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Coordinators:
Vasile Cândea
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We hope that this book will serve as a source for fertilizing and evoking new scientific thoughts and experiments in the cardiovascular surgery field.

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Part 2. Congenital cardiovascular pathology

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FOREWORD

The present volumes that totalize 1373 pages with 348 authors and co-authors, reflect the advances made in the field of the cardiovascular surgery within a decade, since the foundation of the Romanian Society of Cardiovascular Surgery, and in a more restrictive way, of the Archives of the Balkan Medical Union and the Annals of the Academy of Scientists in Romania, the medical sciences series.

In the inaugural article of the "Romanian Journal of Cardiovascular Surgery" "Words to the Journal", the famous scientist and romanian surgeon Pr Dr Marian Ion Ionescu wrote: "In any specialty, the great treaties or monographs remain ephemeral facing the inexorable time which runs away. Everything advances too fast in this post-modern period of time that we live, so that the single publication which is not prone to caducity is the periodical; it dies with any published and read issue, but it renews with the following one.

The publication of a specialized journal proves the maturity reached by a scientific community in the respective field. Such a journal represents the ligature that relates people of the same activity from different places by means of subtle mechanisms, through the very participation to the life of this journal."

One knows that only those involved in battles have the chance to win. And I believe having won, because all the romanian or foreign attendees to the achievement of these advances, along with the big companies of medicines and ultramodern advanced technologies permitted this qualitative bound, towards which we express our entire gratitude.

General (r) prof. univ. dr. Vasile Cândea

Part 1.

EXPERIMENTAL AND CLINICAL RESEARCH

Contributions to the biopathologic study of myocardium by repeated intraoperative myocardial biopsy*)

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Abstract

The paper synthesizes a whole, long experience of the collective of authors of morphological evolution during open heart surgery, as in the literature have also reported data and methodology of the study. In 269 cases of acquired heart disease, especially cardiac malformations and various valvular heart disease. V. Candea performed myocardial biopsies, both before installing extra-body circulation (E.B.C), as a focal point of previous injuries and at every 5-6-10-15-17-20-30-35 sometimes 54 minutes after clamping the aorta to the involutive influence of E.B.C. and to the cardioplegic prefusions. Different morphological examinations were performed, especially using electonomicroscopy at Victor Babes Institute by the team led of dr. D. Laky. Under the influence of situation of "shock-controlled" ultrastructural changes – type stunning occur in the first minutes predominantly in the mitochondria, sarcoplasmatic reticulum, followed progressively by hypoxic injury at the vascular and cellular membranes. Evolution of mentioned lesions at the level of organites determines advance of the transition from limited reversibility of lesion, those 15-20 minutes, to the alterations appearance with irreversible evolution, from 30 minutes, with disorganization and lisis at sarcomers by lysosomal enzymes, edema peri and intrasarcoplasmatic, to apoptosis and necrosis. The beneficial aspect of treatment with phosphocreatin over. In cases of cardiac ischemia are given morphological aspects of myocardial hibernation as adaptive differentiate embryofetal, viable but with evolutionary potential in the absence of lesion of revascularization surgery. The paper pleads for the benefits of scientific and practical application of these methods by cardio surgeons as intraoperative investigation.

Keywords: *open heart interventions, intraoperative myocardial biopsy, biopathology*

Rezumat

Lucrarea sintetizează în ansamblu, îndelungata experienţă a colectivelor autorilor privind evoluţia morfologică în cursul intervenţiilor chirurgicale pe cord deschis, întrucât în literatură nu s-au semnalat asemenea date şi metodologii de studiu. Pe 269 cazuri de cardiopatii dobândite, îndeosebi valvuulopatii şi variate malformaţii cardiace, V. Cândea a efectuat biopsii miocardice, atât înaintea instalării circulaţiei extracorporeale (C.E.C.), ca punct de referinţă al leziunilor

*) **Annals of Academy of Romanian Scientists, Medical Sciences, Volume 1, No 2, 2010, pg. 131-144**

anterioare şi la interval de 5-6-10-15-17-20-30-35 uneori 54 minute după clamparea aortei pentru a decela involutiv influența CEC şi a perfuziilor cardioplegice. Variatele examene morfologice, îndeosebi cele electronomicroscopice, au fost efectuate la Institutul "Victor Babeş" de colectivul condus de dr. D. Laky. Sub influența stării de "şoc controlat", modificări ultrastructurale de tipul siderării apar în primele minute predominând la nivelul mitocondriilor, reticulului sarcoplasmatic, urmate progresiv de leziuni hipoxice interesând sistemele de membrane vasculare şi celulare. Evoluția leziunilor organitelor menționate a activării leziunilor determină progresiv trecerea de la limita reversibilității lezionale, respectiv 15-20 minute, la apariția alterărilor cu evoluție ireversibilă, de la 30 min. cu dezorganizări şi lize ale sarcomerelor prin enzimele litice lizozomale, a edemului peri şi intrasarcoplasmatic, până la apoptoze şi necroze. Este redat aspectul benefic al terapiei cu fosfocreatină asupra structurilor cardiomiocitelor. În cazurile cu ischemii cardiace sunt redate aspecte morfologice ale hibernării miocardice ca diferențieri embriofetale adaptative, viabile dar şi cu potențial evolutiv lezional în absența revascularizării chirurgicale. Lucrarea pledează pentru beneficiile ştiințifice si practice ale aplicarii de catre cardiochirurgi ale acestor metodologii de investigare intraoperatorii.

Cuvinte-cheie: *Intervenții pe cord deschis, biopsii miocardice intraoperatorii, biopatologie*

Introduction

The wide range of laboratory investigations of the myocardium subjected to open heart surgery under extracorporeal circulation (E. B.C.) lacks sequential biopsy studies on changes and evolution of intraoperative myocardial injury in the adoption of appropriate protective measures. Description of morphological cardiac lesions were performed only on single intraoperative myocardial biopsy by various authors.

This is done on open-heart surgery, clamping off the aortic bulb in terms of shock control (6) of stunning, named by various authors mentioned especially by Braunwald and Carp, defining contractile disturbances duration variable (in our case by clamping the aorta) and restore circulation (after declamping) persisting contractile disorders. During this period a number of series of metabolic injuries occur due to the changes at the level of organites, cytosol and extracellular matrix. These biochemical changes are necessary to know, considering the fact that due to high degree of congestive heart failure (CHF) in many patients, the prolonged duration of the operation, in some cases, and cardioprotective effect infusions with various cardioplegic effect solutions (in continuous improvement) so still performing poorly, reversible changes may develop into lesions with irreversible trends. In the absence of such data in the literature, we considered useful to our experience, first performed in Romania, modern morphobiochemistry study, myocardial biopsy performed at specified time interval. In the period 1976-1981 were made in the Service of Cardiovascular Diseases, founded by V. Candea, at the Central Military Hospital, 242 various heart disease by the team led by V. Candea, whose myocardial biopsies were examined separately by Dr. D. Prunescu only electonomicroscopical at the Institute of Biology. Between 1982-1998 a total of 269 cases operated for valvular (mitral, aortic, mitral-aortic, tricuspidien sterile or effusion), or to correct heart malformations (DSIP, DSIV or both, Fallot disease), some associated with drainage anomalous vein, transposition of great vessels. (6) intraoperative repeated biopsies were studied by team led by Dr. Laky at V. Babes Institute performed numerous histopathological, histochemical, biochemical and electronomicroscopical studies (13).

In this study we included cases of pre, intra and postoperative myocardial protection with phosphocreatin (24). The results obtained conferred us the motivation to present the methodology of the study, adding to the usefulness of expanding knowledge on the evolution of all morphological and biochemical substrates in the context of these surgical interventions and non-identify electrocardiographic and sometimes disagreeing with the clinical assessment of a class of ICC in order to adapt appropriate therapeutic means. Stress that in any such case had operated physiological disturbances during and after the repeated biopsies in the context of most of the cardio surgeons adopt this methodology to study, many expressed their fear of complications or unmotivated considering morphological study in the context of range of laboratory investigations.

Material and Methods

Of the large number of operated heart disease, we selected for this study, 269 cases in which intraoperative biopsies were performed at the same intervals and morphological investigations remained unchanged. For interpretation of the results were taken into account by the ICC class (NYHA), most falling within the third class, the existence or not of HTP, mostly moderate, other associated diseases (especially diabetes, atherosclerosis, systemic hypertension) as the age (predominantly from childhood in malformations and in valvular disease sometimes exceeding 70 years with male predominant) The lot of study was formed by:

- Acquired heart disease and degenerative especially Valvular postrheumatic disease and, mitral, aortic, mitroaoric, tricuspidan less sterile and septic rarely subject valvulotomy and valvuloplastia.
- Different Congenital Heart Disease DSIA, DSIV, often combined, sometimes associated with anomalous venous drainage, Fallot Disease (Penthalogy, Tetralogy, rare Syndromes Pizzi-Lauby Trilogy) and Transposition of Great Vessels undergo surgical correction.
- Genetic Heart Disease consisting of a small number of Hypertrophic Heart Disease, Restrictive, Dilatative, topography corrected surgically.
- Atheromatous Ischemic Cardiomyopathy were performed biopsies only in atrial areas and diskinetic zone which bypass were performed by the collectives (Goleanu, Patrut, Mocanu) on 50 cases from their rich collection of cases, studies in which D. Laky performed immunohistochemical investigations.

Surgical interventions were performed under conditions of moderate hypothermia in open heart under E.C.B., cooled with ice cubes and serum physiological at 4 degrees Celsius cardioplegic infusion of crystalloid solutions, discontinuous and continued (Al. Popa), taking myocardial biopsies before clamping the aorta from the right auricle reflecting the morphological status of the heart and aorta after clamping and installation E.C.B., especially biopsies of papillary muscles, every 5, 6, 10, 15, 17, 20, 30, 35, sometimes 54 minute. The material collected was cut to perform the following techniques:

- Histological and histochemical on fragments fixed in 10% neutral formalin included in paraffin, performed the color HE, VG, PAS with amylase, Lie, alcian blue, Scherlach

- Histoenzimological, the frozen fragments at cryostat: techniques for SDH, citochrom-oxidants, LDH, acid and alkaline phosphatase, ATP-aze of membranes, LDH, catepsinaB, nonspecific esterase
- Biochemistry: enzyme marker, mitochondrial and lysosomal, determining values imunogramei K+, Mg++, Ca++, Na+ and water
- Electronomicroscopical transmission on myocardial tissue fixed in glutaraldehyde 2.5%.

Results and Discussions

The originally lesion pattern, built gradually in years, we studied bioptic samples before clamping the aorta, the set up criterion for assessing aortic lesions after clamping. Histological examinations revealed little information: vacuolation, deleting sarcoplasmatical structures, acidification of the cardiomiocytes cytoplasm (eosinophilia, glycogen changes, interstitial fibrosis, hypertrophy and hypercromation nuclear, thickening of arteriolar walls). We noticed histoenzimologic decreases to mitochondrial marker enzymes (citocromoxidase, SDH), leads to the biochemical and tissue fragments.

Electonomicroscopical exams revealed a range of progressive lesions whose emphasis we present below.

Literature data show normal structure organites and other components cardiomiocytes, injuries issues and their interpretation. Although, they revealed from the first minute in detail, the unfisiological effects of E.C.B., but and infusion cardioplegic solutions, suffering undergone cardiac "shock control" in stunning state.

Deterioration of circulation through the created shock by clamping the aorta, generating an infusion leading to inadequate tissue ischemia progresses to the extent that the shock and consecutive metabolic disorders. Thus in terms of metabolic cardiomiocytes from cell that consumes lactate for energy becomes a producing lactic cell. So an acidose cellular was installed with changes in cellular metabolism, decreased energy production, disturbance phenomena in the pump cell membranes, accumulation water and Na+ in the cell with edema cell subsequent. After clamping the aorta and installation of E.C.B. we found chronologically (6), progressive deterioration of subcellular organites and citostructural, at baseline were viable, adaptive of stunning-type (13, 14).

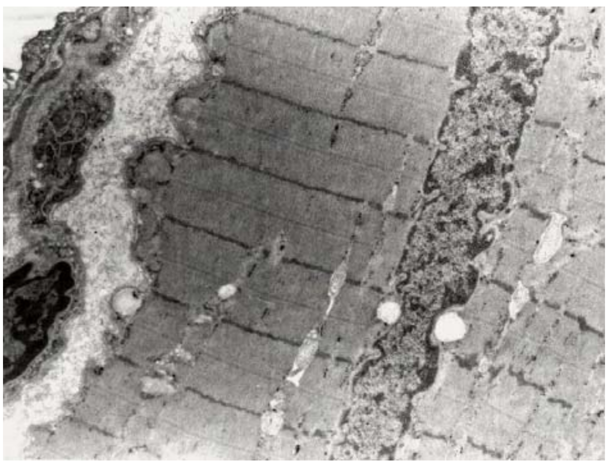


Figure 1: Sarcolemal injury, vacuolisation, edema and intra perisarcoplasmatic, mitochondrial damage near the Z lines (9500X), 13 minutes after clamping the aorta

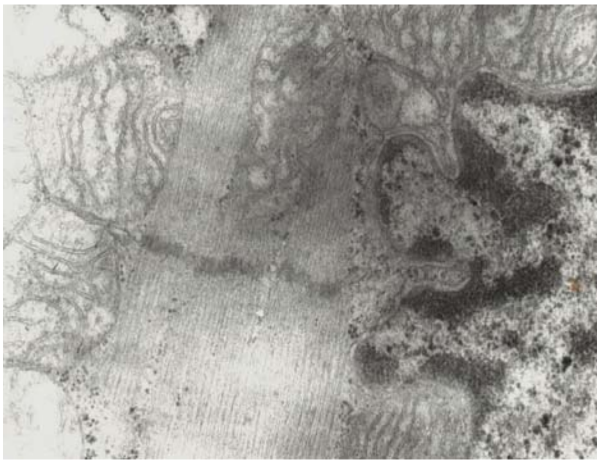


Figure 2: Sarcolema presents early hypoxic alterations, ultrastructure illustrated vesicles of pinocitoza, and later by vacuolization subsarcolemal dehiscence, disturbances of diffusion hypoxia. Starting from the first minutes 2, 5, 6, 10, mitochondria.

First organites affected appear (15). This is of particular importance because they represent 25-30% of the entire cell, disposing it in regular rows between miofibrile and are its principal place of oxidative phosphorylation, electron transport, through oxidative phosphorylation plays a role in the formation of DNA and RNA at different levels (external membrane, internal, matrix) to store Ca^{++}.

Their visual appearance varies, passing through a series of steps from the reversible to the irreversible, fragmentation and deletions of myofilamente, loss of granules to their disappearance, obtaining detailed images on mitochondrial suspensions (Figure 3). The appearance of electronodense deposits, represented by precipitates of Ca 2+, indicating the worst stage of lesions of the organites (Figure 4). Following the disturbances of physiological alterations of oxidative phosphorylation as reflected by decreasing the ratio P/Ca. Occurring disorders of permeability of membranes expressed through failure of Na^{+} and water influx of K^{+}, Mg^{++}, deficiencies Ca^{2} transport.

Figure 3: Irreversible damage to mitochondria with granular deposits with Ca. (4500X), 30 minutes after clamping the aorta

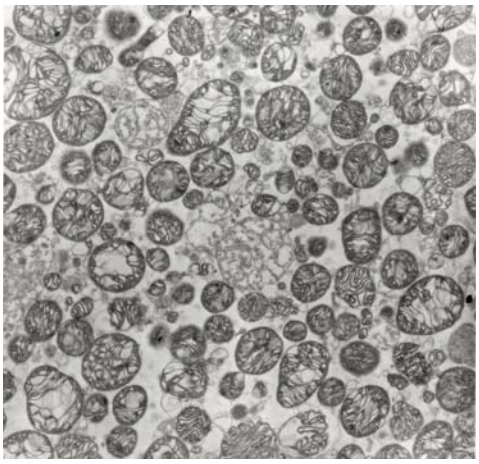


Figure 4: Suspension mitochondrial: mitochondria vacuolation, avoid of content or being vacuolation (9500X) 30 min from clamping the aorta.

Sarcoplasmatic reticulum presents early postischemic alterations, which are characterized by an expansion in the early stages that progress to the fragmentation of membranes and the appearance of plexiform areas in sarcoplasma (Figure 5). Lysosomes are organites that play an important role in the economy and the life cycle of cells especially in advanced stages. Lysosomal alterations proliferated from perinuclear area (Figure 6) with various shapes and arrangements, issued by the disturbance of permeability of the membrane, protease, lipase, phospholipase, sulfatase, glicoronidaze, acid phosphatase, catepsine. They may alter the integrity of surrounding structures and function of cell metabolic changes incurred during the duration of clamping along with the advancement of the aorta.

Figure 5: Cardiomiocyte portion expansion of various sarcoplasmic reticulum, nucleus with chromatin marginalisation, 20 minutes after aortic clamping (8000X).

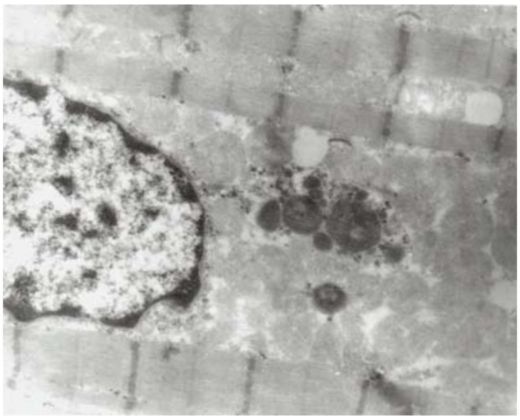


Figure 6: Perinuclear lysosomes with extensive trend within sarcoplasm, with various injuries (11000X), 25 minutes after clamping the aorta.

All these stages of evolution from hyperplasia appear second lizozoms forming fagolisosoms (Figure 7). Finally, determine the enzymes released by the disintegration of structures leading to cell death concomitantly with the appearance of myelin bodies (Figure 8).

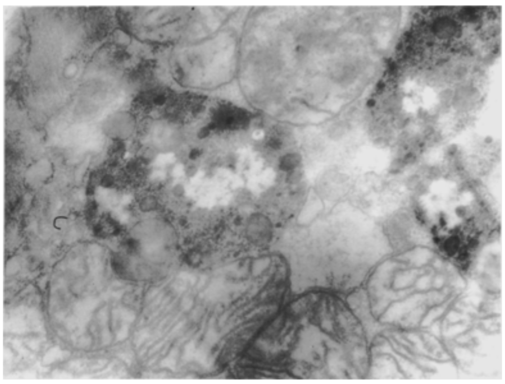


Figure 7: Fagolizozomi crowded perinuclear (9500X) in 30 minutes

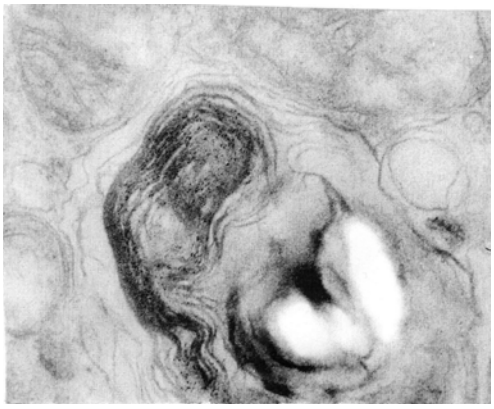
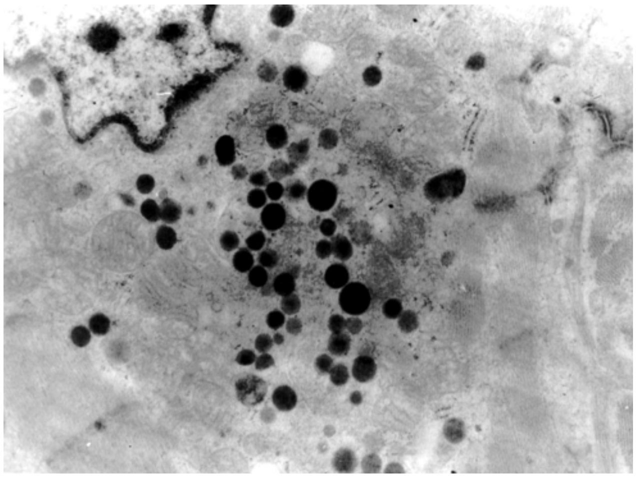


Figure 8: Myelin body in the vecinity of mitochondria with rupture of growth and tendency to vacuolation (25000X)

Atrial natriuretic granules (16), become visible in growing numbers in conditions of hypoxia (17). The repeated biopsies, we have met and in the ventricles (18). The aspect is spherical with electron dens content of 2.75 (Figure 9) located near Golgi apparatus and that secrete hormones and peptides. Through its activity give endocrine feature to the heart (18). Fluid balance influences Na-H_2O issued consecutive ion pump damage (17, 18). They are characterized by changes of the inflow intracellular hidroionical Na+, water and Ca 2+ and the efflux of K+ and Mg 2+. Resting potential decreases hence the decrease of excitability cellular. The number and their extension increases with worsening heart failure.

Figure 9: Proliferated natriuretic granules in the vicinity of the nucleus inside sarcoplasm



Myofilaments and discs gradually suffer interlacing dissociation and disintegration mainly due to the intrasarcoplasmatic edema, tapes and discs is fragment insertion, the intherior sarcomer structure, nuclear changes occur in advanced stages and, ultrastructural, they are showed by marginalization heterocromatin and by the appearance of dense chromatin.

Extracellular matrix suffers progressive morphobiochemical alterations, finally leading to myocardosclerosis and increased heart failure (31), capillaries present changes of basement membrane, with vesicles of pinocitosis increasingly numerous and endothelial cells appear turgid and festoned.

Ultrastructural aspects vary from one microscopic field to another even within a sarcomer, that the labeling stage lesion requiring multiple sections. The accuracy of these changes electronomicroscopic is certified by experimental results which simulate various forms of myocardial ischemia observed by the team led by Dr. Laky for a decade, and described in his monograph (14). Both valvulopaties (19, 20) and malformations (21) painting ultrastructural lesion was nonspecific and intercept compared with the previous state of the patient especially ICC class (NYHA), a pre-existing hypoxia, alterations observed in the previous biopsy experience and caution required by the Examiner. In this way, were determined adaptive changes within sideration process, reversible early lesions from those, that are at the limit of reversibility after 15-20 minutes morphofunctionaly viable and the lesions that evolved after 20-30 minutes to irreversible status of apoptosis and necrosis. Following the dynamic changes in myocardial cardioplegic infusion solutions, we found in the majority of cases, their efficiency in myocardoprotection (14), lesions, with few exceptions, not exceeding reversibility limits of lesions.

Alexandru Popa has devoted his doctoral thesis to efficiency continuous infusion of cold cardioplegic hyperkalaemic solutions (22). Inauspicious results, demonstrated electronomicroscopicaly, were noticed in cases of ICC class IV (NYHA) in endocarditis with septic embolism (22, 23) and in some patients, in whom the time of surgical operators have exceeded 45 minutes, such as, in double or triple valves prosthetic process or complex malformations. In these patients we found hyperplasias and lysosomal activation, frequent phagolisosoms, increased tendency to swelling of mitochondries, the interstitial and intrasarcoplasmatic edema. Myofiaments appear dissociated from edema, with changed Z band with appearance of structures called "Z band material", dilatation, with plexiform images of the sarcoplasmatic reticulum, increasing numbers of natriuretic granules, subsarcolemal vacuolisation.

Capillaries present vesicles of pinocitosis common in basement membranes, and in the final stages of lysis, appear myelinic bodies, mitochondrial swelling and progressive sarcoplasmatic lisis with nuclear picnosis. Biochemical exams were consistent, signaling decreases in mitochondrial enzymes and increases in the those lysosomal. From histoenzimological point of wiew, values of acid phosphatase, catepsin B (lysosomal enzymes), as well as LDL, were consistent with the severity of lesion images. A particular aspect we studied was that of miocardoprotection pre, intra and postoperative with fosfocreatina (Neoton) (24). For accurate results were studied two groups of patients operated for valvulopaties respectively untreated and treated. In these groups, biopsies and investigation techniques were the same as in previous cases. In cases where myocardial biopsies from patients treated with Neoton them, the picture appears with lesions morphologically reversible (Figure 10), compared with untreated group presents severe lesions (hyperplasias of fagolizozomi, sarcomeres with advanced disintegration with mitochondrial damage and edema) (Figure 11).

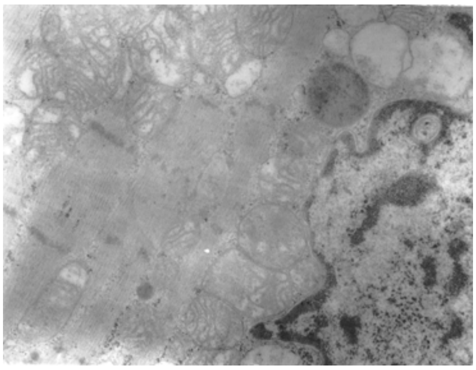


Figure 10: Miocardium after pre and intraoperative treatment with phfosphocreatin- injuries lightweight, reversible, with moderate dilation of the reticulum sarcoplasmatic, light mitochondrial changes, disruptions of the Z lines (12000X), 20 minutes after clamping the aorta

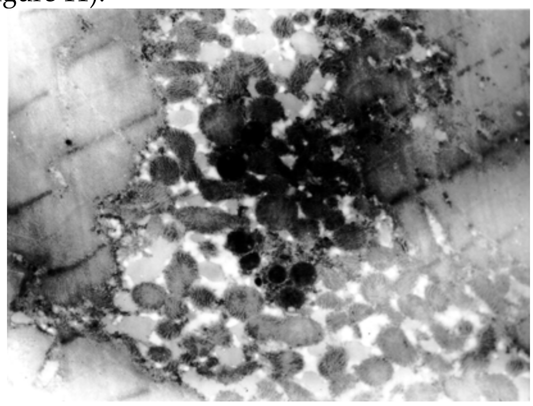


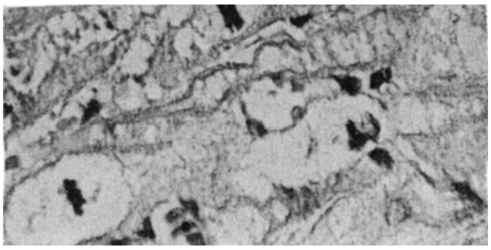
Figure 11: Myocardium in a patient with untreated fosfocreatin (Neoton) presents: fagolizozom severe alteration of mitochondries and deleting sarcomeres structures (12000x), 20 minutes after declampation

So, the apparent tendency of glycogen recovery and sarcoplasm acidification and myocitic edema are much lower. Histoenzimological appearance of ATP-asis membrane, the mitochondrial enzyme and LDH remain in limits before installing CEC. Lysosomal enzyme activity is reduced, so the aortic clamping the changes appear smaller.

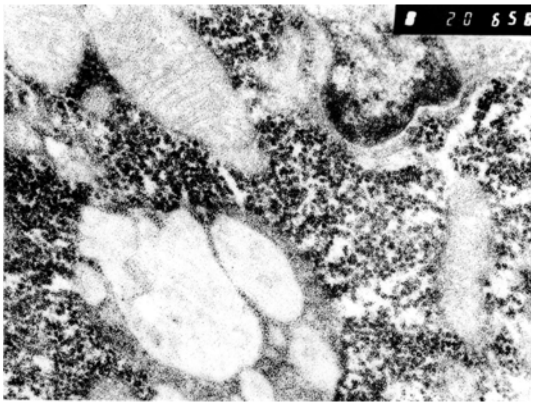
Electronomicroscopic examination (Figure12) also observed a better preservation of cellular organits, storage non-fragmented miofilamentes [12a], Z bands and disseminated intrasarcoplasmatic glycogen granules [12b], and between miofilamentes, mitochondries with membranes and crests preserved. Vacuolo-lysosomal system is reduced by untreated group, suggesting a slow phenomenon cytolysis [12c].

Bazal membran of endothelial cells present an increased stability, causing perivascular edema reduction, inter and intramyocitar.

1. Restoration of spontaneous heart rate.
2. Reducing energy needs due defibrilation.



12a - ***myofibrilar severe depletion leading to waved arrangement of sarcomers, with a tendency to vacuolisation (4500X)***



12b - ***glycogen granules heavily congested in sarcoplasm (4500X)***

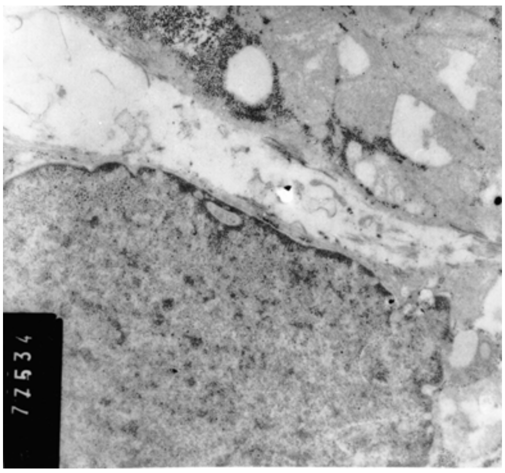


Figure 12: Electronomicroscopic imagies of myocardium in patients with chronic myocardial ischemia, with biopsies harvested during by-pass aortocoronarian site.

12c - ***The core of pulverized chromatin, deletions of sarcomere structures (4500X)***

These findings have been demonstrated both experimentally and clinically. In ischemia, the myocardial energy reserves (ATP, CP), are fast consumers and glicolysis stops at gliceraldehidphosphat, step leading to loss of oxidation phase of cellular NADH- causing acidification of cytoplasm.

Neoton, is a source necessary to prevent oxidative phosphorylation stop and avoid metabolizing phospholipids in membranes, resulting sarcomeres stabilization and membranes capillary. It is used to restore mitochondrial ATP reserve, sarcolemal and myofibrilar. Neoton prevent irreversible changes in reperfusion by maintaining tissue pH, blocking sarcoplasm acidification because accumulation from lactate and alanine, results in high consumption of glucose and lactic acid, preventing injuries.

In cases with varying degrees of chronic ateromatos painful ischemia subject revascularization by aortocoronarien by-passuri, were performed electronomicroscopic examinations on biopsies from ear before practiced graft (50 cases-Dr. Laky), and during bypass from dikinetic area (Dr. Patrut, Goleanu and Mocanu), showing contraction disturbances by adaptive changes, states of stunning, hibernation and various injuries viable reversible, with a tendency toward irreversibility, characterized by apoptosis and necrosis.

Siderotic changes have show viable lesions, especially of mitochondria and reticulum sarcoplasmatic, which were in a study and can pass to hibernate and evolving lesions. In these chronic ischemic heart disease, I met a state of hibernation, the chronic disorder, consecutive to moderate chronic ischemia severity, in which cardiomiocytes remain viable, their contractile function is impaired, can be restored by surgical reperfusion, preventing passage of moderate hypoxic lesion.

Emphasize the fact that myocardial hibernation isnot a lesion state but adaptive, remodeling, the self-protection and adaptation to infusion.

Can be identified morphologically and histologically by the appearance of pale cardiomyocites by lysis of miofilaments and persistence of glycogen.

Electronomicroscopic, along with miofilaments lysis (substrate of diminishing contractility evidentiated clinical mainly by stress on dopamine and nuclear medicine techniques), I met the dense granules of glycogen, nucleols with various aspects prevailing in chromatin, pleading for embryo differentiation, state in which contractions are reduced compared to postnatal cardiac activity.

These data were certainly evidenced by immunohistochemical examinations, prezence of actinic smooth muscle, modification of contractile proteins that titina and cardiotonin and persistent sarcoplasma growth factors, changes in some quantities of calcium and the absence of fibronectin in citosol, the nuclear lamininei H and C. In the basic data, add the rare observation of tubular T system, as reticulum sarcoplasmatic, absence of mitochondrial swelling and lysosomal activation as well as the extracellular matrix changes. These processes consist in changes of mucopolizaharidic parts, cell growth, that of macrophages, fibroblasts, miofibroblastes, capillary density and alterations of their endothelial function. In chronic hibernation increase mainly structural proteins collagen type I and III.

Diagnosis of state hibernation by means of physiological and nuclear medicine techniques, requires emergency surgical revascularization of these diskinetic areas, there can return to normal, but also to prevent their growth by chronic hypoperfusion to progressive ischemic lesions, reaching on apoptosis, necrosis and substitutions collagen.

Revascularization should be noted that all areas ischemic oxygen free radicals have bad efects, being necessary to combat their drug means.

Conclusions

Intraoperative myocardial biopsy repeated by our team during open heart surgery under E.B.C., on a large number of cases, within two decades and examined morphologically complex, especially electronomicroscopic, evidentiated the evolution of lesions for operations, enriching data literature.

This study, advocates for intraoperative cardioprotection continuous such as cardioplegia infusion, administration of drug solutions in the prevention of postoperative complications.

Intraoperative myocardial biopsies at different intervals of surgery during bypass aorto-coronary sites in diskinetic areas, have not shown in our studies or postoperative intra accidents. We reccommend Cardiochirurgia application as useful.

Evolution of pre-and intraoperative myocardial injury, suggestive compensated stages, to avoid irreversible damage.

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Observations of apoptosis in myocardium in some cardiopathies on intraoperative and experimental material*)

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Abstract

With a view of apoptosis signification in progression of cardiopathies, our studies have been used morphological investigations on specimens from human intraoperatory biopsies and experimental material. It has been used histologically, histoenzimologically, electrono-microscopically and in some cases molecular biologically investigations. The differentiation between necrosis and apoptosis were difficult, these being isolated thought decreasing cellular volume, cytoplasm densification, slow lose of organelles affection, except mitochondria and nucleus. The certification was due by molecular biology techniques applied TUNEL-DIG and propidium iodide methods which distinguished no reversible lesions of DIVA from apoptotic bodies in myocardial infarcts and myocardium sclerosis border lines, in chronic ischemia areas of hibernation, myocardial hypertrophies, in advanced heart failure. On experimental models similar to angina pectoris(ischemic and reperfusion alterations) and chronic ischemia through partial coronary obstructions, it had appeared apoptotic images like those which are find in human pathology. There are mentioned genetic mechanisms involved in apoptosis and stimulating factors that perturb its, determined the progression of heart failure, and the benefic therapy that would have applied.

Keywords: *apoptosis, myocardium pathogenesis, cardiopathies, experimental researches of apoptosis, long term therapeutic prospect.*

Introduction

In the last decades, the studies about apoptosis, especialially concerning molecular mechanisms, have progressive increased. In the frameword of these dynamic studies, we shall try to present our experience about apoptosis in cardiopathies because in literature there is a few data about this subject. In this sense we have see again the extensive material which we have gathered in almost 3 decade [1, 2, 3, 4, 5, 6, 7, 8, 9, 10] and have processed the recent harvest references [11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26]. We have compared the results of our researches with those who are appeared in literature and we do some reflection about the pathogenesis of these lesions.

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Material and methods

For this study we have used:

Biopsia material – intraoperatory harvested over 250 cases from *Center of Cardiovascular Disease of the Army* (Cândea, Ţintoiu, Pătrauţ, Goleanu, Mocanu et al.) and from Institute of Cardiovascular Diseases "Prof. Dr. C.C. Iliescu" (Cândea, Făgărăşanu et al.). The biopsies are harvested from different areas of myocardium at various time intervals, in the framework of the same case with a view to praise the hypoxical myocardium changes consecutive extracorporeal circulation (C.E.C.) with continuous and discontinuous perfusions with cardioplegic hiperpotasemia cold solutions.

– postatherisclerotic ischemia cardiopathies,

– congenital cardiac malformations.

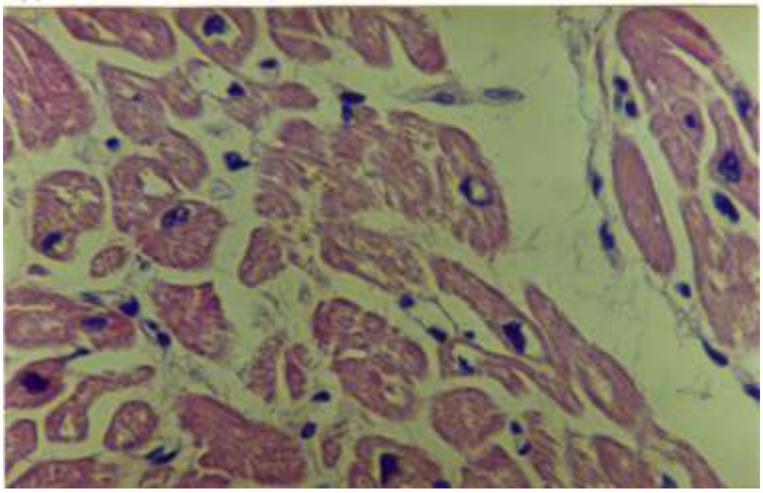

Figure 1: Myocard, chronic ischemic cardiomyopathie intraoperatory Biopsie (I.G.).N.E. staing 400x cardiomiomyocites with apoptotic and necroting appearance;

Experimental matheried harvested from 117 dogs, in years interval 1971 - 1980 from "Victor Babes". Institute by a group leaded towards D. Laky and N.M. Constantinescu ("Carol Davila" Institute for Medicine and Pharmacy). At these animals it was effected acute ischemia from 5 at 60 minute [3, 4]; at other dogs – the partial obstruction of left circumflex coronary branch or left anterior descending during 10 days (5, for following the acute myocardium infarct evolution; the transitory ischemia [6, 8], coronary stenosis follow on recirculation's, while at others animals after the same proceeding incomplete bundle of that coronary brands during 60 days. At all cases the specimens are fixed in neutral formaldehyde 10% and are embedded in paraffin, they were sectioned at 5 microns and were staining utilizing the following histological technique: Haematoxilin - Eoxin, Van Giexin, Lie, PAS, PAS+Amilase, PAS-Aleian, Gomori.

For histoenzymological investigation the fragment were frozen sectioned at cryostat (-20°C) and were affected the techniques for SDN, citocrom oxidase, NADM - C - Citocrom-C reductase, membrane-ATP-ase, acide phosphatase, LDH.

For imunohistochemical techniques on human material, the sections were affected from paraffin block, were investigated for evidence of smooth muscle actin, VIII factor and methods of macrophages.

For electronomicroscopy studies, the fragments of 1 mm were fixated in glutaraldehide solution H%, processed for embedding in 812 semifine and fine sections, were examinated and photographed at electonomycroscopies Optan and Jeol.

In some causes we are affected research of molecular biology on frozen myocardium tissue and paraffin sections, respective TUNEL-DIG and propidium iodide for visualize the state of nuclear DNA.

On experimental material we have done in an addition, biochemical technique (Sm. Constantinescu, Gab. Filipescu) on mitochondrial suspension with a view to spotting the marker enzymes [3], while on lisosomal suspensions, acid phosphotase and beta-glucuromidaze. In some experimental cases it was affected on myocardia tissue specimens establishing of water amount and ionograme (particularly of K, Wa and we have measured the ATP quartiby [7].

Results

We have examinating and reexaminating the older histological images that are specific apoptosis state. We are found histological descriptions that are specific feature of apoptotic state. We are found that the detailed histological descriptions that are done even before of elaboration by Kerr in 1972 [23] the apoptosis term and subsequent amplification have corresponding entirely with specific features who are précised up to date through microscopic methods inclusive some morphological stage of this evolution. The fact that we are not mentioned the apoptosis term were clone of these still unelaborated nomination that are difficult established, even it is missing from reputate monogephies of contain know authors [24, 25]. Only in very obvious cases we have utilized the term of irreversible lesion of apoptotic type; we have mentioned particularly after electronmicroscopical exams the term that "limit of morphofunctional reversibility" that is equivalent today with apoptotic states or reversible lesions (especially in sideration and hibernation states) [1, 2]. The great difficulties to specify the cellular viability or death on usuales staines because of intricated images who included between they areas the fibrosis focuses. In this sense we are become precise after the amplification of our investigations and study of recent literature the busis features of apoptosis and necrosis with a view to their differentiation [8, 11, 13, 14, 23, 24]. Thus in apoptosis cases the nuclear lesions early appeared their evolution is able to watch electronmicroscopicaly in sense that in early studies the nuclear cromathin is perinuclear condensed then undergoes progressive fragmentations until disintegration of diereses portions of nucleus. The cells apoptotic affected appeared isolated, in small groups, separated from the neighboring cells. The cell volume decrease until half, the cytoplasm density consecutive of dehydration the organelles appear in majority unmodified except the mitochondria which are early damaged. The sarcolemal lesions appeared to late and cytoplasm disintegration as well as of nucleus and made up the apoptotic bodies with acidified cytoplasm. All around, we aren't found the inflammatory reaction, we are found only macrophages and nuclear changes, show apoptotic changes, the nucleuses are hyper chromatics, irregulars here and the clivates and doubles and poliploids sometimes (**Figuere 2, 3, 4**).

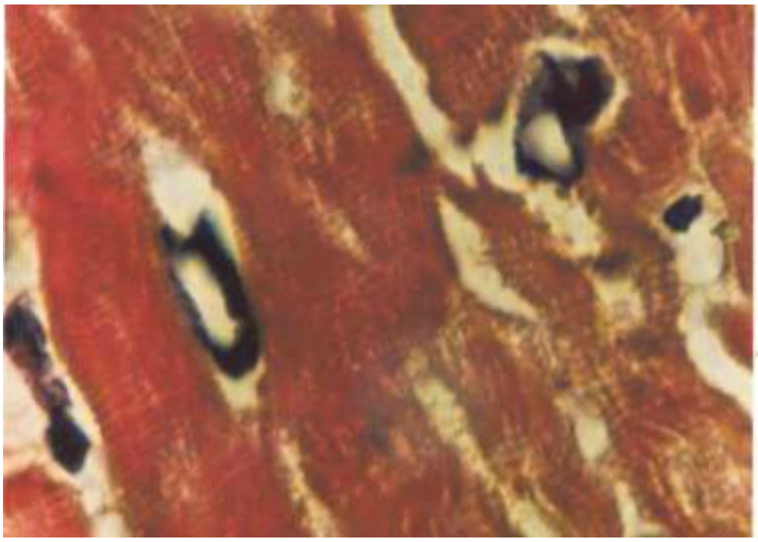

Figure 2: Myocard, chronic valvular disease, intraoperatory biopsie; Lie staining, H.E. staining, immersion;Hypertrophic cardiomyocites with large hipercro matic nuclei with apoptotic appears;

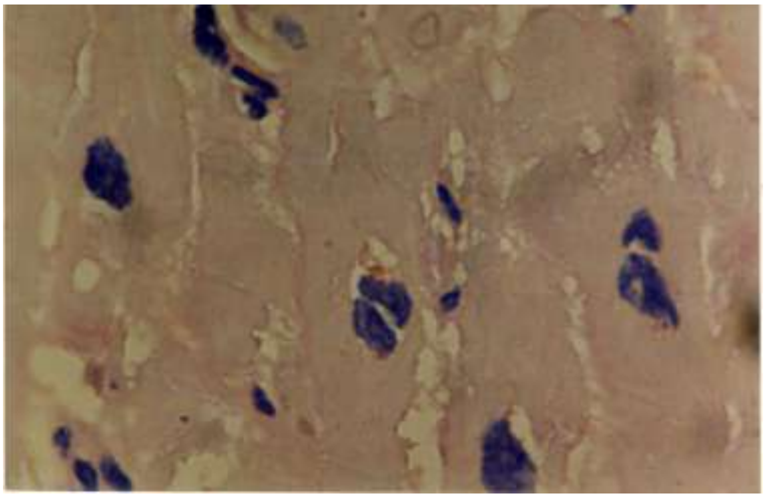

Figure 3: Myocard intraoperatory with malformations (SDA, SDIV), PAS-amilaze staing 400x myocardial cells with double nuclei; Hiperchromatic and with vascuolization

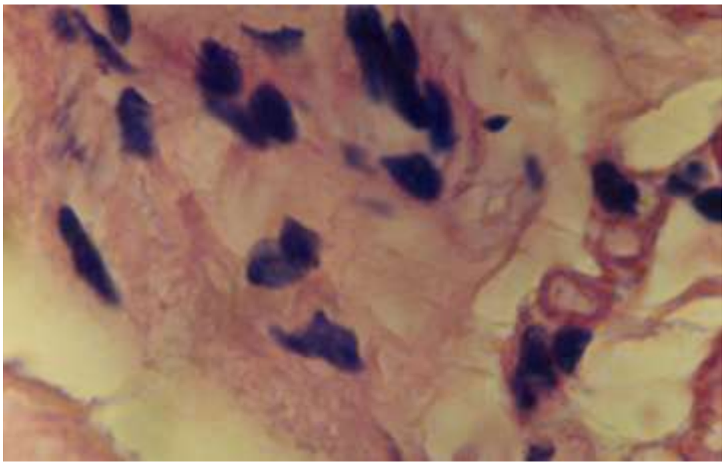

Figure 4: Myocard intraoperative with malformations, PAS - amilaze staining, imersin; Other image with nucleary modifications to poliploide;

The process spended with energy consumption, is a mechanism of cellular programmed death [17], named of some authors as well as “cell suide” [26]. In the end, the apoptotic bodies are fagocitate from macrophages or the neighboring cells and they are digested of lysosemal enzymes.

The necrosis are late nuclear lesions who are gradually installed through irregularly condensed and then homogenized nuclear chromatin. The organelles undergoes to severely lesions consecutive their early evolutive modification while the sarcolema had membranes lesions. The mitochondria appeared swelling with disruption and disintegration of crests. The necrosis process doesn’t required energy consumption. Both lesions are unspecific for some organ gived, they presented and of myocardial level the some images. The new techniqs of immunohistochemia show embryofetalis dedifferentiations of some cardiomyocites throng presence of smooth muscular actine in their sarcoplasma and of macrophages in their neighboring [1, 26]. The stainings Lie and aleian-blue, show acidification of sarcoplasmatic medium who is favorable for apoptotic processes. The Gomori staining as well as ultrastructure praised the presence of fibrosis focars in zones with cardiomagocitare depletions consecutive above mentioned processes. The capillaries presented endothelium turgesence this aspect is augmented ultrastructuraly detailed appeared at capillary basal membrane level.

Electronomicroscopicaly we can establish because of disseminated character of lesions, organelle’s modifications, rather of nucleus, chromatin appeared irregularly dispersed in clusters with tendency to vacuolization [5, 6, 7]. The appearance of lysosomes and phagolysosomes indicate the possibility of evolution to necrosis of these [4, 5] alternative cellular changes.

The osetiacellular matrix edema, rather in condition of organization, acidification and hyaline, the fibrins transformation through the presence of collagen synthesized by fibroblasts is a cellular worsening index-lesion [21, 22].

Apoptotic changes who evaluated to necrosis can appeared through physiological stimulus rather in older age but consecutive the emphasis of light preexistent lesions through the appearance of some hipoxical, toxical and mechanical damage who are quickened thus the installation of apoptosis and then, of necrosis [3, 4, 7, 9, 10, 15].

Depending on severity of harmful agent, the lesions can evaluate to necrosis, to apoptosis (**figure 3, 4**) or structural restoration. Thus, in acute myocardium infarcts, the central area is always necrotic but in peripherical areas are intricated myocites with manifest tendency of necrosis with the other [4, 5, 6, 7, 8, 19] which often presented the waved aspects while electronomicroscopicaly features of hibernation [10, 21, 26] with agglomeration of glycogen granules, endoplasmic reticulum changes, fine and dispersed nuclear chromatin who can evaluated to apoptosis or structural restoration rather in conditions of an suitable treatment that are limited the extension of infarct [19]. Such heterogeneous cardiomyocitares changes we have been met in the neighboring of ventricular anevrism consecutive on sclerohialinisation of myocardium infarcts [10].

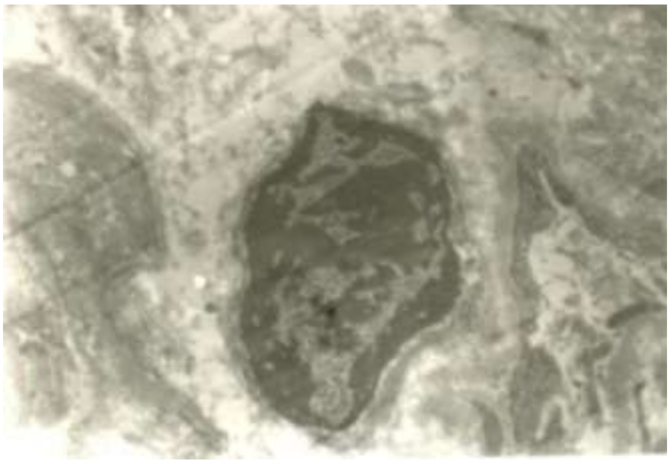

Figure 5: Myocardium: intraoperative biopsy E.M.9100x: disintegration of nuclear structures;

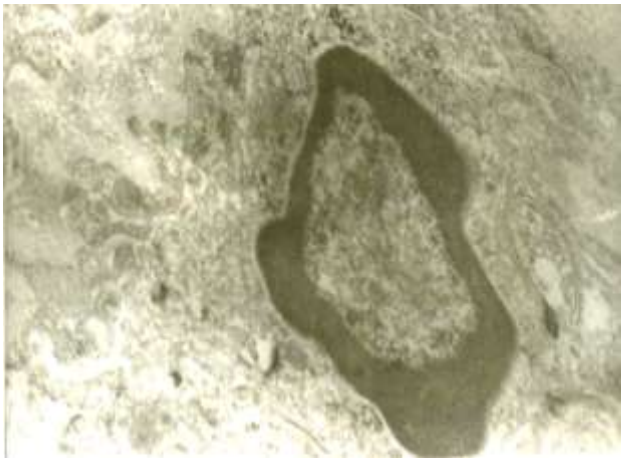

Figure 6: Myocardium: intraoperative biopsy from left myocardium, chronic valvular disease (SDIV, SDA); Cardiomyocite with nuclear vacuolization E.M.X9100;

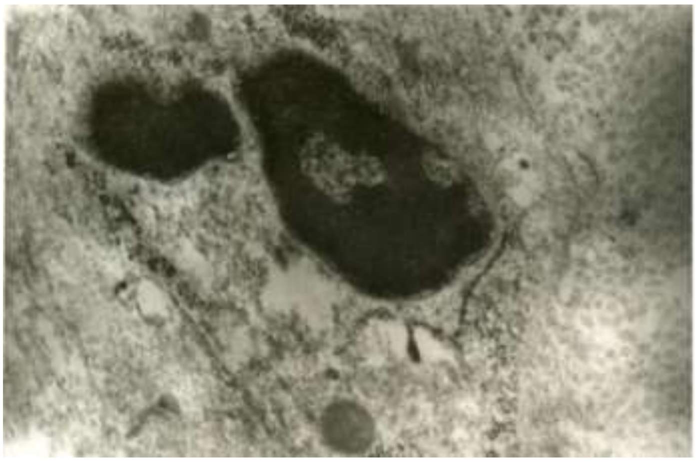

Figure 7: Myocardium with chronic valvulopathie, severe cardiac failure E.M.9100x; Hiperchromatic nucleus with central structural disintegration, nuclear body with hyperchromas;

In zones with consecutive myocardial ischemia of advanced coronarian atherosclerosis, they are such intricates lesions often of hibernation type with nuclear reversible apoptosis through the vascularisation of these areas through aortocoronarian by passes [22].

In valmeopathies [2], rather mitroaortical, we have been met apoptosis, as well as atrial level after fibrillations and ventricular level because the hypertrophy of cardiomyocites with formation of news sarcomeres and multiplication of myofibrilar contractile apparatus. In these situations because of great size of nucleus and of chromatinian and nucleolar volume is sometime difficult to specify the moment of transitions toward apoptosis. That take place rather in the case when arised sarcoplasmatical micro vacuoles and acidification of sarcoplasma. Their energic resources exhaustion consecutive of constraint trawell asa well as the hypoxic state in which they will be because the inadegvatic development of neighboring capillary network size. Similar aspects we have been met also in cardiac malformations, the lesions are unspecific [9]. At histological routine methods appeared nuclear changes who indicated apoptotical states; the cromathin condension under the nucleolema, the appearance of vacuolisations in the middle of the nucleus, their intended outline, tendency to clivatien and their session, appeared cells with 2 nucleus.

In our casuistry we have been met displasia we haven`t been met the right ventricular arritmogenic right ventricular dysplasia in which the literature data show an increased number of apoptosis [16].

Immunohistochemicaly, we have been establishing [10] existence of smooth muscle actin show their embriofetal dedifferentiation and they have keeping the morphological features of their viability.

The same processes we have been observing in case of hipertrophias of certain zones in the framework of inheritance heart malformations through similar mechanism [9].

We can certainly précised the apoptotic states by molecular-biology investigations, that can through the visualizations, the degree of DNA-chain lesson, utilizing TUNEL-DIG technique (**figure 8**) and propidium iodatum rather in the cases of treatment of section with triposine (**figure 6**) that have permit the evidention of diverse states of apoptosis from those reversible to appearance of apoptotic bodies.

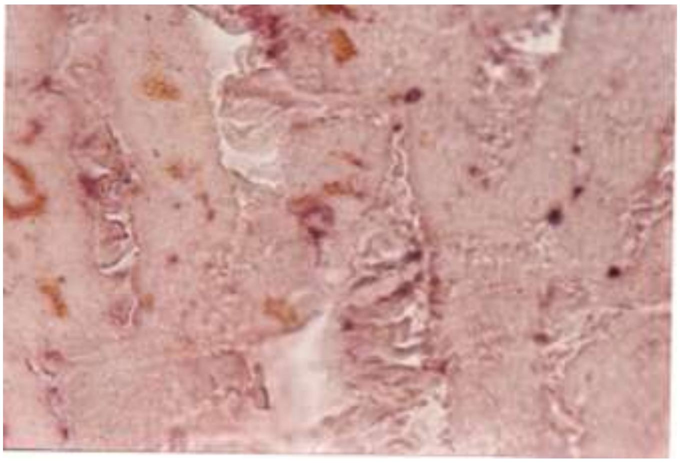

Figure 8: Myocardium, aortic valvular stenozis. TUNEL-DIG molecular biological staining, disintegration of nuclear chromatic x400;

On experimental material we were met in some models which we were effect the images alike with those observed on human matheria. The conception of these models is similar of certain human cardiac affections above-mentioned.

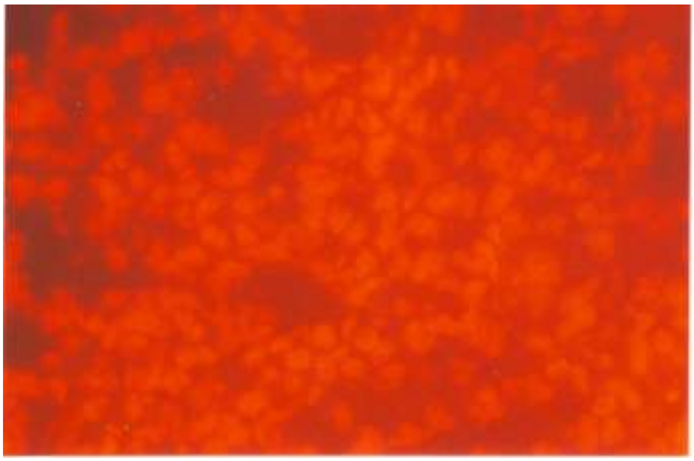

Figure 9: The same. Propidium iodatum, molecular biological staining on view apoptotic bodies.

Discussions

Our researches as well as the latest which are arising in literature [2, 5, 10, 14, 15, 17, 22, 24, 25, 26] show the two patterns of cellular death of myocardium level: - necrosis-considered in past like the singular modality of cellular death, apoptosis-after recent researches.

Our researches are doing to differentiate the apoptotical lesions from necrosis although the both lesions have the same denominator: the lesion of nuclear DNA.

Apoptosis is a physiological state of cellular programming death [12, 13] named by certain auto cell-suicide view of maintain of quantitative homeostasia in rapport of the cellular cycle evolution, the age, the remarking and the differentiation of respective structures through energy consumption.

Because that, the apoptosis have been presenting small organelles lesions (rather mitochondria`s) cell volume decease with cytosol condension because of dehydrations, the nuclear lesions appear early while these of sarcolema arise late. They appear isolated from the neighborings cells without the inflammatory reaction all around. The length of apoptosis evolution is small but the number of these lesions and their evolution to necrosis can be accelerated through nociceptives stimulus's [10, 11, 12, 13, 14, 17, 26].

Necrosis have been appearing consecutive of the damage in cells groups because of some strongs or prolonged noxes have increased cell`s volume through sarcoplasmatical edema, early sarcolema lesions, severe nuclear damages but belated appeared through prolonged evolution; the mitochondrial lesions appeared early and are intenses (swelling) and don't required energy consumption.

We considered necessary to present in brief the mechanisms of apoptosis [10, 12, 17, 27]. These are multiple mechanisms complexes, started on inducing factor and continued on the genetical, biochemical changes witch can goes to cell death. Among the determination role of cellular cycle [17], the restoration capacity of DNA; the free intercellular Ca++ ions concentrations RNA or certain protein synthesis or degradation modifications of phosphorilution and dephosphorilution; the oxidatives cell-mechanisms with generated of free radicals (reactive oxygen).

They have been coinciding by early morphological changes, chromatin condensation undergoes to clivatien of internucleosomales DNA which have been evidently through agar-gel electrophoresis [26].

The selective lose of water and ions with cell volume decrease on half in the earlier states of apoptosis, will contribute subsequently to fragmentation as well as cytoplasm to the nucleuses and apoptotic bodies-formation. The increased level of catabolic ionized Ca++ can activate the enzymes like transglutaminase and precocious induced apoptosis. That in why, the cardioplegic solutions [10, 22] antioxidant drugs can block the basic lesion of DNA and, consecutive the apoptosis installation. An important role has the cistein - proteases. Among these we mention: the interleukine conversion enzyme (ICE) and especially the causes [20].

The apoptosis activation are effectuate through an series of factors which accentuate the histological and phisiologicical changes preexisting like the stimulation of myocitare hiperthrophy, interstitial fibrosis, vasoconstrictors like the others umoral factors: norepinephrine, angiotensine II, inflammatory cytokines, nitric oxide, GMPc - atrium, nathriuretic factor which induced apoptosis through still not clear up mechanism.

The genetic determinism of apoptosis have been observed initially at unverthebrates, they existed the apoptotic gene like ced-3 and ced-4 between ced-9 gene which have seen protecting the cells by programmed family bcl-2 which inhibited the cell death [27]. This gene can be inactivated by the genes bax and bel-x through combination with bil - 2 [6, 7, 20].

The intervention of suppressor gene P53 can suprimate the bel-2 activity; the gen P53 have been determinating to stopped of cell cycle in G1 state permitted the lesions restoration or determined the apoptosis. The gene c - myc can induce also, the apoptosis.

In this processes have been intervening and the Max-gen [26, 27]. The mitochondrias represent the decision factors about the cell-death type. Through the cytochrome - c releasing apoptosis are been induced [17]. Among the modulators of apoptosis, a decisive role has the caspases from cistein protheasis family which, as well as ced - 3 actionated like effector of this processes. The caspasis can be inhibit by be - 2 and bel-x1 homolog ced - 9.

Determined the irreversible proteolysis would be beneficially by drug. The treatment with peptidic inhibitors of caspases which reduced the cerebral infarction dimensions with 50%. The limiting framework of this paper haven't been permitting the presentation of atherosclerotic lesions evolution consecutive the apoptotic process [23], initial endothelial and smooth cells due to expression in excess of E_{as} antigene of endothelial cells. The evolution of the enzymatic proceses have been determinating the evolution of atheromplagues, those stables presented the weak lymphomonocytar neighboring reaction, towards differentiation by the richness of these inflamatories reactions of the neighboring athrom plagues in evolution [10].

Conclusions

In myocardial affections induced by different causes, the apoptotic processes arised relatively frequent at 35% from myocitary cellularity (by some data), like in condition in which is studied especially in the entirely heart experimental material, in severs heart failure, in the extirpated hearts with a vieu to transplantation. The application of methods of molecular biology certified the existence of these lesions like apoptosis having the histological features and the ultrastructure above described also in intraoperatory myocardial biopsies.

The future researchers will be great amplified the numerous aspects not yet cleared up, uncerted, in the framework with the apoptosis and consecutive, the adequate therapy wich can be applied.

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Histoenzymological and ultrastructural studies in repeated pulmonary biopsies effected during open heart operations under extracorporeal circulation*)

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Abstract

In condition when the number of electronomicroscopical and histoenzymological studies about the pulmonary lesions during heart is low, we effected on 100 patients with valvular and congenital diseases intraoperatory repeated pulmonary biopsies.

The aim of this original studies was to establish the dynamic of alveolar and macrophagic reactions in conditions when the lung is in mechanical repose during open heart surgery under extracorporeal circulations.

These changes are due prioritary to phagocytosis of alterated red cells, microhaemorrhages, haemolysis and consecutive ferric from pigment liberation in stasis conditions, especially in advanced pulmonary hypertensions.

Our studies about the biology of pulmonary cells through repeated intraoperatory biopsies in this conditions is prioritary in medical literature.

Keywords: *intraoperatory lung biopsies, open heart surgery, extracorporeal circulation, pulmonary stasis, lung mechanical repose, red cells alterations, macrophages, phagocytosis, histochemistry, electronomicrospy, prioritary study*

Rezumat

Se prezintă studii electronomicroscopice şi histoenzimatice din leziuni pulmonare pe parcursul ischemiei cardiace pe 100 de bolnavi cu boli congenitale sau valvulare, evidenţiate prin biopsii pulmonare repetate intraoperatorii.

Aceste studii originale stabilesc dinamica reacţiilor alveolare şi macrofagelor pulmonare, în condiţiile unui răspuns mecanic din timpul unei operaţii cardiace cu circulaţie extracorporeală.

Modificările sunt datorate prioritar alterării fagocitozei celulelor roşii, microhemoragiilor, hemolizei şi eliberării pigmentului feric în condiţii de stază, în special în stadii avansate de hipertensiune pulmonară.

Studiile noastre despre biologia celulelor pulmonare prin biopsii intraoperatorii repetate, fiind prioritare în literatura medicală.

Cuvinte-cheie: *biopsie pulmonară intraoperatorie, chirurgie pe cord deschis, circulaţie extracorporeală, stază pulmonară, răspuns mecanic pulmonar, alterarea celulelor roşii, macrophage, fagocitoză, imunohistochimie, elecronomicroscopie, studiu prioritar*

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Introduction

In the last decades, the histological studies about the pulmonary lesions in various heart diseases (1, 2, 3, 4, 5, 6) were been enlarged with electronomicroscopical and histoenzymological techniques but their numbers is low (7, 8, 9, 10, 11, 12, 13). The biology of the lung during heart operations under extracorporeal circulation [ECC] was effected on intraoperatory repeated lung biopsies only in this study.

Material and methods

Fragments of the anterior languette of the right pulmon were obtained from 100 patients (59 women, 41 men) with acquired valvular (94 cases), congenital heart diseases (5 patients) and 1 case of left atrial myxoma. The congestive heart failure was missing in 7 cases, 93 patients corresponded to the NYHA classification: 1 patient in the class I-II, 10 patients in class II, 17 in class II-III, 42 in class III, 12 in class III-IV, and 6 in class IV. The pulmonary hypertension (PHT) was absent at 13 patients, 9 had a low PHT, 1 – non severe PHT, 68 – medium PHT.

The fragments that were intraoperatory obtained were immediately processed: fixing in 4% cold glutoaldehy (1 mm size) to be further processed by techniques for electronomicroscopical examinations; fixing a part of the fragment in 10% neutral formalin for histological examination and cryostat freezing at -20°C of other fragments for histoenzymological examination. As for histological examination the embedded paraffin section were stained with Hematoxylin – Eosin, Van Giesen-Weigert, PAS–alcian blue, Perls, Gömöri. For histoenzymological examinations the non-fixed fragment (at 7-7.5 pH) and by cryostat sections, were stained for membrane ATP-ase, alkaline-phosphatase, acid phosphatose, peroxidase.

In view of the electronomicroscopical examinations, the fragments were embedded in Epon 812 and 8 blocks were made from each case. They were cut in semifine sections, out of which were chosen pieces for fine section (4 blocks each) for ultratome LKB. The sections were examined and photos were taken under electronomicroscope Opton and Jeol. All morphological techniques were effected at "Victor Babeş Institute" by professor Laky Desideriu collective.

We mention the fact that, simultaneously with the pulmonary biopsies, on effected myocardial biopsies from the right ear and papillary muscle and in some case from liver before, after extracorporeal circulation and they were processed by some techniques.

Results

The histological aspects (1, 2, 3, 4, 5, 6) which we obtained were classified acording to Health and Edwards [1] comprising the pulmonary lesions in pulmonary hypertension (PHT) in 6 groups depending on the evolution and intensity of vascular lesions. Beside these vascular lesions, we also found a series of lesions at the level of pulmonary parenchyma, that are not found in Health and Edwards classification and they should be introduced in it, because they reduce progressively the capillary alveolar barrier and contribute to evolution of the lesions mass. In this respect, we saw the various thickening of the alveolar walls *(figure no.1)* by hypercellularity with cuboidal metaplasia of the alveolar epithelium, appearance of macrophages, namely siderophages, fibroblasts, fibrocytes, hyperplasia of colagen and elastic fibres, flattenings of the thickened alveolar walls and in advanced stages, various images of hemosiderosis.

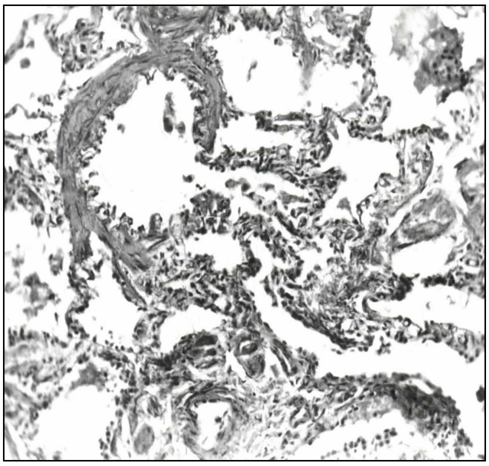

Figure no.1: Pulmonary intraoperatory biopsy before extracorporeal circulation (EC), Hematoxilin-Eosin staining (X125). Ensamble view: alveolar wall thickning by various hypercelularity

We also saw peribronchovascular immunoreactive lymphoid infiltrates at the level of some pulmonary acini [13,14].

The hystoenzymological investigations [13,14] support and go deeply into the morphopathological findings and wheir corelation in a great number of cases with histological images (never found in the literature) contribute to study of the pathogenesis of lesions, the reactions increases progressively, less in pneumocytes and more in macrophages, fibroblasts, interstitial tissue, revealin the stasis lysosomal activation, fallowing the chronical stasis microhemorrhages, hemolysis and phagocytosis of the iron pigment. Histoenzymological, we found similar reactive aspects after the rendering of peroxidase reaction.

Moreover, the reactions intensity progressively increase inside the macrophages with PHT grade caused also by same extravasate and desintegrated red cells whose constants in be partial phagocyted. Instead of reaction for membrane ATP-ase decreases progressivelly together with PHT advancing. A rather simmilar evolution is also be found in the reaction for alkaline phosphatase, a certain enzymes being implied in the metabolism of membrane phospholipids for acid-phosphatases.

Thus in the early stages of PHT, the reaction for acid-phosphatases is positive in the capillary walls, larger vessels and some endothelial cells and rarely in interstitial cells and its intensity is decreasing in the most advenced stages when the reaction become.

The electronomicroscopical examination [7, 8, 9, 10, 11, 12] enlarges the histological horizon. At the level of the alveolar walls, cuboidal metaplasia of the alveolar epithelium (*figure no.2*) has a corresponding hyperplasia of granular pneumocytes type II with their characteristic: voluminous aspect, intraplasmatic vesicles and electronodense bodies are abundent in many cases where hemosiderosis appears.

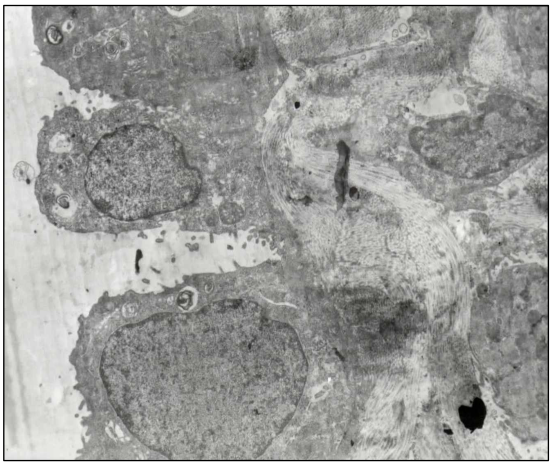

Figure no.2: Pulmonary biopsy before E.C. (E.M. X6000), cuboidal metaplazia of pneumocytes II, macrofages with some vacuoles and elecron dens bodies.

Sometimes we observed some aedematosis aspects in the interstices between endothelial cells and pneumocytes by detaching of endothelial cells from the basal lamina, the presence of hyperplasiated cels elements and numerrous collagenosis fibres whereas the thickens of capillary alveolar membrane is obvious. The capillary and the arterioles have the muscular coat thickened by an increased number of smoath muscular fibres helicoidally arranged including microfilaments, dens bodies and sarcolemmal vesicles surranding collagenous fibres inside them.

At the level of the intima level of the membrane and cytoplasm and the nucleus are big; in the rest of the internal coal there are fibroblasts, collagen and reticular fibres, rare myoid cells. At the level of the adventice there are quite fibroblast and fibrocyte-type cells and prevailing collagen fibres as well as macrophages with hemosiderin pigment were found. The capillaries have their basal membrane much thickened and they have some mesenchymal pericite cells, reticulin collagen fibres in their neighbourhood.

The pulmonary biopsies before extracorperal circulation (ECC) were made for evidence the evolution of previous lesions due the stasis and PHT during EC.

During EC when the pulmon is in mechanical repose the alveolar and macrophagic cells, in condition of stasis and PHT become actives in phagocytosis action phagocytal alterated, desintegrated red cells, debris as iron pigments.

Electronomicroscopical, this biological action appeare litle and more obvious in the pulmonary cells without PHT or in reversible stage. On remark the hyperplasia of pneumocytes II and macrophages *(figure no.3)* that become a voluminous aspects with intraplasmatic vesicles beging myelin figures and electon dense bodies (iron pigments).

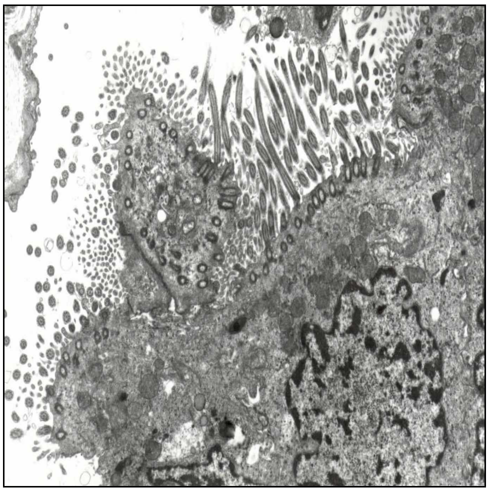

Figure no.3: the same (E.M. X6000).

These are abundent in some cases where hemosiderosis appears, with tendency to narrow of the alveolar lumens and diminishing the pneumocytes I.

The histoenzymological investigations contribue to profound the pathogenesis of the metabolic disturbances, the reactions varing with the PHT grade: increase the peroxidase reactions in the macrophages decrease of the membrane ATP-ase, also the reaction implied in membrane phospholipids, increase the acid phosphatase (lysosomal enzymes).

In advanced stade of PHT near almost alveolar cells are siderophages in frame of hemosiderosis (the advanced stade of PHT).

Discussions

The pulmonary biopsies before and during extracorporeal circulation (ECC) were made for evidence the evolution of previous lesions due to stasis and PHT during this conditions. ECC in a non physiological, artificial pulmonary by-pass that suppose a complex system the solve for a reduced a transient solve (during 6-8 hours) of the cardiac and pulmonary functions to place in functional repose for surgical approach.

In this mechanical repose of the lung in stasis and PHT conditions, the alveolar and macrophagic cells become an phagocytosis actions to remose the altered and debris of red cells as iron pigment and others.

Electronomicroscopical, this biological actions appeare little dearly in pulmons without PHT or in reversibles stady. On remark the mielin hyperplasia *(figure no.4)* of pneumocytes II and macrophages that beging a voluminous aspect with intracytoplasmamtic vesicles *(figure no.5)* and dense electron bodies *(figure no.6)* (histologicaly with Perls positive reactions) where are abundent in advanced stadies when hemosiderosis appear *(figure no.7)* and pneumocytes I diminish. In this condition, the alveolar lumens manifest tendincy to narrow and consecutive to diminish the alveolar capillary barrier.

Our prioritary studies with repeated intraoperatory lung biopsies to be able to prove the evolution of cellular dynamic reactions and morphological lesions the role of mediators as complement system during BCP, the role of neutrophiles after BCP, the increase of pulmonary capillaries related by Tintoiu and al. [15].

The precocious medical and surgical treatment of chronic congestive cardiac diseases can prevent the installation of this pulmonary lesions.

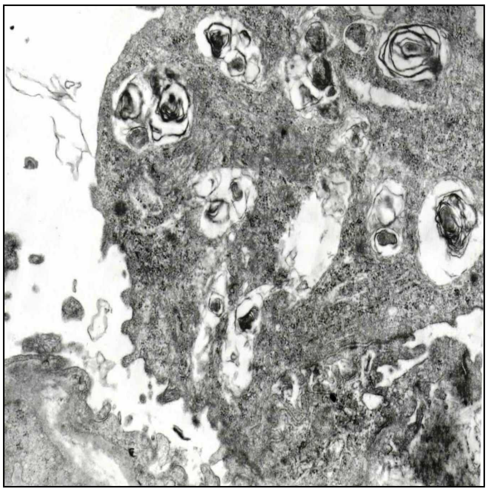

Figure no.4: Pulmonary biopsy to end of extracorporeal circulation (E.M. X 15000): pneumocytes II with hard lesions: myelin gigures, vacuoles, electron dense bodies.

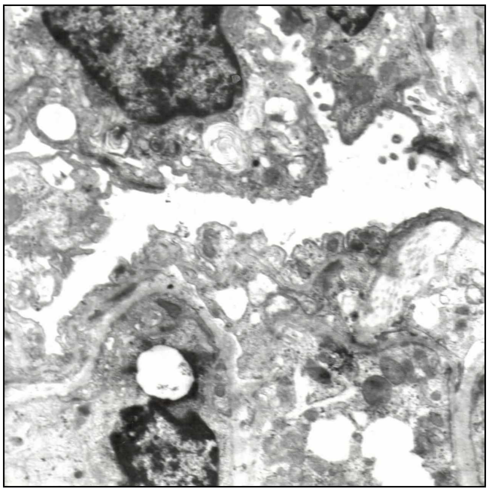

Figure no.5: The same (E.M. X15000): pneumocytes II with various alterations: numerous vacuoles, electron dense bodies.

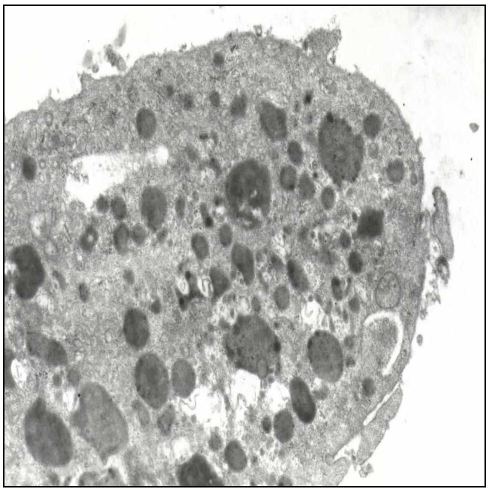

Figure no.6: The same (E.M. X15000): numerous electron dense bodies, activated lysosomes and Vacuoles.

Figure no.7: Intraoperatory biopsy in advanced PHT with hemosiderosis, syderophages with iron pigments (E.M. X 30000).

Conclusions

During open heart surgery, though the lung is in mechanical repose, in the alveolar cells and macrophages, in observed marcked metabolic processes due to phagocytosis in stasis conditions of the altered red cells and wheire depris at the alveolary septums, to determine the alveolo-capillary barrier and gradually instalation of the pulmonary heart. To present of this phenomenon is necessary the precocious cardiac operations in absence of in the reversible PHT stages.

This study about the biology of the pulmonary cells through repeated lung biopsies during cardiac surgical interventions is priorytary in the literature.

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Technologies avancées avec applications en médecine. Le dispositif d'assistance mécanique cardio-circulatoire avec coeur artificiel de type NOVACOR (expérience roumaine)*)

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L'esprit inventif et créatif de l'homme a contribué aux progrès dans le domaine de la connaissance et implicitement à l'obtention de certaines performances de plus en plus grandes dans le domaine des technologies avancées aux applications dans tous les domaines, la médecine incluse.

Les progrès et les performances en médecine, en général, sont en étroite interdépendance avec leur application, tant dans la pratique médicale courante (ordinateurs pour l'interprétation automatique des données, dispositifs d'imagistique invasive et non invasive, microscopes électroniques, etc.) que dans des domaines ultra spécialisés de la chirurgie, la neurochirurgie, la chirurgie cardio-vasculaire, etc.

Aujourd'hui, dans la pratique médicale, inclusivement dans celle de Roumanie, sont entrées la télémédecine, la robotique, etc.

Par rapport à certaines technologies avancées aux applications dans la chirurgie cardio-vasculaire, je vais vous présenter l'utilisation du coeur artificiel de type Novacor-autonome, dans le traitement chirurgical de l'insuffisance cardiaque avancée (le syndrome de débit cardiaque réduit par l'insuffisance de la pompe). C'est une des causes majeures avec laquelle la cardiologie contemporaine se confronte.

Le risque d'insuffisance cardiaque, est estimé à présent de 1 à 5 souffrants de maladies cardiaques, tant aux hommes qu'aux femmes. Également, les études statistiques montrent qu'il y a approx. 100.000 cas nouveaux par année, qui nécessiteraient un transplant cardiaque.

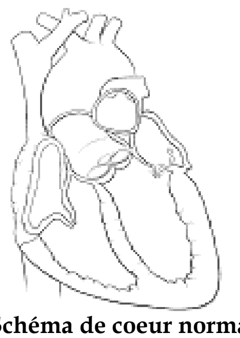

Schéma de coeur normal

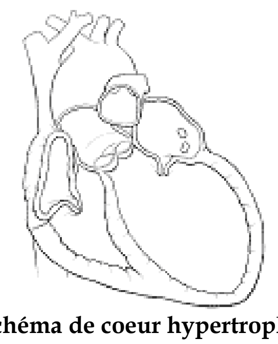

Schéma de coeur hypertrophié

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*) Proceedings - *XXIX-ème Congrès International de la Société de Chirurgie de la Méditerranée Latine, VIII-ème Congrès de L'Entente Medicale Méditerranéenne, XXVIII-ème Seminaire International de Chirurgie Génerale,* **22-24.XI.2007, Alicante-Espagne**

L'insuffisance cardiaque, déjà installée, pour la plupart des cas ne guérit pas, elle est traitée par voie médico-chirurgicale. Les malades qui ne répondent pas au traitement, évoluent inexorablement vers l'insuffisance cardiaque irréversible, réfractaire à tout traitement chirurgical. Une partie de ces malades ont une indication de transplant cardiaque ou, dans certains cas, de transplant coeur-poumon.

Le manque chronique de donneurs d'organes pour le transplant a imposé la création de dispositifs spéciaux qui permettent une "assistance" mécanique du coeur, dans la situation donnée, du ventricule gauche, parfois biventriculaire, de sorte qu'il soit déchargé partiellement ou totalement, jusqu'à la récupération d'une fonction adéquate ou jusqu'au remplacement définitif du coeur par transplant ["bridge to transplant"]. En même temps, on obtient aussi la récupération fonctionnelle des autres appareils et systèmes de l'organisme (foie,rein, poumon, etc) affectés par l'existence du débit cardiaque réduit, fait qui a pour conséquence une amélioration du pronostic aussi.

L'assistance mécanique cardiaque aux dispositifs d'assistance ventriculaire peut être faite à l'aide de:

A) **pompes non pulsatiles** (à flux continu):
centrifuges: Heart Mate III [fig. 1], Tandem Heart [fig. 2],Ventracor-VentrAssist [fig. 3], BioMedicus, Gyro Pump, etc.
á flux axial: Heart Mate II [fig. 4], Jarvik 2000 [fig. 5], Impella [fig. 6], Hemo Pump etc.

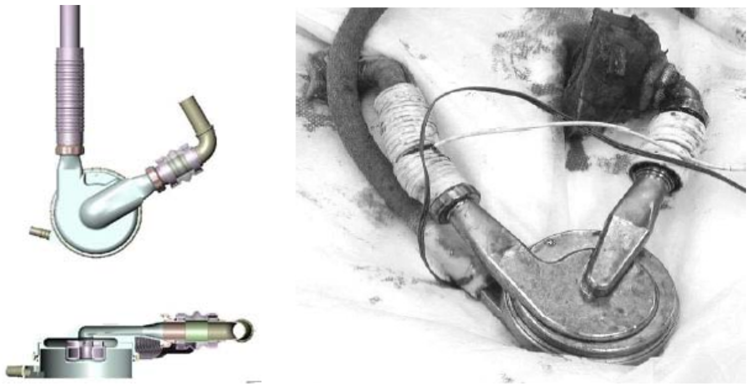


Figure 1: Pompes non pulsatiles à flux continu centrifuges: Heart Mate III

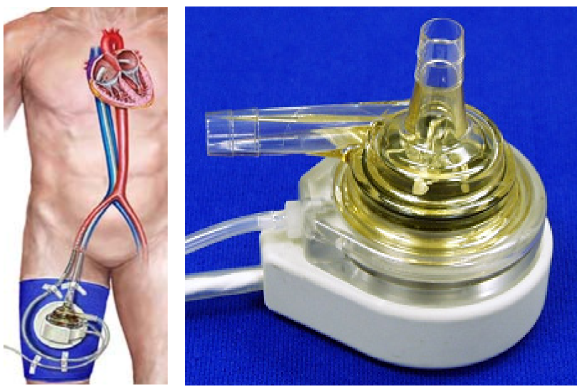


Figure 2: Pompes non pulsatiles à flux continu centrifuges: Tandem Heart

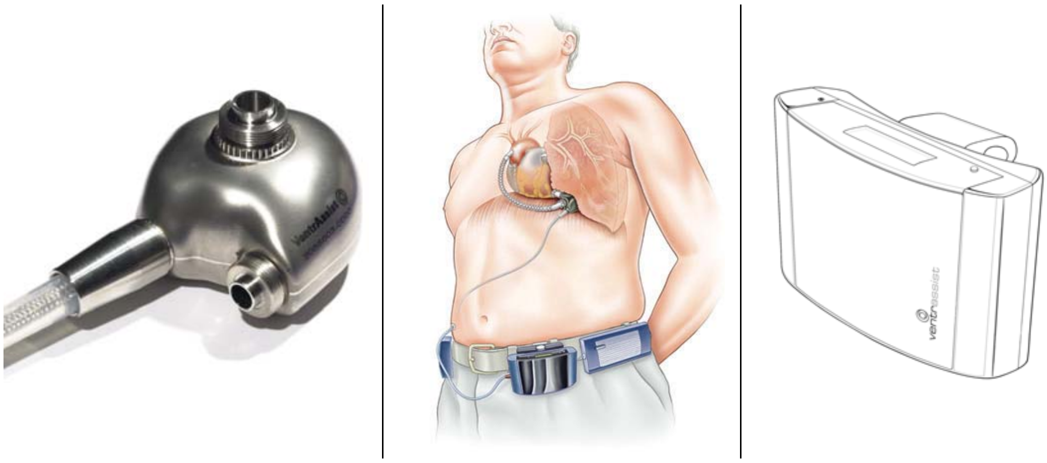


Figure 3: Pompes non pulsatiles à flux continu centrifuges: VentrAssist

Ventracor-VentrAssist/pompe	VentrAssist – Procédé d'implantation	Controller VentrAssist

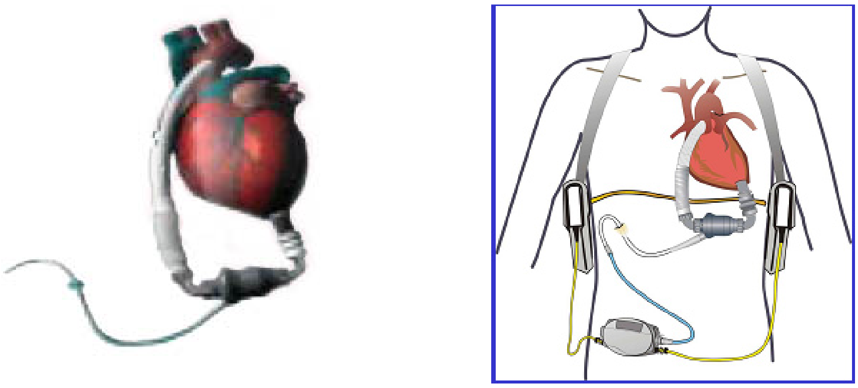


Figure 4: Pompes non pulsatiles à flux continu - axial Heart Mate II

Figure 5: Pompes non pulsatiles à flux continu - axial Jarvik 2000

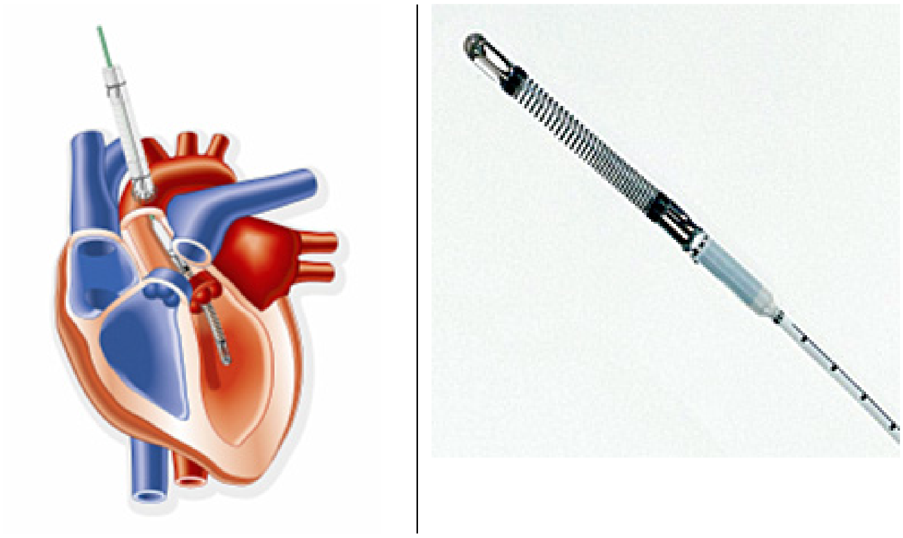


Figure 6: Pompes non pulsatiles à flux axial **Impella**

B) pompes pulsatiles:

Pneumatiques: Thoratec [fig. 7], AbioCor / Abiomed [fig. 8], Medos [fig. 9] etc.
Electriques (électromagnétiques): Novacor [fig. 10], Heart Mate I [fig. 11], Lion Heart [fig. 12] etc.

Ces dispositifs ont été implantés aux animaux, et lorsqu'on a eu de bons résultats, la plupart d'eux ont été et sont aussi implantés à l'homme sous une surveillance stricte. Les dernières années ont apparu des dispositifs d'assistance de plus en plus réduits "en miniature", d'emploi pédiatrique.

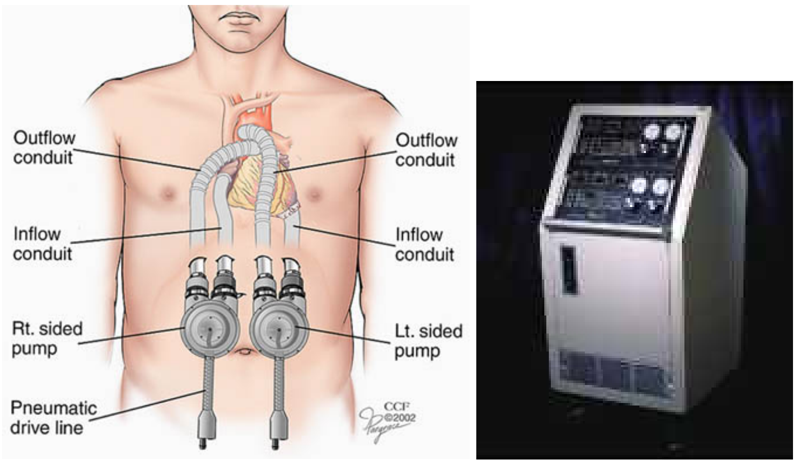


Figure 7: Pompes pulsatiles pneumatiques: Thoratec

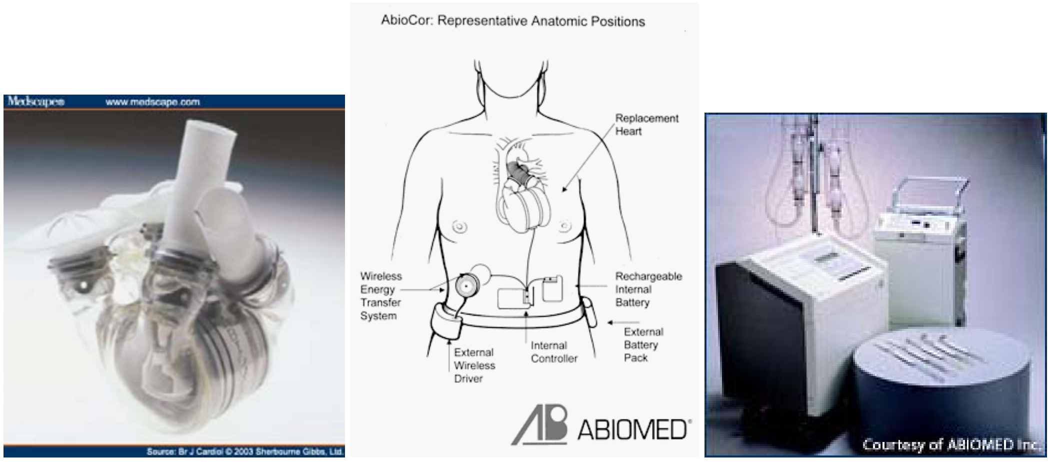


Figure 8: Pompes pulsatiles pneumatiques: AbioCor / Abiomed

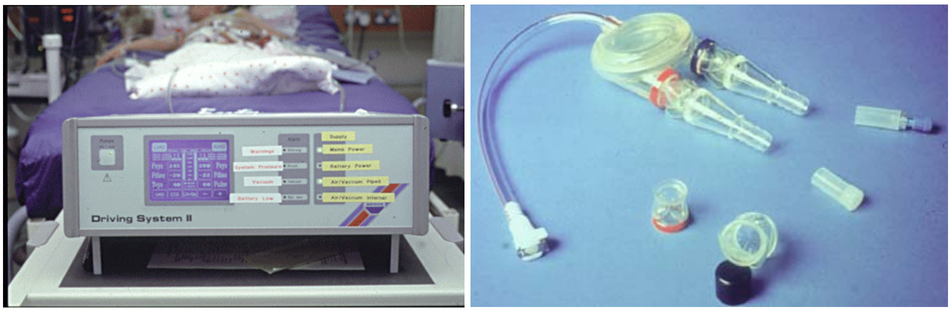


Figure 9: Pompes pulsatiles pneumatiques: Medos

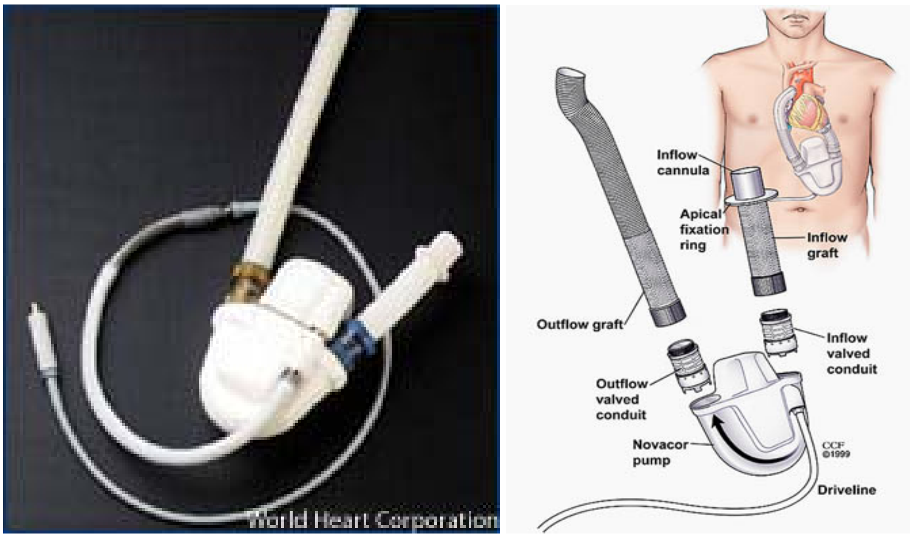


Figure 10: Pompes pulsatiles électriques (électromagnétiques): Novacor

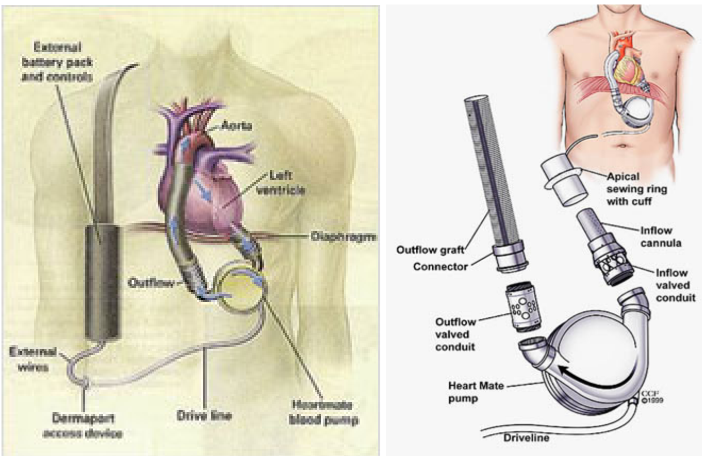


Figure 11: Pompes pulsatiles électriques (électromagnétiques): Heart Mate I

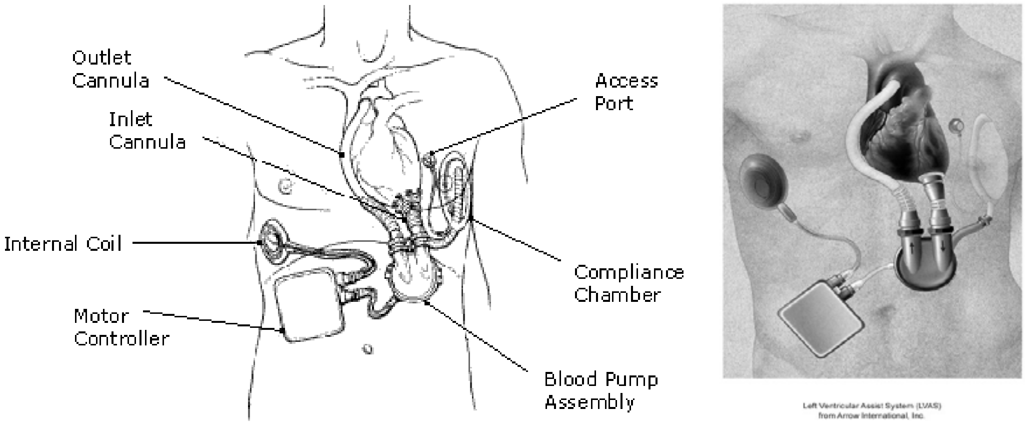


Figure 12: Pompes pulsatiles électriques (électromagnétiques): Lion Heart

Coeur artificiel avec pompe électromagnétique de type NOVACOR"

Nous allons faire référence plus loin au "coeur artificiel avec pompe électromagnétique de type NOVACOR" (réalisé dans les biolaboratoires Edwards-Baxter), qui est un système d'assistance du ventricule gauche implantable dans une poche abdominale, propéritonéale sur le flanc gauche. Il est raccordé au pic du coeur et sur l'aorte ascendente à l'aide de deux prothèses vasculaires pré-coagulées (celle d'influx est localisée au pic du ventricule gauche et celle d'eflux sur l'aorte ascendante) (Fig. 13).

Les valves de la pompe sont des bioprothèses porcines, modèle Carpentier Edwards et peuvent fonctionner:

- avec une fréquence fixe,
- avec trigger EKG,
- avec une fréquence par rapport au remplissage,
- simultanément au cycle cardiaque.

La pompe communique avec une console de commande ou peut être couplée à une batterie rechargeable, portable, ayant une autonomie de jusqu'à 5 heures, pendant que le malade peut être mobilisé.

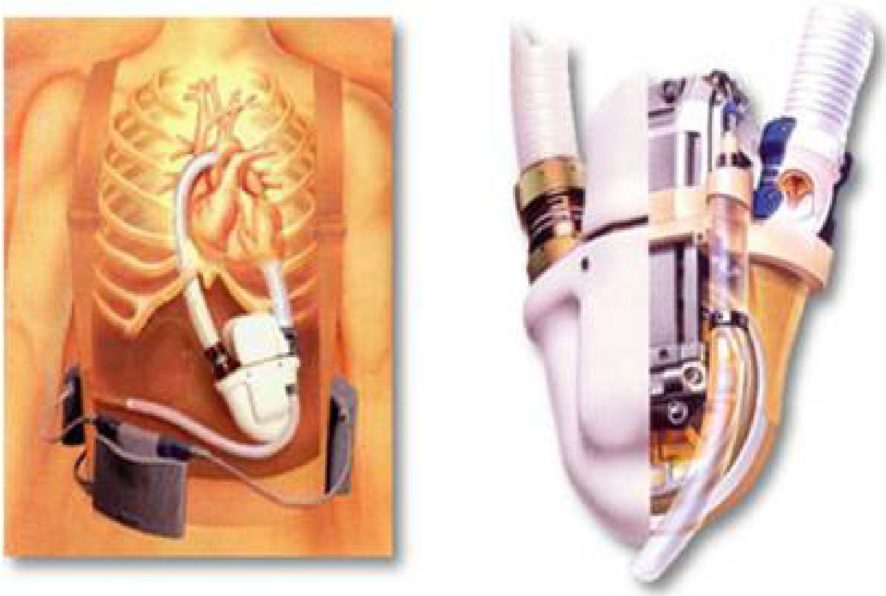
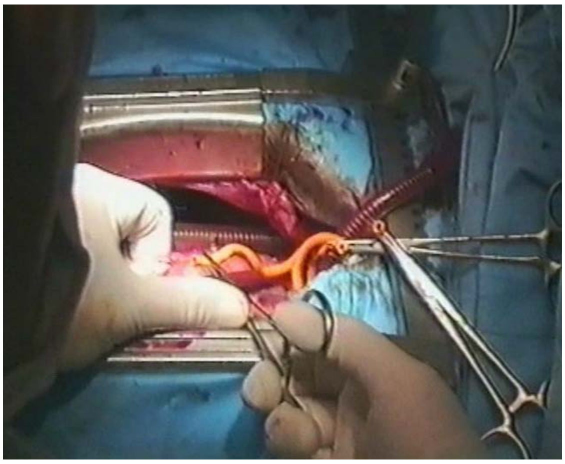
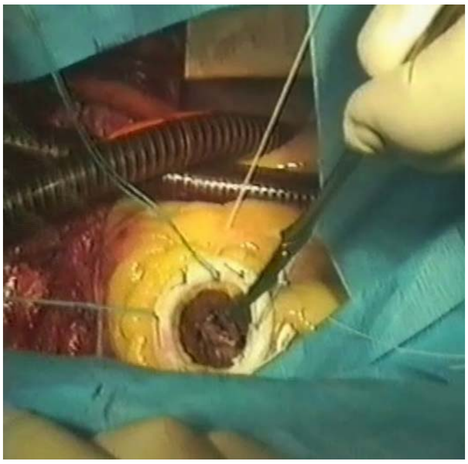


Figure 13: Pompes pulsatiles électriques (électromagnétiques): NOVACOR

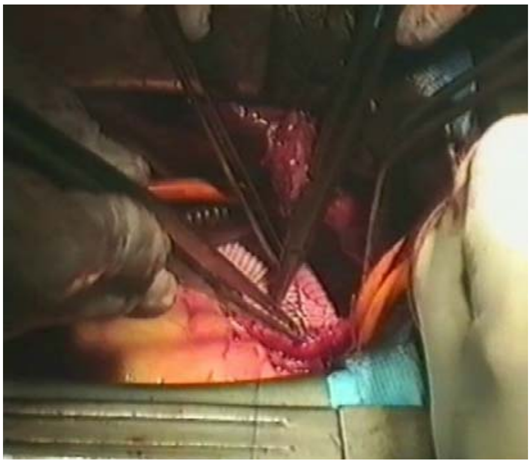


Placement des canules

Incision de la paroi ventriculaire



Orifice dans l'apex du ventricule gauche *Placement de la conduite d'afflux*



Suture de la conduite

Figure 14: Photos pendant l'opération ouverte

En Roumanie, en 2001, a été implanté le premier dispositif de ce type de l'Europe centrale et de sud-est, représentant le cas no. 1462 du monde!

Les indications de l'assistance mécanique

1. Les critères hémo-dynamiques:

a) pour l'assistance du ventricule gauche:

- la pression dans l'atrium gauche > 18-25 mm Hg
- la pression artérielle moyenne < 70 mm Hg
- l'indice cardiaque < 2 l/min et m^2
- l'oligurie

b) **pour l'assistance du ventricule droit:**
   - la pression dans l'atrium droit > 18-25 mm Hg
   - l'indice cardiaque < 2l/min et m^2
   - l'oligurie

2. Indications selon la durée estimée:

a) **assistance à court terme (**heures ou jours jusqu'à la récupération de la fonction cardiaque)
b) **assistance à moyen terme (**jours-semaines) pour la récupération après une myocardite, récupération partielle avec pontage pour le transplant ou jusqu'au moment ou une pompe d'assistance prolongée peut être implantée;
c) **assistance à long terme** (mois-années) en tant qu'alternative au transplant cardiaque (Novacor)

3. Indications selon le degré de l'urgence:

a) **de choix** – chez les patients avec une indication de transplant sans souffrance de malperfusion évidente ou chez les patients chez lesquels a survenu une contre-indication pour le transplant (indication "chronique");
b) **implantation d'urgence** chez les malades avec indication de transplant avec altération clinique sévère avec malperfusion évidente (syndrome de débit cardiaque réduit qui ne répond pas à la thérapie médicamenteuse maximale). Dans ces cas, l'implantation est réalisée dans les 48 heures suivantes;
c) **urgence maximale en cas de choc cardiogène avec malperfusion sévère.** Dans ces cas l'implantation s'exécute immédiatement, en l'absence même d'une indication ferme pour le transplant.

Les contre-indications de l'assistance par pompe de type Novacor

Les contre-indications de l'assistance par pompe de type Novacor ne sont pas absolues, mais elles expriment seules les situations associées aux résultats faibles d'après l'implantation et sont similaires à celles pour le transplant:
- l'affection rénale, hépatique ou pulmonaire chronique et irréversible
- l'insuffisance aiguë d'organe secondaire à l'insuffisance cardiaque
- bilirubine > 5 mg/dl
- l'urée > 100 mg/dl ou la créatinine > 5 mg/dl
- tumeurs malignes avec métastases
- l'artériosclérose centrale ou périphérique
- l'infection systémique active
- diathèse hémorragique incontrôlable

Les contre-indications spécifiques pour la prothésation ventriculaire gauche par pompe Novacor:
- L'insuffisance ventriculaire droite primaire
- L'insuffisance aortique
- La prothésation mécanique aortique vu que dans la valve mécanique peuvent apparaître des thrombi à cause du flux sanguin réduit ou absent qui passe à travers elle.

La durée de l'assistance mécanique

Sur le plan mondial on a enregistré – jusqu'à l'an 2000 – 88 cas d'assistance qui dépasse 1 année. La durée maximale de l'assistance a été de 1200 jours (voir la Fig. no. 28). Au niveau de l'an 2005, dans plus de 100 centres médicaux du monde qui utilisent Novacor® LVAS, le dispositif est reconnu pour sa fiabilité, durabilité et applicabilité. Parmi les plus de 1700 patients avec implant de Novacor® LVAS, 172 patients "Bridge-to-Transplant" l'ont porté initialement un peu plus d'une année. Parmi ces porteurs, 45 ont résisté plus de 2 années, 24 plus de trois années, 11 l'ont supporté temps de 4 années et un seul plus de 6 années. Seulement 1,4 % des pompes ont du être remplacées. Aucun patient n'a décédé à cause d'une défection du dispositif.

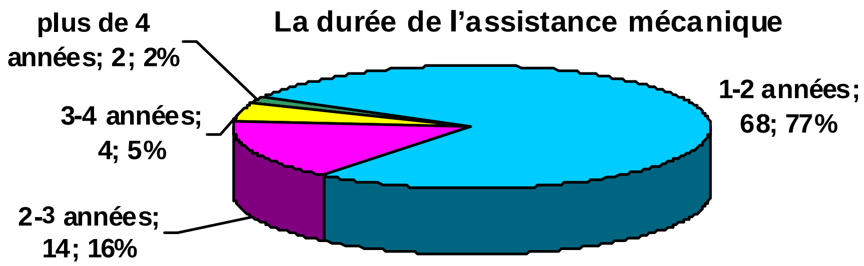


Figure 15: **La durée de l'assistance mécanique**

Les critères de sélection pour la prothésation par le système Novacor sont:

[1] Patients avec insuffisance cardiaque progressive réfractaires au traitement médical ou/et chirurgical. Les effets sont meilleurs autant que l'intervention est plus précoce.

[2] Patients avec insuffisance cardiaque chronique ou se trouvant sur la liste de transplant et qui souffrent d'une décompensation aiguë.

[3] Patients avec choc cardiogène (nécessitent une évaluation précoce pour l'implantation de DAV gauche).

[4] Insuffisance cardiaque post cardiotomie à condition que le pontage cardio-pulmonaire n'ait pas été de longue durée.

Les facteurs de risque pour l'assistance avec pompe de type Novacor:

- L'assistance ventilatoire prolongée
- Le support inotrope maximal prolongé
- L'âge > 45 ans
- La créatinine > 3 mg/dl aux tendances accrues
- La fièvre (plus de 38,5° C dans le rectum)
- Les leucocytes en nombre de plus de 15. 000, sans preuves évidentes d'infection
- La maladie aortique
- Les arythmies atriales incontrôlables
- L'arrêt cardiaque dans les antécédents
- L'assistance circulatoire mécanique ((inclusivement MCIA)
- Les interventions chirurgicales cardio-thoraciques dans les antécédents

Les complications de l'assistance mécanique du ventricule gauche sont **précoces** et **tardives.**

Les *complications précoces* sont: l'hémorragie, l'insuffisance cardiaque droite, l'embolisme, l'insuffisance multiple d'organe [A.R.D.S.].

Les *complications tardives* sont: l'infection, le thrombo-embolisme et les complications mécaniques. Les infections peuvent être causées par un nombre important de micro-organismes comme les bactéries Gram positives (Staphylocoques, en spécial les staphylocoques aureus, les Entérocoques) ou les bactéries Gram négatives (Pseudomonas aeruginosa, espèces d'entérobactéries, espèces de Klebsiella, etc), ou des fongi de type Candida sp.

Le traitement des infections visant les dispositifs d'assistance ventriculaire [DAV] est extrêmement difficile et nombre de patients meurent à cause de l'omission de ces traitements. Le traitement initial devrait viser les antibiotiques à spectre large, de dernière génération, ciblé selon l'antibiogramme fait pour chaque branche microbienne. Dans le cadre du traitement général, on ne doit pas ignorer – par rapport à chaque cas – la thérapie immunosuppressive, anticoagulante et de combat des saignements secondaires provoqués par les anticoagulants.

Par le remplacement des prothèses vasculaires d'influx de type Cooley avec celles de type Vascutek, l'incidence des embolies cérébrales s'est réduite de 21% à 12%.

L'expérience roumaine dans la période 2000-2004 a été représentée par un partenariat entre l'Institut de Maladies Cardio-Vasculaires "C. C. Iliescu", la Clinique de Chirurgie cardiovasculaire de l'Hôpital St. Luc Bruxelles, les Laboratoires Edwards (USA). Dans cet intervalle de temps ont été opérés et suivis deux patients sélectionnés à partir d'un groupe de 15, qui avaient en principe l'indication de transplant cardiaque.

L'équipe roumaine (chirurgiens cardiovasculaires, cardiologues, anesthésistes, réanimateurs avant l'implant, assistants médicaux ATI et techniciens dans la circulation extracorporelle) a suivi un programme de formation dans deux étapes: à Bucarest et à Bruxelles, ou, à part les problèmes théoriques, on a implanté à deux veaux le coeur artificiel de type Novacor, dans le Laboratoire de Chirurgie expérimentale.

Dans cet intervalle, les thèmes ont été: l'évaluation clinique et de laboratoire des malades avant l'implant, discussions sur la sélection des patients, discussions sur des thèmes chirurgicaux (implant-explant), discussions sur le management des patients, le rôle de l'échographie trans-oesophagienne, les complications infectieuses, hémorragiques et/ou multiorganiques [ARDS], films vidéo, les notions sur la console de suivi des patients, les notions d'instruction des patients opérés – en spécial après la période d'hospitalisation- les actualités sur le management des dispositifs, la manipulation des pompes, la solution des dysfonctionnalités, actualités sur l'anticoagulation / l'antiagrégation, etc.

Pendant la période Bruxelles, Hôpital Saint Luc, y ont participé:

De la part de l'Institut de Maladies Cardiovasculaires "C. C. Iliescu" Fundeni: prof. Dr. Vasile Cândea, Dr Dan Paul Gherghiceanu, Dr Horatiu Moldovan, Dr Serban Ioan Bubenek, Dr Daniela Filipescu, Dr Luminita Iliuta, Assist. Vasilica Olteanu.

Y ont participé: de la part de la Corporation **WorldHeart:** Dr P. Jansen, de la part de la compagnie **Edwards:** Dr S. Scuri, Dr R. Halfmann, Marc-Antoine Perez, de la part de la compagnie **Baxter:** G. Sofianos, G. Krinos. Invités spéciaux: Dr A. El-Banayosy, Dr L. Jacquet. De la part de l'Hôpital St. Luc, Bruxelles (Chirurgie Cardiovasculaire): Prof. Dr. P. Noirhomme.

- **Situation à l'admission à l'hôpital:** Débit cardiaque: 4,5 l/min, Indice cardiaque: 1,93 l/min/m², PCWP: 33 mmHg, FEVS: 18%, Volume télédiastolique du Vg: 76 ml
- **L'implantation a eu lieu le 18 juin 2001,** la pompe Novacor ayant un débit de 6-7 l/min après l'implant

L'équipe opérationnelle a été formée par le Prof. Dr. Phillip Noirhomme (Belgique), assisté par le prof. Dr. Vasile Cândea, Dr Horatiu Moldovan et Dr Bogdan Radulescu. Anesthésie: Dr Serban Bubenek. Cardiologue: Dr Luminita Iliuta

L'évolution postopératoire immédiate a été bonne. Le 11-ème jour en post-opératoire on a réintervenu pour l'évacuation de certains hématomes grands dans le péricardium et dans la poche abdominale. Le 99-ème jour - réintervention pour l'évacuation d'une collection de pus dans la poche abdominale. Le 102-ème jour, réintervention pour une péritonite aiguë généralisée et le 123-ème jour on procède à l'intervention pour l'explant.

Le patient est renvoyé le 21 novembre 2001, 156 jours après l'implant.

La fonction cardiaque du patient s'est considérablement améliorée et on peut observer en comparant les valeurs à l'admission et au renvoi de l'hôpital, notamment: la croissance du débit cardiaque de 4,5 l/min à 6,5-8,5 l/min, de l'indice cardiaque de 1,93 l/min/m² à 3,5-3,7 l/min/m² et de la FEVG de 18% à 35-37%.

Le patient est mort le 28 avril 2002, à 306 jours depuis l'implantation du DAV, la cause du décès étant due à une hémorragie foudroyante de la branche aortique.

Le patient no. 2: S. M., 39 ans, sexe masculin.

Diagnostic: cardiomyopathie dilatative avec dysfonction systolique sévère biventriculaire; en insuffisance cardiaque stade IV NYHA.

- **Condition à l'admission:** Echographie cardiaque: L'atrium droit 54/64; L'atrium gauche 73; Le ventricule droit 41; Le ventricule gauche 97/86. FEVg = 23%, FEVd = 25%. Cathétérisme:artères coronaires perméables PSAP = 49mm Hg.
- L'implantation du coeur artificiel [la pompe Novacor] a été réalisée le 23 avril 2002.

L'équipe opérationnelle a été formée par le Prof. Dr. Vasile Cândea assisté par le Prof. Dr. Phillip Noirhomme, le Dr Horatiu Moldovan et le Dr Bogdan Radulescu. Spécialiste d'anesthésie-réanimation: Dr Serban Bubenek. Spécialiste de cardiologie: Dr Luminita Iliuta.

L'évolution post-opératoire dans les premiers jours a été très bonne. Le 7ème jour en post-opératoire [le 30 avril 2002] comme suite d'un saignement, on procède à une réintervention pour contrôler l'hémostase (médiastin et poche abdominale) et on a évacué 3000 ml de caillots. On a fait la toilette chirurgicale dans le médiastin, la poche propéritonéale du côté gauche sous-costal et du trajet sous-cutané du conduit (drive-line) électrique qui faisait la connection entre la pompe Novacor et la source d'énergie électrique (prise ou accumulateurs).

Le malade est maintenu sous une stricte surveillance post-opératoire, ayant une très bonne évolution jusqu'en décembre 2002, lorsqu'il est renvoyé de l'hôpital à 8 mois depuis l'implant.

Le **25 avril 2003,** à un an depuis l'implant, il est hospitalisé en urgence avec syndrome sous-occlusif et infection localisée au niveau du trajet intrapariétal abdominal du conduit sous-cutané (drive-line).

Il est opéré par laparotomie exploratrice et toilette chirurgicale du trajet drive-line avec une bonne évolution, sans complications.

Les examens échographiques montrent un débit cardiaque propre mis en évidence par l'ouverture des valves aortiques natives. Le test de sévrage montre la baisse progressive du débit de la pompe simultanément avec l'évaluation échocardiographique: DC/IC=5,5-6/2,6-3 l/min et m², maintenu aussi à un débit de la pompe de 2 l/min et m². Dans ces conditions, vu qu'on a obtenu une bonne récupération fonctionnelle du myocarde, on procède, le 13 juin 2003, à l'explant de la pompe, **après 14 mois d'assistance.** L'évolution après l'explant est bonne et permet le renvoi le 4 aout 2003.

Le 30 décembre 2004, le malade meurt à 2 ans depuis l'implantation et 10 mois depuis l'explant, avec le diagnostic de cirrhose hépatique à virus C avec décompensation portale et parenchymateuse. La survie a eu une durée de 2 ans et 8 mois.

Discussions. Le rôle des systèmes d'assistance ventriculaire mécanique dans l'insuffisance de pompe cardiaque est, en général, bien établi et documenté. Leur utilisation est en augmentation comme pontage vers le transplant en spécial. Malheureusement, les complications de l'utilisation de ces pompes restent importantes. Parmi celles ci, l'infection est la plus importante.

Le pronostic des patients auxquels on a implanté un système d'assistance ventriculaire dépend, de manière essentielle, des dysfonctions pré-existentes des divers appareils et systèmes.

Conclusions concernant l'assistance par système d'assistance ventriculaire:

*Les systèmes d'assistance ventriculaire ont gagné une place bien définie dans le traitement de l'insuffisance cardiaque (pontage vers le transplant ou vers la récupération de la fonction ventriculaire et plus rarement comme implant définitif).

- La pompe Novacor a démontré au long du temps des caractéristiques techniques très bonnes sans dysfonctions significatives.
- Il y a encore un taux important de complications dominées, de manière évidente, par l'infection et le saignement.
- La colonisation bactérienne des systèmes est très fréquente encore (50-90% des cas), mais dans la plupart des cas elle ne cause pas un syndrome septique et peut être contrôlée efficacement sous traitement aux antibiotiques.

Perspectives

L'avenir appartient aux systèmes complètement implantables (qui existent déjà), à condition qu'ils deviennent performants à long terme. Également, ces systèmes implantables doivent être minimisés et réalisés avec une moindre consommation d'énergie.

En ce qui concerne l'évolution technologique du perfectionnement et de la minimisation des systèmes d'assistance pulsatile du ventricule gauche, "*World Heart Corporation*" – le leader mondial de ceux-ci - a mis au point le modèle Novacor II LVAS (R), qui a été expérimenté sur des animaux afin de vérifier sa biocompatibilité à long terme. Le Novacor LVAS actuel est un dispositif électrique pulsatile implanté aux côtés du coeur du patient pour qu'il se charge d'une grande partie du travail du coeur naturel, aidant ainsi les malades dans des stades terminaux de l'insuffisance cardiaque. Son utilisation est déjà autorisée aux USA, Canada, Japon et Europe.

En 2005, l'insuffisance cardiaque affecte approx. 5 million d'américains et est devenue la cause principale d'hospitalisation, ce nombre représentant plus que toutes les formes de cancer prises ensemble. Pour cette raison, la Société Américaine de Cardiologie, l'Association Américaine du Coeur et la Société Américaine d'Insuffisance Cardiaque ont recommandé l'implantation à but permanent des dispositifs d'assistance ventriculaire, mécanique de la circulation chez les patients avec cette grave souffrance cardiaque et qui ne sont pas des candidats au transplant cardiaque.

Le problème extrêmement important est que ces dispositifs perfectionnés soient accessibles comme prix, étant donné qu'à l'heure actuel ce prix est prohibitif, d'environ 85.000 USD.

Correlation "pressure gradient - flow" in accordance with the dimension of aortic cannula*)

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Abstract

From all the elements of extracorporeal circulation circuit, the aortic cannula represents the one which realizes the highest pressure gradient.

***Objective**: to determine the correlation between the pressure drop at the level of the aortic cannula and the flux in the arterial line, by analyzing a series of cannulas currently used in our clinic.*

***Material and method:** within the study, cannulas sized from 8 to 24 French were tested (see Table 1). The pressure drops at cannulas' level were recorded corresponding to the different flows in the arterial line. The determinations were made using different circulating liquids: water, on the one hand, and blood with hematocrit 26% and of 33 C degrees, on the other hand.*

***Results:** The pressure gradient values corresponding to different flows were recorded in tables (see Tables 2 and 4). At the same time, for cannulas of different sizes, the flows that determined a gradient of 100 mm. Hg were recorded (see Tables 3 and 5).*

***Conclusions:** at low flows of the arterial pump, the 8 French cannula produces high pressure gradients. The use of this type of cannula is recommended in the cases of children under 2.5 kg. Angulated cannulas have lower haemodynamic performances than the straight ones, producing high pressure drops at similar sizes.*

***Key words:** pressure gradient, aortic cannula*

Introduction

The good functioning of the extracorporeal circulation circuit represents one of the major conditions for a successful operation in open-heart surgery. The hemodynamic of the circuit of the cardio-pulmonary "by-pass" is influenced by multiple factors: the length and dimensions of the lines and connectors, the type of the oxygenator, the blood viscosity, density and temperature, the existence of laminar flux, the correct positioning of the cannulas. Of all the elements within the arterial circuit of the pump (oxygenator, lines, connectors, aortic cannula), the biggest pressure drops is found at the level of the aortic cannula (3). Especially in the case of paediatric patients, the dimension of the aortic cannula is the result of the compromise between the technical factor, which has to assure a certain flux, and the anatomical situation, which tends to reduce as much as possible the dimensions of each catheter introduced in the vascular bed (6). On the other hand, at

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adult patients, the too high velocity of the flux at the level of aortic cannula can erode the atherosclerotic material from aorta, causing non-cardiac complications such as cerebral vascular attack, multiple dysfunctions of the organ or death (5). The mechanism by which these lesions (injuries) occur is based on the so-called "sand-blasting effect" of the aortic cannula flux on the aortic walls (2).

Classically, it is recommended to orientate the output orifice of the cannula, and implicitly the blood flow, towards the distal area of the aortic arch. In this context, the injuries induced especially at the cerebral level occur through the following mechanisms: the too high velocity of the blood flow, turbulences, cavitations and "sand-blasting effect". The too high velocity of the blood flow through the aortic cannula might also produce haemolysis and/or proteinic denaturation (2).

Stark and De Leval suggest that the dimensions of the cannula must be selected in such a manner that at the highest predicted flow, the pressure gradient through the aortic cannula should not exceed 100 mmHg (4). At the same time, in order to avoid the turbulent flux, Gates and Hessel suggest as a limit of the pressure gradient 100 mmHg (1).

Material and Method

In spite of all the attempts to imitate the anatomic and physiologic situation it is impossible to simulate all the surgical events. An experimental circuit has been realized, consisting of a roller pump, a set of lines and a reservoir with thermic control (see Figure no. 1).

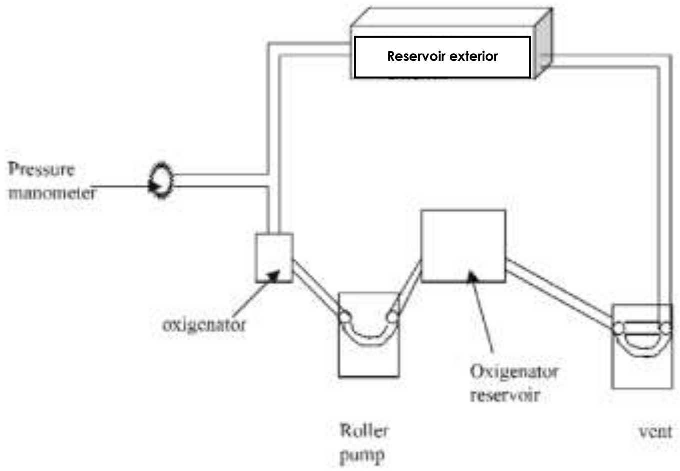

Figure 1: The experimental circuit:

- **Reservoir exterior**
- **Pressure manometer**
- **Oxygenator**
- **Roller pump**
- **Oxygenator reservoir**
- **vent**

In order to be as close as possible to the real situations, a typical circuit with oxygenator, arterial pump with latex of 1/2 and arterial line of 3/8 has been used, the active aspiration being realized through another roll, usually dedicated to vent aspiration, thus draining the blood from the exterior reservoir into the reservoir of the oxygenator. In order to create a laminar flux at the level of the output of the arterial cannula, a latex tube of 1/2 and 20 cm in length has been placed at this level, inside the reservoir (see Figure 2, next page).

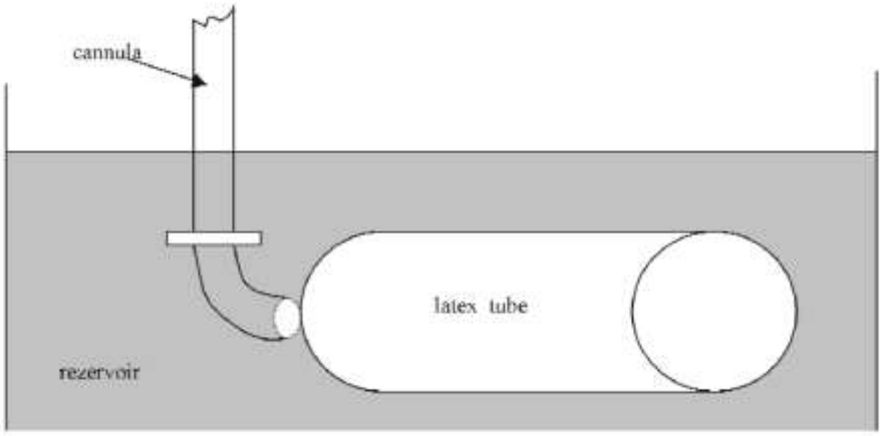

Figure 2: Positioning of cannula in a latex tube

Two sets of determinations have been realized, the first one for water at a temperature of 33 degrees C, and the second one for blood at 33 degrees C and hematocrit at 25-26 mmHg. All the arterial cannulas usually used at present in our clinic have been tested (see Table 1).

Table 1: Types of cannulas

Cannula size (Fr.)	cannula type	Code	Angulation
8	Medtronic DLP	75008	straight
10	Medtronic DLP	75010	straight
12	Medtronic DLP	75012	straight
14	Medtronic DLP	70014	straight
16	Medtronic DLP	70016	straight
18	Medtronic DLP	75318	straight
20	Medtronic DLP	88020	angulated
22	Medtronic DLP	86022	angulated
24	Medtronic DLP	86024	angulated

In all the cases, in order to avoid the big pressure drops at the level of arterial line, a line of 3/8 has been used, although in the case of cannulas under 18 Fr lines of 1/4 are usually used. The pressure detector used was a manometer type with spring, placed, as usually intraoperative, at the exit of the arterial line from the oxygenator. Both the maximum and the minimum pressure were determined, but, for an easier appreciation of the results, we preferred to take into consideration only the maximum pressure recorded by the manometer during the cycles induced by the rotation of rolls of the pump.

The pressure gradient was assessed through the maximum value indicated by the manometer, considering that the pressure within the external reservoir can be approximated as 0 mmHg, the proposed experimental model generating a laminar flux (through the latex tube) at an immersion depth of 2-3 cm blood.

The pressure values were recorded at increasing fluxes (according to the type of the cannula). At the same time the flux at which the pressure gradient reached the critical point of 100 mmHg was recorded for each cannula.

Table 2: Flow-pressure correlation for water

Size of cannula (Fr.)	Flow 0,3 l/min	Flow 0,5 l/min	Flow 0,75 l/min	Flow 1 l/min	Flow 1,25 l/min	Flow 1,5 l/min	Flow 2 l/min	Flow 2,5 l/min	Flow 3 l/min	Flow 3,5 l/min	Flow 4 l/min	Flow 4,5 l/min
8	62	92	140	212								
10	48	64	88	124	155							
12		50		64		96	140	185				
14		45		54		64	84	110	140			
16				52		60	75	94	120	142		
18				50		58	62	75	90	102	118	130
20						50	58	70	82	98	110	128
22							53	60	68	78	88	98
24							50	55	60	68	75	80

Results

During the test with water, the pressure values obtained were recorded (in mmHg) and synthesised in a table (see Table 2).

In order to achieve a pressure gradient of 100 mm Hg the following fluxes were required (corresponding to different dimensions of the cannula) (see Table 3).

Table 3: 100 mm. Hg. gradient flow for water

Dimension of cannula (Fr.)	8	10	12	14	16	18	20	22	24
Flow (l/min)	0.55	0.85	1.57	2.30	2.65	3.40	3.55	> 4.50	> 4.50

These are the values recorded in the case of the test using blood (see Table 4).

Table 4: Flow-pressure correlation for blood.

Size of cannula (Fr.)	Flow 0,3 l/min	Flow 0,5 l/min	Flow 0,75 l/min	Flow 1 l/min	Flow 1,5 l/min	Flow 2 l/min	Flow 2,5 l/min	Flow 3 l/min	Flow 3,5 l/min	Flow 4 l/min	Flow 4,5 l/min
8	60	110	180	240							
10	60	78	108	150							
12	55	60	70	85	120	170					
14	65	75			92	120	140				
16	55	72			85	105	120	145			
18				75	80	90	100	115	130		
20				72	80	90	105	120			
22				70	80	85	90	105	115	120	
24					75	80	88	96	105	110	115

And the flows corresponding to the pressure gradient of 100 mmHg were as following (see Table 5).

Table 5: 100 mmHg gradient flow for blood

Dimension of cannula (Fr.)	8	10	12	14	16	18	20	22	24
Flow (l/min)	0.45	0.67	1.2	1.7	1.85	2.5	2.25	2.75	3.3

Discussions

As expected, the pressure gradient of 100 mmHg is reached at smaller fluxes in the cases when the circuit is filled with blood, in comparison with the test made with water.

The interesting point is the fact that when comparing the fluxes required to reach a gradient of 100 mmHg, the fluxes at which the French cannulas of 14 and 16 reach this gradient are not sensibly different. The explanation lays in the fact that in the case of the cannula of 14, which has an extension of distal plastic, the equivalent diameter for the blood seems to be close to the one of the cannula of 16, at which the distal orifice is monobloc with the cannula (in the case of the models used in our clinic).

Another fact worth to be mentioned is that, as it can be observed from the pressure diagrams, the equivalent diameter of the cannula of 20 Fr is smaller than the one of the canula of 18 Fr, the pressure gradient of 100 mmHg being reached at smaller fluxes in the case of the cannula of 20 Fr than in the case of the cannula of 18 Fr. The explanation sits in the fact that, starting with the cannulas of 20 Fr, the cannulas are angulated, this having negative repercussions on the hemodynamic parameters.

Conclusions

Of all the arterial circuit of the heart-lung machine, the biggest pressure fall takes place at the level of the cannula for arterial canulation. Generally it is not recommended to exceed the fluxes through the arterial cannula which reach a pressure gradient over 100 mmHg.

The use of arterial cannulas of 8 French is quite limited, being reserved for the cases under 2-2.5 kg, because they realise high gradients at low fluxes.

The angulated arterial cannulas realize higher pressure gradients at similar fluxes, in comparison with the straight ones, their use being reserved for the cases in which the dimension of the aorta allows the placement of a cannula oversized when compared with the weight of the patient.

When there is a possibility of choice (according to the calculated flow) between the cannulas Medtronic DLP 70014 and 70016, and the anatomic situation imposes the choice of the one with smaller dimensions, we can make this choice without hesitation because the equivalent diameters of the two cannulas for blood do not differ that much.

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Thermal shape setting process influences the cutting performance of Nitinol Blades*)

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Abstract

Machining of shape memory alloys (SMA) based on Nitinol (NiTi) creates difficulties due to its ductility and severe strain hardening, particularly during the process of sharpening. Up to date, no data exists, if different steps of annealing during shaping process compromise the sharpness of NiTi-made cutting edges. We therefore thought to determine whether heat treatment during the shape setting process influences sharpness and cutting performance of NiTi blades. The present study clearly showed that the process of annealing resulted in a decrease of cutting performance and in attrition of blade-sharpness as measured by scanning electron microscopy (SEM). This could be related to the generation of a thin oxide layer formed at the surface of NiTi following the shaping process.

Key-words: *Nitinol, oxide layer, cutting edge, sharpness, scanning electron microscope, aortic valve resection*

Introduction

NiTi shape memory alloys have been extensively used in medicine, due to their unique properties, like shape memory effect, super-elasticity, good biocompatibility, durability and corrosion resistance [1-4]. These properties have encouraged many investigators to establish new fields for SMA-application and therefore, the use of NiTi is increasing in many devices. Although NiTi has many superior and advantageous characteristics as compared to stainless steel, its mechanical machining is extremely difficult. High ductility and severe strain hardening and furthermore the unconventional strain-stress-behaviour influences the machining of NiTi-based SMA´s [5]. In addition, the stress-induced martensic transformation at the work surface complicates the contact between tool and workpiece [6].

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Up to date, percutaneous aortic valve implantation, either via transfemoral or transapical approach, is an increased propagated, forward-looking procedure, which has been suggested as an alternative to conventional valve surgery in selected high-risk cases [7-9]. However, by using these sophisticated techniques, the calcified valve remains in-situ and has to be dilated with a balloon into the aortic wall prior to implantation. As a result, the valve prosthesis has to be implanted in a rather inhomogeneous and non-circular layer. Therefore, it might be advantageous, if the pathology of the calcified native valve can be removed by the use of a new developed valve resection tool prior to valve implantation of the catheter-mounted prosthesis, in order to avoid several valve-related complications [10].

A variety of different resection tools have been evolved, however, all of the current resection tools are far from clinical routine or are not feasible.

So far in the present study, a new instrument for minimal-invasive resection, equipped with foldable NiTi cutting edges was tested [11]. Due to the ability of shape memory, which enables blade-folding and later expanding in a preformed circular shape, NiTi, as material substance was selected.

We describe our first experimental "in-vitro"-results, if the essential thermal shape setting process does affect the sharpness or cutting performance of blades made from NiTi intended for minimal-invasive aortic heart valve resection.

Methods

Study design

Fourteen NiTi sheets were primarily sharpened under defined conditions [11]. Specimens underwent an electropolishing procedure in order to remove surface oxides and residues prior to heat treatment. The shape setting involves a combination of strain, temperature, and time to optimize the "remembered" shape. Therefore, seven sheets underwent a contact-free annealing procedure for 420s at 873 K (Linn Electronic, Hirschbachtal, Germany) following quenching in water (room-temperature). Cutting performance and blade sharpness were evaluated subsequently under defined conditions (ISO 8442-5, 2005, cutting length 20mm, pressing force 50N). All blades underwent a total of 60 cycles during testing. Initial cutting performance (ICP) and total card cut (TCC) were measured. Blades were observed after test-procedure via scanning electron microscope (SEM) and abrasive wear was quantified.

Specimen

The material used in this study was a commercial available binary NiTi alloy (Endosmart® GmbH, Stutensee, Germany), and its composition was Ni51% at Ti49 %. Specimen were laser cut from 0.3 mm sheetings. The final specimen were 40mm in length and 12mm in width. Grinding of NiTi-made specimen creates difficulties as previously described [11-12]. In this study, grinding was performed mechanically (Cera Gloss diamond, Edenta AG, AU/SG, Switzerland) using a high-speed milling cutter (Aciera F1, Muller Machines, Brügg, Switzerland) at 10.000 rpm.

Sharpness testing

Blade sharpness was tested using a special sharpness tester (Knife&Cutting Test Machine, Catra Cutlery and Allied Trades Research Association, Sheffield, UK; figure #1), which is designed to carry out sharpness testing to very high quality and international standards (BS EN ISO 8442-5, 2005). The principle of this method is subsequently described in detail: The specimen is mounted in a position with the edge vertical and a pack of specially developed synthetic paper is lowered on to it (with constant pressure force of 50N). By oscillating the blade back and forth the specimen cuts into the paper, while the depth of the cut being the measurement of sharpness. The test media (paper) is loaded with 5% silica, which has a wearing effect on the blade edge. By repeating the back and forth motion, the further cuts are made, which wears the cutting edge. The measurement of cut depth at each subsequent stroke can then be plotted to produce a wear curve for each blade tested. The test produces two indications: ICP (Initial Cutting Performance) representing the cutting ability (sharpness) of the blade. ICP is the addition of the first three cutting strokes. Furthermore, TCC (Total Card Cut) is obtained, which represents the life of the blade by giving a measure of its total cutting ability, which is calculated by adding a total of 60 cycles.

Figure 1: Testing machine

Scanning electron microscopy

The structures of NiTi compounds are commonly examined by SEM, X-ray diffraction and photoemission spectroscopy (XPS) or Auger spectroscopy [13]. In our experiments surface structure was examined by scanning electron microscopy with a magnification of x1000 (DSM 960 A, Zeiss GmbH, Oberkochen, Germany). The maximum nicking was identified and maximum flank-wear land width (Vbmax [µm]) and depth (Vtmax [µm]) was quantified.

Statistical analysis

Continuous and normally distributed data were reported as mean ± standard deviation, and categorical variables as number (%). A Student t-test was used for paired data testing. For all statistical tests, a two-tailed *P value* < 0.05 was considered as statistically significant. All statistical analyses were performed using the Sigma-Stat® software package 2.0 (Systat Software Inc., San Jose, CA, USA).

Results

All blades underwent the cutting performance tests (n = 14), but in the heat untreated group, three blades did not pass the required 60 cycles for testing, whereas in the heat-treated group, two blades did not end whole testing period, resulting in a lower number of TCC tests.

Initial cutting performance results

ICP could be obtained in all 14 blades. The cutting distance of the first three cycles was added as previously described and compared between the two groups (untreated and the heat-treated group). — In the non-treated group ICP (n = 14) was 25.7±5.8cm compared to 15.7±9.9 cm in the heat-treated group (p = 0.04), indicating statistical difference.

Total card cut results

Due to the fact, that a total of five blades (two of the heat-treated group and three of the heat untreated group) did not passed and therefore did not end up the whole testing period, TCC could only obtained in 9 out of 14 blades. In the untreated group, TCC was 75.2±17.9 cm, whereas in the heat-treated group a TCC of 41.6±20.7cm was observed (p = 0.037). During the first sixteen cycles of testing, heat-untreated blades showed within ten time points statistically significant higher values in TCC than heat-treated blades (cycle 2, 7, 9, 10, 11, 12, 13, 14, 15 and 16; $p < 0.05$). A comparison of the TCC of both groups is shown in figure 2.

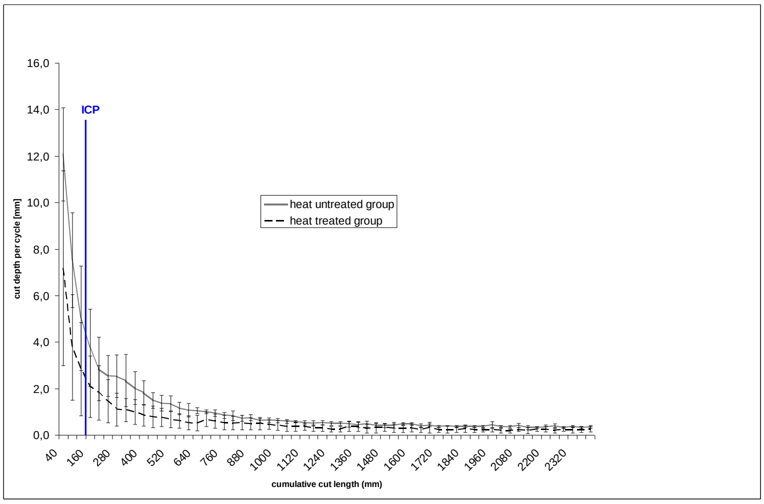

Figure 2: TCC in the treated and untreated group (mean±SD) *: p < 0.05, calculated by *Student t-test*

Scanning electron microscopy results

Each blade was evaluated concerning abrasive wear and in addition, the maximum notch of each cutting edge was identified and sized using SEM. Maximum flank-wear land width (Vbmax [µm]) and depth (Vtmax [µm]) was measured. Vbmax was 38.3±10.7 µm in the heat treated group, whereas in the non-heat treated group Vbmax was 27.9±15µm (p = 0.28) showing no statistically significance. Values of Vtmax in both groups, were 3.5±2.0 µm compared to 2.9±0.5 µm, respectively (p = 0.53). An SEM-example is given in figure 3.

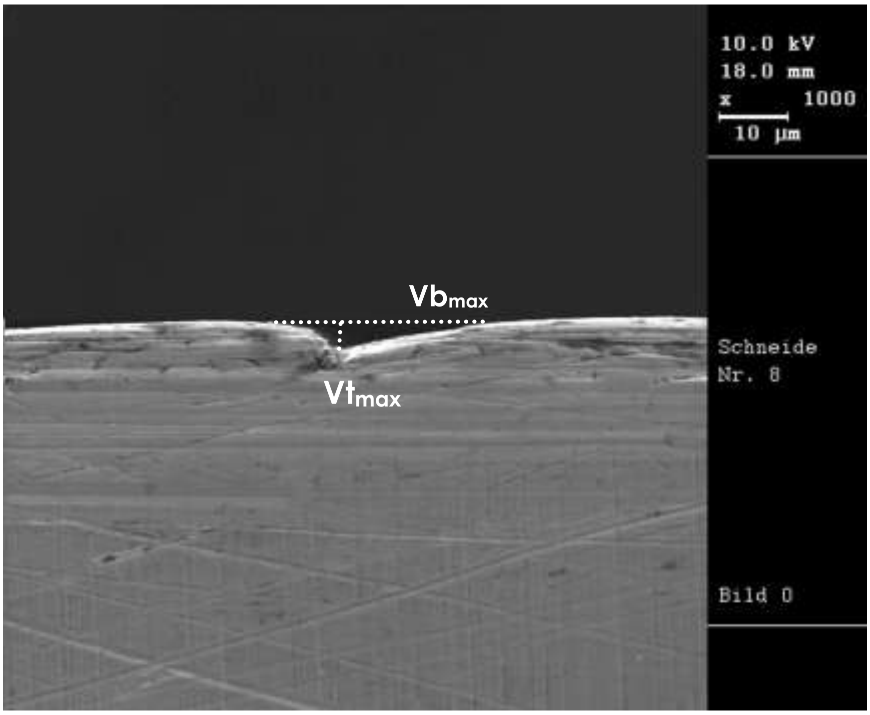

Figure 3: NiTi blade (SEM), magnification x1000, Vbmax and Vtmax indicated as dashed lines

Discussion

Our experimental data showed that the thermal shape setting process, which is used obligatory in machining of SMA influences the cutting performance of NiTi cutting blades. These results were confirmed by a decrease in ICP and TCC in the heat-treated group of NiTi-made cutting edges using an international standardized and well accepted method for testing. Furthermore, we observed a statistical difference within the first sixteen cycles of cutting (heat treated and untreated group), especially in the ICP results (25.7±5.8cm vs. 15.7±9.9cm, P = 0.04). After the first 20 cycles the line graph approximates an almost linear curve without any differences between the two groups. This *equilibration* suggest that the difference in card cutting within the first cycles may confirm the influence of heat treatment in the one group and due to the logarithmic form of the line graph, it could be assumed, that the sharpness of NiTi cutting edges decrease and the wear rapidly increase during the test.

There are some potential reasons for this decrease in cutting performance comparing the heat treated with the untreated group: One of the potential factors can be the heat effect during the annealing process on the microstructural behaviour of the specimen, which was suggested by an increase of thermal peak height shown by Yoneyama et al. [14-15]. Tensile strength tended to decrease by the heat treatment. Considering this situation, another reason for this decrease in cutting performance came up: The process of oxidation during the annealing procedure and therefore the generation of a thin oxide layer, which may influence the sharpness of the blade. Oxides formed on NiTi surfaces can alter the stability and integrity of the material and may affect the corrosion resistance [16]. Due to the fact, that NiTi normally requires shape setting prior to implantation or to function, like in the present study, the heat treatment process modifies the surface of the material. A more precise identification, analysis and quantification of the NiTi blade oxide layer should be the aim in further studies. A suitable method for this aim is the Auger Electron Spectroscopy (AES) which comes with the possibility of obtaining depth profiles, and giving furthermore a hint of the element distribution on these surfaces. Another possible solution to exclude the influence of this oxide layer on the cutting performance of NiTi blades is the removal of the attached oxide layer using etching or pickling techniques with the intent of attacking only the oxide itself. Electropolishing or other chemical treatment such as passivation may solve this problem and as a result of this the in vivo stability of heat treated NiTi may be improved [17]. Furthermore, different surface covering techniques, like DLC (diamond-like-carbon), may improve the sharpness and cutting performance of NiTi cutting edges.

In this study NiTi was used for the purpose of preforming cutting blades into a circle, which can be folded, and afterwards providing recoiling into the prior defined diameter. But NiTi is difficult to process, especially concerning the ease of sharpening. A blade, intended for this purpose will be sharpened easily, when the material has the necessary criteria: (1) Hardness to prevent deformation, (2) toughness to prevent fracture, (3) corrosion resistance to prevents rust and (4) wear resistance to prevent abrasion. The highest grinability will be possible while maximizing the above properties in order to minimize damage to the edge. But therefore, the high ductility and the high degree of work hardening of NiTi lead to difficult processing of this very specific material [11].

Since NiTi is known for its remarkable properties like shape memory, pseudoelasticity and exceptional biocompatibility, it has been as very important and useful addition to materials which were used generally in medical device manufacturing. NiTi shows a huge potential for the future due to functional qualities which enhance the invention of more and less invasive strategies [1]. Therefore, SMA are becoming more noticeable in the biomedical field and due to our knowledge the influence of heat treatment influencing the sharpness of NiTi-made blades has yet not been reported.

Limitations of the Study

There are indeed some limitations of this present study. One limitation is that the small study size of test specimen is underpowered to identify significant differences and not all cutting edges passed all 60 cycles for the TCC measurement. Although all blade specimens underwent the same grinding and annealing procedure, further parameters, like additional DLC-coating or other surface treatments as mentioned above should be evaluated.

Conclusions

In summary the present study suggests, that the essential heat treatment process of NiTi which is used for the shaping may result in a decrease of cutting performance and blade-life (TCC). This decrease in cutting performance could be shown by a lower ICP and TCC in heat untreated blades. A possible reason for this observed sharpness- and cutting performance decrease is yet unclear and more studies concerning sharpness of NiTi are of particular importance to increase knowledge of the machining of this innovative material.

ACKNOWLEDGMENTS

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The role of cell therapy in cardiovascular disease*)

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In adult organisms, each tissue and organ are generally accepted to contain a small subpopulation of cells capable of self-maintenance, of indefinite proliferative potential, and with the ability to give rise to a large family of descendants with defined spectra of specialization (1). Every somatic cell in a human being possesses the full genetic information of that human being. As a human being grows, however, the somatic cells become specialized or differentiated and they shut down the other parts of the DNA except for the ones relevant for their particular function. For example, the cells that make up the heart will function only as that. They will not become or function as liver or brain cells, even though they possess the DNA to do so.

Stem cells are the most undifferentiated human cells. They are characterized by their potential to renew and develop into different cell types and become more differentiated (2). Human stem cells were isolated in late 1998 by two groups of researchers, Thomson et al. (3) and Solter and Gearhart (4), for the first time.

Stem cells from the inner cell mass of the blastocyst (ICM) are thought to have the greatest range of potential; these cells are essentially pluripotential (1). They are capable of giving rise to cells found in all three germ layers of the embrio, and this property along with certain requisite technological steps has allowed embryonic stem cells to be used to engineer strains of mouse, pig, sheep, and potentially humans. There are serious ethical concerns over the use of human embryonic stem cells (ES), although several dozen lines have been made. Some of these ethical considerations would not apply if multipotent cells could be derived from a person for its own use. For this purpose, using adult cell nuclei reprogramming and encouraging them to function in denucleated ova, very early embrios were generated (5). Such techniques might be used to generate cultures of multipotential cells to use for repair of that person's own tissues (6).

It has been recently shown that circulating cells originating from the bone marrow contribute to the regeneration of different tissues after injury. The advent of robust methods for tracking cell lineage has allowed us to identify this contribution (7). The capacity of one circulating cell to engraft in another organ and assume some or all of the phenotypic traits of that organ is called transdifferentiation. It is still under debate whether aside from transdifferentiation such a circulating multipotent cell can also become a local stem cell in its new niche, cell that is capable of self renewal and can produce a family of descendants that eventually become fully functional.

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There is still controversy regarding the degree of multipotentiality of adult stem cells. There is evidence that some adult stem cells may even be pluripotential, albeit in the context of creating chimeric animals, for example in the ability to contribute to all three germ layers in the pre-immune fetal sheep (8) and mouse or chick embryo (9). Adult stem cells reside in adult tissues. Most if not all of these are considered to have a more limited differentiation capacity.

Satellite cells in striated muscle have a certain differentiation capacity that allows them to contribute to the regeneration of striated muscle after injury. They are therefore considered the local stem cells capable of division and self-renewal. They are mononuclear cells located normally between the sarcolemma and the basal lamina of muscle fibers. Their origin is uncertain, however, several reports indicate that a common hematopoietic and muscle precursor exists in adult muscle and in marrow, and it is interesting to speculate that the SP (side-population cells) fraction of many tissues contains a population of multipotent or pluripotent stem cells (1). When purified from adult mouse skeletal muscle, cultured, and then injected into mice (along with other distinguishable whole marrow), satellite cells generated a full range multi-lineage engraftment of the hematopoietic stem-cell compartment. A further round of bone marrow grafting successfully transferred these lineages to other mice (10). It was by this means proven that the satellite cells are the local stem cells that reside in the skeletal muscle that possess the capacity of trans-differentiation.

The endothelium of vessels in a variety of settings turns over through circulating cells and this is detectable after transplantation of organs or marked cells. A proportion of the adult endothelium derives from circulating angioblasts that can be harvested during preparation of hematopoietic grafts (11). Progeny of these cells integrate into new microvessels in skin, heart, skeletal muscle, endometrium and corpus luteum (12). Circulating precursor numbers increase following ischemia, various other conditions that generate endothelial damage or pretreatment with GM-CSF (13). These observations also help support hypotheses formed some 30 years ago that endothelial replacement in grafted organs is encouraged where endothelial damage is severe. It has also recently been suggested that the extent of endothelial replacement of endothelial cell lining is related to the severity of vascular rejection (14).

Endothelial cells alone can initiate the formation and sprouting of endothelium-lined channels, namely angiogenesis. Periendothelial cells are required for vessel maturation. Recruitment of smooth muscle cells is called arteriogenesis and provides these vessels with essential viscoelastic and vasomotor properties (21). Arteriogenesis has a major role in collateral growth (22).

Until recently, the heart of mammalians was supposed to be terminally differentiated, incapable of any cellular regeneration for replacement or repair. Cardiomyocites appear to have a modest capacity for self-renewal in areas adjacent to infarcted myocardium (15). A number of studies have shown cardiomyocyte differentiation to occur in vivo and in vivo from cell lines, circulating cells or directly from bone marrow. Six weeks after direct injection of the cell line WB-F344, clonally derived from a young male rat liver, into the left ventricle of female nude mice, donor cells showed cardiomyocyte differentiation, as they expressed cardiac troponin T and formed intercalated discs with host myocytes (16). Cells derived from sorted bone marrow cells can also differentiate into cardiomyocytes. In female mice, direct injection of certain bone marrow cells into the contracting area bordering an experimental infarct results in more than half the infarcted area being colonized by donor cells within 9 days. Transplanted cells had proliferated in situ and expressed proteins characteristic of cardiac tissue (including connexin 43, suggesting intercellular communication) (17).

In humans, a series of patients suffering from myocardial infarction, who were treated by coronary angioplasty and injection of autologous bone marrow into their coronary arteries, were reported to show a functional benefit following this treatment (18). Based on observations in the rodent models, this benefit could be from microvascular improvements alone, although the technique of Y-chromosome detection in sex-mismatched cardiac transplants revealed that a small proportion of cardiomiocytes were of extracardiac origin, as well as coronary arterioles and capillaries (19).

Some recent studies have brought proves supporting the concept of myocardial regeneration after myocardial infarction. It is the case of a work by Beltrami et al (20) where 13 hearts of patients who died within 2 weeks after an acute myocardial infarction were autopsied and the data were compared with those obtained from 10 hearts of 10 control subjects who died of unrelated causes. Cardiomiocyte regeneration in the free wall was assessed by counting the cells engaged in cell cycling. Also the percentage of cells engaged in the final stage of cell cycle (namely mitosis) was calculated. In the area bordering the infarct 84 times as many cells were engaged in the cell cycle as compared to the control hearts (4% vs. 0.047%), as many as 0.08% of cells were in mitosis. Meanwhile regeneration was smaller in areas further away from the infarct zone. If such a rate of cell cycling and renewal would be maintained for three weeks following an acute myocardial infarction the process would be sufficient to replace all lost myocytes! Unfortunately it seems that the reported level of cardiomyocyte is not extensive enough to counter the massive necrosis that follows a heart attack and cannot prevent ventricular remodeling and progression to heart failure.

An astonishing capacity to regenerate is present in the myocardium of certain species or strains. It is the case of lizards and frogs as well as of a certain mutant strain of mouse called the MRL mouse. In these the necrotic myocardium is replaced by new cardiomyocytes who fill the transmural lesions restoring normal myocardial architecture with little or no scarring. This is unlike the case of normal mice in whom such a regenerative process is unavailable. Identification of genes and molecules which are altered in MRL mutant mice and that mediate this regenerative capacity is now needed to understand this unique myocardial regenerative capacity (21).

The purpose of cell therapy in cardiovascular medicine is to replace necrotic, dysfunctional cardiomyocytes with functional, contractile cells, to promote local angio and arteriogenesis and to induce cardiac protection and anti-apoptotic effects (22). These goals could theoretically be achieved in a number of ways.

One of these ways is to use stem cells for myocardial regeneration. Adult circulating noncommited stem cells will engraft in the adult heart in vivo and differentiate into mature cardiac myocytes. This raises the possibility to harvest adult circulating stem cells from a patient, culture them and re-administer them to support the patient's diseased heart. Certain agents, as 5-azacytidine, added to the cell culture, induce differentiation toward a cardiovascular line in animal (mouse) models by a yet unknown mechanism (23). A promising agent that is supposed to stimulate adult stem cells and mobilize those toward neo-angiognesis in the infarct vascular bed is granulocyte colony stimulating factor (G-CSF) (24).

Some more differentiated circulating or bone marrow cells could also possibly be used for myocardial regeneration. It is the case of endothelial progenitor cells that are capable of incorporation into sites of physiological and pathological neovascularization in vivo (25). This process can result after local or systemic administration (26). Bone marrow contains many angiogenic growth factors but also several progenitor cells involved in vascular regeneration.

That is the rationale for using whole bone marrow aspirate for transplantation. Catheter based intra-myocardial injection of autologous bone marrow cells was shown to promote collateral development in ischemic porcine myocardium (27).

Cells other than stem cells may also represent a source for myocardial regeneration. The most promising are satellite cells from skeletal muscle. They present a number of advantages as the possibility of harvesting from the same individual with the consecutive lack of immunological response and ethical concerns. After satellite cell autotranslantation islands of elongated, striated cells develop. These cells retain characteristics of both skeletal cells and cardiomyocytes in the rabbit model (28).

Philippe Menasche and his team pioneered the first autologous myoblast implantation in a human patient in June 200028. Myoblast implantation was performed at the time of bypass surgery in areas with no evidence of viability prior to surgery that was not grafted. Myoblasts were harvested from the patient's legs two weeks prior to the cardiac operation and were purified and expanded in vitro. The results of the application of this technique are difficult to assess and no definite conclusion can yet be drawn.

Conclusions

There is now a large body of evidence indicating that organ specific stem cells need not rely entirely on their own resources for maintenance and repair. In some circumstances, populations of stem cells normal resident outside the organ are able to contribute to the renewal of quite different lineages. Perhaps a key factor in the generation of self renewing clones in the new tissues is the exposure to (and successful occupation of) niches emptied by damage, with the local environment of the niche defining the cell repertoire that will be produced (29).

Tougher proofs are now needed to show a robust, sustained multi-lineage engraftment and functional activity representative of multiple phenotypic characteristics of the converted cells to show that full conversion has occurred (30). This is needed because the partial repopulation of the heart with cells that have come to resemble their neighbours is not the same as showing a functional competence as diverse and as broad as that expected of an indigenous population of an organ capable of regeneration and self renewal. Yet this is what will be needed for tissue regeneration therapies that will rely on adult stem cell, progenitor or blast cell transplantation. Clonal expansion will certainly be required to yeld cell types to respond to demands of growth, adaptation and repair.

Given the considerable interest in the therapeutic applications of stem cell plasticity, the truth should be worth waiting for.

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Results of the use of plasmidic encoded Vascular Endothelial Growth Factor and Hepatocyte Growth Factor as gene therapy in patients with end stage lower limb ischemia*)

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Abstract

Critical limb ischemia (CLI) represents the most advanced stage of lower extremity peripheral artery disease (PAD) and is associated with high rates of cardiovascular morbidity, mortality, and major amputation. Therapeutic angiogenesis is a novel strategy under investigation for the treatment of PAD that utilizes angiogenic growth factors, genes to encode these growth factors, or stem cells to promote neovascularization. Early clinical trials of gene transfer for therapeutic angiogenesis have been promising and provide hope for CLI patients who are unsuitable candidates for revascularization. In the present study we tested the hypothesis that simultaneous administration of Vascular Endothelial Growth Factor *(VEGF) and* Hepatocyte Growth Factor *(HGF) would synergically promote new blood vessel formation. Materials and methods: We present our results with the use of combined plasmidic encoded VEGF and HGF on 12 patients with end stage lower limb ischemia. A single dose of therapeutic agent was given to 4 patients while a second dose at 3 months (4 patients) or 1 month (4 patients) was given in the remainder. Extensive clinical and paraclinical data were provided at enrollment. All patients were followed up at discharge, 1, 3 and 6 months. Results: No major side effects were noted with administration. The amputation rate was 33% at 6 months. Two of the patients who suffered amputation presented with extremely severe ishemia and were amputated within one month from growth factor administration. Improvement of the status of the ischemic limb with healing of trophic ulcers or increase in walking distance was noted in 6 patients. Conclusions: Our data provide encouraging initial evidence of a potentially important therapeutic approach in the treatment of vascular disease. There were no signs of significant toxicity or serious side effects. Larger clinical trials are needed to evaluate the safety and efficacy of gene therapy with plasmidic encoded growth factors.* **Key words:** *gene therapy, VEGF, HGF, critical limb ischemia*

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Background

Critical limb ischemia (CLI) represents the most advanced stage of atherosclerotic, lower extremity peripheral artery disease (PAD) and is associated with high rates of cardiovascular morbidity, mortality, and major amputation. The incidence of CLI is expected to grow as the population ages. The 1-year mortality rate of patients with CLI is 25% and may be as high as 45% in those who have undergone amputation. The current standard of care for individuals with CLI includes lower extremity revascularization, either through open peripheral surgical procedures, endovascular techniques, or lower extremity amputation (i.e., if revascularization has failed or is unfeasible). Despite advanced techniques in endovascular and surgical procedures, a considerable proportion of patients with CLI are not suitable for revascularization. Of these patients, 30% will require major amputation and 23% will die within 3 months. Therapeutic angiogenesis is a novel strategy under investigation for the treatment of PAD that utilizes angiogenic growth factors, genes to encode these growth factors, or stem cells to promote neovascularization, in an attempt to increase perfusion to ischemic tissues through various mechanisms of action (1). Early clinical trials of gene transfer for therapeutic angiogenesis have been promising and provide hope for CLI patients who are unsuitable candidates for revascularization (2, 3).

Objective

In the present study we tested the hypothesis that simultaneous administration of HGF and VEGF would synergically promote new blood vessel formation.

VEGF and HGF

Human growth factors are compounds made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory by genetic engineering and are used in biological therapy. Growth factors are significant because they can induce angiogenesis. These growth factors also encourage cell proliferation, differentiation, and migration on the surfaces of the endothelial cells—cells found inside the lining of blood vessels. There are approximately 20 proteins that activate endothelial cell growth. *Vascular endothelial growth factor* (VEGF) is a chemical signal produced by cells that stimulates the growth of new blood vessels. It is part of the system that restores the oxygen supply to tissues when blood circulation is inadequate (4). Among the many factors implicated in angiogenesis, VEGF has been identified as the most potent and predominant. The scope of scientific research involving VEGF continues to grow exponentially (5). Vascular endothelial growth factor (VEGF) is an important signaling protein involved in both vasculogenesis (the formation of the embryonic circulatory system) and angiogenesis (the growth of blood vessels from pre-existing vasculature, collateral circulation to bypass blocked vessels. As its name implies, VEGF activity is restricted mainly to cells of the vascular endothelium, although it does have effects on a limited number of other cell types (e.g. stimulation monocyte/macrophage migration, neurons, cancer cells, kidney epithelial cells). In vitro, VEGF has been shown to stimulate endothelial cell mitogenesis and cell migration. VEGF also enhances microvascular permeability and is sometimes referred to as vascular permeability factor.

VEGF may elicit several responses – it may cause a cell to survive, move, or further differentiate (6).

Hepatocyte growth factor/scatter factor (HGF/SF) is a paracrine cellular growth, motility and morphogenic factor. It is secreted by mesenchymal cells and targets and acts primarily upon epithelial cells and endothelial cells, but also acts on haemopoietic progenitor cells. It has been shown to have a major role in embryonic organ development, in adult organ regeneration and in wound healing. Its ability to stimulate mitogenesis, cell motility, and matrix invasion gives it a central role in angiogenesis, tumorogenesis, and tissue regeneration. *Hepatocyte growth factor* (HGF) - initially identified and molecularly cloned as a potent mitogen of primary cultured hepatocytes - has multiple activities in a variety of tissues during the course of development and also in various disease states. HGF plays key roles in the attenuation of disease progression as an intrinsic repair factor. It is also evident that HGF levels are regulated under different conditions, for example, during the course of pregnancy, aging, and disease (7).

Methods

There are 12 CLI patients enrolled in the case study, who presented in the vascular surgery clinic or in the *Cardiovascular Surgery Clinic* of the *INUBCV "Prof. Dr. C. C. Iliescu" Bucharest* beginning with January 2008. Selection criteria for inclusion in the trial: CLI patients aged between 39 and 79 years with no option for surgical or endovascular revascularization and total or subtotal occlusion of at least 1 main artery in a limb confirmed by angiography. All participating patients gave written informed consent. Exclusion criteria included contraindications to growth factor therapy that have been published previously (eg., history of cancer within 5 years, active diabetic retinopathy, and inflammatory arteritides).

Study Design

Extensive clinical and paraclinical data were provided at enrollment, including screening tests for cancer, angiography, eye examination. All patients were followed up at discharge, 1, 3 and 6 months. Safety variables included adverse event reports and changes from baseline in physical examinations, clinical laboratory evaluations, retinal eye examinations, as well as observations related to limb status as changes in ischemic rest pain, healing of ischemic ulcers and ankle brachial index (ABI). Healing of trophic ulcers, resolution of the rest pain or increase in walking distance was considered an improvement. A single dose of therapeutic agent was given to 4 patients while a second dose at 3 months (4 patients) or 1 month (4 patients) was given in the remainder. A dose was administered as 8 direct intramuscular injections into a single limb and the placement of the injections was at the discretion of the investigator and based on patient anatomy and the location of the occluded artery or arteries within the affected limb.

Patient demographics and baseline characteristics:

- Age, median (range), *y*: 66 (39-79);
- Gender, *n* (%): Male 10 (83.33%) Female 2 (16.66%);
- Diabetics, *n* (%): 2 (16.66%);
- Current/ previous tobacco user, *n* (%): 6 (50%);

- Rest pain, *n* (%): 11 (91.66%);
- Ischemic ulcers, *n* (%): 9 (75%);
- Both rest pain and ischemic ulcers, *n* (%): 8 (66.66%);
- Bypass or endovascular procedure in the past, *n* (%): 4 (33.33%).

ABI measurement was not available for all study patients because of arterial calcification or amputation.

Results

At base line and during the study patients were on acetylsalicylic acid (1 patient), metamizolum natricum (6 patients), pentaxifyllinum (5 patients), sulodexidum (2 patients), detralex (1 patient) or tramadolum (4 patients). Growth factor patients experienced adverse events, but most of these were mild or moderate in severity and were not serious. No patient died while during the course of the present study. Four patients underwent amputation, the amputation rate was 33% at 6 months. Two of the patients who suffered amputation presented with extremely severe ishemia and were amputated within one month from growth factor administration. From the 4 amputated patients 2 of them were diabetics and 2 were former smokers. Our experience with growth factors has not identified an increased risk for malignancies, retinopathy, or acute coronary syndromes. Less serious adverse effects have been reported, which include hypotension, transient lower limb edema, injection site reaction, fever. Improvement of the status of the ischemic limb with complete healing of trophic ulcers, resolution of the rest pain or increase in walking distance was noted in 6 patients with the remainder of 2 patients showing no change compared with baseline.

Conclusions

Plasmidic encoded VEGF and HGF as gene therapy appeared to be safe when delivered into skeletal muscle in the leg in no option critical limb ischemia patients. An important point is that no safety problems emerged, including no evidence of malignancy or ocular neovascularization disorders related to the growth factor therapy, at least in the short term. Further dose escalations may be attempted. Overall, the present study confirmed the high rate of progression of disease in advanced CLI, with amputation rate of 33% at 6 months. Improvement in limb status (i.e., complete ulcer healing and/or resolution of rest pain and the increase in walking distance) was observed in 6 patients (50%) at 6 months. Complete resolution of rest pain occurred in 5 patients at 6 months and complete ulcer healing occurred in 4 patients at 6 months. Our data provide encouraging initial evidence of a potentially important therapeutic approach in the treatment of vascular disease. Longer term follow-up in a larger number of patients may be needed to firmly establish the safety and efficacy of the plasmidic encoded VEGF and HGF gene therapy.

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Risk factors for progression of atherosclerosis after primary CABG: gene polymorphisms predispose for adverse events*)

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Abstract

Progression of ***coronary artery disease*** *(CAD) after primary* ***coronary artery bypass grafting*** *(CABG) is frequent and leads to recurrent symptoms and reinterventions. We hypothesized that classical risk factors and genetic dispositions may be associated with the progression of CAD. We investigated 192 patients (18% female, age: 59.2 ± 8.4 years) who had primary CABG more than 5 years ago. Progression of CAD was defined as the need for reoperations (n = 88; 46%), reinterventions (n = 58; 30%), or angina at follow up (n = 89; 46%). Polymorphisms of genes encoding for factors involved in lipid metabolism (Apolipoprotein E, hepatic lipase, cholesteryl ester transfer protein), coagulation (platelet activator inhibitor-I, prothrombin, activated protein C resistance), and endothelial NO synthesis (eNos) were determined. Classical atherosclerotic risk factors at the time of primary CABG did not correlate with CAD progression. Single polymorphisms (i.e. eNos, ApoE) provided limited information on reintervention rate (p = 0.042 and p = 0.001). Construction of a gene risk profile facilitated to discriminate among patients with a fast and slower progression of their CAD with respect to all endpoints (p = 0.0012). Single gene polymorphisms of patients after primary CABG permit a limited prognosis for CAD progression. Gene risk profiles allow risk stratification and may individualize secondary prevention in the future.*

Key words: *coronary artery disease, atherosclerosis, risk factors, gene polymorphism, coronary artery bypass grafting*

Background

Coronary artery disease (CAD) is a multifactorial disorder. Classical risk factors for CAD such as smoking or obesity are well known for decades to increase the incidence. More recently, distinct gene polymorphisms were identified as risk factors for the development of CAD [1, 2]. Medical therapy of risk factors and patient counseling have become the base for the secondary prevention of CAD after primary coronary artery

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bypass grafting (CABG). However, the influences of these factors, particularly gene polymorphisms, on the progression of CAD in patients after CABG with contemporary medical treatment await further investigations.

We hypothesized that classical risk factors for CAD, perioperative parameters, and genetic predispositions determine the progression of CAD primary CABG. The hypothesis was tested by retrospectively investigating a group of patients who underwent primary CABG at our institution more than 5 years ago. Genetic polymorphisms known as risk factors for CAD were determined in this patient cohort. Reoperations, reinterventions, and angina at follow-up served as clinical correlates of CAD progression.

Methods

Patients

One hundred and ninety two patients who underwent their first isolated CABG between 1979 and 1999 were investigated. Perioperative data and postoperative therapy are listed in table 1.

Table 1: Demographics of Patients and Medical Therapy at the Time of Primary CABG

Patients [#]	**192 (100%)**
Female [#]	**34 (18%)**
Age [Years]	**60.9 ± 7.4**
Ejection fraction [%]	**63.0 ± 14.5**
Angina Class	**3.0 ± 1.0**
Bypasses [#]	**2.4 ± 1.0**
Left internal thoracic artery grafts [#]	**1.0 ± 0.5**
Saphenous Vein Grafts [#]	**1.5 ± 1.0**
Additional Grafts [#]	**0.4 ± 0.5**

All patients made a follow-up visit at our department between March and October 2004. After informed consent was given, blood was drawn for genetic analyses. Clinical surrogates for CAD progression were reoperation for CAD, reintervention (PTCA and/or stenting and/or hospital admission for myocardial infarction), angina at the time of follow-up, and a combined endpoint of the three previous further referenced as recurrent symptoms. Most patients (n = 137; 71%) had either a second CABG (n = 88; 46%; 9.3 ± 3.3 years p.o), a reintervention (n = 54; 28.1%; 10.4 ± 5.9 years p.o.), or suffered from angina at follow-up (n = 80; 41.7%; 12.6 ± 5.8 years p.o). All patients received medical therapy at follow-up; most commonly aspirin (87%), beta blockers (70%), statins (50%), ACE inhibitors (35%) and calcium antagonists (24%) were prescribed. Patients with progression of CAD were more likely to receive intensified therapy with ACE inhibitors (p = 0.04), and beta blockers (p = 0.008).

Gene analyses

Seven polymorphisms previously described to play a role in the development of CAD were chosen for this investigation. The polymorphisms encode for factors involved in the NO-donor system (endothelial NO Synthase (eNOS) [3]), the lipid metabolism (Apolipoprotein E (ApoE) [4]; hepatic liapse (hL) [5], cholesteryl ester transfer protein (CETP) [6]), and the coagulation system (plasminogen activator inhibitor 1 (PAI 1) [7], activated protein C resistance (APC) [8], prothrombin (PT) [9]). Details of the polymorphisms are summarized in table 2. To investigate the selected polymorphisms, reverse transcriptase polymerase chain reaction (RT-PCR) was carried out with standard methods [10].

Table 2. Investigated gene polymorphisms

Gene	Function	Mutation	Reference	Primer	Kind of Primer	5 → '3' Orientation	Base length
endothelial Nitric Oxide Synthase **eNos 4ab**	*production of nitric oxide (NO); regulation of vasomotor tone and thrombotic actions*	*Insertion/Deletion of tandem repeats*	[3]	eNOS-1	**Forward**	**AGGCCCTATGGTAGTGCCTTG**	**21**
				eNOS-2	**Reverse**	**TCCTGCTACTGACAGCACCG**	**20**
Apolipo-protein E **ApoE**	*polymorph protein; component of chylomicrons and VLDL lipoprotein remnants as well as ligands for LDL receptors*	**112 C → A**	[4]	ApoE-1	**Forward**	**GCTGTCCAAGGAGCTGCAGGCGG**	**42**
		158 C → A		ApoE-4	**Reverse**	**TGCAGGCCCGGCTGGGTGC CTCGCGGGCCCCGGCCTGGTA**	**21**
Hepatic Lipase **HL**	*mediator of lipid metabolism*	**202 C → G**	**[5]**	HL5-1	**Forward**	**GCTTTCCCATTAGGGCTGGATG**	**22**
				HL 5-2	**Reverse**	**TCATTCTCACCATTGAAGCCGTG**	**23**

Cholesteryl Ester Transfer Protein - **CETP**	*mediator of lipid metabolismus (HDL and Lipoprotein B) and regulates HDL plasma level and size of HDL molecules*	**629 C → A**	**[6]**	CETP-3	**Forward**	**CATCTGGTCACAGTTGCTGCAG**	**22**
				CETP-4	**Reverse**	**GTAGACTTTCCTTGATATGCATAA AATACCACTGGG**	**36**
Plasminogen Activator Inhibitor 1 **PAI-1**	*inhibition of conversion of plasmin to plasminogen*	**Guanin insertion**	**[7]**	PAI-1	**Forward**	**AGCCCTCAGGGGCACAGAGA**	**34**
		4G-668/5G		PAI-1	**Reverse**	**GAGTCTGGCCACGT TCTAGGTTTTGTCTGTCTAGGA CTTGGGGCCA**	**32**
Activated Protein C Resistance **APC**	*inactivation of Factor* Va *mediated by activated protein C*	**1691 G → A**	**[8]**	APC-1	**Forward**	**GGAACAACACCATGATCAGAGCA**	**22**
				APC-2	**Reverse**	**TAGCCAGGAGACCTAACATGTTC**	**23**
Prothrombin , Mutation **PT**	*conversion to thrombin*	**20210 G → A**	**[9]**	PT-2M	**Forward Primer**	**CAGAGAGCTGCCCATGAATAGCACT**	**39**
				PT-3	**Reverse Primer**	**GGGAGCATTGAAGC GGCTGTGACCGGGATGGGAAATATGGC**	**27**

A: *Arginin;* **C:** *Cytosin;* **G:** *Guanin;* **T:** *Thymin;*
HDL: *high density lipoprotein;* **LDL**: *low density lipoprotein;* **VLDL**: *very low density lipoprotein.*

Gene risk profile

Because single mutations had a relatively low prevalence in our limited patient cohort and CAD is a multifactorial disease we constructed a gene risk profile according to the definitions in table 5. Carriers of the gene risk profile were defined as having one of the following polymorphisms: hetero- or homozygous for the variants of eNOS 4 ab, the alleles combination 2 4, or 4 4 of Apoprotein E, homozygous expression of the hepatic lipase variant, homozygous expression of the cholesteryl transfer protein variant, and hetero- or homozygous for the prothrombin variant. Patients had to be not homozygous for PAI-1 mutation.

Statistics

Values are expressed as mean and standard deviation of mean. The *Student's t*-Test was used to compare absolute quantitative values. Angina was censored at the day of follow-up, because a precise onset of angina could not be determined. Freedom from reoperation, reintervention, and the combined endpoint (reoperation, reintervention, or angina at follow-up) were calculated by the actuarial method and tested with the log-rank test. Every univariate parameter reaching or approaching significance ($p < 0.2$) was then tested in a Cox multivariate model using the conditional backward method.

Results

Preoperative risk factors of CAD and its progression (table 3).

Table 3: Preoperative risk factors of CAD and its progression

Factor	Definition	*n*	Outcome	Freedom from [%] at			*p*
				5 years	10 years	15 years	
Diabetes	Yes	33	Reoperation	100	56.9	32.5	0.49
	No	159		94.2	73.3	20.8	
	Yes	33	Reintervention	100	95.7	81.8	0.095
	No	159		90.1	81.1	67.5	
	Yes	33	Combined	100	51.0	24.3	0.26
	No	159		83.6	52.3	10.2	
Obesity	BMI < 24	136	Reoperation	96.6	69.6	22.6	0.79
	BMI > 24	56		91.7	69.7	30.1	
	BMI < 24	136	Reintervention	91.1	84.3	70.0	0.37
	BMI > 24	56		93.7	81.8	78.4	
	BMI < 24	136	Combined	87.6	52.4	10.4	0.39
	BMI > 24	56		83.8	50.5	13.7	
Hypercholesterinemia	Yes	159	Reoperation	94.2	64.7	21.5	0.11
	No	33		100	89.7	34.4	
	Yes	159	Reintervention	90.8	83.5	67.6	0.19
	No	33		96.4	89.3	89.3	
	Yes	159	Combined	84.4	46.2	10.0	0.073
	No	33		96.7	76.7	18.5	
Smoking history	Yes	86	Reoperation	96.1	77.2	28.4	0.33
	No	106		94.5	63.6	20.1	
	Yes	86	Reintervention	90.3	83.1	69.0	0.75
	No	106		93.1	83.9	74.0	
	Yes	86	Combined	87.0	61.5	12.2	0.34
	No	106		86.2	44.1	10.4	
Hypertension	Yes	140	Reoperation	94.2	69.9	31.4	0.27
	No	52		97.8	70.3	0	
	Yes	140	Reintervention	90.6	81.7	66.4	0.04
	No	52		95.2	88.9	88.9	
	Yes	140	Combined	83.9	50.7	15.3	0.62
	No	52		93.5	55.4	0	

Significant differences are in *italics* ($p < 0.05$) or **bold** ($p < 0.01$) print

Documented risk factors at the time of primary CABG had limited impact on the progression of CAD. Only hypercholesterinemia tended ($p = 0.077$) to increase the risk of recurrent symptoms. Obviously, patients were postoperatively fairly efficiently treated for their classical risk factors, so that these risk factors did not develop a more significant influence.

Perioperative parameters and the progression of CAD (Table 4)

Table 4: Perioperative parameters and the progression of CAD

Factor	Definition	*n*	Outcome	Freedom from [%] at			*p*
				5 years	10 years	15 years	
Age	≤ 60 years > 60 years	110 82	Reoperation	95.3 93.8	65.7 78.7	19.9 46.3	0.052
	≤ 60 years > 60 years	110 82	Reintervention	93.2 90.8	88.6 79.1	77.4 58.1	0.150
	≤ 60 years > 60 years	110 82	Combined	88.0 85.5	55.0 47.2	12.4 15.0	0.400
Gender	Male Female	158 34	Reoperation	96.1 87.8	70.4 70.9	21.5 23.6	0.690
	Male Female	158 34	Reintervention	92.5 90.6	85.5 78.9	75.6 38.6	0.120
	Male Female	158 34	Combined	88.6 79.2	53.2 45.3	11.3 10.1	0.490
# of bypasses	**< 3** **≥ 3**	**110** **82**	**Reoperation**	**91.6** **98.7**	**61.8** **81.6**	**24.8** **22.2**	**0.005**
	< 3 ≥ 3	110 82	Reintervention	91.4 93.2	83.1 84.7	70.0 77.2	0.360
	< 3 ≥ 3	110 82	Combined	83.6 91.4	47.1 58.1	14.1 11.7	0.240
Use of LITA	Yes No	151 41	Reoperation	97.3 85.4	74.6 55.4	22.8 18.3	0.340
	Yes No	151 41	Reintervention	91.5 94.7	82.5 91.6	76.9 70.9	0.430
	Yes No	151 41	Combined	88.1 82.9	52.6 49.3	12.5 11.1	0.570

LITA: *Left internal thoracic artery.*
Significant differences are in *italics* ($p < 0.05$) or **bold** ($p < 0.01$) print

Perioperative parameters demonstrate selection bias for future therapy. Elderly patients (>60 years at primary CABG) were less likely to undergo reoperation ($p = 0.05$), but tended to be more often selected for reinterventions ($p = 0.15$). Moreover, patients with 3 or more bypasses had less reoperations than patients with 2 or less ($p = 0.005$).

Gene polymorphisms and the progression of CAD (Table 5)

Mutation of eNOS increased the risk for reinterventions (0.041) and for recurrent symptoms ($p = 0.042$). A similar effect on reinterventions (0.001) and recurrent symptoms (0.077) was observed in patients missing the most common type 3 allele of ApoE. Patients homozygous for the hepatic lipase mutation had a higher incidence of reoperations ($p = 0.049$).

Table 5: Gene Polymorphisms and the progression of CAD

Factor	Definition	*n*	Outcome	Freedom from [%] at			*p*
				5 years	10 years	15 years	
eNos 4ab	bb	141	Reoperation	95.6	69.5	26.1	0.87
	aa / ab	51		92.0	72.1	12.3	
	bb	*141*	*Reintervention*	*93.9*	*88.7*	*75.9*	*0.041*
	aa / ab	*51*		*87.5*	*67.9*	*62.7*	
	bb	*141*	*Combined*	*89.3*	*56.0*	*13.2*	*0.042*
	aa / ab	*51*		*80.4*	*40.6*	*5.1*	
ApoE	2 3 / 3 3 / 3 4	182	Reoperation	94.4	71.0	22.6	0.63
	2 4 / 4 4	10		100	52.5	52.5	
	2 3 / 3 3 / 3 4	**182**	**Reintervention**	**92.3**	**84.5**	**75.1**	**0.001**
	2 4 / 4 4	**10**		**90.0**	**64.3**	**32.1**	
	2 3 / 3 3 / 3 4	182	Combined	87.3	53.3	12.3	0.077
	2 4 / 4 4	10		80.0	30.0	0.0	
hL	*WW / WM*	*144*	*Reoperation*	*96.4*	*74.6*	*27.5*	*0.049*
	MM	*48*		*89.5*	*54.5*	*9.9*	
	WW / WM	144	Reintervention	91.1	84.7	69.2	0.97
	MM	48		95.5	79.4	70.5	
	WW / WM	144	Combined	87.5	55.5	12.9	0.24
	MM	48		85.4	40.2	4.8	
CETP	WW / WM	152	Reoperation	93.9	68.7	23.2	0.31
	MM	40		97.4	51.2	0	
	WW / WM	152	Reintervention	90.1	81.5	68.9	0.82
	MM	40		100	91.2	76.7	
	WW / WM	152	Combined	85.4	49.9	14.0	0.73
	MM	40		92.5	34.7	0	
PAI 1	WW / WM	162	Reoperation	94.4	68.9	22.3	0.13
	MM	30		96.4	76.9	36.1	
	WW / WM	162	Reintervention	90.9	85.0	73.6	0.14
	MM	30		100	80.4	59.3	
	WW / WM	162	Combined	85.8	50.0	11.0	0.24
	MM	30		93.2	63.0	11.0	
APC	WW	177	Reoperation	94.8	71.5	24.0	0.63
	WM / MM	15		93.3	53.9	26.9	
	WW	177	Reintervention	92.1	83.3	70.6	0.55
	WM / MM	15		93.3	85.6	71.3	
	WW	177	Combined	87.0	53.5	11.1	0.43
	WM / MM	15		86.7	32.5	10.8	

PT	WW	189	Reoperation	94.6	70.6	24.6	0.17
	WM / MM	3		100	50	0	
	WW	189	Reintervention	92.0	83.2	71.6	0.80
	WM / MM	3		100	100	100	
	WW	189	Combined	86.7	51.9	11.4	0.78
	WM / MM	3		100	50	0	

A: *Arginin*; **C:** *Cytosin*; **G:** *Guanin*; **T:** *Thymin*; **M:** *Mutation*; **W:** *Wildtype.*
HDL: *high density lipoprotein;* **LDL**: *low density lipoprotein;* **VLDL**: *very low density lipoprotein.*
Significant differences are in *italics* ($p < 0.05$) or **bold** ($p < 0.01$) print

Gene risk profile and the progression of CAD (Figure 1)

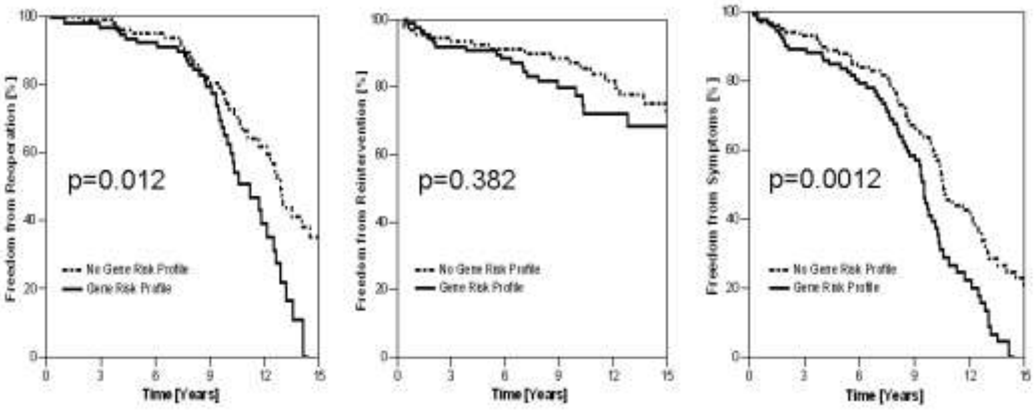

Figure 1: Gene Risk Profile and Progression of Coronary Artery Disease. Out of the seven investigated gene polymorphisms 6 were combined for a gene risk profile (see text). Patients with the gene risk profile had significantly more reoperations (0.012) and were more likely to have recurrent symptoms (0.0012). The incidence of cardiological interventions (PTCA, stent, myocardial infarction) were not different among groups (p = 0.38). However, multivariate Cox regression analysis revealed that only the gene risk profile had significant impact on the progression of coronary artery disease (p = 0.004)

Patients with the gene risk profile had significantly more reoperations (0.012) and were more likely to have recurrent symptoms (0.0012). The incidence of cardiological interventions were not different among groups (p = 0.38). However, multivariate Cox regression analysis revealed that only the gene risk profile had significant impact on the progression of CAD (p = 0.004).

Discussion

Progression of CAD after primary CABG was significantly influenced by genetic polymorphisms; among the seven evaluated polymorphisms the eNos and the ApoE variants had the highest impact on reoperations and reinterventions. The investigated eNos variant has been associated with a higher susceptibility to coronary lesions in smokers [3] and NO metabolites were 20% decreased in patients with the 4 aa variant[11]. Several studies focused on the effects of ApoE polymorphisms after cardiopulmonary bypass and reported a higher incidence of inflammation [12] and nephropathy [13] in patients with the E4 allele; more neurological sequelae were seen with the E2 allele [14]. Interestingly, in our study patients without the most frequent allele E3, thus only having the risk alleles E2 and E4, had a more aggressive type of CAD.

Certainly medical therapy, particularly lowering of low-density lipoprotein cholesterol levels, has been proven to reduce the advancement of CAD after CABG [15]. Due to the design of our retrospective study we were unable to prove the beneficial effects of medical therapy, because therapy after primary CABG was determined by the cardiologist and patients with recurrent syndromes received intensified medical therapy. Likewise, the role of classical risk factors on the CAD progression is difficult to interpret. Risk factors at the time of primary CABG were medically treated; patients stopped smoking and started training programs. Therefore, these classical risk factors lost their predictive value. Obviously, we investigated only long-term survivors of CABG surgery, who were willing to cooperate. This selection bias may also limit our results.

Knowledge of gene polymorphisms and their influence on outcome in cardiac surgery is rapidly growing. However, most studies investigated the acute effects of polymorphisms outcome during the postoperative phase. Data on the progression of CAD after primary CABG is rare. Recently Taylor and associates [16] reported on the influence of lipoprotein lipase locus on the progression of atherosclerosis in coronary artery bypass grafts and identified the LPL-HINDIII 2/2 genotype as an independent risk factor.

In our study we randomly investigated a subset of gene polymorphisms known from other investigations as suspects in the development of CAD. For endothelial NOS at least 4 frequent polymorphisms (G894T, Glu298Asp, T786C, and the one used in this study) are well established and described to be risk factors for CAD. The argument of having no specific hypothesis to investigate just one and not all other polymorphisms is valid. However, a simple gene risk profile constructed out of 7 randomly chosen polymorphisms was more predictive for the advancement of CAD than any cluster of classical risk factors.

This study is only preliminary, because of its limitations in patient sample size and number of investigated polymorphisms. More investigations are warranted and will most likely improve the predictive value of polymorphism tests. We proved the concept, that risk stratification by a simple gene test for the future advancement of CAD after primary CABG is possible. The concept is intriguing, because the detected gene variants give clues to the individual pathophysiology in every single patient in this multi-factorial disease [17]. Therefore, this cheap diagnostic tool may hopefully lead to an individualized secondary prevention after primary CABG.

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Foreign Body Reaction is the Trigger for Intimal Hyperplasia after Prosthetic Arterial Bypass Placement*)

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Introduction

Improvements in surgical technique and development of synthetic vascular grafts allow us to perform the reconstruction of arteries. Although most bypass procedures with synthetic grafts have good early results, they may later fail. An important factor of late graft failure is the development of intimal hyperplasia, mainly in synthetic grafts.

On the contrary, artery grafts are less affected (ex. internal mammary artery). It is therefore very important to improve the performance of synthetic grafts making it as successful as autologus arterial grafts.

Control of the formation of intimal hyperplasia in synthetic grafts is hereby crucial. After implantation, the synthetic arterial prostheses become encapsulated; the surrounding tissue reaction to Teflon or polyethylenterephtalat is similar to the inflammatory reaction to aseptic, inert foreign bodies. There are three chronological phases to the encapsulation process: early, organization and late.

Material and methods

In order to analyze the encapsulation process of the synthetic arterial prostheses, a high-pressure system, we examined 66 prostheses or segments of prostheses; 61 were removed during reinterventions for thromboses and five postmortem.

There were two types of prostheses in our study: 59 were polyethylenterephtalat (47 Terom and 12 Dacron) and seven expanded polytetrafluoroethylene (ePTFE, Gore-Tex). The mean implantation time was 31.5 weeks (range one day to nine years).

After the prostheses were cut longitudinally, fragments from the anastomotic and central areas were obtained for macroscopic and microscopic examination; they were prepared according to the standard protocol for optical microscope, using hematoxylin-eosin and Trichrom-Masson.

We elected not to use any special coloring techniques for the endothelial cells. All the specimens were examined by an experienced pathologist using optical and polarized light microscopy.

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Results

The "early" phase

Considering that in the early encapsulation process the host versus graft reaction is trivial, we focused on the changes occurring after the first two weeks after implantation.

Organization phase

This phase begins after the first two weeks and ends in six months; the changes that occur during this phase are similar to the normal inflammatory process: monocytes, lymphocytes, fibroblasts and macrophages are dominant, accompanied by rare foreign body giant cells and new capillaries formation. Twenty-six prostheses were in this stage.

1. Polyethylenterephtalat prostheses

The external capsule

In two to three weeks, a granulation tissues rich in young cells starts penetrating the prostheses interstitials. This process ends in three to four weeks and leads to a tissue tightly adherent to the prostheses that contains a markedly increased number of foreign body giant cells. Some of these cell display phagocytosis of small synthetic particles.

Other cells seen are increased number of fibroblasts and macrophages that also penetrate the prostheses interstitials. The thickness of the external capsule in our specimens was 0.5-1.8 mm and its cellular proliferation is much more pronounced than the internal capsule.

Prostheses interstitials

Thin filaments of connective tissues can be found in the prostheses interstitials, especially in its external layer. Monocytes and macrophages from both the internal and external connective tissue penetrate the interstitials (Figure 1).

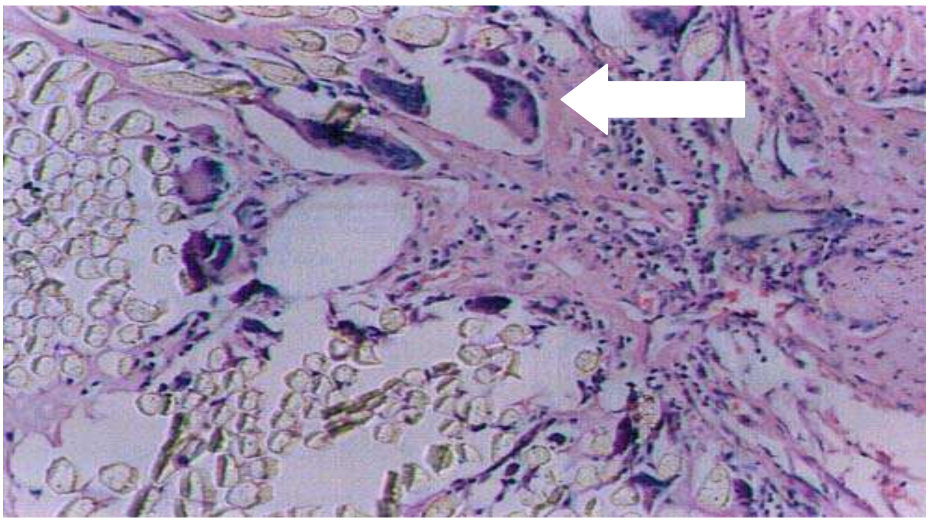


Figure 1: Terom prostheses – IInd phase, 15 weeks from implantation. Giant cells marked with arrow. Col. H-E ×200

The internal capsule macrophages originate in the blood circulating through the prostheses and are most commonly seen around neocapillaries.

They have increased phagocytosis around the prosthetic material with subsequent transformation into foreign body giant cells. The neocapillaries continue to proliferate having a tendency to merging and dilation. Also at this level, the internal and the external capsules send extensions that merge in the middle and form the intercapsular or transprosthetic bridges.

The internal capsule

This part is thin, discontinuous, and has areas covered by fibrin alternating with bare areas. It has an increased number of round cells, lymphocytes, plasmocytes, and small macrophages. The lack of complete endothelization is the main substrate for thrombosis. The endothelization process starts at the prostheses margins where the native arterial endothelium extends covering the luminal prosthetic surface. As shown in previous studies [2, 3, 8], the distal anastomosis have an increased neointimal proliferation associated with an intense foreign body reaction, stimulated by the presence of synthetic material. Occasionally, some prostheses displayed endothelial cell that are not uniformly and continually organized.

2. Teflon (ePTFE) prostheses

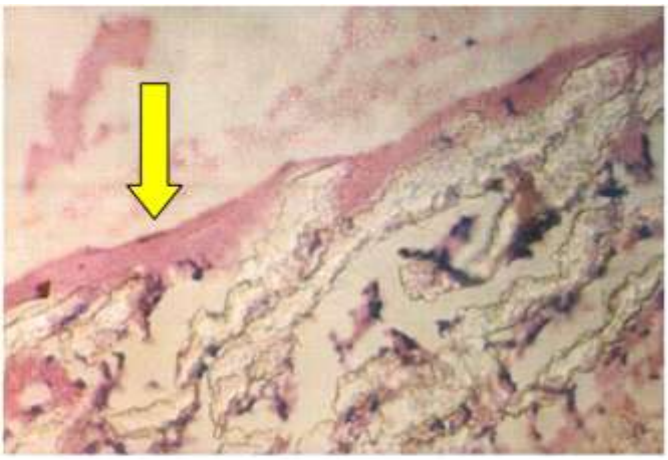
The external capsule

In comparison to the polyethylenterephtalat prostheses, ePTFE prostheses with the same implantation time have a thin external capsule with a limited, focal giant cell reaction.

Prostheses interstitials

The interstitials are occupied by young hypocellular granulation tissue and type I collagen.

The internal capsule



There is a thin internal capsule without foreign-body reaction and endothelial cells originating in the native artery endothelium. Near the anastomoses, it has increased thickness and rare giant cells neighboring the prostheses (Figure 2).

Figure 2: ePTFE prostheses, II-nd phase, 7 weeks from implantation. Endothelial cells at the distal anastomoses (yellow arrow). Col. H-E ×400.

The "late" phase

This stage begins after six months post-implant; the mesenchyme is rich in fibers and hypocellular and occasionally the protein structure is lost. The mesenchyme proliferation, somewhat limited, can be found in the internal capsule.

Twenty-nine prostheses were in this stage.

3. Polyethylenterephtalat prostheses

The external capsule

The thickness of the external capsule in our specimens was 0.8-2.5 mm; it contains mature connective tissue, rich in cells and neocapillaries located in the immediate vicinity of the prostheses. Inside the dense connective tissue rich in fibrils, located in the prostheses transition zone, an almost perfect circle of monocytes, macrophages, and foreign-body giant cells is found.

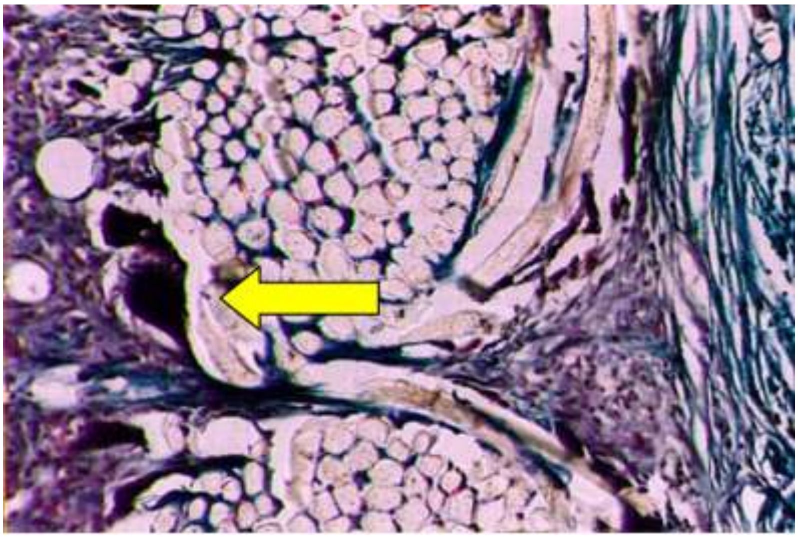


Figure 3: Terom prostheses – IIIrd phase, 24 mounth from implantation. Giant cells reaction arround the prosthetic graft (yeloow arrow). Col. Tricrom Masson ×200

Foreign-body reaction is present in all the examined prostheses with the multinucleated foreign-body giant cells arranged around the synthetic fibers. Some areas display fragmentation and phagocytosis of the synthetic fibers by the multinucleated giant cells (Figure 3).

Prostheses interstitials

These areas contain a fine fibrous connective tissue with macrophages and multinucleated giant cells that penetrate from the internal and external capsule and are attached to the synthetic particles. During the long period of encapsulation, the synthetic particles continue to be degraded. Occasionally, the phagocytosis can be inferred from the loss of regular pattern in the synthetic fibers. The interstitials are crossed by intercapsular bridges containing neocapillaries and multinucleated foreign-body giant cells (Figure 4, next page).

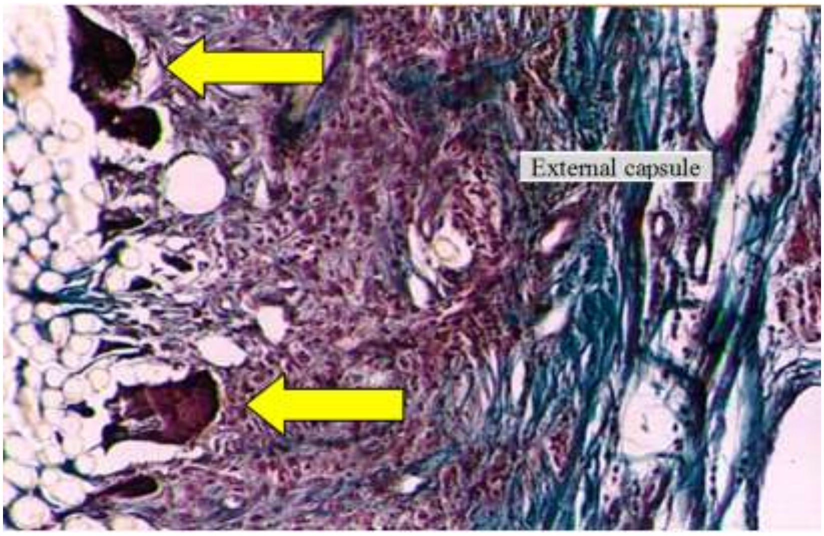


Figure 4: Terom prostheses – IIIrd phase, 24 mounth from implantation. Giant cell (yellow arrow). Col. Tricrom Masson ×200

The internal capsule

In this phase the capsules are completely organized with a minimal activity still occurring in the internal capsule. The internal capsule has mesenchyme proliferation that includes monocytes, macrophages, capillaries and blood vessels. The foreign-body giant cells are also present and occasionally the monocytes and macrophages form a line in the transition zone to the prostheses. In some Terom prostheses, the foreign-body reaction leads to foreign-body granulomas surrounding the synthetic fibers (Figure 5).

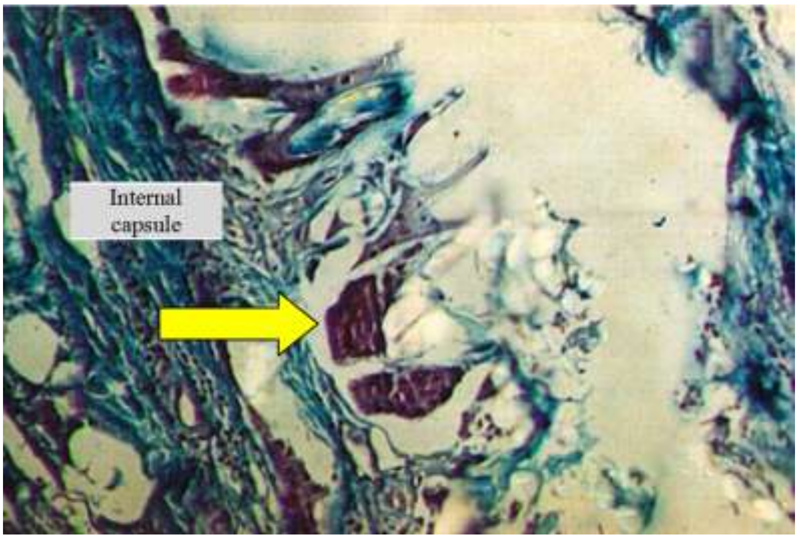


Figure 5: Terom prostheses – IIIrd phase, 36 mounth from implantation. Giant cells (yellow arrow). Col. Tricrom Masson ×200.

In these area, the internal capsule thickness is markedly increased, especially at the distal anastomoses sites, up to levels of 2.0-3.5 mm (average 2.6 mm) versus other areas with lesser degrees of foreign-body reaction (average 1.2 mm). Only 30% of the prostheses have a uniform layer of endothelial cells on the luminal surface and only on a 1.5 cm length near the distal anastomoses. The remaining of the internal or luminal surface has only sporadic endothelial cells.

4. Teflon (ePTFE) prostheses

The external capsule

The ePTFE prostheses have a thin, fibrous, external capsule with small areas displaying multinucleated giant cells (Figure 6). Teflon prostheses external capsule has cavities filled with prosthetic material, massive numbers of macrophages and multinucleated giant cells crossing the entire thickness of the prostheses. These form real "highways" that are perpendicularly oriented on the prosthetic ring-like structures.

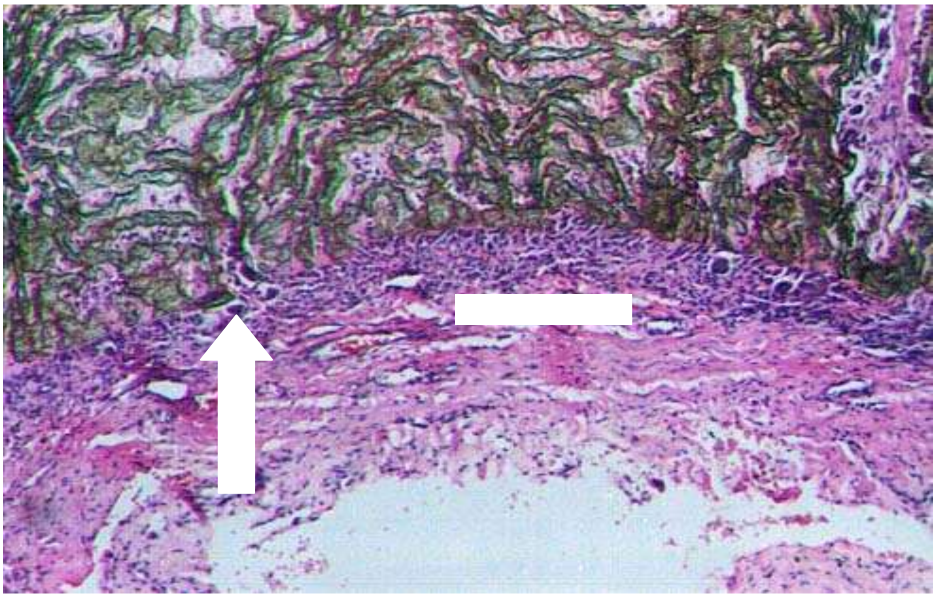


Figure 6: ePTFE prostheses - IIIrd phase, 8 mounth from implantation. Giant cells in the external capsule of the prostheses. Col. H-E ×40

The internal capsule

There is a very thin one or two-layer cell internal capsule with rare foreign-body reaction. Near the distal anastomoses, the thickness reaches 1.0 mm and there are giant cells neighboring the prostheses. The endothelial cells are only present near the anastomoses and are not organized into a uniform layer (Figure 7).

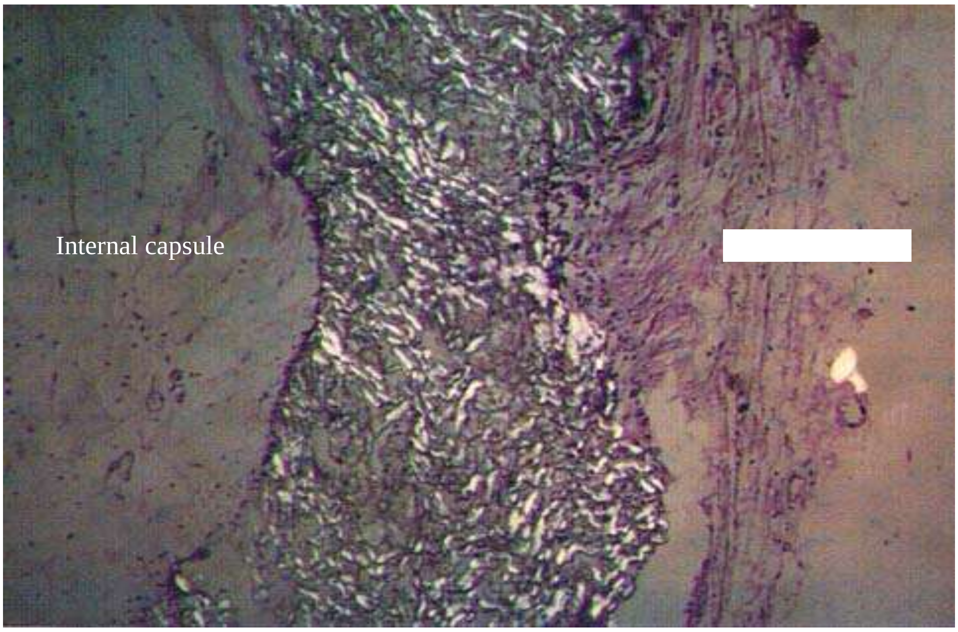


Figure 7: ePTFE prostheses - IIIrd phase, 18 mounth from implantation. Internal capsule, at the distal anastomoses. Low giant cell reaction. Col. H-E ×40.

Discussions

Earlier studies hypothesized that the prostheses encapsulation process is similar to the foreign body encapsulation process, consisting in undifferentiated cells originating in the surrounding tissue and the circulating blood. More recent theories offer an alternate model for the process. Florey [1] describes for the first time in 1962 the presence of neointimal orifices of 120 microns diameter located at the anastomosis level.

In 1986, Clowes [2] identifies the so called “endothelial channels” that open on the endothelial surface through small orifices. These channels are transprosthetic neocapillaries as shown in experimental studies involving micro-corrosive molding and were documented only in the areas where endothelization was present. Because these channels are absent in ePTFE prostheses that have decreased porosity, the authors concluded they are the main source for a complete and uniform endothelization.

Kogel et al [3] showed the presence of endothelial channels in four human prostheses, and Zhang et al (citation needed) together with Usui et al [4] also agree that native artery vasa vasorum plays an important role in the endothelization process. All prior studies agree that unlike the animal model, the endothelization in humans is very slow and never completes. Why does this happen?

One possible answer is that synthetic material, especially polyethylenterephtalat prostheses, inhibit somehow the encapsulation.

Clowes et al [2] and Greisler et al (5) demonstrated that Dacron prostheses have a different encapsulation process than ePTFE and hypothesized that this was due to several factors:

- the existence of large structural differences in the polymers used to woven the prostheses leading to different degrees of peri-graft inflammation with the release of different inflammatory products in the surrounding tissues;
- Dacron prostheses allow less transparietal capillary formation compared to ePTFE;
- the internal surface of Dacron prostheses have larger quantities of In^{111} radioactively marked thrombocytes versus the ePTFE, potentially inhibiting endothelization;
- the Dacron prostheses also attract polymorphonuclear leukocytes and can activate both the classic and alternate complement pathways more than ePTFE; activating polymorphonuclear leukocytes has been shown to inhibit endothelization [10];
- macrophages activation accompanied by TGF-beta release is also more pronounced in Dacron prostheses.

Cavallaro et al [6] demonstrated in an experimental study that the Dacron threads led to an early, intense inflammatory reaction, with inflammatory cells penetrating the prostheses and leading to a chronic inflammation. Polypropylene and ePTFE threads lead to mild to moderate inflammatory reactions. Using another experimental model, Zippel et al [7] found the presence of a chronic inflammatory reaction associated with thromboses inside Dacron prostheses, suggesting that Dacron prostheses led to an unfavorable host response.

Our study demonstrates, in the polyethylenterephtalat prostheses, the existence of an intense inflammatory reaction characterized by the presence of multinucleated giant cells in the internal and external capsules one month post-implantation and also by a persistent chronic inflammatory reaction with foreign-body granulomas in both capsules and the surrounding tissue at over one year post-implantation.

These changes were not found in the ePTFE prostheses in our study, and also are not described in the previously published literature. Camileri [9] and Xue et al [10] identified giant cells in the external capsule of one ePTFE prosthesis obtained 18 months post-implantation.

There are several consequences of a chronic inflammatory reaction that should be considered: inhibited transparietal neocapillaries formation, inhibited vasa vasorum growth in the prostheses wall, neointimal hyperplasia, and lack of endothelization [2, 3, 4, 5]. Thickening of the intimal layer and external capsule in the polyethylenterephtalat prostheses lead to increased prostheses wall rigidity after implantation [8, 9].

Conclusions

Implanted synthetic vascular prostheses cause a foreign-body reaction dependent on the material used.

In the polyethylenterephtalat prostheses there are giant multinucleated cells in the external capsule, interstitials, and internal capsule, in the anastomotic areas (especially distal) seen even in prostheses implanted for more than 9 years. In ePTFE prostheses, the giant cells are only found in the external capsule.

In the distal anastomotic areas of the polyethylenterephtalat prostheses, where foreign-body granulomas are present, the neointima has a markedly increased thickness compared to the areas with decreased foreign-body reaction.

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Cardiac protection by anterograde administration of warm blood cardioplegia during cardiac arrest and evolutions of myocardial ischemia markers*)

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Abstract

In 35 patients undergoing elective valvular surgery using trans right atrial approach (mitral transeptal and tricupid procedures), with intermittent anterograde administration of warm-blood cardioplegic solution for myocardial protection, we analyzed metabolic changes by assay of global ischemia indicators (pH, lactate, glucose and BE) - which were measured into the coronary sinus and arterial blood during the administration of the cardioplegic solution and post-ischemic periods: immediately after declamping of the aorta and after 10 minutes of reperfusion. A typical cumulative ischemic pattern with progressively decreasing pH, BE values and progressively increasing lactate values could be observed in all patients, In our study group, this cumulative ischemic pattern was observed in all patients: at 20 minutes of ischaemia, the ischaemic markers were different from normal values but at or after 30 minutes these alterations were more severe, which suggests differences in perfusion efficiency and a corelation beetween that and ischemic time. It was not the degree of lactate washout, but the lactate concentration at the end of each reperfusion, that correlated significantly with global metabolic recovery time, which suggests the importance of effective perfusion and reperfusion.

Key-words: *Acidosis, valvular replacement, myocardium metabolism, heart arrest, coronary sinus, monitoring, intraoperative myocardial ischemia, myocardial reperfusion*

Introduction

During intermittent warm-blood cardioplegia as described by Calafiore and colleagues (1) the progressive lactate accumulation and intracellular acidosis, the decrease of the pH and of the BE are well-known phenomena. Prolonged lactate production induced by ischemia is associated with adenosine triphosphate depletion and therefore with alteration of myocardial contractile function (2, 3). Therefore, continuous "blood gas analysis" monitoring of coronary sinus (CS) blood during the ischemic period has been recommended as an adjunct, in order to evaluate the quality of myocardial protection (4). The continuous monitoring of myocardial recovery during the post-

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ischemic phase might prove useful in improving the management of patients undergoing cardiac surgery.

Patients and Methods

In order to monitor the global metabolic imbalance during the ischemic period and to assess its impact on the post-ischemic period, we chose for our prospective study 25 patients (22 men and 13 women) aged 43 to 68 years (mean age - 61 years), who undergo valvular surgery, in whom intermittent warm-blood cardioplegic solution was used for myocardial protection. The inclusion criteria were mitral or tricuspid procedures and normal left ventricular (LV) function together with the intermittent antegrade administration of warm-blood cardioplegic solution according to the Calafiore protocol (1) for myocardial protection: 300 ml per minute at pressure of 40-80 mmHg and surgery performed on an elective basis, by the same surgeon.

All patients were operated on under extracorporeal circulation and in normothermia. In order to monitor the metabolic changes, global ischaemic indicators such as pH, BE, lactate were measured simultaneously in the CS and in the arterial blood during blood cardioplegic administration at 20 or 30 minutes, at the beginning and at the end of each cardioplegic delivery and in the post-ischemic periods immediately after the release of aortic clamp and at 10 minutes after that. The COP (recovery time) was reached when the lactate values - measured simultaneously in the CS and in the arterial blood - were equal.

For adequate sampling of the coronary blood, we used total cardiopulmonary bypass, both venae cavae were cannulated and snared, and an Edwards Research Medical RCP014MIB catheter (Edwards Lifesciences LLC; Irvine, Calif) was placed in the CS with the tip positioned at the level of the middle cardiac vein. Samples were drawn simultaneously from the cardioplegic line and from the CS catheter and sent for blood gas analysis by means of a Cobas b221 Roche. Care was also taken to keep the successive samples admixture-free by purging the aspirate from each previous sample. In order to avoid data misinterpretation, the concentration of CS metabolites was also considered in relation to the concentration of metabolites in the arterial blood.

The data then underwent multifocal analysis with the following research interests in mind: influence of global ischemia on recovery time (COP time); change-over-time analysis of lactate and pH value differences (CS vs arterial blood) and analysis of values obtained solely from CS blood, at the beginning and at the end of each cardioplegic administration and after reperfusion; analysis of lactate and pH value differences (CS vs arterial blood) at the beginning and at the end of each reperfusion.

For the different analytes (lactate and pH), regression lines were calculated at the endpoints, at the beginning, and at the end of each reperfusion. In calculating of the mean, we found that if the 12 regression coefficients for a value (either at the beginning or at the end) were significantly different from zero, we could expect either a positive or a negative trend (a pattern) of this analyte during ischemic time. For testing the regression coefficients of the values against zero, the one-sample *T-test* was used. The regression coefficients were calculated with Excel (Office 2003), and, for the *T-test*, the means procedure was used Excel (Office 2003).

Results

The mean aortic cross-clamp time was 62 minutes (range, 50-96 min). The mean ischemic period between each cardioplegic administration was 22.5 minutes and ranged between 18 and 35 minutes. It is of interest that, in all patients, we observed a conspicuous congruence between arterial and CS blood in regard to lactate content, pH value and BE, with one directions of movement: upward movement of these parameters. The regression analysis revealed that *t* values - that for lactate, for pH and for BE showed a significance in favor of the alternatives of increasing values over time (*lactic acid P*=0.023, EB *P*=0.0318, pH *P*=0.0036, c HCO_3 *P*=0.014411). All *p-values* were lower than 0.05 (**table 1**).

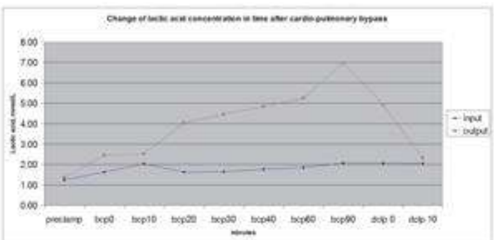
Tabel 1. Variations of metabolic markers during cardiac ischemia *T*-test and *p* values

Lactic acid							
Stage	**Input**			**Output**			***T-test p value***
	average	**min**	**max**	**average**	**min**	**max**	
preclamp	1.23	0.5	1.8	1.35	0.6	2.0	0.0023
bcpO	1.62	0.5	2.8	2.45	0.9	5.2	
bcplO	2.02	1	3.2	2.52	1.9	3.0	
bcp20	1.61	1.2	2.3	4.02	2.0	6.1	
bcp30	1.63	1.3	2.1	4.46	2.4	8.5	
bcp40	1.76	0.6	2.4	4.84	1.3	8.3	
bcp60	1.85	1.4	2.7	5.24	3.4	8.9	
bcp90	2.07	1.2	2.5	6.97	5.6	9.1	
dclp O	2.08	0.6	3.1	4.94	1.4	9.9	
dclp 10	2.04	1.4	2.7	2.33	1.4	3.4	

pH							
Stage	**Input**			**Output**			***T-test p value***
	average	**min**	**max**	**average**	**min**	**max**	
preclamp	7.43	7.16	7.55	7.44	7.35	7.55	0.0036
bcp0	7.47	7.4	7.55	7.38	7.2	7.53	
bcp10	7.49	7.43	7.55	7.46	7.4	7.53	
bcp20	7.48	7.43	7.54	7.24	7.12	7.43	
bcp30	7.49	7.43	7.56	7.30	7.17	7.46	
bcp40	7.45	7.43	7.47	7.25	7.13	7.37	
bcp60	7.45	7.24	7.57	7.29	7.11	7.44	
bcp90	7.44	7.43	7.45	7.06	6.74	7.3	
dclp 0	7.47	7.41	7.56	7.31	7.13	7.49	
dclp 10	7.45	7.39	7.58	7.43	7.35	7.54	

EB							
Stage	**Input**			**Output**			***T-test p value***
	average	**min**	**max**	**average**	**min**	**max**	
preclamp	0.63	-6.0	5.2	1.65	-3.5	6.9	0.0318
bcp0	0.38	-2.4	4.1	-0.88	-6.0	6.8	
bcp10	5.98	0.1	26.5	5.96	-2.2	26.8	
bcp20	1.13	-3.5	3.9	-1.77	-6.0	3.3	
bcp30	1.08	-2.1	5.8	-1.49	-5.3	4.0	
bcp40	-0.90	-1.9	0.3	-3.10	-5.3	-1.2	
bcp60	0.06	-1.7	6.3	-1.71	-5.5	6.6	
bcp90	-2.07	-2.2	-1.9	-7.50	-13.0	-3.2	
dclp 0	-0.69	-4.8	5.1	-1.59	-6.3	3.4	
dclp 10	-1.52	-3.9	3.9	-0.81	-5.0	6.4	
c HCO_3							
Stage	**Input**			**Output**			***T-test p value***
	average	**min**	**max**	**average**	**min**	**max**	
preclamp	24.96	19.6	28.9	25.71	21.5	30.2	0.0144
bcp0	24.58	20.3	27.9	23.55	18.5	30.1	
bcp10	25.94	24.5	29.9	25.42	22.5	28.9	
bcp20	25.00	21.6	27.7	22.48	19.2	27.0	
bcp30	25.29	22.7	29.3	23.36	19.6	29.1	
bcp40	23.62	22.8	24.6	21.05	19.6	22.6	
bcp60	24.46	23.0	29.7	22.59	19.5	29.8	
bcp90	22.70	22.6	22.8	17.80	12.9	21.6	
dclp 0	23.84	20.5	28.7	22.79	18.8	27.2	
dclp 10	23.49	21.2	27.7	23.72	20.3	29.8	

The analyses of lactate, glucose and BE levels during the post-ischemic period revealed a striking congruence in all patients. A representative tracing (in patients) of simultaneously sampled lactate, acidosis and BE and standard bicarbonate values, in CS and in arterial blood, is presented in (figure 2). In all patients, 10 minutes after declamping the aorta, values of all parameters measured in CS blood reached the levels of values measured in arterial blood (table 1, figure 1)



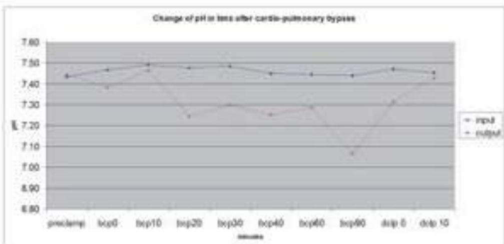


Figure 1: Metabolic markers during cardiac ischemia

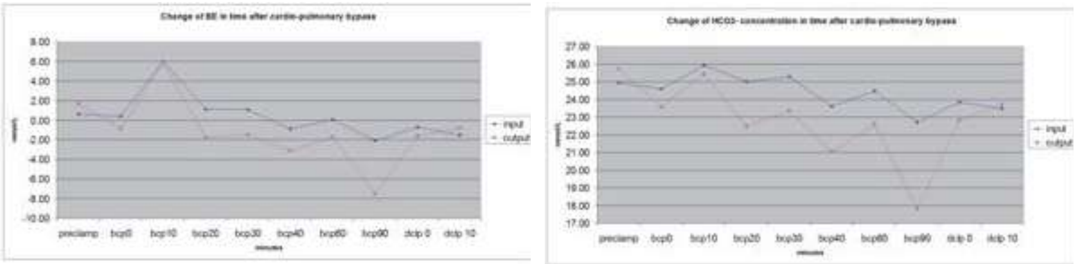


Figure 1: Metabolic markers during cardiac ischemia

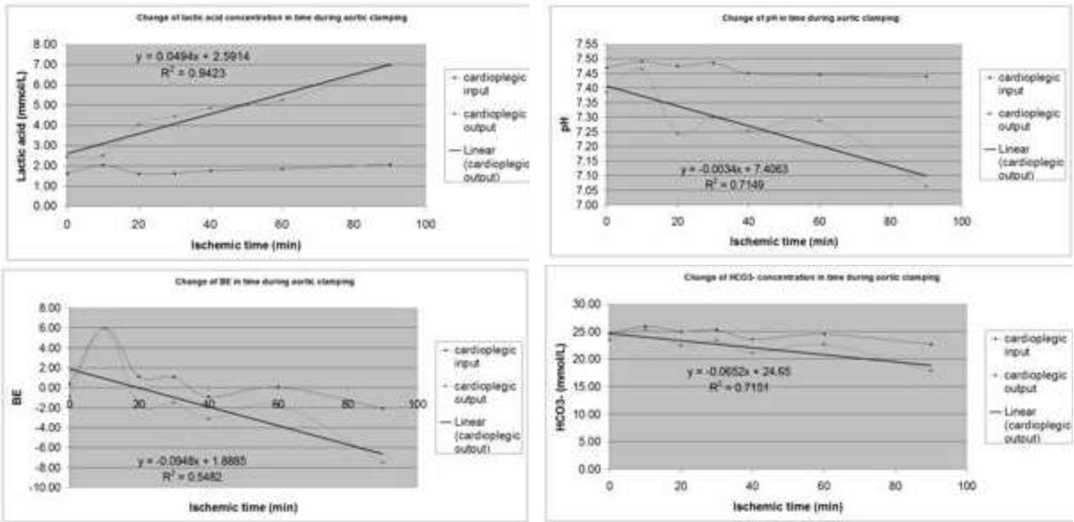


Figure 2: Metabolic markers trend during cardiac ischemia

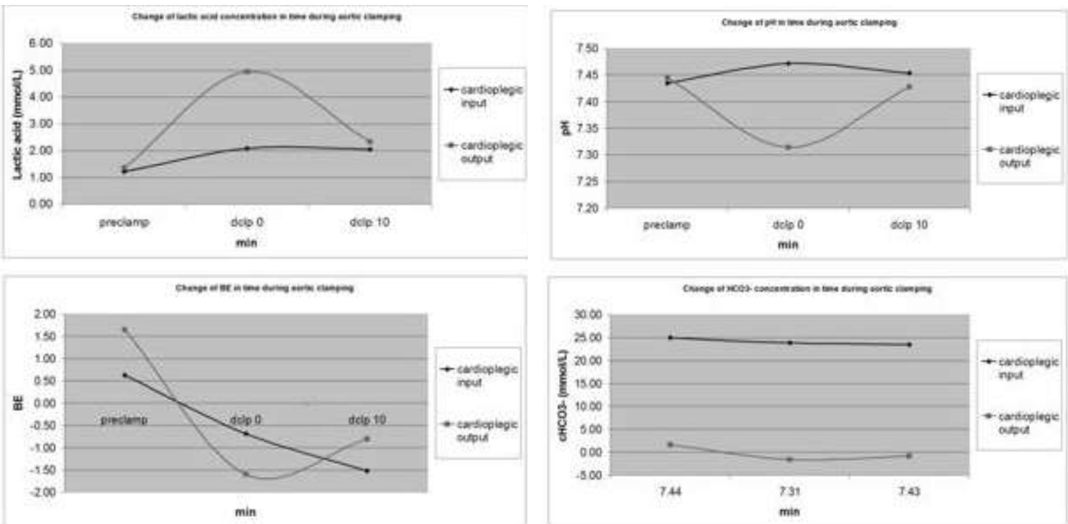


Figure 3: Metabolic markers after aortic declampation

We observed a linear correlation between mean values from all lactate, BE and pH samples and ischemic times from the beginning of first administration of the cardioplegic solution until the end of cardioplegic administration (figure **2**) and we did observe a positive correlation, with progressive decrease of these values, at the beginning of reperfusion until 10 minutes after declamping of the aorta (tabel **1**). In regard to this we found a nonlinear correlation between lactic acid, pH and BE values from all samples and partial ischaemic times (after 20 minutes in all cases these value increases exponentially) (figure **1**).

The analysis of lactate, pH and BE value differences (CS vs arterial blood) at the beginning of the last reperfusion (data not shown) showed correlation with partial ischemic times, after 30 minutes of ischemia these values presented more severe alterations than after 20 minutes of ischemia. At 30 minutes of ischemia these values are three times higher than basal value and there was a strong positive correlation between lactate values and ischaemic times at the end of the last reperfusion (aortic declampation) (figure **3**). No correlation was found between these metabolic value differences and ischemic time at the end of 10 minutes after reperfusion (figure **1**).

Discussion

Graffigna and colleagues (2) investigated the metabolic state of ischemic myocardium in 19 patients who underwent CABG or valve surgery (or both) with myocardial protection afforded by the intermittent administration of warm-blood cardioplegic solution, antegrade or retrograde (or both). They detected a typical pattern of blood-gas change with progressive deterioration of PCO_2 and pH values: at subsequent intermittent doses of warm-blood cardioplegic solution, pH and BE failed to return to previous levels, so that at the end of every ischaemic period progressively lower pH levels and higher PCO_2 values were recorded.

We found, in our study group, a clear pattern of progressively decreasing of the pH and BE values and progressively increasing lactate values. Generally, we observed during the ischemic period, changes of lactate and pH content in CS blood that were not congruent with changes in the arterial blood. Even in patients who underwent longer ischemic periods, constant lactate and pH values could be registered at the next cardioplegic administration and at the end of reperfusion. Furthermore, longer ischemic periods after 20 minutes of ischemia were necessarily associated with cumulative patterns of ischemic metabolites and longer ischemic periods after or near 30 minutes times were associated with severe cumulative patterns of ischemic metabolites. Neither the degree of lactate washout nor the pH values measured at the beginning of each reperfusion were correlated significantly with cardiac ischemic times but at 10 minutes after reperfusion all the value from coronary sinus became normal. However, our regression analysis revealed a significant change over time for lactate pH and BE values obtained at the end of all reperfusions. We also observed a positive linear correlation between the mean lactate concentration at the end of all reperfusions (including the last). These data indicate the importance of effective reperfusion time.

According to a report published by Johnson and co-authors (5) an immediate increase of contractility after cardiac surgery can be expected in patients who have good preoperative LV function. We observed this phenomenon in all but 4 patients - those in whom the longest ischemic time were recorded. Despite metabolic recovery with demonstrable normal lactate metabolism at 10 minutes, diminished contractility persisted in all 3 patients even longer than 20 minutes after declamping the aorta.

Conclusion

Therefore, lactate and acido-basic markers monitoring seems to be useful in the assessment of myocardial protection quality and hence in the management of the post-ischemic heart. In our study group, a cumulative ischemic pattern was observed in all patients: at 20 minutes of ischemia, ischemic markers were different from normal values but at or after 30 minutes these alterations were more severe, which suggests differences in perfusion efficiency and a corelation beetween that and ischemic time. Additional research is warranted to prove the notion that changing reperfusion conditions (for example, pressure, volume, or duration) can contribute to the improvement of quality of myocardial protection.

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The left ventricular diastolic filling pattern as prognostic predictor in patients with idiopathic dilated cardiomyopathy*)

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Abstract

Background: *Previous studies have demonstrated that the presence of restrictive left ventricular (LV) diastolic filling pattern in patients with dilated cardiomyopathy have an unfavorable prognostic.*

Aim: *1. To establish the value of LV diastolic filling pattern as prognostic predictor in patients with idiopathic dilated cardiomyopathy. 2. Assessment of the betablocker treatment on these patients.*

Material and method: *Prospective study on 143 patients (63%male, mean age 52 ±15) with dilated cardiomyopathy who were divided in 2 groups taking into consideration the LV diastolic filling pattern. 1.Group A - 87 patients with restrictive LV diastolic filling pattern, 2. Group B - 56 patients with nonrestrictive LV diastolic filling pattern. 49 patients (56%) from group A and 31 patients (55%) from group B underwent betablocker treatment (carvedilol). Patients were evaluated every 3 months during a 2 year follow-up. Statistical analysis used SYSTAT and SPSS programs for the simple and multiple linear regression analysis, correlation coefficient and relative risk calculations.*

Results: *1.Mortality rate after 2 year follow-up was significantly higher in group A (68.96%) compared to group B (51.78%). The restrictive LV diastolic filling pattern (E wave deceleration time DT<130msec, E/A>2) has increased twice the risk of death (RR=2.6, p=0.007). 2. Clinical amelioration after 2 years was more frequent in patients with nonrestrictive diastolic filling pattern (DT>130msec, E/A<2). 3. Survival rate in patient undergoing betablocker treatment was similar in both groups (46.93% versus 51.61%) but significantly higher in these patients versus patients without betablocker treatment (46.93% versus 10.53% in group A, p=0.002, respectively 51.61% versus 44% in group B, p=001). 4. The LV diastolic pattern has remained restrictive at 2 year follow-up in 84.21% patients without betablocker treatment and only in 30.6% patients with betablocker treatment.*

Conclusions*: 1.The persistence of the restrictive LV diastolic filling pattern at 2 years is associated with an increasing in the risk of death in patients with cardiac failure due to nonischemic dilated cardiomyopathy. 2. The association of restrictive LV diastolic filling pattern leads to a more unfavourable prognostic, with increasing the risk of death and worsening the clinical status of these patients in a 2 year follow-up. 3. The restrictive LV diastolic filling pattern is reversible on betablocker treatment.*

Key words: *dilatative cardiomyopathy, left ventricular diastolic filling pattern*

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Abbreviations: *DCM - dilated cardiomyopathy, LV - left ventricle, LVEF - left ventricular ejection fraction, DT - deceleration time, NYHA - New York Heart Association*

Introduction

Dilatated cardiomyopathy is a significant cause of morbidity and mortality among patient with congestive heart failure and aging population. In United States, the reported incidence of cardiomyopaties is 400,000-500,000 cases per year, with a prevalence of 2-3 million people [1].

In spite of modern therapy which associates vasodilators, angiotensin-converting enzyme inhibitors to digitalis treatment, and of progresses on surgical treatment, the overall prognostic remains poor. Facing this heart condition, clinician is in the position to decide which of various parameters should be used in order to evaluate the severity and the prognostic of disease.

The long and medium term prognosis in patients with idiopathic dilated cardiomyopathy is influenced by many parameters among which left ventricular diastolic function is one of the most important. It is also appears to be the one of the earliest detectable abnormalities in many of the heart disorders.

Diastolic dysfunction is a condition in which filling of the left ventricle is impeded, leading to symptoms of low cardiac output or/and elevated pulmonary venous pressure. There are two distinct abnormal filling patterns which can be detected by Doppler echocardiography [2]: "impaired relaxation" characterized by a prolonged isovolumetric relaxation time, an increased deceleration time of early transmitral filling velocity (E wave) and a decrease in E/A ratio and "restrictive pattern" characterized by a shortened isovolumetric relaxation time, a decreased deceleration time, and an elevated E/A ratio.

It is known that the presence of a restrictive left ventricular diastolic filling pattern is associated with a more unfavourable prognosis in most of cardiac diseases (valvular, coronary or congenital). The impact of restrictive left ventricular diastolic filling pattern presence on the evolution and prognosis in patients with idiopathic dilated cardiomyopathy has been evaluated in some previous studies and we tried to evaluate it also taking into consideration the beta-blocker treatment in these patients as well.

That is why the purpose of this study is to establish the implication of the left ventricular diastolic filling pattern on the evolution and prognostic in patients with idiopathic dilated cardiomyopathy. We have also tried to assess the impact of betablocker treatment on the left ventricular diastolic filling pattern in these patients.

Material and Methods

We carried out a prospective study on 143 patients with idiopathic dilated cardiomyopathy admitted to the *Institute of the Cardiovascular Diseases* "*C.C. Iliescu*" between 1 January 2000 and 1 January 2003. Most of the patients were male (62.72%), with a mean age of 52±15 years and the mean left ventricular ejection fraction was 25±5.2%.

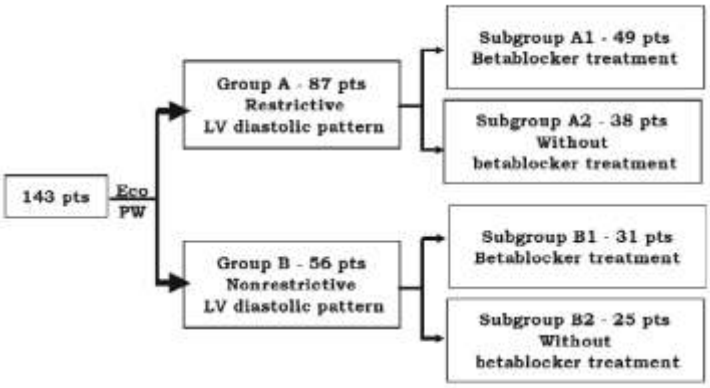
The patients were evaluated clinically and by echocardiography at the enrollment into study and during the treatment at every 3 months for two years. For each patient taken into study we assessed echocardiographically the left ventricular systolic and diastolic performance and the left atrium function.

All patients received the standard treatment for heart failure with digitalis, diuretics, converting enzime inhibitors and spironolactone. At the enrollment into study all the patients were in sinus rhythm.

The left ventricular diastolic filling was evaluated by Doppler examination and the restrictive diastolic filling pattern was defined as an E wave deceleration time less than 130msec and the E wave / A wave velocity ratio more than 2.

Depending on the LV diastolic filling pattern the patients were divided in two groups (fig. 1):

a. Group A - 87 patients with a left ventricular restrictive diastolic filling pattern, and
b. Group B - 56 patients with a left ventricular non restrictive filling pattern.



Depending on both diastolic performance of the left ventricle and the type of the treatment, each group was divided in two subgroups as follows:

Figure 1: Patients Structure depending on the LV diastolic filling pattern and treatment undergone

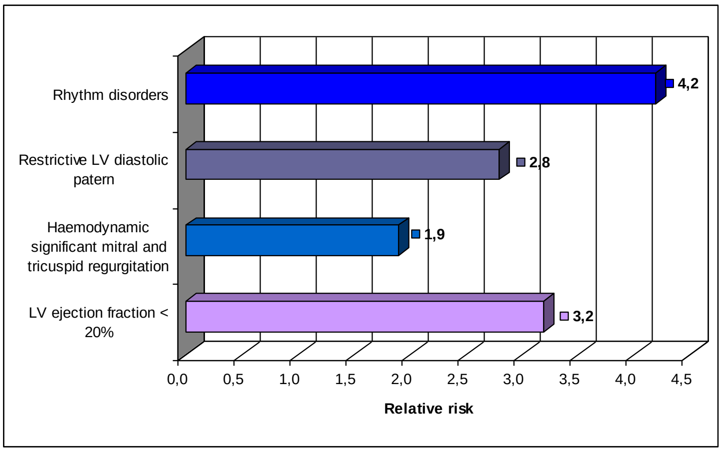


Figure 2: Risk of death at 1 year in patients with idiopathic dilated cardiomyopathy

a) Subgroup A1 with 49 patients with a restrictive LV diastolic filling pattern undergoing betablocker treatment;

b) Subgroup A2 - 38 patients with a restrictive diastolic filling pattern without betablocker treatment

c) Subgroup B1 comprising 31 patients with an non restrictive LV filling pattern who underwent betablocker treatment, and

d) Subgroup B2 - 35 patients with a non restrictive LV filling pattern but without betablocker treatment.

The two groups were comparable concerning:

- mean age;
- gender;
- mean LVEF;

• secondary mitral regurgitation degree;
• the mean pulmonary artery pressure. Statistical analysis used SYSTAT and SPSS programs for the simple and multiple linear regression analysis, correlation coefficient calculation and relative risk calculation. The most important endpoints used for the estimation of the medium term prognosis were:
• type of LV diastolic filling pattern;
• NYHA class for heart failure;
• quality of life (appreciated on a scale from 1 to 10 using a questionnaire filled in by the patient at each visit);
• death.

Results

1. Mortality rate at 2 year follow-up was significantly higher in patients with restrictive LV diastolic filling pattern (68.96% in Group A) compared to patients with nonrestrictive LV diastolic filling pattern (51.78% in Group B), regardless the LV systolic performance.

2. The presence of the restrictive LV diastolic filling pattern (E wave DT< 130msec, E/A>2) has increased the risk of death by 2.8 times at 1 year and by 2.6 times at 2 year follow up, regardless the presence of other parameters known to increase mortality in patients with dilated cardiomyopathy. The restrictive left ventricular diastolic filling pattern turned out to be an independent predictor for increasing the risk of death or hospitalization for heart failure decompensations ($p = 0.001$), regardless the left ventricle dimensions or performance, the presence of a secondary mitral regurgitation haemodinamically significant or pulmonary hypertension.

These data are presented in figure 2 which shows the relative risks of death at one year follow-up for the patients with dilatative cardiomyopathy associated with different parameters known for increasing the mortality rate. Thus, the risk of death at one year was increased by 4.2 fold by the presence of rhythm disorders, by 2.8 fold by an associated restrictive left ventricular diastolic filling pattern, by 3.2 fold by a severe left ventricular sistolic dysfunction with an ejection fraction less than 20% and by 1.9 fold by the presence of an associated haemodinamically significant mitral or tricuspid regurgitation.

In figure 3 there are represented the relative risks of death at two years follow-up for the patients taken into study associated with different known parameters that increase the mortality level in idiopathic dilated cardiomyopathy (such as the presence of atrial or ventricular rhythm disorders, an associated haemodinamically significant mitral or tricuspid regurgitation, systolic performance of left ventricle). The relative risks are also represented distinctly depending on the type of left ventricular diastolic filling pattern.

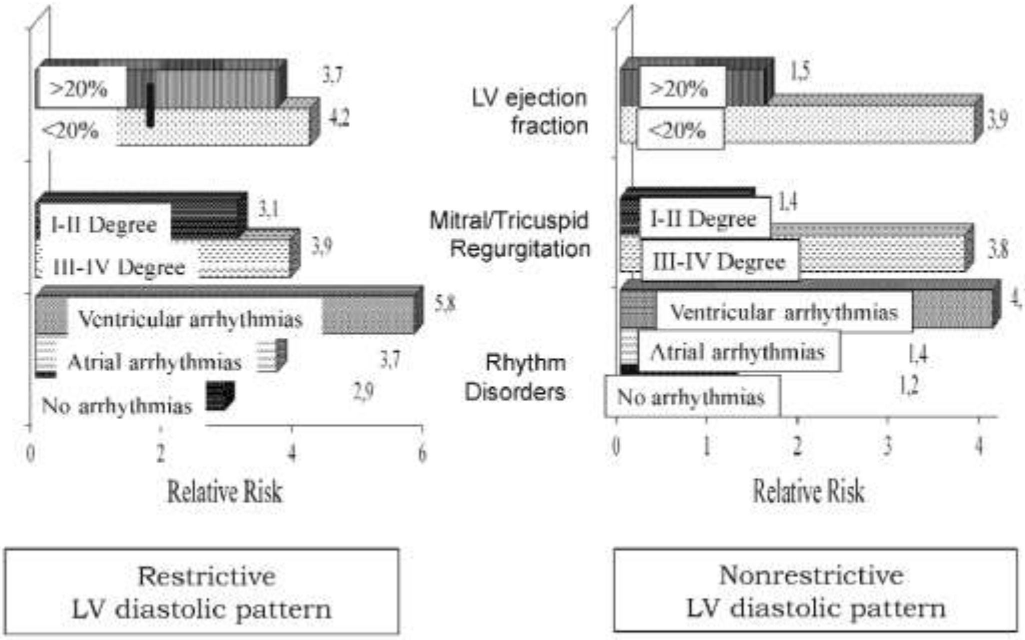
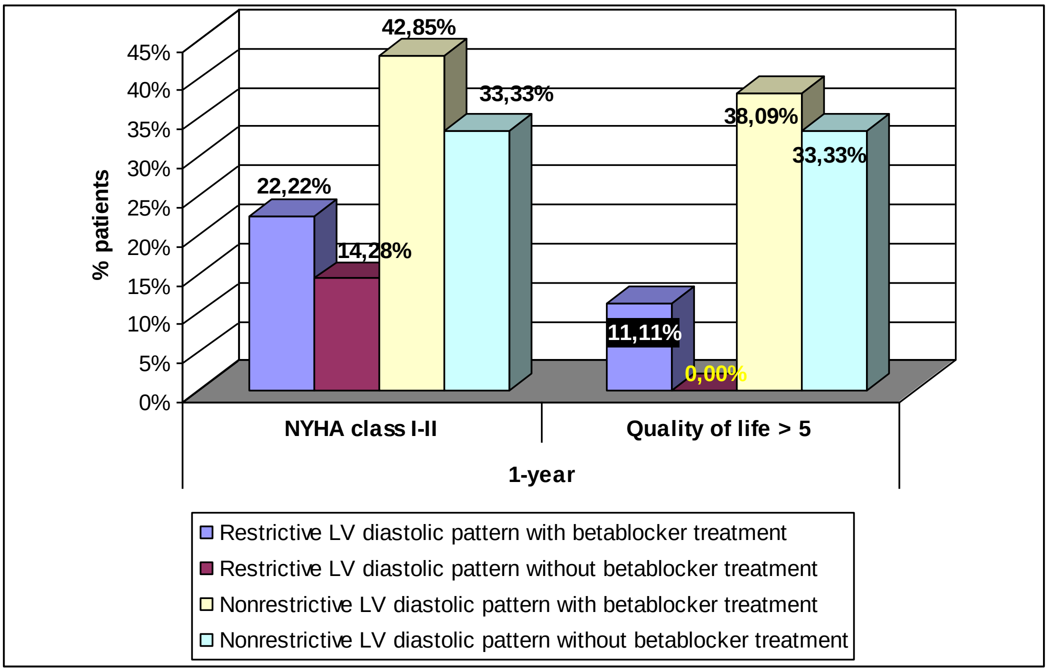


Figure 3: Risk of death at 2 years in patients with idiopathic dilated cardiomyopathy depending on the type of LV diastolic filling pattern

The predictive value for death at two years follow-up of the left ventricle systolic dysfunction, of the atrio-ventricular valve regugitation or of the arrhythmias was higher in patients with a non-restrictive LV diastolic filling pattern. In these patients, values of left ventricular ejection fraction less than 20%, the presence of a mitral or tricuspid regurgitation three or four degrees or ventricular arrhythmias increased about four times the risk for death at two years follow-up.

The presence of a restrictive left ventricular filling pattern homogenized the relative risk values. In patients from group A, the risk for two years mortality was increased by the type of the diastolic filling regardless the left ventricular systolic performance or the presence of mitral or tricuspid regurgitation or atrial arrhythmias. In these patients, the only independent predictor for increasing the risk of death at two years follow-up was the presence of ventricular rhythm disorders.

3. Taking into consideration the patient evolution, the percent of those with a favourable evolution quantified as NYHA class of heart failure less than 3 and the quality of life score >5 was higher in the group of patients with a nonrestrictive left ventricular diastolic filling pattern, regardless whether they received betablocker treatment or not. Thus, at one year follow-up, the percent of patients in a low NYHA class was nearly double in group B and at two years follow-up three times higher compared with patients with a restrictive left ventricular diastolic filling pattern (group A), regardless the betablocker treatment undergone. In addition, the quality of life score >5 was found at about three fold more patients with a nonrestrictive LV diastolic filling compared with a restrictive one in both years of follow-up (figure 4):



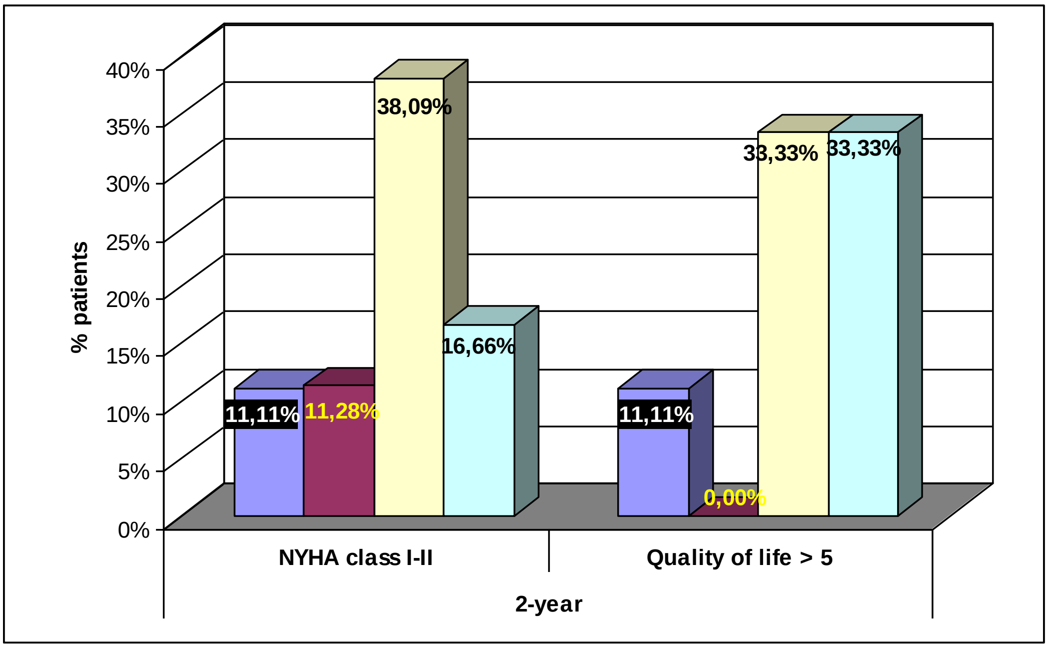


Figure 4: NYHA class and quality of life in patients depending the LV diastolic filling pattern and year of follow-up

4. Follow-up at 2 years showed that survival rate in patients undergone betablocker treatment was similar in both types of the left ventricle diastolic filling pattern but significantly higher compared with patients without betablocker treatment:

- in Group A: 46.93% patients with betablocker treatment respectively 10.53% in patients without betablocker treatment, $p = 0.0022$;
- in Group B: 51.61% patients with betablocker treatment respectively 44% in patients without betablocker treatment, $p = 0.001$.

In figure 5 the percents of survivors at one year and two years follow-up are presented for all four subgroups taken into study depending on both the type of left ventricle diastolic filling and on the type of treatment (patients who received or not beta blockers):

- in group A (*patients with a restrictive left ventricular filling pattern*) the survival rate at one year was aproximatively 2.5 times higher in patients who received betablocker treatment compared with those without betabloker treatment (about 66% versus 28%). In addition, at two years follow-up the survival rate in subgroup AI was 3 times higher in patients with betablocker treatment (about 44% versus 14%);
- in group B (*patients with a non restrictive left ventricular filling pattern*) the percent of survivors at one year and at two years was aproximatively 1.5 times higher in patients with betablocker treatment compared with patients who did not receive this treatment.

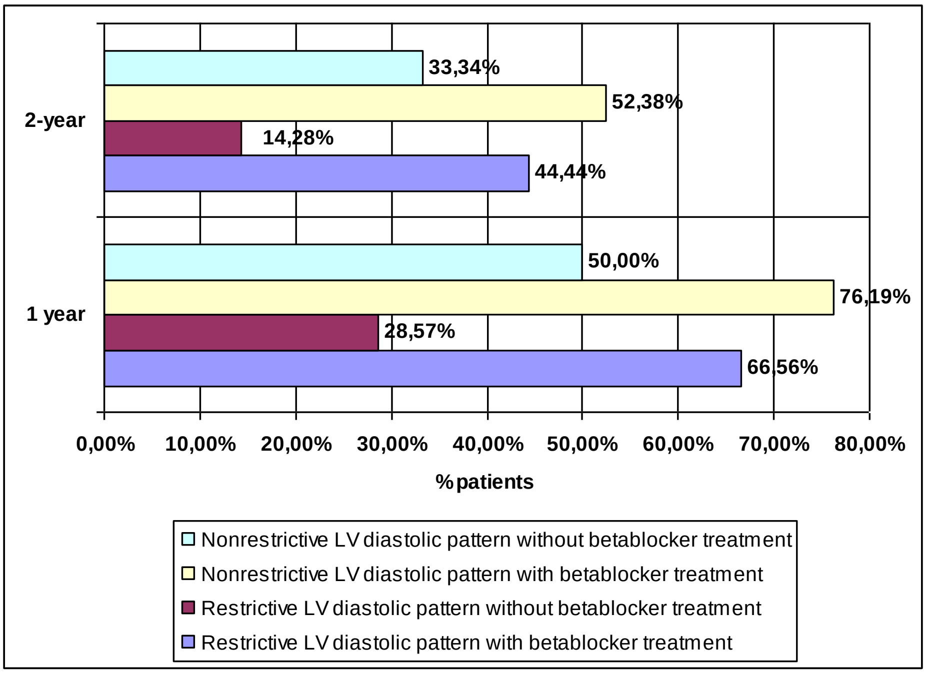


Figure 5: Survival rate at 1 at 2 years depending on the treatment undergone and the LV diastolic filling pattern in patients with idiopathic dilated cardiomyopathy

5. Betablocker treatment has influenced the LV diastolic filling pattern evolution, too. Thus, LV diastolic filling pattern has remained restrictive at two years follow-up in 84.21% patients without betablocker treatment and only in 30.6% patients undergoing betablocker treatment.The evolution of the left ventricular diastolic filling was influenced by the betablockers. Thus, at two year follow-up, left ventricular diastolic filling pattern has remained restrictive in about 84% patients who did not received betablockers and only in aproximatively one third - thirty percent of the patients undergoing betablocker treatment.

Discussions

Data from present study support the hypothesis tested in other previous studies which highlighted the importance of LV diastolic filling as predictor of severity and prognosis in dilated cardiomyopathy.

Dilated cardiomyopathy is characterized by an abnormal LV diastolic filling and severe cases showed the restrictive type of diastolic pattern [19] with a E/A > 2 cases with a poor prognosis and cases with a E wave DT < 150ms usually indicating bad outcome.

The literature showed also that the restrictive LV diastolic filling pattern is frequent in dilated cardiomyopathy and is associated with more severe disease being the best predictor for cardiac death in these patients [6, 8, 10, 13, 15].

The mortality rates showed in our study are in line with those from literature. Thus, the mortality rate at 2 year follow-up found was of 68.96% in patients with dilated cardiomyopathy with a restrictive filling pattern and of 51.78% for those with a nonrestrictive filling pattern.

The clinical evaluation by NYHA class of heart failure and quality of life has shown an amelioration at 2 years which was more frequent in patients with nonrestrictive diastolic filling pattern, which is in line with the literature studied [5, 7, 8, 10, 11].

The survival rates presented by literature in patients with dilated cardiomyopathy have shown different figures. The survival rates at 2 year follow-up was 52% for patients with restrictive LV diastolic filling as compared with 94% in patients with a nonrestrictive filling pattern (defined as prolonged DT) [4]. Another study has shown a survival rate with standard therapy of 84%, 73% and 61% at 1, 2 and 4 years respectively that is significantly poorer than that of age- and gender-matched population [9].

In our study the survival rates were calculated separately for the patients who underwent betablocker treatment or not. The figures at the 2 year follow-up for those who received standard treatment seams to be slightly lower than in the literature maybe because of the transplantation surgery which is not very well developed yet.

Previous studies have demonstrated that beta-adrenergic blocking therapy has a consistent beneficial effect on LV ejection fraction in cardiomyopathy patients [24] with a more variable and controversial effect on diastolic relaxation properties [20, 22, 23, 24, 25]. There was initially reported [23] an improvement in LV end-diastolic pressure with metoprolol. Subsequently, the MDC Study Group evaluated LV diastolic filling using transmitral Doppler echocardiography [20]. They reported that metoprolol resulted in a significant improvement in early LV diastolic deceleration times in cardiomyopathy patients. The maximum improvement in deceleration times occurred within 3 months of initiation of betablocker therapy. These observations in a large group of cardiomyopathy patients are consistent with an improvement in diastolic relaxation properties [21]. These was shown by our study in which the betablocker treatment associated to the standard therapy has influenced the diastolic filling pattern which remained restrictive at 2 year follow-up in 84.21% patients without betablocker treatment and only in 30.6% patients with betablocker treatment.

Conclusions

In patients with dilated cardiomyopathy, the presence of a restrictive left ventricular diastolic filling pattern is associated to a more unfavorable prognosis. This type of filling increased the risk of death and worsened the clinical status of the patients (quantified as NYHA class and the quality of life). On medium term, the use of betablockers associated with conventional therapy of heart failure was shown to improve the left ventricle diastolic filling and, in the same time to decrease the mortality rate and to improve the quality of life.

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Is it useful to review diagnosis criteria in arrhythmogenic right ventricular dysplasia? Update from literature data and case report*)

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Abstract

The purpose of this study is to determine whether it is useful to review the diagnostic criteria for arrhythmogenic right ventricular dysplasia (ARVD) and to compare the original criteria established in 1994 with the new criteria imposed by the current Task Force of European Society of Cardiology in 2010. Next, we choose a case report to highlight the diagnostic methods and means by which they are applied in current practice taking into account the guidelines indications. In the center of these complex and modern diagnostic methods, clinical judgement, remains a key element.

Keywords: *arrhythmogenic dysplasia, ventricular tachycardia, epsilon wave, syncope.*

Rezumat

Scopul acestei lucrări este de a determina dacă este utilă revizuirea criteriilor de diagnostic pentru displazia aritmogenă de ventricul drept (CAVD), precum şi de a realiza o comparaţie între criteriile originale stabilite în 1994 şi noile criterii impuse de Grupurile de Lucru ale Societăţii Europene de Cardiologie din 2010. În continuare am ales ca exemplu un caz clinic pentru a evidenţia metodele de diagnostic precum şi mijloacele prin care acestea sunt aplicate în paractica curentă, ţinând cont de indicaţiile ghidurilor. În centrul acestor metode complexe şi moderne de diagnostic, judecata clinică rămâne în continuare un element cheie.

Cuvinte-cheie: *displazie aritmogenă, tahicardie ventriculară, unda epsilon, sincope.*

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"You see only what you look for; you recognize only what you know."

Merril C. Sosman, [1]

In 1977, *Fontaine* and colleagues provided an anatomical and clinical description of several cases of ARVD (Arrhythmogenic Right Ventricular Dysplasia) discovered during surgical treatment of ventricular tachycardia [2]. "*Dr. Fontaine introduced me to this condition when I visited him in Paris in 1979. At that time he had personally seen 15 cases with ARVD since 1973. Since the patients were referred from a large geographic area, I realized that this was a condition that physicians were not recognizing because it was unknown to them. I decided to spend my sabbatical year studying this entity. Together with others at the* Jean Rostand Hospital, Ivry, France, *we published a composite clinical description of ARVD in 1982 [3]. In the 15 years since the publication of this paper, there has been considerable progress in our understanding of this disease in the following areas*", writes M. Sosman.

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a predominantly genetically determined and heritable form of cardiomyopathy (30-50% of cases have a familial distribution) characterized by pathologically replacement of myocytes with adipose and fibrous tissue leading to arrhythmias, right ventricular failure, and sudden cardiac death [4]. The estimated prevalence of ARVC/D in the general population ranges from 1 in 2, 000 to 1 in 5, 000, men are more frequently affected than women, with an approximate ratio of 3:1. ARVC/D can be inherited as an autosomal dominant disease with reduced penetrance and variable expression, autosomal recessive inheritance is also described. There have been 12 genes identified which are linked to ARVC/D, encoding several components of the cardiac desmosome [4].

The pathogenesis of ARVD is largely unknown. Apoptosis appears to play a large role. It is unclear why the right ventricle is mainly involved. Other authors suggested a pathogenic role for viral infection [4]. The disease process starts in the subepicardial region and works its way towards the endocardial surface, leading to transmural involvement (possibly accounting for the aneurysmal dilatation of the RV) [5]. Residual myocardium is confined to the subendocardial region and the trabeculae of the RV. These trabeculae may become hypertrophied. Aneurysmal dilatation is seen in 50% of cases at autopsy. It usually occurs in the diaphragmatic, apical, and infundibular regions (known as the *triangle of dysplasia*). The left ventricle is involved in 50-67% of individuals. If the left ventricle is involved, it is usually late in the course of disease, and confers a poor prognosis [6].

According to *Dalal et al.*, the median age at presentation of disease is 29 years. The most common symptoms are palpitations, syncope, and sudden cardiac death in 27, 26, and 23% of patients, respectively. Cardiac arrest may also be the first manifestation of disease due to malignant arrhythmias [7].

ARVD diagnosis should be considered in young pacients with syncope effort related, ventricular tachycardia which are also found in the presented case.

Ventricular tachycardia has a typically left bundle branch block morphology due to the fact that it arises from the right ventricle. The ventricular complexes could have multiple forms because of the multiple origins in different areas of the ventricle.

Arrhythmias are induced by adrenergic stimulation and this mechanism is probably responsible for the increased prevalence of ARDV among deceased during physic exercise [5].

There are discussions about the importance of new criteria and about the sequence of investigations used to achieve a quickly diagnosis.

Next, we choose a case report to highlight the diagnostic methods and means by which they are applied in current practice.

We report the case of 21 years old boy without significant medical history, complaining of palpitations with sudden onset and irregular rhythm that occur after meals and exercise, lasting on average between 1h and 2h, which led to two syncopes. Note that the palpitations history started about three years ago, but intensified a month ago when the patient went through a time of intense mental stress accompanied by an important exercise. Mind that the young man is not a professional athlete, but during free time he plays basketball, and he does mountain climbing.

The family history was negative for cardiovascular disease. He went to see a doctor after palpitations with rapid rhythm, prolonged duration (> 2h), which occurred while he was at rest, followed by a syncope.

Clinical and biochemical examination, in ambulatory setting, were within normal limits.

ECG examination (Figures 1a & 1b) and ECG Holter monitoring (Figure 2) was performed, followed by treatment with a beta-blocker agent.

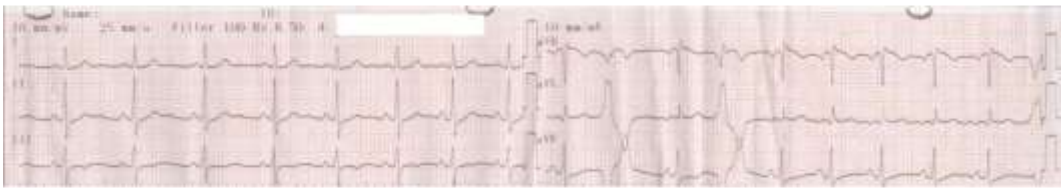

Figure 1a

Figure 1b

Figure 1: ***Ambulatory ECG examination: sinus rhythm, HR= 77 b/min, QRS axis at + 60 degrees, PR = 130 ms, QRS duration = 95ms, negative T waves in precordial leads V1-V3, consistent appearance of epsilon wave at the end of ORS complex, more obvious in V1 lead.***

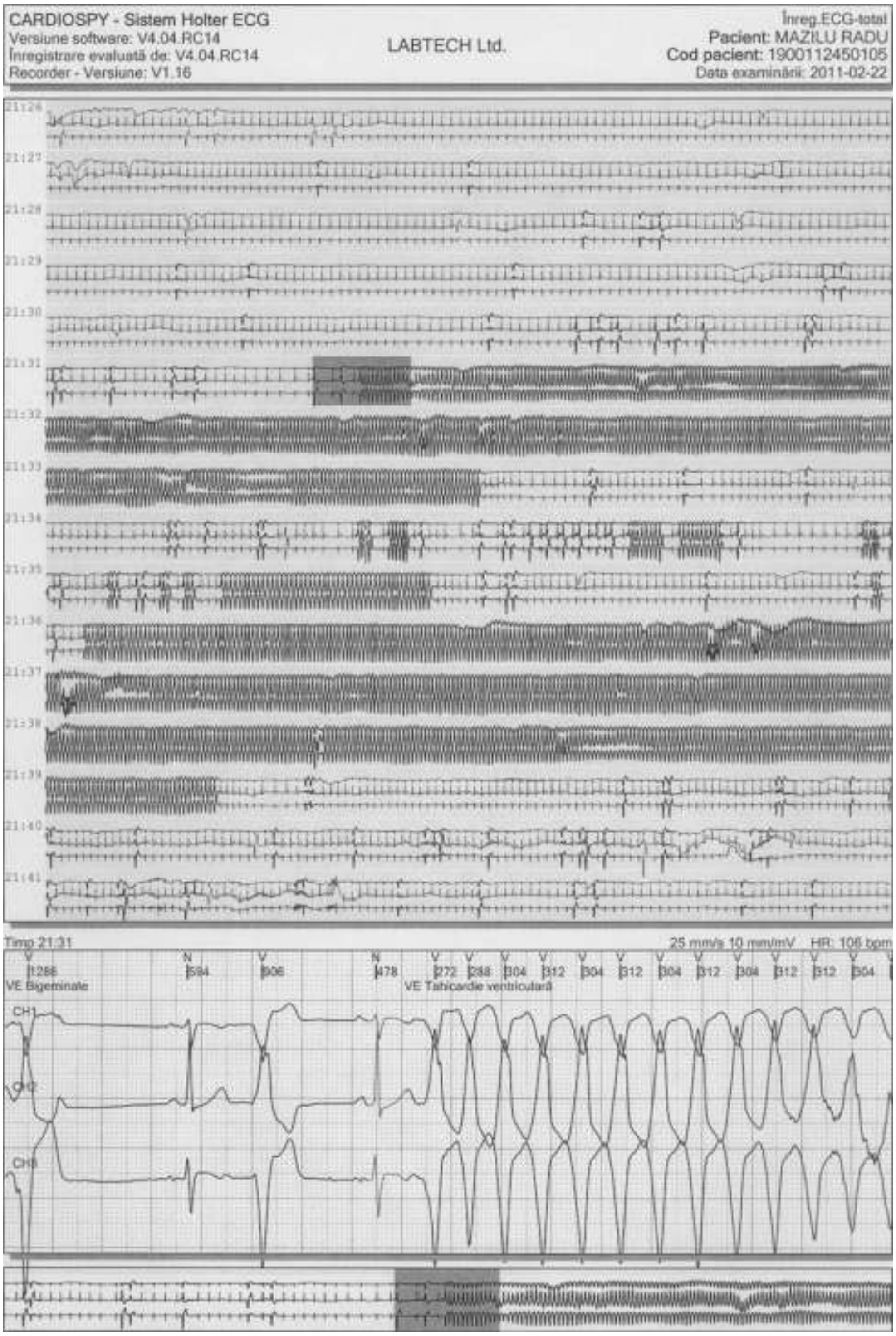

Figure 2: Holter ECG examination; shows episodes of ventricular tachycardia

Ambulatory Holter ECG examination, (done under treatment with beta-blocker agent, the recording corresponded with a symptomatic episode that the patient describes as the most intense he ever felt) indicates complex rhythm disorders: frequent supraventricular ectopic beats, premature ventricular complexes with systematisation tendency. The analysis of the entire Holter registration shows unsusteined ventricular tachycardia with two different morphologies of the QRS complex.

Given the symptoms correlated with exploration results and patient's history, ***the stage diagnosis*** was: recurrent syncope, unsustained ventricular tachycardia, premature ventricular complexes with systematic tendency (LBBB morphology), supraventricular extrasystoles.

The findings in the ECG (negative T wave in precordial leads and premature ventricular complexes with LBBB morphology), the ventricular tachycardia in Holter ECG examination the age of the patient and the temporary loss of consciousness after palpitations occurring with exercise, all led to the suspicion of arrhythmogenic right ventricular dysplasia.

The patient was hospitalized for further investigation to establish a diagnosis. On admission he performed an ECG at rest and an ECG with amplifier (+20) (Fig.3), late ventricular potentials were questioned (Fig.4), followed by investigation of cardiac morphology and function (Fig.5) and cardiac MRI examination (Fig.6).

Figure 3: ***Epsilon wave*****-detailListen**

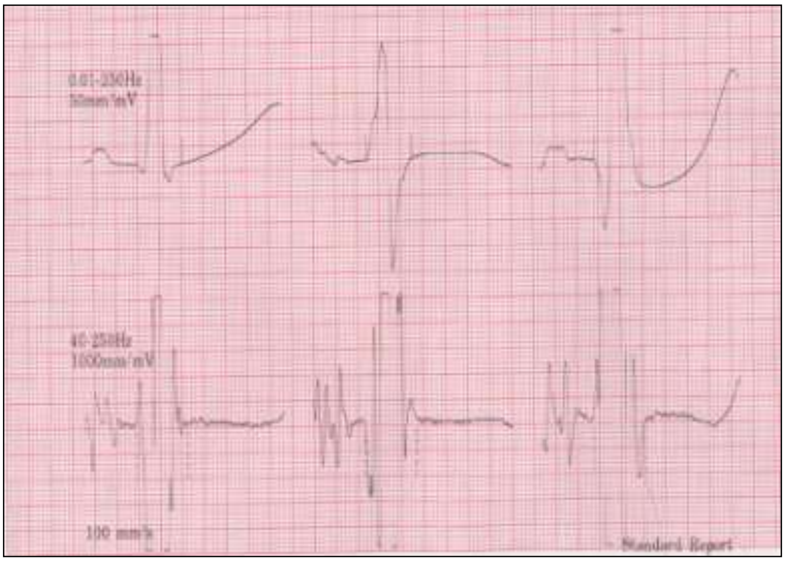

Figure 4: ***Ventricular late potentials:*** **indicates a total duration of filtered QRS > 113 ms, a single criterion was met, the sample was negative: late ventricular potentials were absent.**

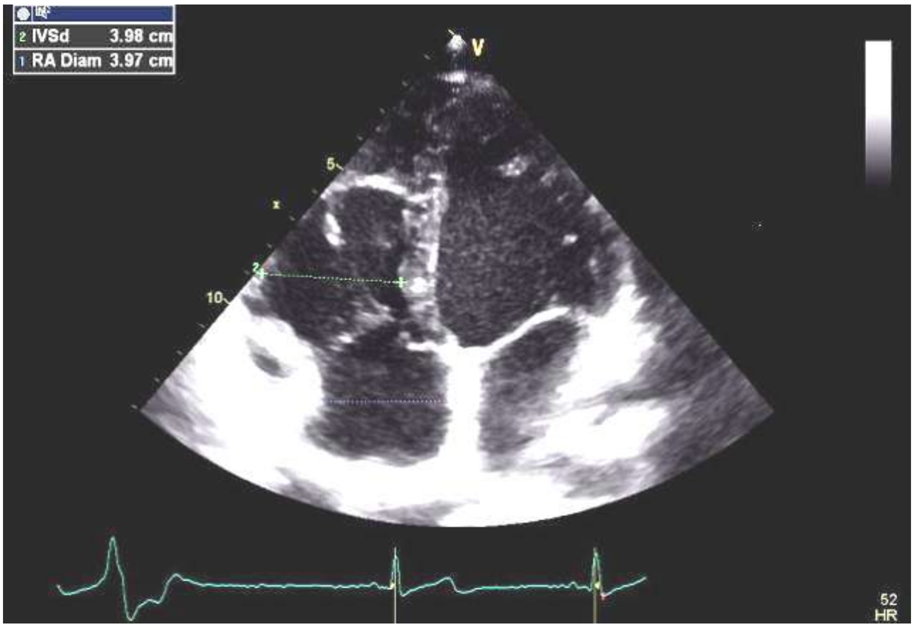

Figure 5: ***Transthoracic echocardiography:*** **in apical four chambers section indicates a dilated right heart with right ventricle with a diameter of about 40 mm.**

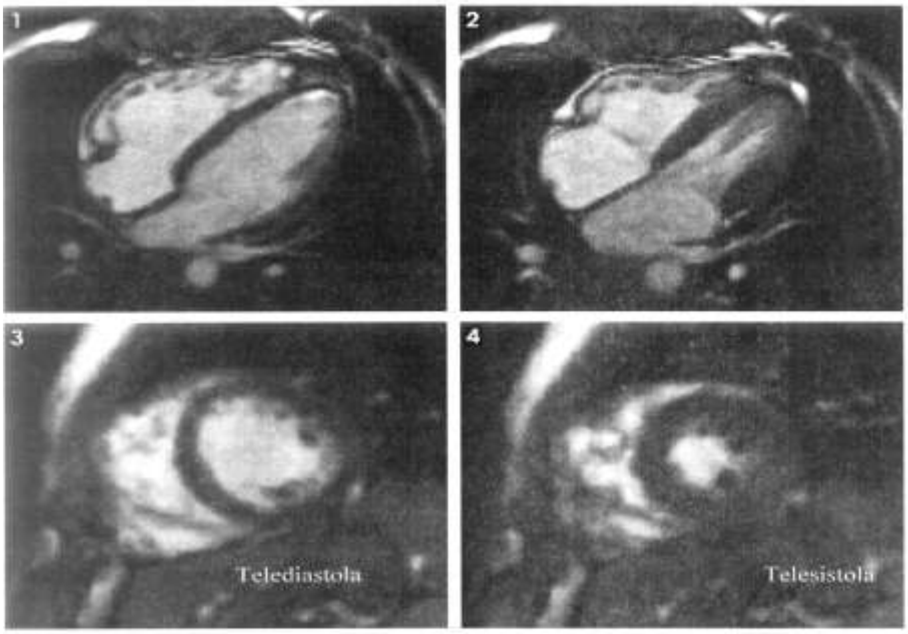

Figure 6: ***Cardiac MRI examination: end-systolic images (1.2) in apical four chambers section (1.2) shows a dilated right heart with an enlarged right ventricle that is restricted by the sternum during contraction, resulting in a fold of the free wall, and end diastolic images (3.4) in parasternal short axis section, is observed the left ventricle noncompaction and the presence of trabeculae in the LV wall.***

Echocardiographic data provides us with major criteria correlated to data from ECG and Holter ECG examination have led to **final diagnosis**: ***arrhythmogenic right ventricular dysplasia***, recurrent syncope, unsustained ventricular tachycardia, premature ventricular complexes with systematic tendency (LBBB morphology), supraventricular extrasystoles.

The patient in the presented case has a class IA indication for implantable cardiodefibrillator according to the current guidelines ACC / AHA / HRS 2008 on "*Implantable Defibrillator and resynchronization therapy in patients with arrhythmias"[8]* in order to prevent sudden deaths that overlaps with class IA indication of ACC / AHA / ESC 2006 for "*Management skills of patients with ventricular arrhythmias and prevention of sudden cardiac death" [9].*

Particularities of the presented case:

The young age at which the disease has become manifest, compared with an average age described in the literature about 29 years (Dalal et al [7]). The difference between the ECG and echocardiographic examination that was suggestive for ARVD and MRI examination that did not provide diagnostic criteria. Presence of numerous trabeculae in the LV from the middle of the cavity to the apex fulfilling the criteria for non-compaction at seven segnents only at the MRI examination unconfirmed by echocardiographic examination (onset of dysplasia in LV)?
Listen
Read phonetically

Discussion

Diagnosis of ARVD can be challenging. Original diagnostic criteria were established in 1994 based on structural changes, histological, echocardiographic as well as arrhythmias and family history. When these criteria were designed experience with ARVD was dominated by studies from patients with symptomatic disease, advanced disease or who died suddenly. Consequently these criteria were highly specific but lacked sensitivity in detecting early cases of disease or familial ARVD. Also, these criteria were rather qualitative than quantitative. In addition, it is known that electrocardiographic changes and arrhythmias may occur long before histological changes or right ventricular dysfunction, which proves the importance of early detection of the disease [4].

Marcus et al. modified the International Task Force Criteria for the clinical diagnosis of ARVD to incorporate new knowledge and improve diagnostic sensitivity. Latest studies comparing old and new criteria showed the superiority of the new criteria because of information from advances in genetic and electrophysiological studies plus they were compared with a significantly control group. New diagnostic criteria will assist clinicians, particularly in borderline cases and 1 degree relatives of patients with ARVD who often have an incomplete expression of the disease [10].

The ECG reveals changes in more than 90% cases. The most frequent findings are: T-wave inversions in V1–V3 in the absence of right bundle branch block (minor criteria for diagnosis). Right bundle branch block, prolongation of QRS complex, epsilon wave are considered distinct markers and major criterias for the diagnosis of ARVD [4]. The epsilon wave is caused by late potentials of low amplitude between the end of QRS complex to onset of the ST segment originating in the viable miocardum surroundead by fibro-faty tissue. From an electricaly point of view the wave reflects areas of delay and can trigger re-entry ventricular tahichycardia [5].

Fontaine named the epsilon waves. His personal account of his discovery was described in his March 5, 1997, letter to me [1], says Sosman. "... after discovering the first cases of late (or delayed) potentials recorded at the time of surgery on the epicardium of patients with resistant ventricular tachycardia. It was quite exciting to demonstrate that these late potentials located on the free wall of the right ventricle of patients with arrhythmogenic right ventricular dysplasia could be recorded on the surface by signal averaging and in some circumstances by increasing the magnification of ECG recording.

As late potentials were supposed to be the result of late activation of a limited group of fibers, the term "post-excitation" looked logical, since it was observed after the main excitation of the ventricle, leading to the QRS complex. The term "epsilon" was nice, because it occurs in the Greek alphabet after delta; thus, delta represents the preexcitation and epsilon the post-excitation phenomenon. In addition, epsilon is also used in mathematics to express a very small phenomenon..." [3]

Specific ECG markers show delay of the electric impulse in ARVD and Brugada Syndrome (BS) also. Althought BS is caracterised as an electrical disease recent data from MRI studies reveals an unexpectedly high rate of mild structural abnormalities. These findings suggest that BS may not be considered solely as a primary electrical disease. It is possible that initial electrical changes occurring in RV may play a fundamental role leading to structural changes [11]. Considering the symptoms and the ECG changes, the presented case is a tipicaly case of ARVD.

The echocardiography provides major criteria for diagnosis, the most suggestive aspect is dilatation of RV associated with local aneurysm. The investigators found that dilation of the RV outflow tract (>30 mm) using the parasternal view was an excellent parameter for diagnosing ARVD in the appropriate setting. They found, for example, that diastolic dilation of the RV outflow tract in the parasternal long axis view (>30 mm) was the most common abnormality occurring in 100% of the probands. Second, they clarified the strength of abnormal RV morphology in establishing the diagnosis. For example, anterior RV wall-motion abnormalities were common (70%), abnormally prominent trabeculations were seen in the majority (54%), and sacculations were seen in 17% [12]. In the case presented the echocardiographic examination showed enlarged right cavities (RA and RV≈ 40 mm), hypokinetic RV with heterogeneous structure of RV lateral wall and dilatation of the outflow tract providing major criteria.

MRI allows precise characterization of the function and anatomic structure of RV, highlighting the areas with akinesia, hypokinesia and regional dissincrone contraction of the RV [4]. The MRI examination of the case presented did not provide a diagnostic criterion for ARVD. Instead MRI confirmed RV dilation with increased volumes and indexed volumes and showed low RV ejection fraction = 41%, without regional or global wall motion changes or aneurysm lesions. It is also remarkable that the right ventricular free wall is compressed and in contact with the sternum. Arguments for which echocardiography was conclusive but magnetic resonance imaging did not provided criteria for ARVD can be explained by the fact that in MRI is difficult to estimate precisely the RV free wall thickness (which is thin and has a poor spectral resolution) and presence of large quantities of fat, compared with epicardial and pericardial fat normally present [5].

One of the most appreciated methods for diagnosis of ARVD is right ventricular angiography, but this exploration is an invasive maneuver, not without risks. In the presented case our echocardiography and MRI have provided sufficient data for diagnosis.

Endomyocardial biopsy can document the typical histological changes ARVD but has important limitations: false negative results due to the mosaic appearance with viable miocardium surrounded by fibro-adipose tissue [13].

Original International Task Force Criteria of ARVC/D were published in 1994, are based on structural, histological, electrocardiography (ECG), arrhythmic, and familial features of the disease (Tabel 1), and were modified by Marcus et al. in 2010 [14] so it can be adjusted to recent discoveries and in order to increase diagnostic sensitivity. In case of family members modification of diagnosis criteria was proposed by Hamid et al. [12] to account for the broader spectrum of disease that is observed in family members. In first-degree relatives of a patient, confirmed to be affected by ARVC/D, the presence of right precordial T-wave inversion, or late potentials on signal-averaged ECG, or ventricular tachycardia with left bundle branch block morphology, or mild functional or morphological changes of the right ventricle on imaging, should be considered diagnostic for familial ARVC/D, as well the threshold of premature ventricular beats of 200 over 24h in Holter monitoring [4].

Positive diagnosis is based on two major criteria, two major and one minor criteria or four minor criteria (Table No. 1.).

Table no 1: ***Diagnostic criteria for arrhythmogenic right ventricular dysplasia [5].***

Comparison between classic criteria with the recently proposed criteria [5].	
Original criteria in 1994	***Revised criteria recently proposed***
Major: ***Global or regional dysfunction and structural alteration*** **Major**: Severe dilatation and reduction of RV ejection fraction, with no (or only mild) LV impairment. Localized RV aneurysms (diskinetic or akinetic areas with diastolic bulging). Severe segmental dilatation of the RV	**Major:** ***2D Echocardiography:*** Regional RV akinesia, dyskinesia or aneurysm and one of the following (measured end diastole): - PLAX ROVT ≥ 32 mm (corrected for body size ≥ 19 mm/m2) - PSAX RVOT ≥ 36 mm (corrected for body size ≥ 21mm/m2) or fractional area change ≤ 33%. ***MRI:*** Regional RV akinesia or dyskinesia or dyssynchronous RV contraction and one of the following: - Ratio of RV end-diastolic volume to BSA≥110 ml/m2 for men and ≥100 ml/m2 in women or RV ejection fraction ≤40% ***RV angiography:*** Regional RV akinesia, dyskinesia or aneurysm.

Minor: Mild RV global dilatation and / or ejection fraction reduction with normal LV. Mild segmental dilatation of RV. Regional RV hypokinesia. Listen Read phonetically *Tissue characterization of walls.* **Major:** Fibrofatty replacement of myocardium on endomyocardial biopsy.	**Minor:** **2D Echocardiography:** - Regional RV akinesia or dyskinesia and one of the following (end diastolic) - PLAX RVOT ≥ 29 to <32mm (corrected for body size ≥ 16 and <19 mm/m2) - PSAX RVOT ≥ 32 and <36 mm (corrected for body size ≥ 18 and <21mm/m2) or fractional area change > 33% and ≤ 40%. *MRI:* Regional akinesia or dyskinesia or dyssinchronous RV contraction and one of the following: - Ratio of RV end diastolic volume to BSA ≥ 100 and <110 ml/m2 men and ≥90 and <100 ml/m2 in women or RV ejection fraction> 40% and ≤ 45%. **Major:** Residual myocytes <60% by morphometric analysis (or <50% if estimated), free wall with fibrous replacement of RV free wall myocardium in ≥ 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy. **Minor:** Residual myocytes 60-75% by morphometric analysis (or 50-65% if estimated), with fibrous replacement of the RV free wall myocardium in ≥ 1 sample, with or without fatty replacement of tissue on endomyocardial biopsy.ListenRead phonetically
Repolarization abnormalities **Minor:** Inverted T waves in right leads precordial (V2 and V3) (people aged> 12 years, in the absence of RBBB).	**Major:** Inverted T waves in right precordial leads (V1, V2 and V3) or beyons in individuals > 14 years of age (in the absence of complete RBBB QRS ≥ 120ms). **Minor:** - Inverted T waves in leads V1 and V2 in individuals > 14 years of age (in the absence of complete RBBB) or V4, V5, V6. - Inverted T waves in leads V1, V2, V3 and V4 in individuals> 14 years in the presence of complete RBBB).
Depolarization/conduction abnormalities. **Major:** Epsilon waves or localised prolongation ([110 ms) of the QRS complex in rightprecordial leads (V1–V3). **Mino**r: Ventricular late potentials	**Major**: Epsilon wave (reproducible low amplitude signals between end of QRS complex to onset of the and T wave) in the right precordial leads (V1-V3). **Minor**: - Late potentials by SAECG ≥ 1 of 3 parameters in the absence of a QRS duration ≥ 110 msec on the standard ECG. - Filtered QRS duration ≥ 114 ms - Duration of terminal QRS <40µV (low amplitude signal duration) ≥ 38ms. - RMS voltage of terminal 40 ms ≤ 20µV - Terminal activation duration of QRS ≥ 55ms measured from the nadir of the S wave to the end of QRS, including R 'in V1, V2 or

	V3 in the absence of complete RBBB). Listen Read phonetically
Arrhythmias **Major** **Minor:** Non sustaind or sustained ventricular tachycardia with LBBB morphology (ECG, Holter, exercise). Frequent PVC (> 1000 per 24 hours) (Holter)	**Major:** Non-sustained or sustained ventricular tachycardia of left bundle-branch morphology with superior axis (negative or indeterminate QRS in leads D II, III, and aVF and positive in lead aVL) **Minor:** Non-sustained or sustained ventricular tachycardia of RV outflow configuration, left bundle-branch block morphology with inferior axis (positive QRS in leads D II, III, and aVF and negative in lead aVL) >500 VES per 24 h (Holter)
Family history **Major:** Family history of ARVC/D confirmed at autopsy or surgery. **Minor:** Family history of premature sudden death (<35 years) because of suspected ARVD. Family history (clinical diagnosis based on present criteria).	**Major:** ARVD confirmed in a first-degree relative who meets current Task Force criteria. ARVC/D confirmed pathologically at autopsy or surgery in a first-degree relative Identification of a pathogenic mutation categorized as associated or probably associated ARVD in the patient under evaluation. **Minor:** History of ARVD in a first-degree relative in whom it is not possible or practical to determine whether the family member meets current Task Force Criteria. Premature sudden death (<35 years) due to a suspected ARVD in a first-degree relative. ARVD confirmed histopathologically or by current Task Force Criteria in a secound- degree relative.

In the case discussed four major criteria were met (presence of epsilon wave, ventricular tachycardia of RV outflow with configuration of LBBB morphology, negative T waves in right precordial leads, right ventricular outflow tract measured in parasternal long axis section ≥ 32 mm) and one minor criteria (the presence of frequent PVC in ECG Holter monitoring).

Pharmacological treatment uses antiarrhythmic agents. Currently there are insufficient data on their effectiveness in controlling malignant arrhythmias.ListeRead phonetically A study of Hiroi et al. [16] suggests that carvedilol is not only useful for controlling arrhythmia but also for improving left ventricular function in some patients with ARVC/D. If this is inadequate to control symptoms or to prevent recurrent VT, membrane active antiarrhythmic agents, such as sotalol and, if necessary, amiodarone should be considered. According to data of Wichter et al. [17] sotalol proved to be highly effective in patients with ARVC/D and inducible as well as non-inducible ventricular tachycardia with an efficacy of 68.4% and respectively 82.8%; In this study amiodarone did not prove to be more effective than sotalol and may not be an alternative because of frequent side effects during longterm therapy, especially in young patients. Verapamil and b-blockers were effective in a considerable number of patients with non-inducible ventricular tachycardia and may be a therapeutic alternative in this subgroup [4].

Indications for catheter ablation in subjects with ARVC/D include monomorphic and well-tolerated VT with localized forms of the disease and drug-refractory or incessant VT or frequent ICD discharges. The current mapping and ablation techniques include activation and entrainment mapping during tolerated VT and substrate ablation using threedimensional electroanatomic mapping systems [18]. In our case Holter monitoring showed episodes of ventricular tachycardia with different morphologies, which implies the existence of several arrhythmogenic areas in the right ventricle. Another aspect worthy of consideration is the fact that while benefiting from a primary successful intervention in 60-90% of cases, due to the progressive nature of the disease, recurrences are common (60%) [6].

The most important decision regarding ARVD management is to choose if implantable defibrillator (ICD) is needed. According to *Wichter et al* [19], an ICD is imperative if an aborted sudden death had occurred. In case of sustained VT and/or syncope, ICD is also indicated in the presence of risk factors (extensive RV dysfunction, LV involvement, polymorphic VT, late potentials and epsilon wave, family history).

The patient received indication according to current guidelines for implantable defibrillator with favorable results and the recommendation to continue the beta-blocker medication.

The treatment for severe right or biventricular dysfunction is in fact the classic treatment for heart failure. Heart transplantation represents an alternative in patients with refractory heart failure [5].

The new criteria increased the importance of early diagnosis of arrhythmogenic dysplasia, thus contributing to the prevention of ventricular tachycardia and sudden death in these patients.

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The saline irrigated radiofrequency ablation in surgical treatment of persistent atrial fibrillation*)

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Abstract

Background: *The study aims to evaluate the efficiency of saline irrigated cooled tip radiofrequency ablation (SICTRA) in the treatment of chronic atrial fibrilation in the patients who need simultaneous open heart surgery.*

Material and methods: *The study comprised 60 patients with chronic atrial fibrillation in association with mitral, aortic valve disease or atrial septal defect (ASD) consecutively randomized to have valve operation either with a Maze procedure (group A) or without (group B). The patients (P) in group A had simultaneously irrigated radiofrequency ablation and the heart surgery for the underlying heart condition. Out of the 30P, 16P needed mitral valve replacement, 6P mitral valve plasty, 3P mitral-aortic repalcement, 4P needed closing of the atrial septal defect (2 of these patients had an associated mitral valve defect), 4P had tricuspid valve plasty. The history of atrial fibrillation disease in the study group was in average 4.8 years. A tissue controlled impedance, saline irrigation monopolar ablation system, was used for the study (Cardioblate Medtronic Inc., MN).*

Results: *At 6 months upon hospital discharge 24P (80%) from group A had sinus rhythm, compared with 9P (27%) from group B. One patient needed a pacemaker implant and 4P needed an electrical conversion to sinusal rhythm in the first 6 months after the surgery. At Hospital discharge the following medications were prescribed: Cordarone in 18P, Digoxin in 8P, Propaphenone in 3P, and a beta-blocker in 5P. Post-op complications were: atrial fibrillation 7P, intermittent atrio-ventricular block 4P, post-op hemorrhage 2P. There were no post-op or follow up deaths.*

Conclusions: *The radiofrequency ablation on the medium and the short term was efficient in 80% of the cases without significantly prolonging the ishemic time onthe cardiopulmonar by-pass. In the study group no complication were noted in regard with the procedure. The method proved it's efficacy in the treatment of chronic atrial fibrillation, justifying an extensive use of the procedure.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2008, vol. 7, no. 1, pp. 7-14**

Background

Atrial fibrillation (AF) is the most frequent cardiac arrhythmia and accounts for 0.4% of the general population (1). In approximately 30% to 40% of patients undergoing mitral valve surgery, chronic AF was present before the operation and in most patients the arrhythmia will persist after correction of the primary disease (2, 3). Several other studies have reported on long-term follow-up of cardiac rhythm after electrical cardioversion after mitral valve surgery but the maintenance rate of sinus rhythm does not seem satisfactory (4, 5, 6, 7). Cox and associates have developed the maze procedure as a surgical treatment for patients with drug-refractory AF (8, 9). Nevertheless the Cox maze procedure is complex with long surgical procedure time and this has been hampering the widespread use in cardiac surgical patients with AF. In an attempt to simplify the procedure modifications have been developed including the use of cryoablation and changes in atriotomies (10, 11) and application of radiofrequency energy (12, 13). In the present study we report the long-term results of the irrigated radiofrequency modified maze procedure as an additional procedure in 200 consecutive patients with chronic AF undergoing concomitant cardiac surgery.

The "cut and sew" technique is most effective to create intra-atrial transmural lesions, which act as electrophysiological barriers, interrupting the multiple wavelet reentry circuits, resulting in extinction of atrial fibrillation. The Maze procedure, as described by Cox and colleagues (14), is a blueprint comprising the precise localization of the various biatrial incisions. However, this operation is, in our opinion, extensive and complex. Substantial surgical experience is required to match the excellent results reported by Cox and colleagues. To facilitate the operative procedure, we used saline irrigated, cooled-tip radiofrequency ablation (SICTRA) to create intraatrial linear lesions. The rationale of the SICTRA is the ability to create intra-atrial transmural functional linear lesions, which act as electrophysiological barriers, but without causing any atrial tissue dehiscence, therefore obviating the need for "sewing the cut edges." However, the effectiveness of the SICTRA to abolish atrial fibrillation and safety of the technique need to be evaluated. Therefore this prospective randomized study was designed and initiated at our institution.

Patients and Methods

From April 2003 to May 2007, 60 patients with documented chronic atrial fibrillation older then 6 months (group A) were randomized consecutively to have cardiac valve operations either with a Maze procedure or without (group B). Thirty patients were simultaneously treated for the underlying heart condition and the atrial fibrillation (group A). Each patient had before surgery a standard 12-lead ECG and a transthoracic echocardiography (TTE). All the patients from the study group (group A) benefited from left atrial model, excepting those associating atrial septal defect or tricuspid plasty in wich we used biatrial lesions. The technique we used was similar with that described by other authors (15, 16).

From the study group most of the patients had mitral valve lesions (18/30); 3P presented tricuspid valve lesions, 1P presented an atrial septal defect and 1P presented an association of these two conditions. 8P were diagnosed with mitro-aortic lesions, one of the patients also had a stent for a coronary disease. Only one patient presented an isolated tricuspid lesion (Figure 1).

The surgical techniques used for the study group patients (Figure 2) consisted mostly in mitral valve surgery (22/30); from this group 16P had a mitral valve (46%) and 6P had valvular plasty (20%). 3P had a double mitro-aortic valvular replacement (9%) and 4P had tricuspid valve plasty (11%), from this 4P, 3P also had other valvular interventions. Only one patient presented an isolated aortic valve lesion (3%).

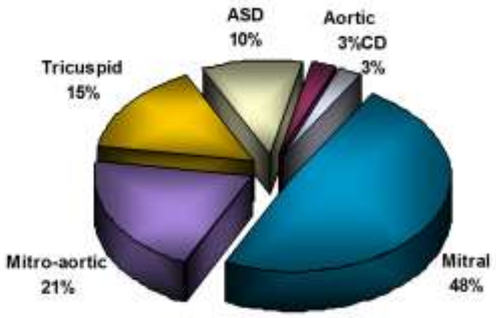

Figure 1: Pathology distribution in group A

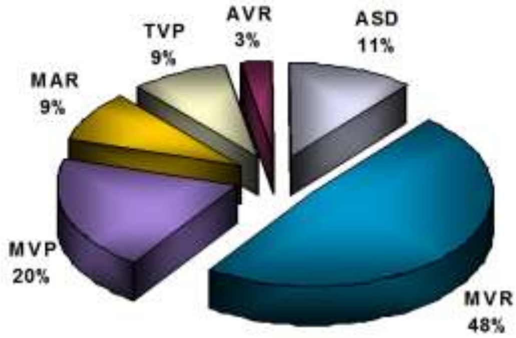

Figure 2: Surgical techniques used for the group A patients: mitral valve replacement (MVR), mitral valve plasty (MVP), tricuspid valve plasty (TVP), mitro-aortic valvular replacement (MAR), aortic valve replacement (AVR), atrial septal defect closure (ASD)

The patients from group B presented mitral valve disease in proportion of 93.3% (28/30), from which 7 had structural lesions of the tricuspid valve that needed valvular plasty. Two patients presented mitro-aortic valvular disease and had bivalvular replacement. Overall, the operations to this group were: mitral valve replacement (21/30), mitro-aortic valve replacement (2/30), tricuspid valve plasty (7/30) (Figure 3).

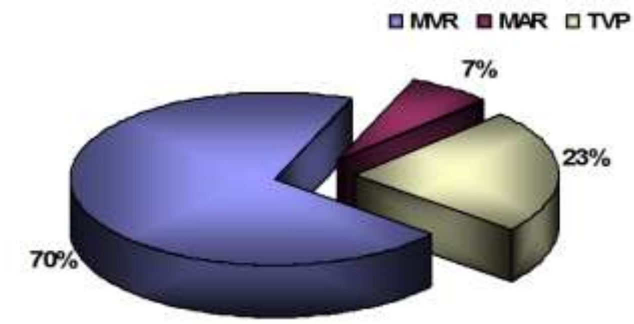

Figure 3: Surgical techniques used for the group B patients: mitral valve replacement (MVR), tricuspid valve plasty (TVP), mitro-aortic valvular replacement (MAR)

The necessary for SICTRA consists of SICTRA (Sprinklr; Medtronic, Minneapolis, MN) catheter, having a 7F diameter (2.33 mm) with a length of 4 mm and with 13 irrigation holes. The catheter was connected to a NaCl 0.9% perfusion bag through an infusomat. The flow volume was 250 ml/hour. The catheter was connected to a radiofrequency generator (Cardioblate-Medtronic). The system was programmed usually to a 25 W power. When we considered that 25 W were to low we increased the power to 30 W. Cardioblate was connected to a neutral electrode, which was fastened by the patient back, and to a pedal for the generator.

The Maze Procedure

The access was made through standard median sternotomy. We cannuled the aorta, *superior vena cava* (SVC), *inferior vena cava* (IVC). After the standard cardiopulmonar bypass was started we administered tepid blood cardioplegia.

Radiofrequency ablation at the right atrium (Figure 4, Figure 5)

Figure 4: Radiofrequency ablation lines and incisions at the right atrium

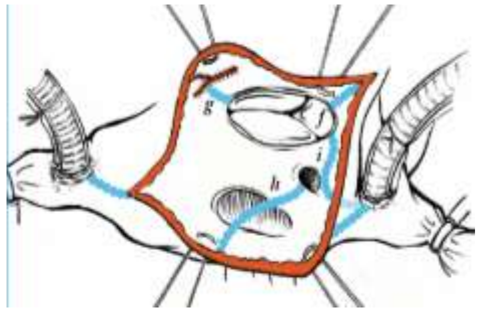

Figure 5: Radiofrequency ablation lines inside the right atrium

It can be done before clamping the aorta, on the beating heart, with both caval canulas snared. Because we used right atrial ablation only in patients who needed tricuspid valve plasty or closing of DSA, all the right atrium procedures were done on the stopped heart, after cardioplegy administration.

Radiofrequency ablation at the left atrium (Figure 6, Figure 7)

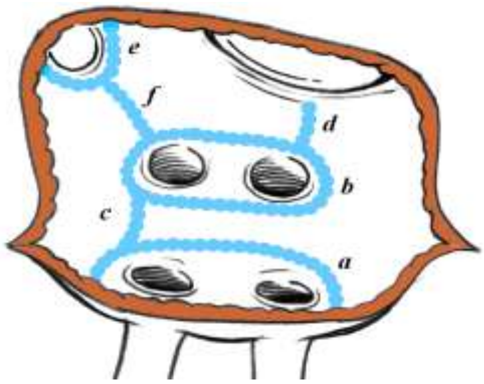

Figure 6: Radiofrequency ablation lines at the left atrium

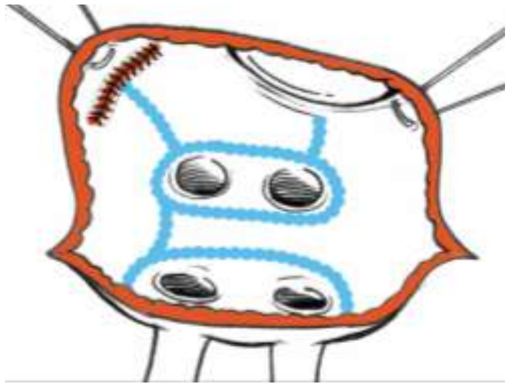

Figure 7: Radiofrequency ablation lines at the left atrium with suture of the left atrial appendice

After the aorta was clamped and the antegrade cardioplegia administred, the left atrium was opened at the level of interatrial groove with extension to the left atrium roof.

Recognizing the anatomic landmark of the left atrium requires the adequate traction of the anterior wall of the atrium with a Cooley retractor or with 2 retractors. Similar to the mitral valve surgeries only an adequate venous drainage may provide an efficient traction and a better access and a better blood control in the operatory field.

With regard of the isolation of the left atrial appendage there is a wide discrepancy of opinions. At first the resection and the suture of the appendage were practiced but this technique proved a significantly increase of the post-op morbidity by hemorrhagy. Because of that, most authors today prefer the endo-cavitar closing of the appendage with a Prolen 4-0 suture. We considered the closing of the left appendage only if a blood clot was found inside it or if embolic episodes were present in the patient history. The closing of the left appendage was usually done through an external ligature and only in the case of adherences or for second surgery the left atrial appendage was sutured from inside. All the time, we marked a circumferential ablation line at the base of appendage and another line from the level of the left lateral margin of the superior pulmonary vena to the level of the left appendage.

At the heart level we placed a pacemaker with the atrial inhibition mode (AAI), if possible, or DDD mode. The patient was disconnected from the cardiopulmonary bypass and the thorax was closed in the standard mode.

Post-op care

The patients were supported with atrial inhibition mode (AAI) or DDD mode pacing if the pulse was under 75 (*beats per minute*) bpm in the first 7 days after surgery. The post-op antiarrhythmic protocol consisted in iv administration of amiodarone (Cordarone) immediately after intensive care admission at a dose of 900-1200 mg/24h, continued with 600 mg/day tid in the first day after surgery and lowering gradually the dose to a maintenance dose of 200 mg/day. The proportion of patients to follow the Cordarone treatment was 66% (20/30). No Cordarone was administrated in the patients who developed sinusal bradicardia or AV block in the surgery follow-up course. In the same time 3P had a contraindication to the amiodarone treatment (alergy, thyroid condition) and 2P were treated with propaphenone for arrhythmias. A patient had her medication changed by another doctor from Cordarone to propaphenone, afterwards being electrically converted to sinus rythm at 6 months post-op (BD). Most of the patients who were on digitalis medication before surgery continued the digitalis treatment after surgery (9/30, 30%). Overall, we avoided the administration of beta-blockers, like Metoprolol or Sotalol, for the treatment of arrhythmias in the post-op care. This was due partly to the fact that most of the patients were already on antiarrhythmic medication (amiodarone or digitalis) which assured a good cardiac heart rate control. But on the other side from the literature evidences and our experience there is a relatively high risk of sudden death or life threatening rhythm disturbances in this category of patients, especially after Sotalol administration. All the patients who followed the betablockers treatment already had this treatment before the surgery (Metoprolol 50-100 mg q 12h) to which Cordarone was added when considered necessary.

The patients who during the hospital treatment had a atrial fibrillation relapse were administered the quick iv amiodarone loading protocol (300 mg/h, followed by another 300 mg in the next two hours, continued with 600 mg in the next twenty hours). If the Cordarone did not re-establish the sinus rhythm electric cardioversion was taken in consideration. Cardioversion protocol consisted in administering a sincron electric shock of

240 J after administering Propofol iv; if needed, another shock of 360J was administered. After 6 months no cardioversion was done anymore. All patients received coumadin from the first post-op day, with an endpoint of INR 2.8-3.2.

Follow-up period

The data was obtained from each patient in the first, tenth, day after the surgery and then in the third, sixth, ninth, twelveth and the twenty-forth month after the surgery. At each visit the history of the condition, the clincal exam and the ECG were taken. A transthoracic echo including the transmitral and transtricuspidian Doppler examination were done at three, six and twelve months. The survival related information was complete. The variables followed were expressed as an average value with a standard deviation. The survival rate was calculated through the Kaplan-Meier method. The cumulative rates of sinus rhythm in the postoperative period were calculated.

Results

The patient characteristics, except for age (53 versus 59.7 years; p = 0.0031) and sex distribution (female to male ratio: 20:10 versus 21:9), were similar in both groups (Figure 8).

	Group A	Group B	p
Age (years)	53.0	59.7	0.0031
AF History (years)	4.8	3.8	0.1642
LA Diameter (mm)	53.4	57.4	0.5981
EF (%)	53,8	54,1	0.9032
Aortic Clamping (min)	67,56	64,33	0.0205
SR at 6 months (%)	80	27	0.0001

Figure 8: patients' characteristics in mean values and the correlation factor (*p*) between the 2 groups

The 30-day mortality was zero. Postoperative morbidity included post-op bleeding (2 patients in group A). One group A patient received a permanent pacemaker because of a bradycardia. The 12-month follow-up was complete, although 2 group B patients were unable to revisit our outpatient cardiology clinics. The respective cumulative frequencies of sinus rhythm after 3 and 6 months for the group A and B patients were 0.76 and 0.8 for group A and 0.3 and 0.267 for group B (p = 0.0001) (Figure 9, Figure 10). The number of group A patients who were in SR with an atrial contraction (transmitral A-wave) was 16 (69.5%) at 3 months postoperative and 20 (83.3%) at 6 months. For the group B, all patients who were in SR had left atrial contraction. Right atrial contraction (transtricuspid Awave) was detected in all patients in SR.

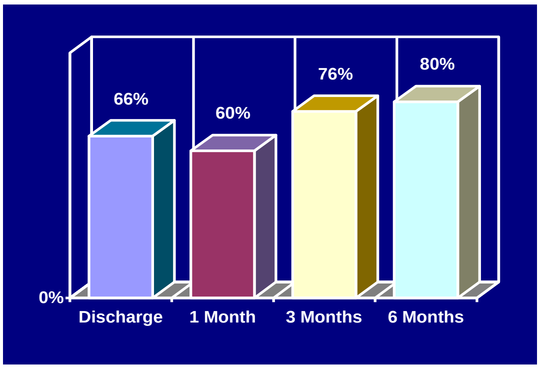

Figure 9: The cumulative rate of sinus rhythm at 1, 3 and 6 months in group A

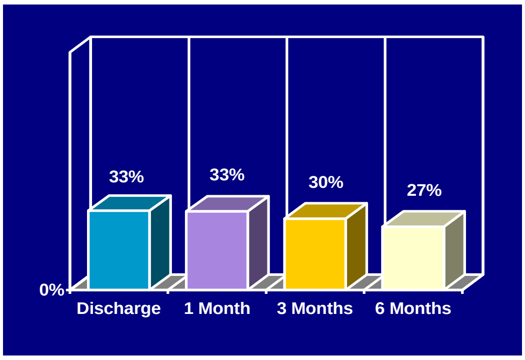

Figure 10: The cumulative rate of sinus rhythm at 1, 3 and 6 months in group B

Statistical data

Continuous variables were expressed as mean standard deviation (median). Student's unpaired *t-test* (two-tailed) was used for comparison in between the two groups. Differences were considered significant at a p value less than 0.05. The survival rate and maintenance rate of sinus rhythm (SR) were calculated according to Kaplan-Meier method and groups were compared using *log rank-test* (significant difference postulated at $p < 0.05$).

The group A patients ($n = 30$), from which 20 females and 10 males had an average age of 53.03 ± 7.8 years (in between 32-69), an average history of atrial fibrillation before surgery of 4.74 years (58 months), an average left atrial diameter of 53.4 ± 0.67 mm, an average ejection fraction of 53.8 ± 0.95 %. In 24 patients the left atrial lesional model was used while for 6 patients the biatrial lesional model was used.

The post-op complications included transitory bradicardia in 13.3% (4/30) of the cases atrial fibrillation episodes which necessitated electric or drug induced conversion 3.3% (10/30) and post-op bleeding 6.6% (2/30) of the cases.

Post-op hemorrhage occurred in 2 cases. The site of post-op hemorrhage was located at the level of the sternum and diffuse bleeding secondary to a coagulation disturbance (INR-6.99) in the third post-op day. In the first patient we intervened three hours after surgery, the indication being provided by the increased retrosternal drenage (>200 ml/hour) and the hemostasis was achieved at the sternal level with a favorable outcome. The second case developed a late cardiac tamponade which necessitated the placement of a drainage tube through a subxiphoid incision, eliminating 400 ml sanguinolent liquid. In this case too the outcome was favorable.

During the follow-up, none of the patients died. Considering all patients who remained in SR, the cumulative rate of SR is overall shown in Figure 9 and 10.

At three months 23 patients in group A had a stable sinus rhythm defined by the 95-100% presence of sinusal rhythm at the Holter ECG. The biatrial contraction was noticed at 16 (69.5%) patients, the atrial right contraction in 5 patients (21.7%), the absence of atrial contraction was noticed 2 (8.6%) patients. At six months 24 patients had a stable sinus rhythm defined by the 95-100% presence sinusal rhythm at the Holter ECG. The biatrial contraction was noticed at 20 (83.3%) patients, the right atrial contraction in 3 (12.5%) patients, the absence of atrial contraction was noticed in 1 (4%) patient.

Complications

In our series, the incidence of post-op complications was under the expected rate. Post-op hemorrhage was never associated with a radiofrequency ablation. During the follow up none of our patients presented signs or symptoms of injured esophagus, circumflex artery or the pulmonary vein orifice.

The safety and efficiency are two important criteria for evaluating the different techniques. Two potential causes may increase the post-op morbidity and mortality: first, prolonging the surgical procedure and second, the surgical technique, including the ablation and lesional model per se. The aortic cross-clamping time for performing the anti-arrhythmic procedure varies in between 10 and 17 minutes in the patients with the mitral valve affected. (17) In the patients with aortic valve replacement or myocardial revascularization the clamping time was doubled because it is more difficult to penetrate the left atrium to perform the various ablation lines at a small left atrium. Moreover the additional time of utilization of the extracorporeal circulation method in the biatrial procedure is 26 minutes, compared with the procedure performed at the left atrium only.

Mortality

In the group of patients taken into the study no death was recorded. The indication and selection of the patients presenting high risk who needed the combination of surgical procedures should be established carefully when an increase in the morbidity and mortality after the surgery is expected. However the potential benefits of re-establishing sinusal rhythm with atrial contraction at the high risk patients may be important because an increase in the diastolic volume of the left ventricle is expected.

Sinus rhythm

In our series the cumulative rate of sinus rhythm upon the hospital discharge and at one month, 3 months and 6 months after the surgery were 63.3% (19/30), 60% (18/30), 76.6% (23/30) and respectively 80% (24/30) – see Figure 9. At one month post-op 3 discharged patients in sinus rhythm had an atrial fibrillation relapse, maybe in part due to an insufficient and incorrect antiarrhythmic medication while 2 patients had a spontaneous sinus rhythm induction. After the first 3 months post-op 5 patients recovered sinus rhythm from which one through a drug induced conversion with propaphenone, three through electric conversion and one spontaneously. At 6 months two patients were converted electrically and one drug induced to a sinus rhythm. All 6 patients who had an electric or a drug induced sinus rhythm preserved the sinus rhythm over the entire follow-up duration. One patient, who had a spontaneous sinus rhythm conversion in the first month, had a relapse to atrial fibrillation and refused electric conversion. Our series included the chronic atrial fibrillation patients with an average of 58 month of the fibrillation duration.

All our patients had valve surgery and/or closing of ASD. The atrial fibrillation was never the main reason of the heart surgery. The patients with paroxystic atrial fibrillation were excluded from our study. Therefore our group of patients is not similar with those reported by Cox, Schaff, Millar et al. (18, 19, 20) The rate of sinus rhythm induction after surgery noticed by us resembles more that published by Mohr, Benussi, Williams and Sie, who reported a rate of sinus rhythm in between 66.7 and 81%.

The gradual increase of the conversion rate to a sinus rhythm in our series starting with 66% immediately after the surgery up to 80% after 6 months matches with the other authors' data. Also Cox described immediately after the surgery the appearance of atrial fibrillation in 47% of his patients.

Failures

One month after the surgery 12 patients from group A were in atrial fibrillation. The electric cardioversion was successful in 4 cases and the drug induced cardioversion was successful in 2 cases, by having the sinus rhythm at the next visit (at 6 months), 5 patients still had atriall fibrillation and one patient had a relapse to atrial fibrilation after an initial spontaneous conversion to sinus rhythm. The actuarial failure rate in our series is 20% (6/30), from which one needed a pacemaker (3.33%) implant for atrial fibrillation with low ventricular response. We should consider 2 main causes of these failures: (1) a non-transmural atrial lesion caused by an inadequate ablation line, (2) an inadequate lesional model. The atrial flutter may have two important origins: the isthmus at the right atrium level or a comunication preserved in between the left and right atrium through the coronary sinus. The right atrial flutters were successfully ablated while the left atrial flutters were treated with AV ablation and DDD pacemaker implant.

Conclusions

The completion of a simultaneous antiarrhythmic surgical procedure obviously prolongs the procedure; however it does not cause a significant difference in regard with morbidity and mortality. SICTRA had an increased rate of sinus rhythm outcome in our series, and even in the high risk patients who had a chronic atrial fibrillation we had positive results of conversion to sinus rhythm. No complications were noted in correlation with the ablation procedure per se.

The radiofrequency with irrigation proved to be safe and efficient. The results are promising. The simultaneous antiarrhythmic surgery, especially in the low risk patients is highly recommended. In the high risk patients the indication should be adapted to each particular case, especially when a post-op increase of mortality and morbidity is expected. On the other hand, the high risk patients will have, at least theoretically, an important benefit if the sinus shythm conversion with atrial contraction takes place.

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Electrocardiographic challenges in patients with potassium abnormalities*)

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Abstract

Potassium, the most abundant intracellular cation, is critically important for many physiologic processes, including maintenance of cellular membrane potential, homeostasis of cell volume, and transmission of action potentials in nerve cells. Therefore, potassium is necessary for the normal functioning of the muscles, heart, and nerves. A great number of metabolic disorders could be associated with potassium abnormalities.

Experimental and human studies have demonstrated that serum potassium imbalance is followed by progressively severe electrophysiological derangements in cardiac impulse generation and conduction. These electrophysiological changes are reflected in the electrocardiogram (ECG) manifestations, with specification that the ECG tracing reflects more faithfully the potassium extracellular concentration.

Though laboratory tests are "the gold standard" for the diagnosis of potassium abnormalities, they have the disadvantage of delivering the information with delay. Thus, the electrocardiogram (ECG) becomes a very useful instrument for diagnosis.

Keywords: *cation, hyperkalemia, hypokalemia, electrocardiogram (ECG), repolarization.*

Introduction

Potassium (K) is the most abundant intracellular cation. Almost all (98%) potassium in the body is found inside the cells (intracellular) and only about 2% occurs in the fluids outside of the cells (extracellular). The concentration of potassium is often expressed in units of milliequivalents per liter (mEq/l), rather than in units of millimolarity (mM). Both units mean the same thing when applied to concentrations of potassium ions. Normally plasma potassium concentration ranges from: 3.5 – 5.0 mEq/l.

The contribution of potassium to resting membrane potential is related to this ratio of intracellular to extracellular potassium.

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The mild to moderate changes in plasma potassium value are relatively poor associated with ECG tracing (10 - 30%), while the severe abnormalities have more specific ECG expression (90%).

The specific ECG changes caused by electrolyte imbalance are usually reversible and their development and regression follow a predictable course.

Hyperkalemia

Hyperkalemia is a common electrolyte disorder with potentially life-threatening consequences. Hyperkalemia is often silent, could occur suddenly, and leads to cardiac arrhythmias and potentially to death [1].

In the general outpatient population, the incidence is relatively low and not well reported. In hospitalized patients, incidence ranges from 1% to 10%, with a mortality rate of 1 per 1000 patients [2, 3].

A value of plasma potassium between: 5.5 - 6.5 mEq/l reflects mild hyperkalemia, moderate hyperkalemia for a range of 6.5 - 8 mEq/l and severe hyperkalemia over 8 mEq/l.

The incidence of hyperkalemia in the general population has been reported in less than 5% of people. The most common causes are potassium shift from the intracellular to the extracellular space, impaired excretion due to renal failure, or medications, with most patients having multiple etiologies. Risk factors include advanced age, significant prematurity, and the presence of renal failure, diabetes mellitus, and heart failure. Additionally, one series documented an increased incidence of hyperkalemia with cancer and gastrointestinal disease [4]. Polypharmacy, particularly the use of potassium supplements and potassium-sparing diuretics, in patients with underlying renal insufficiency contributed to hyperkalemia in almost one half of the cases.

Because hyperkalemia can lead to life-threatening cardiac arrhythmias, prompt recognition and diagnosis are crucial. Patients with severe hyperkalemia could present with generalized weakness, paralysis, arrhythmias, or sudden cardiac arrest.

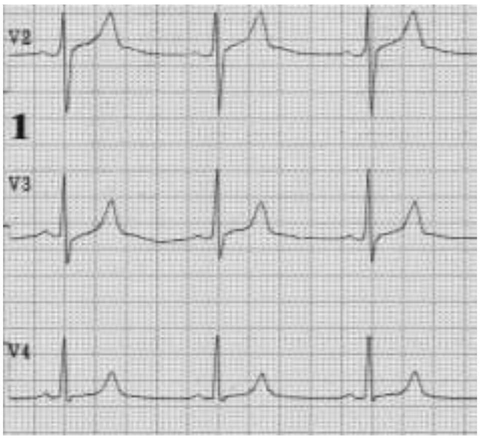
The most prominent effect of hyperkalemia is on the myocardium. The generation of a resting membrane potential is crucial for cardiac myocyte contraction. Movement of potassium into the intracellular space via the sodium-potassium adenosine triphosphatase pump is responsible for the – 90 mV resting membrane potential. As the extracellular potassium concentration increases, the concentration gradient across the myocyte cell membrane decreases, eventually leading to a slowing of myocardial functioning [5].

Electrocardiographic (ECG) findings could provide the first evidence of hyperkalemia, but there are studies which show that a correct ECG diagnosis can usually be made when plasma potassium concentrations exceed 6.7 mEq/l [6]. In contrast, Tarail [7] found that patients with renal insufficiency did not consistently have ECG changes typical of hyperkalemia until the serum potassium concentration exceeded 7.6 mEq/l. It has been postulated that levels of potassium greater than 8 mEq/L are almost always associated with the classic ECG manifestations [8].

The relationship between the degree of hyperkalemia and the ECG changes, however, is variable, and in rare cases of severe hyperkalemia the ECG may even be normal or near normal. Briefly, in mild hyperkalemia T waves changes occur (because of the acceleration of terminal repolarization), than in mild-to-moderate where PR interval is frequently prolonged and QRS complex is wide. In clinical practice it was noticed that ECG changes for mild and moderate hyperkalemia are known, while severe hyperkalemia is often source of error.

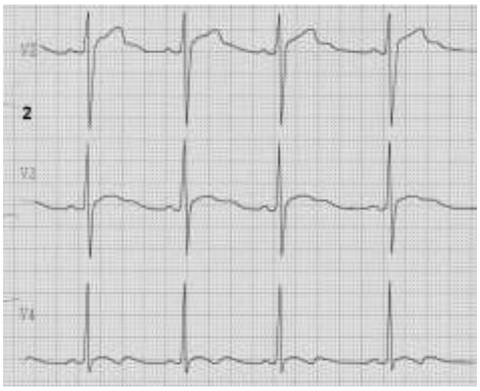
Further, we present some ECG aspects related to plasmatic potassium (Kp) concentration.

When the plasma K concentration exceeds approximately 5,5 mEq/l, the T waves become tall, symmetric, narrow and peaked, tented as if pinched from above because of the faster repolarization of the cardiac action potential; usually they are best seen in leads II, III, V2 and V4 **(Case I)**. The P waves and QRS complexes are normal. The QT interval is shortened at this stage, associated with decreased action potential duration.



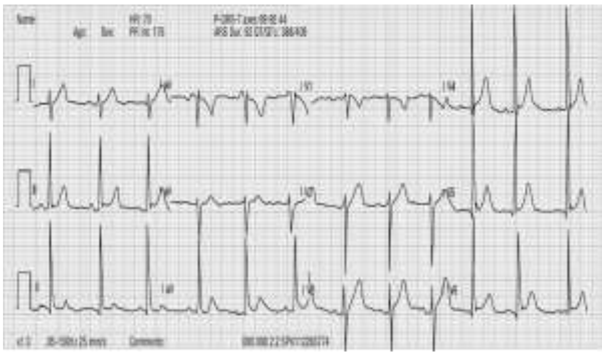
Case I.
Electrocardiograms of a 57-year-old male with dilated cardiomyopathy treated with spironolactone.

(1) Plasma *K* concentration (*Kp*) is 6.1 mEq/l. There is a regular rhythm at a rate of 60 beats/min, T waves are tall, narrow and pointed in leads V2 - V4.



(2) After treatment, *Kp* is 4.2 mEq/l. Note that T waves are lower in leads V2 - V3, and biphasic in lead V4;
U wave is seen too.

Hyperkalemia cannot be diagnosed with certainty on the basis of T wave changes alone. Braun et al. found that the characteristic tall, steep, narrow and pointed T waves were present in only 22 percent of patients with hyperkalemia [9] and so, it is necessary to make the difference with hyperacute ischemic changes (where T waves are symmetric, broad-based, not tented, not pointed; the QT interval tends to be long) or a normal variant (where T waves are asymmetric and not narrow, frequently associated with sinus bradycardia) - **Case II**.



Case II.
Electrocardiogram of a 30-year-old male, sportsman, complai-ning of pricking chest pain. Plasma *K* concentration is normal. There is a regular sinus rhythm at a rate of 70 beats/min and signs of early repolarization.

Progressive extracellular hyperkalemia reduces atrial and ventricular resting membrane potentials, thereby inactivating sodium channels, which decreases *V*max and conduction velocity.

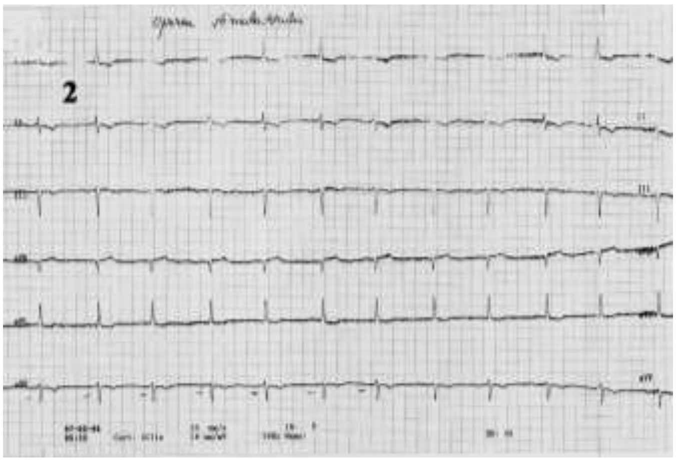
When the plasma K concentration exceeds 7 mEq/l the QRS complex begins to widen, P wave amplitude decreases, and the duration of the P wave increases because of the slower conduction in the atria. The PR interval prolongation can occur, followed sometimes by second or third – degree AV block.

Characteristically, the uniformly wide QRS complex due to hyperkalemia differs from the ECG pattern of bundle branch block or preexcitation because widening affects both the initial and terminal portions of the QRS complex. The wide S wave in the left precordial leads sometimes helps differentiate the pattern of hyperkalemia from that of typical left bundle branch block (LBBB), whereas the wide initial portion of the QRS complex may help differentiate the pattern of hyperkalemia from that of typical right bundle branch block (RBBB).

When the plasma *K* concentration exceeds 8 mEq/l, the P wave frequently becomes invisible (**Case III**).

Case III.
Electrocardiograms of a 65-year-old woman with hypertension, diabetes mellitus and heart failure:

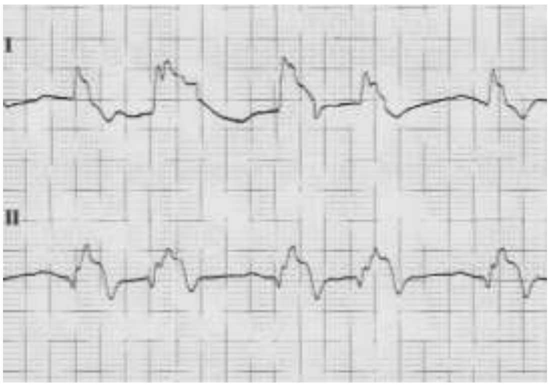
(1) *Kp* is 8.1 mEq/l; the rhythm is regular, at a rate of 21 beats/min, P waves are absent; the QRS duration is 160 ms.



(2) After treatment of hyperkalemia
(Kp is 4.83 mEq/l) there is a sinus rhythm at a rate of 64 beats/min,
T wave is inverted in leads I, II, III, aVF – maybe "memory T waves".

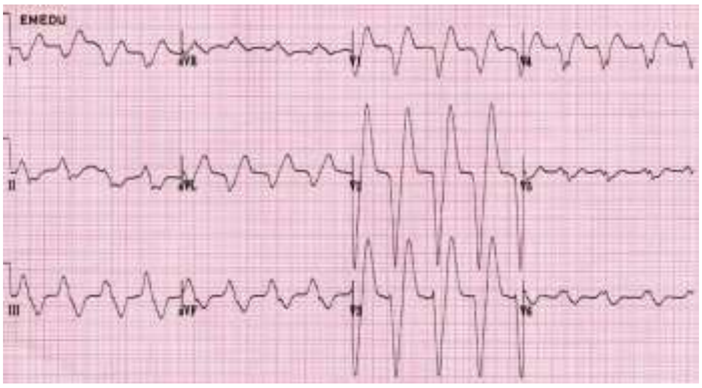
A regular rhythm in the absence of P waves has been attributed to sinoventricular conduction via atrionodal tracts in the presence of atrial (SA) block [10, 11]. Also, a regular rhythm in the absence of P waves can be caused by displacement of the pacemaker into the atrioventricular (AV) junction or the Purkinje fibers, but precise localization of the pacemaker in patients with absent P waves is usually not possible.

Sometimes in patients with advanced hyperkalemia the ST segment deviates appreciably from baseline and simulates the "acute injury" pattern, which resembles the pattern of acute myocardial ischemia (**Case IV**). Deviation of the ST segment or a monophasic pattern can be readily produced by topical application of K on the ventricular surface or an intracoronary KCl injection [12].



Case IV.
Electrocardiogram of a 68-year-old man with hypertension, diabetes mellitus and chronic renal failure, hospitalized with acute pulmonary edema. The plasma K concentration is 10.7 mEq/l. The rhythm is irregular at a rate of 52 beats/min; the QRS complex is wide; there is marked diffuse ST segment elevation in leads I, II

This type of ST abnormality in patients with hyperkalemia rapidly disappears accompanying the regression of potassium concentration with hemodialysis. The ST-segment deviation probably is caused by nonhomogenous depolarization in different portions of the myocardium. According to this hypothesis, a voltage gradient is created between normal myocardial cells and those depolarized by potassium, resulting in current flow between these regions. Since dialysis rapidly normalizes the ST-segment elevation, it is also known as the *dialyzable current of injury* [13] **(Case V).**



Case V.

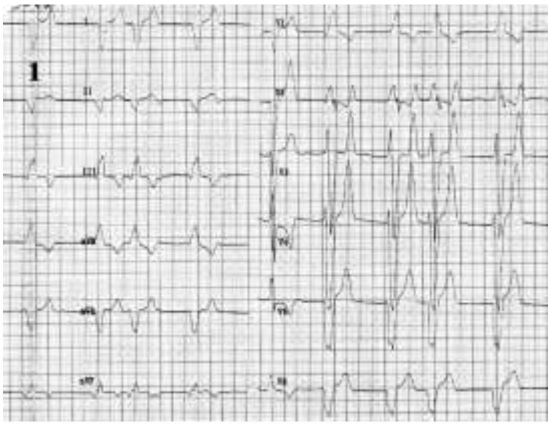
Electrocardiogram of 83-year-old male with hypertension, hospitalized for increased fatigue. The serum potassium level is 9.3 mEq/l. The tracing shows the absence of P waves and wide QRS complexes, with bizarre aspect. After hemodialysis the ECG trace chanced to normal

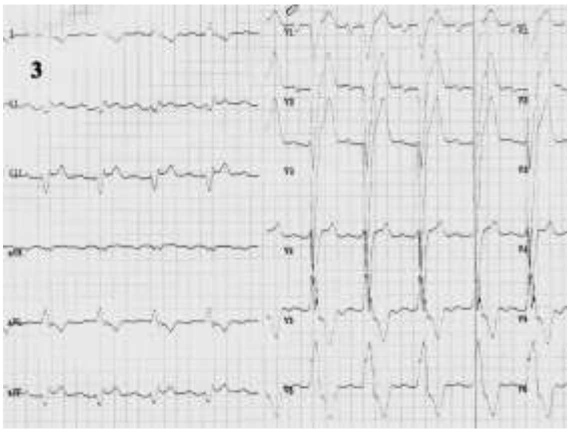
When the plasma K concentration exceeds about 10 mEq/l, the ventricular rhythm may become irregular owing to the simultaneous activity of several escape pacemakers in the depressed myocardium. The combination of an irregular rhythm and an absent P wave may simulate atrial fibrillation. In patients with preexisting atrial fibrillation and hyperkalemia, the ventricular rate is usually slow.

An increase in the plasma K concentration to above 12 - 14 mEq/l causes the final changes: a sine-wave pattern, in which the widened QRS complex merges with the T wave. This is followed by ventricular asystole or ventricular fibrillation. The latter may or may not be preceded by acceleration of the ventricular rate [14]. The danger in the majority of hyperkalemia cases is cardiac dysrhythmia. Although there are many previous reports addressing this threatening problem and associated therapeutic maneuvers, there have not been many previous reports citing the fatal concentration of hyperkalemia irrespective of the causes. However, it is uniformly accepted that a K^+ concentration greater than 10 mEq/l is fatal unless urgent treatment is instituted.

However, even severe hyperkalemia can be associated with atypical or non-diagnostic ECG findings [15]. These include arrhythmias, depression or elevation of ST segment, decrease in the height of the R wave with the development of deep S waves, and QRS axis shift to the left or right, bundle branch blocks, and sino-atrial exit blocks. Some case reports in the literature describe patients with severe hyperkalemia who present with a normal ECG result. Left ventricular hypertrophy, intraventricular conduction defects, and myocardial ischemia all mask ECG manifestations of hyperkalemia. Acidosis, hypoxia, hyponatremia, and hypocalcemia may increase myocardial sensitivity to hyperkalemia, whereas hypernatremia and hypercalcemia may minimize or eliminate the effect of hyperkalemia on the heart. Aslam et al. showed an inverse correlation between serum calcium and the height of the T wave and postulated that the lack of ECG changes of hyperkalemia could partly be due to fluctuations in serum calcium concentration [16].

Sometimes, in the same patient it can be noted a pleiade of ECG changes (**Case VI**).





Case VI.

Electrocardiograms of a 63-year-old, with dilated cardiomyopathy, LBBB, chronic renal insufficiency, treated with sotalol, is admitted with palpitations.

(1) The plasma K concentration is 6.5 mEq/l. The rhythm is irregular at a rate of 64 beats/min; P waves are absent; QRS complex is wide and its duration is 180 ms; T waves are tall, symmetric and narrow.

(2) Two hours later the ECG monitoring records non - sustained ventricular tachycardia.

(3) The treatment with sotalol is stopped and after treatment of hyperkalemia the ECG tracing is: sinus rhythm, at a rate of 72 beats/min, the PR interval is 140 ms and LBBB.

No evidence exists indicating at which serum potassium value life-saving therapies should be administered. Calcium infusion, the first step in emergency management, stabilizes cardiac myocyte membranes. Because of the unpredictable nature of cardiac arrhythmias, calcium infusion should be administered if any ECG change suggests hyperkalemia. Patients without ECG changes but who are at high risk for developing arrhythmias (eg, those with rapidly increasing potassium levels or coexisting electrolyte disorders) might benefit from prophylactic administration of calcium. If ECG changes are present, administration of *intravenous calcium* should normalize the ECG patterns. *Insulin* is a well-established therapy that rapidly decreases serum potassium concentrations by inducing intracellular shift.

When administered intravenously, or by a nebulizer or metered-dose inhaler, *beta-agonists* decrease plasma potassium levels. *Cation exchange resins* bind potassium in the gastrointestinal tract and enhance fecal elimination. It is important to correct metabolic acidosis with *sodium bicarbonate*. *Hemodialysis* can rapidly remove large amounts of potassium and is the treatment of choice for patients with life-threatening hyperkalemia that is refractory to medical management.

Lethal hyperkalemia results predominantly from renal failure and occasionally from an error in the amount of K administrated intravenously. The effect of intravenously administrated K depends on the rate of administration rather than the absolute amount of K given [4, 17].

A particular aspect is about giving much attention to factitious hyperkalemia (part of the differential diagnosis) which occurs when the laboratory potassium value is higher than the actual plasma potassium value. The most common cause is lysis of red blood cells due to specimen handling or collection errors. Hematological abnormalities, such as leukocytosis, thrombocytosis, and polycythemia, can also cause factitious hyperkalemia by increasing cell fragility [18]. When faced with an elevated potassium value of uncertain significance, the physician should consider the patient's risk factors for hyperkalemia. A history of renal disease, obstructive uropathy, clinical features of weakness or myopathy, and use of medications that increase potassium (eg, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], aldosterone antagonists, nonsteroidal anti-inflammatory drugs [NSAIDs], potassium supplements, trimethoprim) should prompt concern. To help differentiate a factitious from a true value, the potassium level should be retested, with care taken to ensure minimal trauma, optimal storage conditions, and rapid analysis. If the patient is at considerable risk for hyperkalemia, an ECG test is warranted. To assess factitious hyperkalemia due to increased cell fragility, additional samples of serum and plasma potassium should be taken using a heparinized tube. A discrepancy of more than 0.3 mEq/l will secure the diagnosis [19].

Hypokalemia

Hypokalemia, defined as a serum potassium concentration less than 3.5 mEq/l, is a common and potentially serious electrolyte disorder.

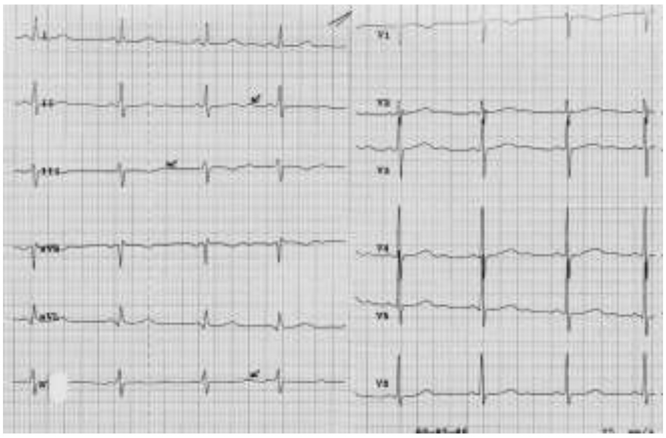
The estimated incidence of hypokalemia in hospitalized patients is 20%, while the incidence of severe hypokalemia, defined as < 3.0 mEq/l, is approximately 5% [20]. Low serum (or plasma) concentrations of potassium may occur in up to 40% of outpatients treated with thiazide diuretics. Of elderly patients, 5% demonstrate potassium levels lower than 3 mEq/l.

Causes of hypokalaemia can be divided in either true potassium depletion, mostly caused by renal or gastrointestinal losses, and a shift of potassium from the extracellular into the intracellular compartment. The electrophysiological changes associated with hypokalemia, in contrast, include hyperpolarization of myocardial cell membranes and increased action potential duration.

Because the duration of mechanical systole does not change during hypokalemia, one can best describe the pattern of hypokalemia as a gradual shift of the major repolarization wave from systole into diastole.

In most circumstances, mild hypokalemia (plasma [K+] 3.0 to 3.5 mEq/l) causes no symptoms. The major disturbances seen with more severe potassium deficiency result from changes in cardiovascular, neuromuscular, and renal function. Cardiac toxicity may be manifested by serious arrhythmias, which occur, as we said, because hyperpolarization of the myocardial cell membrane leads to a prolonged refractory period and increased susceptibility to reentrant arrhythmias.

The ECG diagnosis of hypokalemia is usually based on abnormalities of the ST segment, T wave, and U wave. The major ECG manifestations are ST depression with flattened T waves and increased U wave prominence (**Case VII**). The U waves can exceed the amplitude of T waves.



Case VII.

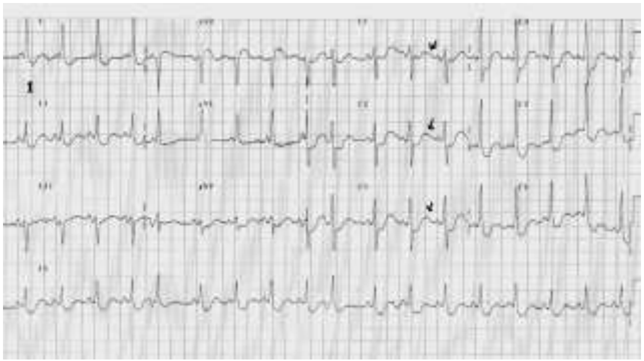
Electrocardiogram of a 19-year - old woman with, treated with indapamide. The plasma K concentration is 2.4 mEq/l. Sinus rhythms is present at a rate 62 beats/min, the amplitude of T wave is decreased in all precordial leads and U wave is present. Note: T wave inversion in III with U wave upright (arrows).

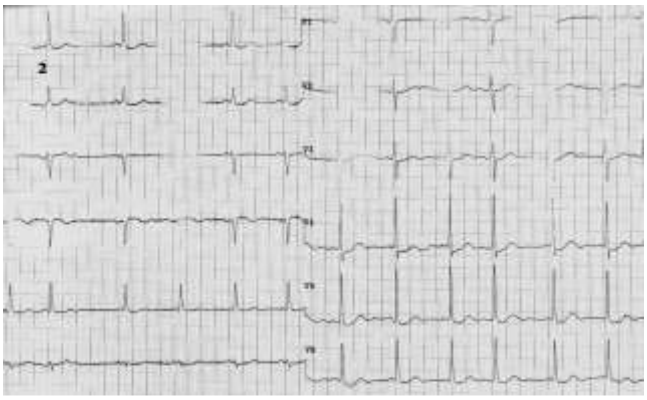
In an attempt to evaluate the pattern of hypokalemia quantitatively, Surawicz et al. considered the following three ECG features:

(1) depression of the ST segment of ≥ 0.5 mm;
(2) U wave amplitude > 1 mm;
(3) U wave amplitude greater than the T wave amplitude in the same lead [2].

The ECG was considered to be ***"typical of hypokalemia"*** if three or more of above feature were present in two leads; it was considered ***"compatible with hypokalemia"*** if two of the above features or one related to the U wave were present. In clinical practice, when the plasma K concentration was < 2.7 mEq/l the ECG was "typical" in the 78 percent and "compatible" in 11 percent of all patients. When the plasma K concentration was 2.7 - 3.0 mEq/l the ECG was "typical" in 35 percent and "compatible with hypokalemia" in 35 percent of patients.

β2 - agonist therapy in patients with chronic obstructive pulmonary diseases (COPD) was associated with significant increases in heart rate and reductions in potassium concentrations, which are known to be common systemic effects of β-adrenergic stimulation. In patients with obstructive airway disease, serum potassium levels could be decreased further with the use of corticosteroids and diuretics, and the cardiac effects of hypokalemia could be aggravated by underlying hypoxemia. (**Case VIII**).





Case VIII

Electrocardiograms of a 55-year-old male with hypertension and chronic obstructive pulmonary disease (COPD), hospitalized for one episode of lipothymia.

(1) The plasma K concentration is 1.85 mEq/l. The sinus rhythm is present at a rate of 120 beats/min, diffuse ST segment depression and T and U waves (arrow) are fused, the U wave amplitude exceeding the T wave amplitude.

(2) After treatment of hypokalemia: the reduction of ST segment depression and low amplitude of the U wave.

In the presence of a left ventricular hypertrophy pattern, the U wave amplitude is frequently increased (as part of the overall amplitude increases). Digitalis usually causes a more distinct separation of the T wave from the U wave than hypokalemia, because digitalis shortens the QT interval. The U wave amplitude is also increased during bradycardia.

When hypokalemia is advanced, both the amplitude and duration of the QRS interval are increased. The QRS complex is widened diffusely. The increased duration of the QRS is the result of widening without a change in shape, which suggests that it is caused by slower intraventricular conduction without changes in the depolarization sequence. The amplitude and duration of the P wave in hypokalemia is usually increased, and the PR interval is often slightly or moderately prolonged.

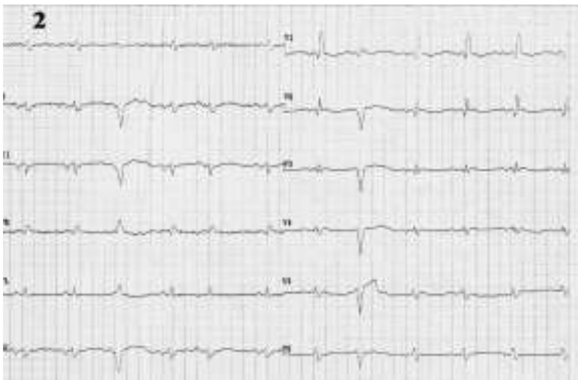
The hypokalemia promotes the appearance of supraventricular and ventricular ectopic complexes. Similar to digitalis, hypokalemia increases sensitivity to vagal stimulation.

In patients with severe hypokalemia, serious ventricular tachyarrhytmias including ventricular tachycardia, torsade de pointes, and ventricular fibrillation have been reported in the absence of heart disease or digital therapy (**Case IX**).

Case IX.

Electrocardiograms of a 68-year-old male with hypertension, diabetes mellitus, and prior inferior myocardial infarction hospitalized after two weeks from an acute anterior myocardial infarction with episodes of non-sustained ventricular tachycardia.

(1) The plasma K concentration is 1.3 mEq/l. The ECG tracing shows polymorphic non-sustained ventricular tachycardia.



(2) After treatment of hypokalemia ventricular tachycardia is no longer present.

Hypokalemia is frequently present in patients with acute myocardial infarction [21, 22] or after resuscitation from out-of-hospital ventricular fibrillation possibly due to treatment with thiazide diuretics or administration of sodium bicarbonate during resuscitation.

In treating hypokalemia, the first step is to identify and stop ongoing losses of potassium; repletion of potassium losses is the second step. The next steps are: monitor for toxicity of hypokalemia and determine the underlying cause to treat and prevent further episodes.

The potassium deficit can be treated with oral or intravenous potassium suppletion and/or a potassium-sparing diuretic. Unfortunately, supplemental potassium administration is also the most common cause of severe hyperkalemia in patients who are hospitalized, and this risk must be kept in mind when one is initiating treatment. The risk is greatest with the administration of intravenous potassium, which should be avoided if possible. When potassium is given intravenously, the rate should be no more than 20 mmol per hour, and the patient's cardiac rhythm should be monitored. Oral potassium is safer, because potassium enters the circulation more slowly.

In conclusion, though frequently included in secondary chapters (“varia”, “miscellaneous”, etc), the potassium abnormalities are a very important subject. The specific electrocardiographic changes caused by imbalance are attributed to the effect of the altered concentration of ions on the transmembrane potentials of cardiac cells. The accuracy of the ECG diagnosis improves when the interpreter is alert to the possibility of an electrolyte imbalance, when control tracing are available for comparison and when the patient is followed with serial tracings.

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Low molecular weight heparin versus unfractionated heparin for the perioperative anticoagulant therapy in patients undergoing mechanical prosthetic valve replacement*)

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Abstract

Background*: Up to now the immediate postoperative anticoagulation regimens in patients undergoing mechanical prosthetic valve replacement are only regulated for unfractionated heparin. Despite widespread use of low molecular weight heparin (LMWH) for the perioperative anticoagulant therapy in mechanical prosthetic valve replacement, there are no protocols or large-scale studies to study the efficiency and efficacy of LMWH given in these patients.*

Purpose*: **a)** To compare the efficacy and safety of Enoxaparin (E) versus unfractionated heparin (UH) during the immediate post- operative period in patients undergoing mechanical prosthetic valve replacement. **b)** To assess the impact of the profile of perioperative anticoagulation regimen on quality of life and prognosis in these patients.*

Materials and Methods: *A randomized, open label study with an open study period. 680 patients operated in our institution randomized in two matched groups. In group A 1mg/kg of body weight of Enoxaparin was given subcutaneously every 12h. In group B unfractionated Heparin was given intravenously. The dose was adjusted according to coagulation assesment (APTT). The clinical parameters that were assessed included: functional NYHA class for heart failure, clinical parameters for the prostheses, patient compliance and quality of life. Laboratory parameters included: the usual blood tests (platelet count, hemoglobin, hematocrit, aminotransferases, LDH, biochemistry), prosthesis echocardiographic assessement and clotting tests (INR for both groups and APTT for group B). Data were statistically analyzed using the EpiInfo, SYSTAT and SPSS programs.*

Results*: The use of Enoxaparin is more effective than the use of UH, with a better cost-benefit report. the use of Enoxaparin was associated with clinical improvement of the patients with decreased immobilization and hospitalization periods, less sacrate ulcerations and less postoperative depression and anxiety episodes. The mean duration of hospitalization in the Enoxaparin group was 10.5±4.3 days, compared to 14.5±5.8 days in the UH group. There were no significant differences between the two groups regarding the combined efficacy and safety outcome as well as the rate of specific complications.*

Conclusions*: Anticoagulation with Enoxaparin in the immediate postoperative period in patients with mechanical prosthetic valve replacement was associated with a better cost-benefit report, proving to be more effective than UH. Enoxaparin should be regarded as an attractive alternative for pharmacological anticoagulation in the immediate postoperative period in patients suffering mechanical valvular replacement.*

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Key words: *valvular replacement, anticoagulation, low molecular weight heparin*

Rezumat

Până astazi, regimul de anticoagulare postoperatorie la pacienții care suferă o înlocuire valvulară cu o proteză mecanică sunt standardizate doar cu privire la utilizarea heparinei nefracționate. În ciuda utilizării pe scară largă a heparinelor cu masă moleculară mică (LMWH), pentru anticoagularea perioperatorie la pacienții protezați valvular cu valve mecanice, nu există încă protocoale sau studii largi care să aprecieze eficacitatea şi eficiența LMWH la aceşti pacienți.

Scop: *Compararea eficacității şi siguranței administrării Enoxaparinei în comparație cu heparina standard în perioada postoperatorie imediată la pacienții care suferă înlocuire valvulară mecanică. Aprecierea impactului profilului regimului anticoagulant perioperator asupra calității vieții şi a prognosticului acestor pacienți.*

Material şi Metodă: *Un studiu randomizat, deschis, cu o perioadă de studiu deschisă. 680 de pacienți operați în instituția noastră randomizați în două grupuri comparabile. La pacienții din grupul A s-a administrat 1 mg/kg corp Enoxaparin la 12 ore subcutanat. La grupul B s-a administrat heparină standard intravenos conform APTT. Parametrii clinici evaluați au inclus: clasa funcțională NYHA, parametrii clinici ai protezelor, complianța pacienților şi calitatea vieții. Parametrii de laborator au inclus: analizele hematologice uzuale (numărul plachetelor, hemoglobină, hematocritul, aminotransferazele, LDH, biochimia serică), datele ecografice cu privire la funcția protezelor, probele de coagulare (INR la ambele grupuri şi APTT la grupul tratat cu heparină standard). Datele au fost analizate statistic utilizând programele EpiInfo, SYSTAT şi SPSS.*

Rezultate: *Utilizarea Enoxaparinei este mai eficace decât a heparinei standard, cu un raport cost-beneficiu superior. Utilizarea Enoxaparinei a fost asociată cu ameliorarea clinică a pacienților cu scăderea perioadei de imobilizare şi de spitalizare, mai puține escare sacrate şi mai puține episoade de depresie şi anxietate. Durata medie a spitalizării în grupul tratat cu enoxaparina a fost de 10,5±4,3 zile comparativ cu 14,5±5,8 zile în grupul tratat cu heparina standard. Nu au existat diferențe semnificative între cele două grupuri cu privire la ținta eficacitate plus siguranță ca şi cu privire la rata de complicații specifice.*

Concluzii: *Anticoagularea cu Enoxaparina în perioada perioperatorie imediată după protezare valvulară cardiacă cu valva mecanică a fost asociată cu un raport cost-beneficiu superior, dovedind că este mai eficientă decât heparina standard, Enoxaparina ar trebui privită ca o alternativă atractivă pentru anticoagularea farmacologică în perioada postoperatorie precoce la pacienții cu înlocuire valvulară cardiacă mecanică.*

Background

It's now well known that low molecular weight heparin, as compared to standard heparin, havs more predictable kinetics, is less protein-bound, has less potential for platelet activation and requires no monitoring of blood coagulation. Therefore *Low Molecular Weight Heparin* (LMWH) provides a strong rationale for better outcomes in patients after cardiac surgery.

The few studies of LMWH used in cardiac surgery, and especially in heart valve replacement interventions, have shown a decrease in the incidence of prosthesis obstructive dysfunctions, as well as an increase in postoperative convenience and quality of life in patients treated with LMWH as compared with patients treated with standard heparin.

Up to now the immediate postoperative anticoagulation regimens in patients undergoing mechanical prosthetic valve replacement are only regulated for unfractionated heparin, whereas the only low molecular weight heparin trial available concerns the use of Nadroparin in pregnant women.

Despite widespread use of LMWH for the peri-operative anticoagulant therapy in mechanical prosthetic valve replacement, there are no protocols or large-scale studies to study the efficiency and efficacy of LMWH given in these patients.

Purpose

The main purpose of this study was to compare the efficacy and safety of *Enoxaparin* (E) versus *unfractionated heparin* (UH) during the immediate postoperative period in patients undergoing mechanical prosthetic valve replacement in the mitral, aortic or tricuspid positions, or combinations of these three procedures.

We also tried to assess the impact of the profile of perioperative anticoagulation regimen on quality of life and prognosis in these patients.

Thus, the second purpose of this study was to assess the immediate and long term implications of the type of the perioperative anticoagulant treatment in patients undergoing mechanical prosthetic valve replacement.

Materials and Methods

We performed a randomized, open label study with an open study period. The main phases of our protocol were:

– Enrollment phase – we enrolled six hundred and eighty patients undergoing mechanical prosthetic valvular replacement, in the immediate postoperative period

– Active treatment phase – by randomisation all patients received anticoagulant therapy with Enoxaparin (group A) or unfractionated heparin (group B) in combination with oral anticoagulation until they achieved an optimal INR level. The parenteral anticoagulant treatment was stopped when an INR value of 2 to 4 was achieved (according to the position and type of the prosthetic valve). The incidence of major and minor bleeding episodes, the occurrence of thrombocytopenia and lab tests abnormalities was also recorded.

– Follow-up phase – all patients were assessed clinically and paraclinically on a daily basis during the first ten postoperative days and at one month from the operation.

In *group A* 1 mg/kg of body weight of Enoxaparin was given subcutaneously every 12h. In *group B* unfractionated Heparin was given intravenously. The dose was adjusted according to coagulation assesment (APTT).

We enrolled in our study all patients undergoing mechanical valvular replacement in our institute in one year who did not confirm any of the non-eligibility criteria.

Exclusion criteria. We did not include in our study patients with peptic ulcer, with conditions associated with increased bleeding risk, history of stroke or any known organic central nervous system disease, who underwent general surgery or organ biopsy within the last 2 months or patients with cardiopulmonary resuscitation for more than 10 minutes within the past 2 weeks. We did not include in our study patients participating in other clinical trials.

We excluded from the study patients who did not comply with the hospital protocol or who absented from the follow-up protocol.

The two study groups were adequately matched. The essential inclusion criteria (gender, age, preoperative diagnosis), the type and the mean number of mechanical prostheses/patient and the duration of treatment were similar in the two treatment groups.

The clinical parameters that were assessed included: functional NYHA class for heart failure, clinical parameters for the prostheses, patient compliance and quality of life. Laboratory parameters included: the usual blood tests (platelet count, hemoglobin, hematocrit, aminotransferases, LDH, biochemistry), prosthesis echocardiographic assessment and clotting tests (INR for both groups and APTT for group B).

The data collected represented the fields of a database using the Visual Fox Pro software. Data were processed using the Epiinfo, SYSTAT and SPSS programs.

No confirmatory statistical hypothesis was pre-specified, but a detailed analysis plan was defined before the database was locked.

This analysis plan was based on generating risk ratios and CI's (CI = confidence index) for the paired comparisons of primary interest. These comparisons were presented with the two–sided 95% CI of the relative risk and with normal p values.

For the primary endpoints Kaplan-Meier curves were constructed and log-rank tests were performed.

For each endpoint, a two-sided 95% CI was also calculated and an overall chi-square test, comparing the three treatment groups was performed.

The most important endpoints used for the estimation of the mid-term prognosis were:

- safety endpoints: the composites of thirty-day mortality and in-hospital prosthesis obstructive dysfunction (thrombosis);
- duration of hospital stay and immobilization;
- quality of life – that was assessed using a scale from one to ten calculated on the base of a questionnaire filled by the patients at each visit);
- efficacy plus safety endpoint: the above end-points plus in-hospital intracranial hemorrhage or in-hospital major bleeding complications.

Results

The main result of our study was that the use of Enoxaparin for anticoagulation in patients suffering valvular replacement with mechanical prosthetic valves in the immediate postoperative period is more effective than the use of UH, with a better cost-benefit report.

Subjectively, the use of Enoxaparin was associated with clinical improvement of the patients with decreased immobilization and hospitalization periods, less sacrate ulcerations and less postoperative depression and anxiety episodes.

The mean duration of hospitalization in the Enoxaparin group was 10.5±4.3 days, compared to 14.5±5.8 days in the UH group. The mean immobilization duration in the immediate postoperative period was five times higher in UH group and, consequently the quality of life was considerably better in the Enoxaparin group.

Objectively, in the Enoxaparin group, all echographic prosthetic parameters were within the normal range; there was no case of early prosthesis thrombosis and the optimal INR was achieved rapidly, consequently decreasing the parenteral anticoagulation period. At hospital discharge and at 30 days, the combined efficacy and safety outcome endpoints were similar but a little bit smaller in the Enoxaparin group.

For the primary efficacy plus safety endpoint, the rates were smaller for Enoxaparin group, as the rates of in-hospital death.

In-hospital prosthesis thrombosis did not occur in patients treated with Enoxaparin and occurred in one of the patients treated with UH. Major hemorrhagic events were also more common in the UH group. Concerning the duration of hospitalisation and immobilisation, they were five to ten times higher in UH group.

Relative risks and 95% confidence indexes for primary efficacy composite endpoints were lower among patients treated with Enoxaparin than among those treated with UH. Also, there were differences depending on the patient's age, functional NYHA class, prosthesis type and placement. Conventional statistical testing for Enoxaparin versus UH resulted in p values of 0.0002 and 0.0003 respectively for the primary efficacy plus safety composite endpoints.

The Kaplan-Meier curves for these primary end-points are shown in figure 1. Early after treatment, the curve for the Enoxaparin group started to separate from the one of the group treated with UH.

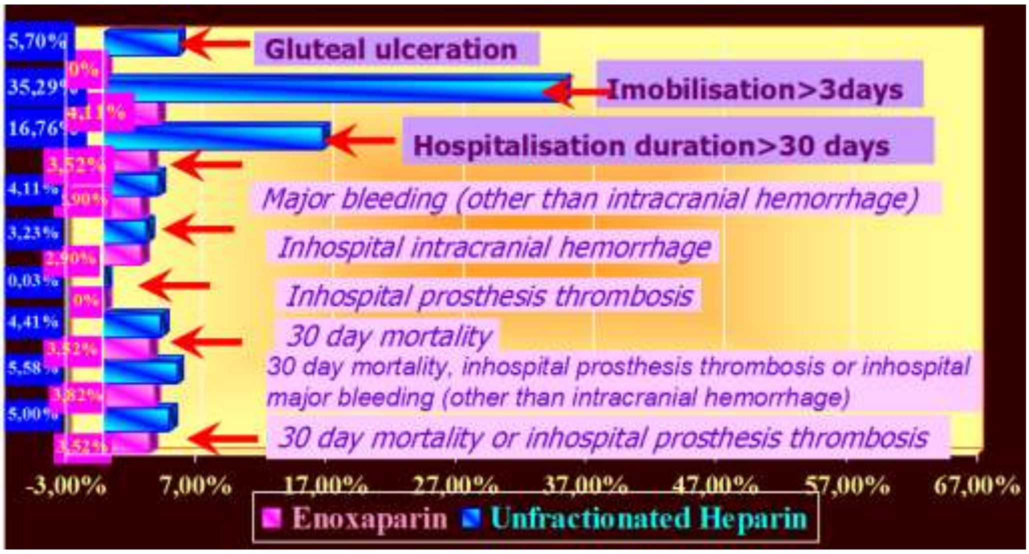

Figure 1: Frequency of composite and single endpoints at hospital discharge and at 30 days was similar but a little bit smaller in *Enoxaparin* group (exception was the hospitalization duration and immobilization which were highly superior in UH group)

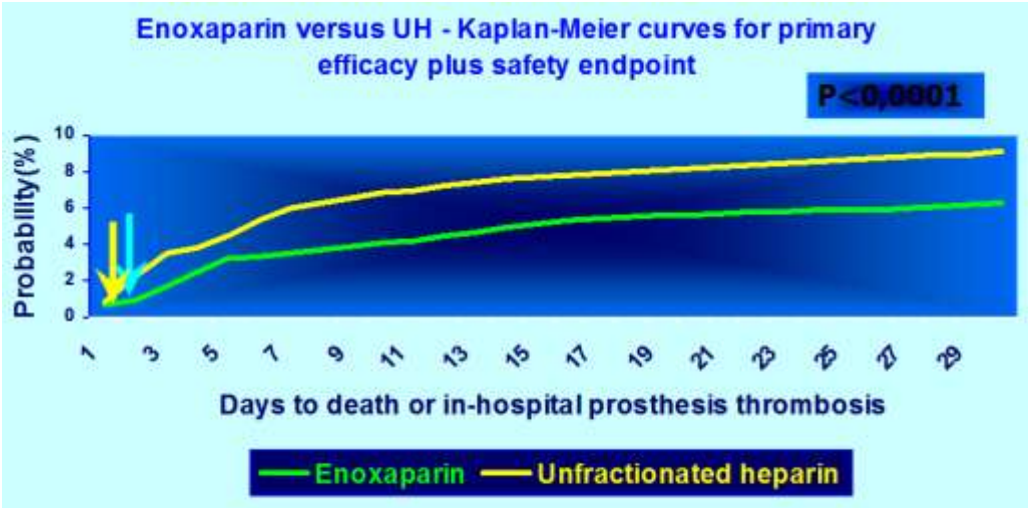

Figure 2: The Kaplan Meier curves for primary efficacy and safety endpoints showed a smaller probability for death or prosthesis thrombosis in *Enoxaparin* group

At 48h, differences in the primary endpoints between the two groups were already present.

Until the end of the follow up, for the primary efficacy endpoint and for the primary efficacy plus safety endpoint, event rates were abut two times higher in the UH group compared with the Enoxaparin group with log rank tests highly significant and p values less than *zero point zero zero zero one* ($p < 0.0001$).

Concerning anticoagulant therapy complications, the dates on in-hospital strokes are summarized in figure 3 [next page]. The rates of stroke (ischemic and hemorrhagic) and ischemic stroke were similar in both groups. A few hemorrhagic conversions were seen in each of the two treatment groups.

More minor or major bleeding complications and blood transfusions were also seen in the UH group compared with the Enoxaparin group, although these differences were not significant.

Significantly more major bleeding complications ($p = 0.0001$), more transfusions ($p = 0.002$) and a higher rate of thrombocytopenia ($p = 0.001$) were seen in patients with associated treatment with Aspirin, Ticlopidine or Clopidogrel. In patients older than 75 years and in diabetics, the rate of major bleeding complications was three times higher in those with associated antiplatelet therapy (4% vs 14% and 2% vs 7%, respectively).

Severe thrombocytopenia occurs less frequently in the Enoxaparin treatment group.

The probability of early prosthetic thrombosis and perioperative myocardial infarction was smaller with Enoxaparin versus UH, the associated relative risks being negative because the studied drugs acted as protection factors for these perioperative complications.

As was shown before, the relative risks for the most severe complication of anticoagulant therapy, hemorrhagic stroke, were similar in the two groups.

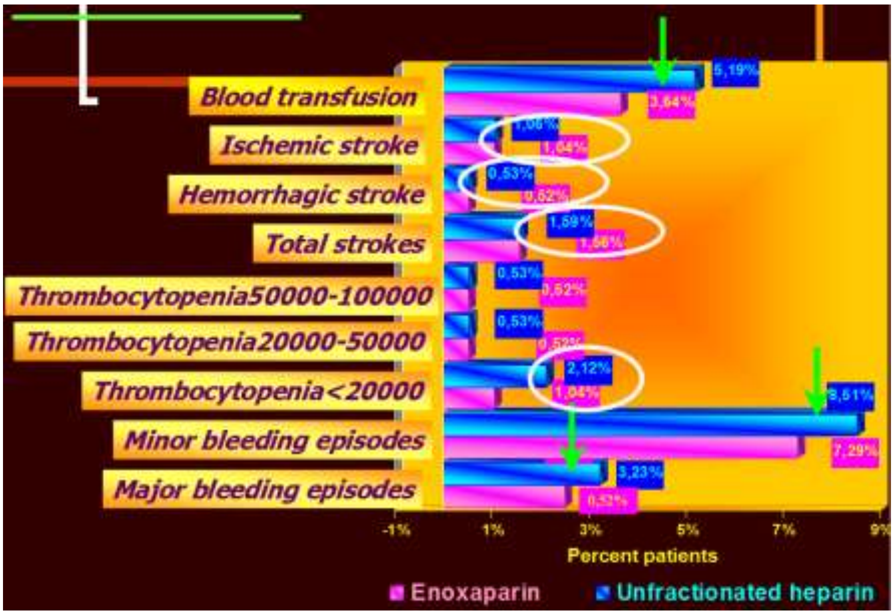

Figure 3: Rates of anticoagulant therapy complications were higher in UH group

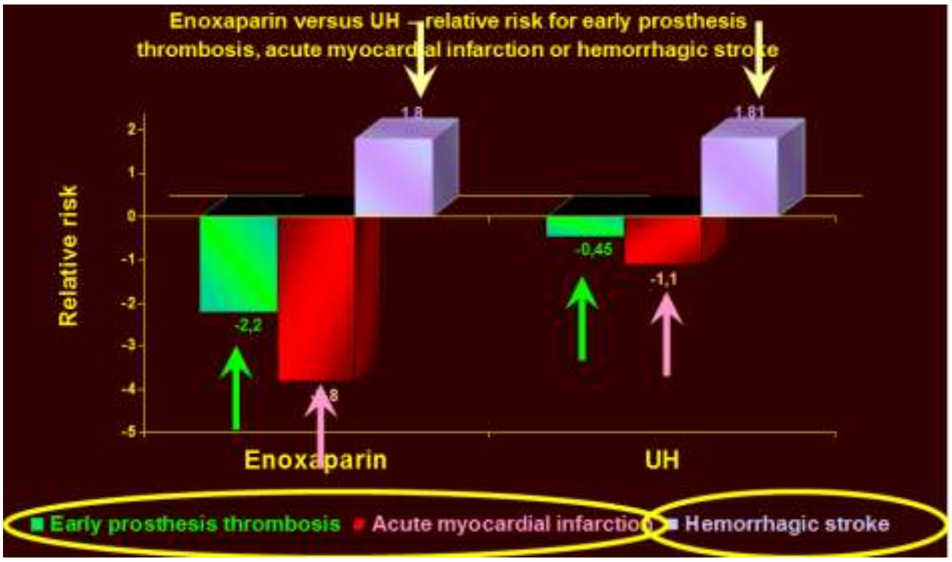

Figure 4: Probability of death, early prosthetic thrombosis and perioperative myocardial infarction was smaller with Enoxaparin versus UH

Enoxaparin was associated with a very good patient compliance, an improved quality of life and of the psychological status of the patients due to shortened hospital stay, less coagulation tests, increased dosing convenience, shortened immobilization during the immediate postoperative period, as well as lack of significant side effects.

Conclusions

Anticoagulation with Enoxaparin in the immediate postoperative period in patients with mechanical prosthetic valve replacement was associated with a better cost-benefit report, proving to be more effective than UH. Also, taking into account both efficacy and safety, the anticoagulation of mechanical valve prosthesis with Enoxaparin resulted as the best treatment in this trial.

Because of the better cost-benefit report and additional advantages such as the ease of administration, the lack of need for monitoring of anticoagulation, reduction of the hospitalization duration, Enoxaparin should be regarded as an attractive alternative for pharmacological anticoagulation in the immediate postoperative period in patients suffering mechanical valvular replacement.

The effect of heparin - protamine dosing in cardiac surgery on bleeding and coagulation parameters*)

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Abstract

Heparin concentration monitoring could be an alternative or supplemental means to confirm adequate anticoagulation. This study was designed to evaluate prospectively the impact of heparin and protamine dosing using the Hepcon-Heparin Management System (HMS) on bleeding and coagulation parameters after CPB.

***Methods:** In a three month period during 2003, 106 patients requiring elective CPB were considered in our study. Systemic anticoagulation during CPB was accomplished with porcine derived heparin. The ACT and heparin concentrations were measured using Hemochron 801 and Hepcon HMS, respectively. The measurements were done 5 minutes following heparin bolus administration and every 30 minutes during CPB. The following parameters were recorded: demographic data (age, sex and weight), perioperative data (perioperative exposure to low molecular weight heparin, type of surgery, aprotinin usage, duration of CPB, temperature on CPB), the heparin and protamine doses, the mediastinal bleeding at 2 and 6 hours, the transfusion requirements during the same interval and the perioperative hematological data (Hb, ACT, number of platelets, fibrinogen level, prothrombin time-PT and activated thromboplastin time-APTT).*

***Results:** The patients were randomized to the control (C) or to the study (S) group. Six patients were excluded for a post-operative mediastinal bleeding requiring surgical reexploration. No differences between the two groups were recorded in reference to age, sex, weight, preoperative exposure to heparin, type of surgery, duration of CPB, perfusion temperature and exposure to aprotinin. Patients in the S group received less heparin and the heparin dose was less variable. The mean protamine dose administered in the S group and the protamine/heparin ratio were significantly lower than that in the C group. Patients in the C group had more mediastinal drainage in the first 2 hours postoperatively and in the next interval until the 6th postoperative hour. Consequently, patients in Hepcon group received fewer blood products. More important is that the percent of transfused patients in the S group is lesser than in the C group (21% vs. 33%).*

***Conclusions:** In our study of patients undergoing cardiac surgery with CPB, the point-of-care testing using Hepcon system was associated with significant reduced protamine dose without affecting the postoperative coagulation parameters by facilitating maintenance of a therapeutic heparin concentration and determination of an appropriate protamine dose.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2005, vol. 4, no. 2, pp. 93-98**

Key words: *heparin, dosing, postoperative bleeding, cardiopulmonary bypass*

Rezumat

Monitorizarea concentrației de heparină în timpul circulației extracorporeale (CEC) poate fi o alternativă sau un mijloc suplimentar de confirmare a unei anticoagulări corespunzătoare. Acest studiu a fost conceput pentru a evalua prospectiv impactul dozării heparinei și al protaminei cu ajutorului Sistemului de Management al Heparinei - Hepcon (HMS) asupra parametrilor legați de sângerare și coagulare după CEC.

Metode*: Au fost analizați 106 pacienți care au suferit intervenții elective sub CEC într-o perioadă de 3 luni in anul 2003. Anticoagularea sistemică s-a realizat cu heparina porcină. Au fost determinate timpul de coagulare activată (ACT) și concentrația de heparină cu ajutorul aparatului Hemochron 801 și, respectiv, Hepcon HMS. Determinările au fost realizate la 5 minute după administrarea unui bolus de heparină și la fiecare 30 de minute in timpul CEC. Au fost înregistrați următorii parametri: date demografice (vârstă, sex, greutate), date perioperatorii (expunerea perioperatorie la heparine cu greutate moleculară mică, tipul de intervenție chirurgicală, utilizarea de aprotinină, durata CEC și temperatura din timpul CEC), dozele de heparină și protamină, sângerarea mediastinală la 2 și 6 ore, necesarul transfuzional în același interval de timp și date hematologice (hemoglobina, ACT, numărul de trombocite, fibrinogen, timpul de protrombină PT, timpul de tromboplastina activata APTT).*

Rezultate: *Pacienții au fost împărțiți aleator într-un grup de control (C) și un grup de studiu (S). Șase pacienți au fost excluși din studiu pentru ca au prezentat sângerare postoperatorie necesitând reexplorare chirurgicală. Nu s-a înregistrat nici o diferență intre cele doua grupuri în ceea ce privește vârsta, sexul, greutatea, expunerea preoperatorie la heparina, tipul de intervenție chirurgicală, durata CEC, temperatura de perfuzie și expunerea la protamina. Pacienții din grupul S au primit mai puțină heparina iar doza de heparină a fost mai puțin variabilă. Doza medie de protamină administrată în grupul S și raportul protamină/heparină au fost semnificativ mai mici decât în grupul C. Pacienții din grupul C au înregistrat un drenaj mediastinal mai mare în primele 2 ore postoperator precum și în următorul interval de timp, până la a 6-a oră postoperator. În consecință, pacienții din grupul S au primit mai puține derivate de sânge. Încă și mai important este faptul ca procentul de pacienți transfuzați din grupul S a fost mai mic decât în grupul C (21% față de 33%).*

Concluzii: *În studiul nostru asupra pacienților supuși unei intervenții chirurgicale sub CEC, testarea concentrației de protamină utilizând dispozitivul Hepcon a fost asociată cu administrarea unei doze semnificativ mai mici de protamină fără afectarea parametrilor echilibrului coagulant postoperator facilitând menținerea unei concentrații terapeutice adecvate a heparinei și determinarea unei doze optime de protamină.*

Cuvinte cheie: *heparina, dozare, sângerare postoperatorie, circulație extracorporală.*

Introduction

Patients undergoing cardiopulmonary bypass (CPB) require anticoagulation to prevent clot formation due to the thrombogenic nature of the CPB. To date, heparin is the anticoagulant drug of choice (1). The dose of heparin is given empirically, based on body weight, and then adjusted to the coagulation response (2). The test currently used to rapidly evaluate the adequacy of anticoagulation is the activated clotting time (ACT), which is performed on whole blood and measures the time to clot using either celite or kaolin as an activating agent (3). However, the use of ACT alone for monitoring of anticoagulation therapy during CPB can be misleading because ACT is affected by many factors during CPB, such as hypothermia, hemodilution of coagulation proteins and activation of platelets (2). Therefore, ACT values may not correlate with heparin concentrations during CPB.

Heparin concentration monitoring has been suggested as an alternative or supplemental means to confirm adequate anticoagulation (1). The most common point-of-care laboratory technique that measures whole blood heparin concentration is a protamine titration assay called Hepcon-Heparin Management System (HMS) from Medtronic Company (1, 2). The device was designed: (1) to evaluate, in vitro, the patient's response to heparin, (2) to calculate the dose of heparin required based on the desired ACT, estimated blood volume, and extracorporeal circuit parameters, (3) to measure the heparin concentration and (4) to calculate the dose of protamine required for reversing heparin. Simultaneous functional evaluation of heparin via the HR-ACT is possible.

Because excess protamine inhibits clot formation and insufficient protamine does not fully antagonize heparin, the channel with the fastest clot formation represents the protamine concentration that optimally neutralizes the existing heparin. If the protamine concentration in the channel is known, the heparin concentration can be calculated by a simple ratio. The titration is performed on whole blood, which offers an advantage for the operating room.

To evaluate the patient's response to heparin (Heparin Dose Response – HDR) the device constructs a 3 point heparin dose-response curve using the base-line, 1.5 IU/mL of heparin and 2.5 IU/mL of heparin. From this curve, extrapolation to the desired ACT or heparin concentration yields the indicated dose of heparin to be given,

This study was designed to evaluate prospectively the impact of heparin and protamine dosing using this system on bleeding and coagulation parameters after CPB.

Methods

Any adult requiring elective CPB in a three month period during 2003 was considered eligible unless clinical history or preoperative laboratory screening identified abnormal blood coagulation. Once enrolled in the study, patients were excluded if postoperative mediastinal bleeding required surgical reexploration.

All patients were anesthetized with an opioid-based technique, and the anesthetic was supplemented with inhalational anesthetic agents, muscle relaxants and benzodiazepines. CPB was performed with roller pump, membrane oxygenator and moderate hypothermia. Systemic anticoagulation was accomplished with porcine derived heparin. The ACT and heparin concentration were measured using Hemochron 801 and Hepcon HMS, respectively. The measurements were done 5 minutes following heparin bolus administration and every 30 minutes during CPB.

The anticoagulation in the control group represented our institutional practice. The initial dose of heparin was 400 UI/kg and 5000-10,000 UI were added as necessary to maintain the ACT above 480 sec. All patients received 10,000 UI in the prime. At the end of CPB, after the patient was rewarmed to 37, heparin was neutralized with an initial fixed dose of protamine. We used 0.8 mg of protamine for each mg of total heparin, including the dose in the prime. Usually protamine was supplemented to obtain an ACT less than 120 sec. The measurement was performed 10 minutes after heparin neutralization.

For the study group, an initial dose of heparin was based on an automated HDR assay. Additional heparin doses were administered if the heparin concentration was less than the reference concentration of 4 UI/mL or for an ACT less than 480 sec. After CPB protamine was given according to the last heparin concentration measured. The ratio was 1 mg of protamine for 100 UI of residual heparin.

The criteria for administering blood products and for the treatment of excessive bleeding and clinical coagulopathy were not standardized. A Hb less than 9 d/dL was a usual trigger for packed red cells administration.

The following parameters were recorded: demographic data (age, sex and weight), perioperative data (preoperative exposure to low molecular weight heparin, type of surgery, aprotinin usage, duration of CPB, temperature on CPB), the heparin and protamine doses (initial, total and the ratio), the mediastinal bleeding at 2 and 6 hours, the transfusion requirements during the same interval and the perioperative hematological data (hemoglobin, ACT, number of platelets, fibrinogen level, prothrombin time-PT and activated partial thromboplastin time-APTT).

Data are expressed as the mean and standard deviation. For statistical analysis a Student's unpaired T test was performed. A p value less than 0.05 was considered indicative of a significant difference.

Results

106 cardiac surgical patients were randomized to control (C) or study group (S). Two patients in group S and 4 patients in the C group were excluded because they returned in OR for hemostasis.

No differences between the two groups were recorded in reference to age, sex, weight, preoperative exposure to heparin, type of surgery, duration of CPB, perfusion temperature and exposure to aprotinin (table 1).

Table 1

Demographic and perioperative data					
PARAMETERS	**Group S (n=52)**		**Group C (n=48)**		***p* value**
Age (years)	**54**	**14**	**54**	**12**	**0.92**
Sex (female/male)	**18/34**		**20/28**		**0.26**
Weight (kg)	**70**		**70**	**14**	**0.91**
Preoperative LMWH <n>	**28**		**25**		**0.55**
Valve replacements <n>	**19**		**22**		**0.16**
Coronary artery bypass (n)	**24**		**21**		**0.52**
Complex procedures (n)	**9**		**5**		**0.18**
Aprotinin (n)	**21**		**16**		**0.27**
Duration of CPU (min)	**106**	**64**	**99**	**47**	**0.50**
Temperature on CPB (°C)	**33**	**3**	**33**	**3**	**0.70**

The ACT before the start of the CPB was similar in the two groups but patients in the study group received less heparin (table 2).

The difference is significant for the initial bolus dose, which is adapted to patient response in the S-group. All patients in the S group achieved an ACT grater than 480 sec after the bolus dose. In addition, the heparin dose was less variable in the S group. However, the average ACT after the initial dose (ACT start CPB) was the same in both groups. In addition, there were no differences in the value of ACT (minimum and maximum) during CPB.

The mean protamine dose administered in the S group and the protamine/heparin ratio were significantly lower than that in the C group (table 2). Although the protamine doses administered in the S group were about half the doses of the control group, the ACTs in the two groups were similar 10 minutes after protamine administration (table 2). The hematological parameters registered perioperatively were not different (table 3).

Table 2

Heparin anticoagulation and neutralization					
	Group S (n = 52)		**Group C (n = 48)**		***p* value**
Initial heparin dose (IU.kg^{-1})	**371**	**72**	**422**	**77**	**0.0006**
Total heparin dose (IU.kg^{-1})	**602**	**138**	**679**	**179**	**0.02**
Protamine dose (mg.kg^{-1})	**190**	**59**	**332**	**74**	**<0.0001**
Protamine / heparin ratio	**0.46**	**0.11**	**0.74**	**0.14**	**<0.0001**
ACT baseline (sec)	**147**	**19**	**130**	**25**	**0.07**
ACT start CPB (sec)	**631**	**136**	**619**	**12**	**0.63**
ACT min on CPB (sec)	**524**	**105**	**494**	**72**	**0.11**
ACT max on CPB (sec)	**791**	**154**	**734**	**167**	**0.08**
ACT after PROT (sec)	**137**	**240**	**132**	**18**	**0 33**

Table 3

Hematological parameters					
	Group S (n = 52)		**Group C (n = 48)**		***p* value**
Haemoglobin prior CPB (g/dL>	**12.9**	**1.7**	**12.9**	**1.5**	**0.88**
Haemoglobin min. post CPB (g/dL)	**9.3**	**1.4**	**9.2**	**1.2**	**0.71**
Haemoglobin ICU entry (g/dL)	**9.9**	**1.5**	**9.8**	**1.5**	**0.68**
Haemoglobin ICU discharge (g/dL) (POD2)	**9.1**	**1.0**	**8.9**	**1.2**	**0.33**
APTT preoperative (sec)	**33**	**5**	**31**	**2**	**0.06**
APTT ICU entry (sec)	**44.0**	**17**	**40.4**	**13**	**0.05**
Plt preoperative (elem.103. cc-1	**282**	**74**	**312**	**69**	**0.06**
Plt ICU entry (clcm.103.cc-l	**160**	**51**	**173**	**71**	**0.30**
PT preoperative (sec)	**12.1**	**1.8**	**11.4**	**0.9**	**0.30**
PT ICU entry (sec)	**17.4**	**3.2**	**18.2**	**4.6**	**0.20**
Fibrinogen preoperative (mg/dL)	**395**	**72**	**355**	**53**	**0.05**
Fibrinogen ICU entry (mg/dL)	**294**	**79**	**272**	**73**	**0.17**

Patients in the C group had more mediastinal drainage in the first 2 hours postoperatively and in the next interval until the 6th postoperative hour (figure 1).

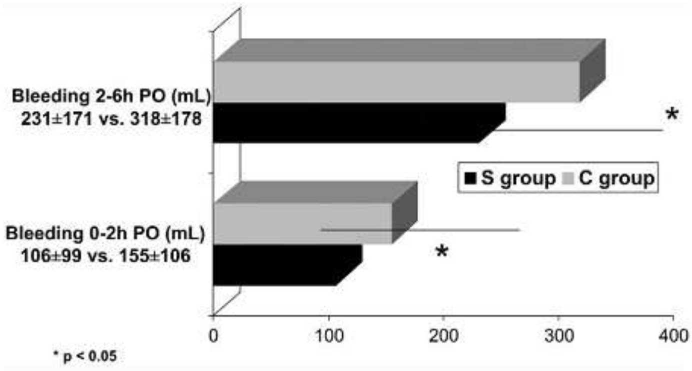

Figure 1: chest drainage data

Although control patients tended to have greater mediastinal drainage in the subsequent postoperative intervals, this was not statistically significant. Total mediastinal loss was greater for the entire period in the control group but the difference did not reach statistically significance (788± 343 ml vs. 741± 438 ml).

Consequently, patients in Hepcon group received fewer blood products (figure 2).

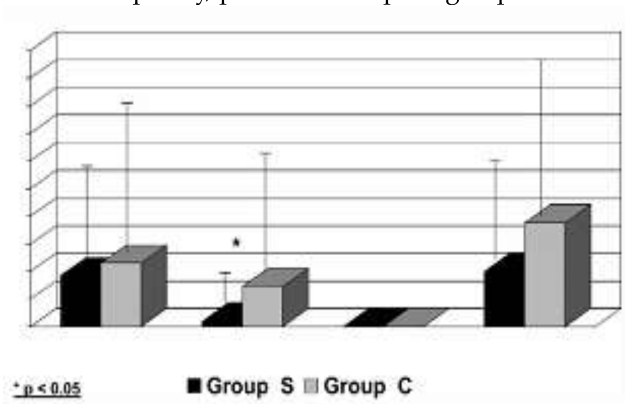

Figure 2: Blood products used (0-6h PO)

The difference was statistically significant only in the first 2 postoperative hours for packed blood cells (PRC) and fresh frozen plasma (FFP). After 6 hours the amount of blood products used in the two groups was similar except for FFP, which still was less for the S group. Anyway, we have to observe that the allogeneic transfusion is small during this interval of time (less than one unit/per patient) and even though statistically significant or not, the difference is not clinically important.

More important is that the percent of transfused patients in the S group is lesser than in the C group (21% vs 33%). This difference reflects the reduced exposure to allogeneic transfusion in the S group.

Allogeneic transfusion in the operating room was similar in both groups (1 ±1.7 U vs 0.85 ± 1.99 U).

Discussions

Management of systemic anticoagulation and its reversal has been a controversial issue since the introduction of CPB. The consequences of an inaccurate management of anticoagulation and hemostasis can lead, either directly or indirectly, to increased morbidity and even mortality (4). In particular, both heparin and protamine play important direct and indirect roles in the onset and amplification of the acute-phase response to CPB (5). Therefore, their respective doses must be carefully prescribed and a number of other issues related to the management of anticoagulation and haemostasis in cardiac surgery must be scrupulously evaluated for use in clinical practice.

Our study demonstrated that in cardiac surgical patients with CPB, the Hepcon-HMS device facilitates to adapt the dose of heparin to patient's response and to decrease significantly the protamine dosage, without affecting the postoperative coagulation parameters. Moreover, heparin-protamine dosing with this system of anticoagulation management allows to reduce the post-operative blood loss and to decrease the postoperative exposure to allogeneic transfusion in the first 6 hours.

Previous reports have attributed reduced blood loss or transfusion to lower protamine dosages but have not identified a mechanism (6, 7). However, the lowest effective dose of protamine is a worthwhile goal (8).

In the literature there is up to five fold difference for protamine given to a patient with the same body weight who has received the same amount of heparin (1, 2, 9). It is assumed that larger doses counteract the heparin rebound (2, 7) but low doses of protamine minimize thrombocytopenia and platelet secretion (7, 10). It was shown that both protamine alone and equivalent concentrations in excess of heparin (1:2) have similar antiplatet effects (7). Protamine excess during empirical heparin reversal may contribute to postoperative bleeding (11).

Conclusion

In conclusion, in our study of patients undergoing cardiac surgery with CPB, by facilitating maintenance of a therapeutic heparin concentration and determination of an appropriate protamine dose, the point-of-care testing using Hepcon system was associated with significant reduced protamine dose without affecting the postoperative coagulation parameters. Bleeding and exposure to allogeneic transfusion were reduced in the first 6 post-operative hours.

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Inhaled iloprost for pulmonary hypertension during cardiac surgery*)

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Abstract

In cardiac surgery, patients with pulmonary hypertension (PH) have markedly increased morbidity and mortality (1). The conventional therapy with intravenous vasodilators has limited results because of lack of pulmonary selectivity. We present our experience with inhaled iloprost, a stable carbacyclin derivative of PGI2 in significant secondary PH (mean pulmonary artery pressure > 30 mmHg).

Methods: *Three adult patients, NYHA III, with moderate to severe pulmonary venous hypertension scheduled to undergo elective valve replacement surgery and coronary artery bypass grafting, preserved high persistent values of pulmonary pressures after CPB. Iloprost was administered, after protamine, by an ultrasonic nebulizer (OPTINEB; Germany) at a concentration of 2 µg/ml. With an average nebulization rate 0.6 ml/min after 20 min a cumulative dose of 2.4 µg had been delivered. The following variables were measured or calculated: cardiac output (CO); systolic, diastolic and mean arterial blood pressures (SAP, DAP, MAP); systolic and mean pulmonary artery pressure (SPAP, MPAP); systemic and pulmonary vascular resistance (SVR, PVR dyne.sec.cm-5), central venous pressure (PVC); pulmonary arterial occlusion pressure (PAOP).*

Results: *In these patients, with persistent PH (after valve replacement and protamine administration), inhaled iloprost decreases MPAP by 30.8%, PVR by 26% and increases CI by 17%. Systemic arterial pressures were stable.*

Conclusion: *Inhaled iloprost appears to be a selective pulmonary vasodilator. The administration procedure is uncomplicated and does not require additional monitoring. Further studies are needed for peri operative routine use of inhaled iloprost in patients with moderate to severe secondary PH and complex surgery.*

Rezumat

În chirurgia cardiacă, pacienții cu hipertensiune pulmonară (HP) au o morbiditate şi o mortalitate crescută. Terapia convențională cu vasodilatatoare administrate intravenos are efecte limitate datorită lipsei de selectivitate pulmonară. Prezentăm în continuare experiența noastră cu privire la administrarea de iloprost inhalator (un derivat carbaciclinic stabil de PGI2) în cazurile de HP secundară semnificativă (presiunea medie în artera pulmonară > 30 mm Hg).

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Metode: *Au fost analizați trei pacienți adulți, aflați în clasa III NYHA, cu HP venoasă moderată sau severă, ce urmau să fie supuşi unei intervenții de înlocuire valvulara şi bypass aortocoronarian, la care au persistat valori mari ale presiunii în artera pulmonară după încheierea circulației extracorporale (CEC). După administrarea de protamină, s-a administrat iloprost cu ajutorul unui nebulizator ultrasonic (OPTINEB, Germania), în concentrație de 2 µg/ml. Rata medie de nebulizare a fost de 0.6ml/min astfel încât după 20 min s-a administrat o doză totală de 24 µg. Au fost determinate sau calculate următoarele variabile: debitul cardiac (DC), presiunile arteriale sistolică, medie şi diastolică (PAS, PAM, PAD); presiunea arterială pulmonară medie şi sistolică (PAPM şi PAPS); rezistențele vasculare pulmonare şi sistemice (RVP, RVS in dyne x s x cm-5); presiunea venoasă centrală (PVC); presiune de ocluzie arterială pulmonară (POAP).*

Rezultate*: La aceşti pacienți cu hipertensiune pulmonară persistentă (după înlocuire valvulară şi administrare de protamină), iloprostul inhalator a scăzut PAPM cu 30,8%, RVP cu 26% şi a crescut indexul cardiac cu 17%. Presiunea arterială sistemică a rămas stabilă.*

Concluzii: *Iloprostul administrat inhalator pare a fi un vasodilatator pulmonar selectiv. Modul de administrare este simplu şi nu necesită monitorizare suplimentară. Sunt necesare studii suplimentare pentru utilizarea den rutina a iloprostului inhalator perioperatorlă pacienții cu HP secundară moderată sau severă supuşi unui act chirurgical complex.*

Background

Significant pulmonary hypertension (MPAP>30 mmHg), the major cause of right ventricular dysfunction, is an independent predictor of outcome after cardiac surgery (1, 2, 3).

Patients with pulmonary hypertension (PH) have markedly increased morbidity and mortality with anaesthesia and surgery. Severe Perioperative exacerbation of the PH leading to acute right heart failure are the major complications of anaesthesia and surgery.

The standard conventional therapy with intravenous vasodilators produces vasodilatation in both the pulmonary and systemic circulation. The systemic vasodilatation may result in systemic hypotension, limiting their use. Inhaled drugs produce selective pulmonary vasodilatation (4). The aim of this study was to evaluate the use of inhaled iloprost in significant chronic secondary PH and aggravation in cardiac surgery (after cardiopulmonary by pass-CPB and protamine infusion).

Methods

Three patients scheduled to undergo elective valve replacement surgery and coronary artery by pass grafting, were assessed by preoperative transthoracic echo-cardiography and cardiac catheterisation. They presented with secondary PH and preserved high persistent values of pulmonary pressures after CPB. All patients were classified as NYHA III.

Preoperative characteristics of patients included are given in **Table 1**.

Table 1: Preoperative characteristics

Pts	Age/sex	Diagn	Operation	SPAP MAP	SVR/ PVR	Therapy preop.
1	70/M	AD + CAD	AVR+ACB	62/40	1324/868	Furosemide metoprolol
2	56/M	MS + IT	MVR+TV	62/45	1529/1032	Furosemide
3	65/M	MR+ CAD	MVR+ACB	72/49	1406/716	Captopril Spironolactone

Abbreviations:

AD = *aortic disease*
AVR = *aortic valve replacement*
ACB = *aorta coronary bypass surgery*
MVR= *mitral valve replacement*
TV = *tricuspid valvuloplasty*
MS = *mitral stenosis*
MR= *mitral regurgitation*
TR = *tricuspid regurgitation*
CAD = *coronary artery disease*
SVR = *systemic vascular resistance (dyne.sec.cm-5)*
PVR = *pulmonary vascular resistance (dyne.sec.cm-5)*
SPAP = *systolic pulmonary arterial pressure (mmHg)*
MPAP = *mean PAP (mmHg)*

These patients with moderate to severe pulmonary venous hypertension complained during the months before surgery of deterioration of exercise capacity and of occurrence of cardiogenic oedema (signs of cardiogenic failure).

The morning of surgery, all patients received dormicum 0.5 mg/kg p.o and morphine 0.1 mg/kg i.m, 45 minutes preoperatively.

While in the operating room patients received oxygen (2 l/min) by face-mask and the usual monitors were used. Under local anaesthesia, a large peripheral i.v catheter and a 20 gauge radial artery catheter were inserted. Patients had anaesthesia induced with fentanyl, dormicum and pancuronium, maintaining mean arterial pressure greater than 60 mmHg. After induction of anaesthesia, a pulmonary arterial catheter (thermodilution catheter, Baxter Edward Swan Ganz) was inserted via the right internal jugular. Anaesthesia was maintained with isoflurane, fentanyl and dormicum boluses. Baseline post induction hemodynamic variables were measured. The temperature during CPB was in keeping with the surgical procedure (slight hypothermia).

During the rewarming phase a *conventional ultra-filtration* (CUF) was initiated. The target for ultra filtrate removal was to achieve a zero fluid balance at the end of CPB. Weaning from CPB was under continuous infusion of 8µg/kg/min dobutamine and of 0.1-0.2 µg/kg/min epinephrine, maintaining a MAP greater or equal to 60 mmHg. 10 min after CPB, protamine was administered to achieve zero heparin level. 10 min after protamine it was decided to administer aerosolised iloprost - single dose.

Delivery of iloprost

Delivery of iloprost: iloprost was administered by an ultrasonic nebulizer (OPTINEB; Germany) at a concentration of 2µg/ml. The nebulizer was introduced in the inspiratory limb of the anaesthesia machine. No filter was interposed between the patient and the nebulizer. The particle size of the aerosols was between 2.5-5 µm, so they deposited by sedimentation and diffusion in the small airways and alveoli. With an average nebulization rate 0.6 ml/min after 20 min a cumulative dose of 2.4 µg had been administered.

Inspiratory oxygen fraction was kept constant at 1. Adjustment of minute ventilation settings on the ventilator aimed to avoid hypoxemia and hypercapnia.

Hemodynamic measurements

The following variables were measured or calculated: cardiac output (CO); systolic, diastolic and mean arterial blood pressures (SAP, DAP, MAP); SPAP, MPAP; central venous pressure; pulmonary arterial occlusion pressure; SVR, PVR.

Measurements were performed: 30 min after induction of anaesthesia, 5 min after separation from CPB, 5 min after protamine (= before iloprost) and after iloprost administration.

Results

The baseline hemodynamic characteristic of the patient is shown in Table 2.

Table 2: Baseline hemodynamic characteristic of the patients

	AFTER INDUCTION			AFTER CPB		
Patient	**1**	**2**	**3**	**1**	**2**	**3**
SPAP	**59**	**62**	**70**	**51**	**60**	**50**
MPAP	**41**	**40**	**48**	**34 (-14.6%)**	**39 (-2.5%)**	**32 (-33.3%)**
SAP	**115**	**85**	**80**	**105**	**88**	**89**
PVR	**250**	**585**	**450**	**158 (-36%)**	**275 (-52.8%)**	**310 (-31.1%)**
PVR /SVR	**0.19**	**0.4**	**0.3**	**0.23**	**0.30**	**0.28**
CO/CI	**3.1/1.6**	**4.2 /2.1**	**3.1/2**	**8.4 /4.1 (+60%)**	**5 /2.41 (+12%)**	**4.4/2.6 (+20%)**

In two patients, the high MPAP and PVR plus the low cardiac output indicated a moderate to severe PH. Duration of CPB was: 197 min for patient 1; 165 min for patient 2; 86 min for patient 3.

After separation of CPB (end of CUF), MPAP decreased (-16.8%), PVR decreased (-40%), cardiac index (CI) increased with 30%. After protamine administration MPAP and PVR remained at high values in patients 2 and 3. In patients 1, PVR increased from 158 to 190 dyne.sec.cm -5, with a decreased in CI from 8.4L/min to 6 L/min. Persistent high values of SPAP and MPAP (>30 mmHg) were noted after separation from CPB and protamine administration. Hemodynamics characteristics of the patients after protamine administration (before iloprost) and after inhaled iloprost are presented in Table 3 (next page).

MPAP decreased by 30.8%, after inhaled iloprost. PVR decreased by 26%. CI increased by 17%. During the experimental procedure the inotrope remained unchanged and there were no significant changes in HR, MAP, CVP, PAOP, SaO2, PaO2, PaCO2. None of the patients experienced reduction in MAP <60 mmHg. There were no side effects in the patients after administration of aerosolised iloprost.

Table 3: Hemodynamics characteristics of the patients after drugs administration

	After Protamine = Before Iloprost			After Iloprost		
Patient	1	2	3	1	2	3
SPAP	51	60	50	37 (-28%)	44 (-27%)	37 (-26%)
MPAP	33	40	32	20 (-39.3%)	25 (-37.5%)	27 (15.6%)
SAP	98	89	90	110 (+10%)	90 (1%)	106 (+15%)
PVR	190	284	327	155 (-18.4%)	180 (-36.6%)	250 (-23.5%)
PVR/SVR	0,22	0,3	0,28	0,19	0,2	0,24
CO/CI	6/3	5.4/2.6	4.4 /2.6	6.7/3.2 (+ 6.25%)	7.6/3.8 (+ 31.5)	5.1/3.0 (+13%)

Discussion

1. Secondary PH due to left sided myocardial or valvular disease was grouped under the category "pulmonary hypertension associated with left heart diseases", according to the Clinical classification of pulmonary hypertension – Venice 2003.

The common characteristic feature of all these disease is an increase in left atrial pressure that means an increased resistance to pulmonary blood flow down-stream leading to "passive" pulmonary hypertension. There is an elevation in the pulmonary artery pressure but no significant elevation in pulmonary vascular resistance.

A chronic rise in pulmonary venous hypertension develop structural changes in parallel with chronic vasoconstriction-remodelling (5). The term remodelling is normally used in according with the changes in the small pulmonary vessels. Remodelling of the vessel wall result in:

a) intimal fibrosis
b) hypertrophy of the media
c) and so called "de novo muscularisation".

The mediator's profile of the endothelial cells shifts from anticoagulatory to predominantly pro-thrombotic and from vasodilation to vasoconstrictive profile. The synthesis of prostacyclin is reduced in chronic pulmonary hypertension, whereas the synthesis of thromboxane A2 and endothelin is increased. The shift in balance from prostacyclin to TxA2 favours vasoconstriction, proliferation, thrombosis and inflammation (6).

2. In the present study, we noted the hemodynamics effects of inhaled iloprost in patients with secondary pulmonary venous hypertension. Due to the high risk of severe peri operative aggravation of the patient's pulmonary hypertension we decided to administer inhaled iloprost after protamine.

3. Perioperative evolution of secondary PH. After corrective surgery on the mitral or aortic valve, both pulmonary vascular resistance and pulmonary hypertensive decline. The major extent of this decline is noted within the first postoperative week (7). PVR is not immediately reversible after CPB. More- over there are some intraoperative vasospastic stimuli, such as: hypoxia, hypercarbia, acidosis, duration of CPB, ischemia-reperfusion injury, free radical formation, microemboli, protamine (8). Levels of TxA2 and endothelin were increased after CPB, whereas PGI2 and NO (nitric oxide) levels were reduced.

Protamine reversal of heparin-induced anticoagulation causes complement activation leading to TxA2 generation and pulmonary vasoconstriction (9).

Acute aggravation of HP, in the presence of decreased right ventricular compliance after CPB could lead to decreased in RVEF (right ventricular ejection fraction).

4. In these patients, the use of conventional ultra-filtration had in view to remove a significant amount of the circulating endothelin 1 (10). Removal of free water may contribute to improved pulmonary mechanics after CPB and results in lower PAP.

Hemodynamic response after separation from CPB (compared to baseline) showed a decrease in PVR and MPAP, an increased in CI. MPAP remained up to 30 mmHg after CPB (CUF) and protamine administration so we decided to use inhaled iloprost as a strategy for decreasing pulmonary pressure and right heart afterload.

5. Iloprost is a stable carbacyclin derivative of PGI2. Prostacyclin is one of the most potent pulmonary vasodilator agent available for clinical purpose. Moreover, in severe PH, local deficiencies of PGI2 may play a role in the genesis and progression of valvular remodelling.

The technique of intra-alveolar deposition of prostacyclin and its analogue seemed the most adequate (11, 12). Inhaled iloprost causes selective pulmonary vasodilation, it proves intrapulmonary selectivity. That means that the pulmonary circulation is redirected to those parts of the lungs that are most well-ventilated (improve in ventilation /perfusion ratio) (13). The effects of inhalation with iloprost on our patients were: a decrease of MPAP by 30%, of PVR by 26% and an increase of CI by 17% without changes in SAP.

75-80 minutes after termination of inhalation of iloprost MPAP and PVR returned to after CPB values.

6. Iloprost-inhaled alternatives to NO. Studies have shown comparable hemodynamic effects of the inhaled agents: NO, iloprost, prostacyclin (PGI2).

The advantages of iloprost over PGI2 include its solubility in saline and a significantly longer duration of action. After termination of aerosolisation, prosta-cycline-induceed changes return to baseline within 10-30 min; iloprost -induced changes within 60-120 minutes and NO-changes in 2-5 minutes.

NO has clinical applications on neonates with acute lung injury and PH and for adults with PH.

The cost of treatment with NO is very expensive (14, 15); the daily cost of PGI2 is only a small fraction of that of NO. In a multicenter trial by the German PPH study group inhaled iloprost was significantly more effective than NO; the increase in CO and the decrease in PVR was greater with inhaled iloprost than with NO. During inhalation with NO, there was a significant drop of 4.3 mmHg in the MPAP. However iloprost produced a larger drop of 10.3 mmHg in MPAP. A decrease of 14% was after NO and of 34% after iloprost (16).

7. We recommend including iloprost in the perioperative protocol for the patients undergoing cardiac surgery with major risk for aggravation of PH and right heart decompensation.

There is still debating over the additive effects of conventional hemofiltration and of iloprost to decrease perioperative PH. The group of patients studied was too small for us to do a statistics analysis of the variables.

Conclusions

In these patients, with persistent PH (after valve replacement and protamine administration), inhaled iloprost decreases PAP, lowers pulmonary resistance and increase cardiac output with no effect on systemic arterial pressure.

The administration procedure is uncomplicated and does not require additional monitoring.

Inhaled iloprost represents an alternative to nitric oxide in the studied patients.

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Betablockers for Prevention of Perioperative Atrial Fibrillation in Coronary Surgery: Lokren (Betaxolol) versus Metoprolol[*)]

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Abstract

Background. *In patients undergoing coronary artery bypass surgery the most common immediate postoperative complication is atrial fibrillation. It's prevention and treatment is only regulated in patients with a risk score significant for atrial arrithmias. There are a few studies testing the benefits of beta blockers used perioperatively in patients undergoing coronary surgery. We have attempted to carry out a randomized, open-label trial comparing the efficacy and safety of Betaxolol (Lokren) versus Metoprolol during the immediate postoperative period in patients undergoing coronary artery bypass grafting irrespective of their preoperative estimated risk for atrial arrhythmias.*

Method. *Open-label, randomized, multicentric clinical trial enrolling 1352 patients undergoing coronary artery bypass grafting. During the perioperative period they were randomised to take Betaxolol or Metoprolol. The primary endpoints were the composites of 30-day mortality, in-hospital atrial fibrillation (safety endpoints), duration of hospital stay and immobilization, quality of life, and the above endpoint plus in-hospital embolic event, bradycardia, gastrointestinal symptoms, sleep disturbances, cold extremities (efficacy plus safety endpoint). Systat and SPSS programs were used in the statistical analysis for the simple linear and multivariate regression analysis, and to calculate the correlation coefficient and relative risk.*

Results

1. *Prevention of perioperative atrial fibrillation with Betaxolol was proven to be more effective than with Metoprolol during the immediate postoperative management of coronary surgery patients.*
2. *Subjective measures in patients achieving a more favorable response included clinical improvement with decreased immobilization and hospitalization periods, less gluteal ulcerations and less postoperative depression and anxiety episodes.*
3. *Objective measures of Betaxolol efficacy in patients with coronary artery bypass grafting included:*

*) **Romanian Journal of Cardiovascular Surgery ■ 2007, vol. 6, no. 4, pp. 178**

- *maintenance of sinusal rhythm or rapid conversion to it in case of atrial fibrillation*
- *absence of early left atrium thrombosis in the study group*

4. *The probability of death was smaller in the Betaxolol group compared with the Metoprolol group.*
5. *No major complication was reported in either of the two groups. Minor side effects as bradycardia, sleep disturbances and gastrointestinal symptoms were more common in the Metoprolol group.*
6. *Patient compliance was good, and quality of life improved due to shortened hospital stay, less atrial or ventricular arrhythmias, increased dosing convenience (once daily for Betaxolol versus every 12 hours for Metoprolol), shortened immobilization during the immediate postoperative period with subsequent improvement in the psychological status, as well as due to lack of significant side effects.*

Conclusions. *Taking into account efficacy and safety, the early postoperative atrial fibrillation prevention in coronary surgery with Betaxolol emerged as the best treatment in this trial. Because of additional advantages such as the ease of administration, reduction of the hospitalization duration and improvement of the quality of life Betaxolol should be regarded as an attractive alternative pharmacological strategy for the prophylaxy of atrial arrhythmias in coronary artery bypass grafting.*

Background

Atrial fibrillation is a common arrhythmia following open heart surgery that is associated with increased morbidity and mortality. Patients who develop postoperative atrial fibrillation are more likely to have other postoperative complications such as peri-operative MI, CHF, respiratory failure [1, 8, 30] and increased hospital length of stay and costs. Postoperative atrial fibrillation is associated with longer ICU and hospital stays and consequently, the economic cost can be considerable (27).

The true incidence of postoperative atrial fibrillation following cardiac surgery is unclear; reported incidence ranges from 10-65% [9, 20]. The reported incidence range is wide because the studies differ in baseline patient characteristics, type of surgery, methods of detection and definitions of atrial fibrillation [23, 28]. There is a lower incidence of atrial fibrillation in patients undergoing only coronary artery bypass grafting (CABG) compared to those patients undergoing valve surgery or combined CABG-valve operations [2, 17, 19, 21,22, 31, 33, 34]. Postoperative atrial fibrillation most often occurs during the first five days with a peak incidence on the second and third day postoperatively [4, 6].

Because of the increased morbidity and mortality associated with postoperative atrial fibrillation, prevention is a reasonable clinical goal, and, consequently, many randomized trials have evaluated the effectiveness of pharmacological and nonpharmacological interventions for prevention of postoperative atrial fibrillation. Trials with different drugs and other therapeutic modalities including beta-blockers, intravenous amiodarone and override suppression of automatic atrial foci by atrial pacing have shown partial success as preventive measures. However, a comparison between those three interventions has not been reported.

Beta blockers have gained wide acceptance and are now recommended for prophylaxis by the American College of Cardiology (ACC) for the prevention of atrial fibrillation in all patients undergoing cardiac surgery unless contraindicated. The ACC guidelines also recommend using sotalol or amiodarone prophylactically in patients who are considered to be at an increased risk of developing postoperative atrial fibrillation [10].

Unlike propranolol, cardioselective beta blockers have have relatively fewer extracardial effect and, consequently, they are more safe in patients with cardiovascular diseases who suffer also from obstructive respiratory tract disease or diabetes, providing a strong rationale for better outcomes in patients after cardiac surgery [29].

The few studies of beta blockers used in heart surgery, specifically in coronary surgery for the prevention of early postoperative atrial arrhythmias, have shown a decrease in the incidence of atrial fibrillation occurrence, as well as an increase in postoperative convenience and the quality of life in beta blockers versus placebo patients [12, 29, 32].

Betaxolol is a beta-1 antagonist with long action duration (biological half life 15-20 hours) and slightly bound to serum proteins (50%). Large-scale studies using Betaxolol given in the perioperative period in coronary artery surgery for the prevention of early postoperative atrial fibrillation have never been done before.

Objectives

1. Assessment of the efficacy and safety of Betaxolol versus Metoprolol given to patients undergoing surgical coronary revascularization in the immediate postoperative period for prevention of atrial fibrillation.
2. To determine whether prophylactic beta blocker therapy with Betaxolol can reduce hospital stay after cardiac surgery by reducing the risk of atrial fibrillation

Material and methods

Randomized, multicentric, two-years clinical trial with open study period, carried out in two parallel groups.

Eligibility criteria

The study included all patients undergoing coronary artery bypass grafting, who underwent surgery in five cardiac surgery clinics from our country *("C.C.Iliescu" Institute for Cardiovascular Diseases and Military Central Hospital from Bucharest, Heart Institutes from Timisoara, Targu Mures and Cluj Napoca)* between November 1st 2005 and November 1st 2007.

Non-eligibility criteria

[1] Second and third degree atrioventricular block
[2] Known hypersensitivity to beta blockers
[3] Conditions associated with increased risk for bradycardia (vagal predominance, sick sinus syndrom).
[4] Heart failure NYHA class > 2.
[5] Cardiogenic shock.

[6] Bradycardia (pulse rate below 50 beats/min).
[7] Severe COPD or pulmonary impairment
[8] Active participation in another clinical trial
[9] Failure to comply with the hospital protocol or absence to follow-up

Study drop out criteria included the occurrence of adverse events (severe bradycardia, skin reactions, gastrointestinal symptoms, cold extremities).

The protocol was approved by the institute management, and every patient signed the informed consent form.

After inclusion in the study, patients were randomized to receive:

- **Group A:** Betaxolol po 20mg once daily (every 24 h)
- **Group B:** Metoprolol po 200 mg in two divided doses (every 12 hours).

The treatment was given for a period of 2 days preoperatively and no less than 10 days postoperatively.

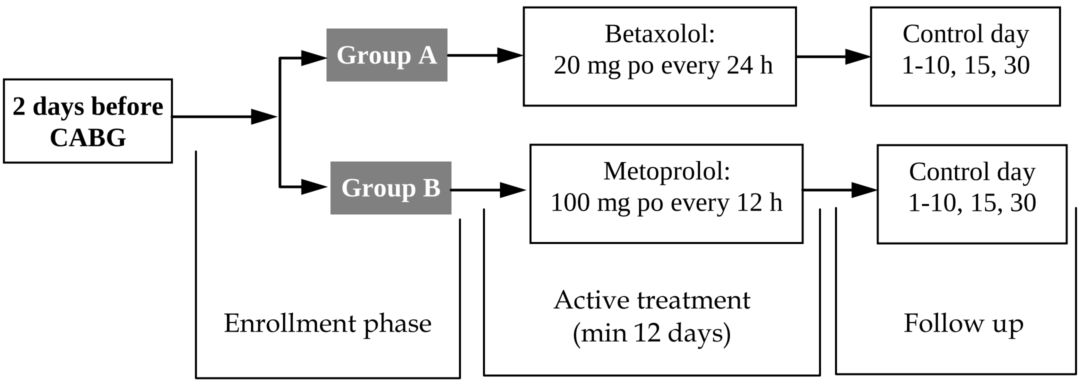

Figure 1. Treatment protocol phases.

Patients were randomized to one of the two treatment groups. The essential inclusion criteria (gender, age, number of grafts, left ventricular ejection fraction), the duration of treatment and assessment criteria were similar in the two treatment groups (p < 0.0001).

Clinical and laboratory parameters were initially assessed, at baseline and at the end of the treatment. The clinical measurements included: NYHA class for heart failure, ventricular rhythm, patient compliance and quality of life. Laboratory parameters included: the usual blood tests (platelet count, hemoglobin, hematocrit, aminotransferases, LDH, biochemistry), electrocardiogram (with the evaluation of rhythm and frequency), 24 hours ECG Holter monitoring and echocardiographic measurements of the left venticular dimensions, sistolic and diastolic performance, left atrium dimensions and compliance prosthetic valves [23].

Early development of heart failure was diagnosed based on clinical criteria and through thoracic and transesophageal echocardiography. The appearance of bradycardia or atrioventricular block second or third degree was diagnosed using clinical evaluation, electrocardiogram and Holter monitoring.

After enrollment in the study, patients were reassessed post-operatively and not randomized until they were shown to be free of low heart rate, low cardiac index, bronchospasm, or need inotropic support (n = 1,000).

The study included 580 patients undergoing coronary artery bypass grafing with arteries (internal mammar, radial, gastroepiploic) or inverted saphenal veins. The patients were randomized to receive Betaxolol 20 mg daily or Metoprolol 100 mg twice daily two days before surgery and in the postoperative period for no less than 10 days. The mean age, gender, number of grafts per patient, the type of the grafts (arterial or venous) and the mean left ventricular ejection fraction and left atrial dimensions (diameters and area) were similar in the two groups. The patients undergoing also venticular remodelling for aneurysms were not taken in our study. All patients received concomitant antiplatelet therapy with Aspirin, immediately after surgery. The patients with exclusive arterial revascularization also received calcium channel blockers agents but their number was similar in the two groups of study. The incidence of bradycardia episodes, the occurrence of gastrointestinal symptoms, sleep disturbances, skin reactions and cold extremities were also recorded.

The primary endpoints were the composites of 30-day mortality, in-hospital occurrence of atrial fibrillation (safety endpoints), total hospital stay and immobilization (measured in days), Intensive Care Unit length of stay and cost, quality of life, and the above endpoint plus in-hospital embolic events, bradycardia, gastrointestinal symptoms, sleep disturbances, cold extremities (efficacy plus safety endpoint).

The data collected represented the fields of a database in the Visual Fox Pro computer program. Data were processed by means of computers, using the Excel, EpiInfo, Systat and SPSS programs.

No confirmatory statistical hypothesis was pre-specified, but a detailed analysis plan was defined before the database was locked. This analysis plan was based on generating risk ratios and Cis (CI = *Confidence Index*) for the pairwise comparisons of primary interest. These comparisons were presented with the two - sided 95% CI of the relative risk and with normal p values. For the primary endpoints Kaplan-Meier curves were constructed and log-rank tests were done. For each endpoint, a two-sided 95% CI was also calculated and an overall Chi square test, comparing the three treatment groups was done [19, 21, 25].

The frequency of the primary efficacy plus safety endpoint for the Metoprolol group as a reference group was 17.7%. On the basis of phase-II studies we assumed that the experimental group with Betaxolol would result in better or at least similar outcomes when compared with standard treatment. The sample size and power calculations were therefore based on non-inferiority of the experimental group versus the reference group. The study has 80% power to exclude, with 95% confidence (one-sided), a 1% higher rate of the primary endpoints compared with the reference group, provided the point estimate in the experimental treatment group was 1.7% lower for the efficacy endpoint and 2% lower for the efficacy and safety endpoint [2-11, 13-18, 22].

Results

1400 patients were enrolled between November 2005 and November 2007 of whom 1352 received study medication.

The baseline characteristics were similar in the two groups (Table 1). Overall, the study populations were similar to those of previous trials on anticoagulants.

Table 1 Baseline characteristics

	Group A - 672 pts	Group B - 680 pts
Mean (SD) age (years)	63 (12)	63 (13)
Age > 70 years	15.75%	15.43%
Women	32.53%	31.88%
Mean (SD) weight (kg)	75 (15)	77(14)
Mean (SD) height (cm)	172 (9)	171 (10)
Mean (SD) heart rate/24h	78 (15)	77 (14)
NYHA class I	37.67%	36.91%
NYHA class II	11.64%	10.06%
Mean (SD) systolic blood pressure (mmHg)	152 (22)	153 (23)
Previous episodes of atrial fibrillation	17.46%	17.11%
Hypertension	65.07%	63.76%
Diabetes mellitus	41.09%	40.27%
Current smoker	32.53%	31.88%
Re-intervention *(previous coronary artery surgery)*	10.27%	10.07%

Depending on the number and the type of the grafts, the two groups were homogenous (Figure 2, 3).

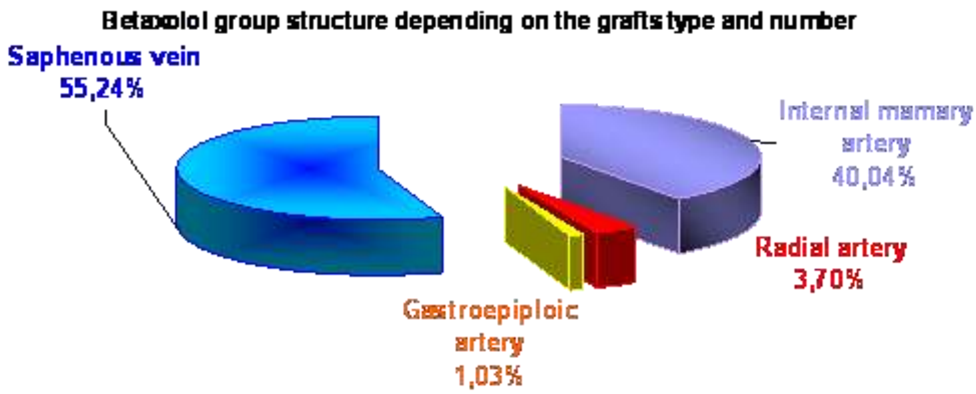

Figure 2: Coronary grafts type and number in Betaxolol group

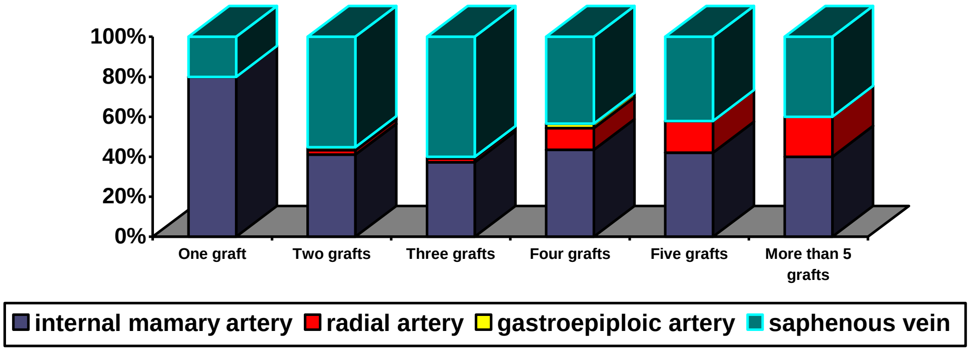

Figure 3: Coronary grafts type and number in Metoprolol group

Concomitant medications given in hospital are listed in table 2

Table 2: Number of patients who received concomitant medications during stay in hospital

	Betaxolol group	Metoprolol group
Digoxin	51 (17.46%)	50 (16.78%)
ACE inhibitors	261 (89.38%)	262 (87.92%)
Angiotensin II inhibitors	15 (5.14%)	13 (4.36%)
Aspirin	256 (87.67%)	257 (86.24%)
Ticlopidine/Clopidogrel	36 (12.33%)	41 (13.76%)
Calcium channel blockers	27 (9.25%)	26 (8.72%)
Diuretics	126 (43.15%)	124 (41.61%)
Aldactone	84 (28.77%)	83 (27.85%)

9.25% of patients received calcium channel blockers (Diltiazem) in group A, respectively 8.72% in group B.

The primary efficacy and efficacy plus safety endpoints and their individual components in the treatment groups are shown in Table 3.

Table 3: Frequency of composite and single endpoints at hospital discharge and at 30 days

	Betaxolol group	Metoprolol group
30 day mortality, in-hospital atrial fibrillation	46/292 (15.75%)	69/298 (23.15%)
30 day mortality, in-hospital atrial fibrillation or in-hospital severe bradycardia/AV block	61/292 (20.89%)	91/298 (30.54%)
Death at 30 days	12/292 (4.11%)	16/298 (5.37%)
In-hospital atrial fibrillation	34/292 (11.64%)	53/298 (17.78%)
In-hospital severe bradycardia/ AV block	15/292 (5.14%)	22/298 (7.38%)
In-hospital heart failure worsening	18/292 (6.16%)	23/298 (7.72%)
Hospitalization duration>15 days	32/192 (10.96%)	38/298 (12.75%)
Immobilization for >3 days	15/292 (5.14%)	23/188 (7.72%)
Sleep disturbances/ gastrointestinal symptoms/ skin reactions	11/292 (3.77%)	24/298 (8.05%)

The combined efficacy and safety outcome in the Metoprolol group of 91/298 patients (30.54%) was similar to that estimated before the trial commenced (31%).

The Kaplan Meier curves for these primary endpoints are shown in figure 4. Log rank tests were highly significant. Early after treatment, the curve for the Betaxolol started to separate from that of Metoprolol. At 48h, differences in the primary endpoints between the two groups were already present. For the primary efficacy endpoint, event rates were 4.11% for Betaxolol group and respectively 5.37% for Metoprolol group ($p < 0.0001$). For the primary efficacy plus safety endpoint, the rates were 15.75% for Betaxolol group and, respectively, 23.15% for Metoprolol group. ($p = 0.02$).

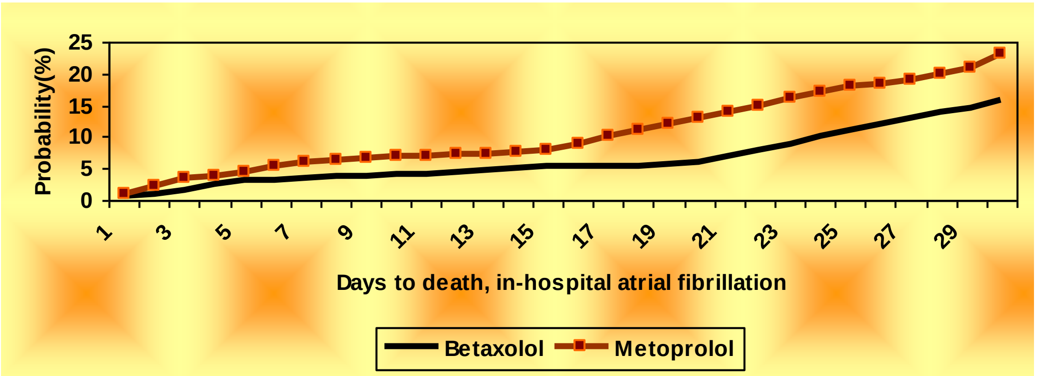

Figure 4: Betaxolol versus Metoprolol Kaplan-Meier curves for primary efficacy plus safety endpoint

The relative risks in the two groups are presented in table 4. The rates of the composite endpoints were lower among patients treated with Betaxolol than among those treated with Metoprolol. Conventional statistical testing for Betaxolol versus Metoprolol resulted in p values of 0.0002 and 0.0003 respectively for the primary efficacy plus safety composite endpoints.

Table 4: Relative risks and 95% CIs for primary efficacy composite endpoint in the two groups.

Death at 30 days, in-hospital atrial fibrillation, hospitalization duration > 15 days, or severe bradycardia	Betaxolol group	Metoprolol group	Relative risk Betaxolol better	Relative risk Metoprolol better
Overall event rate	61/292 (20.89%)	91/298 (30.54%)	0,64	0,94
Age <70 years	19/246 (7.72%)	51/252 (20.24%)	0,40	0,55
Age>70 years	42/46 (91.30%)	40/46 (86.96%)	1,34	3,8
NYHA II class	10/34 (29.41%)	11/30 (36.67%)	1,23	4,2
Type of grafts				
- exclusive arterial	3/28 (10.71%)	3/29 (10.34%)	0,33	0,34
- exclusive venous	5/12 (41.67%)	6/13 (46.15%)	0,91	1,34
- combined arterial and venous	53/252 (21.03%)	82/256 (32.03%)	1,78	3,3

Number of grafts				
- one	1/10 (0.1%)	1/11 (9.09%)	0,2	0,33
- two	20/84 (23.81%)	26/86 (30.23%)	0,3	0,3
- three or more	40/198 (20.20%)	64/201 (31.84%)	0,9	1,2
Previous episodes of atrial fibrillation	32/51(62.75%)	41/51 (80.39%)	1,5	3,8

In-hospital atrial fibrillation occurred less frequently in patients treated with Betaxolol than in those treated with Metoprolol. The rates of in-hospital death were also lower in the Betaxolol group. (4.11%) than in Metoprolol group (5.37%). No significant reductions in other major cardiac complications were seen with the exception of a significantly lower rate for postoperative myocardial infarction in patients with risk factors in the Betaxolol versus the Metoprolol group.

The mean duration of hospitalization in the Betaxolol group was 10.5±4.3 days, compared to 14.5±5.8 days in the Metoprolol group.

The mean immobilization interval during the immediate postoperative period in group A versus group B was 1.02±3 days versus 3.5±2.8 days, respectively. Quality of life was considerably better in the Betaxolol group.

Concerning beta blocker therapy side effects the dates on their in-hospital appearance are summarized in Table 5. Total episodes of severe bradycardia and atrioventricular block second or third degree rates were similar in both groups. A few patients with gastrointestinal symptoms, sleep disturbances, skin reactions, cold extremities or tiredness were seen in each of the two treatment groups.

Table 5: In-hospital rates of side effects

	Betaxolol group	Metoprolol group	*p*-value
Total pts with side effects	12/292 (4.11%)	25/298 (8.39%)	0.95
Gastrointestinal symptoms	4/292 (1.37%)	7/298 (2.35%)	0.92
Sleep disturbances	4/292 (1.37%)	8/298 (2.68%)	0.78
Skin reactions	2/292 (0.068%)	4/298 (1.34%)	0.92
Cold extremities	1/292 (0.034%)	3/298 (1.006%)	0.88
Tiredness	1/292 (0.034%)	3/298 (1.006%)	0.75

Heart failure worsening after beta blocker treatment, severe bradycardia and rates of the appearance of atrioventicular block second and third degree are given in table 6. Significantly more episodes of severe bradycardia (p = 0.0001), more patients with second or third degree atrioventricular block (p = 0.002) and a higher rate of heart failure worsening (p = 0.001) were seen in patients with associated treatment with calcium channel blockers. In patients older than 75 years and in diabetics, the rate of important side effects was three times higher in those with associated calcium channel blockers therapy (4%versus 14% and 2% versus 7% respectively).

More sleep disturbances and cold extremities were also seen in the Metoprolol group compared with Betaxolol group, although these differences were not significant. There was no excess of skin reactions, gastrointestinal symptoms and tiredness in the Betaxolol treatment group. The total number of re-hospitalizations was similar in the two treatment groups (11.41%in Betaxolol group respectively 11.7% in Metoprolol group). A few additional episodes of atrial fibrillation occurred after hospital discharge in the two groups.

Table 6: Rate of in-hospital bradycardia, atrioventricular block and heart failure worsening

	Betaxolol group	Metoprolol group	*p*-value
Any bradycardia	9/192 (3.08%)	14/298 (4.7%)	< 0.0001
Bradycardia			
< 35 beats/min	0/292 (0%)	2/298 (0.67%)	< 0.0001
35 – 40 beats/min	4/292 (1.37%)	6/298 (2.01%)	< 0.0001
40 – 50 beats/minlls/µl	5/292 (1.71%)	6/298 (2.01%)	< 0.0001
Atrioventricular block			
Total	6/292 (2.05%)	8/298 (2.68%)	< 0.0001
Third degree	1/292 (0.34%)	2/298 (0.67%)	< 0.0001
Second degree	5/292 (1.71%)	6/298 (2.01%)	< 0.0001
Heart failure worsening	18/292 (6.16%)	23/298 (7.72%)	< 0.0001

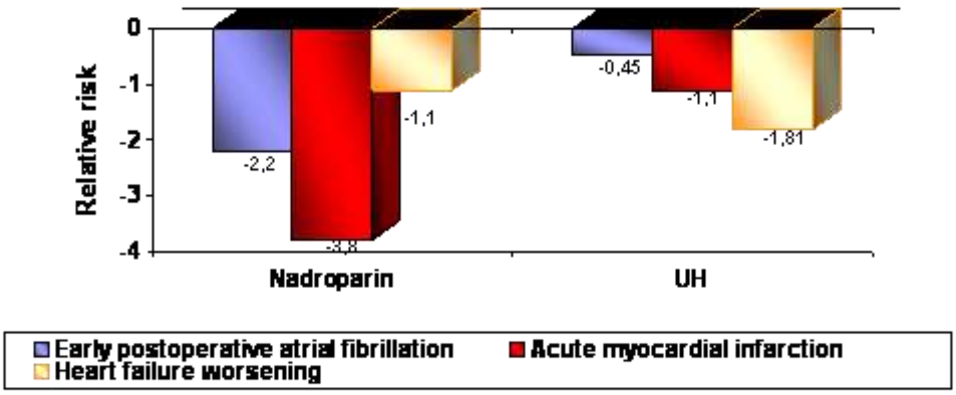

Figure 5: Betaxolol versus Metoprolol – relative risk for early postoperative atrial fibrillation, acute myocardial infarction or heart failure worsening

The probability of death, early postoperative atrial fibrillation and perioperative myocardial infarction was smaller with Betaxolol versus Metoprolol.

No significant change in liver function tests and blood biochemistry was recorded in the three groups.

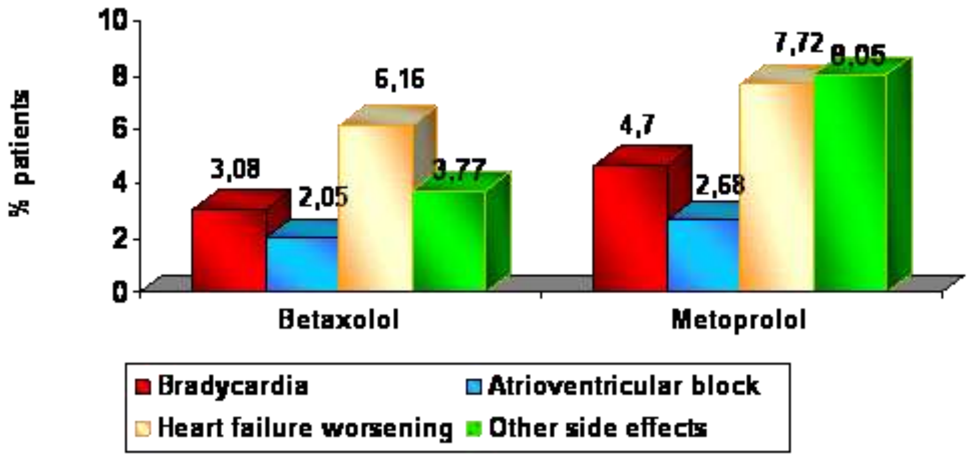

Figure 6: Treatment side effects

Discussions

Atrial fibrillation is a common complication after cardiac surgery that is associated with increased morbidity, mortality and longer hospital stays. Many studies have evaluated ways to decrease atrial fibrillation, however, none of these trials have been strong enough to show an effect on length of hospital stay or stroke. In essence, none of the pharmacologic or pacing modalities have had an impact on length of stay, which remains stubbornly increased by the presence of atrial fibrillation.

Overall, the meta-analysis suggested atrial fibrillation prophylaxis reduces length of stay by only about one half of one day. Length of stay likely remains prolonged because of symptoms and complications of atrial fibrillation, necessity to apply pharmacologic or cardioversion interventions, adverse effects of medications, and intentional clinical observation [13, 14]. The data also suggests that there is no reduction in stroke risk due to any of the effective prophylactic treatments of atrial fibrillation [3, 10, 15, 18].

Patients should be assessed preoperatively for risk factors that may increase their likelihood of developing this postoperative arrhythmia. If no risk factors are identified, patients should receive beta blocker prophylaxis unless contraindicated. The utilization of prophylactic amiodarone or sotalol should be considered in those patients who have been identified to be at increased risk of developing postoperative atrial fibrillation [7, 11, 16, 24, 25, 26].

There are also pilot studies which compare right atrial pacing, intravenous amiodarone and oral beta-blockers in the prevention, time to onset, duration and effect on hospital stay of postoperative atrial fibrillation (AF) after coronary artery bypass graft surgery (CABG) [5, 7]. These studies showed a trend in favor of atrial pacing versus intravenous amiodarone or beta-blockers in the prevention of postoperative AF after CABG but randomization of a larger patient sample would be required in order to ascertain the true value of the observed trend.

Data from a few small studies have suggested that beta blockers reduce the risk of developing atrial fibrillation after heart surgery [12, 29, 32]. Unfortunately, in some of these trials, patients assigned to placebo that had previously been on beta-blockade probably suffered from beta-blocker withdrawal, thus biasing the results against placebo.

Despite this, the largest experience with prophylactic medical therapy is with beta-blockers. A number of clinical trials using a wide variety of beta-blockers have been published. Patients who have used preoperative beta-blockers that are withdrawn after surgery seem to be at particularly high risk of AF. Reinstitution of beta-blockers after surgery has been associated with a reduction of postoperative AF in most clinical trials.

Beta blocker prophylaxis is more effective when initiated preoperatively rather than postoperatively (4,10). Several clinical trials report that prophylaxis with beta blockers will decrease the relative risk of postoperative atrial fibrillation by 50%. These trials have shown a reduction in atrial fibrillation from 40% to 20% in patients undergoing CABG and a 60% to 30% reduction in those undergoing valve surgery [12, 29, 32]. A subsequent meta-analysis of 24 trials reported that beta blocker therapy decreases the incidence of postoperative atrial fibrillation by 72% (OR 0.28, CI 0.21- 0.36) [10].

The 6% reduction in the incidence of postoperative atrial fibrillation in patients with Betaxolol is more than reduction previously reported in smaller studies with other betablockers compared with Metoprolol [12, 29, 32]. It should be noted that about 80% of patients were on pre-operative beta blocker-therapy. The practice in our hospital was to routinely continue pre-operative beta-blocker therapy. Thus, this study suggests that prophylactic beta-blocker therapy with Betaxolol is useful.

In summary, beta-blockers represent the simplest and most cost-effective prophylactic treatment of postoperative atrial fibrillation, and are easy to employ in a patient population that requires betablockers for other purposes as well. Alternative antiarrhythmia drug therapy includes amiodarone and sotalol, and atrial pacing is promising, but not yet of proven benefit. Beta-blockers should be used as a first-line medication to prevent postoperative atrial fibrillation, a common complication of heart surgery. Reduction in length of stay by a simple, inexpensive therapy such as a beta-blocker can lead to a significant cost savings [10].

Conclusions

1. Betaxolol has shown increased efficacy over Metoprolol in the postoperative prevention of the appearance of atrial fibrillation in patients undergoing coronary surgery.
2. Subjective measures in patients achieving a more favorable response included clinical improvement with decreased immobilization and hospitalization periods, less palpitations episodes and less postoperative depression and anxiety episodes.
3. Objective measures of Betaxolol efficacy in patients with coronary artery bypass grating included:
    - maintenance of sinusal rhythm
    - few episodes of atrial fibrillation in the study group
    - rapid achievement of sinusal rhythm with its maintenance after cardioversion in patients with Betaxolol

4. The probability of death was smaller in the Betaxolol group compared with the Metoprolol group. No major side effect was reported in either of the two groups. Minor side effects as sleep disturbances and cold extremities were more common in the Metoprolol group.
5. Patient compliance was good, and quality of life improved due to shortened hospital stay, easy administration (once daily for Betaxolol, twice daily for Metoprolol), shortened immobilization during the immediate postoperative period with subsequent improvement in the psychological status, as well as due to lack of significant side effects.
6. Taking into account efficacy and safety, the prevention of postoperative atrial fibrillation in coronary surgery patients with Betaxolol emerged as the best treatment in this trial. Because of additional advantages such as the ease of administration, the reduction of the appearance of atrial arrhythmias, reduction of the hospitalization duration, Betaxolol should be regarded as an attractive alternative pharmacological strategy.

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The histogenesis of cardiac myxomas
Histochemical and immunohistochemical observations*)

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Abstract

Cardiac myxomas represent a controversial topic. They are considered either organized thrombi or neoplasms. Cardiac myxomas are rare tumors which usually affect the adult population. This paper presents the partial conclusions of a study whose aim was to identify the immunohistochemical profile of the cardiac myxoma and to highlight certain features that could differentiate between cardiac myxomas from organized thrombi, and between cardiac myxomas from primary malignant tumors (cardiac sarcomas).

We studied 45 cardiac myxomas operated on between 1993-2004 in the Cardiovascular Surgery Clinic of the Cluj-Napoca Heart Institute. The study included 25 fetal valves and 20 adult mitral valves removed by using routine procedures. The paraffin embedded tissue blocks were available. Serial sections at 5 microns were performed. The sections were histochemically stained for mucicarmine, Alcian blue PAS, orcein, Masson's trichrome and Gomory's. The immunohistochemical stains used the following primary antibodies: vimentin, desmin, alpha-smooth muscle actin, factor VIII, CD31, CD34, neuron- specific enolase, S-100, chromogranin.

Unilayer or multiplayer rings made of lepidic cells situated around a vascular canal represent the typical structure of myxomas. In two cases we studied the areas of glandular differentiation at the base of the myxoma. Our observations regarding cardiac myxomas, fetal valves and adult mitral valves conclude that cardiac myxomas are neoplasias generated from multipotent mesenchymal cells.

We believe that the identification of a pertinent immunohistochemical profile suggests that cardiac myxomas are neo-plasias; on the other hand, a differential diagnosis with cardiac sarcomas is also possible. This would be of great interest in current clinical practice.

Keywords: *cardiac myxoma, true neoplasia*

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Background

The British surgeon King was the first to describe cardiac tumors in English literature. In 1845 he wrote about six "vascular growths" in the left atrium of heart. Cardiac myxomas are primary cardiac tumors which have generated numerous debates. On the one hand the controversies have concerned its thrombotic or neoplastic origin while on the other hand they have been related to the histogenesis of the cell types present in the tumor. In 1907 Thorel suggested the thrombotic origin of cardiac myxomas for the first time. He believed that patients with cardiac myxomas suffered from circulatory disorders which generated thrombosis in the heart or other parts of the body. Thorel also considered that the histological features of the lesion matched the diagnosis for organized thrombus.

The concept according to which the myxoma is of thrombotic origin was developed by Husten and later by Styler and it continues to be accepted. In 1975 Salyer (6) updated the concept. He considered that the lesion is generated by the formation of a thrombus, whereas the histological aspect differs from that of thrombosis due to the development of the myxoma in an environment with unusual mechanical properties (6, 7). In 1996 the thrombogenic theory was developed by Beffutti and Silvermann (8). The authors studied four cardiac myxomas, embryonal and adult valves and demonstrated that the myxoma had primitive sub-endocardial cells capable of endothelial differentiation (positive cells for CD 31 and CD 34). They also concluded that the cells were mixed with factor XlIIa positive dendrophages whose presence suggested that the morphogenesis of the cardiac myxoma included a stage of abnormal organization that could resemble that of a thrombus.

Sixty years ago Ribbert was the first to focus on the idea that the neoplastic origin of the cardiac myxoma is due to embryonal rests situated near the oval fossa. This theory is currently supported immunohistochemically and by ultrastructural arguments. The comparison between cardiac myxomas and endocardial embryonal tissues found similarities between the superficial endothelial cells, the cells in the tissue of the valvular cusps and the "lepidic" cells of the myxoma. The cells of the embryonal endocardium could be myxoma precursors; the term vasoformative sub-endothelial spare cells refer to this hypothesis. This rationale suggests that the tumor could be generated by multipotent primitive mesenchymal cells present in the heart wall as embryonal remains. In 1927 Ribbert (4) launched the idea that the tumor came from embryonal cell nests situated near the oval fossa. This theory is widely accepted nowadays as it is supported by electron microscopic, histochemical and immuno-histochemical arguments.

Objective

This paper focused on the histogenesis of cardiac myxomas. Its objective was to present the arguments that support the idea that cardiac myxomas are of neo-plastic origin. We present the partial results of a study whose aim was to identify an immunohistochemical profile for cardiac myxomas and to highlight certain features that could differentiate cardiac myxomas from organized thrombi, and cardiac myxomas from primary malignant tumors (cardiac sarcomas).

Materials and method

We studied 45 cases of cardiac myxomas which were removed intraoperatively and analyzed histopathologically between 1993-2004. The cases were sporadic; most patients were women aged between 50 and 60; two of the cases presented cardiac myxomas of glandular structure (4.4%). These two cases underwent clinical examinations which excluded the presence of associated tumors. The patients were young (25-30 years old) and did not present signs of myxomas or familial aggregation. We also studied 25 fetal valves and 20 adult mitral valves, which were surgically removed.

The pieces were routinely processed; paraffin embedded tissue blocks were available and were sectioned at five microns. The serial sections underwent immunohistochemical and histochemical staining according to the standard protocol. The immunohistochemical examination was carried out for vimentin, cytokeratins, alpha-smooth muscle actin, desmin, factor VIII, CD 31, CD 34, neuron-specific enolase, S-100, chromogranin.

Cardiac myxomas, fetal valves and adult mitral valves were examined. These cardiac tumors were analyzed morphologically and immunohistochemically. The same procedures were employed for analyzing the fetal valves which underwent morphologic, immunohistochemical and histochemical determinations.

Immunohistochemical staining was carried out for the following: vimentin, cytokeratins, alpha-smooth muscle actin, desmin, factor VIII, CD 31, CD 34, neuron-specific enolase, S-100, chromogranin.

We also performed histochemical staining for Masson's trichrome, Alcian blue PAS, mucicarmine, Gomory's and orcein.

Results

Atrial myxomas were diagnosed histologically after identifying "myxoma cells" or lepidic cells in the shape of butterfly scales. These cells were detected in all investigated tumors. The term was introduced in 1942 by Orr who regarded these cells as being of endocardiac origin (3, 4, 5). Myxoma cells present an oval nucleus while the nucleolus is not easily noticeable. They are situated in a myxoid matrix; when isolated they have stellate aspect; when more cells are present they form complex structures. Myxomas are characterized by unilayer or multilayer rings situated around a vascular canal (Figure 1).

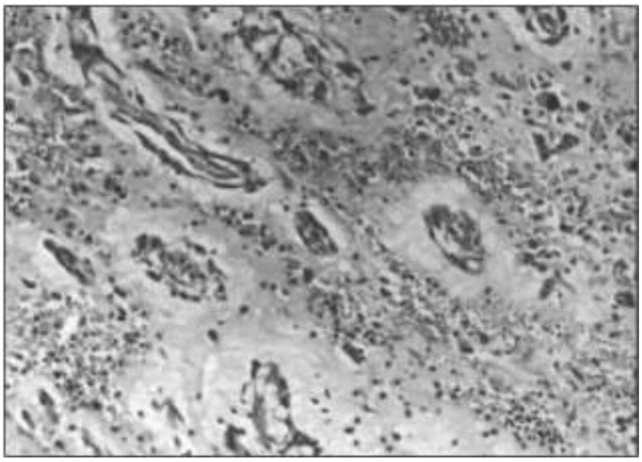

Figure 1: Cardiac myxoma. H.E.X. 100 lepidic cells organized in concentric rings

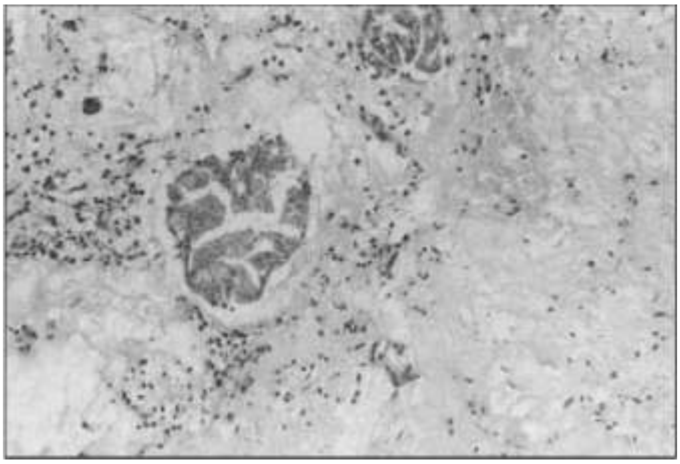

Figure 2a: Cardiac myxoma with glandular structures

We observed the areas of glandular differentiation at the base of the myxoma. Secondary determinations for carcinoma with a different localization were excluded. The tumors in our study did not contain malignant cells. All examined sections contained lepidic cells positioned in various ways, which supported the diagnosis for cardiac myxoma with glandular structure (Figure 2a and b).

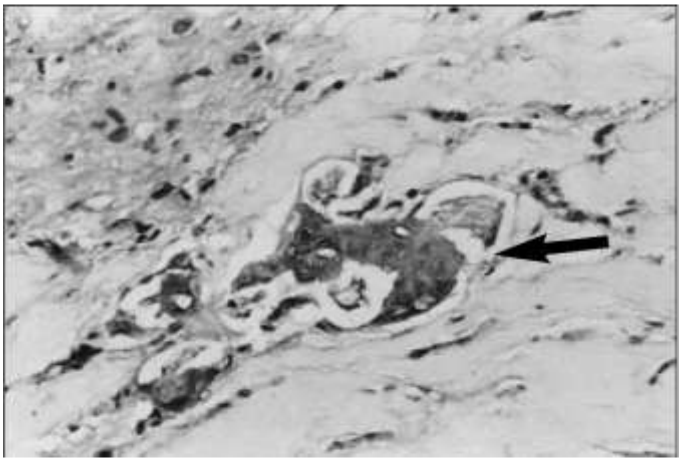

Figure 2b: Cardiac myxoma with glandular structures X 100; H.E.X. 100 staining for cytokeratins (arrow)

These structures were positive for cytokeratins; they were mucosecretant and resembled enteral structures.

The use of the electronic microscope demonstrates that the lepidic cells of the cardiac myxoma present features that belong to primitive mesenchymal cells in which the differentiation between smooth muscle and endothelium could not be made and which sometimes exhibit myofibroblast features. The fundamental substance contains electrondense granules which were described as being identical with the proteoglycans present in the fundamental substance of the cartilage (6, 7, 8). Cardiac myxomas can produce gelatinous matrices. This is an important feature which becomes obvious in embryonal cuspal tissues.

The lepidic cells which are supposed to produce the matrix (13, 14) contain vimentin, fact which proves their mesenchymal nature. Our study did not show positive cells for nervous markers (chromo-granin, neuron-specific enolase, S-100). The positive cells for factor VIII, CD 31 and CD 34 (endothelial markers) fill the primitive vascular spaces and the surface of the tumor. Ultrastructural studies of atrial myxomas confirm their immunohistochemical features by revealing the existence of primitive mesenchymal cells (9, 10).

The fetal endocardium and the adult valves presented various amounts of prolonged cells, which had features similar to those of lepidic cells and were positive for vimentin (Fig. 3).

Figure 3: Fetal endocardium X 200; staining for vimentin

Discussions

Approximately 95% of cardiac myxomas occur in the atrial endocardium. The tumor is located in the left atrium in approximately 75% of cases. The other cardiac myxomas are situated in the right or left ventricular endocardium. Myxomas are most often located in the atrial septum, near the oval fossa, where cardiac thromboses do not usually occur. Other localizations within chambers are rare, although the literature mentions atrial myxomas situated on cardiac valves. Cardiac myxomas are usually pediculate masses with smooth or villous surfaces. The villous surface may cause embolism. The behavior of cardiac myxoma emboli suggests the neoplastic origin. These emboli can develop in the arterial wall and cause fusiform aneurysms. Due to the fact that cardiac myxomas are considered benign tumors without malignant histological features and without the possibility to generate visceral or lymph node secondary localizations, they are not regarded as metastases (2, 11, 12, 13).

The positioning of the myxoma can produce obstructive valvular episodes. Radiologic investigations may show that old cardiac myxomas can become calcified. Such tumors are called "mummified". They fuel the debate thrombus vs. tumor. We believe that detailed microscopic examination and the absence of lepidic cells can establish the correct diagnosis.

The cardiac myxoma is regarded as a true neoplasm generated from undifferentiated mesenchymal cells which occur naturally in the subendocardial layer (14, 15, 16). The morphologic features of the fetal valves and of the myxoma cells, as well as their immunohistochemical profile, support our statement.

Cardiac myxomas are rarely recurrent. The detailed analysis of recurrent myxomas present in the literature lead to two important conclusions. Cardiac myxoma recurrences are more frequent in familial form (21% as compared with 1% for sporadic myxomas). On the other hand, myxoma cases reported as "malignant" were reevaluated and regarded as being inaccurately diagnosed - that is cardiac myxomas mistaken for sarcomas. Therefore, an intracavitary tumor in an adult patient could be both a cardiac myxoma and a primary sarcoma.

There are cardiac myxomas with glandular structures. Their presence is explained either by the existence of primitive remains of endodermal origin or by the fact that the cells that generated the myxoma underwent mesenchymal and epithelial differentiation. Based on these findings some authors consider that atrial myxomas are hamartomas caused either by intracardiac endodermal heterotopia or by intestinal embryonal rests. The idea that cardiac myxomas are hamartomas is based on the glandular elements occasionally present in the myxoma, which were thought to be remains of the primitive intestine. Suvarna (17) demonstrated that cardiac myxomas have proliferative abilities and reduced metastatic potential. Suvarna does not exclude the possible neoplastic origin of myxomas but he regards these results as being closer to a reactive/hamartomatous process.

Recent determinations suggest that the "mystery" of cardiac myxomas is solved by acknowledging the existence of a multipotent progenitor capable of divergent mesenchymal and epithelial differentiation. Immunohistochemical studies which showed the presence of calretinin-positive lepidic cells (18, 19) supported the neoplastic origin of the cardiac myxoma.

Partial conclusions

Although theories suggesting thrombosis or a reactive/hamartomatous process were not completely excluded, we believe that the recent literature supports the neoplastic theory. Our study of cardiac myxomas, fetal valves and adult mitral valves concluded that cardiac myxomas are neoplasias resulting from multipotent mesenchymal cells (2, 3, 4, 18).

We believe that the identification of a pertinent immunohistochemical profile suggests that cardiac myxomas are neoplasias; on the other hand, a differential diagnosis with cardiac sarcomas is also possible. This would be of great interest in current clinical practice.

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The vascularization of the ventricular septum*)

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Abstract

The ventricular septum represents a complex and important structure and its vascularization has long received the attention of anatomists, cardiac surgeons and cardiologists. New studies are continuously added, especially with regard to the endovascular or surgical revascularization procedures. Particular maneuvers such as embolization or alcoholization of the first septal branch, and their potential complications, underline the importance of a deep knowledge of the intimate anatomical details of this region of the heart. An anatomical study was performed on fixed human heart specimens in order to reveal the disposition of both anterior and posterior septal branches. Thirty formalin-fixed adult heart specimens were studied by using macro- and microdissection techniques. The origin, number, and territory o f vascularization of both anterior and posterior septal perforator branches were recorded. The anterior two-thirds up to three-quarters of the ventricular septum are vascularized by the anterior septal branches, the remainder being vascularized by the posterior branches. Important intramyocardial anastomoses between the anterior and posterior septal branches were revealed, as well as anastomoses between the septal branches and the arteries supplying the pulmonary root and the atrioventricular node. The anatomical details are useful to the cardiac surgeon and interventional cardiologist in view of the planning and performing the revascularization and embolization procedures and in order to avoid their possible complications.

Keywords: *anatomy, atrioventricular block, coronary circulation, myocardial infarction, septal arteries*

Rezumat

Septul interventricular reprezintă o structură importantă şi complexă, atrăgând atenţia şi interesul anatomiştilor, a chirurgilor cardiaci şi a cardiologilor de mai mult timp. Noi studii apar, mai ales în ceea ce priveşte manevrele endovasculare şi cele chirurgicale de revascularizaţie. Unele procedee particulare cum ar fi embolizările sau alcoolizările primei ramuri septale, la fel ca şi complicaţiile posibile ale acestora, subliniază importanţa unei bune cunoaşteri a detaliilor ce caracterizează aceasta regiune a inimii. A fost efectuat un studiu anatomic privind dispoziţia

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ramurilor septale anterioare şi posterioare, folosind inimi umane fixate. Au fost studiate treizeci de inimi umane de adult, fixate în formol, folosind tehnici de disecție normală şi de microdisecție. Au fost înregistrate următoarele date: originea, numărul şi teritoriul de vascularizație al ramurilor septale anterioare şi posterioare. Ramurile septale anterioare vascularizează cele două treimi sau trei sferturi anterioare ale septului, restul fiind vascularizate de ramurile posterioare. Au fost evidențiate anastomoze importante la nivel intramiocardic între ramurile septale anterioare şi cele posterioare, la fel ca şi între acestea şi cele ce vascularizează infundibulul pulmonar şi nodul atrioventricular. Amănuntele privind vascularizația septului ventricular sunt utile atât chirurgului cardiac, cât si cardiologului intervenționist, în vederea planificării şi efectuării manoperelor de revascularizație sau a celor de embolizare, şi pentru a evita complicațiile acestora.

Introduction

The ventricular septum represents a complex structure which develops as a result of various mechanisms during the embryological period: apposition of the growing trabeculated parts of both ventricles, closure of the secondary interventricular foramen and with some contribution from the cushion material. These processes are in intimate relationship with the division of the atrioventricular canal, the septation of the bulbus cordis and the formation of the arterial valves and of the coronary vasculature (1 - 4) The resultant two ventricles have different function and form, reflecting the hemodynamic particularities in the systemic and respectively, pulmonary circulation. The angle between the inflow and outflow compartments is totally different, being narrower in the left ventricle and measuring between 45-60° in the right. The right ventricle seems to wind around the left ventricle. The resultant ventricular septum reflects this disposition and in accordance, is a non-planar structure (Figure 1).

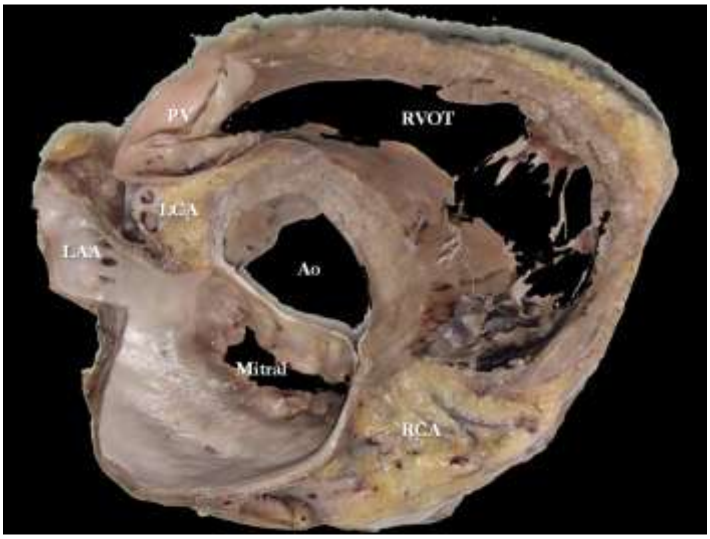


Figure 1: Horizontal section through the heart revealing the disposition of the ventricular septum.

The aortic root is centrally-located (Ao). The right ventricular outflow tract winds around the aortic root. Note the non-planar disposition of the ventricular septum. Ao: aortic root; LAA: left atrial appendage (left auricle); LCA: left coronary artery (main trunk); Mitral: mitral valve; PV: pulmonary valve (cut obliquely); RCA: right coronary artery; RVOT: right ventricular outflow tract;

The various segments of the septum as viewed from the left and right ventricle, are thus not equivalent, as for example, the inlet part of the septum in the right ventricle, corresponds on the left ventricular side to its outlet portion (The parts of the ventricular septum are: the inlet, the trabecular part, the outlet and the pars membranacea which in the case of the left ventricle depicts two portions: the atrioventricular part and the interventricular part, respectively).

The septal structures also serve as the sustaining element of the tricuspid valvar apparatus and are traversed by the elements of the conduction tissue. The most distal part of the septum continues with the aortic root. The arterial supply of the ventricular septum has in accordance an important role in the proper functioning of the afore mentioned elements. Surgical or endovascular revascularization procedures on one hand, and embolization or alcoholization methods, on the other, ask for a thorough knowledge of the anatomical particulars regarding the arterial vascularization of the ventricular septum.

Materials and Methods

An anatomical study was performed on 30 formalin fixed adult human heart specimens (age range 23-84 years). The heart specimens were collected from patients of Caucasian descent, showing no cardiac or cardiac-related diseases. Hearts were harvested at autopsy. Buffered formalin (10%) was injected in the coronary tree both antegrade and retrograde (by catheterization of the coronary sinus), reaching total volumes of 600-1000 ml. The hearts were immersed in formalin for a 1-2 week period. Prior to dissection, hearts were immersed in 50% ethanol and rinsed with water. Regular dissection techniques and magnifications up to x 6 were employed. Photographic documentation was obtained with the aid of digital equipment (Olypmus Camedia E-10, Olympus, Tokyo, Japan).

Results

In the normal heart, the ventricular septum is vascularized by anterior and posterior perforator arteries. The arteries having a diameter above 1 mm, entering the septum and giving off braches to it, were counted as septal branches. Their origin, number and main characteristics, are illustrated in Tables 1-3.

Table 1: Origin of the first anterior septal artery

Origin	No. of specimens	%
Anterior interventricular branch (LAD)	27	90.00%
First diagonal or ramus intermedius	2	6.67%
Circumflex branch	1	3.33%
TOTAL	30	100%

Table 2: Number of anterior septal arteries

No. of septal arteries	No. of specimens	%
7	2	6.66%
8	2	6.66%
9	8	26.67%
10	9	30.00%
11	8	26.67%
12	1	3.34%
TOTAL	30	100%

Table 3: Main septal artery (the largest and the longest in the given specimen)

Origin	No. of specimens	%
S1	6	20%
S2	16	53.34%
S1 + S2	5	16.67%
S2 + S3	2	6.66%
S3	1	3.33%
TOTAL	30	100%

The anterior septal perforators vascularize the anterior two-thirds up to three-quarters of the septum, being longer and more conspicuous as compared to the posterior ones. The septal branches vascularize the aortic root while the pulmonary infundibulum is vascularized by infundibular branches with origin in both coronary trunks but mostly in the right coronary artery. The anterior septal branches contribute to the vascularization of the medial and anterior papillary muscles of the tricuspid valve, but not of the mitral papillary muscles. The first posterior septal branch is the most conspicuous, travels toward the right fibrous trigone of the heart, terminating as the artery of the atrioventricular node. The remainder of the posterior septal branches contribute to the vascularization of the posterior papillary muscle of the tricuspid valve.

The longest and the largest anterior septal perforator branch was defined as the main septal branch and has an important territory of vascularization (Figure 2, next page).

In our study the main septal branch was the second and it vascularized most of the ventricular septum and the medial papillary muscle of the tricuspid valve. It anastomosed with branches of the atrioventricular node artery, with branches of the right coronary artery at the base of the anterior papillary muscle of the tricuspid and eventually, with the posterior septals. Branches from the main septal artery travel through the trabecula septomarginalis, and the moderator band, toward the base of the anterior papillary muscle of the tricuspid valve and anastomosis with the atrioventricular node artery and with the infundibular braches.

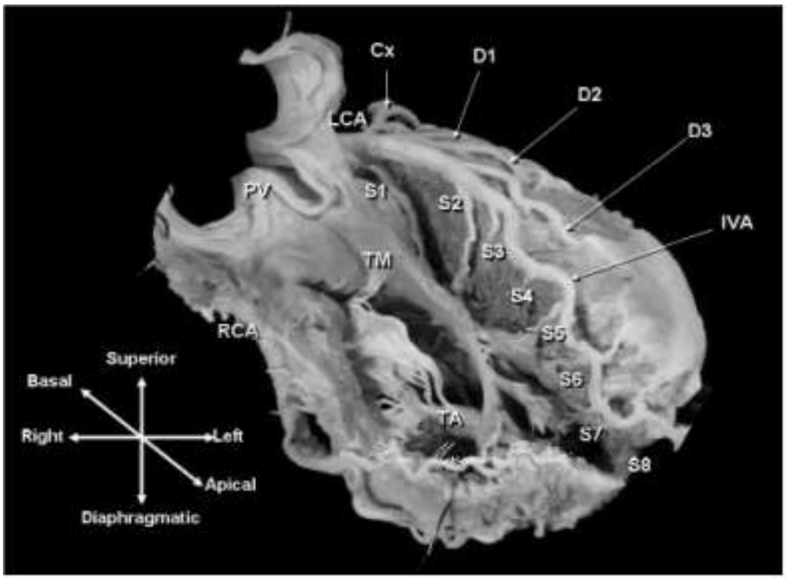
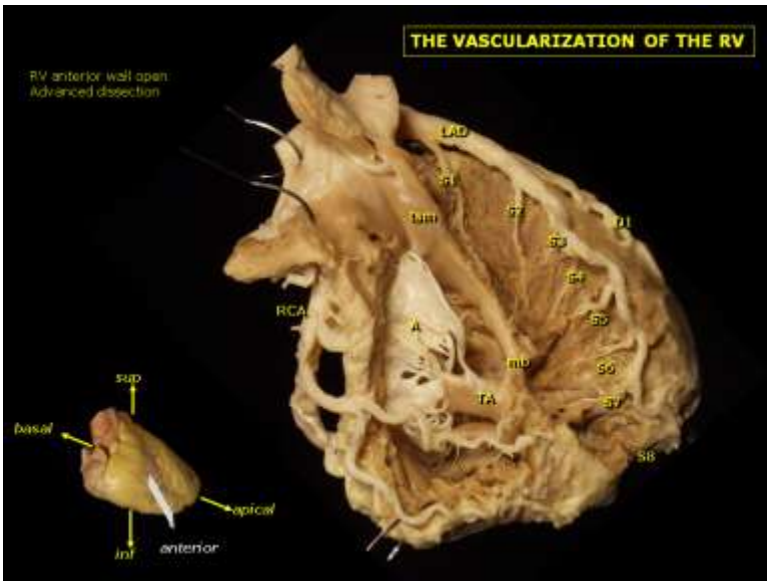


Figure 2: Vascularization of the ventricular septum



The anterior part of the ventricular septum is dissected, depicting the first eight anterior septal braches (S1-S8) with origin at the level of the anterior interventricular branch (IVA). Large parts of the right ventricle have been removed. The pulmonary valve is open. The trabecula septomarginalis and the moderator band are still in place. The tricuspid subvalvar apparatus is intact, with the anterior (TA) and medial (TM) papillary muscles visible. Note the anastomosis between the septal branches and branches from the right coronary artery, at the base of the anterior papillary muscle of the tricuspid. The medial papillary muscle of the tricuspid valve is vascularized by the first two septal arteries in this case. Cx circumflex branch (from the left coronary artery); D1-D3 diagonal branches; LCA: left coronary artery (main trunk); PV: pulmonary valve; RCA: right coronary artery; TA: tricuspid anterior papillary muscle; TM: tricuspid medial papillary muscle; S1-S8: anterior septal branches.

The origin of the posterior septal branches was also studied (Table 4), taking into account the length of the anterior interventricular branch which either ended before reaching the left ventricular apex, ended upon the apex or showed a recurrent course at the level of the posterior interventricular sulcus. In 2 cases (6.67%) this artery ended at the crux cordis and represented the only arterial source of vascularization of the septum.

No coronary anomalies were found in this series.

Table 4: Origin of the posterior septal arteries

Origin	No. of specimens	%
Right coronary artery (RCA)	22	73.33%
Circumflex branch (Cx)	3	10%
RCA + Cx	3	10%
Anterior interventricular branch (recurrent tract)	2	6.67
TOTAL	30	100%

Comments

The ventricular septum represents a complex structure depicting various portions from a didactic and a practical point of view: inlet, trabecular, outlet, membranous. Diagnostic interrogation and therapeutic maneuvers addressed to this particular region of the heart, should take into account the disposition of the septal arteries.

The larger part of the septum is vascularized by the anterior septal branches, having origin mainly in the anterior interventricular branch ("left anterior descending") or adjacent vessels such as the first diagonal, *ramus intermedius* or circumflex branch (rarely). The territories of these branches frequently overlap and establish numerous anastomoses. Moreover, the septum represents an area of intra- and intercoronary anastomoses (5) i.e. between the territory of the three main coronary trunks: anterior interventricular branch, circumflex branch and the right coronary artery (6). Some intraventricular landmarks such as the trabecula septomarginalis might serve as reference points for the intraseptal course of the main septal branch (7) although some studies did not prove such a constant relationship (8).

The significance of stenotic-occlusive lesions of the anterior interventricular branch is different from case to case, as the length of this artery and its contribution to the vascularization of the septum is variable. The coronary typology and the balance between the three main trunks are essential in defining the particulars of the septal vascularization.

The septal branches have been implicated in various other disease processes besides ischemic cardiac disease (9). The new diagnostic tools allow a better characterization of the vascular disposition and on larger number of cases (10).

Septal protection represents an essential step in open heart surgery, as its dysfunction is reflected none only on the function of the left ventricle, but on the right ventricular function too. Cardioplegia delivery must be thoroughly planned and performed, taking into account the particular disease and the disposition of the stenotic-occlusive lesions. Incisions through the septum as in the Ross-Konno aorto-ventriculoplasty procedure may intercept one or more septal branches (11) but consequences are still difficult to predict in the individual patient.

Anatomic variations of the coronary arteries and their septal branches have also been implicated in various disease processes (12).

Percutaneous maneuvers can be also complicated by septal artery interception (13) and the course and relationships of the main septal artery ideally must be precisely known for the planning and for the approach of the chosen procedure (14, 15). Surgical or percutaneous stenting of the main septal branch represent useful revascularization techniques, gaining more and more indications (16).

Final Remarks

The thorough knowledge of the anatomical particulars regarding the vascularization of the ventricular septum, represents an obligatory condition for any specialist performing endovascular or surgical procedures on this region. This anatomical study offers new details specially regarding the number, position and territory of vascularization of the anterior and posterior septal arteries and serves as a basis for further research.

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Left ventricular remodeling clinical anatomy for the cardiologist and the surgeon*)

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Abstract

Left ventricular remodeling is characterized by progressive dilation, hypertrophy, distortion of cavity shape and deterioration in contractile function, that appears and develops after myocardial infarction. Various degrees of remodeling are also encountered and represent a characteristic of dilative cardiomyopathies of any cause. The frequently used parameters for assessing the form and function of the left ventricle are however limited and incomplete or ambiguous data often emerge. Moreover, individual variations are prominent and diagnostic interrogation and surgical therapy should address many particulars, in various individuals affected by the numerous diseases that eventually are characterized by left ventricular remodeling. This review article makes a careful analysis of the left ventricular development, structure and three-dimensional architecture, revealing the normal asymmetries and non-uniformities that characterize the structure and function of the left ventricle. Important and valuable clinical applications emerge, as such data may aid the diagnostician and surgeon in the prevention, the planning, the treatment and the follow up of the patient who might develop or has already started to develop ventricular remodeling.

Key words: *acute myocardial infarction; dilative cardiomyopathy; left ventricle; left ventricular restoration*

Introduction

Left ventricular (LV) remodeling after myocardial infarction is characterized by progressive dilation, hypertrophy, distortion of cavity shape and deterioration in contractile function (1, 2).

Cavity dilation occurs in 1/3 to 1/2 of survivors of acute myocardial infarction. The progressive dilation of LV increases systolic and diastolic wall stresses, which activate cell surface mechanoreceptors, that initiate intracellular signaling for myocyte hypertrophy and modulate the activity of matrix metallo-proteinases, neurohormones and local trophic factors. The extent of LV dilation after myocardial infarction is an important determinant of risk for major adverse cardiovascular events including ventricular arrhythmias, heart failure and death.

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Ventricular tachycardia is believed to be due to anisotropic reentry (3). There is a dynamic imbalance between distending forces and the stretch-resistant extra-cellular collagen scaffold during postinfarction remodeling and this propensity may be amplified by elevated plasma levels of adrenergic neurohormones after infarction.

The most frequently used ventricular shape index (the ratio between the LV short axes to LV long axis), however is not representative of distorted postinfarction ventricles.

A deeper insight into the surgical anatomy and intimate structure and function of the ventricular wall, is thus necessary.

Developmental and physiological view on ventricular myocardial architecture

The beating heart of higher vertebrates transforms from a single tube intro a four-chambered organ while meeting continuously increasing circulatory demands of the rapidly growing embryo. Three distinct stages can be pointed out in this continuum. (4)

1. The stage of cardiac tube (initially straight, later looped)

The myocardium forms a single, then a double cell thick mantle (endocardium, myocardium and the intervening cardiac jelly), being not yet covered by the epicardium. Even at this stage, anisotropic arrangement of myocytes can be found. The inner cell layer is more differentiated and along the length of the tube, preferential circular alignment of myofibrils is seen in the regions of the atrio-ventricular canal and the outflow tract. There is no coronary circulation and nutrition and oxygen are supplied by diffusion from the lumen.

2. The trabeculation stage

The heart gets the epicardial covering but the coronary circulation is not yet established. Trabeculation represents the only way to increase myocardial mass without hitting the diffusion barrier. Trabeculation patterns are different among species and between the left and right ventricle. The general arrangement is radial with some indication of spiraling during systole (or in response to experimentally-induced pressure overload). The development of spiraling can be accelerated or delayed by manipulating the loading conditions.

3. Formation of compact myocardium

This is mainly achieved by trabecular compaction, which coincides with the functional development of the coronary circulation. Formation of compact myocardium is critical for cardiac performance. Activation and contraction patterns are also different in the three stages.

4. The stage of cardiac tube

The ventricular activation sequence reflects the changes in blood flow and geometry. Activation follows the direction of blood flow, proceeding toward the outflow tract resulting in a peristaltoid pattern of contraction.

5. The trabeculation stage

Heterogeneities in conduction properties appear; the trabeculae located on the inside being activated first and spread the excitation radially towards the outside. These structures are the precursors of the specialized conduction network (His-Purkinje system).

6. The ventricular compaction

It is the geometry of the ventricle that helps explaining the transition from apparent base-to-apex to the mature apex-to-base adult pattern. At the earlier stages the two ventricles are widely connected and the inflow and outflow portions are widely separated, since the heart still resembles a tube rather than an ellipsoid.

By the completion of looping and ventricular septation, both inflow and outflow portions of the LV are found closely aligned at the top of the ventricle. Thus, it is necessary to start the activation from the apex, to move the blood towards the aortic outlet.

During the development, the myocardial wall matures from a single-layered structure to a complex multilayered structure supplied by epicardially-derived vasculature and is reinforced by collagenous supporting network while continuously pumping blood. The cell layers are added to both the inside (by compaction of trabecular network) and the outside (by continued myocyte proliferation). Activation patterns change during development and we do not know how the patterning of the Purkinje-myocyte junctions is controlled or how mechanical and electrical connections among working myocytes providing functional coupling across the layers are remodeled. The ventricular components of this system are significant because they remain insulated until they become the Purkinje fibers within the apical trabecular ventricular compartments.

The ventricular architecture

The primary components of ventricular myocardium are the cardiac myocytes.

The atrial and ventricular muscular masses are made up of millions of individual myocytes set in axially coupled endless chains, embedded in a supporting matrix of fibrous tissue. Each myocyte nonetheless is an entity in itself. Thus, in man, each cardiac myocyte is about 80 micrometers in length and 15 micrometers in cross section and depicting lateral offshots. The multiple branches join with adjacent cells through the intercalated disks, thus producing a network of branching and anastomosing cylinders. There are however controversies regarding the further organization of myocytes, i.e the existence (or non-existence) of secondary and even tertiary structures.

The secondary structures are aggregates of myocytes, or fascicles, together with the supporting connective fibrous matrix, which may appear to the various authors more or less regularly-disposed. Whether this arrangement produces lamellas that extend in an orderly fashion from epicardium to endocardium or if instead these lamellas of connective tissue constrain the myocytes into sheets of thickness of four to six cells - is still a matter of debate.

The existence of tertiary structures, i.e. tracts or bands, has been recently popularized and has created a lot of debate. (5, 6) It seems, nonetheless, that the purported "unique myocardial band" is artificially created by the dissector, while dissecting boiled or fixed heart specimens, with no anatomic or physiologic correspondent.

The heart is composed by a large amount of muscular tissue but it is not a muscle. The other components are frequently overlooked: the epicardium, the parietal pericardium, the endocardium, the interstitial connective tissue, the nerve fibers and mechanoreceptors, the intrinsic arterial, venous and lymphatic systems. The heart is also an endocrine organ (secreting the atrial and brain or ventricular natriuretic peptide). The heart resembles more a blood vessel, depicting the same layers - although it is not really a blood vessel. The heart presents autorhythmicity and conduction properties as other internal organs in the body do, but its electrical characteristics are totally different from those of the alimentary canal or uro-genital tract. The muscular and electrical patterns make the heart resemble more skeletal muscle, when considering the frequency and the force of contraction; on the other hand, its autoregulatory properties and the independence with respect to the voluntary control, make it more resemble the visceral system.

Characteristically, the heart shows high metabolic rates, with a predominant aerobic metabolism, and with a continuous activity (even during the periods of rest or during sleep). The arterio-venous difference and the oxygen uptake are the highest. The heart can "rest" and be perfused during diastole, although a new concept of diastole has recently emerged, as this part of the cardiac cycle is not a passive relaxation, but a rearrangement of the muscular fascicles, a reorientation of the myocytes and an active dilation of the heart cavities.

Tetany is never achieved in cardiac muscle, under normal conditions. Each myocardial contraction resembles a single skeletal muscle twitch. The length-tension relationships are totally different from those of the skeletal muscle and the concept of "origin" or "insertion" is not applicable to the cardiac muscle. The mechanical response has a longer latent period (25 ms) and declines more slowly, being between that of the faster skeletal muscle (10 ms) and that of the visceral muscle (200 ms).

The myocardium contracts as a whole, and variations in the contraction pattern, come about through changes in the properties of the individual muscle cells and not by the number of active fibers (as in skeletal muscle). Such changes are due to the innate structure of the myocyte and are under the influence of the physical and chemical environment.

The major determinants of ventricular function are intrinsic and extrinsic. Among the intrinsic determinants (autoregulation), we can cite: the end-diastolic fiber length (depending on the filling pressure, on the duration of diastole, and on the diastolic ventricular distensibility), the myocardial tension (load), the frequency of contraction and the temperature. The extrinsic determinants are: the autonomic nervous system, the humoral factors (O2, CO2, cathecolamines), the coordination of contractions (timing of atrial systole and the sequence of ventricular activation). Each of the afore mentioned determinants, can be further separately analyzed, but this in beyond the scope of the present work.

The muscular tissue in the ventricles represents less than 50% of the total mass. A large amount is represented by the connective tissue. The spatial disposition of this latter, has important role in the ventricular physiology both in normal and disease.

The myocytes (the contractile elements) have attached elastic elements, both in series and in parallel. The connective tissue offers both resistance and elasticity. A clear distinction must be made between successive processes. The electrical activation of the myocyte produces mechanical activation resulting in an increase of contractile tension within the cell - with or without shortening of its myofibrils. The myocytic shortening produces changes in the shape of the ventricles - with or without ventricular narrowing. Ventricular constriction however is the mechanism that results in emptying of the ventricles. Shortening (and hence the measured strain) starts thus after the mechanical activation, when the resistance to shortening has been overcome by the necessary increase in tension. A subpopulation of myocytes nonetheless is refrained in its shortening - namely, the population that because of its alignment is able antagonistically to counteract systolic ventricular thickening (and thus controlling rather than promoting ventricular shortening). (7)

Three-dimensional disposition of ventricular components

The spatial disposition of the ventricular components must allow a proper conduction and delivery of the depolarization impulse ensuring that each myocyte contracts at the right moment, at the appropriate speed and to the necessary extent.

The myocardial mass is best understood as a mesh-work of endless sequences of myocytes coupled axially in one preferential direction - this latter direction marking "the grain" (visible to the naked eye after peeling the epicardium). There is nonetheless some ordering of the overall pattern. When the superficial covering of myocytes is stripped away to reveal the middle and subendocardial portions it can be seen that, with slight variations between species, the superficial myocytes are oriented at angles between 60 and 80° relative to the ventricular equator, with the myocytes occupying the middle portion of the left ventricle being circular, and the deeper (subendocardial) portion returning to a still more longitudinal orientation than the subepicardial grain. This angle relative to the ventricular equator is known as the helical angle. The circular fibers of the left ventricle had previously identified as the actuating fibers of systolic ventricular constriction (Triebwerkzeug) (8).There is no clear evidence supporting the concept of a regular organization of the fibrous matrix so as to produce lamellas that extend in orderly fashion from epicardium to endocardium. Instead, lamellas of fibrous tissue constrain the myocytes into sheets of thickness of four to six cells. Histologic examination of the various portions of the ventricular wall fails to reveal any regular lamellar arrangement. Each myocyte is wrapped within an endomysial weave with adjacent myocytes joined together by endomysial struts. Small collection of myocytes is then unified within a perimysial weave with the entirety of the myocardial mass enclosed within the epimysium.

The only recognized orderly arrangement of discrete isolation of collections of myocytes within the remainder of the ventricular walls is found subendocardial, here serial histologic sections reveal the sheaths of fibrous tissue that ensure the continuity and discretness of the right and left bundle branches of the ventricular conduction system. In man, histologic studies failed to reveal lamellar fibrous shelves extending from epicardium to endocardium.

Changes in mural thickness are more likely to be related to the number of myocytes aligned across the wall rather than to changes in individual dimensions. Chains of axially coupled myocytes aligned side-by-side and parallel to the ventricular surface must move in radial direction with two adjacent rows of myocytes becoming three or four by alternate interleaving.

Extended areas of muscular heterogeneity are found at the bases of the papillary muscles where the parallel fibers within the bodies of the papillary muscles coalesce with the spiraling musculature at the apex. Right ventricular structure is far less regular when compared to the left counterpart.

From a physiologic point of view, the amount of contractile force engendered by a sequence of axially coupled myocytes is independent of the number of myocytes thus coupled in series. The amount of maximally developed force increases proportionally to the number of myocytes arranged in parallel. The amount of shortening increases proportionally to the number of myocytes coupled in series. The myocardium shortens most efficiently in the direction that parallels the epicardial surface, thus supporting ventricular ejection. Numerous short side branches cross between adjacent myocytes with the potential of linking them together. These branches intrude in a direction from the epicardium toward the endocardium. The contractile force engendered by these short contractile bridges fuses to provide a measurable force in more or less radial orientation. As the maximal deviation of these aggregates is less than 45° they probably need to work in concert with the supporting fibrous matrix so as to achieve the oblique deviation of forces required to control the amount of regional mural thickening that is known to take place during systole. These myocytes also constitute the major determinant of cyclical realignment of the three-dimensional arrangement of cells being thus involved in diastolic reopening of the ventricle and in regional stabilization of ventricular shape.

Regional non-uniformity of normal human left ventricle

Myocyte sarcomere shortening can eventually lead to ventricular ejection through different but otherwise related mechanisms (at the macroscopic level): wall thickening, circumferential shortening and longitudinal shortening. The demonstration of the relative contribution and the regional nonuniformity of these different mechanisms in humans, became feasible after the introduction in clinical practice of the noninvasive myocardial magnetic resonance tagging and the possibility to measure regional ejection fraction (EF) and strain. (9) Endocardial regional EF can be viewed as a composite measure of the local contribution to the ejection. Because of the conical shape of the LV the end-diastolic circumferential radius of curvature gradually decreases from base to apex. In contrast, the end-diastolic longitudinal radius of curvature increases toward the apex, expressing a flattening of the myocardium toward the apex.

The LV posterior wall shows the largest endocardial EF but the least systolic wall thickening. The anterior wall and septum demonstrate the largest systolic wall thickening but a smaller EF (due to the lower degree of circumferential and longitudinal shortening in this part of the LV). At the level of the LV septum, the epicardial fiber shortening (i.e. corresponding to the RV endocardium) exceed LV endocardial fiber shortening. The differences in the strain in the septum are likely due to the presence of the right ventricle. The regions with a higher wall thickening have a lower EF except at the LV base.

The diastolic wall thickness varies significantly. The largest differences are found in the LV long axis. In the short axis direction the LV cavity has an oval rather than a circular configuration at end diastole. The anterior part of the LV is the flattest and shows the largest systolic wall thickening. The relative contribution to ejection increases toward the apex, although the myocardium significantly thins from base to apex.

A transmural nonuniformity can also be demonstrated. Circumferential-longitudinal shear strains - expressing ventricular torsion - are significantly larger epicardially than endocardially. Wall thickness and radius of curvature are important determinants of wall stress. A more curved wall will exhibit less wall stress, leading to a thinner wall at end diastole, which will show a relative larger thickening for the same amount of increase in wall thickness. On the other hand, a smaller systolic stress will allow a larger systolic regional EF. Different regions of the ventricle exhibit a variable contribution of thickening, global circumferential inward motion and longitudinal shortening to the ejection of blood, and wall thickening certainly does not show the most simple, direct and easy relation. Thus, when wall thickening is used as a regional parameter of function, these complex relations have to be kept in mind when interpreting differences among patients and in the same patient when comparing various regions If the LV. The influence of other parameters such as nonhomogeneity in myocardial perfusion or myocardial innervation, is unknown (10).

The electrical activation sequence of the heart proceeds from the septum to the lateral wall and does not correspond to the mechanical sequence of the onset of shortening which starts in the lateral wall and ends in the inferior and inferoseptal wall. It has been suggested that the delay between the electrical and mechanical activation (E-M delay) is spatially heterogeneous in order to ensure a mechanically synchronous contraction. Variations in E-M delay could arise either from differences in load or from differences in initial sarcomere length. Earlier onset of shortening in the lateral wall may be caused by a local increase in initial fiber length due to the atrial contribution to ventricular filling. The lateral wall may be stretched more than the septum by the atrial filling because it is thinner and because the septum is subject to counterbalancing effects from the left and right ventricular pools.

Gross anatomic appearance of the left ventricle

Surgical restoration of the left ventricular shape, volume and function, must certainly take into account some of the gross anatomical particularities of its structure.

Both ventricles can be described as having three portions: inlet, trabecular and outlet. The ventricular septum is shared by both the right and left ventricles, although the various regions as described on the septal wall, are not corresponding exactly on the right and left sides. This is partly due to the fact that the angle between the inflow and outflow compartments of the two ventricles differ: the angle is about 45-60° at the level of the right ventricle, while it appears more acute at the level of the left ventricle with the anterior mitral leaflet and the aortic-mitral curtain separating the two compartments. In consequence, the LV appears conically-shaped and having thicker walls, being built as a pressure pump. The right ventricle, on the other hand, is the thinner tube-like volume pump, winding around the LV. The right ventricle has larger volumes and lower EF while the LV has smaller volumes and higher EF. As no important physiologic shunts between the systemic and pulmonary circulation normally exist in man, the right and left ventricular stroke volumes should match over long periods of time. Only slight variations can be compensated by variations in the pulmonary and systemic capacitance and resistance.

The morphological right ventricle is characterized by the prominent shelf (crista supraventricularis) separating the atrioventricular from the arterial valve. The apical trabecular zone has coarse trabeculations with the trabecula septomarginalis being the most prominent.

The morphological left ventricle depicts the characteristic fibrous continuity between the atrioventricular and arterial valve, the apical zone has fine trabeculations and the septal surface appears smooth, with no septomarginal trabecula.

The LV wall has a thicker compact zone, which is essential for the proper ejection of blood into the systemic circulation. In adult hearts, both the compact and the trabecular zones are vascularized by the coronary arteries, predominantly the left.

The anterior interventricular branch (the left anterior descending artery = LAD) vascularizes the anterior 2/3-3/4 of the interventricular septum, and a variable portion of the anterior LV wall, through the diagonal branches. Marginal branch(es) from the circumflex branch vascularize(s) the larger parts of the lateral and infero-lateral wall of the LV. The remainder posterior part of the interventricular septum and the inferior LV wall, are vascularized by the posterior interventricular artery (posterior descending artery = PDA) and posterior LV branches, which can originate from the right coronary artery, the left coronary artery or in rarer instances, from both.(ll) Coronary arterial typology, collateralization, type and onset of disease, are reflected in case of ischemic cardiomyopathy.

From the point of view of its arterialization, the interventricular septum can be imagined as a morphologically and functionally bilayered structure potentially supplied by different coronary arteries. The revascularization procedures represent thus an important step of the LV restoration.

There is a linear relation between scar size and EF and LV volumes, but this relation is independent of scar location and transmurality. The surgical objective is to rebuild the LV form (12) rather then restricting restoration surgical procedures to only addressing the particular disease.

The mitral subvalvar apparatus has a long-recognized role in the geometry and normal function of the LV. The papillary muscles and their corresponding chordae, connect the apical trabecular system to the anterior mitral leaflet and indirectly to the aortic root and the two fibrous trigones. The dilating LV assumes different shapes with respect to the number and disposition of papillary muscle fascicles or heads. Papillary muscle sling or repositioning begets an important role in LV restoration, together with the re-establishment of LV volume and shape. Additional procedures are associated to the LV restoration: mitral ring plasty or edge-to-edge fixation. New techniques such as the septal anterior ventricular exclusion (SAVE) with mitral reconstruction represent an useful option for the treatment of advanced dilated cardiomyopathy in extremely dilated LV with akinetic septum (of idiopathic or ischemic origin) (13, 14).

The gross anatomic appearance of the LV is thus complex and shows individual variations. The surgical reconstruction, the indication, the timing of surgery and the technique chosen, should address all these multiple particulars. Numerous details regarding the intimate structure and function of the ventricular wall continuously emerge, allowing a better characterization of this complex organ. Surgery represents only a step in the context of an intricate system beside the pharmacologic or endovascular approach.

The thorough knowledge and implementation of clinical anatomical concepts, aids the physician in understanding better the natural history of some deleterious diseases among which, ischemic heart disease occupies a notable position. Not least, it offers a basis for further research in the associated fields.

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Ebstein's anormaly: from wet-lab to therapy*)

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Background

Ebstein's anomaly (1, 2) is a polymorphous congenital heart disease, otherwise difficult to include in a unique classification system due to its rarity and because of the infinite possibility of combinations of severity of the involved structures.

It counts less than 1% of all congenital heart diseases. The main and the best known anatomical feature is represented by the apical displacement of the tricuspid leaflets. Besides, Ebstein's anomaly includes many other morphological alterations with important pathophysiological consequences: abnormal adherence of the leaflets to the underlying myocardium (failure of delamination; the absence of a valvar free edge), apical displacement of the functional annulus (septal > posterior > anterior), the presence of an atrialized portion of the right ventricle which becomes dilated (with variable degrees of thinning or hypotrophy), dilatation of the right atrioventricular junction (the true annulus), dysplasia of the leaflets (tethering, fenestrations, redundancy - important especially at the level of the anterior leaflet when thinking toward a surgical reconstruction) (3, 4, 5, 6).

From the practical point of view, the apical displacement of the leaflets is not of great importance "per se", if not associated with other morphological alterations.

The pathophysiological consequences include: tricuspid insufficiency, tricuspid stenosis, stenosis of the right ventricular outflow tract, shunts at atrial level (usually right-to-left), paradoxical emboli, dysrhythmias, left ventricular dysfunction, mitral insufficiency.

Although a rare pathological entity, Ebstein's disease requires a correct and early diagnosis, a thorough management and follow-up of the patient, a correct and properly-timed surgical indication (7). Because of its protean clinical manifestations due to the polymorphous anatomical aspects, a thorough study of the disease, a correct characterization and classification are important issues and an individualized and systematic approach should be performed in every single case.

Mimics of Ebstein's anomaly should be differentiated from true Ebstein's anomaly, as the surgical approach and prognosis, differ greatly (8, 9).

The present work takes into account a review of the literature (especially from the

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anatomical, echographical and surgical points of view), comprises a wet-lab section and the analysis of 22 operated cases.

The wet-lab sessions have been performed at the Institute of Pathology at "Niguarda" Hospital in Milan, Italy and included the study of normal hearts (30 adult hearts of both sexes, ages between 20-81 years, deceased from non-cardiac causes) and the study of 10 hearts with Ebstein's anomaly (of which 4 pediatric cases). The normal anatomy of the right heart chambers and the tricuspid valve was studied, revised and depicted. The heart specimens with Ebstein's anomaly have been dissected and photographed in order to illustrate particular anatomical forms.

The analysis of surgical cases, comprising 22 cases, was performed at the *Cardiac Surgery Department at "San Donato" Hospital, Milan, Italy.*

The continuous feed-back with anatomy is particularly necessary in this case, due to the fact that a complete characterization is often either difficult to perform or frequently overlooked.

Embryology (10, 11, 12)

Although the tricuspid valve can be viewed from the anatomical point as consisting of two leaflets (i.e. a septal and a "parietal" one, the latter including the anterior and posterior leaflets) (13, 14) from the embryological one, it consists of three leaflets: anterior, posterior and septal. The anterior leaflet inserts on the parietal band, by means of the papillary muscle of the conus and on the anterior papillary muscle. The posterior leaflet inserts on the anterior papillary muscle and by means of multiple heads at level of the posterolateral right ventricular wall. The septal leaflet inserts by means of several fascicles, directly on the septum. The insertion on the septum represents one of the major differences between the mitral and tricuspid valves.

The development of the future tricuspid valve is intimately related to the septation process. After the formation of the cardiac loop, the atria are connected only to the future left ventricle and the cono-truncus is situated distal ("above") the future right ventricle. A posterior muscular crest will mark the boundary between the primitive A-V canal and the future right ventricle. With further right "shift" of the A-V canal, this crest becomes funnel-shaped directing the blood from the right atrium towards the right ventricle and the cono-truncus ("the tricuspid funnel"). Fenestrations appear at the level of the inferior extremity of the funnel; by their confluence these will generate the inferior aperture of the tricuspid valve. The right ventricle develops in an apical direction. The right ventricular cavity and its trabeculations augment. The process of delamination takes place, in an apical-basal direction, first at level of the posterior leaflet, followed by the septal one, till at the level of the papillary muscle of the conus. Thus, the tricuspid funnel generates the posterior and septal leaflets of the tricuspid, their subvalvar apparatus, together with the septo-marginal trabecula. On their atrial side, the afore mentioned leaflets receive material from the atrioventricular endocardial cushions.

The anterior leaflet has a completely different origin. The anterior leaflet has also a double origin: from ventricular myocardium (parietal band) and the conal septum (fused superior A-V endocardial cushion and the endocardial cushions of the cono-truncus). The delamination process takes place in an opposite direction (i.e. in a basal-apical direction).

Little is known on the exact embryological mechanisms in Ebstein's anomaly. There is certainly a faulty delamination process whose origin remains obscure. The different timing in the formation of the three leaflets explains the constant and more severe involvement of the posterior leaflet, as compared with the septal and eventually, the anterior one (the insertion of the anterior leaflet is almost always normal in position only its distal attachments are usually abnormal).

Pathology

The pathological modifications can be systematized as follows (Figures 1 and 2):

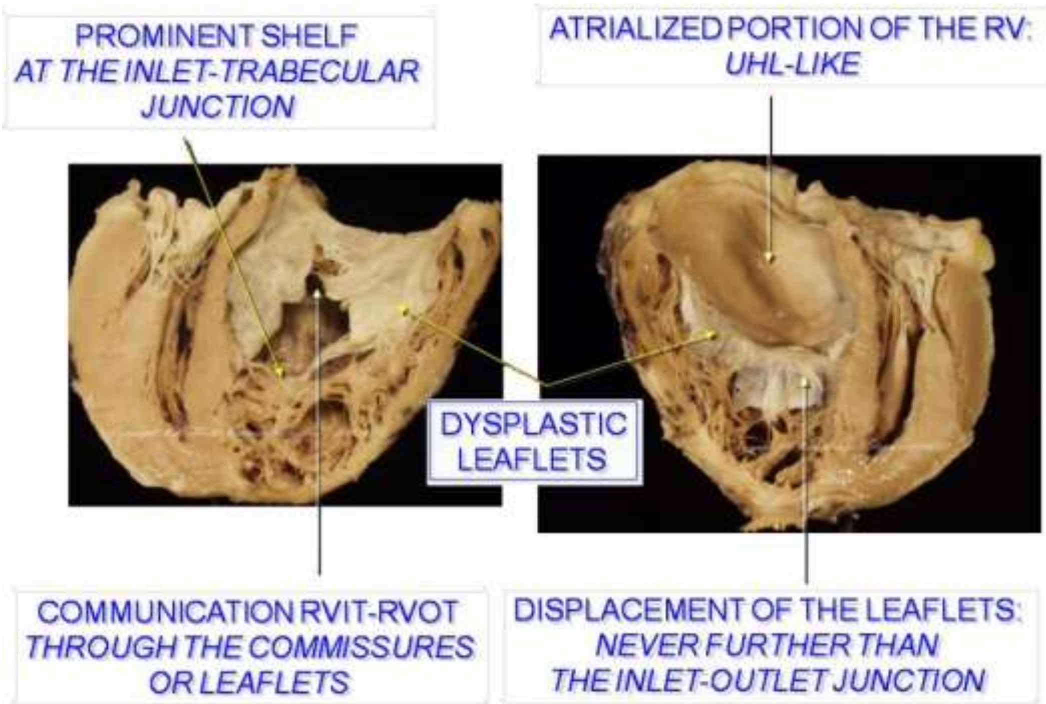


Figure 1: Pathology. Adult heart, frontal section depicting only the ventricles and A-V true annulus (both atria have been removed). The figure shows the anterior aspect (on the left) and the posterior one (on the right). The main pathological modifications are shown. The displacement of the septal and posterior leaflets of the tricuspid valve is evident. The atrialized portion of the right ventricle is easily to delimit: the position of the true annulus of the tricuspid is at the same level with the annulus of the mitral valve. This latter one shows moderate modifications of the myxomatous type.

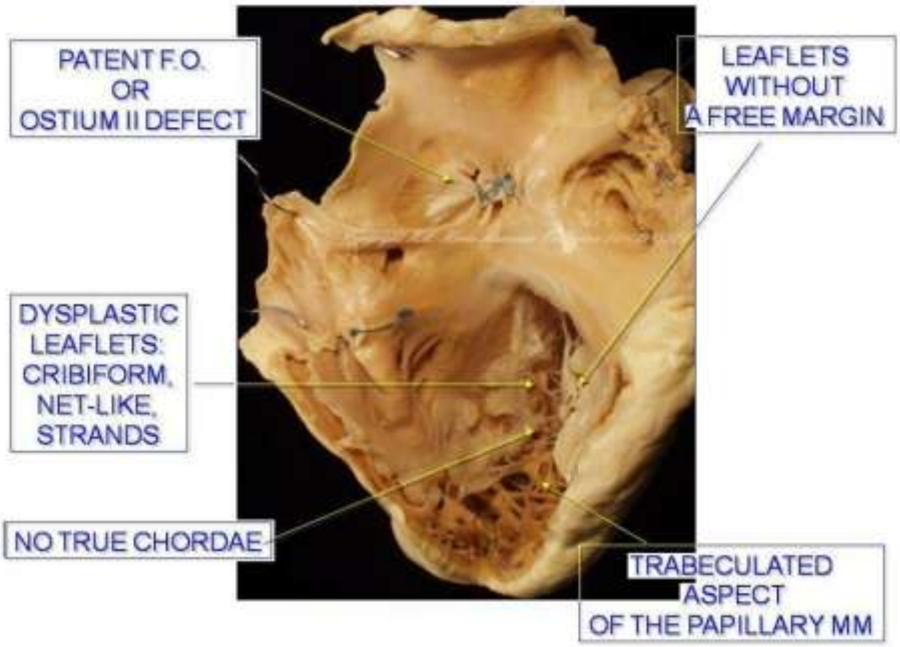


Figure 2: Pathology. A different adult heart specimen, opened at level of the right margin of the heart; right heart chambers are thus seen from the right side. Surgery has been performed on this patient. The atrial septal defect (fossa ovalis type) has been sutured (note the fact that some of the stitches have cut through the tissue: a plea for patch closure of any ASD in Ebstein). A plasty on the posterior tricuspid annulus has also been performed. The septal leaflet is dysplastic arid hyphenated; the posterior leaflet is the most affected. The anterior leaflet has no true free edge. The communication with the RVOT takes place between the anterior and septal leaflets. In this particular case, the remaining part of the right ventricle is highly-trabeculated, with no true papillary muscles, no true chordae.

1. The abnormal leaflet insertion

a. The posterior and septal tricuspid leaflets. Their maximal apical displacement is encountered at level of the commissure between them, i.e. at level of crux cordis in correspondence with the right fibrous trigone. This would also explain the frequent anomalies of the conduction pathways and especially the existence of accessory pathways. The displacement never goes down beyond the inlet-trabecular portion of the right ventricle, where frequently there is a prominent shelf (this assertion is somewhat tautological, in the way that the very definition of the "inlet" and respectively "trabecular" portions of the RV septum is given by the insertion of the tricuspid subvalvar apparatus).

b. The anterior leaflet can present an anomalous "annular" insertion at its posterior extremity, otherwise it has a normal insertion. The leaflets of the tricuspid valve in cases of Ebstein anomaly, have thus a spiral insertion: starting from the anterior part, there is a normal insertion and proceeding towards the septal leaflet, the insertion becomes more apical, reaching the utmost apical displacement at level of the commissure between the septal and posterior leaflets., where the distance between the true and respectively, the apparent annulus is greatest.

Besides these details, the anterior leaflet can have three types of distal insertion (i.e. papillary insertion):

- focal insertion, i.e. a normal papillary insertion, with normally formed commissures and a normal tricuspid orifice. The valve is usually competent;
- discontinuous insertion: tethering of the valve, which becomes inserted by means of multiple fascicles directly attached to the RV wall. This represents a frequent cause of tricuspid insufficiency;
- linear insertion at level of the muscular shelf at the inlet-trabecular limit, with a "sail-like" aspect of the anterior leaflet; the valve can be either insufficient or stenosed.

2. Dysplasia of the leaflets

The leaflets frequently show a eribrform or net-like appearance, usually in concordance with the status of the subvalvar apparatus (vide infra). In severe cases of Ebstein's anomaly, the very GOTMiianication with the right ventricular outflow tract is made through commissures or clefts in the leaflet substance.

3. The subvalvar apparatus

There are no true chordae and both their cuspidal as well as their parietal attachments are abnormal, rendering the leaflet totally non-functional. The mobility of the anterior leaflet and the presence of a free edge are important prerequisites for the surgical plasty.

4. The atrialized portion of the right ventricle

The additional chamber is dilated but it seems that this dilatation is not only due to hemodynamic factors: the histopathological aspect is almost "Uhl-like" with scarce and hypoplastic myocardial cells. This would explain the presence of associated dysrhythmias and the necessity of eliminating this abnormal, additional chamber, with surgery. The atrialized portion of the RV can become huge and impinge on the IV. This dilatation manifests at septal level too; in severe cases of Ebstein's anomaly, the LV can show a hypodiastolic insufficiency and associated mitral insufficiency.

5. The remaining part of the right ventricle

Is reduced in various degrees. In most severe cases, it can be practically absent. An important issue is that not only the absolute dimensions of the RV count but also its morphology. Often, the remaining RV cavity is almost sponge-like, crossed by numerous trabeculae and aberrant chordal material. The free wall is thin and hypocontractile. (15)

6. The dilatation of the right atrioventricular function (the true annulus) and of the right atrium

The limit between the right atrium and respectively right ventricle, can be usually traced, both anatomically, echographically and intraoperatively. There is frequently a difference of thickness between the right atrial wall and the atrialized RV wall (usually thinner). The true annulus dilates as well as the right atrium. Trabeculae in the RA are usually prominent. More Thebesian veins usually open in the RA in cases of Ebstein's anomaly. At times, the coronary sinus is slender. The anatomical relationship between the right coronary artery and the true tricuspid annulus, is of extreme importance when performing the reduction of the atrialized right ventricular chamber (vide infra).

7. The communication RVIT-RVOT

In normal cases, this communication is bordered by the inferior margin of the anterior leaflet, the anterior papillary muscle, septo-marginal trabecula and parietal band and papillary muscle of the conus. In case of Ebstein's anomaly, the communication takes place at level of the commissure between the septal and anterior leaflet or even thorough clefts or orifices in the leaflets when these latter ones are highly-dysplastic. The general aspect is of a small functional orifice. With redundant anterior leaflet material, the orifice can be practically obstructed.

The RVOT is either reduced in size or partially obstructed by the abundant leaflet material. In cases with predominant tricuspid insufficiency and pulmonary hypoplasia, the RVOT can be also dilated.

8. Associated anomalies (including the left heart chambers)

The most frequent is a defect in the atrial septum (94% of the patients who are referred to the surgeon): a "forced" foramen ovale or an ostium secundum atrial septal defect. Ostium primum defects in case of associated partial A-V canal forms, are also encountered. The ventricular septal defects are by no means rare; these can be perimembranous, conal or even of muscular type. Subpulmonary stenosis or pulmonary valve hypoplasia usually are acquired during fetal life. Less frequent, there are associations with complex cardiopathies as transposition of the great arteries (SLL), double-outlet right ventricle. A patent ductus arteriosus may be present in severe forms of neonatal Ebstein's anomaly.

The marked dilatation of the right ventricle affects in a significant manner the function of the LV (and septum). These structures are compressed, displaced posteriorly towards the verterbral column. The septum itself can become flattened, bulging leftward and even showing a paradoxical movement. In severe and/or chronic cases, interstitial fibrosis can also develop at level of the left heart cavities.

Besides the afore mentioned consequences at level of the left heart chambers, there can be various degrees of mitral alterations (myxomatous, redundant leaflet material, cleft mitral valve, parachute mitral valve). There is associated mitral insufficiency and compression of the lungs; the pathophysiological consequences are evident. The atrial septum is not only discontinuous but also thin. This represents an important detail for the surgeon, indicating that a closure of the ASD should be performed by using a patch (instead of a simple suture).

Extracardiac structures frequently involved are: the lungs (compression, important especially in infants), congestive hepato-splenomegaly, hepatic fibrosis, renal insufficiency. Diffuse coagulopathy and the respiratory problems represent important issues especially in neonates and during the perioperative period.

9. Particular forms

"The left-sided Ebstein" is encountered in case of A-V discordance; it actually represents an Ebstein anomaly located on the left-sided tricuspid valve. (16) Only one case of true left-sided Ebstein (i.e. true Ebstein of the mitral valve) has been described so far: Rushaupt, Bharati and Lev (1976). The spectrum of morphological alterations of the tricuspid, can show two extremes: "the unguarded tricuspid orifice" (practically no functional tricuspid valvar apparatus) at one end and "the imperforated Ebstein", at the other (17, 18). From a longer list of diagnostic procedures. I will present only the most indicated and useful ones, in case of Ebstein's anomaly.

Radiology

The cardiothoracic index (Figure 3), that actually reflects the amount of cardiac dilatation (cardiomegaly), represents a factor of poor prognosis and an indication for surgery, if greater than 0.65, even in the oligosymptomatic patient. In neonates, a cardiothoracic index greater than 0.80 has been taken as the cut-off point for surgery (vide infra).

Figure 3: Chest X'Ray. Two typical chest x-rays of patients with Ebstein's anomaly, are shown. Note the almost characteristic appearance of the cardiac sillhouette and the ratio between the cardiac and pulmonary areas (the cardiothoracic index or ratio).

Echocardiographies examination (19, 20)

The diagnosis of Ebstein's anomaly can be made with confidence from the two-dimensional echocardiogram.

The ultrasound examination can offer details regarding the anatomical forms and their pathophysiological consequences. I would like to stress at this point some particular aspects of the echographical examination and of its inherent benefits for the clinician and the surgeon.

The general aspect of the heart is important. The measurements of the cavities, volumes, ejection fraction, pressures, etc., should be performed in the usual manner. A special attention should be given to the remaining part of the right ventricle, its volume, contractility and cavity. Another point of interest is represented by the right ventricular outflow tract and the pulmonary valve - details which can radically change the surgical indication. The left heart chambers should not be overlooked. The performance and anatomy of the left ventricle are important issues, especially in young patients. The determination of the ejection fraction is less reliable due to the paradoxical movement of the septum. The degree of apical displacement of the leaflets is best measured at the level of crux cordis. The main echocardiographic characteristic that differentiates Ebstein's anomaly from other forms of congenital tricuspid regurgitation, is the degree of apical displacement of the septal leaflet at the crux cordis (> 0.8 cm/m^2) (21).

The Echo Score ("Great Ormond Street" Ebstein Score) (22) represents an easily-obtainable parameter, with a direct applicability in the classification, surgical indication and follow-up of patients with Ebstein's anomaly. A four-degree severity score can be thus obtained; patients with a severity score grade 3 or 4 have a poor prognosis (Figure 4).

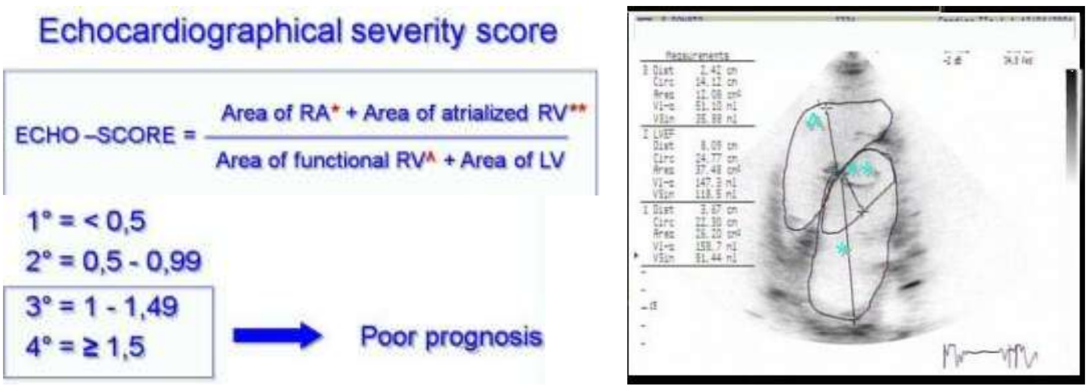
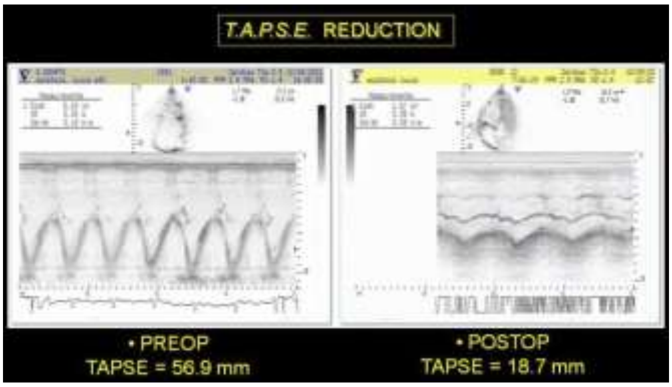


Figure 4: The ultrasound image depicts the general measurements needed in order to calculate the echographic severity score (Great Ormond Street Ebstein Echo Score: see text for reference). Grade 3 and 4, indicate a poor prognosis [negative foto processing]



In the neonate: a grade 4 echo score implies a mortality reaching 100%. A grade 3 echo score is associated with an early mortality of 10% but with a late mortality of 45% usually in early childhood. A grade 1 or 2 is associated with 92% survival. The systolic apical displacement of the tricuspid valve (TAPSE) (Figure 5), represents an important marker.

Figure 5: TAPSE reduction. The systolic displacement of the tricuspid valve is reduced in the postoperative period, due both to the surgical procedure and the right ventricular dysfunction (small remaining RV cavities, poor contractility etc.). At repeated follow-ups, the patients should recuperate; nevertheless normal values will never be attained. The surgeon must make a clear distinction between the normal reduction of the TAPSE values due to surgical plasty and die right ventricular dysfunction.

In the postoperative period, lower-than-normal values of the TAPSE are encountered reflecting the result of the surgical plasty but also a reduced contractility of the right ventricle. After an initial lowering, TAPSE values should normally increase over time, during the postoperative period.

Classifications

Few classifications have been proposed so far, due both to the rarity of the anomaly and to its polymorphous presentation. Basically, two major classifications are currently in use, and these reflect the larger experience of two major cardiological and surgical centers. THE CARPENTIER CLASSIFICATION is noteworthy for its simplicity and practical point of view. This includes four major types of lesions (Figure 6).

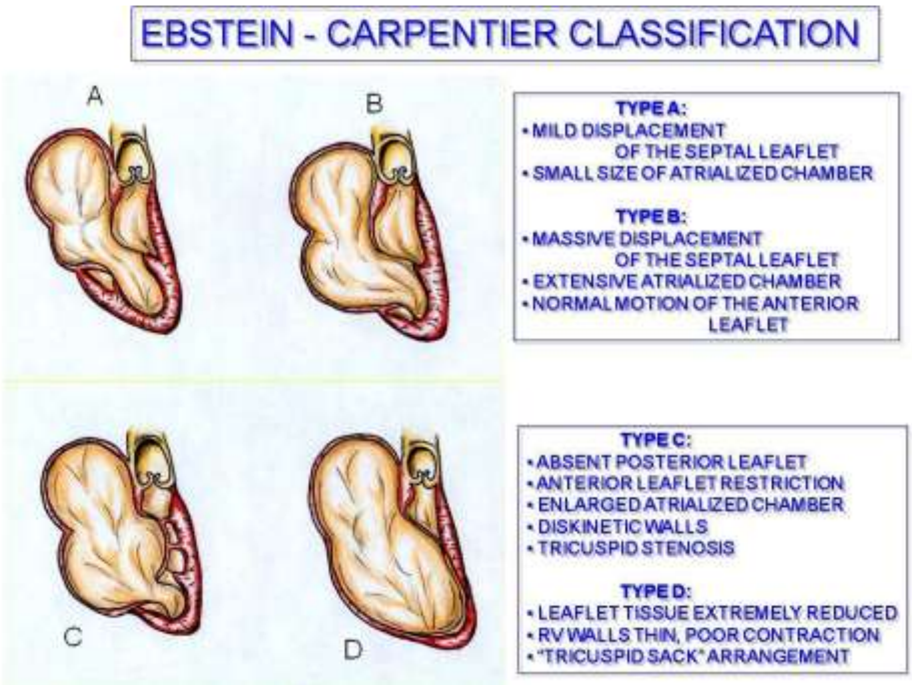


Figure 6: The Carpentier classification. The drawings depict the main alterations in Ebstein's anomaly and divided in the four types that characterize the Carpentier classification

In Type A, the volume of the true RV is adequate with a mild displacement of the septal leaflet, in Type B, the there is a large atrialized portion of the RV but the anterior leaflet is freely mobile; in Type C the anterior leaflet is severely restricted and may cause significant obstruction to the RVOT; in Type D, there is an almost complete atrialization of the RV (with the exception of a small infundibular component).

Going further and from a slighlty different point of view, the classification proposed by Dearani and Danielson (21), takes into account not only the displacement of the leaflets, the size of the atrialized portion of the right ventricle and the remaining portion of the RV, but it brings into attention also the shape and mobility of the anterior leaflet (which is utmost important for the surgical plasty).

The Dearani & Danielson classification (21)

Type I: the anterior leaflet is large and mobile, complete delamination of > 50%. The free edge can be either mobile or with hyphenated or linear attachments. The posterior and septal leaflet can be present, displaced, dysplastic (or absent). Fenestrations are common. The atrialized portion of the RV can be either small or large.

Type II: anterior and septal leaflets are present but small and displaced in a spiral fashion (vide supra); leaflets are mobile and these are often supported by small, short papillary muscles and chordae. The anterior leaflet has a free edge; the atrialized portion of the right ventricle is moderately large.

Type III: the anterior leaflet has a restricted motion, chordae are shortened, fused, tethered. Some papillary fascicles insert directly on the leaflet. The leaflet itself can be either large or small; the free edge has hyphenated or linear attachements. The remainder of the leaflets are displaced, dysplastic and usually non-reconstructable. Fenestrations are common. The atrialized portion of the RV is large.

Type IV: the anterior leaflet is severly deformed and displaced into the right ventricular outflow tract. There may be few or no chordae; direct insertion of the papillary fascicles onto the free edge is common. The free edge is hyphenated or with a linear attachment. The septal and posterior leaflet are either dysplastic or absent. There is obstruction of the RVOT. Nearly all of the RV is atrialized.

Beyond any of the classifications, the cardiologist and the cardiac surgeon should have in mind the fact that this anomaly has its very particular manifestations and those indications should be put in the case of the individual patient. Anyway, the two afore mentioned classifications are very helpful in that they orient the surgeon (before the moment of the operation). Type I hearts are ideal for tricuspid valve repair (if the free edge is not hyphenated or attached). Type II hearts are also ideal for tricuspid plasty + annuloplasty (inserting a ring at the level of the displaced annulus). Type III hearts are borderline for repair and if results are not satisfactory (intraoperative echocardiography); the tricuspid valve can be also replaced. Type IV hearts require tricuspid replacement or other types of surgery.

Surgical Indications (23, 24, 25, 26, 27, 28, 29, 30)

In the natural history of this anomaly there is a reduced life expectancy, with a mean age at death at about 20 years (although the oldest patient described with Ebstein's anomaly lived throughout his ninth decade) depending of course on the anatomical form and the associated pathologies (especially dysrhythmias). The major causes of death are: congestive heart failure and dysrhythmias but as stated previously, the left ventricular dysfunction should not be overlooked. Only about 5% of the patients will reach the age of 50. The factors of poor prognosis are: the presence of atrial fibrillation (expected death within 5 years), tachyarrythmias (with a high risk of sudden death), cardiomegaly (as revealed by a cardio-thoracic index greater than 0.65), the forms showing a high tricuspid dysplasia and the young age (Table A, few pages next).

There are two main categories of Ebstein patients: asymptomatic and symptomatic. The latter category is regarded as a good-prognosis one, although this may be misleading.

The symptomatic patient, can present with dyspnea, cyanosis, dysrhythmia, cardiomegaly, intractable cardiac insufficiency, embolic phenomena - at any age. The younger the age, the more severe the disease.

Oligo- or asymptomatic patients with a cardio-thoracic index greater than 0.65 should be operated on, as soon as possible.

The high proportion of dysrhythmias and especially due to the presence of aberrant pathways, indicates the necessity of performing the electrophysiological study and ablation therapy (in the cath lab or as an associated procedure during surgery). In addition to the afore mentioned dysrhythmias due to one or more accessory pathways, severe atrial and ventricular dysrhythmias can be the result of anatomical changes of the right chambers and right ventricular ischemia - these represent an important cause of morbidity and mortality. As stated previously, these latter categories of dysrhythmias are (in part) acquired. This mitigates strongly for an earlier surgical repair.

The main surgical indications, are: Class III and IV NYHA patients, Atrial fibrillation and other severe dysrhythmias (tachyarrhythmias), wide atrial septal defect and/or other cardiac lesions amenable to repair, cyanosis, stroke, cardiothoracic index > 0.65 and echo severity grade 3 or 4.

Surgical Techniques

The aim of surgery is to restore the normal anatomy and/or function of the tricuspid valve (as much as possible), to reduce the dilatation of the annulus, the dilatation of the right atrium, to reduce or eliminate the atrialized portion of the RV, to ablate the accessory pathways, to eliminate the obstruction of the RVOT (when present), to eliminate the tricuspid insufficiency, to treat the associated intracardiac lesions. When severely compromised (unfavorable anatomical forms), surgical interventions that bypass the right chambers or that will unload these, can be performed. Not infrequently for example, the Glenn procedure is associated to the Carpentier or Danielson technique.

The Carpentier and Danielson techniques try to restore the mobility of the anterior leaflet as well as the anatomy and function of the right chambers - a task not always easy to accomplish. The "limiting" factors of a satisfactorily surgical repair are:

- the anatomy of the anterior leaflet: dimensions, displacement, the presence of a free edge (or of a mobilizeable free edge);
- the atrialized portion of the RV and consequently, the remaining part of the RV; this latter one can be very small or having thin, dysfunctional walls;
- the RVOT and the pulmonary valve: severe obstruction or hypoplasia will preclude any repair at the tricuspid level.

The unfavorable anatomical forms and patients in class IV NYHA, will orient the surgeon towards various other surgical solutions, as Glenn, Fontan, univentricular repair or even heart transplantation (*d'emblee*) (31, 32, 33, 34, 35).

Between these two "extremes", there is also a place for the tricuspid valve replacement (though very arguable in the author's opinion) (36, 37, 38, 39).

The Carpentier technique is illustrated in Figures 7-10 (40, 41). The plication of the atrialized RV chamber is performed in an apical-annular direction (longitudinal).

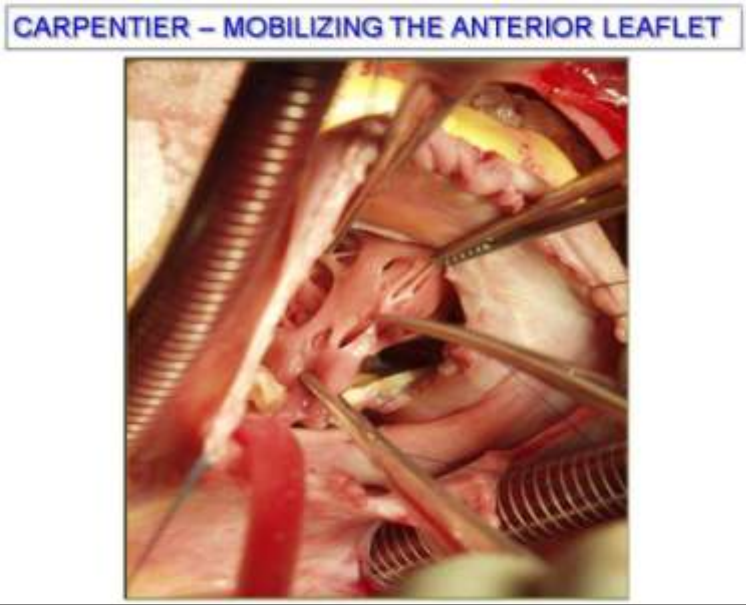


Figure 7: Surgery. Carpentier technique. The mobilization of the anterior leaflet. The leaflet has been disinserted from the annulus. Note the trabeculated aspect of the right ventricle proper and the fact that the surgeon must perform a good and complete mobilization of the leaflet detaching it from the underlying tissues (muscular and chordal). Care should also be taken in order to not open the RV or the septum.

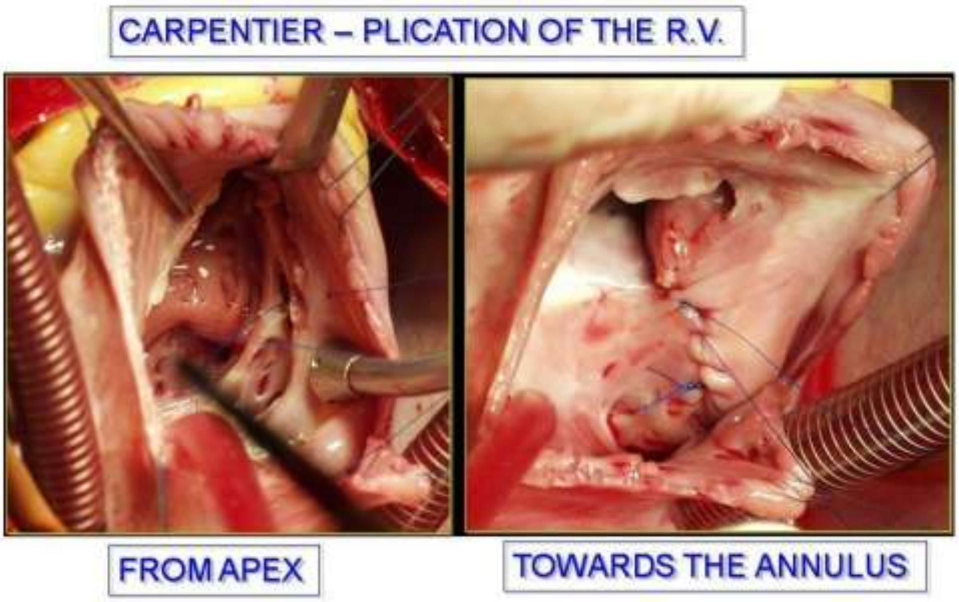


Figure 8: Surgery. Carpentier technique. The plication of the atrialized portion of the right ventricle, takes place posteriorly, in a longitudinal manner, starting from the apex.

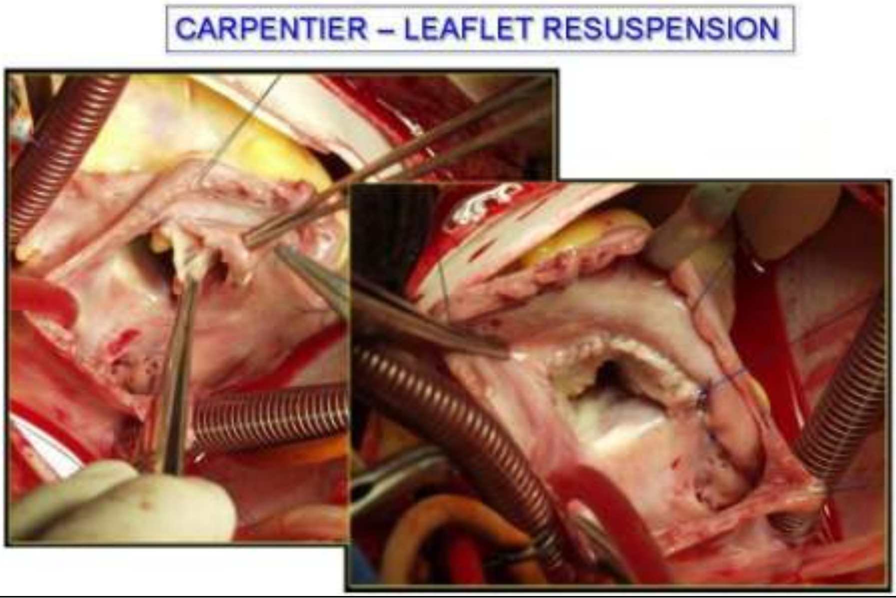


Figure 9: Surgery. Carpentier technique. The anterior leaflet is reinserted at level of the true annulus (which has been reduced by plication). The tricuspid valve becomes a monocuspid leaflet. See also text for details.

Figure 10: Surgery. Carpentier technique. An artificial ring is inserted in the usual manner, in order to stabilize the true annulus and the complex plasty performed. About the sizing, see the corresponding references

The Danielson technique includes the following steps (21) (Figure 11):

- electrophysiologic mapping;
- perinodal cryoablation;
- reconstruction of the tricuspid;
- right reduction atrioplasty;
- plication of the atrialized portion of the RV (in a circumferential manner);
- patch closure of the atrial septal defect;
- correction of any associated lesions.

The surgical techniques used on the 22 Ebstein patients operated in the *Cardiac Surgery Department at San Donato Hospital Milan*, is illustrated in Figure 12. Anatomical forms are illustrated in Figure 13. Causes of death and mortality are illustrated in Figure 14.

DANIELSON'S TECHNIQUE

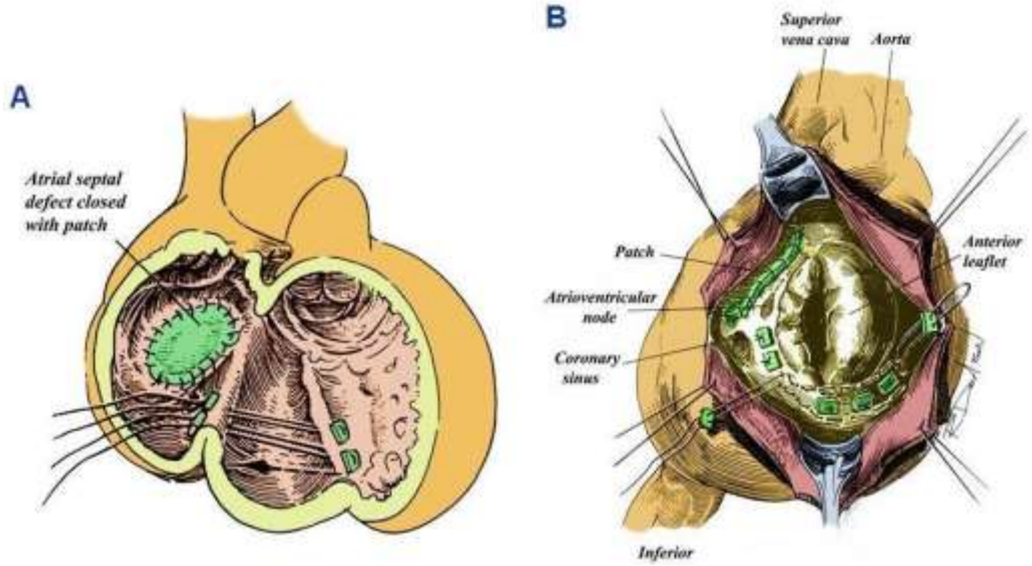


Figure 11: Surgery. Danielson technique. The drawings demonstrate the principles of the Danielson technique (see text for details). Note the different plication of the atrialized right ventricle. Care should be taken not to include the right coronary artery (i.e. to differentiate between the true and respectively, the apparent tricuspid annulus).

EBSTEIN - 22 cases (San Donate 1988-2002)		
Surgical Technique	**No. of cases**	**Deceased**
Carpentier	14	1
Valvar replacement	4	1
Carpentier + Glenn	2	1
Danielson	2	-
Total	**22**	**3 (13.6%)**

Figure 12: San Donate statistics. The statistics of *the Cardiac Center San Donate Hospital* is shown. Type of surgery comprises mostly plasties. Note that two patients had associated Glenn procedures.

EBSTEIN - Operatory Statistics (San Donate 1988-2002)	
No of pts.	22
Age	25 + 6 y (3 m - 45 y)
NYHA class	III - IV
C.T.I.	0.75 (0.55-0.90)
Type B - C	13
Type D	2

Figure 13: San Donate statistics. Some of the main characteristics of the patients groups is depicted. Note that 15 out of 22 patients had unfavorable anatomy. All were in an advanced NYHA class and with high cardiothoracic indexes.

EBSTEIN - Causes of death, SAN DONATO (1988-2002)						
	Age	Technique	CTI	Arrythmia	NYHA	Cyanosis
C1	26	TVR*	.85	SVT	III	+ + +
C2	28	Carpentier	.80	AF (chron.)	IV	+
C3	7	Carpentier + Glenn	.90	AF (parox.)	IV	+ + +
*TVR = *Tricuspid Valve Replacement* C1, C2, C3 = *case* 1,2, respectively 3						

Figure 14: San Donate statistics. The causes of death in the three deceased patients are shown. Mortality and causes of death are comparable to the published statistics.

Various surgical centers depict different cohorts of patients with different results **(Table A)**

Table A: Ebstein statistics

Authors and year	No. of patients (and age)	Surgical technique	Mortality in hospital (%)	Mortality late (%)	Follow-up	Redo (%)	Causes of death
BOCKERIA 2000	12 (7-48 years)	"Bioglis" bioprosthesis	0	-	2-10 weeks		-
SARO-SERVANDO, 2000	9 (31-248 months)	Mechanical (1) Bioprosthesis (8)	0	12	11-264 months		arrhythmia CHF
TANAKA 2001	10 (only adults)	Bioprosthesis supra-annular	0	0	12.4 ± 5.5 years	-	-
BRANCACCIO 2001	48	Carpentier	8	12,5	63 ± 54 months		RV failure
SAN02002	3 (pediatric)	Glenn	0	-	not specified	-	-

Authors and year	No. of patients (and age)	Surgical technique	Mortality in hospital (%)	Mortality late (%)	Follow-up	Redo (%)	Causes of death
CHAUVAUD 2001	**48 (33+/-15 years)**	**Carpentier**	**8.33**	**-**	**57 ± 50 months**		**arrhythmia RV failure**
KUPILIK1999	**4 (pediatric) 6 (adults)**	**Carpentier**	**0**	**0**	**53 ± 23 months**	**-**	**-**
CHAUVAUD 2000	**142* (25 +/- 15 years)**	**Carpentier** (138 patients) Replacement (4 patients)**	**10**	**-**	**75% survival at 10 years**	**3.52**	**Acute RV failure**
KHOSITSETH 1999	**6 (neonates and infants)**	**Plasty**	**83.3**	**-**	**3-72 months**	**-**	**age cyanosis low insert°**
DANIELSON 1992	**189 (11 m-64 years)**	**58.5% Danielson 36.5% bioprosthesis 5.3% Fontan**	**6.3**	**5,29**	**in progress**	**3,6**	**cardiac 7 patients non-cardiac 2 patients unknown 1 patient**
KNOTT-CRAIG 2002	**8 neonates and infants**	**Danielson De Vega**	**12.5**	**0**	**not specified**	**-**	**RV failure**

* = 142 *patients with Ebstein anomaly*, of which:
Type A = 5%,
Type B = 35%,
Type C = 51%,
and **Type D = 8%**

** = *associated procedures*: tricuspid ring (in 94 patients), Glenn (in 30 patients)
° = i.e. lower insertion of the septal leaflet of the tricuspid valve; high ratio between RA + atrialized RV over RV

One can obviously notice that these results are by no means comparable, either due to the reduced number of cases or because of the highly-different categories of patients. Also, there is rarely possible to encounter on such statistics, the experience of a single surgeon or a single surgical technique - amenable to more pertinent comparisons. Mortality is also variable, but a percentage of about 8-12% is generally accepted (highest in neonates). The poor prognosis factors are: younger age, unfavorable anatomical forms ("low insertion" of the leaflets), preoperative congestive heart failure (reflecting altered right heart chambers and/or concomitant LV dysfunction). Causes of death are mainly congenstive heart failure and dysrhythmias (42). There are also various other therapeutic approaches (43).

(Table B). The anatomical form and the presence of associated lesions - are the most important factor in the therapeutic approach: medical vs. surgical therapy.

Table B: Therapeutical options. The therapeutical options and possibilities are different with respect to the age and severity of the disease. Temporary or definitive medical solutions are also available. Surgery is performed in all age groups

	Clinical picture	Therapy
Fetus	• Cardiomegaly • Heart failure • Dysrhythmias	Abortion Medical therapy for mother
Neonate and Infant	• Cianosis (reversible) • Cardiomegaly • Heart failure • Dysrhythmias	Medical therapy Operation if CTI ? 0,65 Or if eco score = 3° or 4°
Adolescent Adult	• Dysrhythmias (SVPT, AF-Flutter) • Murmurs • ECG (RBBB, AVB 1° W.P.W.) • Heart failure - Cardiomegaly	Clinical follow-up Medical therapy Ablation Surgery

Borderline cases should be judged and should receive a special attention too, because delaying the surgical intervention can be deleterious for the patient. The addition in the therapeutic plan of new parameters as the cardiothoracic index, the echo score (besides a more complete ultrasound examination as performed nowadays), helps undoubtedly the physician and orients him better toward the choice of medical therapy or surgery.

A special reference should be made in cases of NEONATAL EBSTEIN'S ANOMALY (44, 45). At a younger age, patients present with signs and symptoms of progressive heart failure whereas, adults usually present with exercise intolerance or dysrhythmias. There is no consensus about which neonates with Ebstein's anomaly should be operated on. In literature, data suggest that 20-40% of the neonates diagnosed with EA will not survive 1 month and that less than 50% will survive to reach the age of 5. Symptomatic neonates have a fatal course. Mildly symptomatic neonates, could also be treated medically or can have an indication for a temporary bicavo-pulmonary shunt. This procedure, performed without cardiopulmonary bypass could delay a more hazardous intracardiac radical repair. This is to be taken into account in the context of the decreasing pulmonary vascular resistance that normally takes place during the first 6 months of age and which offers a chance of potential clinical improvement. Palliation with single ventricle repair has also been revisited lately. The presence of cyanosis is associated with 50% mortality during the neonatal period; this parameter becomes 100% predictive when associated with an echo score grade 3 or 4. Thus, the proposed INDICATIONS for neonatal repair of Ebstein's anomaly are as follows:

- *asymptomatic neonates: echo score 4; cardiothoracic index > 0.80; severe tricuspid regurgitation;*
- *symptomatic neonates: severe cyanosis; mild cyanosis + echo score 3 or 4; cardiothoracic index > 0.80; severe tricuspid regurgitation; associated cardiac defects.*
- *The perioperative aggressive supportive care is critically important in the very ill neonates: immediate intubation, continuous muscle paralysis, high-dose fentanyl, large tidal volumes hyperventilation with minimal PEEP, peritoneal dialysis, nitric oxide, prostaglandins for maintaining ductal patency, daily echocardiograms (46).*

Surgical Technique in the neonates

- radical reduction atrioplasty - in order to create more room for the lungs and a more efficient right atrium. The right coronary artery lies in the thin-walled atrialized portion of the right ventricle, which might be easily confused with the right atrial wall. It is thus important to differentiate between the true tricuspid annulus (that is closely approximated by the right coronary) and the apparent (displaced) tricuspid annulus (that is demarcated by the hinge of the displaced valve leaflets);
- tricuspid valve repair, consisting of reduction annuloplasty (with a probable potential to grow) and respectively, the construction of a monocuspid valve. This is obviously highly-dependent on the shape and status of the anterior leaflet of the tricuspid valve. The longitudinal plication of the atrialized chamber of the RV can be performed also using the Knott-Craig technique by using a two-pledgetted nonabsorbable suture placed between the commissure between the anterior and posterior leaflets and respectively the opening of the coronary sinus;
- subtotal closure of the atrial septal defect, leaving a 3-4 mm. fenestration, allowing some right-to-left shunting during the early postoperative period;
- creation of a functional right ventricular outflow tract. Because the right ventricle is compromised, it is important to create a good antegrade flow toward the pulmonary arteries without loading the right ventricle and concomitantly avoiding pulmonary insufficiency. The RVOT should thus not be oversized and usually a 7-8 mm diameter will suffice.

Final Remarks

Ebstein's anomaly represents a complex and polymorphous cardiac disease and the therapeutic choice remains challenging. The surgical techniques are not all difficult by themselves but imply a sound and thorough knowledge of the spectrum of anatomical modifications that characterize this anomaly and their functional resonance. The ultrasound examination has brought many new details that orient both the cardiologist and the cardiac surgeon toward the type of therapy to be chosen in the individual patient. The study of the anatomical forms renders this disease more easily to comprehend and hopefully, more curable. Surgical options are multiple and have better indications today. More experience is still needed as is the analysis on larger statistics and longer follow-ups. The anatomical forms and the thorough knowledge of the structural modifications that characterize this anomaly, as well as their pathophysiological consequences, represent the first and most important step for a sound judgment and approach of the Ebstein patients.

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Hospitalization rates of acute myocardial infarction and distribution of major cardiovascular risk factors in Bulgaria (Bulgaria heart study 1998/1999)*)

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Abstract

*The **aim** of study is to investigate the rates of hospitalization of Acute Myocardial Infarction and its relation to the distribution of the main cardiovascular risk factors in Bulgaria on a representative sample of urban population.*

***Material and Methods:** Cross-sectional study on 3994 subjects of age ranges 25-64 was conducted. Data on Acute Myocardial Infarction rates of hospitalization was collected from hospital admissions documentation. Information on risk factors was obtained by the standardized interview and screening.*

***Results:** The average annual rates of hospitalization were three times higher in males as compared to females. The differences in rates by gender in the younger age groups (< 44 years) are distinguishing in order of 10:1 (male: female). Males of age group 35-44 differ significantly from women of the same age range for the proportion of hypertensives (49.2% vs 27.4%), smoking (62.0% vs 47.8%) and subjects with hypercholesterolemia (27.5% vs 15.2%); p<0.01.*

***Conclusion:** Differences in distribution of risk factors by sex in younger age groups are significant. Unfavorable pattern of hospitalization for Acute Myocardial Infarction of males could be related as to the effect of gender as well as to the differences in the distribution of cardiovascular risk factors by age.*

***Key words:** cardiovascular disease, risk factors, myocardial infarction*

Introduction

Cardiovascular diseases (CVD) are leading cause of death in the world. The average proportion of deaths attributed to CVD for 50 countries by the data of the World Health Organization (WHO) for 1998 is in order of 46 percent. Proportion of deaths attributed to CVD for Eastern Europe is considerably higher i.e. from 51 to 66%. Bulgaria is a country experiencing one of the highest rates of cardiovascular mortality: 66.2% for 1998 or

*) **Romanian Journal of Cardiovascular Surgery ■ 2004, vol. 3, no. 3, pp. 238-143**

814.1/100000 which is almost threefold higher than the average mortality rate for the countries from the European Commission (269.8) (1).

The "rejuvenate" of coronary mortality in males in terms of mortality rates for age groups 35-54 in Bulgaria is another disturbing fact (2). The same unfavorable trend is observed concerning incidence rates of CVD: from 93.6/ 1000 in 1992 incidence of CVD increases up to 142.1/ 1000 in 2002 (3). Males have higher rates than females and the reasons for differences in rates are not very well clarified, yet.

This was the basis for conducting a national study with the aimed at investigation rates of hospitalization of Acute Myocardial Infarction (AMI) and its relation to the distribution of the main cardiovascular risk factors in Bulgaria on a representative sample of urban population.

Study objectives include answers to the following questions:

1. What are the rates of hospitalization of AMI by age and sex?
2. What is the distribution of the major risk factors by age and sex?
3. Is there any relationship between rates of hospitalization for AMI and distribution of the main cardiovascular risk factors by sex?

Material and Methods

Data on AMI rates of hospitalization was collected from 1998 to 1999 from both the database of Central Statistical Office and hospital admissions' documentation (3).

Information on risk factors distribution was obtained on the basis of a cross-sectional study, conducted on a representative sample of Bulgarian urban population aged 25-64 years including stratified groups for both sexes. The study was conducted on 3994 subjects (1983 males and 2011 females) resident in one of the 28 regions (Oblast) included in the study.

Information on risk factors was obtained by the standardized interview and screening. Standing height and weight for calculation of body mass index (BMI) were measured and recorded by the trained interviewer to the nearest of 200 gr and 1cm. BMI was calculated as weight (kg)/height (m^2). Blood pressure was measured by mercury sphygmomanome-ter after 5 minutes rest in a sitting position by the standardized method of the WHO (1984) (4).

Laboratory tests include determination of serum total cholesterol (TSC), high-density lipoprotein cholesterol (HDL) and triglicerydes levels. Concentrations of TSC, HDL and triglycerides were measured directly by colorimetric method after precipitation with a diagnostic test of Roche, Cobas - Mira and enzymatic method (Merckotest Triglicerid GPO-PAP-Method, Merck).

Statistical analysis

Quantitative data were compared by *Student-Fisher t-test*. Comparison of percentages was done by X2- test.

Results

Rate of hospitalization of AMI

In 1998 in each of the County hospitals of the all of the 28th included in the study regions have been admitted 7748 subjects with a diagnosis AMI. Annual rate of hospitalization of AMI is three times higher for males (39,39/100000) as compared to females (12.27/100 000). The differences in rates by gender in the younger age groups (below 44 years) are distinguishing in order of 10:1 (male: female). In the oldest ages over 74 years the rates tend to get equal. Mean age of hospitalization for men is 56 years, 6 to 8 years lower than for women. Almost half of diseased in the hospital males (48.4%) are in active creative age whereas 65.6% of diseased women have already been retired.

Characteristic of the major risk factors

Frequency distribution of the main risk factors by categories is presented on Figure 1. Frequency of the main risk factors is higher in men than in women with an exception for both the frequency of diabetes and obesity, where the differences are not significant.

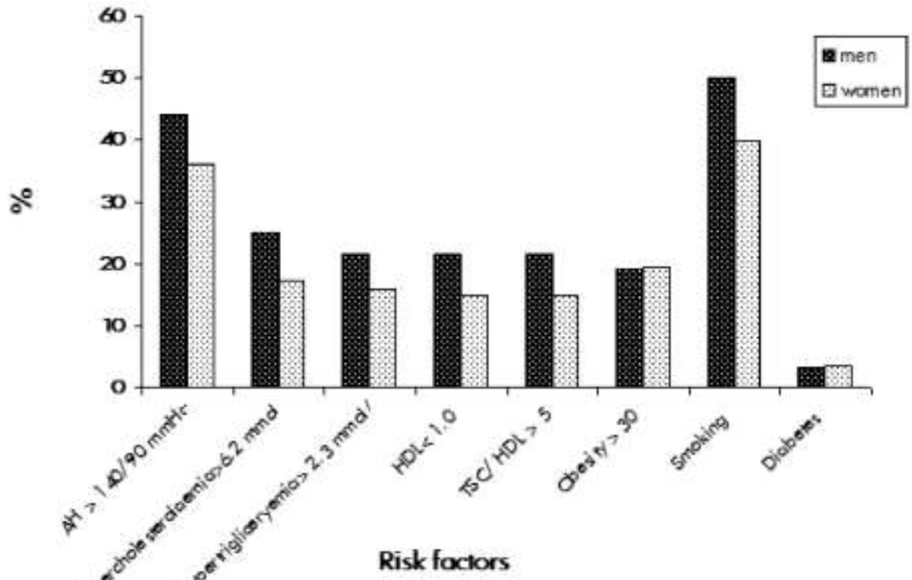


Figure 1: Distribution of cardiovascular risk factors by gender, 1998/1999

Arterial hypertension

Frequency of arterial hypertension (AH) (BP > 140/ 90 mm Hg - WHO -1997) for the age range 2564 is 40.1% (44.2 % in males, 36.1% for females) (Table 1). Gender differences in the distribution of arterial hypertension are statistically significant ($p < 0.001$).

Table 1: Frequency distribution of arterial hypertension by sex* in age groups 25-64 (Bulgaria Heart Study 1998-1999)

Age group	Men No	AH		Women No	AH		Both sexes	AH	
		No	%		No	%		No	%
25-34	521	150	28.8	542	125	23.1	1063	275	25.8
35-44	606	298	49.2	635	175	27.4	1241	473	38.1
45-54	515	264	51.3	470	231	49.1	985	495	50.3
55-64	341	164	48.1	364	194	53.3	705	358	50.8
Total	1983	876	44.2	2011	725	36.1	3994	1601	40.1

** differences in percentages of AH by sex in all age groups are statistically significant at p < 0.001; AH-Arterial hypertension*

On the basis of results could be made the following considerations:

1. Frequency of AH increases with age in both sexes ($p < 0.001$).
2. The pattern of increase in frequency of AH with age is not the same for males and females. An excessive increase is observed in males of age range 35-44 and in females of age range 4554 (Figure 2)
3. Medians of systolic blood pressure (SBP) are 132.0 and 130.0 mmHg for males and females, respectively.

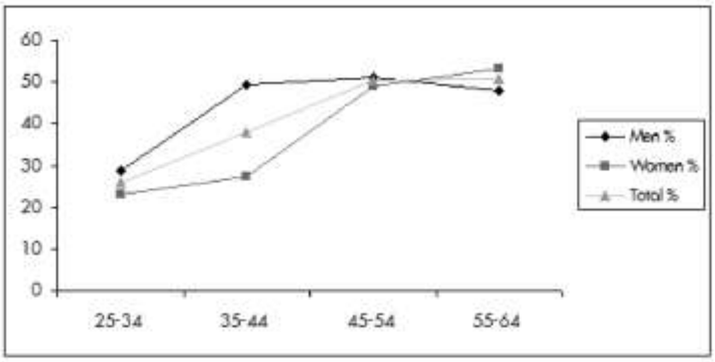


Figure 2: Dynamics of arterial hypertension (140/90 mm/Hg) in parallel with increase in age in both sexes

Lipid status

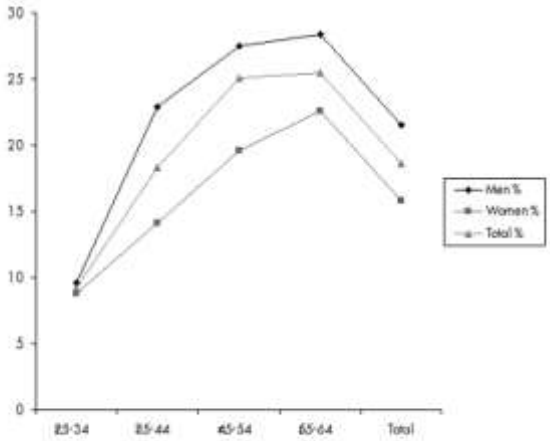
Mean values of TSC, standardized by age are 5.38 mmol/l and 5.26 mmol/l for males and females, respectively. Higher values of TSC (≥ 6.20 mmol/l) have 25.1% of males and 17.1% of the investigated women ($p < 0.01$).

Values of TSC and triglicerydes are moderately increased in males as compared to females with statistical significance for the observed differences in age ranges 35-54 ($p < 0.05$) (Table 2).

Table 2: Distribution of hypercholesterolemia by sex (Bulgaria Heart Study 1998-1999)

Age group	Men	*TSC > 6.2		Women	*TSC > 6.2		Both sexes	*TSC > 6.2	
	No	No	%	No	No	%	No	No	%
25-34	250	34	13.6	251	24	9.6	501	58	11.6
35-44	262	72	27.5	283	43	15.2	545	115	21.1
45-54	211	67	31.7	230	47	20.4	441	114	25.8
55-64	190	56	29.5	208	52	25,0	398	108	27.1
Total	913	229	25.1	972	166	17.1	1885	395	20.9

**mmol/l; p < 0.05*



Similar results have been received for triglicerydes as well (Figure 3).

Figure 3: Hypertriglicerydemia* by gender (Bulgaria Heart Study 1998-1999)

*** > 2.3 mmol/l**

Mean value of HDL- cholesterol after standardization by age is 1.2 mmol/l for males and 1.5 mmol/l for females. Atherogenic index (TSC/HDL - cholesterol > 5) is 21.4 for males and 14.7 for females ($p < 0.01$).

Body Mass Index

Mean height and weight for the investigated males are 175.2 sm and 79.9 kg. For females the figures for height and weight were 159.7 sm and 67.2 kg. Proportion of individuals found to be with a different degree of obesity is in order of 59.3% or 1599 subjects. Around two thirds (64.2%) of males and more than a half of the women (56.6%) are overweighed (BMI > 25 kg/m^2). Clinically obese (BMI > 30 kg/m^2) were 337 males (19.0%) and 391 (19.4%) females (Table 3, next page). Standardized by age mean values of BMI are 26.3 kg/m^2 and 26.4 kg/m^2 of men and women, respectively.

Mean value of the wrist to hip ratio is 0.90 for men and 0.80 for women.

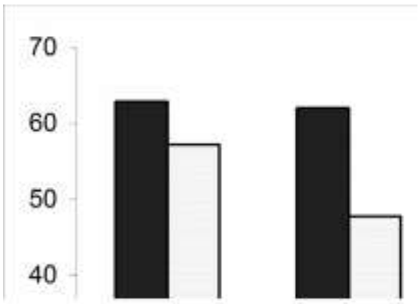
Table 3: Frequency distribution of obesity* by age groups and sex (Bulgaria Heart Study 1998-1999)

Age group	Men	Obesity		Women	Obesity		Both sexes	Obesity	
	No	No	%	No	No	%	No	No	%
25-34	521	50	9.6	542	31	5.7	1063	81	7.6
35-44	606	110	18.2	635	134	21.1	1241	244	19.7
45-54	515	118	22.9	470	121	25.7	985	239	24.3
55-64	341	99	29.0	364	105	28.8	705	204	28.9
Total	1983	337	19.0	2011	391	19.4	3994	768	19.2

** (BMI>30 kg/m^2)*

Smoking

Results on frequency distribution of smoking could be summarized as follows:



- There is a considerable difference in proportion of smokers by gender;

- It has been observed high proportion (> 50%) of smokers in younger age groups (< 45 years) for both sexes and a trend to over two times decrease in proportion of smokers in age groups over 55 years ($p < 0.001$) (Figure 4);

Figure 4: Percentage of current smokers by age and sex

- There is a trend to give up smoking in the older age groups observed in both sexes;

- 33.8% of males and 19.7 % of females were smokers that never try to give up cigarettes

- There are considerable differences in number of cigarettes smoked per day. Proportion of men who smoke more than 20 cigarettes per day is four times higher than the same proportion of women. Proportion of men that smoke less than 5 cigarettes per day is also three times lower compared to women.

- Proportion of "heavy" smokers (>20 cigarettes /daily) is 49.7% and 12.4% in men and women, respectively. Moreover, three forth of smoking men below age of 45 years reported frequent use of alcohol.

Distribution of combinations of risk factors by sex

Without the investigated risk factors were 9.4% of males and two times more females 15.9%. The most frequent combination presented by the registration of two risk factors in both sexes was observed in the case of combination of either obesity and smoking or AH and smoking. A combination of three risk factors was observed in one third of men (31.6%) and one forth of women (24.4%). Combination of four and more risk factors was observed advantagely for men 8.2% against 4.7% in women. It is a disturbing the fact that the combination of three and more than three factors is with high frequency starting from the young ages from 35 to 54 years. The reported differences in the distribution the different combination of risk factors by sex are statistically significant.

Independently, on the big number of CV risk factors, the information on traditional major risk factors and their combinations ensures simple and useful summary on risk factors situation in the country on the whole.

Discussion

The received results show that males' population in Bulgaria experience considerably higher rates of hospitalization of AMI and higher frequency of caring different combination of CV risk factors in comparison to females. This picture is aggravated by the young age at which the risk factors start their effect. It is, however, difficult for explanation considerably higher values of blood pressure in men than in women as well as the sharp increase in blood pressure in men aged 35-44 years. A possible explanation relates higher level of stress as a consequence of financial problems, insufficient control of existing AH, physiological mechanisms, higher number of harmful habits, etc.

Increase in frequency of AH in women, aged over 44 years could be a consequence to hormonal changes in this age or to the effect of obesity, frequently observed in that age, etc.

Independently on the fact that AH is one of the most strongly related to AMI risk factor in epidemiological studies, it should be noticed that the median values of systolic blood pressure in both sexes are around the mean values found for the countries included in Monitoring trends and determinants in cardiovascular disease (MONICA), European Project On Genes in Hypertension Risk factors (EPOGH) and Countrywide Integrated Noncommunicable Diseases Intervention (CINDI) (4, 5, 6, 7, 8). Thus the explanation for the high incidence and mortality rates of AMI in Bulgaria is unlikely to be related only to the effect of arterial hypertension.

Mean values of TSC in both sexes is low and the values are skewed to the left coming closer to the values of countries with low rates for CVD in contrast to the results from MONICA (6).

Our results in terms of population mean values of TS? are comparable to the data from other population studies including Sofia Heart Study (1994), CINDI-Bg (1998) conducted in Bulgaria in the last ten years reporting similar low levels of TSC for both sexes (9, 10, 11).

The results from our study confirm the doubts of many authors about the role of TSC in interpopulation differences in CVD frequency as well as the conclusion of MONICA Project that "Traditional risk factors could partly explain the variations in population trends".

Comparison with the standardized data from other European countries coming from CINDI and MONICA, show considerable differences in terms of the higher proportion of smokers and high percentage of overweighed subjects among the Bulgarian population. Ranging by proportion of both smoking and obesity places Bulgaria along the countries of MONICA, situated on the right side (6).

Conclusion

Rates of hospitalization of AMI in Bulgaria are higher compared to other countries. Differences in distribution of risk factors in younger age groups (<44) by sex are considerable in the range of 10:1 (male: female). The observed differences could be a consequence of the multiplicative effect of more than three CV risk factors among the young Bulgarian males and increased intensity of some of them in the last decade, including stress, physical inactivity, increased alcohol consumption etc. The observed unfavorable pattern of hospitalization rates could be linked as to the effect of sex as well as to the differences in the distribution of the main cardiovascular risk factors by age. The results are a cause of concern in terms of determination and prevention of high-risk groups for development of AMI among the Bulgarian population. The results reveal the need of prospective studies on AMI in Bulgaria.

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Part 2.

CONGENITAL CARDIOVASCULAR PATHOLOGY

Cardiopathies infantiles relevant du traitement chirurgical dans le service de cardiologie de l'hôpital Gabriel Touré*)

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Résumé

Introduction: *Les cardiopathies infantiles occupent une place de plus en plus importante en Afrique sud saharienne (1.6). Les auteurs rapportent une série de 268 enfants, d'une étude épidémiologique descriptive et rétrospective s'étalant sur 14 ans. Les objectifs assignés à cette étude étaient les suivants: décrire les aspects épidémiologiques des cardiopathies infantiles relevant du traitement chirurgical, la nature des cardiopathies et leur évolution.*

Matériels et méthodes: *Il s'agit d'une étude épidémiologique descriptive et rétrospective s'étalant sur 14 ans et portant sur une série de 268 enfants âgés de 0 à 15 ans du service de cardiologie de l'hôpital Gabriel Touré tous présentant une cardiopathie relevant du traitement chirurgical confirmée par examen écho cardiographie.*

Résultats: *Il existait une prédominance du sexe féminin avec un sexe ration = 0,8; de la tranche d'âge 10-15 ans avec 42,54% des cas (N= 114); une prédominance des cardiopathies congénitales avec 49,25% des cas (N= 132); l'insuffisance mitrale était la valvulopathie la plus fréquente avec 60,58% des cas (N= 36); la CIV était prédominante avec 56,07% des cas (N=74). Sur les 268 enfants, 75 ont bénéficiés d'une prise en charge chirurgicale soit 27,98%.*

Conclusion: *nécessité de création de structure locale de prise en charge.*

Mots Clés: *Cardiopathies infantiles chirurgicales*

Abstract

Introduction: *The infantile cardiopathies occupy a more and more important place in south saharien Africa. The authors report on a series of 268 children, a descriptive and retrospective epidemiological study spread out over 14 years. The objectives that they assigned to this study were the following: to describe the epidemiological aspects of the infantile cardiopathies requiring surgical treatment, the nature of the cardiopathies and their evolution.*

Materials and methods: *It is about a descriptive and retrospective epidemiological study spread out over 14 years, and concerns a series of 268 children aged 0-15 years from the cardiology department of Gabriel Touré Hospital all presenting a cardiopathy requiring surgical treatment confirmed by echocardiograpy.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2008, vol. 7, no. 1, pp. 3-6**

Results: *There was a predominance of the female sex with a sex ration = 0.8; of the 10-15 year age group with 42.54% of cases (N=114); a predominance of congenital cardiopathies with 49.25% of cases (N = 132); mitral insufficiency was the most frequent valvulopathy with 60.58% of cases (N=36); VSD (ventricular septal defect) was predominant with 56.07% of cases (N=74). Out of 268 children, 75 benefitted from surgical case management or 27.98%.*

Conclusion: *the necessity of creating a local structure for case management*

Key words: *Infantile cardiopathies*

Introduction

Les Cardiopathies Infantiles occupent une place de plus en plus importante dans le paysage cardiovasculaire en Afrique subsaharienne.

Selon l'Organisation Mondiale de la Santé, on estime que 9 à 15% des enfants en âge scolaire sont porteurs d'une atteinte cardiaque rhumatismale dans les pays en voie de développement. Et de nombreuses études réalisées en Afrique ont montré une fréquence élevée des cardiopathies infantiles (4, 10). Sachant que 6 à 8 pour 1000 enfants à la naissance sont porteurs de cardiopathie congénitale.

Dans cette étude nous tâcherons d'illustrer ces notions en faisant part de notre expérience.

Les buts de ce travail étaient de:

- Décrire les aspects épidémiologiques des cardiopathies infantiles relevant du traitement chirurgical.

Plus particulièrement:

- Étudier la nature des cardiopathies infantiles.
- Déterminer l'évolution des cardiopathies infantiles opérables.

Matériel et Méthodes

Il s'agit d'une étude épidémiologique descriptive et rétrospective allant de janvier 1990 à décembre 2004. L'étude a porté sur 268 enfants de 0 à 15 ans admis dans le service de cardiologie de l'hôpital Gabriel Touré Bamako, structure de 3ème référence situé au sommet de la pyramide sanitaire au Mali.

Tous les enfants retenus dans l'étude étaient porteur d'une cardiopathie congénitale et ou acquise confirmée par échographie cardiaque, et dont le traitement nécessitait un geste chirurgical.

Résultats

Aspect socio-démographique

Il existait une prédominance du sexe féminin avec un sexe ratio de 0,8. 145 filles et 123 garçons représentant respectivement 54,10% et 45,90% (figure 1)

La tranche d'âge 0-5 ans 49 cas, 5-10 ans 105 cas, 10-15 ans 114 cas représentait respectivement 18,23%, 39,38%, 42,54% (figure 2).

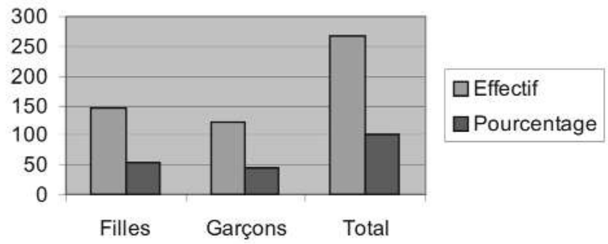

Figure 1 :
Répartition selon le sexe

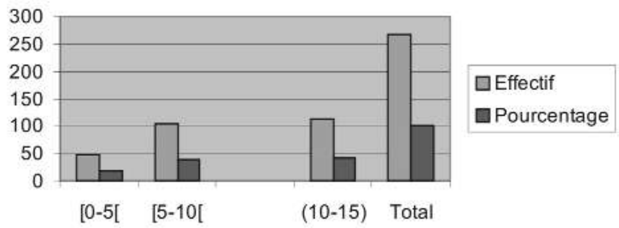

Figure 2 :
Répartition par tranche d'âge

On notait une prédominance de la tranche d'âge de 10 à 15 ans avec 42,54% des cas (N = 114). Il y avait une prédominance des cardiopathies congénitales avec 49,25% des cas (N = 132) (*tableau 1*).

Tableau 1. Répartition selon le type de cardiopathie

Types de cardiopathies	effectif	%
Cardiopathies acquises	**104**	**38,80**
Cardiopathies congénitales	**132**	**49,25**
Association de cardiopathies	**32**	**11,95**
Total	**268**	**100**

L'insuffisance mitrale isolée était prédominante dans 60,58% des cas dans les cardiopathies acquises (N = 63) (*tableau* 2).

Tableau 2. Répartition selon le type de cardiopathies acquises

Cardiopathies acquises	effectif	%
IM pure	**63**	**60,58**
IM + IT	**8**	**7,69**
MM	**6**	**5,77**
IAo	**6**	**5,77**
IM + IAo	**5**	**4,80**
RAo	**5**	**4,80**
RM	**4**	**3,85**
IM +RAo	**4**	**3,85**
MM + IAo	**3**	**2,89**
Total	**104**	**100**

La CIV était prédominante avec 56,07% des cas (N = 74) (*tableau* 3).

Tableau 3. Répartition selon le type de cardiopathies congénitales

Cardiopathies congénitales pourcentage	effectif	%
CIV	**74**	**56,07**
CIA	**22**	**16,67**
Tétralogie de Fallot	**19**	**14,39**
Canal atrio-ventriculaire	**8**	**6,07**
Persistance de canal artériel	**7**	**5,30**
Membrane sous aortique	**1**	**0,75**
I.M congénitale	**1**	**0,75**
Total	**132**	**100,00**

L'association insuffisance mitrale et CIV étaient la plus fréquentes avec 56,25% des cas (N = 18) (*tableau* 4).

Tableau 4. Répartition par associations de cardiopathies congénitales et acquises

Association de cardiopathies	effectif	%
I.M + CIV	**18**	**56,25**
I.M + CIA	**6**	**18,75**
CIV + PCA + I.M	**3**	**9,38**
IAo + CIV	**2**	**6,25**
Cardiopathies congénitales complexes + I.M	**2**	**6,25**
CIV + MSAo + I.M	**1**	**3,12**
Total	**132**	**100,00**

Devenir des enfants enregistrés: Sur 268 enfants, seuls 75 ont pu bénéficiés d'une intervention chirurgicale à l'étranger soit 27,98%. Onze enfants étaient décédés avant évacuation soit 5,7% des cas. 182 étaient encore en attente.

Devenir des cardiopathies acquises: Sur les 104 cas de cardiopathies acquises recensées, 41,35% ont pu être opérés (N= 43).

Devenir des cardiopathies congénitales: Sur les 132 cas de cardiopathies congénitales, 20,45% (N=27) ont bénéficié d'une sanction thérapeutique chirurgicale.

Devenir des enfants avec association de cardiopathies:

Les 55,56% (N=10) des enfants porteurs de cardiopathies associées était encore en attente; 14 enfants sont restés sans nouvelles.

Pour les enfants non opérés, l'évolution s'était faite de la manière suivante: Pour le devenir des enfants non opérés 193 au total: 78,24% (N= 151) (*tableau* 5).

Tableau 5. Évolution des enfants non opérés

Type	effectif	pourcentage
Stabilisation	**151**	**78,24**
Aggravation	**31**	**16,06**
Décédé	**11**	**5,70**
Total	**193**	**100**

Se sont stabilisés sous traitement, contre 16,03% (N = 31) d'aggravation; 11 décédés.

Devenir des cardiopathies acquises non opérées: Nous avons eu 64% de stabilisation (N=39) des cardiopathies acquises non opérées contre 29,5% (N = 18) d'aggravation.

Devenir des cardiopathies congénitales non opérées: Nous avons enregistrés 86% (N = 89) de stabilisation contre 12% d'aggravation (N = 12).

Commentaires et Discussions

268 enfants porteurs de cardiopathie relevant d'un geste chirurgical ont été inclus de janvier 1990 à décembre 2004. La prédominance du sexe féminin dans notre échantillon avec un sexe ratio de 0,8 s'explique par un biais de recrutement car la survenue d'une éventuelle grossesse reste un facteur d'aggravation. Ceci est contraire à Ould Zein H et collaborateurs qui trouvaient un sexe ratio de 1,3.

La tranche d'âge comprise entre [10-15 ans] avait portée le plus grand nombre d'enfants avec 57,33% s'explique par le retard dans le diagnostic et l'absence de structure chirurgicale.

Dans la répartition selon le type de cardiopathie, les cardiopathies congénitales avec 49,25% des cas (N = 132) constituent un autre biais de sélection favorisé par la préférence des associations humanitaires qui interviennent dans la prise en charge à l'étranger.

En ce qui concerne les cardiopathies acquises, l'insuffisance mitrale isolée est prépondérante avec 60,58% des cas (N = 63) conformément à la répartition générale des atteintes valvulaires rhumatismales.

Les cardiopathies congénitales dans leur ensemble étaient dominées par la communication inter ventriculaire avec 74 cas conformément aux résultats de Ould Zein H et collaborateurs (5) et de Baspinar O et all (3).

Par ailleurs l'association I.M + CIV représentaient 18 cas soit 56,25% de cardiopathies congénitales et acquises. Sur les 268 enfants recensés au départ, 75 ont pu bénéficiés d'un geste chirurgical soit 27,98% taux supérieur à celui de l'équipe de médecins du monde à Madagascar qui avait en 2005 454 patients dont 89 cas opérés.

Ceux-ci à concerner 43 cardiopathies acquises sur 104 avec 6 cas de décès et 27 cardiopathies congénitales sur 132 et 2 cas de décès.

Les cardiopathies acquises non opérées se sont stabilisées dans 64% des cas (N = 48). Alors que les cardiopathies congénitales se sont stabilisées dans 89% des cas sur 100 retrouvés.

Conclusion

Cette étude montre à suffisance la nécessité d'une prise en charge régionale ou nationale des cardiopathies infanto juvéniles.

Elle met en exergue le retard accusé dans le recrutement et le traitement des patients.

Elle souligne encore une fois l'importance de la prévention des cardiopathies rhumatismales dont le coût sera toujours inférieur au traitement surtout dans nos pays aux ressources limitées.

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The cardiac surgery of congenital diseases - Necessity and reality*)

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Abstract

Between 1998 and 2005 (march) in the Department of Cardiac Surgery (TIM-CENTER) of the Timisoara Institute of Cardiovascular Diseases, 1020 children (aged from 2-3 days) with congenital heart diseases (CHD) were operated, comprising all the aspects of the malformative pathology. Around 80% were infants (under 3) and 50% young infants and newborns. Although enough large, the studied group represents around 20-30% of the surgical activity of the Department and it is far from the surgical necessity of treating CHD, which are frequent but not in time and correctly diagnosed, leading to a 60% mortality in the first year and 75% in the first two years of life. This creates a large distance between the real necessity and the practical reality of the pediatric cardiac surgery and the study, for the first part, is emphasizing that and presents the practical corrective conclusions. The second part of the study presents the pathology treated surgically and the early postoperative results (mortality, morbidity) in order to emphasize the difficulties and possibilities in pediatric cardiac surgery, especially in very young children.

Keywords: *cardiac surgery, congenital heart disease, incidence, evidence, prevalence*

Background

The current issue of the children with congenital heart diseases in Romania is especially serious and in the same time eluded or ignored by the institutions or persons in charge of its management and resolution. So, more than 1000 children with CHD are born annually in Romania; from them around 60% die in the first year, which means that 2 children die daily because of CHD.

Objectives

Starting from the clinical and statistical basic multifactorial analysis of a large group of children with CHD operated in TIM-CENTER in a relatively short period of time (more than 1000 children operated in about 7 years), inclusively and preponderant newborns (from 2 to 3 days after birth) and infants, with a large spectrum of diagnostics and operations, the commented data allow us to emphasize the current status of this pathology

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from many angles: incidence and prevalence, morbidity, mortality and the populational consequences of this pathology, the difficulties and possibilities of the management of this pathology between necessity and reality.

Incidence

The congenital heart malformations are frequent and permanently growing in number, because of the multiple maternal and fetal malformation generating aggressions and also in consequence of the current diagnostically possibilities, especially the echography, which is largely accessible. Corresponding to the knowledgeable statistics (EU, OMS), at the current population of Romania (around 22 millions) and at the reported rate of births (1.08%) and at a known and admitted incidence of CHD of 0.4% at newborns, results a number of 1073 children born yearly with CHD. But those are not retrieved in the statistics also because there is no National Registry of CHD and because, even if it would exist, 60% of children with CHD die in the first year of life and 75% in the first two years. This means that approximately 600 children die annually by CHD or two children per day, which is much more than the children with HIV-AIDS or the children of the streets, excessively known and press covered.

Those numerous malformative diseases, which are not, in general, but partially diagnosed (the 25% that gets beyond 2 years or just the 15% that survived after the age of 3 years, are like the tip of the iceberg, with its very large base still unknown), generates two important and severe statistical parameters: the morbidity and mortality caused by cardiovascular diseases (In Romania, it is the first cause of mortality ad morbidity, and, as it concerns this, Romania is on a regrettable first place in Europe); the high mortality in children, which leads to two important populational consequences: the depopulation of Romania, by the reduce in natural increase (negative already) and especially the depopulation of young age, the aging of population and the increase of the unfavorable proportion between the economical active and independent persons and the economical dependent persons.

Evidence

The known incidence of CHD is far from real and that is for at least two reasons:

1. The lack of a proficient and opportune diagnosis, starting from birth, through the existence of an activity of neonatology or even fetal cardiology.
2. The lack of a managerial algorithm of reporting and registration.

This inadequate evidence has as a consequence the erroneous interpretation of the existing data, especially in comparison with similar data from other countries.

Hence, the incidence of congenital diseases at 100000 alive births is reported a lot smaller in Romania than in the developed countries, which is totally false because it not reflects the lack of diseases but the lack of diagnosis (Figure 1).

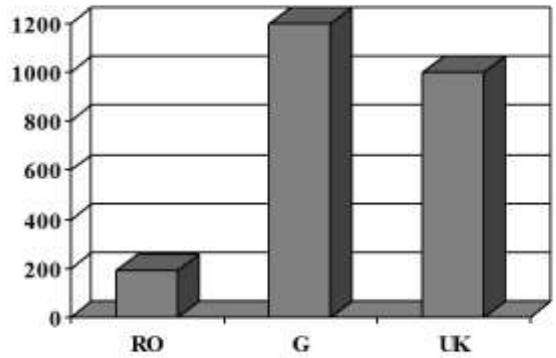


Figure 1: Compared (reported) incidence of congenital anomalies at 100.000 alive births

Instead, the neonatal perinatal mortality and at infants are much higher in Romania than in the developed countries (Figure 2, 3, 4).

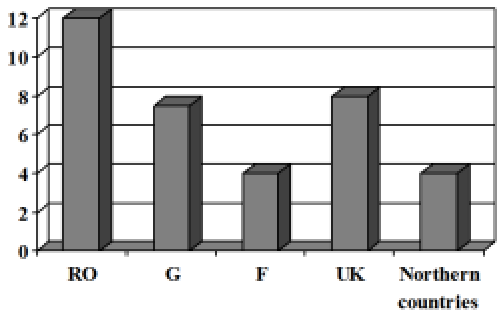


Figure 2: Compared perinatal mortality RO-developed countries (at 1000 births)

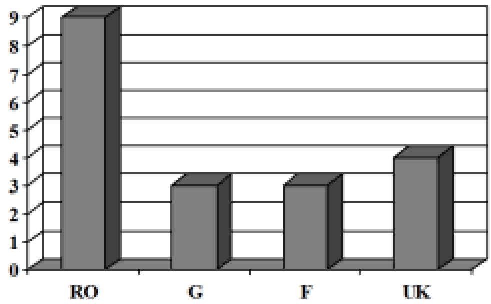


Figure 3: Compared neonatal (first 30 days) mortality RO-developed countries (at 1000 births)

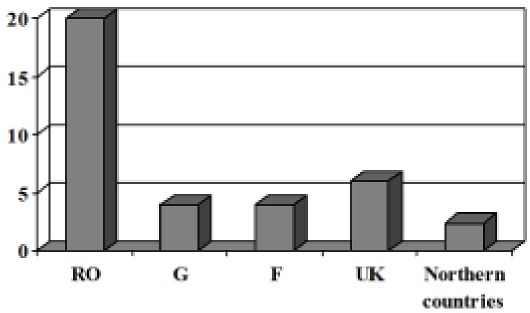


Figure 4: Compared first year mortality RO-developed countries (at 1000 births)

The conclusion that could be drawn is that the child mortality (perinatal, neonatal and at infants) is actually high and the congenital malformations are misleadingly reduced, because they are not correctly diagnosed and reported.

Other statistical data that include and hide the unfavorable consequences of the morbidity by CHD are: life expectancy, at birth, in years (Figure 5), life expectancy, at 1 year, in years (Figure 6) and the probability of dieing before reaching 5 years at 1000 alive births (Figure 7).

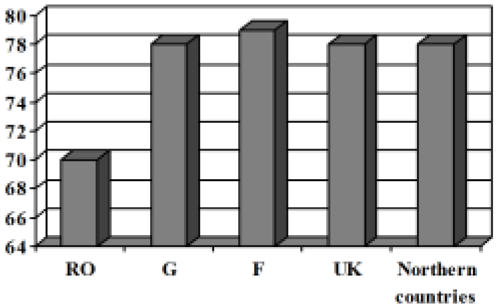


Figure 5: Compared life expectancy, at birth, RO-developed countries

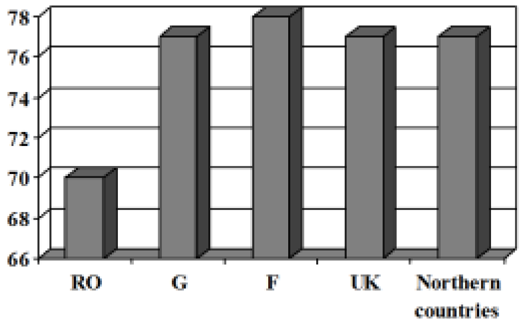


Figure 6: Compared life expectancy, at 1 year, RO-developed countries

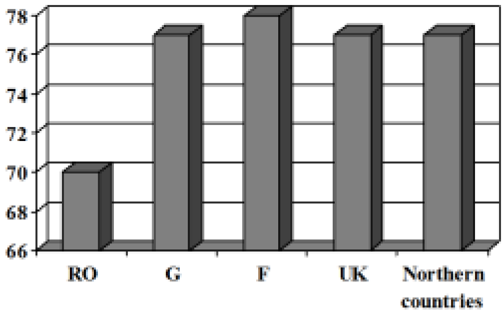


Figure 7: Compared probability of dieing, before reaching 5 years, at 1000 alive births, RO-developed countries

Therefore, Romania is not registered in Europe with any pediatric cardio-surgical activity, institutionally or as number of operations. Those statistics can be interpreted like this:

1. There are not children with CHD in Romania, because they are not diagnosed nor operated, the cause of death being reported erroneously.

2. The children with CHD are not operated – meaning they are not timely operated (newborns, infants), waiting for them to grow-up, and they don't grow because they are sick, and, because they are sick, they die. The pediatric cardio-surgery in Romania takes care only of the tip of the CHD iceberg.

In this context, the pediatric cardio-surgery in TIM-CENTER can be useful for comments and conclusions or practical use.

The pediatric cardio-surgical experience in TIM-CENTER

a. The patients

Between 1998 - march 2005, 1020 children with CHD, from all the counties of Romania, with an age starting from 2-3 days postnatal, with various and complex malformations, were operated in TIM-CENTER, often arrived in emergency, with a severe clinical status, by transportation means that were frequently without adequate monitorization and life support equipments, or with improvised ones. It is remarkable that this type of operations have not been done previously in TIM-CENTER and the gained experience overlapped with the learning curve of the complex team – cardiologist, anesthetist-reanimator, extracorporeal circulation technician, and collaborating surgeon. Also it is to say that this activity began with infants and school children (1998-2000) and then continued inclusively with newborns and young infants (2002-2003).

A surgical activity of barely 140-150 operations for CHD per year is very feeble, but is the kind of activity possible within the limitations of a modest center,with insufficient founds and a surgical activity oriented especially to adults.

In comparison, a multicentre study (ECSUR – EACTS Database – sept. 2001) reported 5249 cases operated for CHD in 31 hospitals, with a number of reported cases between 10 and 1200, in average 170 cases, through a period of 4 years, which is much less than TIM-CENTER:

- TIM-CENTER: 140-150 CHD/year
- ECSUR – EACTS: 40-45 CHD/year

In the activity of TIM-CENTER, the pediatric cardio-surgery represents around 20-30%, the cardio-surgery of the adult being concomitantly practiced in the same environment. The taking in charge of pediatric pathology in a modest and relatively recent center was imposed by a larger addressability and a relatively reduced availability of the larger and more experienced cardiology centers. We have to specify that the whole activity has been done without foreign collaboration (the only foreign help was in the training phase).

b. Demographics

- The sex ratio has no significance in the whole of that pathology; significant differences appeared only in some malformative patterns.
- The repartition by age of the patients (Figure 8) is a very important statistical parameter for the defining of the surgical activity.

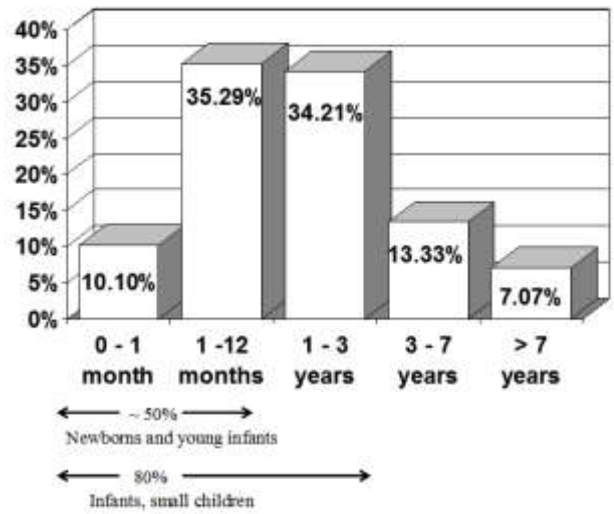


Figure 8: Repartition by age of the patients operated for CHD in TIM-CENTER

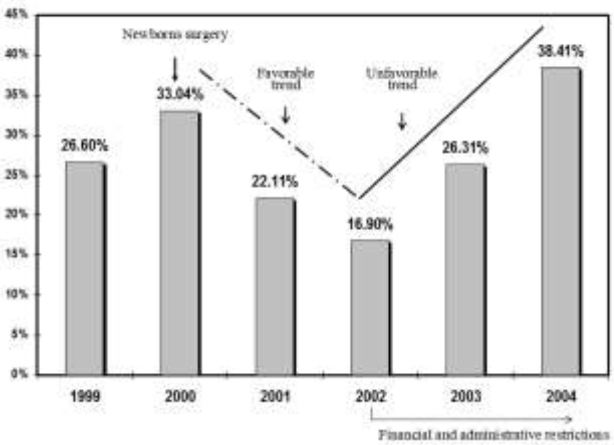
We have to emphasize the percentage of newborns, 10.1%, which is obviously less than the necessary, but the effort for the operations at that category is in reverse proportion to their statistical percentage and represents the intention and possibility to practically approach this pathology, in time (some malformations are loosing their corrective and life-saving surgical indication after the first days or maximum first weeks of life).

That percentage has a relative significance, because the surgical activity for newborns and young infants begun only in the year 2000. 35.29% from the operated children were between 1 and 12 months old; this percentage is similar to those reported by competent specialty centers. We also emphasize that almost 50% from the children operated for CHD were newborns or young infants. Together, newborns and infants represents around 80%, which is a favorable statistical parameter in that field; the other children were of preschool (13.33%) and school age (7.07%), together 20% from all the children operated.

Making a comparison with the same multicentre study (ECSUR – EACTS Database – sept. 2001), we found, as a positive aspect of the activity, similar statistics (Table 1).

Table 1: Repartition by age of the patients with CHD in ECSUR – EACTS Database – September 2001

Age	*Nr. of patients*	%
Newborns	**809**	**15.3**
1-12 months	**1601**	**30.2**
> 1 year	**2884**	**54.5**
Total reports from 31 centers	**5294**	**100**



A tender subject by its significance is the percentage of the un-operated children from the hospitalized children (Figure 9).

Figure 9: The percentage of the un-operated children from the hospitalized children

Three moments are to be highlighted:

1. the year 2000, when we begun the surgery at newborns and the cases were excessively selected;

2. a period when the trend was favorable (2000, 2001, 2002);

3. a period with an unfavorable trend, when the number of the un-operated children was higher because of the financial and administrative-managerial impediments in the Institute (2002, 2003, 2004).

c. Prevalence

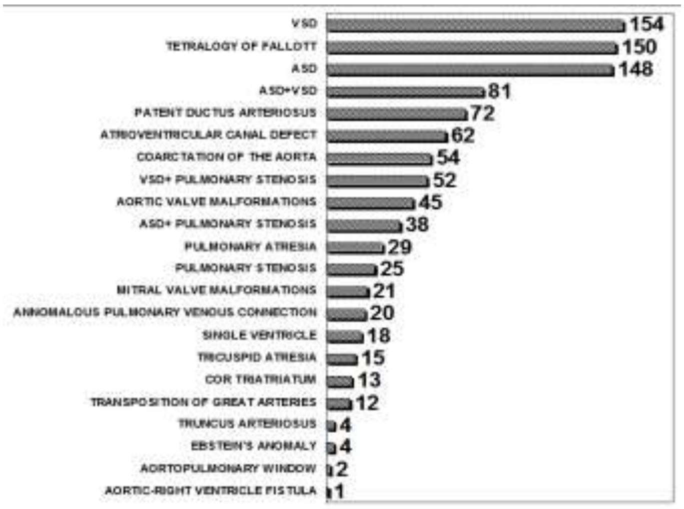


Figure 10: The number of cases by diagnostics

The approached lesional types (Figure 10) comprise the most common CHD, with the exception of hypoplastic left heart syndrome (Norwood operation) which necessitates surgery immediately after birth and that is possible only with fetal diagnosis and delivery near to a proficient cardiac surgery hospital, announced previously in order to maximally synchronize the birth with the operation.

The incidence of the lesional types is resulted from the addressability of the cases, but is similar with the lesional prevalence in other centers (Table 2).

Table 2: Comparison of the lesional prevalence between TIM-CENTER and ECSUR-EACTS (2001)

CHD	TIM-CENTER (%)	ECSUR-EACTS (%)
Ventricular septal defect	15.1	16.74
Tetralogy of Fallot	14.7	11.09
Atrial septal defect	14.51	12.32
Patent ductus arteriosus	7.06	4.06
Atrioventricular canal defect	6.08	7.58
Coarctation of the aorta	5.29	5.76
Aortic valve malformations	4.41	5.18
Pulmonary atresia	2.84	3.36
Pulmonary stenosis	2.45	1.04
Mitral valve malformations	2.05	1.38
Anomalous pulmonary venous connection	1.96	0.11
Single-ventricle	1.76	3.36
Tricuspid atresia	1.47	1.85
Cor triatriatum	1.27	0.09
Transposition of the great arteries	1.17	6.71
Truncus arteriosus	0.39	0.98
Ebstein's anomaly	0.39	0.3
Aortopulmonary window	0.19	0.26

Transposition of great arteries neonatal treatment*)

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Abstract

Objective: *Anatomic surgical correction (arterial switch) of transposition of great arteries has become in the last decades the elective approach in the western countries. In this study, we reviewed 32 patients with transposition of great arteries, referred to our hospital, and surgically corrected in the neonatal period.*

Patients and method: *We analyzed 32 patients submitted in our hospital between January 2002 and July 2006, in the first days of life. They were immediately diagnosed by echocardiography, (complete diagnostic), prepared for surgery with Rashkind septostomy and/or prostaglandin infusion, according to the patient's state, and operated on, 2 - 14 days after referral, performing an arterial switch operation - 30 patients, and intracardiac conduit + R.E.V. operation - 2 patients.*

Results: *The principal measures of preoperative management were Rashkind septostomy and prostaglandin infusion. The surgical procedure consisted in extensive dissection of the aorta and pulmonary arteries, coronary translocation by punch orifices in neoaorta, reconstruction of the pulmonary artery by pantaloon patch technique and closure of ASD. The immediate post-op. course depended on the possibility of maintaining the neonates in negative fluid balance. The "open-sternum" technique was applied to 24 patients (75%), in 8 patients the sternum was closed per-primam. The patients were weaned from mechanical ventilation and extubated between the 2-nd and the 68-th post-op. day. The intensive care unit stay ranged between 10 and 165 days. The overall post-op. mortality was 31.2% and was related to myocardial ischemia - 3 patients, and post-op. complications - 7 patients (total -10 patients). There were also 4 late deaths (12.5%), due to infectious complications.*

Conclusions*: The diagnostic and surgical approach of the patients with transposition of great arteries in neonatal period involves a perfect collaboration between all physicians dealing with these patients. The surgical procedure time has to be as short as possible, and the post-op. therapy may be eventful, even in well operated patients.*

Rezumat

Obiectiv: *Corecția chirurgicală anatomică (switch arterial) a transpoziției de vase mari a devenit în ultimele decade intervenția de elecție în țările dezvoltate. În studiul de față am revăzut o serie de 32 pacienți cu transpoziție de vase mari, internați în serviciul nostru şi corectați chirurgical în perioada neonatală.*

Material şi Metodă: *- Am studiat o serie de 32 pacienți internați în serviciul nostru în perioada Ian. 2002 - Iul.2006, în primele zile de viață, care au fost diagnosticați imediat ecografic*

*) Romanian Journal of Cardiovascular Surgery ■ 2006, vol. 5, no. 2, pp. 77-86

(diagnostic complet), pregătiți preoperator cu septostomie Rashkind sau infuzie cu prostaglandine, în funcție de situație şi operați la interval de 2-14 zile de la internare, efectuându-se operația switch arterial - 30 cazuri şi conduct intracardiac + operatia R.E.V. - 2 cazuri.

Rezultate: *Măsurile principale de pregătire preoperatorie au fost septostomia sau infuzia cu prostaglandine. Tehnica operatorie a constat în disecția extensivă a aortei şi arterelor pulmonare până în hilii pulmonari, translocarea coronarelor prin orificii practicate în neoaorta, refacerea arterelor pulmonare prin tehnica "pantaloon patch" şi închiderea DSA. Evoluția postoperatorie imediată a depins semnificativ de posibilitatea menținerii pacienților în bilanț hidric negativ. Tehnica 'stern-deschis' s-a aplicat la 24 pacienți (75%), la 8 pacienți sternul a fost închis per primam (25%). Pacienții au fost sevrați de ventilația mecanică şi detubați între ziua a 2-a şi ziua a 68-a. Pacienții au fost internați în terapie intensivă între 10 şi 165 zile. Mortalitatea postoperatorie a fost 31,2% şi s-a datorat ischemiei miocardice - 3 cazuri, şi complicațiilor postoperatorii - 7 cazuri (total -10 cazuri). Au mai existat 4 cazuri (12,5%) de decese la distanță, după 30 zile p.o., determinate de complicații septice.*

Concluzii: *Abordarea diagnostică şi terapeutică a pacienților cu transpoziție de vase mari în perioada neonatală presupune o foarte bună conlucrare între toți medicii implicați în rezolvarea acestei afecțiuni. Durata intervenției chirurgicale trebuie să fie cât mai scurtă, iar terapia postoperatorie poate fi grevată de multiple complicații, chiar şi la pacienții bine operați.*

Introduction

The transposition of great arteries represents approximately 80% of all cardiac congenital malformations, occurring approximately once at 3000 births. Continuous concerns to solve this cardiac malformation have led to the development of the correction surgical techniques, until the appearance of the anatomic surgical correction (arterial switch), made public for the first time by the Brazilian surgeon Jatene in 1976 [7]. The initial technique of surgical correction was continuously improved, the most important modification being made by Lecompte, by inversion of the distal extremities of the pulmonary artery and aorta, for the accomplishment of an anastomosis without prosthetic conduit and without tension [9]. In the last 20 years, this technique has become the election technique for surgical correction of transposition of great arteries abroad [3, 4, 10, 11]. The difficulty of this type of operation consists in the complexity of the surgical technique itself and due to the fact that this operation must be performed, generally, in the first two weeks of life [13]. The experience gathered in the pediatric cardiac surgery within the Heart Institute in Cluj-Napoca, as a result of some repeated visits of some medical teams from Italy and USA, allowed the approach of this very complex type of operation in our institute too. The present paper studies 32 patients with transposition of great arteries, diagnostically and therapeutically approached in the first 4 weeks of life. The patients' morphopathology, largely, resembled, but physiopathologically, the patients' preoperative state was quite variable.

Patients and Method

Patients

The study analyses a series of 32 patients, hospitalized and treated in our department between January, 2002 and July, 2006. The series contains 25 male newborns and 7 female newborns. The patients were urgently transferred from neonatology departments from different areas of the country, including Bucharest. Upon hospitalization, patients were aged between 2 and 30 days, with an average of 7 days. The patients' weight upon arrival in our department varied between 2.8 kg and 4.2 kg, with an average of 3.45 kg. The diagnosis immediately established by cardiac echography was: Transposition of great arteries - 32; associated malformations: patent ductus arteriosus - 32, atrial septal defect - 29, patent foramen ovale - 3, ventricular septal defect - 4, pulmonary artery stenosis - 2, subpulmonary stenosis - 1, aortic coarctation - 1, situs inversus - 1. The coronary anatomy showed the following distribution: Yacoub Type A - 28, Type B - 1, Type C - 1, Type D - 2. Surgery was performed within a range that varied from 2 to 14 days from patient hospital admission, and was carried out at the age of 6 - 32 days, with an average of 15 days.

Preoperative treatment

Upon hospital admission, the patients were immediately monitored from a cardiovascular and respiratory point of view, so that their clinical and paraclinical state could be exactly assessed, considering that many patients were sent from long distances, and these newborns bear hardly enough the transportation conditions.

After the patients' state was stabilized upon hospital admission, they were urgently diagnosed by cardiac echography. The transposition of great arteries can be easily diagnosed by underlining an artery that curves (Ao), which starts from the RV and an artery that bifurcates (AP), which starts from the LV (Figure 1 & 2).

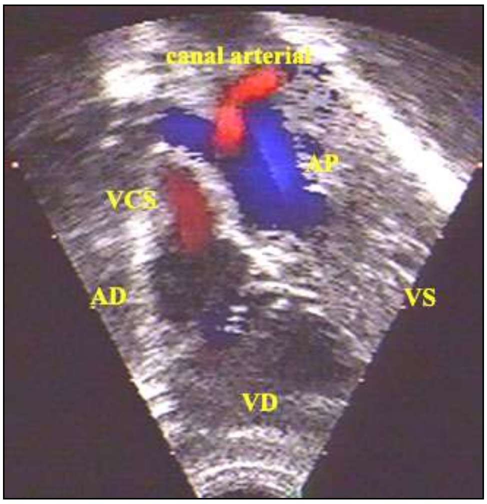

Figure 1: LV origin of PA and left-right shunt across PDA

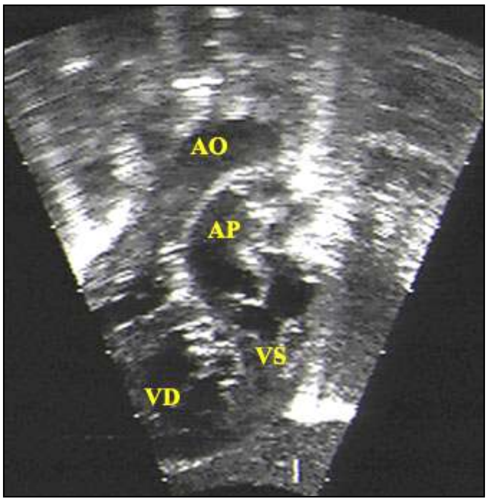

Figure 2: TGA (subcostal long axis): LV origin of PA and RV origin of Ao

The comparative size of the two great arteries is then considered, one's position with respect to the other, considering the fact that the position side-by-side implies supplementary intraoperative technical difficulties. Usual lesions associated in TGA, PDA, ASD or VSD are then studied. Another malformation that can occur, pulmonary stenosis, counter indicates the performance of an arterial switch.

The echographic assessment of the ventricular function is important, as the underdeveloped left ventricle, with interventricular septum that bulges towards the left ventricle, not towards the right one, counter indicates the arterial switch, LV no longer being able to support the systemic circulation. In these cases, the LV retraining can be performed, by a PA banding with a systemic to pulmonary shunt, for 7-10 days, followed then by an arterial switch.

Special attention must be paid on the precise description of the coronary anatomy, considering the fact that this is very important in choosing the surgical technique and strategy (Figure 3). The coronaries are relatively easy to visualize at origin. It's more difficult to specify the way, the bifurcations and the distribution, but strictly compulsory to be known by the surgeon, before entering the surgery room.

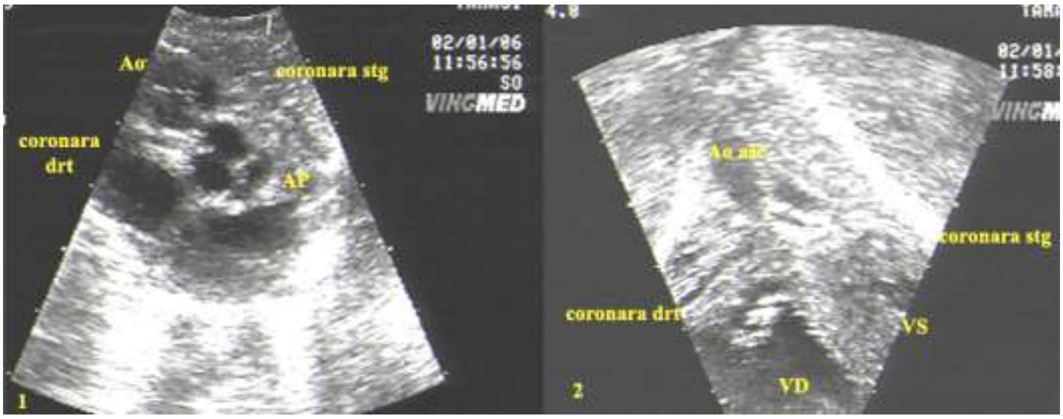

Figure 3: Coronary origin and initial course in parasternal short axis (1) and in subcostal wiew (2) - Yacoub Type A

Upon echographic diagnosis, the preoperative preparation begins, by setting up a central catheter for volemic and drug infusion, and an arterial catheter for the permanent measurement of the arterial pressure, the blood gases and the biological samples, for the exact appreciation of the hypoxia and acidosis degree, considering the fact that many patients had preoperatively severe hypoxia and acidosis. If there was the case, Rashkind septostomy (Figure 4) was performed in our department (6 cases), other 5 cases being transferred with Rashkind septostomy performed in other cardiology departments. 28 patients benefited from an infusion with prostaglandin, in order to maintain the permeability of the PDA. The patients' nutrition was naturally practiced in stable patients or through naso-gastric catheter in intubated patients after the septostomy, or large doses of prostaglandin, that induces apnea.

**Figure 4: Patent foramen ovale (1); Rashkind septostomy (2);
atrial bidirectional shunt post-Rashkind procedure (3, 4)**

Surgical technique

Surgical procedures performed on the 32 patients were: 30 arterial switch operation (ASO), and 2 intracardiac conduit with R.E.V. procedure (*réparation a l'étage ventriculaire*), in the 2 patients with pulmonary stenosis, on whom arterial switch operation could not be performed. Preoperatively, the acid-basic re-equilibration of the patients was tried, considering the fact that entering in the surgery room with a patient with hypoxia and acidosis, dramatically cuts down the chances of success for these operations, by poor ventricular contractility after weaning of extracorporeal circulation and uncontrollable diffuse bleeding, caused by coagulation disorders. However, surgical procedure was performed on these patients at limit, the operation being considered the only chance of survival for these newborns. The great majority of these critical patients deceased during the operation or immediately after, increasing the perioperative mortality, so that, as a result of the gathered experience, in the last period, we counter indicated the surgical operation in the case of this category of patients.

The arterial switch operation was performed by median sternotomy. A large patch of the pericardium was harvested, which was fixed in glutaraldehide solution, for the reconstruction of the pulmonary artery. In the last 8 surgical procedures for the reconstruction of the pulmonary artery a patch of bovine pericardium was used, which adapted very well to the sutures on the pulmonary artery. The extensive dissection of the aorta was performed (Figure 5) and of the pulmonary arteries (Figure 6), up to the pulmonary hila, in order to avoid the tensions on the pulmonary branches, according to the Lecompe maneuver.

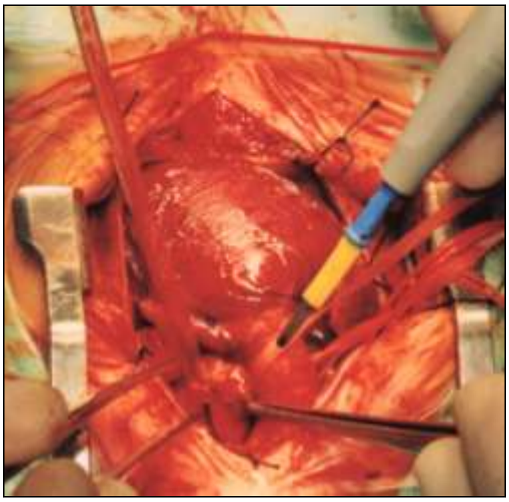

Figure 5

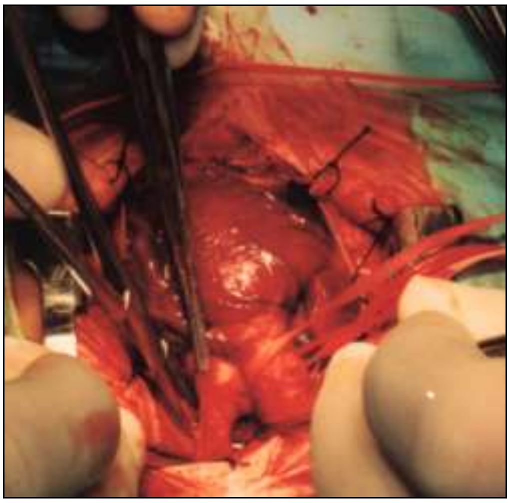

Figure 6

The canulation of the aorta was performed distally, close to the emergence of the innominate artery. We initially performed bicaval canulation, then, in the last 22 interventions, we used unique caval canulation, in order to shorten the surgery time. Sometimes, canulation and emergency by-pass were performed, because of the patient's hemodynamic instability. The extracorporeal circulation was performed in deep hypothermia at 18 degrees with "low-flow", with blood cardioplegia, repeated every 20 minutes.

After initiation of the extracorporeal circulation, the PDA was immediately divided and sutured. Venting of the LV was used in order to avoid the distension of the left side of the heart, venting that is very useful at the end of the operation too, after weaning of the extracorporeal circulation.

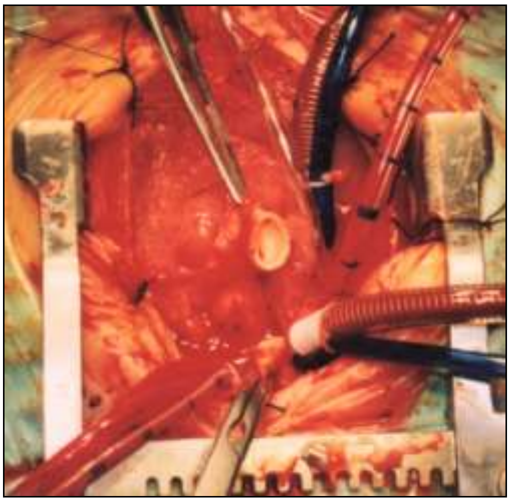

Figure 7

After stopping the heart with antegrade blood cardioplegia, the division of the great arteries (Figure 7), at a distance of 1 cm from the emergence, and the harvesting of the coronary buttons were performed. The dissection of the coronary buttons was extremely difficult in the case of coronary distribution of Yacoub B and C type.

The dissection of the first section of the coronary arteries was extensively performed, within a distance of 7-8 mm, for a translocation on the neo-aorta without tension and kink-kink.

Figure 8

The re-implantation of the coronaries was performed in neo-aorta by orifices made with a punch of 4 mm, in order to avoid the intersection of the suture lines with the termino-terminal suture for remaking the continuity of the aorta, according to the Lecompte maneuver (Figure 8). In the cases when the coronaries had particular anatomy (Yacoub B, C and D), the dissection of the coronaries was extremely difficult and the reimplantation was performed in more distanced or higher positions on the neo-aorta, in order to avoid kink-kink or tension, with consecutive myocardial ischemia, objective that couldn't always be reached.

Sometimes, in order to perform coronary anastomoses, the circulatory arrest was used, in order to obtain a clean, bloodless surgical field.

Upon performance of coronary anastomoses, the circulatory arrest was used, in order to solve the intracardiac defects (ASD, VSD). In cases when surgery was performed with bicaval canulation, the circulatory arrest was not used. After solving the intracardiac defects, rewarming was started, considering the fact that this lasts, on an average, 45-50 min.

The pulmonary artery was reconstructed using the "pantaloon patch" technique, using a patch of autologous pericardium or bovine pericardium, fixed in glutaraldehide (Figures 9 & 10).

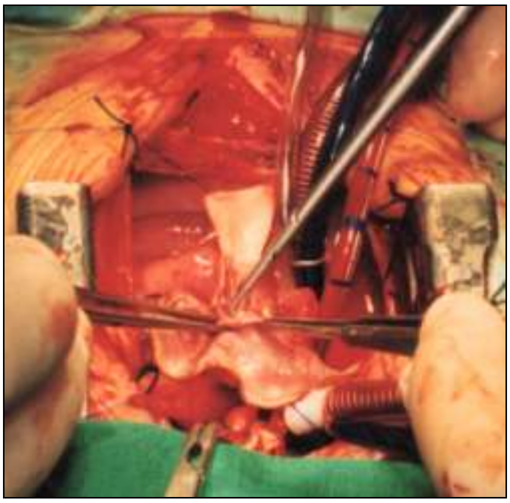

Figure 9

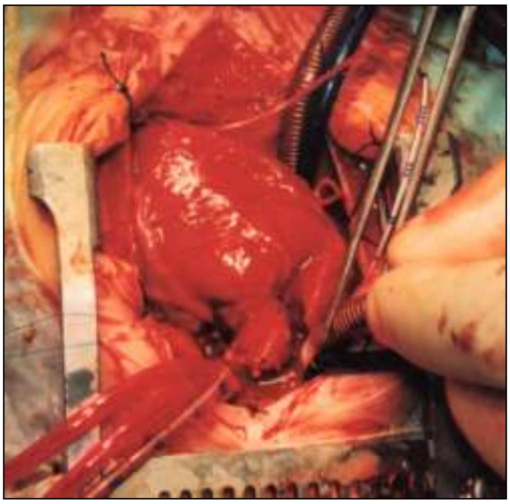

Figure 10

This surgical stage was performed within the first cases with unclamped aorta, in order to shorten the time of aortic clamping, but after improvement of the experience and shortening the surgery times, it was passed on to the reconstruction of the posterior half of the pulmonary artery with the clamped aorta, due to the possibility of performing a more precise suture, without no danger of bleeding after weaning from the extracorporeal circulation. Among the first operations in the series, in 2 cases, the reconstruction of the pulmonary artery was done with two pericardium separate patches, in the place where the coronary buttons were harvested, and termino-terminal anastomosis of the two extremities of the pulmonary artery, but their postoperative course was difficult, with respiratory insufficiency and consequently with cardiocirculatory insufficiency with 1 death, the reason why we abandoned this technique. The physiopatho-logical mechanism was probably the tension on the pulmonary hila, by traction of the too short pulmonary artery, mechanism that does not appear in the "pantaloon patch" technique.

The longer the clamping time was, the more difficult the weaning from the extracorporeal circulation was, but it also depends on the preoperative acidosis, and on the possible myocardial ischemia, due to the imprecise coronary translocation. After weaning from the extracorporeal circulation, modified ultrafiltration was performed, in all cases, to reduce the myocardial and other organs edema.

In patients with TGA and valvular pulmonary stenosis, when the arterial switch operation is not indicated, the pulmonary valve having to be perfect to become the neo-aortic valve, the R.E.V. operation and intracardiac conduit procedure was performed. The operation is performed by a longitudinal right infundibulotomy, by which the closing of the ventricular septal defect is done by the help of an intracardiac conduit that leads blood from LV, through VSD, into the aorta. The pulmonary artery is divided at the base, the proximal extremity is sutured, and the distal extremity is translocated before the aorta by the Lecompte maneuver, and is sutured directly to the infundibulotomy, in the postero-superior part, the anterior continuity of the artery being accomplished by a patch of autologous or bovine pericardium, fixed in the glutaraldehide. This procedure, R.E.V. is an alternative to the Rastelli procedure, for lack of pulmonary homografts or xenografts. After weaning from the extracorporeal circulation, modified ultrafiltration was performed in these patients too.

Postoperative treatment

Postoperative treatment in these patients is very difficult, sometimes even more difficult than the intraoperative management, even in the patients where surgery developed with no problems. Sometimes, these patients need inotropic combinations in high doses, in order to sustain the contractility of the left ventricle, which must sustain the systemic circulation. In some cases, vasodilators are being used, in order to reduce the after-load. Maintaining the patient in negative fluid balance is essential, immediately after the surgical procedure, because, in case of fluid overload, the left ventricle can severely decompensate within a few minutes. In the cases when weaning from extracorporeal circulation is difficult, the "open-sternum" technique is used, by leaving the sternum open for 2-3 days and closing the skin with a Gore-Tex patch, until the improvement of the hemodynamics. In the studied series, 24 patients leaved the operation room with "open-sternum", and 8 with the sternum closed per-primam. The cases of myocardial ischemia (3 in the studied series) are very difficult to treat with drugs, these having to be remade surgically. In the studied series, all these cases ended with intra-operative death, in spite of the efforts made by the surgeon and the anesthesiologist to improve the situation.

After closing the sternum, or if necessary, control echography is performed (Figure 11), which can show the possible persistent problems from the intra-operative stage, or which appeared after the operation, problems which, most of the times, can be remedied, by postoperative treatment. In this way, repeated control echographies are absolutely necessary for a qualitative postoperative therapy.

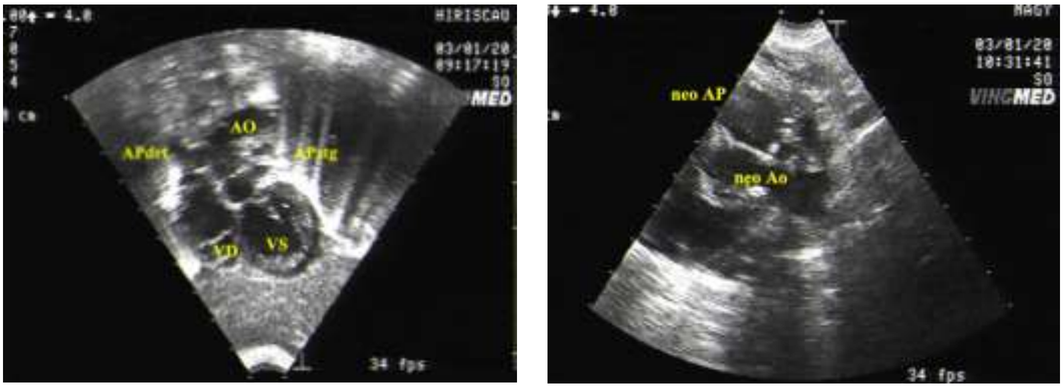

Figure 11: TGA after arterial switch - subcostal and parasternal short axis

The mechanical ventilation of these patients is, most of the times, of long standing, due to many reasons: the precarious preoperative state of the patients, who, most of the times, need intubation within a few hours or days from birth (so that these patients breath spontaneously a short period of time after the operation), long time intervention, which predisposes to interstitial edema, even if modified ultrafiltration was performed, the pulmonary complications that can appear in the period of the mechanical ventilation (athelectasia, pneumothorax, pulmonary infection, bronchopneumonia, pleural effusion). Sometimes, one can end in a vicious circle: the mechanical ventilation is prolonged by the very complications that can occur due to mechanical ventilation. So, the patient's extubation in these patients is delicate, with a preparation of the patient of approximately 24 hours, sometimes re-intubation of the patient being necessary, even several times. In the studied series, the mechanical ventilation lasted between 2 and 68 days, with an average of 19 days.

After the patient's extubation, natural alimentation can be started again, in the beginning by naso-gastric tube, then by natural way, with the mention that, during the whole mechanical ventilation, parenteral nutrition is also administered, or if the ventilation is prolonged, natural nutrition is also administered by naso-gastric tube, but continuously, on automatic syringe. When nutrition is administered again, pulmonary complications can appear, because of the fact that the patient can vomit and then, pulmonary aspiration syndrome can occur.

When passing on to complete natural nutrition and ceasing the use of the parenteral medication, the patient can leave intensive care. In the studied series, the intensive care stay lasted between 10 and 165 days, with an average of 34 days.

Thus, the 4 critical moments of the postoperative course are: the first postoperative hours (bleeding, myocardial ischemia, left ventricular failure with acute pulmonary edema), closing the sternum (death by acute cardio-circulatory insufficiency), extubation (respiratory insufficiency with the necessity of re-intubation, or other complications) and nutrition restart (vomiting with bronchial aspiration syndrome).

The complications appeared in the studied series were as follows:

- myocardial ischemia -	3 cases, 3 deaths
- left ventricular failure -	13 cases, - 3 deaths
- postoperative bleeding -	7 cases, 5 reinterventions, 3 deaths
- postoperative wound infections -	3 cases
- mediastinitis -	2 cases, 2 deaths
- pulmonary athelectasia -	25 cases
- bronchial infections, bronchopneumonia -	15 cases
- toxic-septic shock -	4 cases, 4 deaths
- pneumothorax -	3 cases
- pleural effusion -	4 cases
- stroke -	2 cases (1 ischemic, 1 hemorrhagic)
- arrhythmias -	6 cases
- acute renal failure -	2 cases
- third degree AV block -	1 case
- ileal perforation on vascular malformation -	1 case

The reoperations and the invasive maneuvers performed after surgery were as follows:

- secondary closing of the sternum for "open sternum"	24
- mediastinal lavage and secondary suture of the sternum for mediastinitis	2
- bleeding control	5
- median laparotomy for digestive complications	2
- pacemaker implantation	1
- thoracotomy and pleural drainage for the hemothorax	2
- pleural drainages for hydrothorax and pneumothorax	5
- bronchoaspirations with fiberscope for athelectasia	14
- emergency opening of the sternum for acute cardio-circulatory insufficiency	2

Postoperative mortality was of 31.2% (10 cases), and the mortality at distance through septic complications was of 12.5 % (4 cases). There weren't any deaths along the follow-up, which varied between 58 and 3 months, with an average of 25.4 months. The somatic and psychological development of the patients who survived was very good, corresponding to their age.

Disscusion

Having in mind that anatomic surgical correction of the TGA is a difficult surgery, very delicate, and must be performed in the first weeks of life, the results shown in the present paper give us the right to believe that the experience gathered in our department, in diagnosis, surgical therapy and postoperative treatment, in the field of congenital cardiac defects in the newborn allows the future evolution and the possibility of gradual approach of very complex cardiac malformations. We mention that the group studied in the present paper represents a personal statistic, and the surgical procedures and the postoperative therapy were realized by a Romanian medico-surgical team.

A first condition for the success of these procedures was the very early diagnosis, most of the times in the first days of life, with the possibility to perform the Rashkind septostomy and the infusion of prostaglandin, in order to stabilize the patients and to be able to approach them surgically, in optimal conditions. Sometimes, we were forced to perform surgery in patients with very high hypoxia, acidosis or with metabolic disorders, but the great majority of these patients died during the surgical procedure, so that, in the last period, we counter indicated from the beginning the surgical correction in these cases. Another essential condition is the detailed investigation of the patients, in order to find out their sufferings from birth, which complicate very much the postoperative course.

Under these circumstances, an elective surgical approach was preferred. The newborn anesthesia and the placement of the catheters require special experience and ability from the part of the anesthesiologist. After opening the sternum, a large pericardium patch was harvested, fixed then in glutaraldehide. The extensive dissection of the aorta and the pulmonary arteries were done as far as possible, before performing the extracorporeal circulation [1, 2]. For the extracorporeal circulation, we initially used bicaval canulation and "low-flow" deep hypothermia, with blood cardioplegia repeated every 20 minutes, but after development of the surgical experience, we passed to unique caval canulation, managing to shorten the intervention with approximately 30 min. We used permanent venting of the left ventricle, which we consider very important, especially in restarting the contractile ventricular function after unclamping the aorta, when the left ventricle must not be overloaded.

The aorta has always been divided with approximately 3-5 mm higher than the pulmonary artery in order to avoid tension at reconstruction of the new pulmonary artery. The coronaries were harvested from the aorta following the classical technique [1, 2, 6, 8, 13], and the re-implantation in the neo-aorta was performed in a very carefully chosen position, before dividing the great arteries [1, 2] and, within the possibilities, through an orifice made in the neo-aorta with a punch of 4 mm, in order not to cross the suture line of the coronary buttons with the suture of the distal and proximal extremities of the aorta (intersections that present, afterwards, high possibilities of bleeding).

The suture of the coronary buttons was performed with PDS 7-0, in order to prevent the later ostial stenosis. The translocation of the coronaries was technically easier in patients who had coronary distribution Yacoub type A [13], and much more difficult in patients that had other types of coronary distribution. The pulmonary artery was reconstructed using the "pantaloon patch" technique, but only posterior and lateral, the anterior part being directly sutured at the bifurcation of the pulmonary artery, in order to keep a contiguous portion of native material, for growth. Initially, we totally reconstructed the pulmonary artery, after unclamping the aorta, but the bleeding points between the aorta and the pulmonary artery are very difficult to be controlled, so that, in the last 22 cases, we sutured the posterior section of the pantaloon patch on the pulmonary artery, before unclamping the aorta (in view of a precise suture on an immobile heart), with much better results, without postoperative bleeding. In the last 8 cases we used bovine pericardium patch, which proved to be very suitable for reconstruction of the pulmonary artery. Weaning from the extracorporeal circulation was performed by gradually and easily reducing the debit, as to give the left ventricle the possibility to adapt and by keeping a reduced after-load by vasodilators. We performed ultrafiltration in all cases to reduce the post-CEC edema [1, 2, 5, 11]. We inserted sequential pacemaker wires, and the "open-sternum" technique in 24 cases, in the other 8, the sternum being closed per-primam.

The gathering of surgical experience and some technique modifications that we performed on the way, determined the possibility to shorten the surgery time. Thus, the perfusion time diminished from 310 min. to 161 min. (average - 211 min.), the clamping time from 167 min. to 81 min. (average -124 min.), and the circulator arrest time varied according to the chosen technique between 5 and 81 min. (average - 27 min.). In the R.E.V. procedure, the average perfusion time was 159 min. and the average clamping time was 117 min. The total operative time dropped in the arterial switch operation from 8 to 5 h. This shortening of the operative time was the essential improvement factor in time of the results, besides the more careful selection of the patients and the increase of experience in the postoperative therapy.

The postoperative course was diverse, due to the different physiopathological conditions. What is essential in the postoperative intensive care is the reduction of the left ventricle after-load through vasodilators, to give the left ventricle the possibility to adapt to the passing from pulmonary circulation to the systemic one. Maintaining a systolic systemic pressure of 60 - 70 mmHg is ideal. The inotropic agents used were dopamine, adrenaline, milrinone, dobuthamine and isoprenaline, according to the *physio-pathological* conditions. We met one single case with pulmonary hypertension, due to the aspiration syndrome at birth, which was successfully treated with nitric oxide, which, generally, with children under the age of one year, is the only postoperative practically efficient treatment of pulmonary hypertension, so that we do not recommend approaching such procedures, in lack of nitric oxide.

Another very important element in the postoperative therapy is the fluid load, which must not be excessive, closely following up the central venous pressure and especially the left atrium pressure, which must not be higher than 10 mmHg. Antibiotic therapy must be performed with strong and large spectrum antibiotics, considering the fact that some of these patients have their sternum open for 2-3 days and their immunity is deficient.

The second critical point, after getting out of the operation room, in the postoperative course of these patients, is closing the sternum, moment that must be carefully chosen, after 2-3 days when the patient must evolve in negative fluid balance, otherwise closing the sternum will be impossible.

The third critical point is the weaning from the mechanical ventilation, weaning that must be done gradually, with a period of assisted ventilation. In spite of all these, it can happen that the patient can not be weaned from the mechanical ventilation from the first attempt. On the other side, mechanical ventilation in these patients, even if very well chosen, can get complicated with suprainfections of the tracheobronchial tree, pneumothorax or lesions in the upper breathing ways.

A fourth difficult point is restarting the nutrition, which must be done gradually, via the naso-gastric catheter, with permanent control of the digestive tolerance (vomiting can lead to pulmonary aspiration syndrome), because restarting the transit in these patients is frequently difficult, due to the fact that they have been fed only few days before surgery, and after the surgical procedure, the evolution can be long until the possibility to restart oral nutrition. In these cases, the patients had initially parenteral nutrition. After getting out of the therapy, patients are generally on vasodilator, diuretic and cardiotonic treatment.

The follow-up was performed, in the beginning, twice a month, and then monthly by clinical, radiological and echographic examinations, without showing, in this period, postoperative complications.

Conclusions

The approach of the patients with transposition of great arteries in the neonatal period, in view of anatomic surgical correction needs, besides routine in the postoperative and operative treatment, and diagnosis of the patients aged under one year, a very good collaboration between surgeons, cardiologists, anesthesiologists, perfusionists, pediatricians and neonatologists.

The surgical technique was, mainly, the same, but with slight changes that were adopted upon experience gathering, changes that reflected in a better bleeding control, an easier exit from the extracorporeal circulation and the shortening of the duration of the surgical procedure.

The postoperative therapy of these patients has not yet become a routine, due to the multiple complications that can occur, even in well-operated patients, because of the immaturity of the biological functions in the newborns.

In the future, a better collaboration with the neonatologists in the area is required, for immediate tracing of the patients with transposition of great arteries, having in view the fact that the anatomic surgical correction is possible only in the first weeks of life.

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Surgical Approach in Grown-up Children Diagnosed with Tetralogy of Fallot*)

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Abstract

Objective: *To study the surgical approach in children diagnosed with Fallot' Tetralogy and operated in Targu Mures Institute of Cardiovascular Diseases and Transplantation, depending on the complexity of the malformation and the particular conditions of each patient.*

Methods: *This is a retrospective study performed on 45 children (31 boys and 14 girls) aged over three years, diagnosed with tetralogy of Fallot, operated in our institute between January 2005 - February 2011. The surgery type was palliative - systemic to pulmonary shunt - in one case (2.2%), primary total repair performed on 21 (46.6%) of the children, complete secondary repair in 17 children (37.7%), pulmonary valve replacement in 6 children (13.3%) and right ventricle-pulmonary artery valved conduit implantation in 1 case (2.2%). The short and mid term postoperative follow-up was performed by clinical examination and echocardiography.*

Results: *Mean age of children at the time of surgery was 6.8 years (7.5 for boys and 6.5 for girls), with a mean weight of 19.9 kg (19.7 for boys and 20.5 for girls). Perioperative mortality was 0% and at 3 years 2.22% (one patient). Palliative surgery was performed in one patient who presented a shunt thrombosis, which was replaced with a larger diameter shunt in emergency conditions. Primary total repair was performed in patients primarily diagnosed with tetralogy of Fallot, and secondary repair was performed in those who had undergone a systemic-to-pulmonary shunt previously. Older children, with postoperatory severe pulmonary insufficiency and signs of right ventricle dysfunctions at long term follow up, underwent pulmonary valve replacement with bioprosthesis.*

Conclusions: *Children with Fallot tetralogy aged over three years represent a challenge because of anatomical and physiological particularities, the primary surgical repair being performed preferably between 6-12 months of life. It is preferable to perform primary or secondary repair, palliative procedures being reserved for extreme forms of hypoplastic pulmonary branches and emergency procedures. Surgical repair at this age can be performed with low mortality and morbidity, with optimal anatomical and functional outcomes and complete social reinsertion.*

Key-words: *Tetralogy of Fallot, "grown up children", repair*

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Rezumat

Obiectiv: *Studiul abordarii chirurgicale la copiii diagnosticați cu Tetralogia Fallot operați în Institutul de Boli Cardiovasculare şi Transplant Târgu Mureş, în funcție de complexitatea malformației şi a condițiilor particulare ale fiecărui pacient.*

Metode: *Studiu retrospectiv pe un lot de 45 de copii (31 băieți şi 14 fete) cu vârsta de peste trei ani, diagnosticati cu tetralogie Fallot, operati în institutul nostru în perioada ianuarie 2005 - februarie 2011. Tipul operației a fost paliativ - şunt sistemico-pulmonar (systemic to pulmonary shunt) - într-un singur caz (2,2%), reconstructia primară completă efectuată la 21 (46,6%) dintre copii, reconstrucția secundară completă la 17 copii (37,7%), înlocuirea valvei pulmonare la 6 copii (13,3%) şi implantare de conduct valvulat ventricul drept – artera pulmonară în 1 caz (2,2%). Urmărirea postoperatorie pe termen scurt si mediu s-a realizat prin examen clinic şi ecocardiografie.*

Rezultate: *Vârsta medie a copiilor în momentul intervenției chirurgicale a fost de 6,8 ani (7,5 pentru băieți şi 6,5 pentru fete), cu o greutate corporala medie de 19,9 kg (19,7 pentru băieți şi 20,5 pentru fete). Mortalitatea perioperatorie a fost de 0% şi la 3 ani 2,22% (un pacient). S-a efectuat intervenție chirurgicală paliativă la un pacient care a prezentat tromboză de şunt, acesta fiind înlocuit cu un şunt cu diametru mai mare în condiții de urgență. Reconstructia primară completă s-a efectuat la pacienți diagnosticați cu tetralogie Fallot, reconstrucțiile secundare fiind realizate la cei care au fost supuşi unui şunt sistemico-pulmonar anterior. Copiii mai mari, cu insuficiență pulmonară postoperatorie severă şi semne de disfuncție ventriculară dreapta, la urmărirea postoperatorie pe termen lung, au fost supuşi intervenției de înlocuire a valvei pulmonare cu proteză biologică.*

Concluzii: *Tratamentul copiilor cu tetralogie Fallot în vârstă de peste trei ani reprezintă o provocare datorită particularităților anatomice si fiziologice, reconstrucția chirurgicală primară fiind realizată de preferință între 6-12 luni de viață. Este de preferat efectuarea reconstructiei primare sau secundare, procedurile paliative fiind rezervate pentru forme extreme de hipoplazie pulmonară şi intervențiilor de urgență. Reconstrucția chirurgicala la această varsta poate fi efectuată cu mortalitate şi morbiditate scăzută, cu rezultate anatomice şi funcționale optime, cu reintegrare socială completă.*

Cuvinte-cheie: *Tetralogia Fallot, "copii în creştere", reparare*

Introduction

65 years have passed since Blalock performed the first systemic-to-pulmonary shunt and 40 years since Barratt-Boyes performed the first repair in tetralogy of Fallot. If during the pioneering period, the surgical attitude of this pathology was to perform the first stage palliative operation (systemic-to-pulmonary shunt) offering the child the opportunity to grow to an age considered optimal for repair, nowadays the surgical approach is to correct this malformation at an early age by primary repair technique.

At the Institute of Cardiovascular Diseases and Transplantation of Targu Mures, the attitude is to repair at the age of 6 to 12 months in all cases diagnosed with tetralogy of Fallot, palliative interventions being reserved for cases with extreme hypoplasia of pulmonary branches, with Z score < -2 and in emergency situations at newborn and small infants with pulmonary atresia or preocclusive stenosis. As pediatric cardiology network is underdeveloped in Romania, children over 3 years of age with tetralogy of

Fallot, with or without a history of palliative surgery, continue to present for diagnosis and treatment. Due to the anatomical-clinical evolution, these patients represent a challenge for surgeons, pediatric cardiologists and anesthesiologists as well. At these children, surgical solution is quite often accompanied by postoperative complications and a longer postoperative evolution compared to patients operated in optimal time.

The surgical techniques were different, adapted to each case for best postoperative results and for a longer distance for reinterventions.

Materials and methods

This is a retrospective study on 45 children over 3 years of age who were diagnosed with tetralogy of Fallot and who underwent surgery during 2005-2011. We have performed primary or secondary repair after a previous palliative or corrective technique in these childrens. In 21 cases (46,6%), primary repair consisted in closing the ventricular septal defect and repairing the pulmonary outflow tract stenosis, which was performed by infundibular muscle resection and outflow tract enlarging plasty with heterologus pericardial patch for preserving the valvular ring at a Z score > -2 or with transanular posterior monovalved patch. The transanular patch was tailored using heterologous pericardium, and posterior valve from Gore-Tex membrane 0.1 mm thick, in triangular shape, sutured at the ventriculotomy level in "sandwich" technique.

The ventricular septal defect was closed in all cases using heterologous pericardium patch, in running suture fashion at a safe distance from the conduction system and aortic valve. Infundibular muscular resection was performed in all cases, knowing that grow up children at this age presents a massive hypertrophy of the muscular bands at the level of the right ventricular outflow tract. Transection was carried out with extreme care to avoid damaging the papillary muscles or the moderator band, but "aggressive" enough to provide the best possible right ventricular outflow tract and to obtain a good right ventricular cavity (Figure 1).

In cases with successful pulmonary valvuloplasty (9 cases, 20%) the right ventricular outflow tract plasty was performed using a patch of heterologous pericardium (Figure 2).

If sparing the pulmonary valve ring was not possible (30 cases, 66.6%), the incision was extended at the pulmonary artery trunk level, transecting the pulmonary annulus, the RVOT reconstruction being performed by using PTFE monovalved heterologus pericardium patch (Figure 3).

Considering that in nine (20%) cases pulmonary artery stenosis (trunk or branches) was associated, the patch was extended at this level.

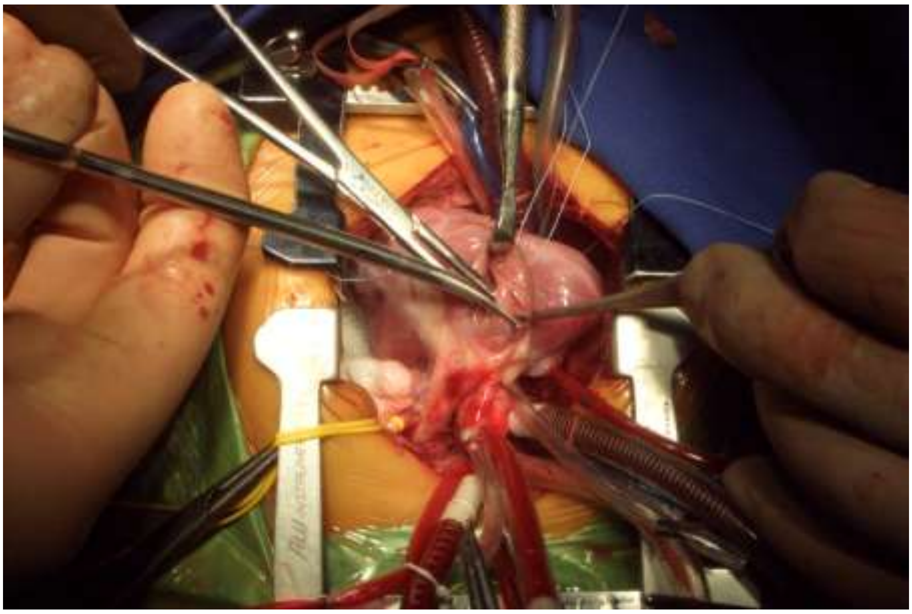

Figure 1

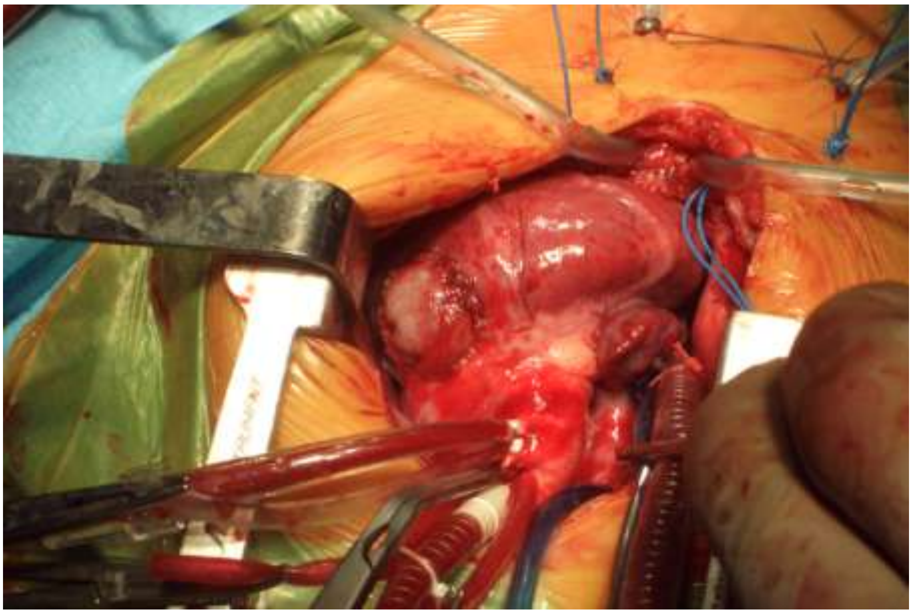

Figure 2

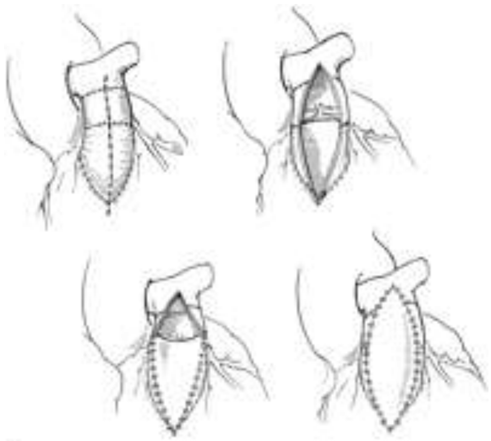

Figure 3

The associated patent ductus arteriosus was ligated in all 6 cases (13.3%). Atrial septal defects associated in (14 cases - 31.1%) cases of our study were primary sutured. Moderate or severe tricuspid insufficiency was corrected by "de Vega" tricuspid valvuloplasty (2 cases - 4.4%) or with flexible ring (1 case - 2.2%). In three cases (6.6%) with atrio-ventricular septal defect we have performed mitral valvuloplasty along with ostium primum type atrial septal defect closure.

In secondary repair, the systemic-to-pulmonary shunt take-down was performed as the first step, cardiac lesions being corrected by the techniques described above.

In one case (2.2%), with severe stenosis of the RV-PA valved conduit at three years, this was replaced with a larger Contegra type conduit. Distal suture of Contegra conduit was made in the first step (Figure 4).

Figure 4.

Figure 5
In the next step, we made the proximal ventrcular suture of Contegra conduit

Final aspect with Contegra conduit in place (Figure 6).

In redo procedures, the surgical risk was increased by the presence of adhesions. In 6 cases (13.3%) with severe pulmonary insufficiency and signs of right ventricle dysfunction at long term follow up, pulmonary valve replacement with bioprosthesis was performed. Bioprosthesis implantation was performed by suturing it in two thirds of the circumference of the pulmonary ring, and one third of the circumference of the heterologous pericardium transannular patch (Figure 7).

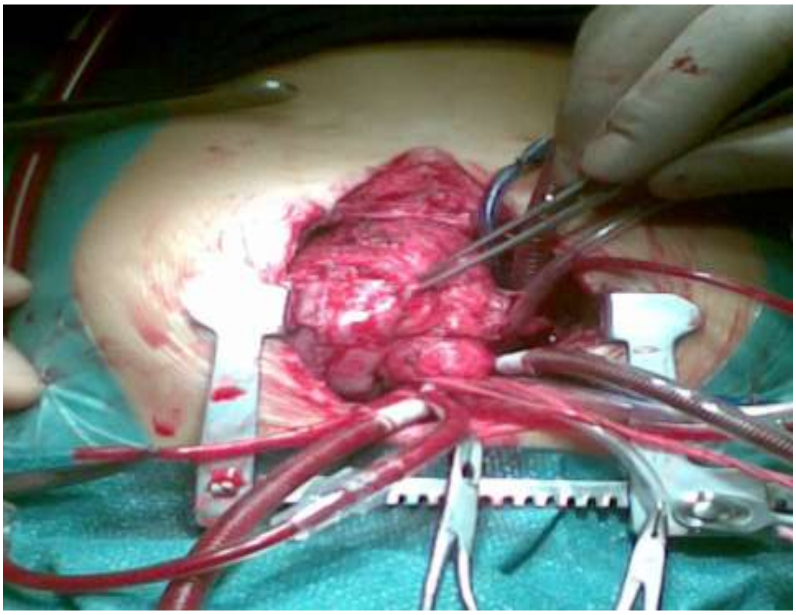

Figure 6

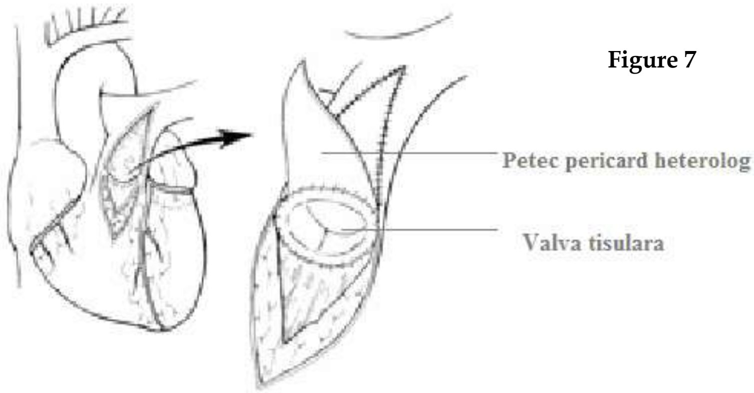

Figure 7

All patients were followed postoperatively every 3 months by echocardiographic method for assessing right ventricular and right ventricle outflow tract morphology and function.

Results

In the period 2005-2011, 45 children aged over 3 years and diagnosed with tetralogy of Fallot were operated in our institute. The number of boys (31-68.8%) was almost double compared to the number of girls (14-31.1%). The age of children was between 3 and 16 years with mean age of 6.82 years (6.51 for boys and 7.55 for girls). The children's weight was between 10.5 and 51 kg, with a mean weight of 19.9 kg (19.7 kg for boys and 20.5 kg for girls). Out of these interventions, 21 (46.6%) were primary repair, 18 (40%)

were secondary repair or other procedures post-primary repair and in one case (2.2%) we have performed a palliative operation.

As an associated cardiac malformation we have encountered Patent Ductus Arteriosus in six cases (13.3%), atrioventricular septal defect in 3 cases (6,6%), atrial septal defect in 14 cases (31.1%), moderate to severe tricuspid insufficiency in three cases (6.6%), and in 9 cases (20%), pulmonary artery trunk or branches stenosis / hypoplasia was found. One (2.2%) patient presented left superior vena cava, which required canulation at the time of procedure.

Among the 16 children who underwent secondary repair, 10 (22.2%) presented a patent shunt and in five (11.1%) the shunt was occluded. In one case (2.2%) we have performed the replacement of right ventricle to pulmonary artery valved conduit for proximal stenosys due to intimal hyperplasia and moderate calcification. The conduit was replaced with a Contegra valved conduit. In 9 cases (20%), pulmonary valvuloplasty and right ventricle outflow tract plasty was corrected using heterologus pericardium patch.

In 30 (66.6%) cases, in which we could not preserve the pulmonary ring, outflow tract enlargement with a PTFE monovalved heterologous pericardium patch was used. In cases (9 cases, 20%) with pulmonary artery (trunk / branches) stenosis or hypoplasia, patch plasty was extended to this level. In 6 children (13.3%) all of them over 8 years of age, with previous total primary or secondary repair, diagnosed with severe pulmonary insufficiency and signs of right ventricle dysfunction at long term follow up, pulmonary valve replacement with bioprosthesis was performed (no.19 in two cases, no.21 in two cases, no.23 in two cases).

In all cases of secondary repair the cell-saver was used. The most common early postoperative complication was bleeding with or without cardiac tamponde in 4 cases (8.8%), all after secondary corrective surgery.

Mean duration of extracorporeal circulation was 107 minutes (range 82 to 197 minutes) and mean aortic cross clamp time was 78 minutes (range 45 to 143 minutes). Duration of extracorporeal circulation was higher by an average of 18 minutes in the secondary repairs comparing with primary repairs and mean aortic cross clamp time was 12 minutes higher in secondary repairs versus primary repairs. The mean time of postoperative mechanical ventilation was 12.3 hours, range from 3 to 39 hours.

Dobutamine, Milrinone and Simdax were used as first choice for inotropic support, associated with Adrenaline, Noradrenaline or Dopamine if necessary, for a mean duration of 5.3 days. Low cardiac output syndrome was present at 24-72 hours in 36 (80%) patients requiring the increase of inotropic support and sustained diuresis. As major complications, two childrens (4.4%) presented late tamponade (which required resternotomy), one case of chilotorax (2.2%) and one case (2.2%) with complete atrioventricular block (which required pacemaker implantation).

There were no perioperative deaths, and at 3 years one death was noted (2.2%). The mean length of stay in ICU was 5.6 days. Mean hospital length of stay time was 12.1 days and post-operative follow-up was performed by clinical and echocardiographic evaluation every 3 months. There was one case (2.2%) with residual ventricular septal defect with trivial left-to-right shunt. In 24 childrens (53.3%) we found a low dynamic stenosis (peak gradient below 25 mmHg) in the right ventricular outflow tract, moderate stenosis (peak gradient 25-50 mmHg) in 13 patients (28.8%) and severe stenosis in one child (2.2%) (Peak gradient over 50 mmHg).

Discussions

If the modified Blalock Taussig shunt was innitial considered to be the the optimal first surgigal step for patients with Tetralogy of Fallot, performing the repair later on, at the age of 3 (Nørgaard et al., 1999), currently majority of the surgeons recommend that the primary repair should be performed early in life, the age of operation decreasing year-by-year. The palliative surgery maintains in some degree a suboptimal clinical status, with hypoxia and cyanosis, with deleterious effects for the child development. Therefore, whereas in some studies the authors recommend primary repair after 6 months (Jonas, 2010) or after the age of 8 months (Van Arsdell et al, 2000), others recommend the primary repair under the age of 6 months (Tamesberger et al, 2008) (Parry et al, 2000) (Kazaa et al, 2009) (Al Habib et al, 2010). The revolutionary attitudes where progressive decline of the age for primary repair is due to increased experience of pediatric surgeons, increased access to knowledge, with access to new medical technology and advancements in better understanding of the newborn physiology, encourage surgical repair in tetralogy of Fallot at the newborn and infant age.In our department, according to our experience and as a result of flattening the learning curve, we believe the optimal age for primary repair of tetralogy of Fallot is 6-12 months, most primary corrections being performed in this period of life. For this reason, primary repair in children over 3 years of age are becoming increasingly rare, most secondary repairs being performed at childrens with palliative surgery performed in the first year of life. Favorable results obtained in primary repair performed within 6-12 months of life encourage us and progressively reduce this type of surgery in children over 3 years. However, the repair (primary or secondary) for tetralogy of Fallot is performed with good results, with extremely low mortality rate and a significant reduction in intra- or postoperative complications.

Conclusions

The best attitude is to repair at the age of 6 to 12 months in all cases diagnosed with tetralogy of Fallot, palliative interventions being reserved for cases with extreme hypoplasia of pulmonary branches, with Z score < -2 and in emergency situations at newborn and small infants with pulmonary atresia or preocclusive stenosis. In children over 3 years, primary or secondary repair after palliative surgery will be in a progressive decline, the current trend being to primarily correct Tetralogy of Fallot in the first year of life. However, these types of interventions can be performed after the age of 3 years in very good conditions and with good survival rates, with significant reduction of complications, providing to little patients a more comfortable life and a low rate of reinterventions.

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Les résultats du traitement chirurgical des atresies pulmonaires a septum ouvert*)

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Abstract

We presents the results of the surgical treatment of the pulmonary atresia with ventricular septal defect on 31 patients operated on at the "Marie Lannelongue Surgical Center", Le Plessis Robinson, France (professor Jean-Yves Neveux), between 1990 and 1999. The principle was to made first a "pulmonary unifocalization" by anastomosing the aorto-pulmonary collaterals with the central pulmonary arteries that are recalibrated or created using vascular conduits. The unifocalizated pulmonary tree is perfused by a subclavian shunt or by a palliative connexion between the right ventricle and the pulmonary trunk. The complete repair was done in a second time by connecting the pulmonary tree with the right ventricle and by closing the ventricular septal defect. We report 22 complete repairs on 31 patients operated for unifocalization. Two patients are waiting for the complete repair, four patients are dead after unifocalization surgery and in three cases the complete repair is not allowed: two cases of thrombosed construction and one case of fixed pulmonary hypertension. We discuss our results in comparisson with other reported series.

Keywords*:* *pulmonary atresia, ventricular septal defect, aorto-pulmonary collaterals, unifocalization*

Introduction

L'*atrésie pulmonaire a septum ouvert* (APSO) est définie par une obstruction complète entre la voie d'éjection du *ventricule droit* (VD) et l'*artère pulmonaire* (AP), associé à une *communication interventriculaire* (CIV) large et une suppléance artérielle pulmonaire d'origine systémique (canal artériel ou collatérales aorto-pulmonaires. L'APSO a été inclue par erreur dans autres catégories dans l'histoire de la chirurgie des cardiopathies

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congénitales: 1949 - truncus arteriosus de type IV (Collet et Edwards); 1968 - Stuckey propose le terme de "VI-ème arc aortique absent"; 1975 – pseudo-truncus (Bharati); 1973 - Macartney utilise le terme de "MAPCA" (*major aorto-pulmonary collatéral artéry*) pour différencier les collatérales aorto-pulmonaires et les artères bronchiques; 1980 - Haworth et Macartney donnent une description détaillée des MAPCA et de la physiologie de la circulation pulmonaire dans les APSO; 1981 - Haworth introduit le concept d'unifocalisation des sources de flux artériel pulmonaire comme une étape préliminaire a la cure complète des APSO. D'après Tchervenkov et Roy [1], l'APSO représente un groupe de cardiopathies congénitales caractérisé par une discontinuité et une absence de flux entre le VD et l'*artère pulmonaire* (AP), dans un cour bi-ventriculaire qui a une CIV. Dans les formes sévères les artères pulmonaires centrales sont partiellement ou complètement absentes [2].

On peut évaluer que les APSO représentent entre 0,5 et 2% des cardiopathies congénitales [3]. Des études génétiques [4] ont démontré que les APSO sont reliées au génotype 22q11 (microdéletion du chromosome 22). Le pronostic des APSO est sombre parce que seulement 30% des patients dépassent une année d'espérance de vie et les patients qui ont une collatéralité aorto-pulmonaire qui leur permet d'atteindre l'age adulte ne dépassent pas l'age de 30 ans [3].

L'anatomie intracardiaque est superposable à la tétralogie de Fallot, caractérisée par un infundibulum du VD sous-développé et un déplacement antérieur et a gauche du septum conal. La voie d'éjection du VD est sténosante et les deux ventricules sont en communication à cause de la CIV. L'origine de l'aorte chevauche la CIV. Les poumons sont vascularisés par le canal artériel perméable ou par des MAPCA qui ont leur origine habituellement dans l'aorte thoracique descendante et plus rarement dans les troncs supra-aortiques ou les artères coronaires. Les MAPCA vascularisent les poumons sous pression systémique et déterminent l'apparition de la maladie occlusive pulmonaire. Les MAPCA peuvent aussi évoluer vers la sténose et l'occlusion rendant donc les territoires pulmonaires inhomogènes en ce qui concerne le régime pressionnel et l'hématose.

L'évolution immédiate après la naissance est dépendante de l'arborisation artérielle pulmonaire et des sources de flux pulmonaire: 1) la forme la plus simple est celle dans laquelle existent des artères pulmonaires centrales qui alimentent un arbre pulmonaire complet; la source est le canal artériel et il n'y a pas de MAPCA. La fermeture du canal artériel est tragique, mais l'administration des prostaglandines a changé le pronostique de ces patients. La réalisation d'une anastomose systemico-pulmonaire type Blalock modifié permet le développement des *artères pulmonaires centrales* (APC) et la réalisation de la cure complète avec connexion VD-AP et fermeture de CIV dans un deuxième temps thérapeutique; 2) dans la forme la plus compliquée, il n'existe pas des APC et les poumons sont vascularisés par les MAPCA. Entre les deux formes extrêmes, il existe une multitude des formes intermédiaires.

Du point de vue embryologique, les plexus vasculaires pulmonaires primitifs seront alimentés dans un premier temps par les artères inter-segmentaires ventrales, branches de l'aorte dorsale. Dans le même temps, la 6-ème paire d'arcs aortiques évolue vers la formation des APC qui vont se connecter avec les extremitées des plexus vasculaires pulmonaires. A ce stade, les artères inter-segmentaires ventrales régressent et à l'age de 60 jours de vie intra-utérine la vascularisation fonctionnelle pulmonaire est assurée entièrement par les APC. Les seules collatérales systémiques sont les artères bronchiques.

L'anomalie embryologique primitive est la septation inadéquate du septum conal avec sténose infundibulaire ce qui provoque une sténose de la voie d'éjection du VD et une atrésie de l'orifice pulmonaire. Le débit des deux ventricules est dirigé préférentiellement vers la IV-ème paire des arcs aortiques (qui donne naissance a la crosse aortique et tronc artériel brachio-céphalique) en défaveur de la VI-ème paire des arcs aortiques qui va involuée et qui donne naissance normalement aux APC [5]. C'est pour cette raison que les poumons restent vascularisés par les artères inter segmentaires ventrales qui se transforment en MAPCA avec origines et distributions variées.

Les APSO sont classifiés [6] en fonction de l'anatomie des APC, les sources de flux pulmonaire et leur distribution.

Le type A - discontinuité VD - AP, absence du tronc pulmonaire, le reste de l'arborisation pulmonaire est normal. Il existe deux sous-types: A1 - bifurcation pulmonaire normale, sans sténose, canal artériel perméable et absence de MAPCA; A2 - il existe une sténose a l'origine de l'AP gauche ou droite.

Le type B - discontinuité VD - AP, absence du tronc pulmonaire, bifurcation pulmonaire hypoplasique ou inexistante; il existe des défauts de vascularisation pulmonaire, des territoires pulmonaires étant vascularisés par les APC et autres territoires par les MAPCA qui peuvent êtres communicants (elles s'anastomosent avec les APC) ou de type terminal.

Le type C - la vascularisation pulmonaire est assurée seulement par les MAPCA, les APC intra péricardiques manquent.

Les premières interventions chirurgicales pour les APSO ont été de type palliatif (des anastomoses systemico-pulmonaires type Blalock modifié ou connexions VD-AP sans fermeture de CIV). L'étude des origines et de révolution des MAPCA a été faite dans les 20 dernières années et a permis la reconstruction de l'arborisation pulmonaire par des interventions d'unifocalisation pulmonaires qui préparent l'arbre pulmonaire à la cure complète. Les principes de la réparation chirurgicale des APSO sont:

1) réalisation d'un arbre pulmonaire le plus près de la normalité, par l'anastomose des sources de flux pulmonaire, donc par l'anastomose des MAPCA aux APC; ce geste s'appelle "*unification pulmonaire*";

2) réalisation d'une source unique d'alimentation pulmonaire par ligature a l'origine des MAPCA et alimentation de l'arbre pulmonaire unifie par une source unique représentée par une anastomose systemico-pulmonaire ou une connexion palliative VD-AP;

3) le remodelage des AP droite et gauche par calibrage des sténoses ou par la création des APC quand elles n'existent pas [8]. Ces trois gestes portent la dénomination "*d'unifocalisation pulmonaire*" (UF).

Dans un deuxième temps on réalise la "cure complète" qui nécessite la connexion du VD a l'arbre pulmonaire unifocalisé et la réparation complète des malformations intracardiaques avec fermeture de la CIV. Les premières séries des APSO ont été traitées d'après une stratégie en plusieurs temps. On réalisait des unifocalisations séparées des deux poumons par thoracotomie postero-laterale et la cure complète par sternotomie médiane était faite dans un troisième temps opératoire. Les résultats des premières séries sont montrés dans le tableau 1 [9, 10, 11, 12, 13, 14, 15].

Tableau 1: Résultats de la cure chirurgicale des APSO. La mortalité globale inclue les décès pendant les opérations préliminaires, entre les opérations et la mortalité précoce après la cure complète. UCLA, University of California, Los Angeles; UCSF, University of California, San Francisco

Auteur (centre)	Stratégie	Nr. patients	Age moyen (ans)	Mortalité globale		Cure complète	
				nr	%	nr.	%
1988, Sullivan (Hospital for Sick Children, London)	multistage	26	2.0	4	15,4	3	11,5
1989, Puga (Mayo Clinic)	multistage	38	4.7	4	10,5	23	60,5
1989, Sawalari (The Heart Institute. Tokyo. Japan)	multistage	34	6.6	4	11,8	10	29,4
1991, Iyer (Royal Children's Hospital, Melbourne)	multistage	58	1,83	7	12,1	30	51,7
1994, Marelli (UCI.A, Los Angeles. California)	multistage	26	2,8		19,2	10	38,5
1996, Yaghihara (National Cardiovascular Center, Osaka. Japan)	multistage	50	5.9	6	12,0	26	52,0
1995, Redy (TJCSF, San Francisco, Callf.)	one stage	10	2,8	0	0	9	90.0
1997, Tchervenkov (Montreal Children's Hospital, Canada)	multiple and single stage	12	0,7	2	16,7	11	91,7
(100,0)	(single stage)	(5)	(0,54)	(0)	(0)	(5)	

Les études rétrospectives sur les séries opérées pour tétralogie de Fallot et APSO montrent d'après Kirklin [16] que la CIV peut être fermée si le rapport prévisible entre les pressions des deux ventricules Pvd/Pvg < 0,85. Le rapport dépend de la résistance des artérioles pulmonaires qui est proportionnelle avec l'age de la cardiopathie, du calibre de l'APC et de l'existence d'une valve sur la voie d'éjection droite.

Plusieurs études statistiques ont essayé d'établir une corrélation entre les diamètres des APC mesurés sur angiographie et le rapport Pvd/Pvg. Le seul index fiable retenu est celui de Nakata [17] qui est le rapport entre la somme des surfaces des APD et APG d'une part et la surface corporelle du patient d'autre part. La valeur normale est de 300 ± 30 mm^2/m^2, les APC hypoplasiques sont définies par une valeur de l'index de Nakata sous 60 mm^2/m^2, et les valeurs moyennes sont entre 120 et 200 mm^2/m^2.

Au niveau de l'arborisation artérielle périphérique on a comme objectif une réimplantation maximale des MAPCA à un jeune age pour diminuer les risques d'hypertension pulmonaire. Ces critères ont été définis dans les dernières années et ont rendu possible le lancement du concept d'unifocalisation et cure complète dans un seul temps, technique dénommée dans la littérature "one stage" pour la différencie de la technique en plusieurs temps, dénommée "multiple stage" [14].

Matériel et Méthodes

Cette étude a été réalisée dans le Service de Chirurgie Cardio-vasculaire et Chirurgie cardiaque pédiatrique du professeur Jean-Yves Neveux, au Centre chirurgical Marie Lannelongue (Le Plessis Robinson, France). C'est une étude rétrospective sur 31 patients avec APSO qui ont été opères dans le service entre 1990 et 1999.

Chaque patient a été exploré par échographie, cathétérisme cardiaque et parfois par angioscanner 3D avec reconstruction tridimensionnelle. Chaque patient a bénéficié d'une injection de repérage dans l'aorte thoracique et les MAPCA ont été cathétérisées sélectivement pour préciser le trajet, le territoire de distribution pulmonaire, l'existence des sténoses et le type terminal ou communicant avec les APC. L'index de Nakata a été calculé pour tous les malades dans le stade initial et après les opérations d'unifocalisation préparatrices pour la cure complète. Tous les montages d'unifocalisation ont été contrôlés par angiographie postopératoire a l'exception des cas traités dans un seul temps opératoire quand le résultat immédiat du montage était apprécié par le rapport *Pvd/Pvg*. L'index de Nakata prévisible a été calculé pour chaque cas en mesurant le diamètre des APC et le diamètre des MAPCA sur le film. L'agrandissement donné par la projection du film a été corrigé en rapportant le diamètre de la sonde de cathétérisme au diamètre réel de la sonde marqué sur le compte rendu de cathétérisme. La formule générale de calcul pour l'index Nakata est: Nakata = $0{,}085 \times (\mathrm{Tfr/Tf})^2 \sum \mathrm{Df}^{\,2}/\mathrm{Sc}$, ou *Tfr* est la taille de la sonde de cathétérisme en french, *Tf* est la taille de la même sonde mesurée sur le film, *Df* est le diamètre mesuré sur le film de l'APD, APG et des MAPCA.

Résultats

Les caractéristiques des 31 patients de l'étude sont montrées dans le tableau suivant. Sur les 31 patients opérés: 22 ont bénéficié de la cure complète; 2 patients sont en attente après plusieurs interventions d'unifocalisation qui ont permis de reconstruire un arbre pulmonaire compatible avec la cure complète; 2 montages d'unifocalisation sont thrombosées et la cure complète est contre indiquée; 1 patient a une hypertension pulmonaire fixe qui contre indique la réparation complète; 4 patients sont décédés après UF.

Un autre patient est décédé le 6-ème jour post réparation complète par choc septique donc la mortalité globale est de 5 cas pour 31 patients, équivalent a 16,12%. Les résultats sont résumes dans le tableau 2.

Parce que notre série est inhomogène, nous présenteront séparément les résultats pour les trois types A, B et C.

Le type A

Il existe seulement deux patients de type "A" dans notre série donc les résultats ne sont pas significatifs pour ce type d'APSO. Les deux cas ont nécessité une anastomose type Blalock a l'age de 1 mois et de 12 ans. Les deux cas sont de type "A1" à cause d'une hypoplasie d'APS. Dans un seul cas était présente une MAPCA qui vascularisait deux segments pulmonaires et qui a été ligature pendant la cure complète. L'index de Nakata était de 140 et de 275 mm^2/m^2. La réparation complète a été réalisée dans les deux cas et le rapport postopératoire *Pvd/Pvg* était de 0,6 et de 0,43. Les deux patients sont asymptomatiques après deux ans de follow-up.

Le type B

Il y a 17 patients de type "B" dans notre série, dont 10 garçons (58,82%) et 7 filles (41,17%). Dans 9 cas (52,94%) une intervention palliative a été effectuée a l'age de 23,44 ± 28,24 mois (extrêmes entre 1 mois et 9 ans); dans la majorité des cas l'intervention palliative a consisté dans la réalisation d'une ou de plusieurs anastomoses type Blalock ou une dilatation de l'AP avec ballonnet a l'age de 1 mois, dans un seul cas.

Tableau 2: Résultats du traitement chirurgical des APSO (*Centre Chirurgical Marie Lannelongue*)

Type APSO		*Âge moyen première intervention palliative (ans)*	*Âge moyen première UF/ou CC (ans)*	*Cure complète*		*Mortalité globale*	
nr	%			**nr**	%	**nr.**	%
2 A	**6,45%**	**6,04 ± 5,95**	**7 ± 5**	**2**	**100,00%**	**0**	**0,00%**
17 B	**54,86%**	**1,95 ± 2,35**	**6,60 ± 4,66**	**14**	**82,35%**	**2**	**11,76%**
12 C	**38,70%**	**2 ± 0,66**	**8,45 ± 6,78**	**6**	**50,00%**	**3**	**25,00%**

Le défaut d'arborisation pulmonaire était bilatéral dans 71,5% des cas (13 patients) et unilatéral dans 23,5% des cas (4 patients). Le nombre des segments pulmonaires dépendant de MAPCA non-communicantes était de 10,05 ± 3,12 par patient. L'index Nakata initial est de 128,37 ± 51,42 mm^2/m^2. Seulement deux patients ont été traités d'après la technique "one stage".

Quinze unifocalisations gauches ont été réalisées par thoracotomie postero-laterale (14 cas) ou sternotomie médiane (1 cas one stage). Les MAPCA ont été réimplantées directement sur APC dans 7 cas, par l'intermédiaire des prothèses en PTFE dans 3 cas et utilisant les deux techniques dans 4 cas. Trois patients ont subi des embolisations postopératoires des MAPCA. Les résultats immédiats après UF gauche sont: évolution simple postopératoire dans 10 cas, 1 cas de thrombose de montage, 1 décès par hypoxie peropératoire et dans un cas le montage a du être refait a cause d'une MAPCA inconnue. Une circulation extracorporelle d'assistance a été nécessaire dans 2 cas.

Quatorze unifocalisation droites ont été réalisées à un age moyen de 6,62 ± 3,62 ans (extrêmes de 1 et de 13 ans). La voie d'abord a été la thoracotomie postero-laterale pour trois patients et la sternotomie médiane pour 1 malade qui a bénéficié de la cure complète dans le même temps. La réimplantation des MAPCA a été directe sur les APC dans 9 cas ou indirecte par l'intermédiaire de la crosse de la veine azygos (1 cas) ou de tube de PTFE (4 cas). La ligature des collatérales a été effectuée dans 4 cas et un patient a subi une embolisation postopératoire d'une MAPCA. La circulation extracorporelle d'assistance fut nécessaire pour 9 patients. L'évolution postopératoire a été favorable pour tous les patients et a distance le segment de la crosse azygos utilisé pour le montage d'UF a développé un anévrysme qui a été réparé pendant la cure complète réalisé par bithoracotomie.

La cure complète a été réalisée chez 14 patients (82,35%). Parmi les trois autres, un est décédé par hypoxie peropératoire, dans un autre cas le montage s'est thrombosé et le dernier patient est en attente de cure complète après deux interventions d'UF. La voie d'abord a été la sternotomie médiane dans 13 cas et la bithoracotomie dans un cas. La base d'implantation au niveau de l'APC a été la bifurcation pulmonaire pour 5 patients, la bifurcation pulmonaire élargie par une plastie dans 5 cas et les APC artificielles (tubes de PTFE) dans 4 cas. La connexion VD-AP fut réalisée avec des tubes valves (valves biologiques) dans 13 cas et dans un cas la connexion a été faite en cousant un patch antérieur associé à une valve de Carpentier. Le rapport moyen *Pvd/Pvg* était de 0,58 ± 0,09.

L'évolution postopératoire immédiate a été marquée par un décès le 6-ème jour postopératoire (choc septique), par 1 cas d'insuffisance tricuspidienne et par 4 cas d'insuffisance aortique modérée. Le follow-up pour les 15 malades qui ont survécu a été fait sur une période de 31,6±16,09 mois/patients avec des extrêmes de 6 et 72 mois. Les résultats sont résumes dans le tableau 3.

Tableau 3:

Patient	*cure complète*	*Résultats immédiats*	*mois Folow-up*	*Résultats à distance*
1	OUI	IA II, CIV résiduelle	12	Sténose LIG, Pvd#36, gradient T# 10
2	OUI	Évolution simple	24	Pvd#50, IT minime
3	OUI	Sténose APD, gradient T#30, IA I, CIV résiduelle	24	Asymptomatique, Pvd#30, Gradient T# 15
4	OUI	IT minime, gradient T#10	0	DCD J6 choc septique
5	OUI	Évolution simple	48	NYIIA II, IA II,
6	OUI	Évolution simple	48	asymptomatique
7	OUI	Gradient T# 16	48	asymptomatique
8	OUI	Évolution simple	36	IT minime, gradient T#33, sténose APG
9	OUI	Gradient T#27, IT et IA minime	48	Gradient T#48, IT II, HTAP#30
10	OUI	IA I, aorte dilatée	72	Anévrysme VD opéré 1 an après cc; actuellement gradient T#35, sténoses résiduelles dilatées
11	OUI	Évolution simple	12	IT I, gradient T#35
12	OUI	Évolution simple	12	asymptomatique
13	OUI	Évolution simple	24	HTAP mais asymptomatique
14	OUI	IA I, gradient T#10	12	asymptomatique
15	NON	Décès post UF par hypoxie		
16	NON	Thrombose UF avec Blalock perméable	6	IITAP fixe, cure complète impossible
17	NON	2 UF á 3 ans intervalle	48	HTAP droite, lit vasculaire non favorable, a réévaluer

IA = *insuffisance aortique*, **IT** = *insuffisance tricuspidienne*, **LIG** = *artère lobaire inférieure gauche*, **gradient T**= *le gradient sur le tube* VD-AP *en* mmHg, **HTAP** = *hypertension pulmonaire*

Les patients de type "B" ont subi un nombre total des 42 interventions (2,47 ± 0,72 interventions/patient). L'efficacité des gestes d'unification et unifocalisation pour la préparation de la cure complète a été de 82,35% et la mortalité globale a été de 11,76%.

Le type C

Il y a 12 patients de type "C" dont 8 garçons (66,66%) et 4 filles (33,3%). Seulement 3 patients ont nécessité une intervention palliative type anastomose Blalock a l'age de 2 ±

0,66 ans. Le défaut d'arborisation pulmonaire était bilatéral dans 11 cas (91,66%) et on retrouve seulement chez un patient un arbre pulmonaire complet a gauche, vascularisé par une MAPCA qui a l'origine dans l'artère sous-clavière gauche.

Pour les 12 patients on a trouve un nombre total de 47 MAPCA avec une distribution moyenne de 3,91 ± 0,77 par patient. Parmi les 47 MAPCA, 42 sont de type terminales (89,36%) donc non-communicantes. Le nombre total de MAPCA non communicantes est de 3,5±1 par patient avec une distribution aux 20 segments pulmonaires, les malades étant de type "C". L'index de Nakata est nul par définition pour ces malades, parce qu'il n'existe pas d'APC.

Onze unifocalisations droites ont été réalisées à un age moyen de 9,31 ± 6,86 ans. La voie d'abord était la thoracotomie posterolaterale dans 8 cas et la sternotomie médiane dans 3 cas quand la cure complète a été réalisée dans le même temps opératoire. Les MAPCA ont été réimplantées directement sur les AP extra-péricardiques ou par l'intermédiaire de la crosse azygos dans 9 cas (81,81%) et dans 2 cas la réimplantation a été indirecte, en utilisant des tubes de PTFE. Une circulation extracorporelle d'assistance a été utilisée dans 7 cas (63,63%). L'évolution postopératoire a été simple pour 7 patients et 3 sont décédés, 1 par hypoxie peropératoire, 1 par hémoptysie et hémothorax et 1 par hémorragie digestive postopératoire.

Neuf unifocalisations gauches ont été faites à un age moyen de 9,06 ± 7,95 ans. Un seul cas a bénéficié de la stratégie "one stage". La voie d'abord était la thoracotomie postero-laterale dans 7 cas (77,77%) et la sternotomie médiane pour les 2 autres patients qui ont bénéficié de la cure complète dans le même temps opératoire. Les unifications pulmonaires ont nécessite des réimplantations indirectes sur des tubes de PTFE dans 8 cas et dans un cas la réimplantation était directe. La source de flux pulmonaire était chaque fois une anastomose type Blalock. L'évolution immédiate a été simple dans 9 cas, un patient a nécessité une antibiothérapie prolongée pour des problèmes pulmonaires et un montage s'est thrombosé sans pouvoir être récupère après trois ans.

La cure complète a été réalisée seulement a 50% des patients de type "C" (6 sur 12). Trois patients sont décédés après UF droite, un est en attente de cure complète après 2 UF et pour deux autres la cure complète est contre indiquée (un cas avec HTAP gauche fixe et chez qui on a réalisé une UF droite palliative pour augmenter la saturation artérielle de l'oxygène et un cas avec thrombose de l'UF gauche).

Les APC ont été reconstruites avec des tubes de PTFE dans tous les 6 cas et les connexions VD-AP ont été réalisées avec des tubes valves ou avec un patch antérieur (1cas). Le rapport *Pvd/Pvg* était de 0,6±0,09. L'évolution immédiate a été marquée par 1 paralysie phrénique et deux cas d'insuffisance tricuspidienne de 1er degré.

Le follow-up a été réalisé pour les 9 survivants. Un des 6 cas qui ont bénéficié de la cure complète a été perdu de vue et pour les 5 autres le follow-up a été effectué sur une période totale de 108 mois (21,6 ± 12,8 mois/patient). Les cinq patients sont asymptomatiques. Parmi eux, deux ont une dilatation de l'aorte ascendante qui est surveillée régulièrement par échographie et un patient a déjà subi une intervention de Bentall a cause de l'évolution anévrysmale de l'aorte. Un autre patient parmi les cinq a subi un traitement antibiotique prolonge a cause des infections pulmonaires a répétition.

Les trois autres patients qui n'ont pas bénéficié de la cure complète ont eu des évolutions simples: un est en attente de la cure complète après 2UF, celui qui a thrombose l'UF a une HTAP qui contre indique la cure complète et celui qui a bénéficié d'une UF palliative pour augmenter la SaO_2 maintien ce gain.

Le nombre moyen des interventions est de 2 ± 0,66 par patient et si le patient qui a bénéficié d'une UF à titre palliatif est exclu, l'efficacité des interventions d'unifocalisation pulmonaires pour la préparation des patients avec APSO de type "C" en vue de la cure complète est de 54,54%.

Conclusions

Le progrès de la chirurgie cardiaque pédiatrique et de la réanimation postopératoire ont permis a environ 70% des patients avec l'APSO d'atteindre l'age adulte avec une bonne qualité de vie. Le seul espoir pour ce type de patients est la cure complète chaque fois que c'est possible.

La définition exacte de l'anatomie intracardiaque et des MAPCA par angiographie et par angioscanner 3D [18] est indispensable pour la prise en charge chirurgicale. La classification du Barbero-Marcial est fiable et facile à utiliser. Les résultats a distance après la cure complète sont dépendants du rapport *Pvd/Pvg* postopératoire qui doit être inférieur a 0,85. Pour cette raison, la cure complète peut être réalisée si l'index de Nakata est supérieur à 200 mm^2/m^2 et si on connecte un minimum de 15 segments pulmonaires. La technique chirurgicale optimale est la réimplantation directe des MAPCA sur APC pour préserver le potentiel de croissance.

Les résultats obtenus avec la stratégie "multiple stage" nous montre que l'avenir du traitement chirurgical dans les APSO est l'UF et la cure complète dans un seul temps opératoire par sternotomie médiane si l'anatomie est favorable, a l'age de 6 mois - 1 an, quand le lit artériel pulmonaire n'est pas encore affecté par la maladie occlusive.

Le type "C" est le plus complexe et les résultats sont marques par une morbidité et une mortalité augmentées.

Le diagnostique prénatal des APSO peut conduire a une prise en charge précoce des patients qui peut améliorer les résultats. Il est nécessaire une surveillance prolongée de ces malades pour mieux connaître l'évolution des matériaux prothétiques utilisés dans les montages d'unifocalisation et aussi l'évolution du lit vasculaire pulmonaire.

Le traitement chirurgical de l'APSO est complexe, extrêmement difficile mais il n'est pas impossible et il nécessite une équipe medico-chirurgicale entraînée dans la prise en charge des cardiopathies congénitales chez les nourrissons et les petits enfants.

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Parameters of the extracorporeal circulation that influence the postoperative need of inotropics in newborns and infants*)

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Abstract

The management of extracorporeal circulation (ECC) at newborns and infants differs substantially from the one at adults. The purpose of the research is to statistically assess the correlation between the postoperative need of inotropics (as evolution markers) and different parameters of extracorporeal circulation.

Material and method: *the study was both prospective and retrospective. 31 newborns and infants operated in our clinic during the period 1991-2004 were included in this study. Age limits were between 11 days and 12 months and patients' weight varied between 3.1 kg and 9 kg. The surgical intervention consisted in the correction of simple cardiac malformations (VSD, ASD) or complex cardiac malformations (Fallot's tetralogy, the transposition of great vessels, common arterial trunk). The following ECC parameters were taken into consideration: the time of myocardial ischemia, the time of extracorporeal circulation, the use of total circulatory arrest, the use of classical or modified ultra-filtration, the use of priming with packed cells obtained through processing in cell-saver, the use of cardioplegia with blood, the cooling temperature during CEC, pO_2 value during CEC, the value of base excess during ECC. The statistical processing of data was done by using the CHI test.*

Results*: there is a statistical correlation between the postoperative need of inotropic and the following parameters: period of ischemia below 90 minutes ($p = 0.041607$), period of ECC over 120 minutes ($p = 0.041607$), the use of priming with packed cells obtained through pro- cessing in cell-saver ($p = 0.0230557$), the use of classical or modified ultra-filtration ($p = 0.0230557$), the use of cardioplegia with blood ($p = 0.0230557$), maintaining the pO_2 below 350 mm Hg ($p = 0.0297428$).*

Conclusion*: the postoperative need of inotropic correlates with certain ECC parameters, and a careful monitoring and correction of these parameters allows the results' improvement.*

Introduction

The management of extracorporeal circulation (ECC) in newborns and infants require special considerations (2). Pediatric patients are exposed to extremes temperatures, including here profound hypothermia (15-20ºC), haemodilution, low perfusion pressure (20-30 mm Hg), variations of the pump flow (from 200 ml/kgc/min to hypothermic circulatory arrest) and a wide margin of the pH, (depending on the correction method alpha-stat or *pH*-stat, or uncontrolled *pH* - after total circulatory stop, when the *pH* can be

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unpredictable and extremely low). These non-physiological parameters alter the self-regulative functions. Apart from these changes, there are other factors that can impede an effective perfusion during extracorporeal circulation, such as: positioning of the cannulas (1, 5, 7), presence of aorto-pulmonary collaterals, age and size of the patients. Starting from the importance of extracorporeal circulation for the newborns and infants, we explored certain parameters which can be correlated with the postoperative evolution of the new-borns and infants.

Material and Method

The study was both prospective and retrospective. During 1991-2004 31 newborn and infants were operated in our clinic in extracorporeal circulations. The age of these patients varied between 11 days and 12 months, and their weight ranged from 3.1 kg to 9 kg. The cardiac pathology included simple congenital heart malformations (ASD, VSD) or complex ones (Fallot's tetralogy, the transposition of great arteries, common arterial trunk). The following parameters of ECC were analyzed: time of myocardial ischemia, time of cardiopulmonary by-pass, use of circulatory arrest, use of classical or modified ultra-filtration, use of priming with packed cells obtained through processing in cell saver, the use of cardioplegia with blood, cooling temperature, pO2 value during ECC, the value of base excess during ECC. The postoperative need for inotropics was used as an indicator of evolution. The statistical processing of data was done by using the CHI test for pairs. The results were expressed by the value of the p parameter (p values < 0.5 meant statistical significance and p values > 0.5 being interpreted no correlation between the parameters).

Results

The results of the study are presented in table system and charts in the situations where there were statistical correlations.

The increased need for inotropics correlated with the duration of ischemia period over 90 minutes. If we modify the landmark ischemia period to 120 minutes, we realize that there is no more statistical correlation between the two parameters (see table).

Another parameter that was studied is durations of ECC.

The extension of ECC period over 150 minutes correlates with the increased need of inotropic, while the ECC limit of 120 minutes is statistically inconclusive.

The use of circulatory stop does not correlate with an increased post-operation need of inotropics. Either the use of ultra-filtration did not influence the post-operation need of inotropics.

Either the use of ***modified ultra-filtration*** (MUF) does not statistically correlate with the need of inotropics, though the statistical data can change on a greater number of cases, the p parameter being close to statistical significance. Taking into account the fact that 12 patients died after the operation, we considered the statistical analysis of the use of MUF on the group of those who survived the intervention - 19 patients - as being useful. The use of MUF reduced the need of inotropics on this group of patients, thus there is a statistical correlation between the use of MUF and the postoperative need of inotropics.

We notice that the two parameters are at the limit of statistical significance. By applying the CHI test on the group of patients that survived the intervention we obtained a statistical correlation between the use of packed cells (self processed) in priming and the need of inotropic - see table 1-11

Table 1: Correlation number of inotropics - period of ischemia

Ischemia				Estimated values		
Inotropics	below 90	over 90	*Total*		below 90	over 90
0	7	0	7	0	6,096774	0,903226
1	11	0	11	1	9,580645	1,419355
2	9	4	13	2	11,32258	1,677419
Total	27	4	31			

p= 0.041607

Table 2: Correlation number of inotropics - period of ischemia over 120 minutes

Ischemia	Estimated values					
Inotropics	below 120	over 120	*Total*		below 120	over 120
0	7	0	7	0	6,322581	0,677419
1	11	0	11	1	9,935484	1,064516
2	10	3	13	2	11,74194	1,258065
Total	28	3	31			

p= 0.1003139

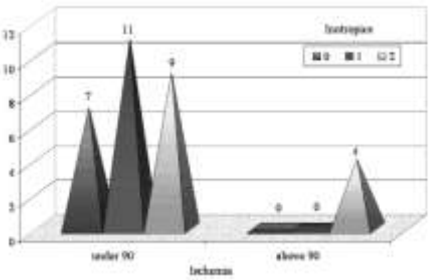

Figure 1: Correlation number of inotropics - period of ischemia (in minutes)

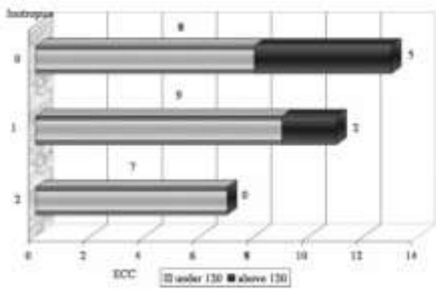

Figure 2: Correlation number of inotropics - period of ECC of 120 minutes

Table 3: Correlation number of inotropics - period of ECC of 120 minutes

ECC — Estimated values

Inotropics	Below 120	over 120	*Total*
0	7	0	7
1	9	2	11
2	8	5	13
Total	24	7	31

	below 120	over 120
0	5,419355	1,580645
1	8,516129	2,483871
2	10,06452	2,935484

p = 0.1327299 - there is no link between the inotropics and a period of ECC of 120 minutes

Table 4: Correlation number of inotropics - CEC of 150 minutes

ECC — Estimated values

Inotropics	below 150	over 150	*Total*
0	7	0	7
1	11	0	11
2	9	4	13
Total	27	4	31

	below 150	over 150
0	6,096774	0,903226
1	9,580645	1,419355
2	11,32258	1,677419

p= 0.041607

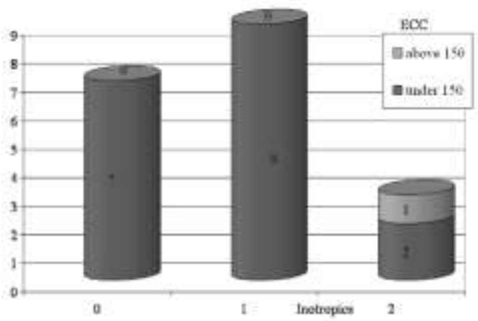

Figure 3: Correlation number of inotropics - ECC of 150 minutes

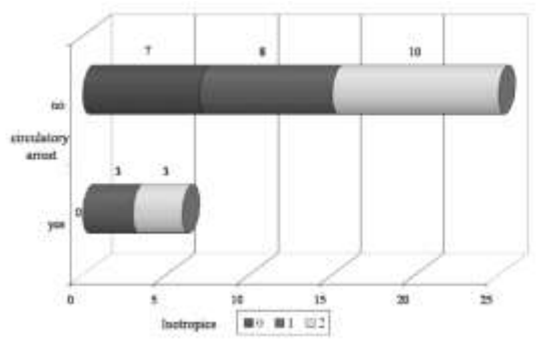

Figure 4: Correlation number of inotropics - use of circulatory arrest

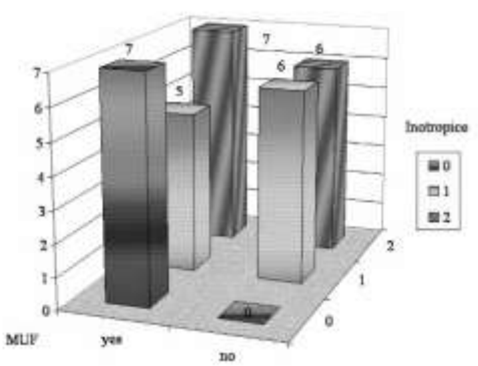

Figure 5:
Correlation number of inotropics - use of MUF

Table 5: Correlation number of inotropics - use of circulatory arrest

Circulatory arrest — Estimated values

Inotropics	Yes	No	Total		Yes	No
0	0	7	7	0	1,354839	5,645161
1	3	8	11	1	2,129032	8,870968
2	3	10	13	2	2,516129	10,48387
Total	6	25	31			

p= 0.3267364

Table 6: Correlation number of inotropics - use of classical ultra-filtration

Ultra-filtration — Estimated values

Inotropics	Yes	No	Total		Yes	No
0	0	7	7	0	0,903226	6,096774
1	2	9	11	1	1,419355	9,580645
2	2	11	13	2	1,677419	11,32258
Total	4	27	31			

p= 0.501328

Table 7: Correlation number of inotropics - use of MUF

MUF — Estimated values

Inotropics	Yes	No	Total		Yes	No
0	7	0	7	0	4,290323	2,709677
1	5	6	11	1	6,741935	4,258065
2	7	6	13	2	7,967742	5,032258
Total	19	12	31			

p= 0.0526711

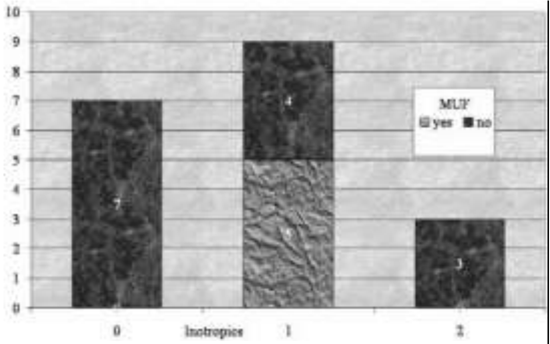

Figure 6: Correlation number of inotropics - use of MUF on patients that survived the surgical intervention

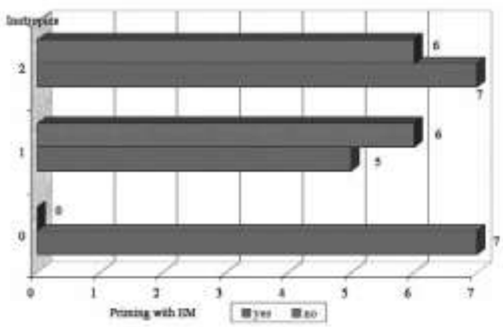

Figure 7: Correlation number of inotropics - the use of priming with packed cells (EM) obtained through cell saver

Table 8: Correlation number of inotropics - use of MUF on patients that survived the surgical intervention

MUF — Estimated values

Inotropics	Yes	No	*Total*		Yes	No
0	7	0	7	0	5,157895	1,842105
1	4	5	9	1	6,631579	2,368421
2	3	0	3	2	2,210526	0,789474
Total	14	5	19			

p= 0.0230557 (statistical signifiance)

Table 9: Correlation number of inotropics - the use of 'priming' with packed cells obtained through processing in cell saver

Priming cu ME — Estimated values

Inotropics	Yes	No	*Total*		Yes	No
0	7	0	7	0	4,290323	2,709677
1	5	6	11	1	6,741935	4,258065
2	7	6	13	2	7,967742	5,032258
Total	19	12	31			

p= 0.0526711

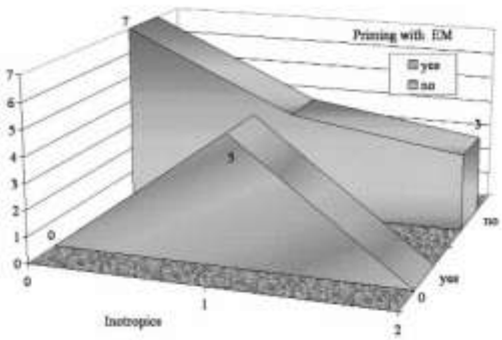

Figure 8: Correlation number of inotropics - the use of EM in priming on the group that survived the intervention

Table 10: Correlation number of inotropics - the use of packed cells (EM) in priming on the group that survived the intervention

Priming with EM — Estimated values

Inotropics	Yes	No	*Total*		Yes	No
0	7	0	7	0	5,157895	1,842105
1	4	5	9	1	6,631579	2,368421
2	3	0	3	2	2,210526	0,789474
Total	14	5	19			

p= 0.0230557

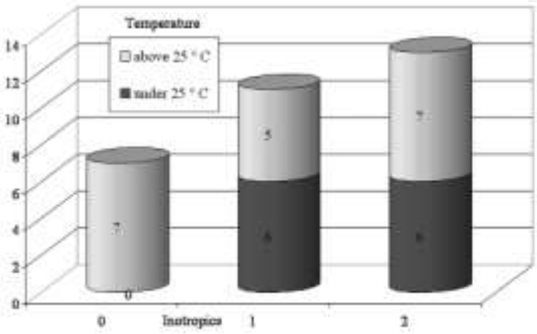

Figure 9: Correlation number of inotropics - cooling temperature during ECC

Table 11: Correlation number of inotropics - the use of cardioplegia with blood

Cardioplegia				Estimated values		
Inotropics	Yes	No	*Total*		Yes	No
0	7	0	7	0	4,064516	2,935484
1	5	6	11	1	6,387097	4,612903
2	6	7	13	2	7,548387	5,451613
Total	18	13	31			

p= 0.0381723

Table 12: Correlation number of inotropics - the use of cardioplegia with blood on the group that survived the intervention

Cardioplegia				Estimated values		
Inotropics	Yes	No	*Total*		Yes	No
0	7	0	7	0	5,157895	1,842105
1	4	5	9	1	6,631579	2,368421
2	3	0	3	2	2,210526	0,789474
Total	14	5	19			

p= 0.0230557

Table 13: Correlation number of inotropics - cooling temperature during ECC

Temperature				Estimated values		
Inotropics	below 25°	over 25°	*Total*		below 25°	over 25°
0	0	7	7	0	2,709677	4,290323
1	6	5	11	1	4,258065	6,741935
2	6	7	13	2	5,032258	7,967742
Total	12	19	31			

p= 0.0526711 (no statistical signifiance)

The group of patients with blood cardioplegia showed a reduced use of inotropics afther the operations. This correlation maintains also in the statistical analysis of the need of inotropic in the group of patients that survived the intervention (see table 14).

Table 14: Correlation number of inotropics – cooling temperature during ECC on the group of patients that survived the intervention

Temperature				Estimated values		
Inotropics	below 25°	over 25°	*Total*		below 25°	over 25°
0	0	7	7	0	1,842105	5,157895
1	5	4	9	1	2,368421	6,631579
2	0	3	3	2	0,789474	2,210526
Total	5	14	19			

p= 0.0230557

Lower temperatures during ECC (or total circulatory arrest) did not correlate with an increased need of inotropic (*p* being above the limit of statistical significance).

There is a clear correlation between the need of inotropic and profound hypothermia on the group of patients that survived the intervention.

Table 15: Correlation number of inotropics - average values of pO2 during ECC

Average O_2				Estimated values		
Inotropics	below 350	over 350	*Total*		below 350	over 350
0	2	5	7	0	3,612903	3,387097
1	8	3	11	1	5,677419	5,322581
2	6	7	13	2	6,709677	6,290323
Total	16	15	31			

p= 0.1647329

Table 16: Correlation number of inotropics - average values of pO2 during ECC on patients that survived the intervention

Average O_2				Estimated values		
Inotropics	below 350	over 350	*Total*		below 350	over 350
0	2	5	7	0	3,315789	3,684211
1	7	2	9	1	4,263158	4,736842
2	0	3	3	2	1,421053	1,578947
Total	9	10	19			

p= 0.0297428

Table 17: Correlation number of inotropics - base deficit value during ECC

DB

Inotropics	below -2	over -2	*Total*
0	4	3	7
1	7	4	11
2	9	4	13
Total	20	11	31

p= 0.862355

Estimated values

	below -2	over -2
0	4,516129	2,483871
1	7,096774	3,903226
2	8,387097	4,612903

The need of inotropic did not correlate with the average value of *p*O2 during ECC. Excluding the cases who died, we obtain a positive correlation between the two parameters (*p*O2 above 350 mm Hg. correlate with increased need of inotropics).

The need of inotropic did not correlate with the decrease of base deficit below - 2 during extracorporeal circulation. The same result is obtained as well if we make the analysis only on the group of patients that survived the intervention.

Table 18: Correlation number of inotropics - base deficit value during CEC on patients that survived the intervention

DB

Inotropics	below -2	over -2	*Total*
0	4	3	7
1	7	2	9
2	1	2	3
Total	12	7	19

p= 0.3530328

Estimated values

	below -2	over -2
0	4,421053	2,578947
1	5,684211	3,315789
2	1,894737	1,105263

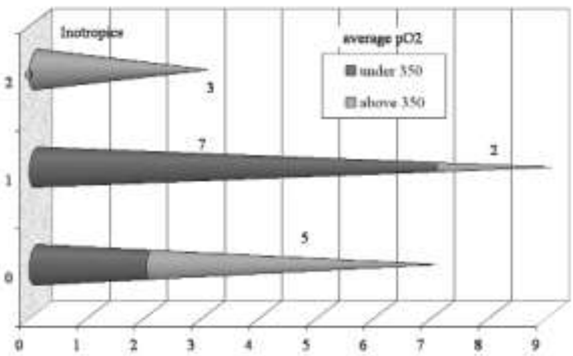

Figure 10: Correlation number of inotropics - average values of pO2 during ECC on patients that survived the intervention

Discussions

One of the main tasks of the present study was to identify the longest period of myocardial ischemia tolerated. In order to do that, within the studied cases we analyzed statistically the association of the aortic clamping period and the post-operation need of inotropics. Aortic clamping periods of 90 and 120 minutes were established as landmarks, since these periods are mentioned in literature (9). We obtained a statistical correlation between the need of inotropic and the period of aortic clamping below 90 minutes. This correlation does not exist in the case of 120 minutes ischemia. Based on these results we can conclude that in this group, the safe aortic clamping period is the one of 90 minutes. The increase of myocardial ischemia period over the 90 minutes results in an increased need of inotropic, no matter what kind of correction is applied.

The same correlation was established between the need of inotropic and the period of extracorporeal circulation. There is no statistical correlation between the need of inotropics and the 120 minutes period of extracorporeal circulation. On the contrary, the increase of extracorporeal circulation period over 150 minutes statistically correlates with an increased need of inotropic. Thus, we can conclude that the safe period of extracorporeal circulation in this group was from 120 to 150 minutes. Over 150 minutes of ECC has negative effect in postoperative evolution.

The introduction of classical and modified ultra-filtration represented an important moment in the reduction of tissular oedema and myocardial depression post extracorporeal circulation (4, 11, 13). Considering the fact that the analytical data is negatively influenced by the cases that died postoperatively (cases that needed high doses of inotropic), these cases were excluded from the study. The statistical analysis concerned only the correlation between the need of inotropic and the use of classical or modified ultra-filtration on the group that survived the post-operation period. A statistical correlation was obtained, thus, in this group, the use of classical or modified ultra-filtration is related with the reduction of inotropic need.

The literature recommends for the preparation of priming the use of packed cells obtained through processing the homologue blood in cell-saver (10). The processing of blood in cell-saver eliminates blood elements with a role in the inflammatory response: leucocytes and trombocytes. This is the reason why the reduction in using whole blood products remains desirable among the methods of reducing inflammatory response. We have analyzed in our study the measure of influence of the use of packed cells from cell-saver upon the evolution. The two parameters are at the limit of statistical correlation if we analyze the open heart surgery cases. If we analyse only the cases involving patients that survived the surgical intervention, we obtain a clear statistical correlation between the use of packed cells processed in cell-saver and the postoperative more reduced number of inotropics.

Crystalloid cardioplegia was used in surgical interventions performed during 80-90's. Cardioplegia with blood was used during the last part of our study, in the majority of the cases the blood being taken from the oxygenator reservoir. By analyzing the correlation with the number of inotropics we notice that there is a link between the use of cardioplegia with blood and a more reduced number of postoperative inotropics, both for the cases of open heart surgery and of patients that survived the intervention. This is in agreement with the data provided by specialized literature (3, 6, 8, 12), but we have to mention that the evolution of the patients with short time of myocardial ischemia during the correction of simple cardiac malformations is influenced less by the type of cardioplegia (crystalloid or with blood).

At a certain moment during the evolution of pediatric cardiac surgery the use of profound hypothermia and the use of total circulatory arrest were recommended. The advantages were considered to be the more reduced tissular inflammatory reaction with a more reduced isolation of volume in the third space, apart from a higher surgical comfort given by the absence of cannulae within a surgical field with reduced dimensions. During the last period of time there is an emphasis on the use of continuous extracorporeal circulation techniques, giving up the excessive cooling of the patients, which involves uncontrollable reactions during re-warming period. Through analysis of the cases of patients that survived the intervention, we have obtained a statistical correlation between the use of total circulatory arrest and a more increased need of inotropic for these patients.

The maintaining of *p*O2 levels that do not exceeded 400 mm Hg during extracorporeal circulation is generally recommended. Excessive oxygenation of blood inside the circuit of heart-lung machine produces negative reactions because it generates in excess free oxygen radicals, followed by the specific metabolic cascade. In the studied cases we established a statistical correlation between the increased need of oxygen and the exceeding of 350 mm Hg level of *p*O2.

There is still a controversy in the specialized literature on the use of a certain type of management of the metabolic status during CEC: alpha-stat or pH-stat (correction or non-correction of bases deficit during hypothermia). The attitude that we consider as being optimal is the one of the alpha-stat management, with the mention that, for short periods of time, we apply a pH-stat management during the re-warming period in the case of medium or profound hypothermia because this has a cerebral vasodilatory effect that allows (at least in theory) a more uniform cerebral re-warming and the disappearance of thermo gradients. In the cases we studied we did not succeed in establishing a statistical correlation between the maintaining of bases deficit within normal limits and a lower need of inotropic.

Conclusions

1. Over 90 minutes of myocardial ischemia statistically correlates with an increased need of inotropic;
2. Limitation of extracorporeal circulation period to 120-150 minutes correlates with a more reduced postoperative need of inotropic;
3. Use of priming with packed cells processed in cell-saver, the use of cardioplegia with blood and the use of classical or modified ultra-filtration reduce the postoperative need of inotropics;
4. Maintaining *p*O2 below 350 during CEC correlates with a more reduced postoperative need of inotropics
5. Use of continuous perfusion techniques and of the low flow is preferred to the use of total circulatory stop with profound hypothermia;
6. The alfa-stat or *pH*-stat management does not influence the postoperative need of inotropic;

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Ultrafiltration in pediatric cardiac surgery*)

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Cardiopulmonary bypass (CPB) induces an inflammatory response in the whole body, which in the uncomplicated cases manifests as a temporary reaction of tissues and organs to aggression, also known as the post-perfusion syndrome. The patient's young age, long time of the ECC, extreme values of hypothermia and hemodilution represent risk factors that may increase the severity of the post-ECC syndrome.

The CPB techniques have improved constantly and lowered postoperative morbidity and mortality rates in congenital heart surgery even in the newborn. However, the inflammatory systemic response associated with the increase of total water after CPB determines organ dysfunctions especially at the level of the heart, lungs and central nervous system that may complicate, sometimes severely, the postoperative evolution. The clinical manifestations of the post-perfusion syndrome include cardiac, respiratory, renal, hepatic and neurological dysfunctions, coagulation disturbances and in severe case even multiple organ failure.

The most important mediators of the inflammatory systemic response are the proinflammatory cytokines TNEalpha, ILlbeta, IL6 and IL8, whose blood concentration increases after CPB. As a contra reaction to the increase of proinflammatory cytokines, the antiinflammatory cytokines will increase. In children, unlike in adults, the post-bypass response of cytokines is less clear and studied.

One certain fact is that the balance between the proinflammatory and antiinflammatory cytokines determines the extent of the tissular lesions and the postoperative outcome. The biochemical markers of the tissular lesions are the organ-specific enzymes of tissular cytolysis.

Chew et al., from the Aarhus University, Denmark, in a well documented descriptive studyl concerning the post-perfusion inflammatory reactions and their tissular response in pediatric patients, have demonstrated that:

- the proinflammatory cytokines behave differently:

  • TNFalpha increases post-ECC by about 4-5 times then decreases progressively in the first 24 hours without reaching the preoperative level, to increase again significantly in the next 24 hours.

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• IL_1beta increases more than 1000 times post-ECC then decreases progressively in the next 48 hours.

• IL_6 increases about twice post-ECC and continues to increase to about 5 times within the next 48 hours.

- Antiinflammatory cytokines have similar patterns:

• IL-1ra increases post-ECC almost 1000 times, decreases within the first 24 hours, then increases again at 48 hours.

• IL-10 increases significantly postECC, then decreases progressively to normal in the next 48 hours.

- The post-perfusion syndrome also involves coagulation disturbances 1:

• Prothrombin fragments 1+2 increase post-ECC about 6 times then decrease, but after 48 hours they are still 2-3 times higher than normal.

• Antithrombin 3 are halved post-ECC and increases to normal within 48 hours.

- The tissular response, assessed through the biochemical markers, becomes significant not immediately after ECC but after the first 6 hours (1):

• ALAT, gammaGT, CK and LDH reach maximum values at 6 hours then CK and LDH decrease or remain constant while gammaGT and ALAT increase (in uncomplicated cases).

• Amylases reach a peak after 24 hours and return to normal very slowly.

Tissular oedema, due both to the capillary leak produced by the inflammatory syndrome and the dilution of the plasma proteins due to the ECC priming, is responsible for the multiorgan dysfunction. Maehara et al. have demonstrated using bioelectrical impedance that total water increases after CPB in pediatric patients by 11-18% as compared to the pre-bypass level (2).

Various methods have been attempted to reduce the post-perfusion syndrome and tissular oedema: cortisone, aprotinine, peritoneal dialysis, aggressive diuretic therapy, ultrafiltration. Ultrafiltration is a convective process at the membrane level, by which the substances with a molecular mass smaller than the membrane pores are filtered due to the transmembrane gradient. This technique, initiated during the rewarming phase of the CPB, also called conventional ultrafiltration (CUF), is used in order to minimize the level of total water and the post-perfusion oedema. The volume of the ultrafiltrate is limited by the volume of the venous reservoir, because the priming is extremely low especially in the newborn, therefore the volume of ultrafiltrate is also limited.

Taking into account the limited capacity of (CUF) to drain excess fluid and counteract hemodilution, Naik, Knight and Eliott introduced in 1991 an ultrafiltration technique after the discontinuation of CPB which they called modified ultrafiltration (MUF) (3, 4). In a preliminary study they compared the total water volume after CPB in the absence of ultrafiltration, with CUF and with MUF. The volume of fluid evacuated by modified ultrafiltration was significantly higher, while total body water was much less increased. In another study (5) performed in children, they reported that after MUF blood loss was lower and arterial pressure increased surprisingly. The authors (6) demonstrated that MUF improved all hemodynamic parameters: cardiac index was increased, pulmonary vascular resistence was lower in conditions in which systemic vascular resistance remained unchanged. Consequently the postoperative requirements of inotrope decreased significantly. These results were directly correlated with the degree of blood concentration.

The interest in this technique has increased while several research teams have investigated its various aspects. Studies performed at the Great Ormond Street Hospital for Children in London (7, 8) have shown that in children with MUF the hemodynamic parameters improved through the decrease of the myocardial oedema and improvement of heart contractility. Ultrasonography also evidenced the decrease in size of the left ventricle (LV) posterior wall, fractional decrease of the LV and reduction of end diastolic pressure of the LV.

The increase of the arterial pressure after MUF raised the suspicion that anesthetic drugs were also filtered with the fluid. Elliott measured the serum level of fentanyl, which remained efficiently increased during the whole ultrafiltration period (9). It is therefore improbable that superficial anesthesia should be the cause of hemodynamic improvement, even less as following ultrafiltration the cardiac frequency and systemic vascular resistance remain unchanged.

Another advantage of MUF is the reduction of the pulmonary interstitial oedema followed by the improvement of pulmonary compliance and decrease of insufflation's pressures (10). Ko Bando et al. have found the endothelin-1 (substance responsible for the increase of the pressure in the pulmonary vessels) concentration to be decreased in children after conventional and modified ultrafiltration (11). At the same time, they have evidenced in these children a decrease of the ratio between pulmonary and system vascular resistances. They consider aggressive ultrafiltration, both modified and conventional, to be an important additional method of preventing early pulmonary hypertension crises after open heart operations in children at high risk. Following the improvement of the pulmonary function, the mechanical ventilation time also decreases (11, 12). In children with cavo-pulmonary anastomoses postoperative pleural drainage decreases significantly (13).

CPB is also associated with an increased level of serum endotoxins, by translocation, both in adults and children, following splanchnic hypoperfusion and then reperfusion. Clinically the increase of circulating endotoxins may cause hypotension, fever, hypermetabolism, coagulation diseases (14). Stig Yndgaard et al. found that circulating endotoxins decreased significantly following modified ultrafiltration in children operated with CPB (14).

Attention has lately focused on the effects of CPB and hypothermia, with or without circulatory arrest, on the central nervous system. A recent experimental study has evidenced that modified ultrafiltration improved brain recovery after the metabolic distress due to deep hypothermia with circulatory arrest (15). The mechanisms supposed to be responsible include the decrease of cerebral oedema, elimination of the vasoactive substances and proinflammatory mediators.

In the initial model proposed by Naik et al. (3, 4, 5) the modified ultrafiltration is performed arterio-venously: after discontinuation of CPB the blood is removed from the aorta, passed through a hemofilter and reintroduced in the right atrium. At the same time the blood from the venous reservoir is also passed through the filter, concentrated and then introduced in the right atrium. In this way, MUF has the capacity to eliminate excess water from the patient's body and concentrate all the blood from the venous reservoir which is then retransfused. Modified ultrafiltration is performed until the circuit is empty or the patient's hematocrit reaches 40%. Subsequent studies were performed with veno-venous ultrafiltration (16). The blood from the right atrium is filtered simultaneously with the blood in the venous reservoir and then reinfused into the right atrium. No comparative studies of the two techniques have been reported. Journois et al. (17) have reported a modified technique of conventional ultrafiltration which they named zero-balanced ultrafiltration. During rewarming, ultrafiltration is continuous, the volume of the venous pool being maintained by adding crystalloids. After the discontinuation of the CPB the blood concentration is achieved by MUF.

At first it was believed that MUF was beneficial only because of the reduction of total body water and tissular oedema. The examination of the ultrafiltrate composition showed increased concentration of vasoactive substances and proinflammatory mediators, in both CUF and MUF (17, 18, 19). One of the benefits of conventional or zero-balanced ultrafiltration is the fact that circulating mediators are removed at an early stage, at the beginning of the inflammatory cascade (20). Daggett et al. (21) have demonstrated in an experimental study that the readministration of the ultrafiltrate in the newborn piglets leads to the alteration of the heart function. This indicates that ultrafiltration removes toxic substances. The positive effects of modified ultrafiltration seem to be directly correlated with the amount of ultrafiltrate. The concentration and composition of mediators in the ultrafiltrate do not differ between conventional and modified ultrafiltration. MUF is more efficient than the CUF, due to the higher volume of the ultrafiltrate.

Worries regarding the possible complications of this technique are purely theoretical. Initially it was believed that MUF may cause hemodynamic instability by the removal of blood from the aorta. A multicenter study performed in 22 centers did not report any morbidity or mortality correlated with modified ultrafiltration (22).

In the *Cardiovascular Surgical Clinic of the Cluj Heart Institute* we have been using for more than three years now conventional and modified arteriovenous ultrafiltration in all the pediatric patients under 20 kg body weight. CUF starts during rewarming at 28°C and the modified one 10-12 minutes after the discontinuation of CPB, in conditions of hemodynamic stability, until the complete emptying of the lines. The blood coming out of the aorta together with the venous blood and are joined in a common line where, after passing through the filter, is warmed at 37°C and administered into the right atrium. No complications have been recorded with this technique.

Since modified ultrafiltration was introduced in 1991 it has been successfully used with well documented benefits. The conclusion is that CUF and MUF are not competitive techniques but rather complementing one another. Optimal results are obtained by the combined use of the two techniques in children operated with CPB (23). Further studies are required in order to identify the mechanisms responsible for the positive effects of ultrafiltration and the type of patients that would benefit the most from the method. Both techniques, conventional and modified ultrafiltration, are safe and free of complications.

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Part 3.

HEART TRANSPLANT PATHOLOGY

Les disponibilités d'organes pour le transplant cardiaque en utilisant des listes alternatives

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Rezumat

În momentul de față, transplantul cardiac reprezintă o metodă acceptată de tratament pentru insuficiența caridacă terminală, având o supraviețuire foarte bună, supraviețuire care depăşeşte în multe centre 85% la un an. Din păcate, însă, disponibilitatea grefelor cardiace este foarte limitată. Mai mult, în ultimii ani s-a constatat o scădere a numărului de grefe cardiace disponibile pentru transplant. Această disponibilitate insuficientă implică desigur o problematică particulară: problematica selecției primitorului şi selecția cordurilor disponibile pentru a fi folosite ca grefă de cord [selecția donatorului]. În lumina acestor realități, organizarea unui program de transplant cardiac are de rezolvat cel puțin trei categorii de probleme:

a) performanța centrului în care se realizează transplantul cardiac;
b) selecția adecvată a primitorului şi
c) selecția adecvată din pool-ul de organe disponibile a donatorilor.

În plus, s-a acceptat conceptul de „liste alternative" pentru pacienții cu risc crescut sau pentru pacienții mai vârstnici. Acestor pacienți li se vor aloca corduri considerate „la limită". În momentul de față, aproximativ 40% din cordurile disponibile pentru transplantul de cord nu sunt utilizate, datorită faptului că sunt considerate „non-standard", însă utilizarea unei liste alternative creşte numărul de grefe cardiace şi accesul la transplant fără să compromită şansa de transplant a pacienților standard cu risc scăzut şi mai tineri.

Xenotransplantul, suportul cardiac mecanic permanent, terapiile medicale noi, stimularea biventriculară, transplantul celular şi terapia genică sunt soluții potențiale pentru penuria actuală de inimi pentru transplant.

Cuvinte-cheie: *transplant cardiac, selecție adecvata primitor / donator, liste alternative, suporturi mecanice cardiace*

A présent le transplant cardiaque représente une méthode de traitement acceptée pour l'insuffisance cardiaque terminale, ayant une très bonne survie, survie qui dépasse chaque année le pourcent de 85%, dans beaucoup de centres. Mais, malheureusement, la disponibilité de greffes cardiaques est très limitée. De plus, les dernières années on a constaté une décroissance du nombre des greffes cardiaques disponibles pour le transplant. Cette disponibilité réduite implique certainement un problème à part: celui de la sélection du receveur et de la sélection des coeurs disponibles afin qu'ils soient utilisés comme greffes de coeur (la sélection du donneur).

En principe, tout patient dont la maladie cardiaque est correctement et maximalement traitée et dont la survie estimée est moindre que celle offerte par un transplant cardiaque peut en bénéficier. Malheureusement, le nombre des patients s'intégrant à cette catégorie est de beaucoup plus grand. Au cas ou tous ces patients auraient été inscrits sur la liste de transplant, les temps d'attente jusqu'au transplant seraient trop longs et par conséquent la mortalité parmi les patients inscrits serait inacceptable. Il en résulte la nécessité de choisir seuls les patients ayant la plus grande probabilité de survie et de réhabilitation postopératoire. Les progrès enregistrés par la technique chirurgicale, mais aussi par la thérapie immunosuppressive ont déterminé que de plus en plus patients s'inscrivent dans ces demandes mêmes très strictes de survie et de réintégration postopératoire, rendant plus difficile le processus de sélection et surmontant la pénurie d'organes. Voilà donc que l'organisation d'un programme de transplant cardiaque a à résoudre, dans la lumière des choses ci-haut présentées, trois catégories de problèmes au moins:la performance des centres ou le transplant cardiaque est réalisé, la sélection adéquate des receveurs et la sélection dans la mare d'organes disponibles de ceux qui seront utlisés pour le transplant. Le problème des couts et de l'appui du programme de transplant par un certain système sanitaire ne constituent pas l'objet de ce travail.

Dès 1984, aux États Unis d'Amérique ont été établies sous la forme de "*The National Organ Transplantation Act*" (l'acte national concernant le transplant d'organes) une série d'exigences que les centres qui réalisent le transplant cardiaque doivent accomplir. Afin d'encourager l'assistance excellente des patients et de décourager les centres dont les résultats ne sont pas optimaux, on a établit que seuls les centres qui effectuent au moins 12 interventions de transplant cardiaque annuellement et obtiennent une survie de plus de 70% après une année, peuvent bénéficier des organes offerts par le réseau de prélèvement et de distribution des greffes d'organes (*United Network of Organ Sharing*). Outre cela, le centre respectif doit disposer de facilités et de personnel qui correspondent aux normes rigoureuses et doit être un membre actif d'une organisation locale de prélèvement d'organes pour le transplant. Le personnel médical (chirurgiens et autres spécialistes) doit aussi accomplir une série de critères de performance et d'expérience.

Un problème extrêmement controversé est celui de la sélection des candidats pour le transplant cardiaque. Au moment présent il n'y a pas de critères précis qui établissent une indication pour le transplant cardiaque. Tout patient qui souffre d'une maladie cardiaque terminale qui détermine une symptomatologie significative et un espoir de vie inférieur à celui offert par le transplant cardiaque pourrait être inscrit sur la liste de transplant. Chez ces patients les procédés chirurgicaux alternatifs doivent s'avérer irréels (respectivement, impossibles à être appliqués). D'autre part, ces patients ne doivent pas présenter des affections extracardiaques qui altèrent le pronostic après le transplant et doivent faire preuve d'un psychique et d'une motivation qui assurent l'adoption d'une manière de vie active doublée d'une bonne compliance aux régimes thérapeutiques indiqués. Par malheur, le nombre des patients qui s'inscrivent dans ces critères est de beaucoup plus grand que celui des greffes de coeur qui peuvent être utilisées. Pour cette raison on a du établir une série de nouveaux règlements d'exclusion et de priorité.

Tableau no. 1. Priorité pour le transplant conformément à l'UNOS

Status I (priorité maximale). Les patients qui nécessitent une assistance cardiaque et/ou pulmonaire avec une/un des suivants:

- coeur artificiel total
- système d'assistance du VG ou du VD
- ballon de contrepulsation intra-aortique
- ventilateur mécanique
- Patients qui accomplissent les deux suivants critères:
    - patients admis dans le service de thérapie intensive
    - patients qui nécessitent des agents inotropes pour le maintien d'un débit cardiaque adéquat

Status II - tous les autres patients admis sur la liste de transplant.

L'un des critères d'exclusion peut être l'âge des patients. Nombre de centres n'acceptent pas pour le transplant des patients au dessus de 55 ans. La raison de l'introduction de ce règlement paraît très simple: pratiquement dans toutes les interventions chirurgicales cardiaques l'âge avancé est un facteur de risque pour une évolution postopératoire défavorable. C'est pour cela que le nombre limité des greffes cardiaques doit être orienté vers les receveurs ayant des perspectives des plus favorables, donc non pas vers les patients âgés. Ce point de vue soulève toute une série de problèmes.

La croissance de l'espoir de vie dans le monde civilisé rencontrée les dernières décennies (croissance relativement constante les 50 dernières années) a déterminé que le segment d'âge de plus de 70 ans soit le segment de la population avec la plus grande croissance parmi les segments populationnels occidentaux. Ainsi, en 1990, aux Etats-Unis d'Amérique l'espoir moyen de vie était de 75,6 ans et on estime une croissance de celui ci. Généralement, l'individu qui atteint à présent 65 ans a un espoir de vie de plus de 15 ans. Cette tendance des changements démographiques est aussi réfléchie dans le domaine de la chirurgie cardiaque. Les patients âgés représentent un pourcent de plus en plus élevé parmi les patients opérés à coeur et ils sont soumis à des opérations d'une complexité de plus en plus grande. Parallèlement, le transplant cardiaque a atteint une performance remarquable.

Les données du registre de la Société Internationale pour le Transplant de Coeur et de Poumon (ISHLT) indiquent vraiment le fait que l'âge avancé représente un facteur de pronostic défavorable pour l'évolution après le transplant. Donc, il y a des arguments qui suggèrent un taux plus grand d'infections et de néoplasies malignes après le transplant, une récupération fonctionnelle faible, une durée de l'hospitalisation plus grande et des coûts plus grands chez les patients âgés. La détermination d'un âge limite qui sépare le groupe à bas risque du groupe à risque élevé est difficile et arbitraire. Dans différents centres il est établi à 50, 55, 60 ou 65 ans.

Conformément aux données du registre ci haut cité, l'âge avancé représente en ensemble un facteur prédictif pour une mortalité accrue tant après un an qu'après 5 ans depuis le transplant. De plus, les facteurs de risque connus avoir de l'influence sur la mortalité après un an depuis l'intervention persistent encore après 5 ans en leur grande majorité. Néanmoins, ces données doivent être analysées dans un contexte correct du point de vue statistique, considérant la grande variabilité concernant la sélection des donneurs et des receveurs dans différents centres. Ainsi, il y a sans conteste la possibilité que toute une série de différences entre les receveurs (il s'agit particulièrement de différences sur la présence de divers facteurs de pronostic) ne soient pas prises en considération lorsqu'on fait la collection des données pour l'analyse statistique.

Une série d'études ont montré que le transplant cardiaque chez les personnes âgées (au dessus de 55 ou plus de 65 ans) peut être réalisé avec succès, respectivement avec une mortalité et une morbidité comparables avec celles observées chez les patients plus jeunes et avec une survie excellente à long terme. Ces études ont souligné que l'âge en lui-même n'est pas nécessairement un facteur de risque pour le décès et qu'il n'est pas obligatoire qu'il soit considéré une contre-indication pour le transplant cardiaque. Dans la lumière de ces études, beaucoup de centres ont admis dans le programme de transplant des personnes de plus en plus âgées. L'âge moyen des patients transplantés a lui aussi accru. En 1988, seulement 1,4% des patients receveurs d'une greffe cardiaque étaient au dessus de 65 ans, tandis que, en 1998, ce pourcent était de 8,8%. Voila donc, pour quelle raison on justifie la question: est-ce qu'il y a un appui médical pour le transplant cardiaque chez le patient âgé? A côté de cette question il y en a d'autres qui se posent, notamment: jusqu'à quel âge le transplant cardiaque est-il justifié? Peuvent les personnes âgées se soumettre et supporter les rigueurs d'un transplant cardiaque? Peuvent-ils se récupérer fonctionnellement et mener ensuite une vie productive? Un problème d'un intérêt à part est celui lié aux greffes cardiaques de qualité sous-optimale. La pénurie des donneurs pousse à l'utilisation de ces organes pour le transplant aux personnes âgées.

Il est certain que seul l'âge chronologique ne doit pas représenter une contre-indication absolue pour le transplant. Pourtant, les critères d'acceptation des patients âgés (même au dessus de 70 ans) sur la liste de transplant doivent être très sélectifs. De manière particulière, chez ces patients le taux de complications postopératoires doit être très réduit. Afin de réduire ce taux de complications les patients âgés sont inclus dans le soi-disant « status 2 ».

Généralement, dans le cas de la détérioration hémodynamique, ces patients âgés sont plutôt écartés du transplant et, en tout cas, ils ne sont pas avancés en tant que priorité maximale (status 1) afin de prévenir qu'un patient âgé "passe avant" un patient jeune. Le soutien mécanique de la circulation (à l'aide d'un ballon de contrepulsation intra-aortique ou d'un dispositif d'assistance ventriculaire mécanique) est plus rare chez les âgés, vu que ceux ci supportent plus difficilement les complications de ces dispositifs.

Le concept de "liste alternative" pour les patients âgés (ou en général avec les patients à grand risque) réside en la formation de certaines listes de transplant parallèles ou sont inclus les patients avec indication de transplant à la limite. A ces patients, qui ne bénéficieraient pas autrement de cette méthode thérapeutique, seront accordés des coeurs également considérés à la limite. Actuellement, environ 40% des coeurs disponibles pour le transplant cardiaque ne sont pas utilisés étant considérés non standard. L'emploi d'une liste alternative accroît le nombre des greffes cardiaques disponibles et l'accès au transplant sans compromettre la chance de transplant des patients standard à bas risque et plus jeunes. Ce système soulève tout de même une série de problèmes théoriques et pratiques. L'utilisation des greffes cardiaques de qualité à la limite pour les patients à risque élevé va très probablement déterminer une survie et un taux de succès moindres tant à court qu'à long terme, continuant ainsi l'idée que l'âge avancé implique des résultats plus faibles. Un argument en faveur de l'utilisation du système de liste alternative est représenté par les résultats communiqués par certains centres de transplant conformément auxquels l'utilisation sélective des greffes cardiaques à la limite est compatible à une très bonne récupération de la fonction cardiaque et est associée à une très bonne survie.

L'incidence des complications néoplasiques malignes chez les receveurs âgés d'un transplant, supposée d'être accrue selon les résultats du registre ISHLT, n'est pas nécessairement différente de celle rencontrée chez les receveurs standard. Les centres qui rapportent des incidences pareilles justifient ces résultats sur la base de l'adaptation de la médication immunosuppressive à la réponse immune naturellement plus faible rencontrée chez la personne âgée. Le développement de certains immunosuppresseurs plus spécifiques et l'établissement de certains protocoles efficaces afin d'obtenir une tolérance immune ont la capacité de réduire les complications associées à l'immunosuppression, complications qui sont en général plus sévères chez la personne âgées. L'introduction à l'avenir des stratégies thérapeutiques immunosuppressives basées sur la pharmacogénomie pourrait éventuellement permettre l'adaptation de la thérapie au profil génique du patient avec un bénéfice maximal chez le patient âgé.

Notre société doit évaluer de manière appropriée le problème de la baisse de la mortalité des listes de transplant tout comme le problème de la croissance de la survie après le transplant. L'accroissement de la disponibilité d'organes par l'utilisation de certains organes non standard (sous-optimaux pour le transplant) pourrait réduire la mortalité sur les listes d'attente. En principe, si l'on clairement prouvait que les résultats de l'utilisation de tels organes soient similaires avec ceux de l'utilisation des greffes de coeur standard (fait suggéré par plusieurs travaux récemment publiés) il s'érigerait la question si ces organes ne devraient-ils être accordés plutôt aux patients à moindre risque. La qualification d'un coeur en tant que sous-optimal (synonyme: limité, non standard (en dehors du standard) est faite sur la base de certains critères qui sont présentés dans le tableau no. 2.

Tableau II. Critères d'évaluation d'un coeur sous-optimal

- le sexe féminin
- l'âge au dessus de 45 ans
- support inotrope avec dopamine en dose plus grande de 10 g/kgc et min
- superficie corporelle du donneur <70% de celle du receveur
- antécédents d'abus des drogues
- diabète
- arrêt cardiaque
- temps estimé d'ischémie de la greffe de coeur > 210 min
- pression veineuse centrale> 10 mm Hg
- hypertrophie ventriculaire gauche
- facteurs de risque pour la maladie coronarienne
- hépatite

Le xenotransplant, le support cardiaque mécanique permanent, les nouvelles thérapies médicales, la stimulation biventriculaire, le transplant cellulaire et la thérapie génique sont des solutions potentielles à la pénurie actuelle de coeurs pour le transplant. Actuellement, le support cardiaque mécanique permanent paraît la stratégie la plus convenable pour les patients réfractaires à tout traitement médicamenteux. Les résultats de certaines études prospectives comme l'étude REMATCH (*Randomized Evaluation of Mechanical Assistance Therapy for Congestive Heart Failure*) vont donner la direction des critères d'utilisation de cette méthode de traitement.

L'objectif d'équilibrer le problème de la mortalité de sur liste de transplant et l'amélioration des résultats du transplant peut être partiellement atteint par l'adaptation du risque de dysfonction du coeur transplanté (greffe de coeur) à la condition immuno-physiopathologique du receveur. Un exemple serait celui sur l'utilisation des coeurs à partir de donneurs jeunes aux receveurs jeunes (d'un âge proche). La solution serait, donc, l'introduction de toutes les greffes de coeur sur une liste étendue, l'appréciation standardisée de chaque organe et son allocation à un récipient adéquat. Toutes les données sur la greffe cardiaque, ainsi que celles concernant le receveur sont analysées ensemble en vue de la réalisation du transplant. Il en résulte que l'utilisation d'une seule liste d'organes et d'une seule liste de patients pour le transplant est une solution qui puisse surmonter les inconvénients que le système des listes alternatives implique. Le système des listes alternatives désavantage les patients trouvés sur la liste alternative en leur offrant des organes "de seconde qualité", mais aussi ceux qui sont sur la liste principale par le fait qu'on ne leur donne pas l'accès à certains coeurs, qui pourraient, d'ailleurs, leur être alloués.

La provocation de l'allocation "parfaite" d'organes envers les receveurs va continuer jusqu'au moment ou nous disposerons de critères clairs concernant la décision d'attribuer un certain coeur à un certain patient. Elle est, de manière certaine, nécessaire, ensemble avec la croissance des efforts pour une information et une éducation meilleures de l'opinion publique en vue de l'acceptation et de l'approbation de l'idée de transplant, une relaxation des critères qui attestent la qualité de donneur de coeur.

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Recipient evaluation in heart transplantation. IBCvT Tg. Mures experience*)

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Introduction

Severe congestive heart failure is a major health problem whose prevalence is continually increasing.

These patients present a wide diversity of severity degrees and prognosis.

Cardiac transplantation is a well-known beneficial therapeutic option offering increased survival rates and life standard in patients with severe symptomatology and severely impaired functional status.

The number of patients enrolled as potential donors has more than doubled in the USA since 1990 whereas cardiac transplantations in the same country decreased by 8%. Due to this significant decrease in the number of donors and consequently crowded waiting lists, selection of potential transplantation receivers becomes crucial.

Method and Material

The purpose of receiver evaluation is the exclusion of patients with medical and psychosocial comorbidities as well as the quantification of severity in cardiac function alteration.

Below is the evaluation protocol of potential receivers used in the Institute of Cardiovascular Diseases and Transplantation from Targu Mures since 1999, the year of the first heart transplantation in Romania. Maximum age limit of admission on the receiver waiting list was 60.

1. Blood tests - hematologic, coagulation profile, including hepatic enzymes;
2. Serological evaluation CMV, toxo, HVA, HVB, HVC, HIV, herpes, EB, VDRL;
3. Anemia-colonoscopy, esogastroscopy, bone marrow biopsy;
4. Increased creatinine values, urine test, renal echocardiography;
5. Increased hepatic enzymes and right heart pressures, hepatic echocardiography;
6. ABO Typing, HLA, PRA (pannel reactive antibody);
7. EKG
8. Bidimensional transthoracic echocardiography, spectral and color-flux Doppler;
9. Coronarography and myocardic viability evaluation;
10. Bilateral carotidian Echodoppler for the patients with atherosclerosis risk (counterindication for the patients with cerebrovascular impairment);

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11. Obesity - determination of the body mass index (140% ideal weight - counterindication);
12. Infections / active systemic diseases - absolute counterindications;
13. Malignancies in the history;
14. Abdominal aorta echocardiography;
15. Metabolic stress testing;
16. Pulmonary functional tests;
17. Peripheral Vascular Evaluation;
18. Psychosocial evaluation (counterindications: currently smoking, excessive alcohol intake, medical noncompliance, significant untreated psychological / psychiatric diagnoses, lack of adequate social and family support);
19. Stomatologic evaluation;
20. Nyha Class.

NAME	Age	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. D. P.	47	*	*	-	-	-	*	*	*	*	*	*	-	-	-	*	*	-	*	*	4
2. G.M.	47	*	*	*	-	*	*	*	*	*	-	*	-	-	*	-	*	-	*	*	4
3. V.O.	48	*	*	-	-	-	*	*	*	*	*	*	-	-	*	-	*	*	*	*	4
4. S.S.	47	*	*	-	-	*	*	*	*	*	*	*	-	-	-	-	*	*	*	*	3
5. F.M.	21	*	*	-	*	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
6. G.A.	47	*	*	*	-	-	*	*	*	*	-	*	-	-	-	*	*	-	*	*	3
7. F.A.	53	*	*	*	-	-	*	*	*	*	*	*	-	-	-	-	*	*	*	*	4
8. A.S.	53	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
9. H.E.	54	*	*	-	-	*	*	*	*	*	-	*	-	-	*	-	*	-	*	*	3
10. P.P.	54	*	*	-	*	*	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
11. S.V.	36	*	*	-	-	-	*	*	*	*	-	*	-	-	-	*	*	-	*	*	4
12. M.V.	28	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
13. K.A.	54	*	*	-	-	-	*	*	*	*	*	*	-	-	*	*	*	*	*	*	3
14. S.M.	39	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
15. S.A.	58	*	*	*	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	3
16. B.S.	23	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
17. K.R.	54	*	*	-	-	-	*	*	*	*	*	*	-	-	*	-	*	*	*	*	4
18. O.A.	57	*	*	*	-	*	*	*	*	*	-	*	-	-	-	-	*	-	*	*	3
19. R.M.	44	*	*	-	-	-	*	*	*	*	-	*	-	-	-	*	*	-	*	*	4
20. M.C.	23	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	3
21. B.A.	32	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
22. V.M.	47	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
23. P.L.	53	*	*	-	-	-	*	*	*	*	*	*	-	-	*	*	*	*	*	*	4
24. P.P.	13	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	3
25. D.A.	32	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	4
26. C.A.	41	*	*	-	-	-	*	*	*	*	*	*	-	-	*	-	*	*	*	*	3
27. P.A.	55	*	*	-	*	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	3
28. H.D.	9	*	*	-	*	-	*	*	*	*	-	*	-	-	*	-	*	*	*	*	4
29. G.C.	29	*	*	-	-	-	*	*	*	*	-	*	-	-	-	-	*	-	*	*	3
30. B.A.	44	*	*	-	-	*	*	*	*	*	-	*	-	-	-	*	*	-	*	*	4

* performed tests, - not performed

The paper presents patients with congestive heart failure referred for treatment to our unit for several cardiac diseases conducting eventually to congestive heart failure (predominantly congestive cardiomyopathy) as well as patients admitted for specific procedures such as surgical or interventional myocardic revascularization or valvular patients with advanced congestive heart failure beyond etiologic therapeutic resources which can be treated only through a congestive heart failure approach.

Results

The current waiting list of the Institute of Cardiovascular Diseases and Transplantation from Targu Mures comprises 30 patients under permanent periodic monitorization clinically, biologically and virusologically, in different stages of cardiac impairment.

In the diagnosis range, 19 patients present idiopathic congestive cardiomyopathy, 10 have ischemic congestive cardiomyopathy and one patient has hypetrophic congestive cardiomyopathy.

The list includes 5 female and 25 male patients aged between 9 and 58 years of age, with a median of 39.66 years, 18 patients being included in the interval 44-54 years. Out of these, nine patients died during the waiting period at a median interval of 18 months after registration.

Discussions

The ever-growing prevalence of heart failure becomes one of the major health problems of the world.

Recent results estimate that heart failure affects 5 million people only in the USA with an annual incidence of 500,000. This number of patients requires up to 15 million visits, over 2 million hospitalizations and over 6 million hospitalization days per year. Its prevalence is expected to increase within the next years alongside with the increase of the mass of aged population and the continuous improvement of coronary-specific therapies. There is no reason to believe that the Romanian situation is better than that reported in western societies regarding this category of patients. On the contrary, we estimate that the real data are even more pessimistic, also due to the current shortcomings of the domain. In this respect, we estimate a modest, often inexistent prophylactic activity of cardiovascular diseases, not only at the overall population level, but also in the medical field.

These facts are complemented by a relatively low degree of addressability to the surgical services at least during the first stages of cardiovascular diseases, when certain therapeutic measures could slow down the evolution towards heart failure. Unfortunately, nor does a significant number of the medical staff react to these patients within the generally accepted methods of approach and treatment of similar diseases in the world.

Diagnosis, adequate therapy and patients' referrals to tertiary centers for specific evaluation and drug or non-drug based therapy, still need improvements. Moreover, insufficient knowledge or unjustified reticence for classically accepted and efficient therapies in heart failure, persistence in employing therapies without long-range results and with no impact on the vital and evolutionary patient prognosis.

It is beyond the scope of the current paper to dwell on the multiplicity of specific problems, nor is it to analyze causes or provide solutions. Our intention is to ascertain coarsely evident facts which are ever poignantly raised in the routine clinical activity and to estimate that the number of congestive heart failure patients is likely to be above the reported figures of civilized medical societies.

Conclusions

We conclude that there is an extremely reduced number of patients referred to the Institute of Cardiovascular Diseases and Transplantation during the five year period under study since the beginning of cardiac transplantation, with the specification that there are only two specialized centers in the country performing cardiac transplantation including our unit.

This might explain the reduced figure of receivers on the waiting list. On the other hand, this is also due to too late referrals for evaluation, often in refractary cardiac heart failure. This category of patients with increased levels of short-term mortality is difficultly assessed, predominantly invasively, and quite often they die before finding an adequate donor. A significant number of patients insufficiently evaluated and treated still benefiting from drug and non-drug treatments which classify them to other categories are referred for heart transplantation, thus remitting both congestive heart failure and the necessity of a possible transplant.

We can hardly overlook the specific conditions of our country where enlisting as waiting receiver was rejected due to the impossibility of telephone contact or arrival in due time. Similarly unsuited candidates are the patients whose post-transplantation follow up and complex medication or life standards disallow minimum safety conditions regarding possible contagious and infectious diseases, whose fatality for an immunitary-depressed patient can easily be discerned.

Average age of enrolled patients is 39.66 years and this highlights once more the importance of this therapy to the reinsertion of young patients whose life and work potential would otherwise be lost. Also to be remarked is the extremely reduced number of patients from the Mures and neighboring regions, this situation posing a number of questions beyond the scope of the present study.

Most potential receivers have congestive cardiomyopathy, the coronary cases being reduced. One explanation could be the large experience of our *Institute of Cardiovascular Diseases and Transplantation* in coronary surgeries and their complications, this type of patient being approached through specific therapies: interventional, aorto-coronary bypass, anevrismectomies, ventricular reconstructions, ICD implants, which limit or improve evolution to congestive heart failure. On the other hand, patients with congestive cardiomyopathy benefit only from relatively reduced therapeutic opportunities as efficient medication is introduced relatively late and the techniques of ventricular resynchronization are difficult due to highly expensive pacemakers - a fact which explains the predominance of these cases.

Patient mortality on the waiting list is of 95% for a 36-months period from the enlisting date as a receiver. Possible explanations are: sudden deaths with optimum therapy being represented by ICD implants - a highly restricted procedure due to their extremely high costs. Furthermore, still more critical is the method of donor recruitment, their report, a critical maintenance therapy (hospital infections render such cases useless as transplant candidates), a distorted outlook of their families who either do not consent to the procedure or sometimes reconsider their initial consent, sometimes consent too late when the donor organs can no longer be used (infections, MSOF).

We consider that different methods of assessing a potential candidate for heart transplantation (except for the specific ones, especially invasive) can be used in most regional hospitals and could serve as primary centers of selection and enrollment. One of the main purposes of this paper is actually the familiarization of the local specialists with this side of the heart transplantation, conferring them an ignored therapeutic method for their patients. In our opinion patient enrollment for possible cardiac transplantation might and should start in regional hospitals, invasive evaluation and final enrollment being reserved to tertiary centers.

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Twenty-seven Years Experience with Heart Transplantation*)

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Abstract

Background: *The objective of this study was to evaluate long-term outcomes of cardiac transplantation (HTx) in different eras of innovation at a single center during a period of 27 years.*

Methods: *We performed a retrospective analysis of 960 cardiac allograft recipients (40 re-HTx) between 1981 and 2008. The results of 6 different eras based on milestones in HTx were analyzed: Era1: the early years (n = 222, 1981 - 1992); era2: introduction of inhalative nitric oxide, prostanoids, University of Wisconsin solution (UW) replacing Bretschneider's solution (HTK, n = 118, 1992 - 1994); era3: statins (n = 102, 1994 - 1995); era4: tacrolimus (n = 115,1995-1996); era5: mycophenolate mofetil (MMF, n = 143, 1997 - 2000) and era6: sirolimus (n = 300, 2000 - 2008). Outcome variables were survival, freedom from transplant vasculopathy (CAV) and from acute rejection episodes (ARE).*

Results: *Differences in survival was found comparing era1 and era2 with era4 and era6 (p < 0.001). Organ preservation through UW demonstrated a significantly better survival compared to HTK (p < 0.001). Less ARE occurred in patients receiving tacrolimus-sirolimus or tacrolimus-MMF (p < 0.001). Patients receiving tacrolimus-MMF showed less CAV than treated with cyclosporine-MMF (p < 0.005). There were more ventricular assist device implantations and more re-HTx in era6 (p < 0.0001).*

Conclusions: *Although the causes for improvement in survival over time are multifactorial, we believe that changes in immunosuppressive therapy have had a major impact on survival.*

Keywords: *Heart transplantation, immunosuppression, survival, chronic allograft vasculopathy, acute rejection.*

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Introduction

On August 19, 1981, the first successful heart transplantation (HTx) was performed by Reichart and colleagues at our center and on July 8, 2008 the one-thousandth heart transplantation. During the last 27 years many advances have been made in the field of surgical care, organ preservation, perioperative management, immunosuppression, and infection control. These advances have contributed to establish heart transplantation as an effective therapy for patients with end-stage heart disease [1]. Nowadays, the patients who undergo HTx differ from those in earlier periods. There are an increasing proportion of older patients with multiple concomitant diseases, patients with mechanical circulatory support devices or re-transplantations (re-HTx). This results in a larger number of sensitized patients who are at high risk for the development of various adverse immunologic effects [2]. On the other hand a large variety of immunosuppressive protocols have been developed and the individualization of immunosuppression provides a powerful tool for the prevention of rejection and the avoidance of side effects [3]. In this study we summarize the data of our 27 year experience in 1000 HTx in order to correlate long-term patient outcomes with different eras of innovation.

Material and Methods

Patients

We reviewed the data of 960 patients who underwent HTx at our center between August 1981 and July 2008 for the treatment of end-stage heart disease. A total of 1000 transplants, including 40 re-transplants in 38 patients, have been performed.

Donor acceptance criteria

Recipients were selected based on ABO blood type compatibility and donor-recipient size matching (usually within 20% of body mass index). Until 2005 the prospective donor-specific HLA cross-matching was only performed when recipients were tested positive for panel reactive antibodies (PRAs) greater than 10%. Since 2005 PRA, ELISA and LUMINEX was performed for all patients. For pre-sensitized patients “virtual cross matching” according to donor HLA typing, prospective and retrospective B- and T-cell cross matching was realized. Donor hearts are accepted, when preformed antibodies have been ruled out by virtual cross matching [26, 27]. In highly pre-sensitized patients plasmapheresis or treatment with monoclonal antibodies was initiated in order to reduce the PRA positivity on retesting. Organ donation and transportation was organized by Eurotransplant International Foundation in Leiden (Netherlands).

Surgical methods

In most of the patients surgery was performed in the biatrial technique first described by Lower and Shumway except patients after atrial switch operations [4]. Furthermore 74 patients were bridged to transplantation by implantation of a ventricular assist device (VAD). The mean ischemic time was 3.43 ± 1.01 hours.

Organ preservation

We used Bretschneider's solution (HTK) for cardioplegic arrest of the donor hearts until 1991 (*n* = 254). In 1992 we replaced Bretschneider's solution by University of Wisconsin solution (UW, *n* = 628) [5]. Other preservation solutions, mostly Celsior (*n* = 107), were used in the remaining patients (n = 118). We did not modify the preservation technique and still use topical cooling with infusion of cold saline via a left ventricular vent after the left atrial anastomosis is finished. The so called "hot shot" is not established at our centre.

Immunosuppressive therapy

In 1981 the standard triple immunosuppressive regimen consisted of cyclosporine (CyA), azathioprine (AZA) and methylprednisolone. Immunosuppression was initiated with administration of methylprednisolone (500 mg) intravenously approximately 20 minutes before releasing the aortic cross clamp. On arrival at the intensive care unit (ICU), CyA was added in order to achieve initial serum levels of 250 to 350 ng/mL for the first 3 months, and 200 to 250 ng/mL for the first year. The trough levels were tapered down individually with regard to acute rejection episodes (ARE), infections and renal function ending up at a maintenance target trough level of 100 ng/mL late after transplantation. Methylprednisolone therapy was continued postoperatively at a dose of 125 mg every 8 hours for 3 doses. The initial daily dosage of 1 mg/kg body weight was continuously tapered down to 0.1 mg/kg body weight in the first month. Since 1995 methylprednisolone was withdrawn 6 months after transplantation in all patients who did not suffer from multiple ARE.

In 1993, tacrolimus (Tac) was introduced and consecutively replaced CyA in most of the de novo patients. Starting with an intravenous dose ranging from 0.01 mg/kg/day to 0.03 mg/kg/day, the daily Tac dose was adjusted in order to reach target trough levels of 10 to 15 ng/mL. After the initial postoperative period Tac was administered orally aiming at the same trough levels of 10 to 15 ng/mL for the first three months. Then the target trough levels were tapered to 9 – 12 ng/mL until month 12 and to 7 - 10 ng/mL for the further course. Completing the triple regimen, azathioprine (AZA) was administered at a daily dose of 2 - 4 mg/kg body weight, depending on the patient's white blood cell count. In 1997, mycophenolate mofetil (MMF) began to replace AZA, and its combination therapy with Tac was found to be associated with suppression of ARE [6]. Therapeutical drug monitoring for MMF was introduced in 1997 and the target levels for MMF were 1.5 to 4 µg/mL. In patients who suffered from ARE under target trough levels on a CyA-based immunosuppression regimen, the immunosuppressive regimen was switched from CyA to Tac. In 2000, sirolimus (Sir) was introduced because of its superior side effect profile in terms of calcineurin-inhibitor (CNI)-related renal failure which represents a frequent complication after cardiac transplantation. In a prospective study Groetzner et al. could show that conversion from CNI-based immunosuppression to MMF and Sir in heart transplant recipients with chronic renal failure was safe, preserved graft function and improved renal function [7].

Diagnosis and management of acute rejection

Endomyocardial biopsies were performed according to a standardized schedule to diagnose ARE. ARE with an ISHLT grade ≥ 2 were treated with 3 doses of 500 mg methylprednisolone intravenously for 3 days. The same treatment was considered in patients with ISHLT grade ≥ 1B and hemodynamic compromise or other clinical signs of rejection such as edema, dyspnea or cardiac rhythm disorders. When endomyocardial biopsy confirmed persistence of rejection after the first steroid pulse, a second intravenous treatment with methylprednisolone was administered or - depending on the severity of rejection - intravenous mono- or polyclonal antibody preparations such as orthoclone monoclonal antilymphocyte antibody (OKT3, until 1994) or antithymocyte globulin (ATG) were administered.

Antiinfective prophylaxis

Since 1994, cytomegalovirus (CMV) prophylaxis was initiated with ganciclovir in patients at high risk for CMV infection (donor CMV-positive, recipient CMV-negative). Patients presenting with other CMV constellations were scheduled for a preemptive approach with CMV-testing and ganciclovir-treatment only after proven CMV-viraemia. Starting with a daily dose of 2.5 to 5.0 mg/kg intravenously for 2 weeks, antiviral therapy was continued for another 3 months with oral ganciclovir and since 2001 with oral valganciclovir. Additionally, inhaled amphotericin B and oral nystatin were administered for 7 days for antifungal prophylaxis. Trimethoprim-sulfamethoxazole was administered at 960 mg twice per week for pneumocystis carinii prophylaxis for the first 6 months after HTx.

Perioperative management

In 1994 we implemented prophylactic and aggressive treatment of hyper-cholesterolemia with statins at our institution in order to reduce the incidence and development of transplant vasculopathy (TVP) [10]. In 1996 perioperative inhalative nitric oxide (NO) was introduced in order to prevent post operative right ventricular failure in patients with high pulmonary vascular resistance [8]. In the same year we started to use inhalative iloprost (prostacyclin analogue) for the treatment of pulmonary hypertension at our institution [9].

Follow-Up

In order to detect acute or chronic rejection and infectious complications, every patient underwent regularly detailed examination including coronary angiography, endomyocardial biopsy, echocardiography, chest x-ray, routine laboratory values, trough level-monitoring for immunosuppressive drugs and CMV-detection.

Definition of the eras

The entire group of 960 transplant recipients (with 40 re-HTx) was divided into 6 eras based on the introduction of new techniques or drugs in the field of HTx. The beginning of each era was set, whenever we used a new innovation for the first time:

- **Era 1:** the early years of HTx at our center with cyclosporine (CyA) and azathioprine (AZA, n = 222, 1981 - 1992);

- **Era 2:** introduction of inhalative nitric oxide (NO), prostanoids, and University of Wisconsin solution (UW) replacing Bretschneider's solution (HTK, n = 118, 1992 - 1994);
- **Era 3:** introduction of statins (n = 102, 1994 - 1995);
- **Era 4:** introduction of tacrolimus (Tac, n = 115, 1995 - 1996);
- **Era 5:** introduction of mycophenolate mofetil (MMF, n = 143, 1997 - 2000) and
- **Era 6:** introduction of sirolimus (Sir, n = 300, 2000 - July 2008).

Statistical Analysis

For computer-assisted statistical data analysis the software package R was used (version 2.6.0; the R Project for Statistical Computing). Values of continuous variables are expressed as mean ± standard deviation. Survival estimates were calculated with the Kaplan-Meier method and the log-rank test (Mantel-Cox) was performed to calculate probability values. A Cox-proportional hazard model was calculated for multivariate analysis where appropriate. For multiple group comparisons in the demographic data an analysis of variance (ANOVA) was used to discriminate significant differences.

Results

Demographics

Between August 1981 and July 2008, 1000 patients underwent HTx at the Medical Center of the University of Munich, Grosshadern. There were 819 male (81.9%) and 181 female patients (18.1%). At the time of transplantation, 91 patients were younger than 18 years (9.1%), 758 patients were aged between 18 and 60 years (75.8%), and 151 patients were older than 60 years (15.1%).

In this study group, end-stage heart disease was caused by dilative cardiomyopathy (DCM) in 540 patients (54.0%), by ischemic cardiomyopathy (ICM) in 276 patients (27.6%), and by other diseases such as congenital heart disease, cardiac tumors, or advanced valvular disease in 184 patients (others = 18.4%). The mean patient age was 45.9 ± 16.3 years, ranging from 1 month to 73.4 years, with a mean donor age of 32.3 ± 14.4 years, ranging from 1 month to 66.7 years at the time of transplantation. In the entire study group 36 patients received a second transplant and 2 patients received 3 transplants.

The mean follow-up time was 7.22 ± 6.2 years. In most of the patients surgery was performed in the biatrial technique first described by Lower and Shumway except patients after atrial switch operations [4]. We found only 15 patients with severe tricuspid valve insufficiency and necessity of surgery (1.5%). 7% of the patients required a pacemaker implantation after HTx (70 patients). Heterotopic heart transplantation was performed in 2 patients (0.2%).

The distribution of age, gender, and pre-transplant diagnosis showed statistically significant changes through the different eras, as shown in table 1.

Table 1: Distribution of demographic variables among different eras of innovation

	Era 1 1981 – 1992 n = 222	Era 2 1992 – 1994 n = 118	Era 3 1994 – 1995 n = 102	Era 4 1995 – 1996 n = 115	Era 5 1997 – 2000 n = 143	Era 6 2000 – 2006 n = 300	*p* Value
Recipient age (years)	45.2 ± 11.9	46.3 ± 15.2	42.9 ± 18.9	49.6 ± 12.8	49.0 ± 17.1	44.1 ± 19.2	< 0.004
Donor age (years)	27.8 ± 10.4	30.8 ± 12.8	28.2 ± 14.0	32.5 ± 13.1	37.6 ± 15.8	34.7 ± 16.0	< 0.0001
Recipient gender in % (m/f)	87.9 / 12.1	81.5 / 18.5	83 / 17	83.3 / 16.7	81 / 19	77.6 / 22.4	0.01
Donor gender in % (m/f)	72.5 / 27.5	67.8 / 32.2	63.8 / 36.2	67 / 33	54.9 / 45.1	72.4 / 27.6	0.09
Age distribution							
< 19 years	2.2 %	9.2 %	11.3 %	4.2 %	10.3 %	14.7 %	
19 – 60 years	90.5 %	77.7 %	71.7 %	84.2 %	71.4 %	64.4 %	
> 60 years	7.4 %	13.1 %	17 %	11.7 %	18.3 %	20.9 %	
Diagnosis							
DCMP	41.5 %	50.8 %	52.8 %	56.7 %	60.3 %	60.3 %	
ICMP	42 %	33.8 %	20.8 %	25 %	32.5 %	25.9 %	ns
Others	16.5 %	15.4 %	26.4 %	18.3 %	7.1 %	13.8 %	
VADs (n = 74)	3 (6.6 %)	7 (5.9 %)	5 (4.9 %)	6 (5.2 %)	10 (6.9 %)	43 (14.3%)	< 0.0001
Retransplants (n = 40)	7 (3.2 %)	3 (2.5 %)	4 (3.9 %)	4 (3.5 %)	4 (2.8 %)	18 (6 %)	< 0.0001
Ischemic time (hours)	2.50 ± 0.51	3.08 ± 0.54	3.02 ± 0.54	3.39 ± 0.49	3.22 ± 0.59	4.00 ± 0.51	< 0.0001

DCMP = *dilated cardiomyopathy*, ICMP = *ischemic cardiomyopathy*,
Others = *congenital heart disease, cardiac tumors, advanced valvular disease etc.*,
VAD = *ventricular assist device.*

There was an increase in the proportion of donors with advanced age ($p < 0.0001$) and of female recipients ($p < 0.01$) in the later eras. The proportion of patients requiring a ventricular assist device (VAD) increased significantly in the later eras (6.6% vs. 14.3%, $p < 0.0001$). Moreover, in era 6 significantly more patients were re-transplanted (6%, $p < 0.0001$) and ischemic time increased up to 4.00 ± 0.51 hours ($p < 0.0001$).

Patient survival

The actuarial survival of the entire study group was 75.9%, 68.5%, 56.3%, 44.0%, 38.2% and 28.2% at 1, 5, 10, 15, 20 and 25 years, respectively **(figure 1a-c)**.

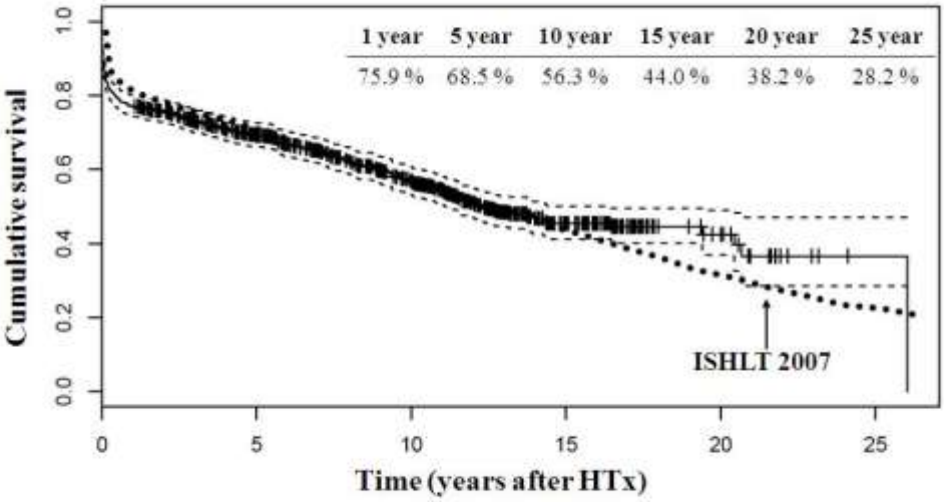

Figure 1a: Cumulative survival of 960 patients undergoing heart transplantation between August 1981 and July 2008

We could show a better cumulative survival 20 and 25 years after HTx comparing with the ISHLT data (figure 1a). The patient with the longest survival of 27 years is still alive.

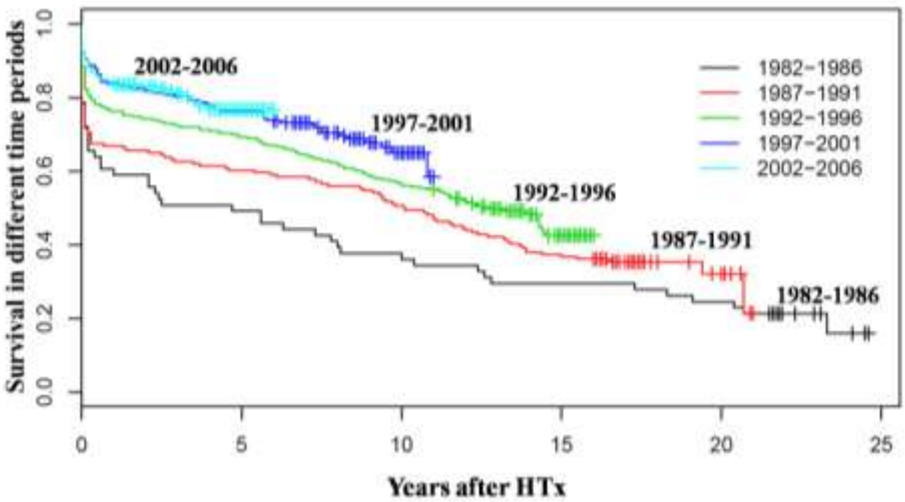

Figure 1b: Cumulative survival improved with every 5 year report

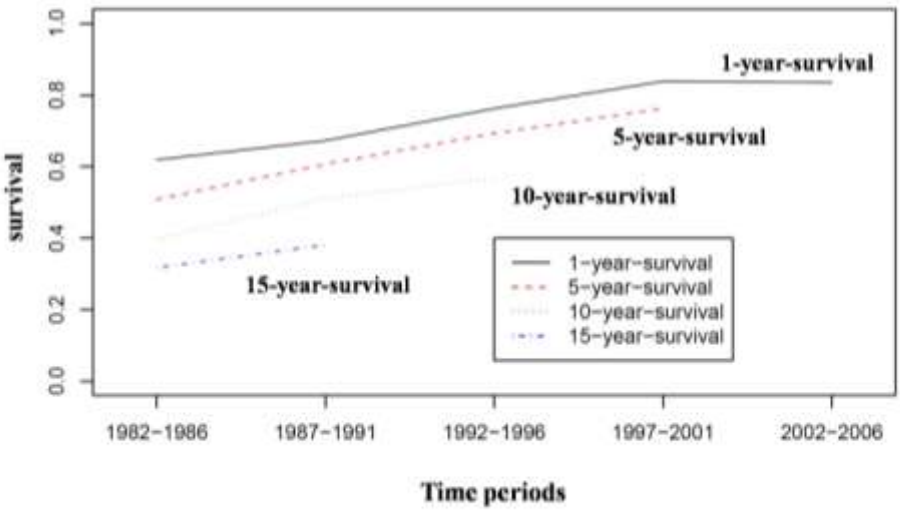

Figure 1c: The improvements of the 1-, 5-, 10- and 15-year survival

With regard to the eras, actuarial survival at 1, 5, 10, 15, 20 and 25 years for era 1 was 65.3%, 57.7%, 46.8%, 35.6%, 30.8 and 22.8; survival at 1, 5, 10 and 15 years for era 2 was 70.3%, 64.4%, 46.6 and 31.4%; survival at 1, 5 and 10 years for era 3 was 70.2%, 68.1% and 61.7%; for era 4 was 83.5%, 73.9% and 61.7% and for era 5, 80.5%, 73.5%, 62.1%. For era 6 the actuarial survival at 1, 5 and 10 years was 82.3%, 74.3% and 61.7%. Significant differences in survival were found when comparing era 1 and era 2 with the tacrolimus-era (era 4) and the sirolimus-era (era 6, $p < 0.001$, figure 2).

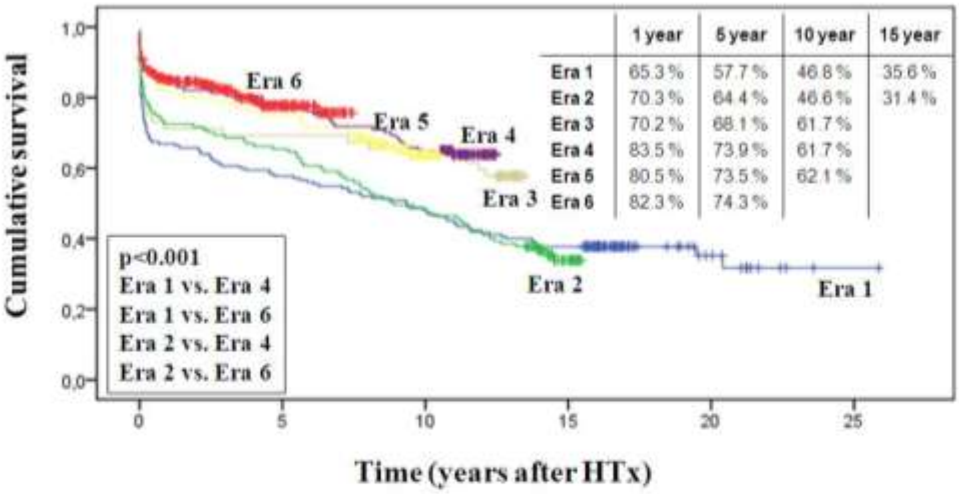

Figure 2: Cumulative survival of patients undergoing heart transplantation between 1981 and 2008 in six different eras of innovation. Era 1: early years of HTx at our center (1981 - 1992); era 2: introduction of NO, prostanoids, and UW replacing HTK (1992 - 1994); era 3: introduction of statins (1994 - 1995); era 4: introduction of Tac (1995 - 1996); era 5: introduction of MMF (1997 - 2000); era 6: introduction of Sir (2000 - 2008), *p* < 0.001.

Actuarial survival at 1, 5, 10, 15 and 20 years based on pre-transplant diagnosis was 80.6%, 74.4%, 64.2%, 54.5 and 48.9% at 20 years for DCM, and 73.5%, 65.1%, 48.1% and 31.1 at 15 years for ICM and 65.1%, 53.4%, 42.1% and 31.1% at 15 years for other diseases (e.g. congenital heart disease, cardiac tumors, or advanced valvular disease). Long-term survival in patients with DCM was superior compared to patients with ICM (p < 0.001). When compared to patients with other diseases, ICM patients revealed a trend towards inferior survival (figure not shown).

Furthermore, there was no significant difference in survival for male patients compared with female patients (p = 0.135, data not shown), but there was a trend towards a better long-term-survival for female patients. Comparing the gender from donors and recipients revealed a trend towards a better long-term-survival for female recipients with male donor hearts (p = 0.238, figure not shown).

Comparing the different groups of age showed that survival of recipients younger than 18 years was significantly better than survival of recipients aged between 18 and 60 years (p < 0.001) and also better than survival of patients older than 60 years (p < 0.001, figure not shown).

There was a superior early and long term survival in patients, who were transplanted after 1992, when UW preservation solution replaced Bretschneider's solution at our institution (p < 0.001, figure 3). Actuarial survival at 1, 5, 10 and 15 years was 80.1%, 72.3%, 58.5% and 46.4%, respectively, when UW was used for preservation, and 66.1%, 58.7%, 47.3% and 36.4%, respectively, when HTK was used.

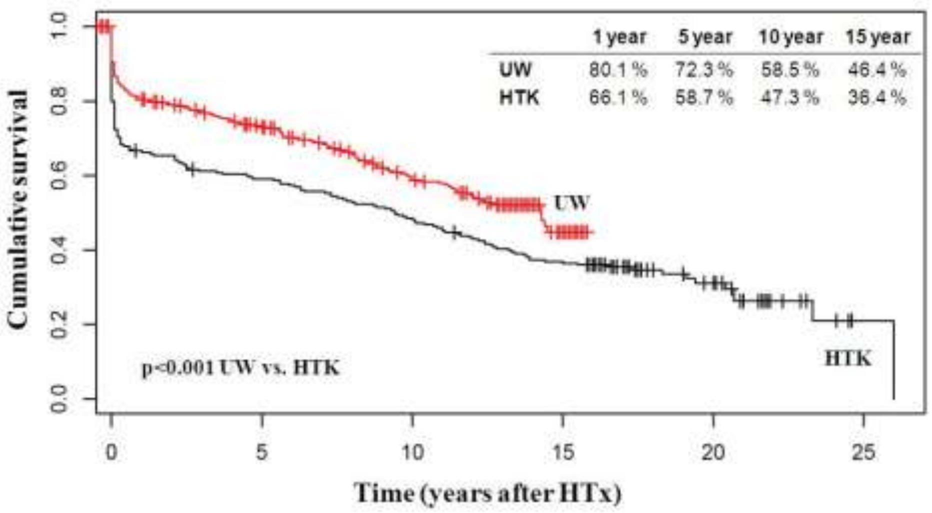

Figure 3: Cumulative survival of patients undergoing heart transplantation between 1981 and 2007 comparing University of Wisconsin preservation solution (UW) versus Bretschneider's solution (HTK), *p* < 0.001.

The survival of patients undergoing re-HTx was inferior to the survival of patients, who were not re-transplanted (p < 0.001, figure not shown). Actuarial survival at 1, 5, 10 and 15 years of re-transplanted patients was 56.5%, 36.9%, 17.6% and 8.8%, respectively, and 76.7%, 69.8%, 57.4% and 45.3%, respectively, in patients, who were not re-transplanted.

Actuarial survival based on immunsuppressive regimen at 1, 5, and 10 years were as follows: 69.5%, 61.3% and 47.6% respectively for CyA-AZA, 87.9%, 83.1%, and 77.0%, respectively for the combination of CyA-MMF, 77.5%, 74.6%, and 68.8%, respectively for Tac combined with AZA, 79.9%, 72.7%, and 63.1%, respectively for the combination of Tac-MMF. Actuarial survival at 1 and 5 years was 92.4%, and 85.5%, respectively for Tac-Sir. Finally, actuarial survival at 1 year was 90.9%, respectively for Sir-MMF (figure 4).

Patients under immunosuppressive therapy with CyA-MMF, Tac-MMF or Tac-Sir had a significantly better survival than patients receiving CyA-AZA ($p < 0.001$, figure 4).

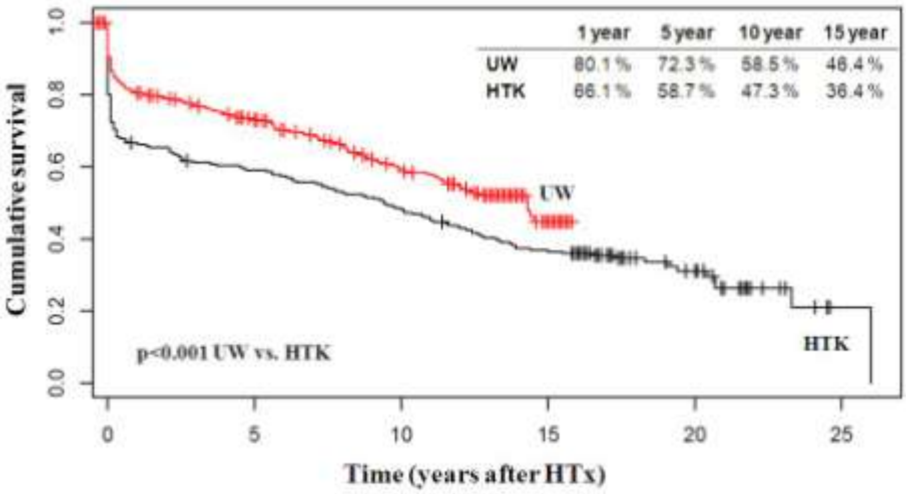

Figure 4: Cumulative 1-, 5-, and 10 year survival of patients undergoing heart transplantation between 1981 and 2007 comparing different immunosuppressive regimen, $p < 0.001$.

Furthermore patients receiving Tac-MMF had an inferior survival when compared to patients receiving Sir-MMF, TAC-Sir and CyA-MMF. This is likely due to the fact that in the Tac-MMF group there were significantly more patients with diabetes than in the other groups (Hazart-ratio 2.1, $p = 0.0009$). The survival of patients receiving MMF in their immunosuppressive regimen was significantly better than patients receiving AZA ($p < 0.001$, data not shown).

Acute Rejection

Freedom from ARE based on different immunosuppressive regimen is shown in figure 5. Freedom from ARE at 1, 5, and 10 years were as follows: 43.5%, 39.7%, and 38.7% for CyA-AZA, 55.0%, 49.1%, and 47.1% for the combination of CyA-MMF, 30.4% and 27.0% for Tac-AZA, 80.4%, 77.5%, and 75.6% for the combination of Tac-MMF. Freedom from ARE at 1 and 5 years was 94.5%, and 87.9%, respectively for the combination of Tac-Sir and 70.0% and 58.3% for Sir-MMF. CyA-MMF and Tac-MMF was significantly better regarding ARE than CyA-AZA and Tac-AZA ($p < 0.001$). The best combination regarding ARE was Tac-Sir ($p < 0.001$ vs. all groups, except Tac-MMF).

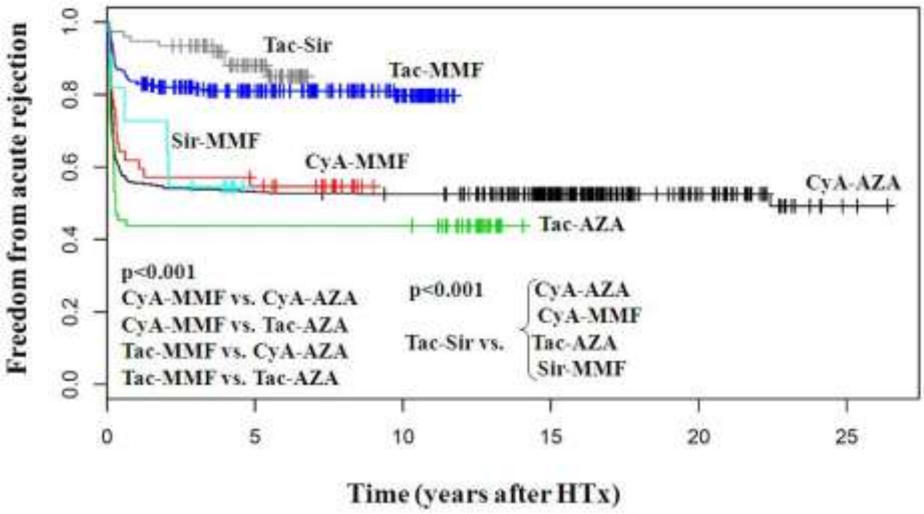

Figure 5: Freedom from acute rejection (ARE) based on different immunosuppressive regimens, $p < 0.001$.

Graft Coronary Artery Disease

Freedom from CAV at 1, 5, 10, 15 and 20 years were as follows: 97.3%, 82.4%, 69.8%, 50.9% and 37.3% for CyA-AZA; 86.5%, 69.8%, and 43.2%, for CyA-MMF; 90.0%, 73.6%, and 61.1% for Tac-AZA; 95.9%, 82.9%, and 69.0% for Tac-MMF. Freedom from CAV at 1 and 5 years was 96.8% and 87.6% for Tac-Sir; 97.2%, and 93.0%, respectively for Sir-MMF (figure 6). Patients receiving Tac-MMF showed significantly less CAV than patients treated with CyA-MMF ($p < 0.005$).

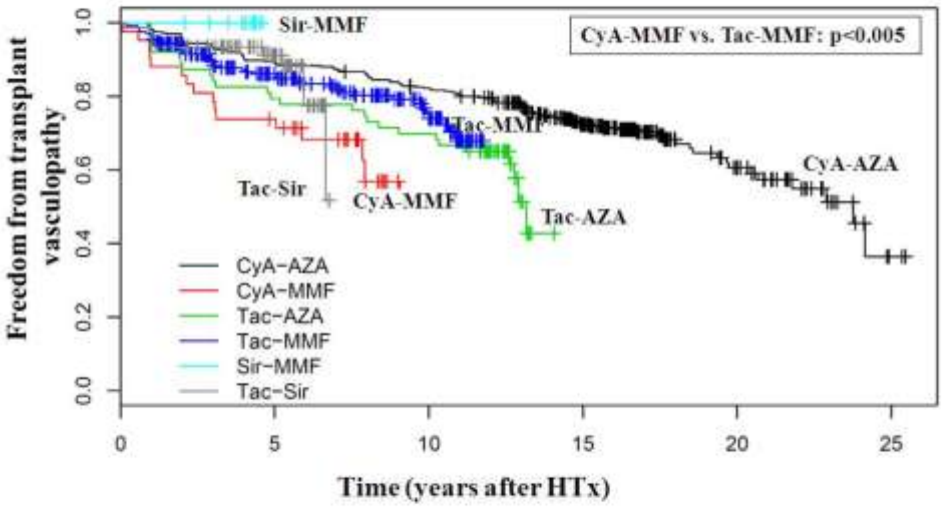

Figure 6: Freedom from cardiac allograft vasculopathy (CAV) based on different immuno-suppressive regimen, $p < 0.005$.

Discussion

This study represents a large series of patients undergoing HTx at a single center by a team whose core members have not changed over time. Even if it seems that the division in 6 different eras did not allow individualized therapy, our patients received an individualized immunosuppressive regimen according to age, co-morbidities and time after HTx. Especially older patients with increased risk for infectious complications, renal failure and neoplasms necessitate a tailored immunosuppression [3]. This division in eras allows to examine trends and study changes which have occurred in the management of patients with end-stage heart disease over a period of 27 years. Here we could show subsequent improvement in survival with each era of innovation (figure 2). Although the reasons for improved survival are of multifactorial origin, we ascribe the main advancements to evolving immunosuppressive therapy and improvements in immunologic monitoring. This hypothesis is supported by the subsequent diminishing incidence of ARE in relation to the gradual refinements in immunosuppressive therapy (figure 5).

Patients Survival

The cumulative survival of 38.2% at 20 and 28.2 % at 25 years after HTx (**figure 1a**) was higher than shown in the ISHLT data [24]. The most likely reasons for these good results are the high rate of freedom from ARE, the use of UW preservation solution and the very experienced team whose core members have not changed over time. Cumulative survival improved significantly during the different time periods (figure 1b) and was lower in the early phase of our HTx program (era 1, 1981 to 1992, figure 2). In this era the immunsuppressive regimen consisted of CyA and AZA. The next era (era 2, from 1992 to 1994) was heralded by the introduction of UW, which replaced HTK-solution because UW had shown superior results for cardiac perfusion in experimental studies [5]. Comparing the cumulative survival of patients receiving organ preservation with HTK vs. UW, we found a significant better survival in the UW group (figure 3). As it is displayed in the survival curve the UW group showed not only a decreased early mortality, but also a better long term survival. The 1 year survival was 80.1% in the UW group versus 66.1% in the HTK group. The long term survival 15 years after HTx was 46.4% in the UW group and 36.4% in the HTK group. As expected the organ preservation solution plays a significant role in early graft survival. Reichenspurner et al could show a decrease in the incidence of early, ischemic time-dependent graft failure [19]. Nevertheless also long term survival improved. In an experimental study from Kajihara et al. UW solution led to a better left ventricular function and a greater potential for long term preservation [20]. Furthermore Michel et al showed in rat hearts that UW resulted in better heart contractility, lower LDH and CK levels during perfusion then HTK [21]. The multivariate analysis we made, did not show differences between the groups regarding age, diabetes, infections or ARE. It is also noteworthy that the use of UW coincided with the introduction of perioperative inhalative nitric oxide (NO) and aerosolized iloprost both to prevent post operative right ventricular failure in patients with high pulmonary vascular resistance [8, 9]. Era 1 and 2 showed an improved survival at 1, 5, and 10 years against era 4 and 6 (figure 2).

No significant increase in actuarial survival was observed after introduction of statins for the treatment of hypercholesterolaemia after HTx in era 3. Nevertheless the aggressive treatment of hypercholesterolemia had proved to lower the incidence and development of CAV in adults [10] as well as in children [11] and survival improved in the following periods also as result of the statin treatment. The next major periods began with the introduction of Tac (era 4), MMF (era 5) and Sir (era 6) as main immunosuppressant agents (figure 2). The survival and freedom from ARE and TVP of patients receiving MMF was significantly higher than patients receiving AZA. A review of major clinical trials with MMF in HTx from Kobashigawa and Meiser demonstrated that MMF provided long-term benefits in reducing CAV and increasing survival [23].

Nevertheless there was no significant difference in survival between era 4, 5 and 6. The multivariate analysis did show differences between these 3 groups regarding age, diabetes, ventricular assist devices, ischemic time and re-HTx. Donor and recipient age increased continuously over time. The patients had significantly more ventricular assist devices during their waiting time. The ischemic time was longer and we had more retransplanted patients (see table 1). Furthermore we accepted more co-morbidities (diabetes, renal insufficiency) in recent eras. Therefore, even with the newer generation of immunosuppressive agents no better survival was observed between era 4, 5 and 6.

In most of our patients surgery was performed in the biatrial technique by Lower and Shumway. This method is easier to perform and does not lead to caval stenoses. On the other hand this technique might result in more tricuspid regurgitations. Nevertheless the data did not support any definite mandate for either of the surgical techniques. Grande et al. observed that tricuspid regurgitation occurs in 53.1% of the patients transplanted with the Lower/Shumway technique and in 41.9% of patients operated in the bicaval technique without significant difference [28]. The largest study examining bicaval vs. biatrial anastomosis techniques, the United Network for Organ Sharing (UNOS) database identified 14.418 patients undergoing heart transplantation between the years 1999 and 2005. Weiss et al. found no difference in survival between the two groups, although the bicaval technique was associated with a shorter lengh of hospital stay and less pacemaker placement [29]. In our group 70 patients required a pacemaker implantation after HTx (7%). If we look at the actual literature, pacemaker implantation after HTx occurred between 5-10% [29, 30, 31].

An increasing problem is the organ shortage with extended waiting lists and increased mortality on the waiting list. Evidence exists that certain “standard” donor criteria can be significantly liberalized to increase the available donor pool by accepting “marginal donors” who would, under conventional transplant guidelines, be declined as potential organ donors [32, 33]. In the last 27 years we accepted marginal donors in high urgent patients. In the future we might have to adjust this policy to organ shortage with extended waiting lists and increased mortality on the waiting list.

Acute rejection

As seen in figure 5, the use of new immunosuppressive drugs plays the key role in the prevention of ARE, especially the use of calcineurin inhibitors such as CyA and Tac. We demonstrated that Tac is superior to CyA in prevention of ARE. Grimm et al. showed in a large European trial that biopsy proven ARE of grade ≥ 3A at month 6 after HTx was significantly lower for Tac vs. CyA [13]. Additionally Kobashigawa et al. found significant differences in the incidence of treated ARE in their Tac/MMF group vs. the CyA/MMF group at 1 year after HTx [24]. In 1997, era 5 began with the addition of MMF to our program. Freedom from ARE was significantly higher in the MMF-based immunosuppression compared with immunosuppression based on AZA. Kobashigawa et al. showed in a randomized double-blind, and active-controlled trial that the use of MMF as part of a triple immunosuppressive therapy was associated with a significant reduction in ARE and mortality when compared to the use of AZA [14]. Furthermore, the ability of MMF to reduce recurrent and refractory rejection episodes was shown in previous studies [15, 16].

After the introduction of Sir in 2000 a trail either in combination with Tac or MMF started. Patient treated with Tac-Sir showed the best results regarding ARE **(figure 5)**. De-novo Sir-MMF therapy revealed significant more ARE than the combination Tac-Sir. We introduced Sir because of its superior side effect profile in terms of CNI-related renal failure as a common problem after cardiac transplantation. In a prospective study at our center Groetzner et al. could show that conversion from CNI-based immunosuppression to MMF and Sir in heart transplant recipients with chronic renal failure was safe, preserved graft function and improved renal function [7].

Transplant Vasculopathy

When comparing the immunosuppressive therapies CyA-MMF and Tac-MMF, freedom from ARE as well as freedom from CAV ($p < 0.005$) were significantly higher in the Tac-MMF-group (figure 6). Weis et al. demonstrated that tacrolimus is superior to cyclosporine with respect to microvascular endothelial function, intimal thickening and vascular remodeling [25].

Limitations

Comparing outcomes of the different eras, we assumed that all events were mutually exclusive. Of course, this was not always the case. It is very difficult to evaluate outcome results in the field of transplantation for each defined milestone because some inventions overlapped.

Conclusions

This study clearly demonstrates that continued efforts in developing surgical care, perioperative management, organ preservation, immunosuppression, and infection control have improved early and long-term survival after cardiac transplantation. however, cardiac transplantation continues to evolve and mature, but many limitations still remain. in the future, highly specific immunosuppression or the achievement of tolerance induction is needed to further improve the results.

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Heart and Lung Transplantation*)

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Abstract

Thoracic organ transplantation (Tx) has become clinical routine for the treatment of end-stage heart and lung disease. The article discusses the current guidelines for the indication of thoracic transplantation. It provides furthermore a brief summary about listing procedures, allocation, post-operative care and the long-term results after heart or lung transplantation.

Ischemic cardiomyopathy and the heterogeneous group of dilative cardiomyopathy represent up to 40% of the causes that lead to heart failure and finally, to heart transplantation (HTx). Other indications for HTx are valvular diseases or congenital heart failure that cannot be corrected surgically.

In the decision for Tx are equally involved the cardiologist, the cardiovascular surgeon and the patient. The main objectives are the quality of life and the success of the transplantation. The time point for placing the patient into the waiting list has to be estimated by considering the individual risk and the expected waiting time. HTx is not an operation to be performed in emergency, because patients on the waiting list must be optimally prepared.

Keywords: *heart transplantation, lung transplantation, immunosuppression*

Rezumat

Transplantul organelor toracale reprezintă în prezent o metodă terapeutică de rutină pentru boli cardiace şi pulmonare în stadiu terminal. Articolul prezintă un ghid practic de indicaţii pentru transplantul de organe toracice, tipurile de tehnică chirurgicală şi tratamentul postoperator, precum şi supravieţuirea la distanţă după transplantul de cord şi de plămân.

Cardiomiopatia ischemică şi grupul heterogen al cardiomiopatiilor dilatative, reprezintă 40% din cauzele ce duc la insuficienţă cardiacă şi, in final, la transplantul cardiac (HTx). Alte indicaţii sunt bolile valvulare şi malformaţiile congenitale cardiace, care nu pot fi corectate chirurgical.

Decizia pentru transplant cardiac trebuie luată în comun de către cardiolog şi chirurg cardio-vascular şi de către pacient. Obiectivele sunt, în aceeaşi măsură, calitatea vieţii şi succesul transplantului. La momentul înscrierii pacientului pe lista de aşteptare, trebuie evaluat bine riscul individual până la momentul operator.

Transplantul organelor toracale nu este o operaţie adecvată pentru a fi realizată în urgenţă, deoarece pacienţii listaţi trebuie pregătiţi în condiţii optime.

Cuvinte-cheie: *Transplantul de cord, transplantul de plămân, imunosupresie*

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Thoracic organ transplantation (Tx) has become clinical routine for the treatment of end-stage heart and lung disease. The article discusses the current guidelines for the indication of thoracic transplantation. It provides furthermore a brief summary about listing procedures, allocation, post-operative care and the long-term results after heart or lung transplantation.

Ischemic cardiomyopathy and the heterogeneous group of dilative cardiomyopathy represent up to 40% of the causes that lead to heart failure and finally, to heart transplantation (HTx). Other indications for HTx are valvular diseases or congenital heart failure that cannot be corrected surgically.

In the decision for Tx are equally involved the cardiologist, the cardiovascular surgeon and the patient. The main objectives are the quality of life and the success of the transplantation. The time point for placing the patient onto the waiting list has to be estimated by considering the individual risk and the expected waiting time. HTx is not an operation to be performed in emergency, because patients on the waiting list must be optimally prepared.

The classic indication for HTx is irreversible end-stage heart failure (NYHA III / IV), with a survival probability of less than 50% at one year. The International Society for Heart and Lung Transplantation states, that in patients with a maximum oxygen uptake (VO2max) of 12 ml/kg/min, indicated by spiroergometry, HTx is recommended (1, 2).

Table 1: Main indications for heart transplantation.

I) Absolute indications:
- VO2max < 12 ml/kg/min - Angina pectoris refractory to therapy - Ischemia refractory to therapy with no option of revascularisation - Ventricular arrhythmias refractory to therapy
II) Possible indications
- VO2max < 14 ml/kg/min with severe limitation of physical activity - Recurrent unstable angina pectoris without option of revascularisation - Unstable fluid balance and impaired renal function despite a good compliance - Left ventricular ejection fraction < 20%

Other prognostic factors to be taken into account in the decision for Tx are: stage IV NYHA heart failure, serum sodium < 135 mmol/L, complex ventricular arrhythmias, brain natriuretic peptide (BNP) > 200 pg/ml, end diastolic left ventricular diameter > 75 mm, end systolic left ventricular diameter > 65 mm, end diastolic left ventricular pressure > 20 mmHg, a cardiac index < 2.0 L/min/m², pulmonary hypertension, as well severe liver and kidney impairment (3).

These prognostic parameters are not applicable to all cardiac diseases, such as congenital heart defects, amyloidosis, sarcoidosis, malignancies, etc.

Mortality on the waiting list is about 20% (Eurotransplant countries). Leading causes of death are cardiac arrhythmias. Therefore, patients on the waiting list should receive a defibrillator. There are also telemetry systems available, that continuously transmit hemodynamic data (4).

Contraindications

There are few absolute contraindications for HTx. The main contraindication is pulmonary hypertension that is unresponsive to drug therapy. Patients are eligible for Tx with a maximum pulmonary resistance of less than 4 Wood units (320 $dyn \times s \times cm^{5}$) or a transpulmonary gradient of less than 12 mmHg. In cases of elevated pulmonary resistance, response to nitric oxyde or prostanoids must be tested. These criteria gain relevance, because nowadays the indication for HTx is often made when secondary pulmonary hypertension is already evident, as a result of modern heart failure and pacemaker therapy.

Relative contraindications are co-morbidities, which may reduce the chances for a successful transplant, such as diabetes, chronic or acute infectious diseases, tumors that cannot be treated curatively, severe systemic disease (amyloidosis, sarcoidosis), severe renal and hepatic insufficiency, advanced pulmonary disease, cerebrovascular or peripheral artery disease, severe obesity (BMI > 40), low compliance, nicotine and alcohol dependency, as well as psychiatric diseases. Current studies show, that nicotine abuse both before and after Tx is a risk factor for posttransplant survival (5). The patient's age alone does not represent a contraindication and the decision has to be made by considering the biological age. It is generally agreed, that the maximum age for HTx is 70 years, although there are many experiences with good results beyond this limit (6, 7).

Examinations before listing for heart transpalntation

Before being placed onto the waiting list, it should be clarified from a health perspective, that the patient is suitable for HTx [see Table 2].

Table 2: Summary of the necessary investigations.

I. Laboratory investigations	
Coagulation tests	**Blood group, blood count, platelets, INR, PTT, fibrinogen, CRP**
Renal function	**Electrolytes, creatinine (clearence), urea, urinary status**
Liver function	**Total bilirubine, AST, ALT, GGT, LDH, AP, CK, amylase, lipase, serum protein electrophoresis**
Metabolism and endocrinology	**Cholesterole, Triglyceride, LP(a), serum lipoprotein electrophoresis, T3/T4/TSH, glucose profile, HbA1c**
Immunology	**Panel reactive antibodies (PRA) test, HLA typing, cold agglutination test, antinuclear antibodies**
II. Microbiology	
Bacteriology	**Urine culture**
Virology	**Coxsackie, Herpes simplex, Varicella zoster, Herpes zoster, Cytomegalovirus, EBV, HIV, hepatitis virus A, B, C**
Serology	**Mycoplasmosis, toxoplasmosis, candida, syphilis**
III. Imaging	
12 channel ECG, echocardiogram, abdominal ultrasound, computed tomography of thorax and abdomen, Chest x-ray, right heart catheterization, spiroergometry, blood gas analysis, cerebral CT	
IV. Specialized expertise	
Dentistry, ENT, gastroenterology, psychiatry, urology, gynecology, anesthesia, neurology, endocrinology	

Chronic infections or malignant diseases must be excluded. In addition, it is also necessary to test the pulmonary function and pulmonary vascular resistance as a key indicator for adverse outcome.

Operability of the patient must be evaluated by the anesthesiologist. Patients must also be investigated for psychiatric and psychosomatic diseases. After completion of these investigations, the patient can be put on the waiting list.

Listing for heart transplantation and the waiting time

In the presence of end-stage heart failure (NIHA III / IV) the patient can be put onto the waiting list after possible contraindications are ruled out.
Mandatory is a thorough preliminary discussion with a transplant specialist is about the risks and prospects of Tx, about the surgical procedure and possible risks, about the social and psychological impact of Tx, about immunosuppression and its secondary effects, as well as the necessity and frequency of regular controls after successful Tx.

A cardiologic checkup is scheduled at least every three months during the entire waiting time. In addition, right heart catheterization should be performed every six months. The transplant center has to be informed in case of transient diseases, such as an infectious febrile syndrome.

Heart transplantation

The technique is based on scientific experiments of Lower and Shumway [8]. According to Lower and Shumway's biatrial method, the recipient heart is excised at the atrial level. Furthermore, the ascending aorta and the trunk of the pulmonary artery are separated. Implantation begins at the left atrium and continues with the right atrium and ends with the anastomoses of the pulmonary artery and the ascending. In the bicaval modified implantation technique, the right atrium is completely resected, preserving the posterior wall of the left atrium. The advantages of this method are a better geometrical integrity of the tricuspid valve and a later reduction in the need for pacemaker implantation (8, 9, 10, 11).

Stenosis of the anastomoses of the inferior and superior caval veins is the main disadvantage of this method.

Immunosuppression

Critical for the success of Tx is an appropriate and individually controlled therapy. In earlier days immunosuppression consisted of cyclosporine A, azathioprine and prednisolone. The immunosuppression induction with mono- and polyclonal antibodies (such as OKT III or ATG) or with interleukin-2 receptor antagonists is currently performed in approximately 50% of the transplant centers. Its use is still controversial. Nowadays immunosuppression consists of tacrolimus or cyclosporine A in combination with mycophenolate mofetil (12). Steroids are not used as regular long term medication, but in the immediate post transplant period or as rejection treatment. New substances such as sirolimus or everolimus, part of mTOR inhibitors group are new immunosuppressive drugs. They may be used to prevent kidney failure caused by calcineurin inhibitors (13). The combination and the dosage of immunosuppressive drugs should result in a balance between the risk of graft rejection and the risk of opportunistic infections and adverse side effects. The extent of the immunosuppressive therapy after Tx can be reduced consecutively in most of the patients during follow-up.

Additional medication

In addition to the immunosuppressive medication, other drugs are used regularly. They should protect the body against infections or they should reduce immunosuppressant toxic side effects. Therefore, the protocol of additional medication administration depends on the needs of each patient. Diuretics stimulate renal function immediately after Tx. Furthermore, diuretics can stimulate renal function, in case of immunosuppressive nephrotoxicity. Statins (HMG-CoA reductase inhibitors) are routinely prescribed after Tx. Many of the immunosuppressive drugs, especially sirolimus and everolimus lead to increased cholesterole and triglyceride levels. Statins can increase survival in cardiac transplant patients. They are therefore administered routinely in some centers, even at a normal level of cholesterole. Besides pre-existing hypertension, calcineurin inhibitors, may increase blood pressure. Antihypertensive therapy consists of ACE inhibitors, angiotensin receptor antagonists and calcium antagonists. Beta blockers may be prescribed but they are often not tolerated. Furthermore, calcineurin inhibitors may induce post-transplant diabetes mellitus. Therefore, antidiabetic therapy may be indicated.

Transmission or reactivation of cytomegalovirus (CMV) is common among transplant recipients. Antiviral prophylaxis (especially with ganciclovir) is used especially in exposed patients (CMV negative recipients of CMV positive grafts). Regular monitoring of blood CMV-PCR is routinely performed in the transplant centers. The optimal duration of antiviral therapy is widely discussed. Costs and side effects, such as myelotoxicity and nephrotoxicity play an important role. On the other hand, an early CMV infection can cause early vascular dysfunction. Patients should receive cotrimoxazole twice a week in order to prevent Pneumocystis jiroveci pneumonia (Pneumocystis carinii) infection. The duration of the prophylaxis varies between two and twelve months after Tx.

There are many drug interactions with immunosupessive drugs. Antibiotics, antiepileptic medication, calcium antagonists and even grapefruit are metabolized via Cytochrome P450 Isoenzyme CYP 3A4, which is the key enzyme for tacrolimus and cyclosporine A metabolism. Therefore thorough evaluation of trough levels after changes in medication are mandatory.

Graft rejection

As a consequence of the effective immunosuppressive therapy acute graft rejection has become a rare complication. Besides a good prevention, early diagnosis plays an important role. Possible signs of rejection are nonspecific and may be limited to dyspnea, edema, cardiac arrhythmias, and sometimes fever. Endomyocardial biopsy represents the gold standard for the diagnosis of rejection after heart transplantation. After a clinical or histological diagnosis of acute rejection, steroid treatment should be started immediately. Rejection refractory to steroids is rare and can be treated with ATG antibodies.

The exact cause of chronic rejection or cardiac allograft vasculopathy (CAV) is not finally elucidated. It may be related to immunological processes that cause or maintain the changes. 5-10% per year of the cardiac transplant patients develop new-onset CAV, and after 5 years, 30-50% show signs of CAV. Therefore, coronary angiography should be performed regularly by an experienced cardiologist familiar to HTx.

The main objective of CAV is not the early diagnosis, but a good prevention. The elimination of risk factors such as rejection, viral infections, hypertension, hyperlipoproteinemia, and diabetes mellitus are crucial. The new generation of immunosuppressants, such as sirolimus and everolimus, possess inhibitory effect on the development of CAV.

Results

After data provided by the ISHLT, survival after HTx during 2002-2006 is 85% at 1 year and 75% at 5 years. The risk factors for mortality in the first year are reproduced in Table 3.

Table 3: Risk factors for 1-year-mortality (all heart transplants in the world between 2002 and 2006, *n* = 8823)

Factor	Relative risk	p-value	Confidence Interval 95%
Extracorporal circulation / assist device / ECMO pre HTx	3.19	< 0.0001	2.32 - 4.37
Diagnosis: congenital vs. cardiomyopathy	1.89	0.0002	1.35 - 2.64
Mechanical ventilation	1.50	0.0044	1.13 - 1.98
Pre-transplant hemodialysis	1.48	0.0021	1.15 - 1.19
Infection with antibiotics i.v. in the 2 weeks pre-HTX	1.30	0.0047	1.08 - 1.56
AB0-unidentical (ex. 0 to A)	1.25	0.0067	1.06 - 1.46
Blood transfusions	1.19	0.0432	1.01 - 1.41
Diagnosis: ICM vs. DCM	1.16	0.0431	1.00 - 1.35
i.v. inotropes pre-transplant	0.85	0.0282	0.73 - 0.98
Recipient age		< 0.0001	
donor age		< 0.0001	
Donor BMI		0.0288	
Center volume		0.0032	
Ischemic time		0.0060	
Pulmonary pressure		0.0004	
Serum bilirubine		0.0006	
Serum creatinine		0.0001	

Lung transplantation

Lung transplantation (LTx) has become a routine therapeutic procedure for lung diseases that cannot be cured conservatively, now counting around 20.000 cases in the world (14).

Indications

The indications for LTx cover a broad spectrum. Depending on the primary disease, some patients reveal a rapid deterioration or a rather stable course. Therefore, the timing in putting the patient onto the waiting list is essential. The International Society for Heart and Lung Transplantation (ISHLT) (14) has developed strict criteria for listing for LTx, as summarized in Table 4.

Table 4: Indications for lung transplantation

COPD/ Emphysema
BODE-Index > 7 or one of the following states: ☐ FEV1 < 20% after bronchodilation and DLCO < 20% or a homogeneous distribution of emphysema. ☐ Multiple hospitalizations due to increasing hypercapnia ($PaCO_2$> 55 mmHg) ☐ Secondary pulmonary hypertension under oxygen substitution
Idiopathic pulmonary fibrosis
Histological or radiological diagnosis of one of the following criteria: ☐ DLCO < 40% predictive value ☐ decrease of vital capacity > 10% in 6 months ☐ saturation of oxygen < 88% at 6 minute test ☐ honeycomb lung in the high-resolution CT
Cystic fibrosis (Mucoviscidosis)
☐ FEVI < 30% predictive value after bronchodilation or sudden drop in FEV1 ☐ Hypercapnia ☐ PaO2 < 55 mmHg at rest ☐ Secondary pulmonary hypertension despite oxygen substitution
Pulmonary hypertension
Heart failure NYHA III-IV
Shortening (<350m) or sudden drop of the walking distance
CVP > 15 mmHg
Cardiac index < 2 L/min/m2
Failure of drug therapy

Single lung transplantation (SLTx) is in principle possible and indicated in patients without infectious complications or pulmonary hypertension. In the later double lung transplantation (DLTx) is recommended. Accompanying right heart failure or congenital heart defects, with Eisenmenger reaction, require a combined heart-lung transplantation. The bilateral sequential technique for DLTx has replaced the en-block-DLTx technique. The two lobes are implanted one after another. This decreases the necessity for the usage of the heart-lung-machine.

Immunosuppression

The established immunosuppressant combination therapy after LTx is a triple therapy, consisting of tacrolimus, mycophenolate mofetil and steroids. Proliferation signal inhibitors (PSI) such as sirolimus or everolimus, should not be administered immediately after LTx, because they interfere with the healing of the bronchial anastomoses. If PSI's can prevent bronchiolitis obliterans, is currently under investigation and there are some encouraging data. There are no consistent data concerning the advantage of an induction therapy after Ltx.

Results

According to the ISHLT data (14), survival after LTx has improved between 1994 - 2006 up to 88% at 3 months, 78% at 1 year and 51% at 5 years. DLTx leads to better results compared to SLTx. Chronic rejection presenting as bronchiolitis obliterans syndrome (BOS) is still the major limiting factor for long-term success after LTx. The prevalence of BOS is 9.2% after 1 year, 33.8% after 5 years and 46.3% after 10 years.

Post-transplant care

Regular ambulatory checkups are necessary in the early stage after Tx. After HTx, endomyocardial biopsies are usually performed on a monthly basis followed by annually performed coronary angiograms.

After LTx lung function testing on a regular basis is mandatory for the early detection of BOS. Trough level monitoring and dose adjustments of the immunosuppressive medication should always be in the hands of a specialized transplant centre.

The importance of a close relation between the patient and the transplantation centre cannot be underestimated and is a key to long-term survival.

The four corner stones in the long-term care of patients after heart and/or lung transplantation are:

- ☐ Close monitoring of the immunosuppressive therapy
- ☐ Early recognition and treatment of drug side effects
- ☐ Recognition and treatment of acute or chronic rejection
- ☐ Psychological support of patients and their families

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Part 4.

POSTOPERATORY PATHOLOGY

Stent restenosis, coronary anatomic-lesional complexity and revascularization possibilities*)

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Introduction

Intrastent restenosis (ISR) after initial succesful revascularization procedure is an unsolved issue in continuos debate (1, 2, 3, 4).

Primary mechanism of ISR is the neointimal tissue proliferation. The re-occurrences rate of ISR remains greater than 30%. (5, 6, 7) The main tool for ISR diagnosis is coronarography analysis. Recently, 64 MSCT started to gain credibility due to its more analytic and noninvasive technique. (8, 9) Based on restenosis complex phenomenon, the development of rapamicine and paclitaxel covered stents (DES) seem to solve this problem, when compared with metallic stents (BMS). This is true only in a small degree because ISR lesions continue to appear even in DES years (10, 11, 12, 13, 14).

Other factors concurring to ISR initiation and progression, beside already mentioned neointimal proliferation, are: lesion complexity, initial coronary anatomic features which needed stenting, prevention measure, endothelial dysfunction, stent thrombosis etc. (9, 15, 16, 17, 19, 20) All these mechanisms interfere with ISR stages, from initialization to endothelial growth. This explains why ISR can be presented under multiple clinical and pathologic aspects.

In this study we focused only on those patients who developed stenotic lesions between 2 months and 2 years after initial PCI. Based on lesions structure we classify patients into 4 lots:

- ⇨ **A** – those with isolated intrastent stenosis;
- ⇨ **B** – patients with patent stents coexisting with stenotic stents and with new appeared hemodynamic significant lesions (new coronary stenosis > 50%);
- ⇨ **C** – patent stents coexisting with stenotic stents;
- ⇨ **D** – patent stents coexisting with new coronary lesions. Based on these admitting criteria we study the restenosis phenomenon and criteria for revascularization for each lot.

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Objectives

The main objective of this study was to reveal the complexity of ISR and to try to find out predictive features for this event. Thus, we focused our analyze on the following bias: lesion pattern before revascularization, location of significant lesions within coronary tree, coexisting patent stents with stenotic ones or/and with new lesions, structural and size issues of different used stents and re-revascularization opportunity (PCI vs CABG).

Material and methods

This is a retrospective study on 286 patients with stent restenosis. Study protocol consisted in: anatomic-lesional quantification (by coronarography done before and after revascularization) using SYNTAX score SYNergy between PCI with TAXus and cardiac surgery), (21, 22); clinical picture examination; analyzing different restenotic particularities in regard to A,B,C and D lots of patients; individualizing restenosis therapy by admission criteria.

Study selection/exclusion criteria

Our study was retrospective taking in account only patients that developed stenosis of the implanted stent after initial revascularization therapy. We excluded from the study patient with severe coronary lesions unable to be treat through revascularization and patients with poor cardiac performance (E.F. < 30%).

Patients' pool structure

Knowing the complexity of ISR phenomenon we studied the patients' pool using "real word" system. Between 2004 and 2007, coronarography check-up was done for 286 patients underwent PCI or surgical revascularization. The entire lot was structured in four pathologic lots: A – patients with ISR; lot B – patients with patent stents coexisting with ISR and with new hemodynamic significant lesions; lot C – patients with patent stents coexisting with ISR; and lot D – patients with patent stents coexisting with new coronary lesions. Working protocol diagrame is presented in figures 1, 2 and 3.

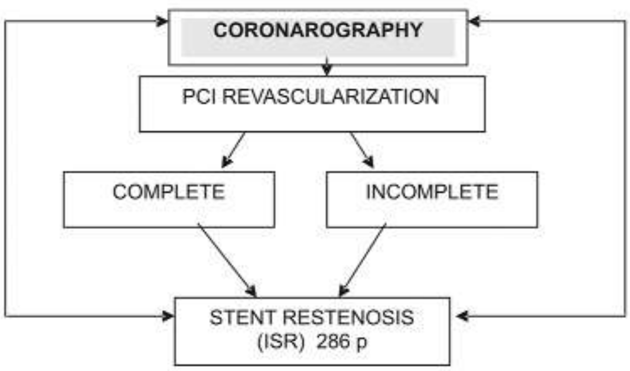


Figure 1: Working protocol

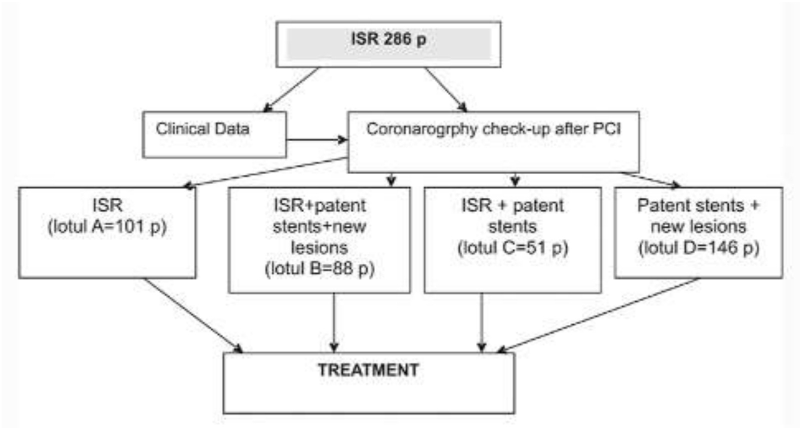


Figure 2: Patients clasification in lot based on presence of ISR, patent stents and/or new coronary lesions

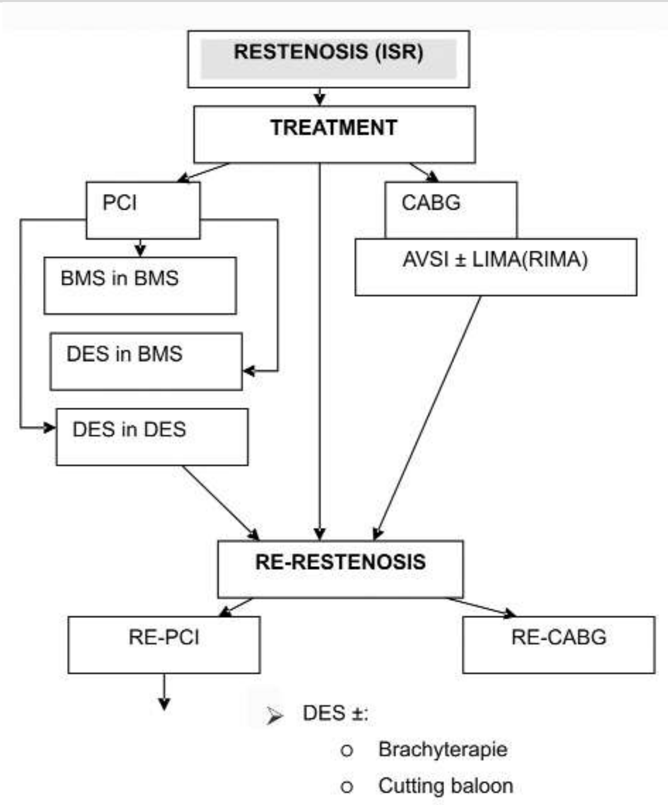


Figure 3: The complex treatment of restenosis and re-restenosis

Results

We will present the results of this study based on the protocol parameters reminded above. Also we will try to present these results with respect of the deductive sequence which guided the study and try to connect these results with the leading control issue, naming here the restenosis and the progression of atherosclerosis in the presence of patent or restenosed stent (table 1).

Table 1: Clinical data collected during the study

		No. Patients	%
Patients		286 p	100,0
⇨ Male		220 p	76,9
⇨ Female		66 p	33,1
Silent ischemia		83 p	29,0
Stable Angina (CCS)1-2	1-2	64 p	22,0
	3	106 p	36,3
	4a	52 p	18,2
	4b	42 p	15,2
	4c	22 p	8,2
Unstable Angina		67 p	23,4
Prior hx of CABG		42 p	
Myocardial infarction		58 p	
Associated pathology	HBP	135 p	47,3
	Diabetes Mellitus	87 p	30,4
	Dyslipidemia		56,3
	MI hx		24,8
	Carotid artery involvement		14,3
	PVD		20,5
	COPD		14,3
Cardiac Insufficiency		26 p	9,1
Pre-PCI medication	antiplatelets	216 p	75,5
	⇨ Clipidogrel		
	⇨ Aspirin		
	Enzime conversion inhibitor	242p	84,6
	Sartans	86p	30,0
	Beta blockers	183p	63,9
	Ca channel blockers	72p	25,1
	Nitrates	236p	82,5
	Statins	94p	32,8
	Trimetazidine	226p	79,0
	K Anti-Vitamines	56 p	19,5

Clasification regarded to admission criteria is presented in Figure 4. ALS pre-PCI and in restenosis, across the 4 lots of patients - Figure 5.

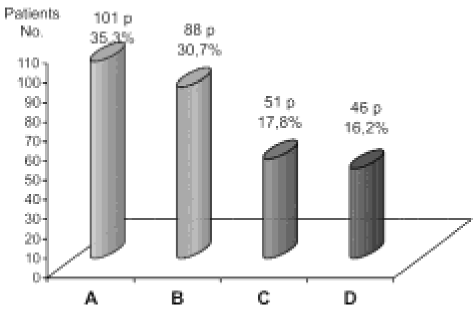


Figure 4: Patients groups after coronarographic evaluation of the restenosis: **A** = *stent restenosis*, **B** = *restenosis + permeability + new lesions*, **C** = *restenosis + permeability*, **D** = *permeability + new lesions*

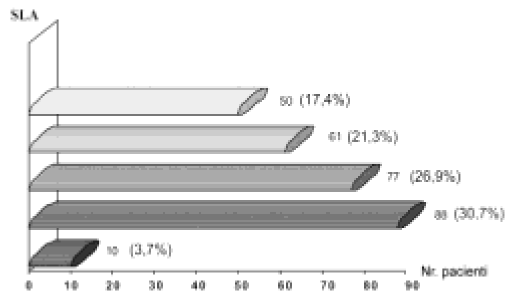
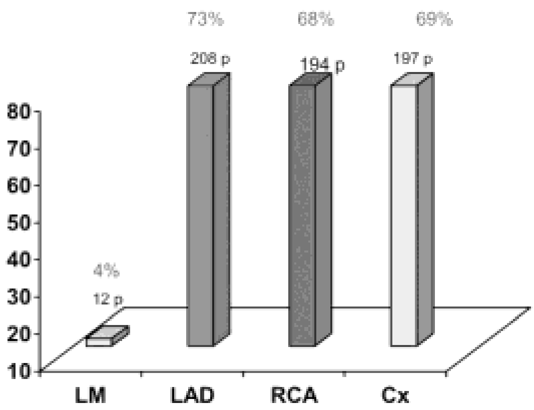


Figure 5: Anatomic-Lesional Score (ALS) distribution of pre-PCI signifiant stenosis compared to total number of patients with PCI and restenosis.



Studying the relation between incidence of restenosis or occlusion and coronary vessel location, we found a lesser incidence on left main ($p < 0.05$) while, between left anterior descendent, right coronary and circumflex artery, there are not significant statistic differences ($p > 0.005$) (Figure 6).

Figure 6: Relative the same percent for LAD, RCA and Cx. Minimal involvement of LM. $P < 0.05$ (LM)

We summarized on table 2 the result of measurements after PCI for A+B+C+D lots, the type of intervention done and the type of stent used.

Table 2

Residual stenosis (%)	15 ± 10%
Lesion length (mm)	31,5 ± 8.1
Reffered diameter(mm)	2,94 ± 0.68
Stent length (mm)	38,4 ± 10.5
Stent diameter (mm)	2,5 ± 0.86
Stents number per segment	2,1 ± 0.7
MDL post PCI	2,54 ± 0.71
Tree coronarians (%)	14.9%
Succes revascularization	97.7%
Stent on bi-, tri-furcation (%)	5.3%
Prior CABG (%)	0.7%
TIMI Flow-3 post PCI (%)	96.9*
EF	57.6 ± 11.8
Type of stent:	
• BMS (p), (%)	188 (65.7%)
• DES 37	(12.9%)
• DES+BMS	61 (21.4%)

The results obtained by analyzing study's parameters on A, B, C, D lots (e.g. involved coronary, the size of the vessel, pre-stenting and restenotic SLA (SYN- TAX), lesion on bifurcation, number of stents per patient, type of stent), were presented on tables 3, 4, 5, and 6. Prevention therapy was administered for 9-12 months; the restenozis time was ranged from 2 to 32 months.

Table 3: ISR (101 patients) – A lot

Stented coronary w/ restenosis	(lesions no.)
⇨ LM	
⇨ LAD	114
⇨ Cx	96
⇨ RCA	101
Vessel size	2,1 ± 1,7
SYNTAX score	
⇨ initial	22 ± 8,1
⇨ Restenosis	25 ± 7,3
bifurcated lesions, stented and w/ restenosis	1 ± 0,9
number of stents	3,8 ± 1,1
stent types:	
⇨ BMS	63 p
⇨ DES	12 p
⇨ BMS+DES	26 p
Prevention medication:	
⇨ Clopidogrel	101 p (100%)
⇨ Aspirin	92 p
Time untill restenosis	2-24 months

Table 4: ISR + patent stent + new signifiant lesions (88 p) - B lot

	Restenosis (Stent No./Patient)	Patent stent (Stent No./Patient)	Signifiant new lesions / patient (Lesions No./patient)
PCI on:			
• LM			2,2 ± 0,3
• LAD	1,8 ± 0,7	2,8 ± 1,6	1,4 ± 0,1
• Cx	1,8 ± 0,6	1,3 ± 0,5	1,1 ± 0,4
• RCA	1,7 ± 0,6	1,1 ± 0,2	1,6 ± 0,2
Vessel size (mm)	1,7 ± 0,6	1,1 ± 0,2	1,6 ± 0,2
ALS (SYNTAX)	1,8 ± 0,9	2,2 ± 0,7	1,7 ± 0,5
• Prior to stenting	21 ± 7,3	36 ± 5,2	44 ± 11,5
• After stenting	24 ± 6,4	12 ± 4,4	-
Lesions on bifurcations	3,1 ± 0,7	0,8 ± 0,5	1,6 ± 0,8
Stent numbers	2,1 ± 1,4	1,3 ± 0,6	-
Stent types:			
• BMS	1,9 ± 0,7	2,0 ± 0,6	1,3 ± 0,9
• DES	0,1 ± 0,02	3,1 ± 1,1	1,4 ± 0,3
• BMS+DES (stent no./patient)	0,11 ± 0,8	1,8 ± 0,5	0,8 ± 0,07
Time to restenosis	2-32 months	2-32 months	2-32 months
Preventive medication	6-12 months	6-12 months	6-12 months

Table 5: ISR and patent stents (51 p) – C lot

	Stent restenosis (Stent No./Patient)	Patent stent (Stent No./Patient)
PCI on:		
• LM	0	0
• LAD	1,4 ± 0,7	0,8 ± 0,06
• Cx	1,1 ± 0,3	0,4 ± 0,08
• CD	1,8 ± 0,6	1,0 ± 0,2
Vessel size (mm)	2,3 ± 1,1	2,3 ± 0,9
ALS (SYNTAX)		
• Prior to stenting	32 ± 7	36 ± 4
• After stenting	34 ± 0,5	26 ± 2
Lesions on bifurcations	0,9 ± 0,07	0,5 ± 0,2
Stent numbers	3,2 ± 0,8	1,1 ± 0,6
Stent types:		
• BMS	2,1 ± 0,6	0,7 ± 0,9
• DES	0,2 ± 0,03	1,1 ± 0,5
• BMS+DES (stent no./patient)	1,4 ± 0,7	1,2 ± 0,4
Time to restenosis	2-32 months	2-32 months
Preventive medication	6-12 months	6-12 months

Table 6: Patent stents with new stenotic lesions (46 p) – D lot

PCI Patent vassel	Patent stent (Stent No./Patient)	New Lesions (Lesion No./Patient)
• LM	0	0,4 ± 0,05
• LAD	3,1 ± 0,6	1,1 ± 0,5
• Cx	2,8 ± 0,7	2,1 ± 0,2
• CD	3,4 ± 0,7	1,8 ± 0,7
Vessel size (mm)	3,1 ± 1,2	1,3 ± 0,7
ALS (SYNTAX)	11,3 ± 1,5	25,4 ± 2,4
• Prior to stenting		
• After stenting		
Lesions on bifurcations	2,1 ± 0,7	1,7 ± 0,4
Stent numbers	3,1 ± 0,9	-
Stent types:		
• BMS	3,2 ± 0,7	1,2 ± 0,9
• DES	1,7 ± 0,5	1,6 ± 0,7
• BMS+DES (stent no./patient)	2,3 ± 0,8	1,3 ± 0,5
Time to restenosis	2-32 months	2-32 months
Preventive medication	6-12 months	6-12 months

Restenosis therapy consisted in interventional revascularization in 106 patients and surgical CABG in 132 patients. Drug therapy only was the best option for 46 patients without revascularization possibilities. Treatment procedures for each lot are presented in Figure 7, 8 and 9.

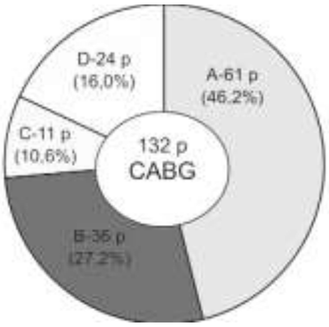


Figure 7: CABG revascularization for each lot of patients (A, B, C, D)

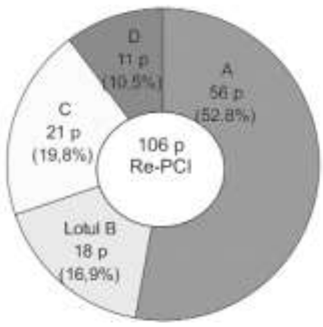


Figure 8: PCI for ISR ("stent in stent") for lots A, B, C, D

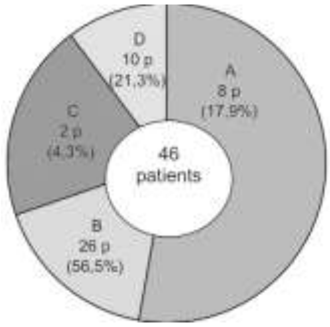


Figure 9: Pharmacologic therapy for patients from A, B, C, D lots

Taking in account the type of stent used previously (DES vs BMS), as an important factor in restenosis genesis, we analyzed in Figure10 their repartition during the different lots.

Other helping techniques used for treating stent restenosis were: bracytherapy, cutting balloon, directed atherectomy and rotablation (Figure 11).

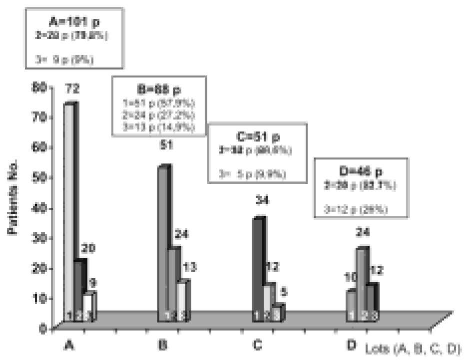


Figure 10: Types of implanted stents (1=BMS; 2=DES; 3= BMS+DES) and ISR on patients' lots A, B, C, D

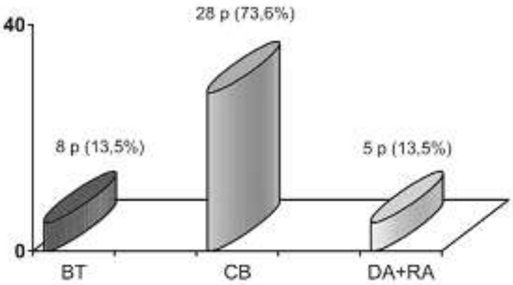


Figure 11: Therapy procedures done for stent restenosis: *Brachytherapia* **(BT);** *Cutting balloon* **(CB);** *Directed Atherectomy* **(DA);** *Rotablation* **(RA)**

Discussions

Stent restenosis (ISR) after successful interventional revascularization is an unsolved problem which changes periodically and tends to become permanent because of multiple factors which determine its genesis: coronary lesions particularities, inflammatory response triggered by stent implantation trauma, the structure and composition of the stent, preventive drug therapy used etc. (15, 23, 24, 25).

We proposed to study the restenosis phenomena in all possible clinical situation encountered using coronarographic control after clinical and ECG criteria. Stent repermeabilization or surgical revascularization was done after criteria imposed by anatomic and lesion particularities. This explained why patients were admitted in 4 different study groups (A, B, C and D).

For pre PCI and restenotic quantification were used SYNTAX criteria because this one analyzes significant lesion by their numeric features.

The anatomic-lesional concordance of ALS before PCI and in restenosis, especially within A lot patients (85.3%), based on the SYNTAX score, made us to presume the importance of this score in pre revascularization stage and to anticipate the grade of future restenosis, with the majore repercussion being the decision of which type of stent to be choose for initial therapy (DES) (21, 22, 25, 26, 27).

For patients in B, C and D lots, the statistic significance of ALS is smaller due to the coexistence of stent patency with ISR and/or new lesions ($p < 0.05$).

We could not find any correlation between restenosis process and constitutive elements of stents because lesion/stent length fraction, stent's diameter and the number of stents were without statistic significance ($p > 0.05$) on all four lots. More, the residual stenosis was in accepted limits (< 10±1.2%) and revascularization was successful in 98.7% of lesions with a TIMI-FLOW-3 post PCI of 96.9%.

Regarding to the type of initial implanted stent which later develops restenosis, we found a more frequent incidence in BMS (186 patients; 65.7%) vs. DES (37 patients; 12.9%). In mixed BMS-DES cases restenoses lesions were found on 61 patients (21.4%).

As per international medical literature, between 2005 and 2007 the use of DES were: in USA and Switzerland more than 90%, Portugal 68%, Germany 21%. Nowadays, there is a descending trend in using of DES. This trend seems to be determined by "BAS-KET-LATE" trial conclusions which stipulate that mortality and nonfatal-MI are more frequent in DES compared with BMS ($p < 0.01$) and after 4 years of follow-up the incidence of MI and death was 6.3% in DES vs 3.9% in BMS ($p = 0.03$).

On the other hand, the "real world" conclusion of this trial is the decrease by 5 times of revascularization needs for patients treated with DES compared with BMS (13, 14).

A particular case in our study was represented by patients from lot B (those with most complex lesions) which raised challenging interpretation issues and questions regarding of why the ISR coexist with stent patency, what is the importance of new lesions for the restneosis, what anatomic features generate the restenosis and how does the lesion's characteristics help in choosing the proper revascularization therapy.

We tried to explain the restenosis through ALS analyze in correlation with vessel size, type of lesion, type of stent (DES or BMS), time to ISR and prevention drug therapy. Another cause of restenosis could be the developing of a new coronary lesion in a location directed by stent presence.

We came to the conclusion that new lesions in immediate proximity (proximal or distal) of the stent can generate ISR by decreasing coronary debit while any other locations of coronary lesions are associated with a greater incidence of stent permeability but the statistic significance of this statement is relative small ($p < 0.05$).

Restenotic mechanism in which coronary flow was not affected by new formed lesions seemed to be generated by inflammatory components and platelets.

We think that if there coexists patent stents, with occluded one as in B and C lots, the explanation should be the same as for lot B (see above), but with specification that the atherosclerotic phenomenon is lent or even stopped, compared to C lot in which this phenomenon doesn't appeared.

Conclusions

Interventional revascularization after coronarography criteria was done to the entire pool of patients (286) taking in account the dominant principle of complete revascularization. In this order, the figures of complet vs. incomplete revascularization is relevant: 231 patients, (87.8%) versus 35 patietns, (12.2%) with a statistic value of $p < 0.05$.

ISR is a complex phenomenon caused by multiple factors: location, new anatomic lesions, coexisting with a patent stent. Its treatment consist in re-PCI, aorto-coronarian by-pass (CABG) or pharmacologic therapy ("no option").

Re-PCI procedure was done mainly by using DES type of stents (rapamicine, paclitaxel etc) and CABG took account of complete revascularization principle.

Stent restenosis phenomenon explaines the continuous concern in finding new types of stents, like: biodegradable, impregnated with pharmacologic agents with progressive release, new anti-restenotic agents, double coated, endothelial progenitors etc. An essential contribution to early discover of restenoses and atherosclerotic progression can be made by using of new coronary studies like angiographic-CT, with its 16 MSCT, 64 MSCT and especially 256 MSCT variants.

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Tardive salvage therapy after ineficient fibrinolysis*)

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Abstract

The purpose for the study: *Our study analize the corelation between coronarografic aspect and the revascularization solution choosed for pacients with restant post-infarction angina after a succesful farmacologic thrombolisis for acute myocardial infarction.*

Method and Results: *Between 2002 and 2004 we encountered 120 patients who developed residual angina in the first 6 months after an acute event (AMI) with ST segment elevation treated with fibrinolitic therapy in the first 12 hours. We investigated this patients underwent coronarographic study. The age panel spreaded from 22 to75 year-old. In 30 p. the location of AMI was in the inferior teritory; in 11 cases was infero-lateral, anterior in 16 p., antero-lateral in 2p., antero-apical in 10 p., antero-septal in 20 p., lateral in 4 p., postero-infero-lateral in 12 p., anterior and inferior in 4 p. We used streptokinase (64 p.), alteplase (26 p.) and reteplase (30 p.). The thrombolitic therapy was applied in the first 6 hours after pain emerge in 86 p. and in the first 12 hours at 34 p. The coronarographic study was done in the first 6 months after AMI. There were detected 37 p. with one coronary lesion, 33 p. with double coronary lesions and 49 p. with triple coronary lesions. One patient had normal coronarographic study. The affected vessels were: left anterior descendent (LAD) - 101 lesions (L), circumflex (CX) - 60 L, right coronary artery (RCA) - 74 (L), left main (LM) - 16(L).*

In 19.5% of patients the stenosis was minimal (<50%) whereas in the rest of 80.5% cases the encountered stenosis was subcritical, critical or suboclusive. Coronary lesions' morphology were of type A (57L), B (175L) and C (19L). All of 120 patients were treated by one of the following methods: CABG (55p – 45.8%), PCI (45p – 37.5%) and improved medical therapy (20p – 16.7%). Our criteria in choosing the therapy was: uni- and bi-coronary lesions underwent PCI and LM and trivessel lesions underwent CABG.

Conclusions: *There is a severe alteration of coronarian circulation after an AMI, which can be included in the recent concept of „pancoronaritis"; this can be proved and quatified through coronarographic study. In our cases fibrinolithic therapy alone proved to be insuficient, patients needing a secoundary therapy for revascularization, so called „tardive salvage therapy" (PCI or CABG, depending of lesions morphology and the degree of stenosis).*

Key words: *Inefficient fibrinolysis, coronarography, tardive salvage therapy, myocardial revascularization*

*) **Romanian Journal of Cardiovascular Surgery ■ 2008, vol. 7, no. 4, pp. 221-234**

Introduction

Using any available reperfusion strategy after an AMI (ideal, in the first hour after pain onset – so called „golden hour”) (1) it showed to improve both, mortality and morbidity (2, 3, 4, 5, 6, 7). In 15-50% (8, 9) of cases pharmacologic thrombolysis is unable to restore the patency of the affected coronary artery (ACA). The blood flow in this artery can be evaluated through TIMI 3 or by analyzing the modification of ST elevation. Unfortunately, in other 5-15% of patients a previous pharmacological restored ACA can early reocclude, which also increases the total AMI mortality (10, 11).

Lincoff and Topol in 1993 came with the idea of “reperfusion illusion” (12).They observed by coronary angiography, that number of patent ACA at 90 minutes after the initiation of pharmacologic thrombolysis was overestimated when compared with cases of real tissu perfusion. In conclusion, there is a real restore of blood flow in only 1/3-1/4 of patients after thrombolysis (13). The rest of cases came together under the „*inefficient fibrinolysis* (IF)” umbrella, other early salvage procedures being necessary in the first 24 hours, as: a secound fibrinolysis attempt (SF), PCI, GPIIb/IIIa medication, CABG or any combination of these techniqs.

The RESCUE trial (Randomized Evaluation of Rescue PCI with Combined Utilization End Points) had showed a decrease of mortality in admitted patients and an improvement of composite end-point, represented by mortality and heart failure, in anterior AMI patients who underwent PCI after a previous inefficient trombolysis. In these cases PCI was done in the first 8 hours from symptomatology onset (14).

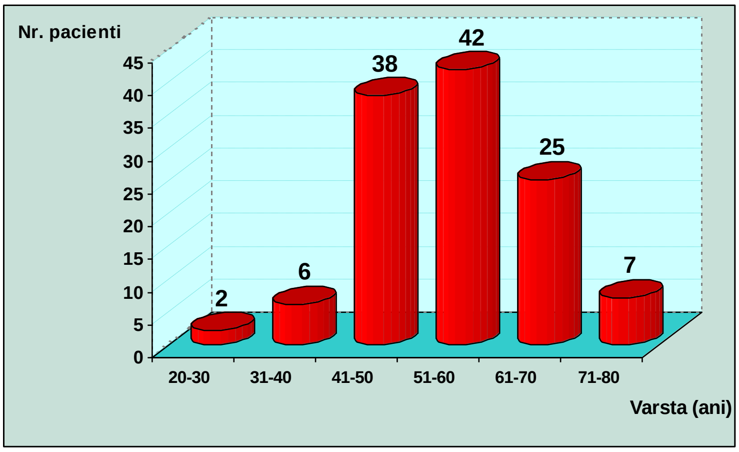
All these studies show that pharmacologic fibrinolysis alone is unsuficient for restoring the blood flow through coronary vessels after AMI. More, a number of patients suffer of late reocclusion phenomenon which can affect 25-30% of previous ACA in the first year after reperfusion. These cases contribute also to the increase of overall AMI mortality (15). All these issues impose the concept of tardive salvage therapy which refers to the new therapeutic strategies after PhF.

Purpose

Our study intends to analyze the correlations between coronarographic features found and the therapeutic solution adopted in AMI patients with post-infarction angina who underwent a previous early PhF, in our center (CCUBCVA).

Material and method

The study group was composed by patients admitted between January 2002 and April 2004 for coronarographic study in our center. Patients were referred for residual angina (early and late) after early PhF-lized AMI. All the coronarographic studies were done between one week and 6 months after AMI with the purpose of evaluate the best therapeutically solution.



There were 120 patients evaluated through CA. Of these, 99 were males (82.5%) and 21 females (17.5%). Patient's age ranged from 22 to 75 years-old (Figure 1).

Figure 1 – Age distribution of thrombolysed AMI (t AMI).

From 120 patients, 61 presented with anterior AMI and 43 had inferior AMI (Figure 2).

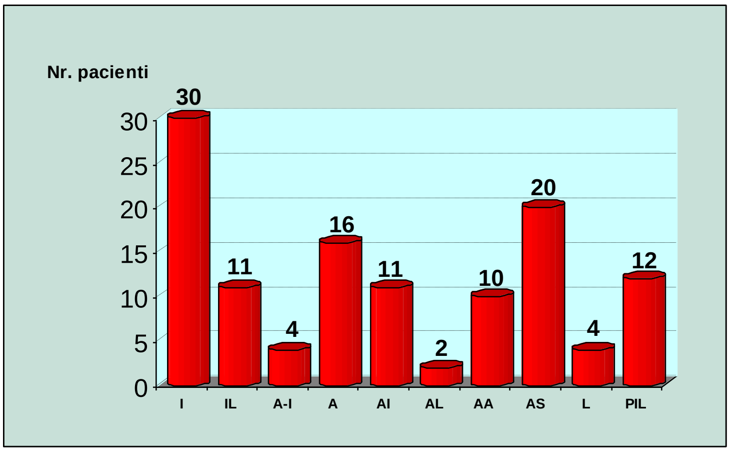


Figure 2: – t AMI territory: inferior (I), infero-lateral (IL), anterior and inferior (A-I), extended anterior (AI), antero-lateral (AL), antero-apical (AA), antero-septal (AS), lateral (L), postero-infero-lateral (PIL). After at most 6 months from the acute event. For 82 of the patients (68%) CA was done in the first month after AMI.

The PhF substances used were: streptokinase for 64 patents (53.4%), alteplase for 26 (21.6%) and reteplase in 30 patients (25%).

Fibrinolysis was done in the first 6 hours from the onset of myocardial infarction for 84 p. (72%) and in the first 12 hours for 36 p. (28%).

After precise evaluation of coronary lesions, a therapeutic strategy was chosen: interventional (PCI), surgical (CABG) or medical (drugs). This late option was reserved for those patients with contraindications for revascularization ("without option").

Results

From the CA point of view, 37 had one coronary lesion (31%), 38 p had two coronary lesions (31.6%), 28 p had three coronary lesions (23.3%), 16 presented with left main - LM – 13.3%) and only one reveled permeable coronary system (0.8%) (Figure 3).

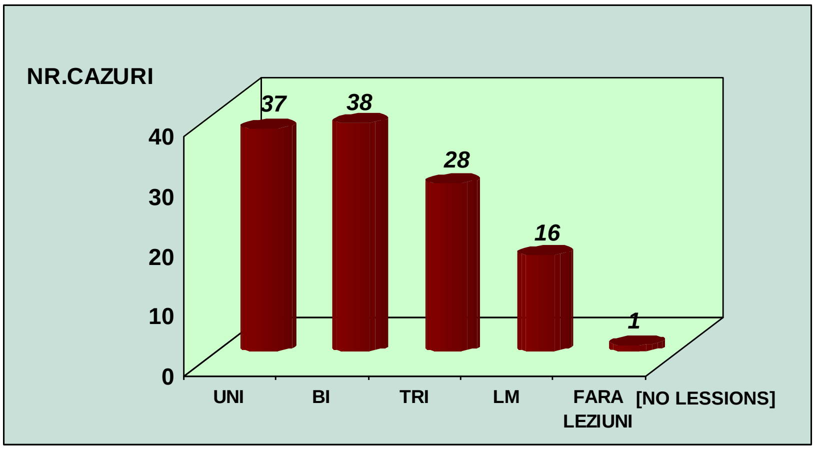
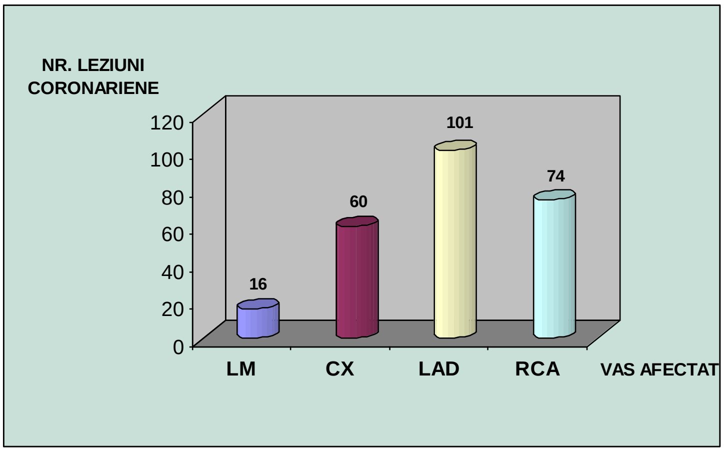


Figure 3: Number of affected coronary arteries after fibrinolysis

From those 37 p. with one coronary lesion, 26 had it on LAD (70%) while 11 p had lesion only on RCA (30%); from those 38 p with two coronary lesions, 17 had major stenosis on LAD and CX (45 %), 16 had lesions on LAD and RCA (42%) and only 5 p had lesions on CX and RCA (3%).



From the total of 120 cases were discovered a total of 251 significant coronary lesions (with > 50% stenosis): 101 on LAD (40.2%), 74 on RCA (29.5%), 60 on CX (24%) and 16 on LM (6.3%) (Figure 4).

Figure 4: Affected vessels after fibrinolysis

The affected LAD was found as unique lesion in 28% from the total number of lesions, whereas it appeared as part of bi-coronarian disease in 39% and as part of tri-coronary disease in 33% of lesions (Figure 5).

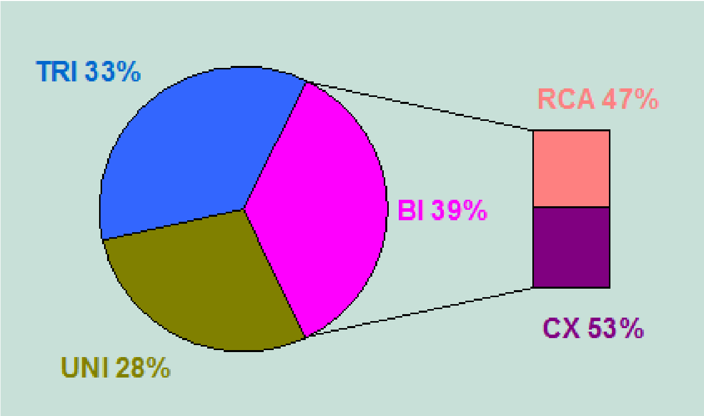
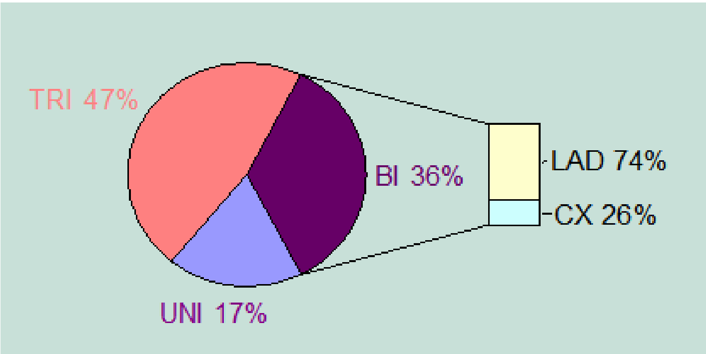


Figure 5 - LAD – unique lesion (UNI) (28%) and associated: bi-(BI) (39%) and tri-vessels (TRI) (33%)



The affected RCA was found as unique lesion in 17% from the total number of lesions, whereas it appeared as part of bicoronarian disease in 36% and as part of tricoronary disease in 47% of lesions (Figure 6).

Figure 6: RCA – Uni-, bi- and tri-coronary cases

The affected CX was found as part of bi-coronarian disease in 46% and as part of tri-coronary disease in 54% of lesions. There was neither one case with CX lesion as a single vessel disease (Figure 7).

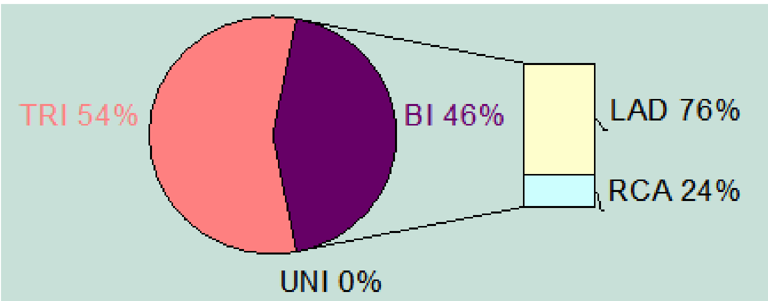


Figure 7 - CX – uni- and tri-coronary cases.

The coronary disease found through CA on this study group of previous PhFed patients was multiple, varying as severity and number of affected vessels. This issue was confirmed by the degree of residual stenosis and their distribution on the coronary map after PhF (Figure 8).

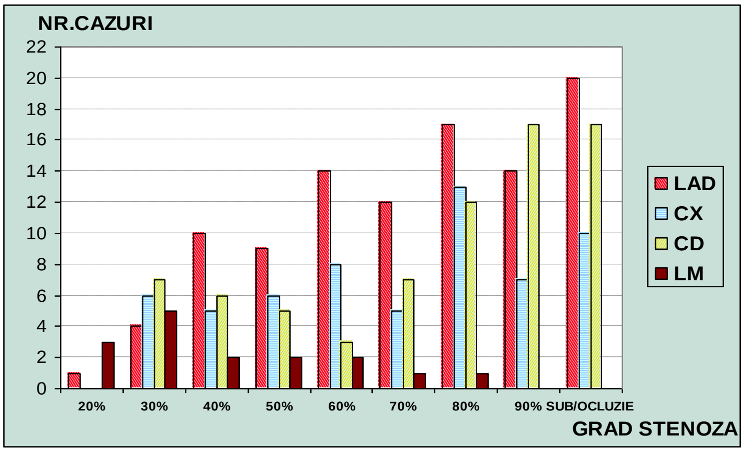


Figure 8: The degree of residual stenosis and the affected vessels

In 20% of lesions there were a minimum residual stenosis (<50%) but the rest of 80% of lesions we countered severe (29%) or critical stenosis (> 70% to occlusion) (51% of lesions) (Figure 9).

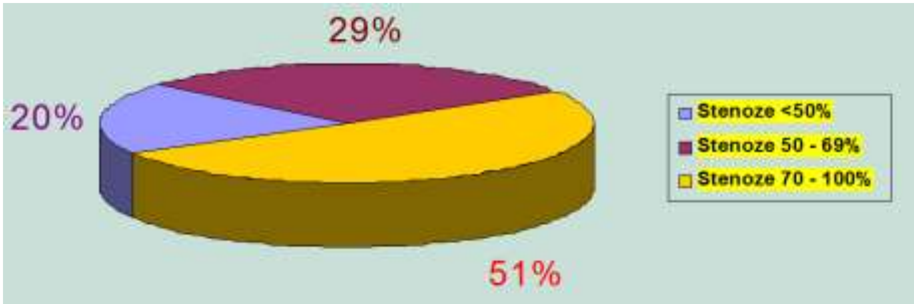


Figure 9: The severity of stenosis by coronarography.

From the total worked-up patients, only 8 p had stenosis less than 50%, 20 p. had stenosis between 50-69%, 91 p. had stenosis > 70% and one patient had permeably coronary arteries (Figure 10).

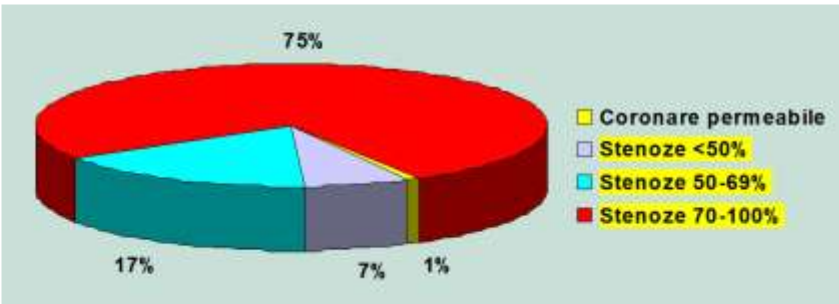


Figure 10: The severity of stenosis by coronarography

It is remarkable that critical stenosis (> 70%) were found in 91 p, which means 75% of those 120 with coronarographic study done. Analyzing the degree of stenosis with the extend of coronary system disease on these patients, the were 22 p with one coronary lesion, 31 p with two coronary lesions, 26 p with three coronary lesions and 12 p with LM (Figure 11).

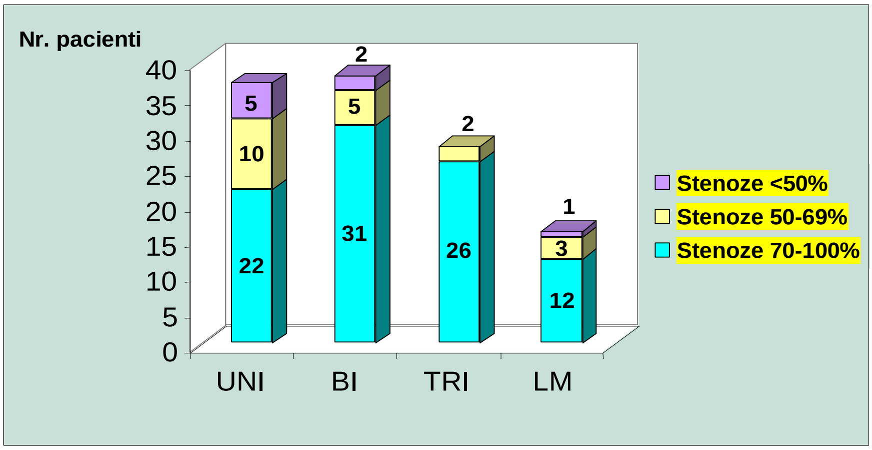


Figure 11: Correlation between stenosis severity and the number of affected vessels.

Morphological we found that the main lesions was of type B, especially on those patients with significant hemodynamic stenosis (> 50%) (Figure 12).

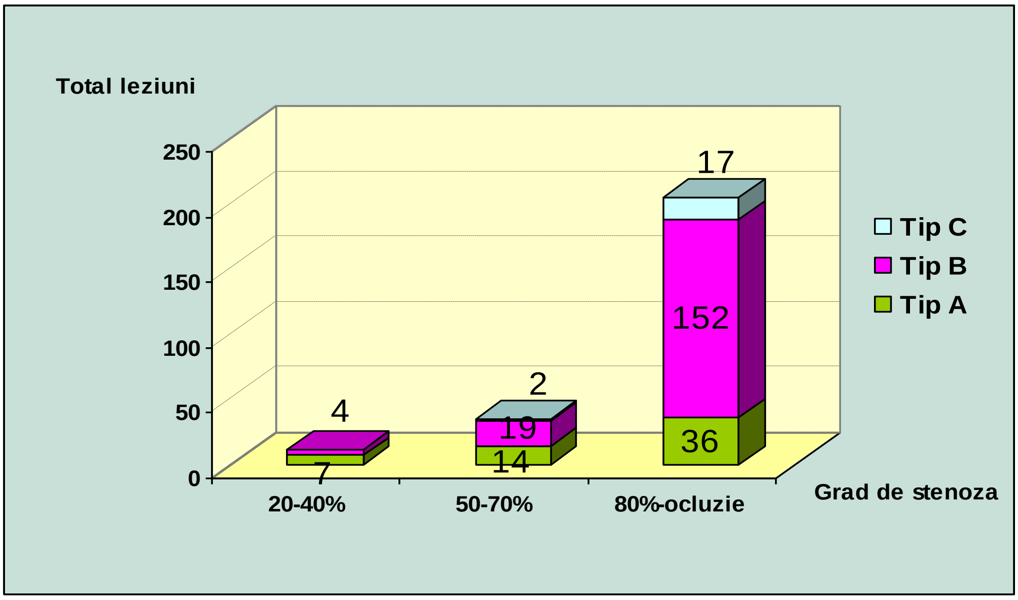


Figure 12: Distribution of morphologic type of lesions.

From 120 p with AMI previously treated by PhF, who undergone through CA study, we found that 100 p beneficed from another revascularization technique as follow: 45 p underwent to PCI and 55 p to CABG. Only in 20 cases patients unable to support a revascularization intervention were prescribed a more optimized medical therapy (Figure 13).

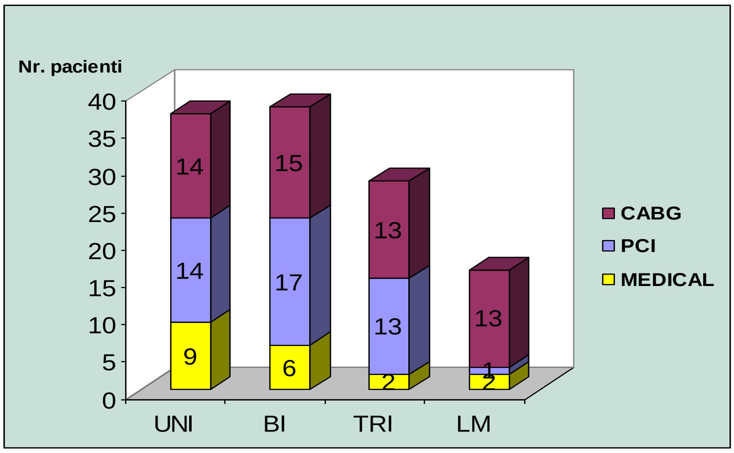


Figure 13: Tardive salvage therapy adopted after post-fibrinolysis coronarography.

Discussions

It is paramount accepted that the primary objective in acute myocardial infarction management is to obtain as fast as possible a sustained recanalization of the blamed coronary. There are three reperfusion options: thrombolysis, PTCA and emergent aortocoronary bypass and, of course, any combination of these.

There is a recent meta-analysis (16) which demonstrates an evident benefice for primary intention PCI versus pharmacologic thrombolysis. A criterion used was the improvement of composite end-point index: death, reinfarctization and stroke. The most important conclusion is that the benefice was obtained even for cases when PTCA was delayed due to the lack of availability of a interventional clinic nearby.

In contrast, the 2004 revised -ACC/AHA guide for management of AMI with ST elevation (17), concludes that there is not one best paramount reperfusion strategy for all cases. Even if the interventional reperfusion seems to be the best primary option therapy for AMI, it lacks points because of its poor availability (it is considered the primary intention therapy if there are a minimum of 200 PTCA done per year and if it has a cardiac surgery unit nearby) (17).

Much more, obtaining angiographic reperfusion after pharmacologic thrombolisis or interventional cardiology is not enough for success due to the „no-reflow” phenomenon which consists of distal micro embolic events post-fibrinolysis and various reperfusion lesions.(20,21,22,23) Also, in 25% of cases, the reoclusion of ARI could happened after the first 2 week from pharmacologic thrombolysis, event which doubles the mortality figures. (24) All these possible events after pharmacological therapy were grouped under the name of „inefficient thrombolysis” (I.F.).

Below is presented a case solved through PCI in the first 2 hours from AMI, after an initial I.F. Figure 14 (A, B, C).

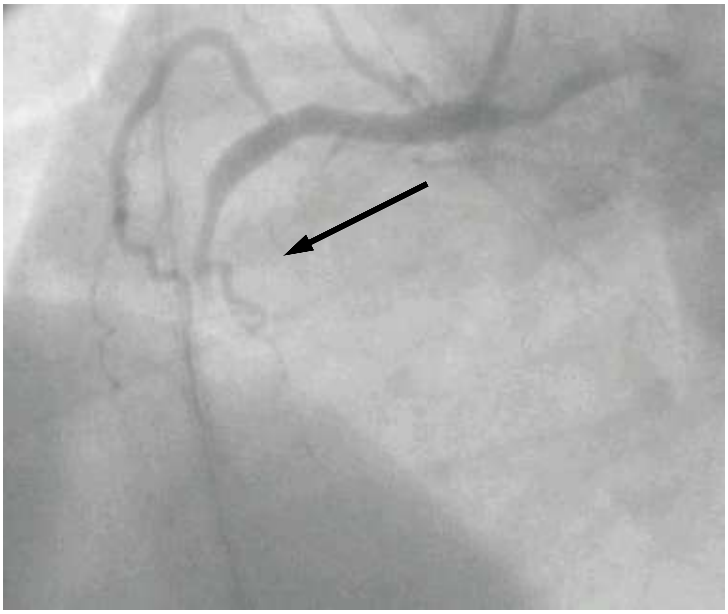
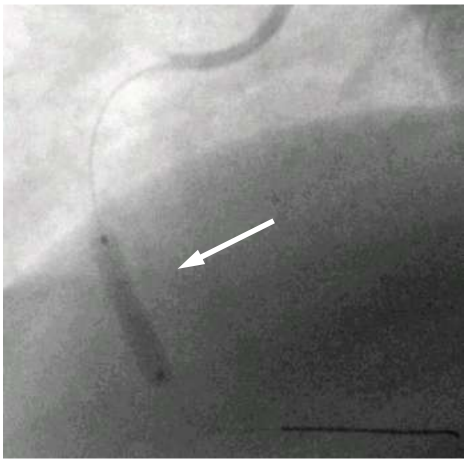
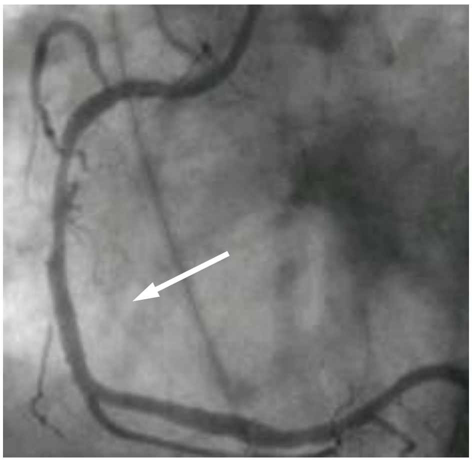


Figure 14 (A): AMI due to thrombosis of RCA – insufficient fibrinolysis.

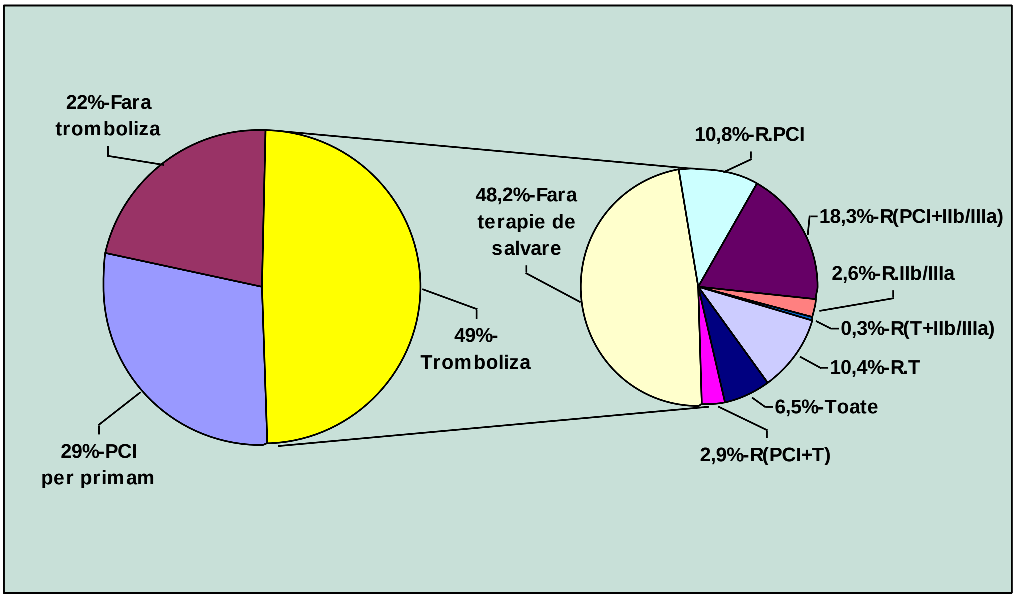




(B) **(C)**

Figure 14 (B, C): PCI (dilation + stent) 2 hours after the onset (B, C).

A recent study (26) shows that after I.F. was diagnosed therapy was diverted toward other options: PCI (74%), redo-thrombolysis (39%), GP IIb/IIIa blocking medication (53%) (Figure 15).



(A) (B)

Figure 15: AMI therapy (A) and salvage therapy(B) - modified after Ronner E. (26)

There are numerous clues that during an AMI the blood flow is decreased not only in the IRA but in the unaffected coronary arteries too, trigger for this being other coexisting high risk lesions beside those responsible of infarctization (27, 29, 30). There are some theories about intrinsic features of cholesterol plaques at the level of IRA and other coronary arteries. This instable plaque phenomenon is not focal to IRA but multifocal which suggested that the infection could occur anywhere in the coronary tree (31).

This dynamic lesion of coronary circulation lyies under the umbrella of „pancoronarities" (31), a phenomena observed after ACS in which both the ACS trigger lesion and those considered initially unsignified, suffer an accelerated atherosclerosing process with unstabilizing the atheroma plaques (32, 33). This is why the pharmacological fibrinolysis is good only in the acute phase of the pancoronarities phenomena and it is insufficient as unique solution for revascularization. Thus it is necessary to adopt further strategies for revascularization (PCI or CABG), so called „tardive salvage therapies", with primary scope of revascularization but also of salvage the hibernating myocardium (34, 35).

In our study, the lesions were multiple and severe, suited to tardiv CABG or PCI.

Most of them were bi- or trivascular and LM (71%) which is specific to the pancoronaritis concept. The incidence of CABG was greater (45.8%) compared with PCI (37.5%) which also indicates a greater incidence of severe lesions (critical stenosis and oclusions).

Due to the presence of multiple affected vessels the ischemia responsible vessel is identified with difficulties. In our study we used for identify this artery all the armamentarium we had: coronarography, echocardiography and ECG. The revascularization procedures, CABG or PCI, were done for all the affected territories.

Both procedures are considered tardive salvage therapies since both increase the the life span and quality after a ST-elevation MI, by reestablishing of coronary patency and normalizing the hibernating myocardial tissue.

Study's limits

This study has a small number of enrolled patients and coronary investigation has been provided only to that patients presenting with post-infarction ischemic symptoms early or tardive angor). Thus, the pancoronaritis phenomenon can't be generalized to all patients with an acute coronary event. Also, it was impossible to follow-up all the patients included in this study. For this reason we cannot provide epidemiologic bias about early and long term mortality and morbidity. On the other hand, the 6 months period between AMI and coronarography could not bring any clue about the evolution of aterosclerosis process on these patients in between. There wasn't done any test for determining the myocardial viability before deciding the need of coronary revascularization, especially for AMI responsible vessels.

Conclusions

The tardive salvage therapy is imposed by coronary lesions preexisting before the acute event. In our study the percent of surgical intervention was of 76 due to the severity, multiple and sequential coronary lesions. Bi- and tri-coronary lesions benefited of surgical revascularization (45.8%) while in the unique coronary lesions was preferred the PCI approach (37.5%). entering on the importance of risk stratification of AMI patients with ST elevation, we should introduce the use of coronary arteriography and revascularization in acute phase. Beside pre PCI evaluation, in AMI an early done coronarography can identify that patient subset with tri-vessel lesions or with Left Main lesions who are candidates for emergency CABG.

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The role of pulmonary hypertension in increasing mortality in surgical aortic stenosis*)

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Abstract

Purpose: *1. Assessment of the predictive factors for the development of the pulmonary hypertension (PHT) in patients with surgical aortic stenosis (AS) 2. Defining the independent predictors for immediate and long term prognosis in these patients and their adjusted value for calculation of a preoperative risk score 3. Evaluation of the PHT involvement as additional perioperative risk factor in patients with AS who underwent aortic valve replacement (AVR)*

Material and methods: *2 years prospective study on 340 pts with AS undergoing AVR. Depending on mean PAP there were identified 3 groups: Group A - 182 pts without PHT, Group B -103 pts with medium PHT and Group C - 55 pts with severe PHT. Statistical analysis used SYSTAT and SPSS programs for simple and multivariate regression analysis and for relative risks and correlation coefficient calculations.*

Results: *1. Multivariate logistic regression analysis has identified as independent predictors for PHT occurence the following parameters: age > 75 years (RR = 6), a LV restrictive diastolic filling pattern (RR = 9), associated moderate mitral regurgitation (MR) (RR = 9, p < 0.0001) 2. The presence of severe PHT has increased the early postoperative risk of death by 7.6 fold, regardless of the presence of other known parameters that increased mortality rate in these patients 3. Regression analysis has identified as independent predictors for early postoperative mortality: mean PAP >50 mmHg, restrictive LV diastolic pattern, age >75 years, interventricular septum thickness >18 mm and the presence of comorbidities. 4. The 2 year follow-up has shown a significant correlation between PHT regression and the LV systolic and diastolic performance (r = 0.19 respectively 0.28), as well as the preoperative dimensions of LV cavities (r = 0.17).*

Conclusions: *1. Relevant independent predictors for PHT occurrence in surgical AS were age >75 years, restrictive LV diastolic filling pattern and the presence of moderate MR. 2.The presence of a severe pHT in patients with AS undergoing AVR is associated with an early postoperative increased mortality rate. The mean PAP is a more reliable parameter for prognosis appreciation than the LV systolic function. 3. The independent predictors for increased early postoperative mortality rate in surgical AS were: mean PAP > 50 mmHg, the presence of a restrictive LV diastolic filling pattern, age > 75 years, IVS thickness >18 mm and comorbidities. 4. PAP regression at 2 years postoperatively was only correlated with pre-operative LV*

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dimensions and systolic and diastolic function and could not be predicted by other clinical or ecographical parameters.

***Keywords**: pulmonary hypertension, aortic stenosis*

Introduction

Severe pulmonary hypertension is present in 15-20% of the patients with surgical aortic stenosos and is associated with higher rates of morbidity and mortality (1-4). Also, long term prognosis in patients with aortic stenosis who added pulmonary hypertension is worse than in those with normal pulmonary artery pressure. Previous studies have not evaluated the influence of pulmonary hypertension on post-operative course in these patients.

Aim

1. Assessment of the predictive factors for the development of the pulmonary hypertension in patients with surgical aortic stenosis.
2. Defining the independent predictors for immediate and long term prognosis in these patients and their adjusted value for calculation of a preoperative risk score.
3. Evaluation of the pulmonary hypertension involvement as additional perioperative risk factor in patients with aortic stenosis who underwent aortic valve replacement.

Material and methods

The study was prospective and included 340 patients with aortic stenosis undergoing aortic valve replacement in our institute between first of January 2006 and first of January 2008. There were not included into study patients with chronic atrial fibrillation, associated aortic valve insufficiency, acute myocardial infarction or coronary lesions, associated mitral or tricuspid lesions. At the moment of study enrolment all patients were in sinusal rhythm.

The majority of patients were male 65%, the mean age of the group was 62 years and the mean gradient between LV and aorta was 75mmHg.

Patients were evaluated both clinically and echographically before surgery and postoperatively at 10 days, 1, 3, 6, months and at 1 and 2 years. For each patient taken into study the clinical measurements included: NYHA class for heart failure, hospitalisation and quality of life. Laboratory parameters included: the usual blood tests (platelet count, hemoglobin, hematocrit, aminotransferases, LDH, biochemistry), electrocardiogram (with the evaluation of rhythm and frequency), and echocardiographic measurements of the left venticular dimensions, sistolic and diastolic performance, left atrium dimensions and compliance Statistical analysis used Systat and SPSS programs for: simple and multivariate, linear and logistic regression analysis, relative risk, confidence intervals and correlation coefficient calculation. The value of pulmonary artery pressure was evaluated using Doppler examination and depending on its value the patients were divided in 3 groups:

- Group A – 182 patients with normal PAP,
- Group B – 103 patients with medium pulmonary hypertension with mean PAP between 30 and 50 mmHg and

- Group C – 55 patients with severe pulmonary hypertension with mean PAP more than 50 mmHg.

Results

1. Multivariate logistic regression analysis has identified as independent predictors for pulmonary hypertension occurrence, the presence in those patients of the following parameters:

- age > 75 years (RR = 6), $p < 0.001$,
- restrictive LV diastolic filling pattern (RR = 9), $p < 0.001$
- Associated moderate mitral regurgitation (RR = 9), $p < 0.0001$.

In this pattern the prediction of the pulmonary hypertension occurrence was made with a sensitivity of 80% and a specificity of 85%.

In Figure 1 there are presented the relative risks associated to the parameters that increase the risk of the pulmonary hypertension occurrence in patients with severe aortic stenosis. The risk of the presence of associated severe pulmonary hypertension to surgical aortic stenosis increased about 6 fold in patients older than 75 years, about 9 fold by the presence of restrictive diastolic filling pattern (respectively by e/a velocity ratio more than 2 by 12 fold and E wave deceleration time < 120 msec 12 fold). In addition, an associated 2 degree mitral regurgitation increased the risk of pulmonary hypertension occurrence by 9 fold, in patients with surgical aortic stenosis.

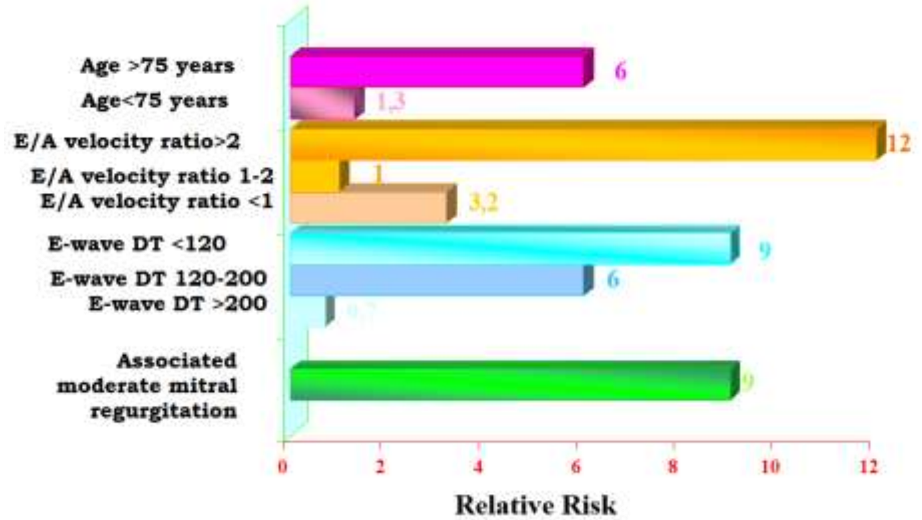


Figure 1: Relative risk for the occurrence of the pulmonary hypertension in patients with aortic stenosis

2. The presence of severe PHT has increased the early postoperative risk of death by 9.8 fold, regardless of the presence of other known parameters that increased mortality rate in these patients.

In figure 2 are shown the relative risks associated to death at 5 and 10 days postoperatively and for the appearance of postoperative cardiovascular complications presented distinctly depending on the pulmonary artery pressure value.

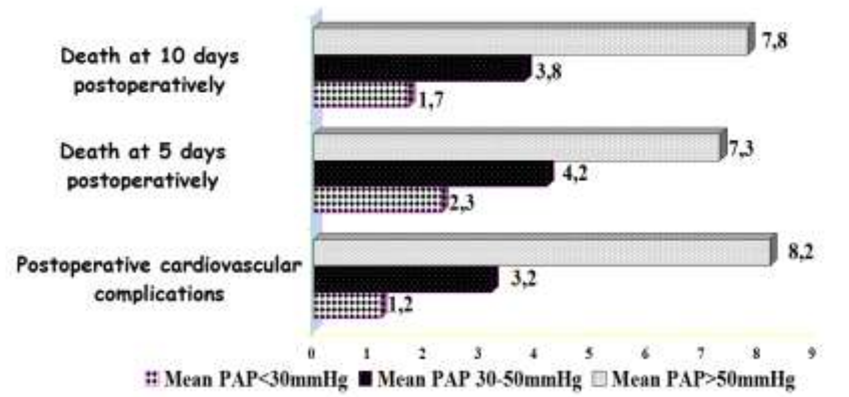
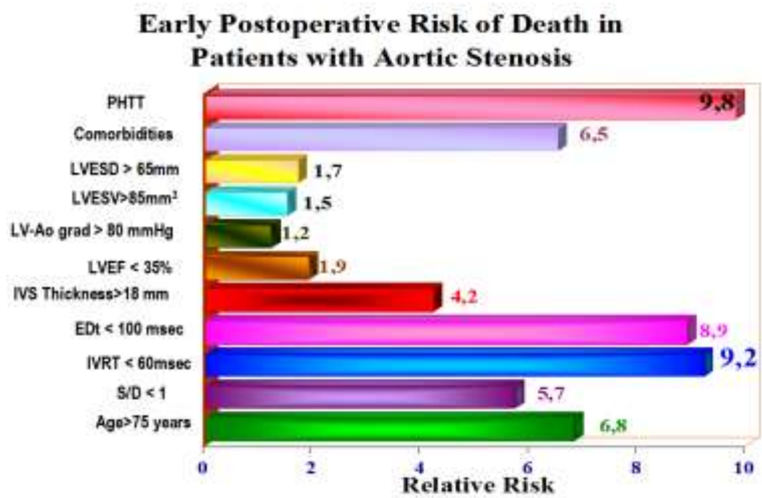


Figure 2: Relative risk for cardiovascular complications and early postoperative death depending on the presence of pulmonary hypertension

3. Regression analysis has identified as independent predictors for early postoperative mortality, the presence in those patients of the following parameters (Figure 3, next page):

- mean PAP > 50mmHg (RR = 9), $p < 0.001$
- restrictive LV diastolic filling pattern (RR = 9), $p < 0.001$
- age > 75 years (RR=6), $p < 0.001$
- interventricular septum thickness > 18mm
- the presence of comorbidities (diabetes mellitus, renal failure) (RR = 9), $p < 0.0001$.

There were not correlated with the increased early postoperative mortality rate in these patients parameters of the LV systolic performance (LVEF), severity parameters of aortic lesion (gradient, area) and LV dimensions.



In figure 3 there are presented the relative risks associated to early postoperative death for the parameters known that they increase the mortality rates in aortic stenosis.

Figure 3: Early postoperative risk of death in patients with aortic stenosis

Thus, the risk of death early postoperatively increased about 10 times by the presence of pulmonary hypertension and by 9 fold by the presence of restrictive diastolic filling pattern (respectively by E wave deceleration time < 100 msec 8.9 fold and isovolumetric relaxation time < 60 msec by 9.2 fold). In addition, a subunitary ratio of systolic and diastolic waves in pulmonary veins increased the risk of death early postoperatively by 5.7 fold, patients age > 75 years by 6.8 fold and the eccentric left ventricular hypertrophy with interventricular septum thickness > 18 mm by 4.2 fold. The early postoperative risk of death was increased as well by the associated comorbidities (diabetes mellitus, obstructive broncho-pneumopathies).

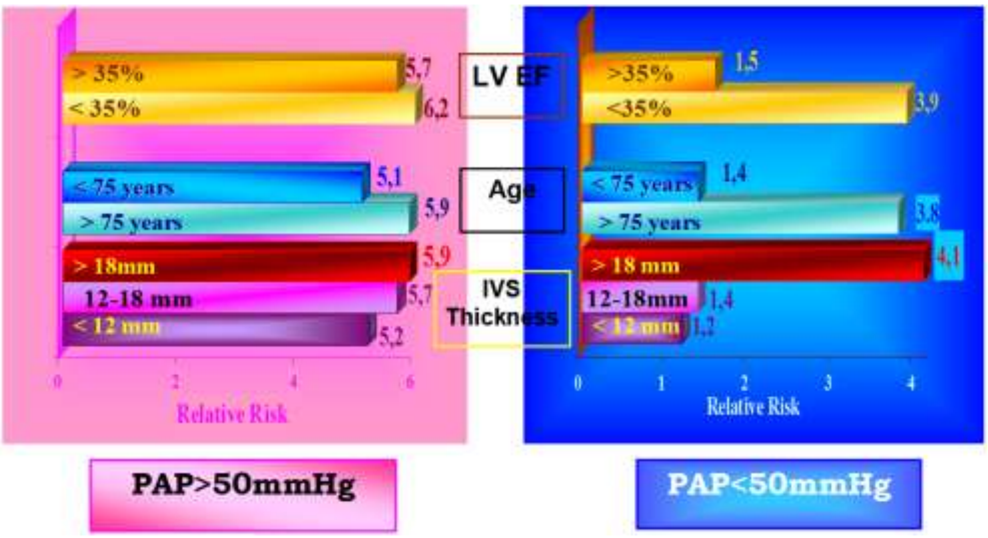


Figure 4: Early postoperative risk of death in patients with aortic stenosis depending on the mean PAP

In figure 4 (page before) there are presented the relative risks for death in early postoperative period for the studied group, associated to different parameters known to increase the mortality rates in aortic stenosis undergone surgery such as: severe left ventricular hypertrophy, age, left ventricular systolic performance. The relative risks are presented separately depending of the pulmonary artery pressure value.

The predictive value of left ventricular systolic dysfunction, elderly or interventricular septum thickness for death at 2 year postoperatively were the same in patients with severe pulmonary hypertension and higher in patients with normal pulmonary artery pressure. In these patients, left ventricular ejection fraction < 35%, age > 75years or interventricular septum thickness > 18mm increased by 4 fold the risk of death at 2 years postoperatively.

The presence of severe pulmonary hypertension has homogenized the relative risk early postoperative risk of death. It was increased regardless the left ventricular systolic performance, patients age or the presence of the left ventricular hypertrophy.

From clinical point of view, the percent of patients with unfavorable evolution (interpreted as NYHA class for heart failure > 3 and quality of life score ><5) was higher in subgroup with severe pulmonary hypertension regardless the left ventricular systolic dysfunction. Thus at 1 year follow-up the percent of patients with NYHA class of heart failure 3 and 4 were almost 8 fold higher in patients with severe pulmonary hypertension in comparison with normal pulmonary artery pressure regardless the systolic dysfunction (Figure 5).

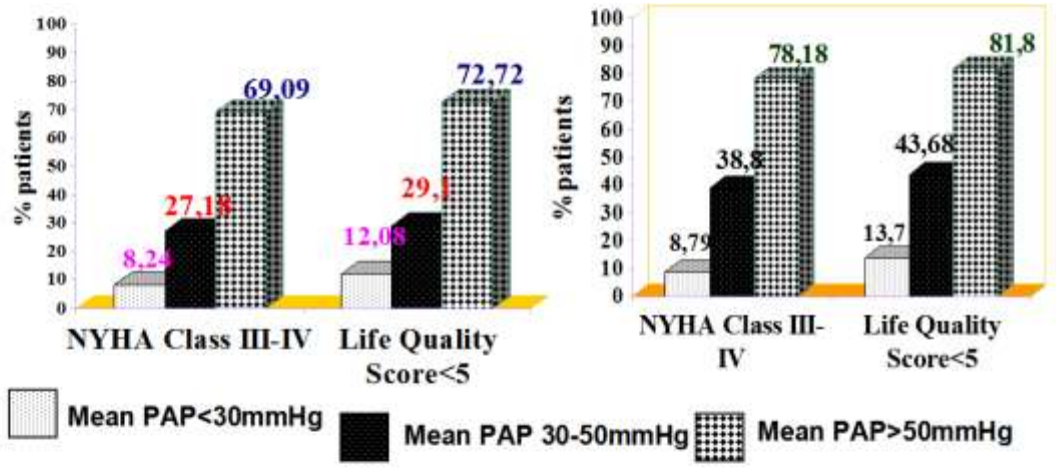


Figure 5: Evolution of the patients from the point of view of NYHA class and quality of life depending on the presence of pulmonary hypertension

In the same time, the quality of life score<5 was found in almost 6 fold patients with severe pulmonary hypertension compared to patients with normal pulmonary artery pressure in both years of follow-up.

5. The 2 year follow-up has shown a significant correlation between pulmonary hypertension regression and the left ventricular systolic and diastolic performance (r = 0.19 respectively 0.28), as well as the preoperative dimensions of left ventricular cavities (left ventricular end-diastolic diameter – $r = 0.17$, $p = 0.02$, LV end-systolic diameter - $r = 0.07$, $p < 0.0001$) (Figure 6).

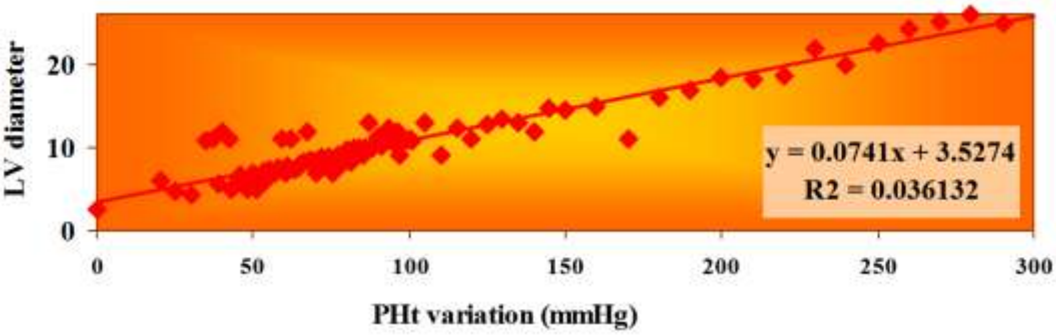


Figure 6: Correlation between pulmonary hypertension regressions at 2 year postoperatively and left ventricular end-diastolic diameter

Other preoperative clinical and haemodinamical parameters or echographic parameters of the aortic prosthesis (LV-Ao gradient, prosthesis functional area) were not correlated with the pulmonary hypertension regression and, therefore, they cannot be used as predictors of its evolution.

Discussions

Presence of transpulmonary pressure gradient in patients with severe aortic stenosis indicates the importance of an increase in pulmonary arterial resistance. (6) One observational study evaluates the risk factors for the development of pulmonary hypertension in patients with severe aortic stenosis and investigates a possible protective effect of statin therapy against the development of pulmonary hypertension (5).

Also, an impressive increase in pulmonary arteriolar resistance has been found in some patients with end-stage aortic stenosis dying suddenly or deteriorating suddenly after catheterisation (7). The rare finding of severe pulmonary hypertension in aortic stenosis should be considered an important marker for sudden death and in association with left ventricular failure may indicate an urgent need for valve replacement, regardless of the apparent clinical condition of the patient.

Severe PHT was an independent predictor of perioperative mortality. However, perioperative mortality was independent of the severity of left ventricular systolic dysfunction or concomitant coronary artery bypass grafting. Aortic valve replacement was associated with significant improvement in left ventricular ejection fraction, the severity of pulmonary hypertension and NYHA functional class. The difference between long-term survival of the operative survivors and the expected survival from life tables was not statistically significant in other studies (2).

Present study is the first one which evaluates long term prognosis in patients with aortic stenosis who added pulmonary hypertension and the influence of pulmonary hypertension on postoperative course in these patients.

Conclusions

1. Relevant independent predictors for pulmonary hypertension occurrence in surgical aortic stenosis were: age>75 years, restrictive left ventricular diastolic filling pattern and the presence of moderate mitral regurgitation.

2. The presence of a severe pulmonary hypertension in patients with aortic stenosis undergoing aortic valve replacement is associated with an early postoperative increased mortality rate. The mean pulmonary artery pressure is a more reliable parameter for prognosis appreciation than the left ventricular systolic function.

3. The independent predictors for increased early postoperative mortality rate in patients with surgical aortic stenosis were:

- mean pulmonary artery pressure > 50mmHg;
- the presence of a restrictive left ventricular diastolic filling pattern;
- age > 75 years;
- interventricular septum thickness > 18mm;
- comorbidities (diabetes mellitus, pulmonary diseases).

4. Pulmonary hypertension regression at 2 years postoperatively was only correlated with preoperative left ventricular dimensions and systolic and diastolic function and could not be predicted by other clinical or ecographical parameters.

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Are there any prognostic factors for the appearance of atrial tachyarrhythmias after valve replacement for aortic stenosis?*)

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Abstract

236 patients undergoing aortic valve replacement for aortic stenosis were analyzed to determine the incidence and predisposing factors to postoperative atrial tachyarrhythmias. Univariate and multivariate analyses were performed on a number of clinical, hemodynamic, radiographic, electrocardiographic, operative and postoperative variables. 97 patients (41%) experienced atrial tachyarrhythmias at a median 3 days after surgery (72% atrial fibrillation, 22% atrial flutter and 6% jonctional tachycardia). Preoperative descriptors associated with an increased prevalence of atrial tachyarrhythmias were age 70 years or older (p < 0.01), mitral regurgitation (p < 0.001), history of paroxysmal atrial fibrillation (p < 0.02), or antiarrhythmic therapy (p < 0.006), diabetes mellitus (p < 0.01), and elevated pulmonary systolic, mean, and capillary wedge pressures (p < 0.02, p < 0.05, p < 0.005). Postoperative descriptors were prolonged respirator therapy (p < 0.001), use of catecholamines (p < 0.01) or vasodilators (p < 0.05), and prolonged stay in the ICU (p < 0.04). Multivariate analysis of these 12 variables showed advanced age, diabetes mellitus, and prolonged respirator use to be independently associated with atrial tachycardias and to predict them with a sensitivity of 62% and a specificity of 77%. Anticipation of atrial arrhythmias in patients with specific clinical descriptors may be used to guide prophylactic therapy.

Key words: *aortic valve replacement, aortic stenosis, tachycardia, atrial fibrillation.*

Rezumat

Am analizat 236 de pacienți care au suferit înlocuire valvulară aortică pentru stenoza aortică cu scopul de a determina incidența tahiaritmiilor supraventriculare postoperatorii precoce şi a factorilor de prognostic pentru apariția acestora. Au fost realizate analize uni- şi multivariate asupra unui număr de variabile clinice, hemodinamice, radiografice, electrocardiografice, operatorii şi postoperatorii. 97 de pacienți (41%) au dezvoltat tahiaritmii supraventriculare la un interval mediu de 3 zile de la operație (72% fibrilație atrială, 22% flutter atrial iar 6% tahicardie joncțională). Parametrii preoperatori asociați cu o prevalență crescută a tahiaritmiilor

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supraventriculare au fost cu vârsta de peste 70 de ani (p < 0,01), insuficiența mitrală (p < 0,001), istoricul de fibrilație atrială paroxistică (p < 0,02), tratamentul antiaritmic (p < 0,006), diabetul zaharat (p < 0,01), presiunile pulmonare sistolică, medie şi capilara blocată (p < 0,02, p < 0,05, p < 0,005). Parametrii postoperatori asociați cu o prevalență crescută a tahiaritmiilor supraventriculare au fost asistarea ventilatorie mecanică prelungită (p < 0,001), utilizarea catecolaminelor (p < 0,01), utilizarea vasodilatatoarelor (p < 0,05) şi o durată crescută a şederii în secția ATI (p < 0,04). Analiza multivariată a acestor variabile a arătat că vârsta avansată, diabetul zaharat şi asistarea ventilatorie mecanică prelungită au fost asociate independent cu o incidență crescută a tahiaritmiilor supraventriculare post-operatorii, având o valoare predictivă cu o sensibilitate de 62% şi o specificitate de 77%. Anticiparea tahiaritmiilor atriale la pacienții cu parametrii clinici specifici poate fi utilizată în viitor pentru ghidarea tratamentului profilactic.

Cuvinte cheie: *înlocuirea valvulară aortică, stenoza aortică, tahicardie, fibrilație atrială*

Atrial tachyarrythmias are a frequent, potentially serious complication after thoracotomy or cardiac surgery. Impaired function of valve prostheses at high heart rates increases the morbidity of tachycardia in such patients.

Prophylactic antiarrhythmic therapy has been proposed, but concerns of efficacy and safety suggest selective use. Unfortunately, not much data are available to provide basis for selective prescription of antiarrhythmic drugs after aortic valvular surgery.

In our study we analyzed patients undergoing aortic valve replacement for aortic stenosis (1) to determine the prevalence of postoperative atrial tachycardias (2), to systematically examine a large number of clinical predictors as possible risk factors, and (3) to develop a profile of those patients at greatest risk for postoperative arrhythmias in whom prophylactic use of anti-arrhythmic therapy might be used most effectively.

Methods

236 patients suffering aortic valve replacement between 01 January 2000 and 31 December 2006 were reviewed. Patients with aortic valve gradients less than 25 mm Hg, chronic atrial fibrillation, and simultaneous mitral valve surgery were excluded, and those undergoing all other additional cardiac procedures such as coronary artery bypass grafting, aneurysmectomy, and resection of the ascending aorta were included. Of the 236 patients 153 (65%) were men, and the average age was 64 ± 13 years (range 23 to 82). 142 (60%) were taking digoxin preoperatively and 43 (18%) were taking beta-blockers.

All surgical procedures included cardiopulmonary bypass with or without systemic hypothermia and multiple doses of cold potassium cardioplegic solution.

201 patients received mechanical prostheses while 41 received porcine heterograft valves. Prophylactic post-operative digoxin or beta-blockade was not used. All patients underwent continuous electrocardiographic monitoring while in the surgical intensive care unit (at least 48 h), and many were monitored also thereafter.

Arrhythmias were defined as any atrial tachycardia (rate > 100/min) with a supraventricular non-sinus mechanism, including atrial fibrillation, atrial flutter, and ectopic atrial tachycardias, occurring after admission to the surgical intensive care unit. All arrhythmias were of long enough duration to confirm diagnosis by 12 lead electrocardiograms in all cases.

The following preoperative clinical, hemodynamic, radiographic, electrocardiographic, intraoperative, and immediate postoperative variables were reviewed to determine those individually predictive or protective of postoperative atrial tachycardias: clinical – age, NYHA class, hypertension, previous myocardial infarction, previous heart surgery, renal disease, pulmonary disease, cerebrovascular disease, diabetes mellitus, hepatic disease; medications – digoxin, vasodilators, anticoagulants, beta-blockers, diuretics, antiarrhythmics; operative – CABG, aortic valve prosthesis type, pump time, aortic clamping time, use of IABP, additional procedures, intraoperative myocardial infarction; postoperative – catecholamine use, vasodilator use, pro-longed respirator use, cerebrovascular accident, wound infection, emergency thoracotomy, abnormal mental status, excessive bleeding, acute renal failure, intensive care unit stay, pericarditis, endocarditis, hospital mortality, late mortality; electrocardiograms – Q-wave scar, first degree atrioventricular block, left atrial abnormality, QRS voltage for left ventriclular hypertrophy, QRS duration > 0.09 ms, left axis deviation, repolarization abnormalities, bundle branch block, permanent pacemaker, paroxysmal atrial fibrillation; roentgenogram – cardiothoracic ratio; hemodynamics – pulmonary vascular resistance, left ventriculogram, presence of CAD, presence of aortic regurgitation, severity of aortic regurgitation, cardiac output, ejection fraction, aortic valve gradient, aortic valve gradient, aortic valve area, left ventricular end-diastolic pressure, mitral regurgitation, arteriovenous oxygen difference, pulmonary arterial systolic, mean, and capillary wedge pressures.

Statistical analysis was performed with the *chi*-squared test or unpaired *t*- test. Multivariate analysis used stepwise logistic regression to determine the simultaneous significance of several variables.

Results

97 patients (41.11%) had atrial tachyarrhythmias at a median of 3 days after surgery (mean 3.6 ± 2.0 days, range 1 to 10). From these patients, 70 (72%) had atrial fibrillation, 22 had atrial flutter (22%), and 5 (6%) had junctional tachycardia.

Clinical variables associated with an increased risk of atrial tachyarrhythmias were age 70 years or older ($p < 0.01$), history of diabetes mellitus ($p < 0.01$), history of paroxysmal atrial fibrillation ($p < 0.02$), and antiarrhythmic drug therapy ($p < 0.006$).

Variables not associated with an increased prevalence of arrhythmias were sex; previous cardiac surgery; previous myocardial infarction; NYHA symptom class; history of hypertension, renal, hepatic, pulmonary, or cerebrovascular disease; and treatment with digoxin, nitrates, vasodilators, oral anticoagulants, beta-blockers, diuretics. No variable was associated with a decreased prevalence of arrhythmias.

Analysis of electrocardiograms revealed no significant associations between arrhythmia and any criterion for left ventricular hypertrophy, including P-wave abnormality, or history of conduction disturbances, or the presence of a myocardial scar. Similarly, there was no association between atrial tachycardias and the cardiothoracic ratio measured on chest roentgenogram. Hemodynamic variables associated with an increased risk of atrial arrhythmia were greater elevations in pulmonary arterial systolic, mean, or capillary wedge pressures ($p < 0.02$, $p < 0.05$, $p < 0.005$, respectively). The presence of mitral regurgitation (1+ or greater) was associated with an increased risk ($p < 0.001$), although the angiographic or echographic severity was not. Variables unrelated to the prevalence of arrhythmia were left ventricular systolic and end-diastolic pressures, cardiac output, arteriovenous oxygen differences, pulmonary vascular resistances, abnormal left ventriculogram, ejection fraction, the presence or severity of coronary artery disease or aortic regurgitation, and aortic valve pressure gradient or estimated valve area.

No operative variables were associated with the occurrence of atrial tachycardia. This included pump and aortic cross-clamp times, type and annulus size of aortic prosthesis inserted, performance of CABG or other additional operative procedures, intraoperative myocardial infarction, or use of the IABP.

Because arrhythmias occurred up to 10 days after surgery, events of the immediate postoperative period could have predictive importance. Descriptors related to an increased prevalence of atrial arrhythmia were mechanical ventilation beyond 48 h after surgery ($p < 0.001$) or need for inotropic support or vasodilators for more than 12 h ($p < 0.01$, $p < 0.05$). Lengthy of stay in the ICU was grater in those with atrial tachycardia (mean 5.5 ± 9.8 days) than in those without (mean 2.4 ± 1.4 – $p < 0.04$). Events unrelated to atrial tachyarrhythmia were hospital mortality, acute renal failure, reoperation for excessive bleeding, emergency thoracotomy, abnormal mental status, cerebrovascular accident, and sternal or wound infection. Subsequent events unrelated to arrhythmia included postpericardiotomy syndrome, prosthetic endocarditis and late mortality.

Logistic regression or multivariate analysis was applied to all 12 variables significantly associated with atrial tachyarrhythmia. Only those patients with complete data sets for these variables were included, reducing the study population to 116 patients. Examination of preoperative variables showed age and mitral regurgitation to be closely related, as were diabetes and antiarrhythmic therapy. Similarly, prolonged respirator use was related to pulmonary arterial pressures, postoperative use of pressors, catecholamines, and vasodilators, and length of stay in the ICU (all $p < 0.05$). The strongest predictor of each of these groups excluded the other variables from the regression model.

The preoperative and postoperative variables proving to be significant were respirator use greater than 48 h ($p < 0.01$), diabetes mellitus ($p < 0.02$), and age 70 years or older ($p < 0.03$). This model had a sensitivity of 62%, a specificity of 77%, and was 71% correct. Although the overall p value was highly significant ($p < 0.0001$) the correlation was only modest, with a coefficient of 0.346.

Discussions

Atrial tachyarrhythmias occur frequently after cardiac or thoracic surgical procedures. The prevalence after CABG ranges from 15.2% to 38%. Although addressed by fewer studies, atrial arrhythmias after valvular surgery have been reported to occur in 4.6% to 53% of patients. Because the incidence of arrhythmias is highly dependent on the methods used for their detection it may be difficult to compare results between institutions. However, our finding of 40% prevalence is considerably higher than the average found after CABG in most studies, although the type and timing of arrhythmias are similar. Extensive examination of potentially associated preoperative and preoperative characteristics shows postoperative atrial arrhythmias to be multifactorial and enables formulation of a demographic profile of patients at greatest risk. Advanced age in particular, is a strongly associated descriptor and is related to the presence of several other significant variables. Most investigators have found age to be unrelated to the development of arrhythmia. However, the number of elderly patients in theses studies is generally small. Our results may be explained by the larger group of elderly patients examined (120 patients aged 65 years or older) and by the higher proportion of these patients (51%) in the study population.

The association of mitral regurgitation and increased pulmonary arterial and capillary wedge pressures with postoperative atrial arrhythmias is not surprising. However, the lack of associations between arrhythmias and pulmonary vascular resistance, LV end diastolic pressure, the severity of mitral regurgitation and ECG left atrial abnormality underscores the complexity of arrhythmia production, and the limitations of our knowledge of their pathogenesis. The association between arrhythmia and the complicated perioperative course but not preoperative pulmonary disease or heart failure indicates the importance of perioperative events.

The mechanism of atrial fibrillation and flutter is unclear, although characteristics of reentry such as slowed conduction, atrial premature depolarization and abnormal refractoriness seem to be important to arrhythmia production. Other studies confirmed the importance of asynchronous atrial activity as a predictor of arrhythmia after CABG surgery. Our observation that paroxysmal atrial fibrillation and pre-operative antiarrhythmic drug use increased the incidence of atrial tachyarrhythmia supports the importance of a preexisting electrophysiologic abnormality as an etiologic factor of early postoperative arrhythmia.

The association between atrial tachyarrhythmia and diabetes mellitus noted in our study may be related to microangiopathic ischemia, to autonomic dysfunction, or even to primary nonischemic myocardial disease.

Although description of the population at risk for arrhythmia is of great clinical usefulness, the lack of association between use of beta-blockers or descriptors of ischemia and atrial arrhytmias is also important. These results are in conflict with postulated mechanisms of arrhythmia production such as adrenergic hypersensitivity caused by beta-blocker withdrawal or inadequate atrial or ventricular preservation.

Analysis of variables by logistic regression determines the relative strengths of their association with atrial tachyarrhythmias and creates a statistically significant profile with moderate sensitivity and specificity with a small number of variables. Although additional underline descriptors may be of value, this profile helps to determine prophylactic therapy. Our data indicate that elderly patients or those with diabetes mellitus, elevated pulmonary arterial pressures, history of arrhythmias, or a complicated postoperative course are at increased risk of postoperative atrial arrhythmias. Because potential benefit may outweigh the risks, prophylactic digitalis and/or beta-blockers should be strongly considered in these patients.

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A comprehensive approach to the intra-aortic balloon counter-pulsation: basic principles and current trend for its use*)

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Abstract

The number of patients affected by coronary artery disease has increased as well as related pathologies and complications. Significant advances were made in the therapy of cardiogenic shock and acute cardiac failure that complicate coronary artery disease or cardiac surgical procedures. The intra-aortic balloon pump (IABP) therapy is used in patients with complicated acute myocardial infarction, in high-risk patients undergoing percutaneous or surgical coronary revascularization, or in those with postinterventional complicated course. The IABP improves myocardial (coronary) perfusion during the diastolic phase, reducing the ischemic area. It also lowers the aortic impedance and contributes to the improvement of the left ventricular pump function; the cardiac output augments and the myocardial metabolic balance improves. Advances in manufacturing and new technology are used to improve quality of IABP devices, increasing the performances and diminishing the rate of device-associated complications. The recent indications have expanded its use in the preoperative care in high-risk patients and have also encouraged its early insertion, anticipating the inherent complications. This manuscript briefly describes the physiological bases of the IABP therapy and offers a synthesis of the recent indications for its use.

Key words: *Acute myocardial infarction, Cardiac surgery complications, Cardiogenic shock therapy, Counter-pulsation mechanical circulatory support*

In the modern world, atherosclerosis represents the main cause of disease and death. Included in this category, coronary artery disease and its complications represent an important group of pathology. The increasing number in ageing population and the achievements of modern medicine have resulted in a prolonged survival rate, but frequently, with a higher percentage of complications. The therapy of acute coronary syndromes and their complications require aggressive interventions, both by pharmacological and respectively technological measures. Cardiogenic shock complicates acute myocardial infarction and represents the main cause of death. In order to sustain the

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circulation and the function of damaged heart during the cardiogenic shock, drug therapies as well as mechanical assist devices are now available.

The intra-aortic counter-pulsation is a well-known method of therapy projected to change the hemodynamic characteristics inside the aorta.

As a result of these changes during the cardiac cycle, in systole the aortic impedance will be reduced while in diastole an augmentation of the aortic pressure will take place (1, 2).

The augmentation of the diastolic pressure will consequently improve the coronary perfusion pressure (increasing the coronary blood flow) (1, 2). The reduction of aortic impedance, downward a suffering left ventricle, facilitates the systolic emptying and improves myocardial energetics (1, 2) (Table 1). With counter-pulsation the metabolic energy balance of the heart is augmented by about 15% and consequently, cardiac output augments by 20-25% [4].

Table 1: Main indications for the aortic counter-pulsation

Coronary ischemic disease and associated complications	Complications of the myocardial infarction	Cardiogenic Shock (1, 2, 5) Anatomic defects (1, 2, 5)	Mitral insufficiency (PM rupture) Interventricular septal perforation
		Cardiac arrhythmia refractory to medical therapy (2) Postinfarction angina (1, 2, 5)	
	Unstable angina with hemodynamic alteration (1, 2, 6) Acute complications during coronary angioplasty		
Cardiac surgery	Preoperative IABP therapy in "high-risk coronary patients". See text (16,17) Difficult weaning from cardiopulmonary by-pass (1, 2, 7, 8, 9) "off pump" coronary revascularization (11, 12) Postoperative hemodynamic instability (1, 2, 7, 8, 9)		
"Bridging" for cardiac transplantation, stabilizing hemodynamics			
Patient with "heavy" coronary situations (multi-vessel disease, unstable angina, recent myocardial infarction) and/or other low-output cardiac diseases, undergoing non cardiac surgery (1, 9, 10)			

These hemodynamic changes are made possible by a special device named "intra aortic balloon pump" (IABP). The main part of this device is a long shaped balloon having a volume of 35 to 50 ml, located at the tip of an intravascular catheter, and placed inside the descending thoracic aorta (just distal to the origin of the left subclavian artery) (1, 2).

The balloon is rhythmically inflated and deflated, corresponding with the two main phases of the cardiac cycle (1).

For their special rheologic properties and for minor complications in case of leakage, both helium and CO2 are currently used as the pneumatic drive inside the balloon (alternating of the inflation/deflation phases).

The two-way catheter contains the gas conduit and the central lumen opening at its tip for blood sampling and pressure monitoring.

The catheter is connected at the console which is monitoring the patient hemodynamic parameters (ECG pattern, blood pressure, the presence and the modalities of the cardiac pacing) as well as the results of counter-pulsation and its effectiveness (the inflation/ deflation graphics) (Figures 1, 2).

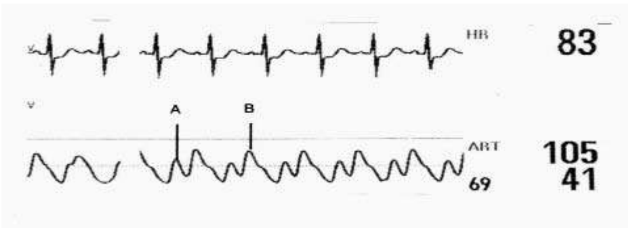

Figure 1: The graphic of the arterial pressure during 1:1 counter-pulsation. Proper counter-pulsation timing. A. Systolic peak pressure; B. Diastolic pressure augmentation as a result of counter-pulsation ("balloon inflation")

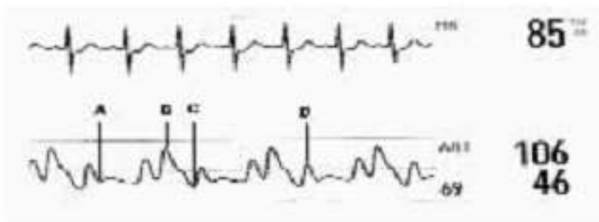

Figure 2: The arterial pressure graphic during 1:2 counter-pulsation. Diastolic dicrotic notch; Diastolic arterial pressure augmentation; Pre-systolic "balloon" deflation. Note the lower arterial pressure value, reflecting reduced aortic impedance; Systolic peak pressure is reduced after the IABP cycle

The console contains the pneumatic system and the computerized system for the timing and the control of the counter-pulsation (1).

A new device comprising a fiber-optic catheter has been recently developed allowing to measure the intra-aortic pressure and to improve the timing (programming) of the counter-pulsation (3).

The balloon is inflated in early diastole corresponding to the dicrotic notch on the pressure graphic.

The inflation of the balloon determines a volume expansion in the aorta. This, in turn, determines a diastolic augmentation of the blood pressure with the resultant improvement of coronary blood flow. Evidently, improved perfusion will sustain the function of an ischemic heart, by reducing the ischemic area and by improving myocardial metabolism and contractility (1, 2).

Prior to the systolic phase, the balloon is deflated, with the consequent reduction of the blood volume in the aorta. This will further reduce the aortic impedance during the ventricular ejection phase (after load reduction). The work of contraction of the left ventricle is reduced (1, 2).

The volume of inflation of the balloon is about 50-60% of the cardiac ideal stroke volume (4).

It is important to understand that the counter-pulsation is not a blood pump. In order to work it requires the presence of cardiac function - even if low as pump performance. In clinical practice however, the counter-pulsation becomes ineffective at systolic blood pressure under 50-60 mmHg.

Designed more than 40 years ago IABP has become the mainstay of therapy for cardiogenic shock and hemodynamic instability (Table 1). Counter-pulsation has also gained popularity as a prophylactic and not only as a therapeutic method. The results are superior if used prior to the appearance of complications and/or before other therapeutic measures have failed (e.g. high level of inotropic drugs).

Insertion techniques

Generally the balloon is inserted through the common femoral artery using the percutaneous techniques (Seldinger) or by cut down (1, 2, 13). Other arterial insertion sites can be used such as the axillary artery 13 and in the operating room the ascending aorta (1).

The proper positioning inside the aorta is with the tip of the balloon a few centimetres distal to the origin of the left subclavian artery. To check and certify this, chest X-ray and, in the operating room, transesophageal ecography (1, 2) are used.

The timing of the counter-pulsation [Figures 1, 2]

As mentioned before, the balloon is inflated at the beginning of the diastolic phase and is deflated at the end of the same.

Normally, the proper timing is made in direct visual, even if the automatic programmation is available. The latter is important in the presence of the cardiac arrhytmias (such as atrial fibrillation) (1, 2, 14).

According to the physiology of the counter-pulsation, two main changes are revealed on the blood pressure graphic: augmentation of the diastolic value, that means a better (higher) coronary perfusion pressure, and the reduction of the systolic value as result of the lower aortic impedance (Figures 1, 2).

The "weaning" off the counter-pulsation is performed gradually: first by reducing the inflation ratio from 1:1 to 1:4 or even 1:8 (1:8 clinically equivalates no counter-pulsation) in accordance with the clinical parameters (1).

The counter-pulsation therapy is ended when the cardiac and circulatory conditions are stable, pharmacological support in the low-medium range. It is important to allow "space" for the therapy [1].

The removal off for the surgically inserted catheter is made also in direct vision, using the surgical technique.

Table 2: Counter-indications to counter-poulsation

1. Aortic valve insufficiency
2. Aortic aneurysm
3. Aortic dissection
4. Peripheral occlusive vascular disease
5. Systemic disease (noncardiac)
6. Trauma

Complications (1, 15, 16, 17)

Generally there are the vascular wall complications such as dissection, perforation etc. There is the risk of the limb ischemia on the side of balloon insertion (thrombosis, dislocation of the atheroamateous plaque). The risk of intraabdominal organ ischemia (renal, intestinal, etc.) is also present; rarely spinal cord ischemia was reported.

Other possible complications are: infection, thrombocytopenia, and haemolysis (1, 16, 17) seldom IABP balloon rupture.

The rate of major complications is about 2%, intended as complication requiring surgical therapy or blood transfusion therapy, while the overall complication rate is about 6.5% (15).

Controls during the counter-pulsation

The patients requiring counter-pulsation are in critical conditions and are generally fully monitored including invasive arterial blood pressure and pulmonary artery catheterisation.

In order to detect limb ischemia the measurement of skin temperature is indicated at distal level. If ischemic complications are present, a difference of more of 4°-6°C of the skin temperature between the two limbs will be noted. In this case, an Echo-Doppler control of the arterial axis is necessary to detect the complication. The clinical signs of reduced limb perfusion are important asking for a regular and periodic checking for: pain, reduction in the articular movements, swelling or tenderness of muscular masses on the involved side (these may be less apparent in the critically ill patient).

Antythrombotic therapy is necessary. Anticoagulation with Heparin is useful (except during the early period after cardiac surgery, for the higher risk of bleeding) and is administrated as a continuous intravenous infusion. The efficacy of Heparin therapy is periodically controlled (at intervals of 4-6 hours) by monitoring the ACT (Activated Clothing Time) for > 200 sec, and / or PTT intended as INR (Partial Thromboplastin Time - International Normalized Ratio) with a target INR of 1.5 - 2.0.

Conclusion

We can conclude, according to the literature and evidence based medicine, that the IABP use is associated with a better clinical outcome, lowers the complications rate related to the low cardiac output syndrome. IABP augments the effectiveness of associated therapy, and the pharmacological support generally, is reduced. The patient's ICU stay is reduced and the survival rate is improved. It is important to understand that IABP results in better outcome and improves physiology if used prior to the appearance of complications. Counter-pulsation should not be regarded as the "last, desperate" therapy to be applied. Moreover: the earlier applied, the shorter its use (12, 15). It was demonstrated that the IABP was used preoperative in high-risk patient it results in positive cost-beneficial (18).

Considering the preoperative use for the coronary revascularization, IABP therapy is indicated in patients with high-risk coronary disease, intended those presenting almost two of the following data: left ventricular ejection fraction less than 30%; stenosis of the left main coronary artery greater than 70%; persistence of the unstable angina at the moment of the surgery despite full pharmacologic therapy; multiple vessel coronary disease necessitating four or more distal anastomosis to perform complete revascularization; reintervention (12, 15).

The rate of complications associated with IABP use can be reduced following a careful clinical evaluation and a proper handling of the device: controlling the position, avoiding excessive inflation of the balloon, using the insertion cut-down technique if percutaneous method seems difficult (small patients, known vascular disease).

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Acute renal failure after cardiac surgery*)

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Abstract

Acute renal failure (ARF) represents a major cause of morbidity and mortality after cardiac surgery. The aim of our study is to assess the incidence and outcome of ARF after cardiac surgery with cardiopulmonary bypass (CPB). Consecutive adult patients operated during 2002 and 2004 were analyzed retrospectively. 11.9% versus 7.6% patients developed ARF in 2002 and 2004, respectively. 3.7% of all patients required renal replacement therapy in 2002 versus 1.4% in 2004. In-hospital mortality decreased significantly in 2004 compared to 2002, from 20% to 4.8%. More patients received perioperative anti-inflammatory prophylaxis in 2004 compared to 2002. These strategies could be involved in decreasing the incidence and mortality of ARF after cardiac surgery.

Background

Acute renal failure (ARF) is a serious complication of cardiac surgery with mortality rates ranging from 28 to 64% (1). The reported incidence of ARF following cardiac surgery is between 1 and 30% (2). In different studies, the need for renal replacement therapy (RRT) in the post-operative period has varied between 0.5 and 15% (1). The aim of our study is to assess the incidence and outcome of ARF after cardiac surgery with cardiopulmonary bypass (CPB).

Subjects and Methods

The study was set in *Cardiac Anesthesia & Intensive Care Unit* of an University Hospital which has full time intensivist cover.

All adult patients having undergone cardiac surgery with CPB in 2002 (544 patients) and 2002 (276 patients) were studied retrospectively. Exclusion criterion was preoperative renal dysfunction. The patient characteristics (age, gender, body weight, NYHA class status and presence of diabetes mellitus) and surgical data are presented in Table 1. Surgical procedures included *coronary artery bypass grafting* (CABG), valve replacements, and complex surgery (combinations of CABG and valve replacements, tumor excisions and corrections of congenital defects or aortic dissections).

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Table 1: Demographic and perioperative data

	Year 2002 (544 patients)	Year 2004 (276 patients)	*p*
Demographic data			
Age (years)	53.8 ± 11.9	54.2 ± 14.7	0.40
Gender Male (%)	61.8	64.6	0.08
Weight (Kg)	69.6 ± 22.7	73.5 ± 14.1	0.05
Diabetes mellitus (%)	21.0	22.4	0.24
NYHA class status = III (%)	26	24	0.12
Type of surgery			
CABG no. (%)	281 (51.7)	144 (52.2)	0.36
Valve surgery no.(%)	190 (34.9)	90 (32.7)	0.52
Complex procedures no.(%)	73 (13.4)	42 (15.1)	0.12
CPB data			
CPB time (min)	97 ± 52	101 ± 41	0.60
Temperature on CPB (°C)	33.0 ± 5.7	32.7 ± 6.1	0.54

CPB was performed using a membrane oxygenator. The pump rate was set at 2.4 l/m2/min and the patient's blood was cooled to 32-34ºC. The a-stat acid-base management strategy was followed. The type of fluid infused perioperatively was not controlled. The patients received crystalloids (0.9% NaCl or Ringer's solutions - B.Braun, Germany) and colloid solutions: succinylated-gelatin (Gelofusine, B.Braun, Germany) and 6% hydroxyethyl-starches (HES) 130/04 (Voluven, Fresenius-Kabi, Germany). Sodium bicarbonate (B. Braun, Germany) and Tromethamine (THAM, Biochemie, Germany) were used as buffers. Potassium chloride 7.45% (B.Braun, Germany) was used postoperatively to correct hypokaliemia.

The fluid used to prime the CPB circuit was usually a mixture of Ringer's solution and Gelofusine. The volume was 800-1000 ml, depending on the patient's weight. It also included 5000-10000 IU of sodium heparin, and 40 mmol of sodium bicarbonate.

Cardioplegic arrest was accomplished using cold crystalloid solution (St Thomas II) (table 2).

Table 2: Incidence of ARF and outcome in patients with cardiac surgery and CPB

	Year 2002 (544 patients)	Year 2004 (276 patients)	*p*
Patients with ARF	11.9%	7.6%	0.0027
Patients with RRT	3.7%	1.4%	0.0290
In-hospital mortality in ARF	20.0%	4.8%	0.0150
In-hospital mortality in ARF required RRT	52.4%	25.0%	0.2300

Blood cardioplegia with a ratio of 2-3:1 of blood to crystalloid solution was administered at approximately 25 minutes intervals. We registered the incidence of ARF and RRT, the use of anti-inflammatory strategies and the in-hospital mortality. ARF was defined as a rise in serum creatinine above 120 μmol/l or a twofold rise of baseline value. RRT was indicated on clinical and biological grounds: fluid overload, uremic encephalopathy, anuria, hyponatremia/hypernatremia, hyperkalemia, creatinine > 300 μmol/l, urea > 15 μmol/l, severe acidemia (pH < 7.1).

Prophylactic anti-inflammatory strategies (aprotinin, metilprednisolon, intraoperative hemofiltration-HF) were used according to the anesthesiologist's preference.

Data were expressed as mean ± SD. Continuous variables were analyzed with unpaired *t*-test. Categorical variables were compared by Fisher's exact tests and a P-value of < 0.05 was considered significant.

Results

There were no differences regarding demographic, perioperative factors and type of surgery between patients operated on CPB in 2004 and 2002 (table 1). The incidence of ARF and the outcome of these patients are presented in table 2.

7.6% of patients developed ARF after cardiac surgery with CPB in 2004 versus 11.9% in 2002 (p = 0.0027). 1.4% of all patients required RRT in 2004 vs. 3.7% in 2002 (p = 0.029).

In-hospital mortality in ARF patients decreased from 20% in 2002 to. 4.8% in 2004 (p = 0.015). There were no statistical differences regarding in-hospital mortality in ARF patients requiring RRT: 52.4% in 2002 vs. 25% in 2004 (p = 0.23).

More patients received prophylactic anti-inflammatory strategies during surgery in 2004 vs 2002 (table 3).

Table 3: Anti-inflammatory strategies used prophylactically during surgery

	Year 2002 (544 patients)	Year 2004 (276 patients)	p
Aprotinin	21%	38.0%	< 0.001
Metilprednisolon	16%	42.0%	< 0.001
Intraoperative hemofiltration	8%	15.3%	0.002

Higher percentage of patients received aprotinin (38% vs. 21%, p < 0.001), metilprednisolon (42% vs. 16%, p < 0.001) and introperative hemofiltration (15.3% vs. 8%, p = 0.002) in 2004 compared to 2002. The distribution of various anti-inflammatory strategies is depicted in figure 1. The incidence of ARF related to anti-inflammatory strategies is depicted in figure 2.

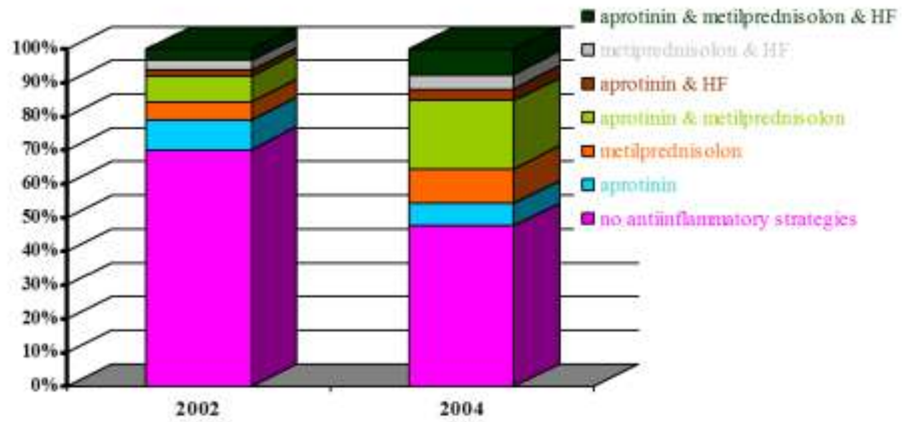

Figure 1: The distribution of patients managed with anti-inflammatory strategies

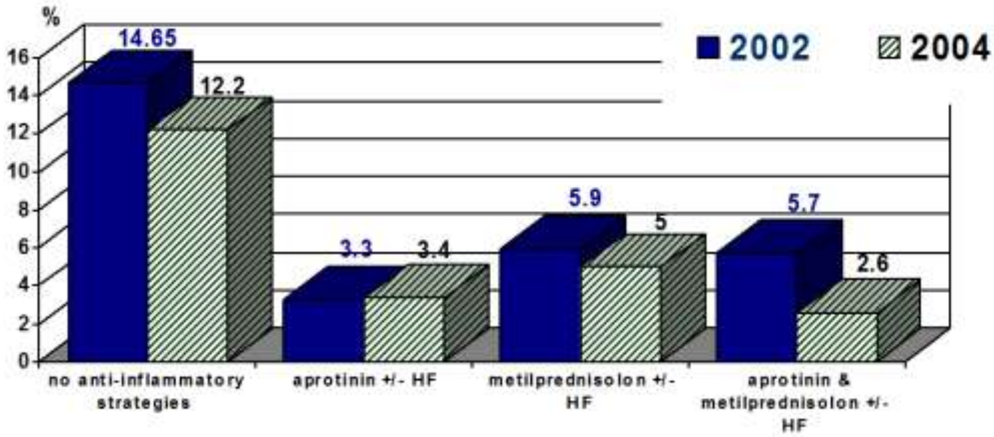

Figure 2: The incidence of ARF related to anti-inflammatory approach

Discussions

ARF has been a challenge over the last five decades (3). In contrast to other clinical settings, the predominant etiology of ARF seen in the ICU is ischemic acute tubular necrosis or nephrotoxic injury (4). As many as 60% of ARF patients in the ICU require dialysis, reflecting the severity of injury in this setting (5). The mortality rate of critically ill patients in the ICU with ARF is high (4). Those patients requiring dialysis have a particularly poor prognosis (2).

In general, the frequency of ARF after cardiac surgery with CPB is 4% to 15% (6). The onset of ARF portends a poor prognosis, not only from the loss of renal function, but also from associated life-threatening complications, including sepsis, gastrointestinal hemorrhage, and central nervous system dysfunction (6). ARF requiring renal replacement therapy (RRT) after cardiac surgery is a cause of major morbidity and mortality (2). The high mortality rates of ARF continue despite advances in CPB technology, intraoperative hemodynamic monitoring, intensive care management, dialysis techniques, and antibiotic therapy (6). In our experience, the inflammatory syndrome post CPB alone or in association with low cardiac output or high doses of vasoconstrictors are correlated with the need of RRT (8).

In our study the incidence ARF was high. However it decreased over time from 11.9% to 7.6%. The need of RRT was also decreased from 3.7% to 1.4% as well as the in-hospital mortality of patients with ARF, from 20% to 4.8%. We speculate that the decreased incidence and mortality of ARF in our patients is due to the extended use of combined prophylactic anti-inflammatory strategies.

It is known that perioperative ARF is often caused by more than one insult, with one risk factor compounding the significance of another (5). One of the kidney insults is the systemic inflammatory response syndrome (SIRS) induced by CPB (7). The clinical significance of this syndrome could be attenuated by the use of anti-inflammatory drugs and techniques (6).

Conclusions

ARF continues to be a serious complication of cardiac surgery. However, the incidence of ARF decreased significantly in 2004 compared to 2002. Also, the outcome of the patients with postoperative ARF was improved. The increased use of anti-inflammatory strategies (aprotinin, metilprednisolon and intraoperative hemofiltration) may be involved in lowering the incidence and mortality of ARF in cardiac surgery. Further prospective studies are needed to confirm the beneficial role of anti-inflammatory strategies in reducing ARF incidence and mortality after cardiac surgery.

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Continuous veno-venous hemodyalisis (CVVHD) in management of the patients with acute renal failure (ARF) after cardiac surgery with cardio-pulmonary bypass*)

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Abstract

Objective: *Retrospective study of the effects of CVVHD on course and outcome of the patients with ARF after cardiac surgery.*

Methods: *In a group of 275 patients after cardiac surgery with CPB, 32 (11.63%) patients developed ARF in the postoperative period, 3 of them being with preoperative dysfunction. ARF was always accompanied by at least one other organ failure. From those 32 patients, 14 patients (43.74% from those with ARF, and 5.09% from all) fulfilled the criteria for starting CVVHD. Those criteria were two or more of the fallowing: oliguria with hyperhydration (78.57%), hyperkalemia (42.85%), metabolic acidosis (7.14%), changes of mental status (14.28%).*

Results: *7 patients {50% of those with CVVHD) had a favorable course, 2 of those with CRF with still functioning kidneys (diuresis maintained, constant levels of BUN). 3 patients had initially a favorable course, but without long term survival, with further complications generated by the other organ failures and died after more than 30 days. 4 patients died in the first 7 days due to MSOF.*

Conclusions: *CVVHD is a very good substitute of the renal function in MSOF, preventing one of the causes of death; CVVHD is not influencing the poor outcome of the patients with MSOF, this being close related with the number of failing organs.*

Introduction

Acute renal failure requiring dialysis develops in 1-5% of patients undergoing cardiac surgery and is associated with higher in-hospital mortality (1). Pre-operative risk factors include age, preexisting renal insufficiency, and combined bypass and valvular surgery (2).

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There are three typical courses of acute renal failure after cardiac surgery, illustrated by creatinine clearance (C-creat) and serum creatinine (S-creat) levels (3). In the pattern A (figure 1) there is a step decrement that is followed immediately by a ramp increment in creatinine clearance. That "abbreviated" pattern, observed in 80 to 90% of patients, usually has an abrupt onset following surgery followed by a brief and mild rise in the serum creatinine, peaking by 3 to 4 days and followed by a rapid recovery.

In the pattern B there is an exponential decrement of clearance that is accompanied by a linear increase in serum level of creatinine (days 1-12). Recovery is manifested during days 16-30 by a ramp increment in clearance that is accompanied by a sigmoidal decline in serum creatinine (figure 2). This "overt" form is associated with a more severe reduction in glomerular filtration rate. This is generally associated with poor cardiac performance following surgery, whereas recovery is associated with improved ventricular function.

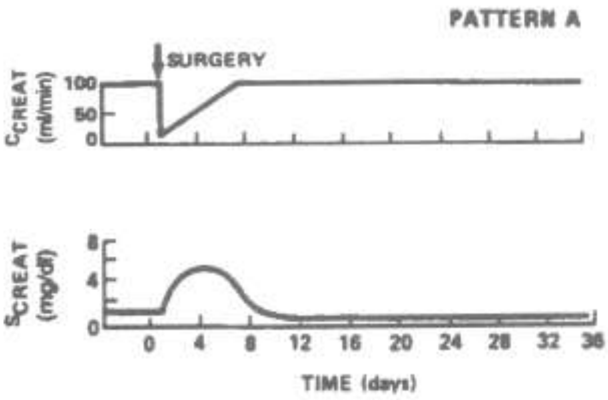


Figure 1

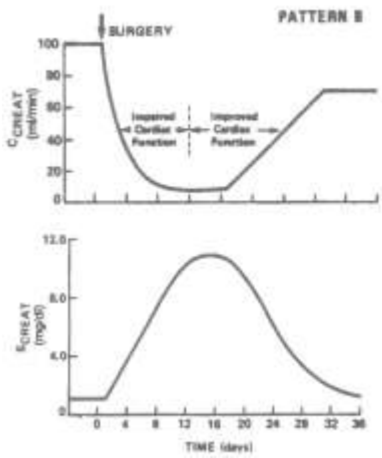
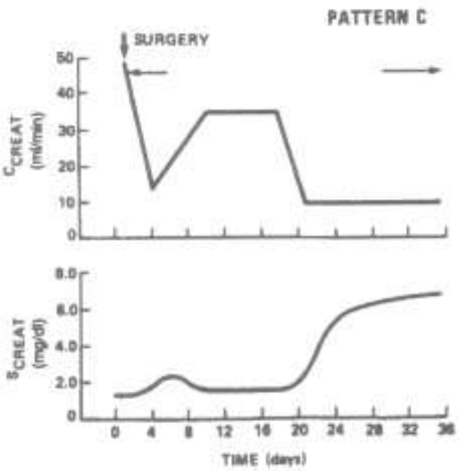


Figure 2



In the pattern C (figure 3) there are successive ramp decrements in clearance (days 1-4 and 18-21), which are accompanied by sigmoid elevation of the serum creatinine level. Recovery of creatinine clearance (ramp increment, days 4-7) is seen only after the first episode. This "protracted" form of ARF generally follows a second insult following surgery, such as sepsis, and is associated with prolonged ARF and poor prognosis. A persistent low cardiac output state prevents recovery from the second insult.

Figure 3

Objective

Retrospective study of the effects of CVVHD on course and outcome of the patients with ARF after cardiac surgery.

Method

In a group of 275 patients in postoperative period, 32 patients (11.63%) developed ARF. From those 32 patients, 3 patients had had preoperative renal dysfunction. 14 patients (5.09% from all, 43.75% from those with ARF) fulfilled the criteria for starting CVVHD. Those patients were after:

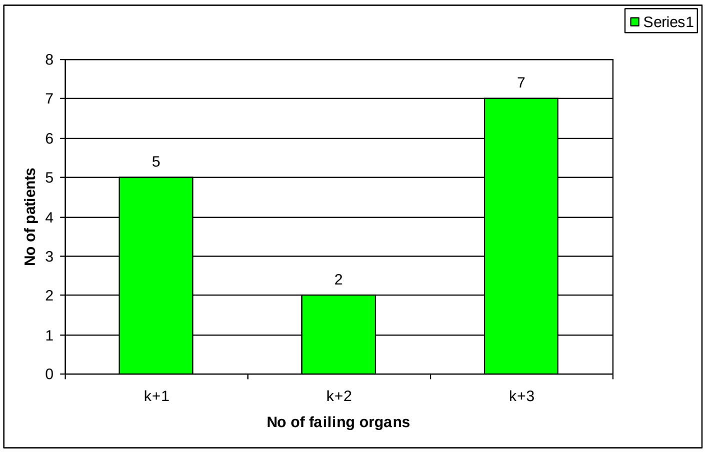


Figure 4

- *CABG* - 7 patients
- *valve replacement* - 3 patients
- *CABG + valve replacement* - 2 patients
- *aortic dissection repair* - 2 patients.

ARF was always accompanied by at least another organ failure (figure 4).

Criteria for starting CWHD were combinations of the following:

- oliguria with hyperhydration (78.57%);
- hyperkalemia, $K^+ > 6$ mEq/1 (42.85%);
- metabolic acidosis, BE under -10 (7.14%);
- changes of mental status (14.28%). CVVHD was performed on a mean period of time of 96 h, using the following protocol:
  - blood flow = 100 - 150 ml/min;
  - dialysate flow = 2500 - 3000 ml/h;
  - removal = according to the patient volemic status, assessed by:
  - pulmonary capillary wedge pressure (PCWP) - with Swan-Ganz catheter;
  - Stroke volume variations (SW) - withPiCCO monitoring system;
  - Transesophageal echocardiography

Anticoagulation was obtained with unfractioned heparin in continuous infusion, in a dose ranged between 300 Ul/h and 1000 Ul/h. ACT was assessed every 2h, with a target of 220-250s. At 4 patients with severe trombocytopenia (Plts < 50,000/mm^3) we flushed the circuit with 100 ml normal saline every 30-60 min, that amount of fluid being taken in account when it was set up the removal.

Results

From those 14 patients who required dialysis, 7 (50%) had a favorable course, with long-term survival. Two of them (14.28%) developed chronic renal failure, with diuresis maintained and constant levels of BUN. Three (21.42%) patients had a good course initially, but after that early period there was a worsening of all organ dysfunctions, evolving toward multiple organ system failure (MSOF) and the death occurred after more than 30 days of illness. 4 patients (28.57%) had an early death due to MSOE. The mortality rate was related to the number of failing organs (figure 5).

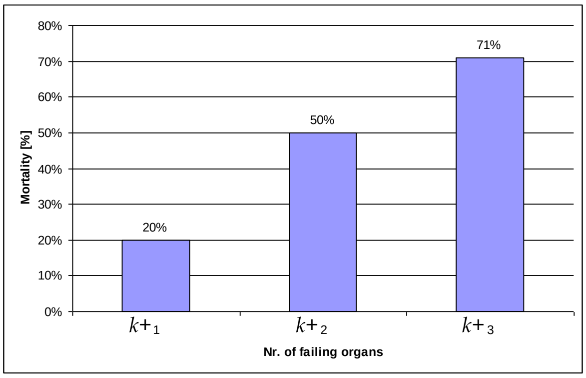


Figure 5

Conclusions

Even our study is done on a small group of patients we can assume that:

- CVVHD is a very good substitute of the renal function in MSOF, preventing one of the causes of death;
- CVVHD is a supporting therapy, not an etiological treatment;
- CVVHD is not influencing the poor outcome of the patients with MSOF, this being close related with the number of failing organs, this being also revealed by other studies (4, 5);

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Predictors of transfusion requirement*)

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Abstract

Background: *Starting with the 1st October 2006, blood donation has become honorific in Romania. This led to a significant decrease of donors' number which in its turn interfered with the scheduling of open heart surgery interventions. The purpose of the present study is to identify the factors that correlate with the transfusion requirement, the groups of patients with transfusional risk being included in a programme of blood prelevation for auto-transfusion.*

Method: *116 consecutive patients operated on open heart in the Cardiovascular Surgery Clinic from Tg. Mures since the 1st February 2006 were included in the study. Surgical interventions consisted of coronary procedures, valvular procedures, congenital procedures or associated procedures, and these interventions were carried out by three surgeons. Pre- and intra-operative factors that statistically correlate with the transfusion requirement were identified by using the CHI or t-STUDENT tests.*

Results: *Of all the 116 subjects included in the study, 32 (27.58%) received blood. Of all the epidemiological factors, the age of the patient correlated with the transfusion requirement (p = 0.034284689). The extracorporeal circulation period and the duration of the surgical intervention were the intra operative parameters that statistically associated with the transfusion requirement.*

Conclusion: *The transfusion requirement does correlate with epidemiological factors (e.g. age) and intra operative factors (e.g. extracorporeal circulation period, duration of the surgical intervention).*

Key words: *Blood transfusion, autotransfusion, cardiac surgery*

Rezumat

Introducere: *Începând cu 1 octombrie 2006, donarea de sânge a devenit onorifică în România. Acest fapt a condus la scăderea semnificativă a numărului de donatori, interferând cu programarea intervențiilor chirurgicale pe cord deschis. Scopul studiului constă în stabilirea acelor factori care se corelează cu necesarul transfuzional, grupele de pacienți cu risc transfuzional fiind incluse într-un program de recoltare a sângelui pentru autotransfuzie.*

Metodă: *Au fost incluşi în studiu 116 pacienți succesivi, operați pe cord deschis în clinica de chirurgie cardiovasculară Târgu Mureş începând cu 1 februarie 2006. Intervențiile chirurgicale au constat în proceduri coronariene, valvulare, congenitale sau asociate, fiind efectuate de trei chirurgi. Au fost identificați factorii preoperatori sau intraoperatori care se corelează statistic cu necesarul transfuzional folosind testul CHI sau t-STUDENT.*

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Rezultate: *Din cei 116 pacienți incluşi în studiu au primit sânge 32 (27.58%). Dintre factorii epidemiologici vârsta pacientului s-a corelat cu necesarul transfuzional (p* = 0.034284689*). Perioada de circulație extracorporeală peste 80 de minute (p* = 0.036389) *şi durata intervenției chirurgicale (p* = 0.00008072*) au fost parametrii intraoperatori care s-au asociat statistic cu necesarul transfuzional.*

Concluzie*: Necesarul transfuzional se corelează cu factori epidemiologici (vârsta) şi factori intraoperatori (timpul de circulație extracorporeală, durata intervenției chirurgicale).*

Background

The evolution of cardiovascular surgery depended on the development of blood prelevation and preservation. During the first years of cardiovascular surgery the blood requirement was very high because of the high priming needed for the oxygenator with disks and because of the coagulation disturbances occurring after cardiopulmonary by-pass. During the above mentioned period of time almost every patient operated on open heart received blood, having transfusional contact with 2-3 blood donors. This resulted in a high number of viral hepatitis cases, as well as other diseases transmitted through blood and blood derived products.

Secondary effects of blood transfusion (4, 7) led to a policy of limitation to the administration of homologous blood. The improvement of the oxygenator by reducing the priming requirement (10), more decreased thrombocyte destruction, a minimal leucocytic activation (5), the development of autotransfusion techniques and of the pharmacological principles with a proven pro-coagulative effect led to the decrease of transfusion requirement to values between 0-30% of the number of cases. Presently, the average of transfusional incidence stands probably between 10-30% of the number of cases. The transfusion requirement is still high in cardiac surgery, in the United States, 10% of the total quantity of transfused blood being used in coronary surgery (1).

Concerning the blood transfusion, the situation was different in Romania compared to the western states. The economical factor has not been such an important incentive in the development of auto transfusion techniques. The blood and blood products are reimbursed at reasonable prices (35 EUR per unit) whilst alternative autologous blood prelevation techniques would incur higher costs. This is a reason why the reduction of transfusion requirement was more a theoretical desideratum than a practical one.

Instead, by legislative harmonisation, blood donation has become honorific starting with the 1st October 2006. This fact led to an under 10% decrease of the number of donors attending the transfusion centers. Implicitly, there has been a disturbance in the scheduling of the open heart interventions caused by the lack of blood. A temporary solution has been the acquisition of blood directly by the patient, through blood donation by the family members or iso-group acquaintances. Practically this represents a form of co-payment of the patient for the medical services performed. Our desideratum is to reduce the requirement of homologous blood by means of developing the auto transfusion techniques. In order to acknowledge the groups of patients with a transfusion requirement, an analysis of the factors that correlate with the post-operative administration of blood is compulsory. And this is the purpose of our study.

Material and Method

116 patients operated on open heart in our clinic starting with 1st February 2006 constitute the subjects included in the present study. The surgical interventions were carried out consecutively and by three surgeons. The study included valvular procedures, coronary artery procedures, the correction of left ventricle aneurism, aorta dissection, congenital malformations and their association. Starting from certain data from the specialized literature there has been an attempt to identify some correlations between the transfusion requirement and certain pre- and intra-operative parameters: gender, age, social environment origin, blood group, diagnosis, the pre-operative level of haemoglobin, of thrombocytes, of creatinine, pre-operative administration of heparin, the surgeon that carried out the operation, the period of extracorporeal circulation, the duration of surgical intervention, the quantity of heparin administered during cardio pulmonary by-pass, the quantity of protamine administered at the end of extracorporeal circulation. The data were statistically analyzed using the *CHI* and *t-STUDENT* tests. The existence of a statistical correlation has been assessed through the value of the parameter p: if p is lower than 0.05 then there is a statistical correlation, and if p is equal or higher than 0.05 then there is no statistical correlation between the two variables. The estimation of the transfusion requirement has been carried out in two stages.

1. It has been established if the blood transfusion has or has not been necessary during the first three postoperative days;
2. The transfusion need has been quantified: reduced, medium – 1 or 2 blood units (or packed cells), high – three or more blood units.

Results

Of all 116 patients, 43 were females (37%) and 73 were males (67%). The age average of the group was 55.2 years, the minimum and maximum limits being 16 and 72 years. 32 patients received blood (27.58%). The number of the administered blood units was 64, that is to say 0.55 blood units per operated patient. By analyzing the correlation between the transfusion requirement and the gender of the patient there has not been identified any statistical correlation between the two parameters (p = 0.952693). 38 patients originated from urban environment, and 78 from rural environment. No statistical correlation between the origin environment and the transfusion requirement (p = 0.818914) was identified. Regarding the age of the patients, they were grouped by decades, and we identified a statistical correlation between the transfusion requirement and a more advanced age (p = 0.034284689) – see table 1 and diagram 1.

Table 1: The correlation between the age and the transfusion requirement p = 0.034285

	Transfusion		
Age	**Yes**	**No**	total
under 30	7	0	7
30-39	6	0	6
40-49	12	1	13
50-59	27	17	44
60-69	26	9	35
over 70	6	5	11
Total	**84**	**32**	**116**

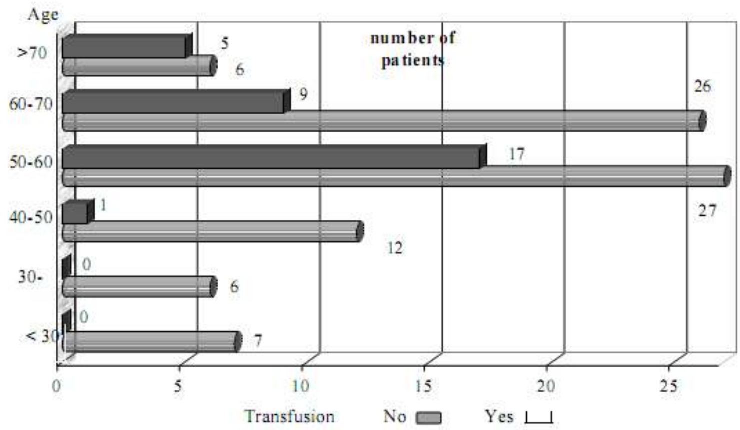

Figure 1: The correlation between the age and the transfusion requirement

The same results was obtained applying t-STUDENT test (p = 0.011959) (figure 2).

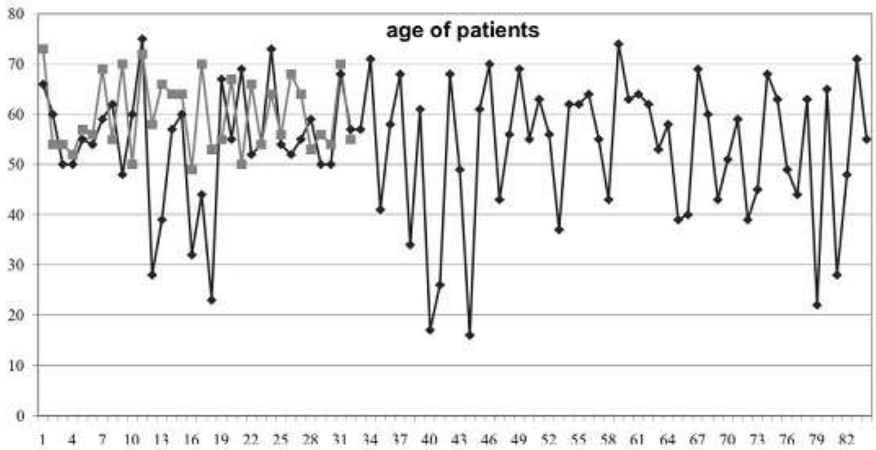

Figure 2: The correlation between the age and the transfusion requirement

The weight does not statistically correlate with the transfusion requirement (p = 0.41006). The distribution of patients in terms of blood group can be seen in Table no 2.

Table 2: The distribution of patients in terms of blood group

	Transfusion		
Blood group	**Yes**	**No**	total
0	36	7	43
A	30	12	42
B	11	8	19
AB	7	5	12
Total	**84**	**32**	**116**

There is no statistic correlation between the transfusion requirement and the blood group (p = 0.113154). Table no 3 represents the distribution of cases in terms of diagnosis type. No statistic correlation has been identified between the diagnosis type and the transfusion requirement (p = 0.064629).

Table 3: The distribution of cases in terms of diagnosis type

	Transfusion		
Diagnosis	**Yes**	**No**	**total**
CAD	33	15	48
valvular	33	10	43
valvular-CAD	10	3	13
CAD + aneurysm	1	4	5
Aortic disection	1	0	1
Congenital	6	0	6
Total	**84**	**32**	**116**

By analysing statistically the preoperative level of haemoglobin corroborated with the transfusion requirement, no correlation was identified between the two parameters of the group studied ($p = 0.322452$). The same result was also obtained in the case of the transfusion requirement correlation with the pre-operative number of thrombocytes ($p = 0.358197$).

The next stage consisted in the statistic analysis of the transfusion requirement association with values of creatinine over 1.2 (see Table no 4). No statistic correlation between the two parameters was identified ($p = 0.09712$).

Table 4: The distribution of patients in terms of creatinine values p = 0.097125

	Transfusion		
Creatinine	**Yes**	**No**	total
normal	79	27	106
over 1.2	5	5	10
Total	**84**	**32**	**116**

Another factor that can be correlated with the perioperative transfusion requirement is the preoperative administration of heparins, especially the fractioned ones. Concerning the group studied, no statistic correlation has been identified between the administration of heparin and the transfusion requirement ($p = 0.877755$). The analysis of the transfusion requirement correlation with the operating surgeon did not finalize with a statistic association ($p = 0.11674$) (see table 5).

Table 5: The distribution of patients in terms of operating surgeon

	Transfusion		
Surgeon	**NO**	**YES**	total
1	24	14	38
2	35	7	42
3	25	11	36
Total	**84**	**32**	**116**

Certain studies suggest a decrease of the transfusion requirement after the administration of antifibrinolytic protocol with Godox. Concerning the lot studied no correlation could be established between these parameters ($p = 0.230961$).

Further, we tried to establish the time threshold of the extracorporeal circulation that associates with the increase of transfusion requirement. For this purpose, we established the statistic correlation for some pre established periods of CEC and we tracked down the moment when the statistic correlation modified. Thus, for the maximum limit of 80 minutes of extracorporeal circulation we identified a statistic correlation with the lack of transfusion requirement: see diagram no 3, table no 6.

By modifying the bench-mark range of the extra-corporeal circulation to 90 minutes the disappearance of the statistic correlation previously mentioned can be observed ($p = 0.082589$). By carrying out the *t-STUDENT test* for the duration of surgical intervention we obtain a statistic correlation with the transfusion requirement ($p = 0.00008072$).

Discussions

After analyzing the epidemiological data of the group we can acknowledge a normal proportion between the male and female gender, 63%/37%, proportion which corresponds to the higher incidence of cardiovascular diseases on the male gender.

The percentage of 27.58% of patients that received blood transfusion is comparable with the results quoted by the literature. The number of blood units administered per patient (0.55) is reduced in comparison with the data mentioned in the literature. We must take into account the fact that the transfusion requirement for this study lot was calculated only for the first three postoperative days. This might be an explanation for the low value of this parameter. Literature data suggest that there could be some differences between the two genders in terms of transfusion requirement, precisely in the sense of an increase of transfusion requirement in the case of female patients (9). This fact can be explained through more factors: more frequent anemia states in the case of female patients, smaller weight which requires administration of blood during the CEC priming in order to avoid excessive dilution during extracorporeal circulation. Concerning the study lot, we have not identified an increased transfusion requirement for the female gender, without finding any particular explanation for this.

By analyzing the patients' rural or urban environment origin from the social and life standards point of view, we can say that Romania stands among the countries with major discrepancies between the two groups. Starting from this premise we assumed a difference in the transfusion requirement between the patients originating from the two environments, in the sense that nutritional, hygienic and dietary lacks would manifest in an increased transfusion requirement for the patients of rural origin. This assumption was not confirmed statistically.

The correlation of transfusion requirement with age has been described in the literature. The decrease of body reaction to aggression, metabolic and coagulation disturbances turn the patients with older age into certain candidates for blood transfusion after cardiac surgery. This propensity was found in our study as well.

We could not establish a statistic correlation between the transfusion requirement and the blood groups of the patients in the study lot. Otherwise, the data from the literature concerning this aspect are controversial in their turn.

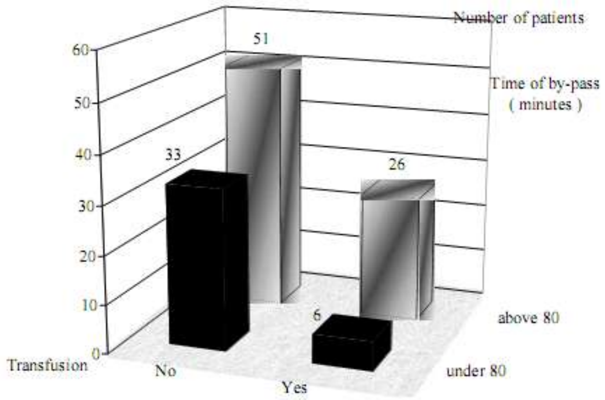

Figure 3: The correlation between the transfusion requirement and the 80 min. CEC period

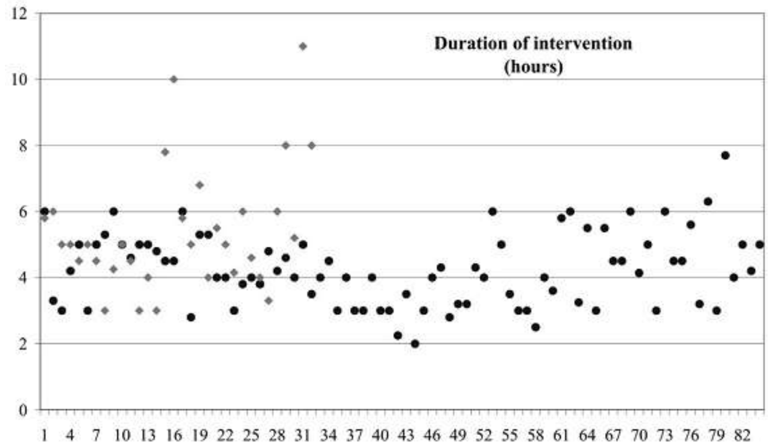

Figure 4: Correlation between the transfusion requirement and the duration of intervention

Concerning the different transfusion requirement in terms of the type of diagnosis type, the statistical analysis did not confirm the existence of such a difference. The explanations can be multiple and they consist mainly in the small number of patients with certain diagnosis which normally would present an increased transfusion requirement. If, for example, we analyze the transfusion requirement for the patients operated for reasons of coronary artery disease and left ventricle aneurysm, we find out that 4 out of 5 patients needed blood transfusion, which is a proportion completely different from the one in the case of patients with a simple aorta coronary bypass, where only 15 out of 48 cases required blood. Even if it is logically obvious that longer and more laborious interventions frequently associate with the transfusion requirement, lack of homogeneity of the study lot from the point of view of diagnosis, probably led to mathematical data that contradict the logical deduction.

Further we analyzed the correlation of preoperative biological constants with the transfusion requirement. The preoperative serum level of haemoglobin is a predictive factor for the transfusion requirement. In the case of an anaemic patient the perioperative blood transfusion is highly probable in order to avoid the extreme dilution during the cardiopulmonary bypass. This statistical correlation did not confirm in the case of the study lot.

The same contradictory data were also obtained concerning other biologic parameters: the transfusion requirement does not statistically correlate either with the low number of thrombocytes or with the increased serum level of creatinine, in spite of the fact that some studies from the literature suggest the contrary. This state of facts has a simple explanation: the achievement of some optimal biological parameters is sought through the preoperative preparation of the patients. This is the reason why the abnormal values of the mentioned biologic parameters appear too seldom for influencing the statistic. Theoretically, the prolonged preoperative administration of heparin may interfere with the postoperative coagulation mechanisms by means of alteration of the function and number of thrombocytes (8). Clinical experience seems to suggest such an effect especially in the case of prolonged administration of heparins with low molecular weight. The statistical analysis of the study lot did not emphasize a correlation between the transfusion requirement and the preoperative administration of different forms of heparins. Also, no statistic correlation has been identified between the transfusion requirement and the operating surgeon, correlation which theoretically should exist because of the different surgical techniques, operation strategy, etc. There are studies referred to in the literature with contradictory results concerning the decrease of transfusion requirement in the case of the administration of the Gordox antifibrinolytic protocol (2, 11). No statistical correlation has been identified between the two parameters in the case of the study lot. There are data in the literature that suggest the correlation of transfusion requirement with the duration of the extracorporeal circulation. No certain duration of extracorporeal circulation which obviously correlates with the increase of blood requirement has been established yet. Regarding the study lot the maximum duration of extracorporeal circulation without repercussions on the transfusion requirement is of 80 minutes. Over this value the transfusion need becomes higher. The duration of the surgical intervention is one of the factors most frequently mentioned as inductors of the transfusion requirement. This fact is explainable by the tissular and sanguine cells destruction subsequent to laborious interventions. This fact has been confirmed on the study lot as well, the *t-STUDENT* test being eloquent for this purpose.

Conclusions

1. There is a statistical corelation between the age of patiens and transfusional requirement
2. Period of extracorporeal circulation less than 80 minutes is correlated with reduced transfusional requirement
3. There is a statistical corelation between duration of surgycal intervention and transfusional requirements.

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Discriminant analysis on survival and severity of infection of patients with postoperative surgical site infections after median sternotomy in cardiac surgery*)

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Abstract

Surgical site infection has two distinct clinical forms: superficial and deep surgical site infection and organ/space surgical site infection. Mediastinitis is an organ/space surgical infection. In medical practice, it is important to know in advance what kind of surgical infection we confront with and have an answer to the following two questions: the case we confront with has a superficial or an organ/space surgical infection (is or not mediastinitis)?; will the patient survive or not? Objective of this study is to find out an answer to these two questions.

Keywords: *surgical site infection, mediastinitis, survival, discriminant analysis.*

Introduction

Mediastinitis incidence in cardiac surgery may be reduced very much applying proved methods in prevention of nosocomial infections (in particular those for prevention of surgical site infections). In spite of this, cardiac surgeon will continue to confront with mediastinitis and the question: "how deep is the infection?" and "will the patient survive or not?"

Aim of the study

The aim of this study is to perform a discriminant analysis and find out the most accurate formula in order to classify in advance patients to the following groups: survivor or deceased and superficial infection or mediastinitis.

Material and methods

The article is based on a retrospective study conducted in "*C.C. Iliescu" Institute of Cardiovascular Diseases, Bucharest, Romania*. The present series consists of 64 patients with surgical site infections following median sternotomy after cardiac surgery. The reference period for the patients included in study is 1-Jan-00 and 31-dec-01. The following two variables split the patients into the following groups:

*) **Romanian Journal of Cardiovascular Surgery ■ 2005, vol. 4, no. 3, pp. 148-152**

Survival:
- survivors
- deceased

Severity of infection:
- Superficiel infection (13 patients)
- Mediastinitis (51 patients)

Descriptive statistics shows that mortality is:
- For the overall set: 359‰.
- For patients with mediastinitis: 451‰.
- For patients with superficial infections: 0‰.

Statistical analysis was performed using SPSS and SPAD software. I analyzed appreciatively 150 variables, grouped in: preoperative, intraoperative and postoperative. I worked effectively with appreciatively 100 variables. The tests performed are:
- For categorical variables: *Pearson Chi-square test*;
- For numeric variables: Student test and one-way analysis of variance (ANOVA).
- Bivariate correlations were made by calculating Pearson correlation coefficient and Spearman correlation coefficient.

Using above mentioned tests, the results are:
- Description of data
- Screening of variance and distribution of data
- Comparison of groups for significant differences
- Identification of significant relationships between variables
- Identification of groups of similar cases
- Identification of groups of similar variables

All the results of this study are included in the Ph.D. thesis entitled: "*Treatment of mediastinitis following median sternotomy in cardiac surgery*" under the supervision of Prof. Ioan Pop de Popa, M.D., Ph.D.

Results

Discriminant analysis of survival in the moment of discovery or intervention for the complication.

I introduced in study variables proved by statistical analysis to be in relation with survival. SPSS program determined the following Fisher's linear discriminant classification coefficients (Table 1.1):

Fisher's linear discriminant functions are F1 and F2.

Each column contains estimates of the coefficients for a classification function for one group. The functions are used to assign or classify cases into groups.

Table 1.1: Classification Function Coefficients

	Survival	
	Deceased	**Survivors**
Extracorporeal circulation time (in minutes)	**0.001681**	**– 0.004016**
WBC count in the moment of discovery or intervention for complication	**2.503**	**0.09043**
ESR (erythrocyte sedimentation rate) in the moment of discovery or intervention for complication	**18.641**	**9.557**
Fibrinogen level in the moment of discovery or intervention for complication	**3.934**	**10.559**
Length of mechanical ventilator support	**29.458**	**11.077**
Use of vasoconstrictors in the first 3 postoperative days	**1.675**	**3.545**
(Constant)	**–59.831**	**–25.115**

The estimate of the classification function for deceased (F1) is:

F1 = - 59.831 +
+1.675 x Use of vasoconstrictors in the first 3 postoperative days +
+ 29.458 x Length of mechanical ventilator support +
+3.934 x Fibrinogen level in the moment of discovery or intervention for complication +
+18.641 x ESR (erythrocyte sedimentation rate) in the moment of discovery or intervention for complication +
+ 2.503 x WBC count in the moment of discovery or intervention for complication +
+ 0.001681 x Extracorporeal circulation time (in minutes)

The estimate of the classification function for survivors (F2) is:

F2 = - 25.115 +
+3.545 x Use of vasoconstrictors in the first 3 postoperative days +
+11.077 x Length of mechanical ventilator support +
+10.559 x Fibrinogen level in the moment of discovery or intervention for complication +
+9.557 x ESR (erythrocyte sedimentation rate) in the moment of discovery or intervention for complication +
+0.09043 x WBC count in the moment of discovery or intervention for complication -
- 0.004016 x Extracorporeal circulation time (in minutes)

Definition of the above variables is found in the annex 1.2.

If F1 > F2, then the individual is classified to deceased group, otherwise to survivor group. Classification uses variables known in the moment of discovery or intervention for complication. The quality of discrimination is shown in the table 1.2.

Table 1.2: Classification Results

			Predicted Group Membership		
		Survival	**Deceased**	**Survivors**	**Total**
Original	**Count**	Deceased	3	0	3
		Survivors	0	17	17
	%	Deceased	100	0	0
		Survivors	0	100	0

100.0% of original grouped cases correctly classified

Discriminant analysis of infection severity in the moment of discovery or intervention for the complication.

I introduced in study same variables as in previous analysis. SPSS program determined the following Fisher's linear discriminant classification coefficients (Table 2.1).

Table 2.1: Classification Function Coefficients

	Severity of infection	
	Superficial complications	**Mediastinitis**
Extracorporeal circulation time (in minutes)	-0,002904	0,008474
WBC count in the moment of discovery or intervention for complication	-1,360	-1,774
ESR (erythrocyte sedimentation rate) in the moment of discovery or intervention for complication	5,070	6 ,166
Fibrinogen level in the moment of discovery or intervention for complication	15,368	18,755
Length of mechanical ventilator support	1,585	2,682
Use of vasoconstrictors in the first 3 postoperative days	4,395	3,967
(Constant)	-20,463	-28,064

Fisher's linear discriminant functions are F1 and F2. Each column contains estimates of the coefficients for a classification function for one group. The functions are used to assign or classify cases into groups. F1 and F2 are calculated as in previous example. Definition of the above variables is found in the annex 1.2. If F1 > F2, then the individual is classified to superficial complications group, otherwise to mediastinitis group. Discrimination uses variables known in the moment of discovery or intervention for complication. The quality of discrimination in shown in the table 2.2.

Table 2.2: Classification Results [90.0% of original grouped cases correctly classified]

		Predicted Group Membership			
		Severity of infection	**Superficial complications**	**Mediastinitis**	**Total**
Original	Count	Superficial complications	2	2	4
		Mediastinitis	0	16	16
	%	Superficial complications	50,0	50,0	100,0
		Mediastinitis	0	100,0	100,0

Discussions

Discriminant analysis opens the way to a concise classification of patients in advance to a certain final outcome (event).

Computation of the discriminant function can appear to be difficult. Using an automated tabular program, which automatically imports data from computerized patient record, this function may monitor patient's evolution and aware the surgeon about a problematic case. The benefit is early diagnosis of complications and difficult cases.

However, anytime we have this kind of signal, medical judgment must pay attention to the power of estimation of the discriminant function. Weak power of classification may end in omitting severe cases as including benign cases.

The goodness of fit of classification varies in time and depends on data collection. A computer program could be created in order to teach the discriminant function in real time and improve the discriminant quality.

Conclusions

Method is useful when the surgeon is aware of the discriminant quality and the classification rule is improved over time. The program performed this discrimination and verified it on 64 patients with surgical site infections after cardiac surgery.

I propose validation of the formula to actual patients from "*C.C. Iliescu" Institute of Cardiovascular Diseases, Bucharest* and other hospitals and new data collection in order to update the formula and generalize the procedure.

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Annex 1.2.

1. Extracorporeal circulation time (in minutes): the number which expresses duration of cardiopulmonary bypass in minutes.
2. WBC count in the moment of discovery or intervention for complication:
   - 0 for WBC count < 8000/mmc
   - 1 for WBC count ≥ 8000/mmc and < 10000/mmc
   - 2 for WBC count ≥ 10000/mmc and < 15000/mmc
   - 3 for WBC count ≥ 15000/mmc
   - 4 for WBC count < 4000/mmc
3. ESR (erythrocyte sedimentation rate) in the moment of discovery or intervention for complication (mm/h):
   - 0 for normal values
   - 1 for ESR: ≥ 10 mm in males, ≥ 12 mm in children, ≥ 13 mm in females and < 20 mm for the whole group
   - 2 for ESR ≥ 20 mm and < 50 mm
   - 3 for ESR ≥ 50 mm
4. Fibrinogen level in the moment of discovery or intervention for complication:
   - 0 for fibrinogen < 400 mg%
   - 1 for fibrinogen ≥ 400 mg% si < 550 mg%
   - 2 for fibrinogen ≥ 550 mg%
5. Length of mechanical ventilator support:
   - 0 for < 24 hours
   - 1 for ≥ 24 h and < 48 h
   - 2 for ≥ 48 h
6. Use of vasoconstrictors in the first 3 postoperative days:
   - 0 for no use of vasoconstrictors
   - 1 for dobutamine
   - 2 for adrenaline
   - 3 for isoprenaline

For WBC count, ESR (erythrocyte sedimentation rate) and fibrinogen introduce the greatest value discovered in the interval between the moment of discovery of complication and intervention for the complication. The other three variables refer to immediate postoperative period.

Treatment of sternal dehiscence after heart operation*)

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Abstract

Objective: *Post-sternotomy wound complications are a major cause of cardiac surgical morbidity, resulting in increased average hospital cost of this contingent of patients. It was developed a protocol for care and treatment of patients with such a complication.*

Method: *From January 2000 to April 30, 2010 (10 years 4 months) were treated 34 patients (22 men and 12 women) with sternal dehiscence. Of them, with clinic mediastenitis were 24 patients, and with no signs of infections - 10. The diagnosis was established at 5-17 days after surgery. The mean age was 60-year (40-71-year) 14 were obese, and only two had diabetes. Treatment is carried out in two stages: (1) postoperative wound early processing, including removal of metal sutures, with daily dressings until complete removal of infected tissue (2)*

Operation: ***a)** mobilizing the subcutaneous tissue and muscle layers separated, **b)** recovery the wound by applying a retrosternal irrigation, **c)** applying sternum osteosynthesis - Robiscek technique, **d)** application lavage system, **e)** wound closure in layers. In acute cases of dehiscence, osteosynthesis is carried out urgently.*

Results: *The cure rate was 98%, the stay in hospital for 14 days (range 12-16 days), with only one death caused by hepatorenal failure. In two patients developed sternal osteomyelitis, which required long-term treatment (3-6 months).*

Conclusion: *Using this protocol is effective and saves the patient from using adjacent tissues (muscles of the abdomen, chest, or even omentum) to cure the infection, and leaves the patient without cosmetic consequences.*

Introduction

Postoperative sternal dehiscence is a serious complication that must be treated promptly (1-5).

Identify risk factors

They identified the various factors that would promote the development of mediastenitis earlier. Postoperative wound infection, diabetes, obesity, use of bilateral IMA for CABG (6-11). As an example to consider in a patient with diabetes a coronary bypass surgery using the bilateral IMA significantly increased risk of unwanted complications such as mediastenitis. Therefore it is mandatory considering the high-risk patients to prevent undesirable complications.

*) **Romanian Journal of Cardiovascular Surgery ■ 2010, vol. 9, no. 3-4, pp. 119-124**

Determining risk factors

(12) Loop FD made the study of Clevel and clinics especially in patients after CABG with single IMA graft, have found that predisposing factors are:

1. Obesity (patients weight is greater than 20% of normal weight).
2. Bilateral IMA + diabetes.
3. Long time surgery.
4. Need of blood transfusion in the early postoperative period.
5. Surgical failures (asymmetric sternotomy, incorrect application of metal sutures).

Pathogenesis of Mediastinal Wound Infections

Patients undergoing heart surgery are at risk to acquire infections due to decreased immune response and failure due to the increased number of ports of entry to bacterial pathogens [13]. Gram-positive bacteria are the most common organisms isolated in mediastenitis, Staphylococcus aureus and S. epidermidis are identified in 70% to 80% of cases [14, 15]. Mixed infections may be responsible for up to 40% of cases [16]. Gram-negative and fungal infections are rarely incriminated as the main cause of mediastenitis [17]. Wound infection after median sternotomy is started as a localized area of the sternal osteomyelitis with minimal external signs [14, 17]. Then the infiltration of bacteria in deeper layers is the key event in the development of mediastinal wound infections [18]. Another hypothesis for the pathogenesis of mediastenitis is improper drainage of the mediastinum, leading to a large retrosternal collection acting as a medium for bacterial growth.

If treatment measures for mediastenitis are not taken timely, complications develop (such as osteomyelitis, sepsis, respiratory failure, or poly-organically failure) and, following which the patient may die (5-9). Probability of survival of patients with septic complications is limited (6).

This report entails a consecutive series of patients who were operated in the department of acquired heart diseases. All patients were treated with the same protocol, without exception, indifferent of appearance during dehiscence. Our protocol aims to restore the normal integrity of the sternum without the use of muscle flap or omental strip. Sparing the sternum, and discharge patients resolving mediastenitis, with anatomically intact (rebuilt) sternum was our power base in the treatment.

Patients and methods

From January 2000 to April 30, 2010 (10 years 4 months) were treated 34 patients (22 men and 12 women) with sternal dehiscence. Of them with mediastenitis clinic were 24 patients, and no signs of infectious -10. The diagnosis was established at 5-17 days after surgery. The mean age was 60 years (40-71 years) 14 were obese, and only two had diabetes.

Treatment is carried out in two stages: (1) postoperative wound early processing, including removal of metal sutures, with daily dressings until complete removal of infected tissue (2). Operation:

a) mobilizing the subcutaneous tissue and muscle layers separated,

b) recovery the wound by applying a retrosternal irrigation,

c) applying sternum osteosynthesis – Robiscek technique,

d) application of lavage system,

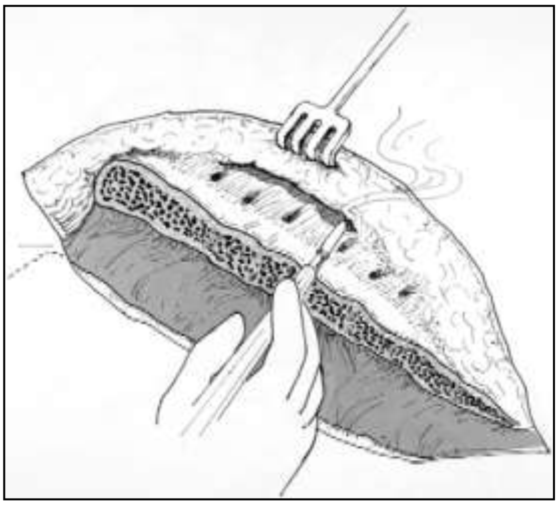
e) wound closure in layers. In acute cases of dehiscence, osteosynthesis is carried out urgently.

The diagnosis of mediastenitis was established in the presence of suppurative eliminations of sternal wound or retrosternal space. Gathering material for bacteriological analysis was prerequisite in all cases. Characteristic of patients operated on are shown in Table 1.

Table 1

Operations	No.
CABG	12
Prosthesis VMtrale + VTricuspid plastic ring	8
Aortic valve replacement	5
Three valve correction	3
CABG + Aortic valve replacement + MtV annuloplasty	2
CABG + RV remodeling (Jatane-Dor) + TrV annuloplasty	1
CABG + MtV annuloplasty	1
Recovery of left coronary from pulmonary artery in Aorta (procedure Takinski)	1
Timectomy	1

Surgical Technique



After wound incision, all sutures and metal are removed. The wound is treated with antibiotic solution (usually 1 g of cephalosporin in 200 ml saline). Betadine 10% solution is applied during application of sutures in the sternum and then postoperative wound. Skin and subcutaneous tissue are prepared as a single layer on both sides until the lateral border of the sternum are carefully identify intercostal spaces (Figure 1).

Figure 1: Mobilization of subcutaneous layer

With a metallic wire leading parasternal (round trip intercostals) is strengthening the sternum (Figure 2), as described by Robiscek, Dougherty, and Cook (15), so that each wire is surrounded by coastal front and rear sometimes it makes a hole in the upper manubriului to allow placement of wire effortlessly promoting a lasting consolidation. This procedure is applied bilaterally binding.

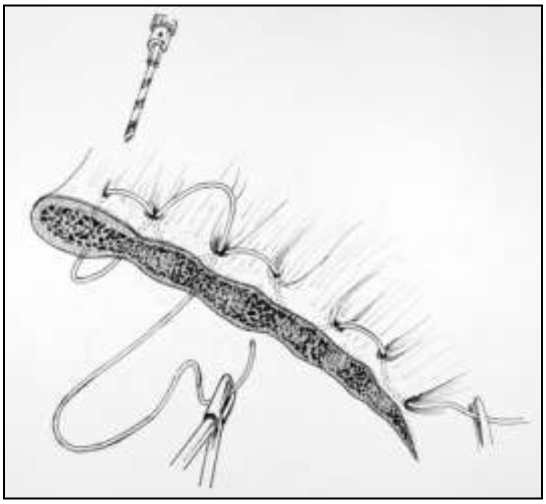


Figure 2: Osteosynthesis, Phase I

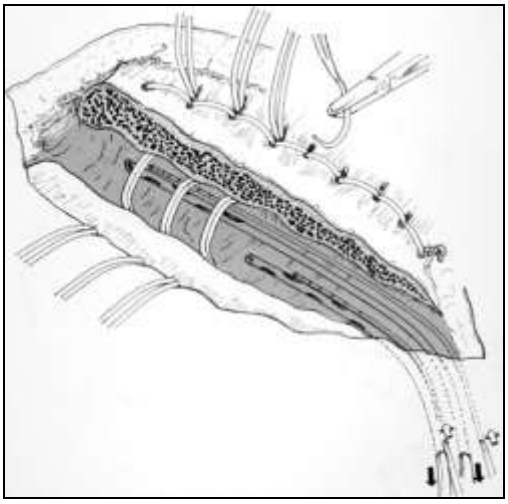


Figure 3: Osteosynthesis, Phase II

Retrosternal lavage system consists of two suction tubes placed along the sternum and one or two tubules for irrigation. Osteosynthesis is finished with metallic sutures application sternum in a way after intercostal suture. Skin and subcutaneous tissue are closed in one layer, which is used by ordinary suture Donate.

Postoperative Care

Patients are extubated after surgery on the operating table (except that some patients are ventilated for longer). Oral feeding is resumed. Wound is irrigated with 100-150 ml per hour continued for 7 days. Suction tubes are permanently active. For irrigation it was used an antibiotic solution (usually saline 3000 ml 3 g of cefazolin or 20 ml Betadine 10%). The only disadvantage of this irrigation system is that it supports patient discomfort, requires immobilization in bed for three days, with maximal decrease of the upper limb movements and is recommended to use chest bandage. To prevent pulmonary thromboembolism was used Fraxiparin 0.6 ml sc., 2 times daily or unfractionated heparin (5000 IU 3 times sc.) under the control APTT for 5 days.

Patients are at rest in bed being allowed only head elevation to 12° (to avoid tension or kinking of tubes).

In the case when, after 48 hours, the drain is clear, with no fibrinous material, clots or debris, the irrigation rate can be decreased to 50-75 ml per hour by the end of treatment week. After that, irrigation is stopped, but active suction is kept. From this on, the patients do not require immobilization in bed. To protect the stability of the sternum, patients are allowed only to extend their arms in front. If the patient gets up from bed to a seating position he should be helped by an assistant to prevent sternal dehiscence and maintain integrity. Patients are not allowed to move their arms or back side.

During the following week (the second postoperative week), tubes are pulled out 2-3 cm from the wound every day until all tubes are taken out (this procedure usually includes no more than 5-7 days).

Patients continue intravenous antibacterial therapy. In our group of patients infection was caused by Staphylococcus epidermidis (47%), antibiotic of choice was Cefaperazon with Sulbactam 2.0 gr 2 times daily. In case of necessity, resistance to cephalosporins, vancomycin and gentamicin was used. At patients who had gram-negative or mixed infections, amikacin 0.5 gr was indicated, 2 times daily iv. Whatever their choice of antibiotics treatment was extended for two weeks in hospital and one week after discharge.

Postoperative wound care: twice a day, cutting through the skin is processed with Betadine. Sutures closing the skin should be kept for a total of 15-20 days.

X-ray control: is made of two days postoperatively and after removal of the lavage system (or necessity). Long-term follow-up need only two visits to the clinic: the first week after removal of sutures and 6 weeks postoperatively to verify the final result.

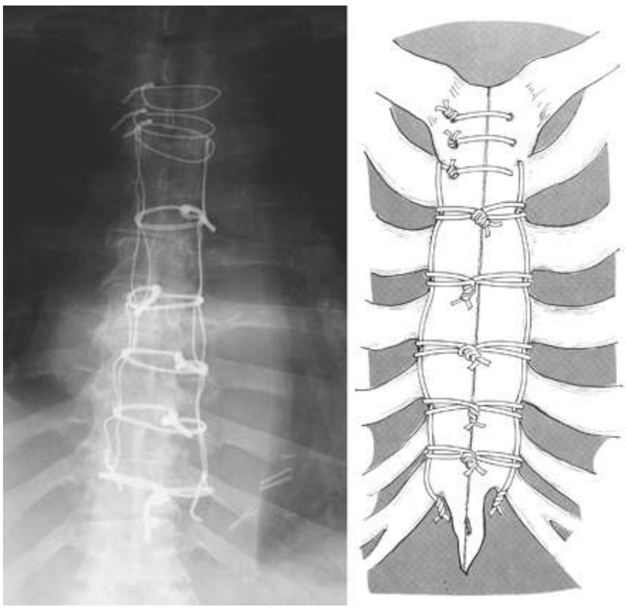


Figure 4: X-ray control

Results

Of 34 patients, 24 had mediastenitis defined earlier. Another 10 patients had a post-traumatic sternal dehiscence as a strong coughing (smoking patients with chronic obstructive bronchitis). Infective organisms in the patients with postoperative sternal dehiscence with mediastenitis are shown in Table 2.

Table 2

Organism	No.
Staphylococcus epidermitis	16
Mixed flora	3
Gram negative bacilli	3
Corynebacterium	2
Streptococcus Viridans	2
Enterobacter aerogenes	1
No growth in culture	7

Only one death occurred throughout the series, caused by heart failure, five years after surgery. Cure rate was 98% staying in hospital for 14 days (range 12-16 days), with only one death caused by hepatorenal failure. Two patients developed sternal osteomyelitis, which required long-term treatment (3-6 months). In one case the repair was not successful, complicated sternal osteomyelitis and required long-term treatment.

In these two patients, who were mentioned, the diagnosis of sternal osteomyelitis was established in the district hospital at 49 and 56 days postoperatively and were hospitalized in the section Acquired Cardiac Department for repeatedly surgery. Both had purulent osteomyelitis with fistula with rib cartilage damage. Operations were conducted according to the protocol established. We obtained total cure at one patient. The second patient required repeated interventions because the progress of osteomyelitis, including removal of rib and reboard cartilage IV to IX.

Operated patients had no thromboembolic complications therefore the use of fraxiparin and heparin seems to be effective in preventing this complication.

No pulmonary complications were observed. Patients who require treatment with anticoagulants, warfarin or trombostop they resumed it the day after surgery.

Discussions

Postoperative sternal dehiscence continues to occur when the median sternotomy approach is used to mediastinal structures. Sternal dehiscence is commonly associated with infection, namely, mediastenitis which is a serious complication, with an increased morbidity. The protocol presented in this text has been designed not only to cure but also to restore the integrity of the sternum.

At reintervention, taking into account the organification, retrosternal mobilization of the sternum is made with caution. The average time for one of these repairs is 3 to 4 hours.

Repeated interventions on the sternum are difficult and can be performed only by experienced surgeons. Even if the sternum is firmly fixed by this repair, bed rest is necessary for the implementation of our method of treatment, because irrigation is discontinued at the end of first week and just after the patient leaves the bed with chest tube suction.

Dehiscence occurs more often in obese patients at whom it is difficult to make a diagnosis by physical examination, because the layer of subcutaneous tissue is too thick to adequately palpate and feel the sternum dehiscence. Therefore, the diagnosis in obese patients is by clinical evaluation.

Our protocol, if strictly followed, leads to a full recovery. Also, the correct placement of the new wires is of utmost importance. Figure 5*A* shows improper placement of the peristernal wires after the dehiscence is treated. Figure 5*B* shows exactly the way the X-ray film should look after a correct repair.

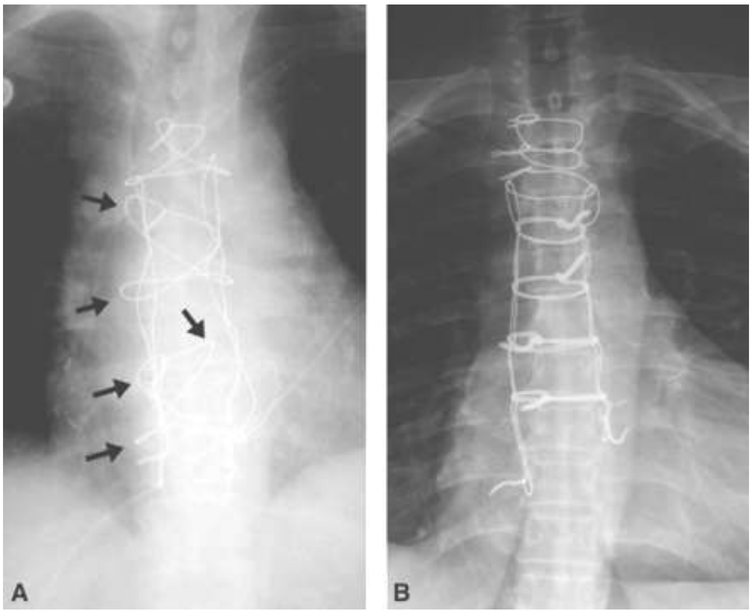


Figure 5

In summary, prompt and accurate implementation of our protocol is effective and therefore recommended for patients with sternal dehiscence and mediastenitis. Meticulous application of this method gives the opportunity to restore integrity of the sternum and patient physical functional status.

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Treatment of recurrent deep sternal wound infection and mediastinitis after cardiac surgery by means of omental flap*)

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Abstract

The treatment of deep sternal wound infection (DSWI) and mediastinitis may create many difficulties. Unsuccessful surgical treatment may lead to sepsis, multi-organ failure and death. Omental flap transposition (OFT) may be the only effective therapy. Twenty-seven patients were treated by OFT after suffering from DSWI and mediastinitis after one or more unsuccessful surgical attempts to cure the infection. Before OFT, forty-one interventions (1.5/patient) consisting of closed irrigation technique, bilateral pectoralis flap reconstruction and vacuum-assisted therapy were performed. There was no operative mortality. Hospital mortality was 7.4% (n = 2). Mean postoperative ventilation time was 1.38 days. Mean stay in intensive care unit measured 4.7 days. Mean follow-up time was 2 years. One patient (4%) died one year after discharge. During follow-up abdominal wall hernia occurred in one patient (4%) and presternal fistula resection was necessary in another patient (4%). OFT is the most effective procedure for treatment of recurrent DSWI and mediastinitis after cardiac surgery. Early mortality is acceptable, morbidity is low and late results are very good.

Abbreviation List: DSWI *= deep sternal wound infection;* ***OFT*** *= omental flap transposition;* ***MRSA*** *= methicillin resistant Staphylococcus aureus;* ***MRSE*** *= methicillin resistant Staphylococcus epidermidis;* ***CIT*** *= closed irrigation technique;* ***BPFR*** *= bilateral pectoralis flap reconstruction;* ***VAT*** *= vacuum-assisted therapy.*

Key words: *surgery, heart wound infection, postoperative, omentum*

Introduction

One of the most devastating complications after cardiac surgery is deep sternal wound infection (DSWI). Subsequent mediastinitis may lead to a life threatening complication such as dehiscence of suture lines. Aggressive surgical treatment consisting of resection of infected tissue and reconstruction of the anterior wall of the chest using muscle flaps (pectoralis major, latissimus dorsi, rectus abdominis) led to reduction of

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mortality and morbidity of this complication. However, recurrence of infection is high 12% [1]. The greater omentum is part of the innate immune system. It is a structure with a remarkable power to repair through cellular proliferation. Therefore, it has been used as an alternative to muscle flaps in the management of a various extraperitoneal wound problems [2, 3]. This paper presents our experience in treating DSWI after cardiac surgery using *omental flap transposition* (OFT) as *ultima ratio* after previous unsuccessful surgical procedures.

Patients and Methods

Data of 27 consecutive patients (19 men and 8 women; mean age 66.4 ± 9.6 years) in whom OFT was used as "*ultima ratio*" to cure DSWI after cardiac surgery between August 2000 and August 2005 was retrospectively reviewed. All patients gave their consent to this surgical procedure. Risk factors for wound complications were summarized in table 1 [4].

Table 1: Patient data: preoperative risk factors for sternal complications after heart surgery

Risk factors	Number (%)
Diabetes mellitus	15 (55.5)
Insulin dependent Diabetes mellitus	7 (25.9)
Obesity	12 (44.4)
Tabacco consume	10 (37.0)
Peripheral vascular disease	10 (37.0)
Dialysis dependent renal insuffiency	4 (14.8)
Chronic obstructive pulmonary diseasse	3 (11.3)

Most of DSWI occurred after coronary surgery (table 2).

Table 2: Primary heart surgery prior to omental flap transposition

Primary heart surgery	Number (%)
Coronary surgery	**22 (81.5)**
• CABVG and LITA	9
• LITA and RITA	5
• CABVG, LITA and RITA	8
Surgery for valvular disease	**2 (7.4)**
• AVR	1
• Bentall DeBono	1
Combinations of interventions	**3 (11.1)**
• AVR, CABVG and LITA	1
• AVR, LITA and RITA	1
• MVR, CABVG and LITA	1

CABVG = *coronary artery bypass venous graft*, LITA = *left internal thoracic artery*, RITA = *right internal thoracic artery*, AVR = *aortic valve replacement*

In 14 patients (51.9%) bilateral internal thoracic artery was utilized. In all cases on-pump surgery was performed. Single surgery for valvular disease or in combination with coronary surgery was performed in 4 patients. One patient had an aortic root replacement with a Dacron valved conduit.

Tissue cultures were obtained in all patients before and at the time of operations. The same germ found preoperatively was identified in all cases in cultures obtained from deep locations of pericardial cavity. The spectrum of organisms encountered was dominated by multi resistant organisms such as methicillin resistant Staphylococcus aureus (MRSA) in 10 cases (37%) and methicillin resistant Staphylococcus epidermidis (MRSE) in one case (3.7%) (table 3). The pathogen was not identified in 6 cases (22.3%), mainly because antibiotics were administered after the appearance of fever, and before the diagnosis of DSWI.

Table 3: Organisms causing DSWI

Organisms associated with DSWI	Number (%)
Coagulase-negative Staphylococcus	8 (29.6)
MRSA	8 (29.6)
MRSA and Escherichia coli	1 (3.7)
MRSA and Enterococcus faecalis	1 (3.7)
MRSE	1 (3.7)
Enterobacter cloacae and Escherichia coli	1 (3.7)
Enterobacter cloacae and Klebsiella pnaeumonie	1 (3.7)
No germ isolated	6 (22.3)

DSWI = *deep sternal wound infection,*
MRSA = *methicillin - resistant Staphylococcus aureus,*
MRSE = *methicillin - resistant Staphylococcus epidermidis*

A total of 41 interventions (1.5 pro patient) was performed to treat DSWI before OFT was used. The closed irrigation technique (CIT) consisted of wound debridement, sternal stabilization and closed mediastinal and pericardial irrigation with saline solution. Sternal refixation occurred mostly using a Robiczek technique. CIT was utilized 26 times (63.4%): in 19 cases as single therapy and in 7 cases in combination with bilateral pectoral flap reconstruction (BPFR) or/ and vacuum-assisted therapy (VAT). The pectoral flaps were mobilized as advancement flaps based on lateral pectoral arterial blood supply. These procedures were performed using the technique described by Gottlieb [5]. BPFR was used in 8 patients (19.5%): in 3 cases as single therapy and in 5 cases associated with CIT or/ and VAT. The VAT was performed by means of the Vacuum-Assisted Closure Device (KCl International, San Antonio, TX, USA) according to the protocol developed by Hersh [6]. The VAT was used in 7 patients (17%): in 2 cases as single therapy and in 5 cases associated with CIT or / and BPFR. Regarding the number of interventions, 18 patients (66.7%) underwent only one surgical treatment between primary heart surgery and OFT, 7 (25.9%) underwent 2 procedures, one (3.7%) underwent 3, and one patient (3.7%) had 6 interventions before OFT (table 4). Therapy was considered unsuccessful if recurrence of infection occurred.

Table 4: *Therapy before OFT*

Type of therapy before OFT	Number of patients (%)
CIT	14 (51.9)
CIT and BPFR	3 (11.1)
CIT and VAT	3 (11.1)
CIT, BPFR and VAT	1 (3.7)
BPFR	3 (11.1)
VAT	2 (7.4)
BPFR and VAT	1 (3.7)

OFT = *omental flap transposition*, CIT = *closed irrigation technique*, BPFR = *bilateral pectoralis flap reconstruction*, VAT = *vacuum-assisted therapy*

Surgical technique

Partial sternal resection was carried out until the tissue was actively bleeding in all patients. Extensive mediastinal debridement and removal of all infected and necrotic tissue was performed. Electrocoagulation was used as less as possible. Then, the wound was irrigated with diluted povidone-iodine solution. Midline incision was prolonged to the upper part of the abdomen. The omental pedicle was harvested on the gastroepiploic artery by dividing the branches to the greater curvature of the stomach. To obtain additional length, the omentum was lengthened using the arch of Barkow. The pedicle was brought up in the anterior mediastinum and fixed using monofilament sutures. No incision in the diaphragm was necessary. Care was taken not to twist the pedicle and to avoid dead spaces by filing the defects completely with omental tissue. One Blake drain was placed posteriorly and one anteriorly to the omental flap. A Robinson drain was placed in the peritoneal cavity. All drains were removed on the first, latest on the second postoperative day. The remaining parts of the sternum or rib ends were stabilized using monofilament sutures. The subcutaneous tissue and skin were then closed. Skin grafting was not necessary in any patient in spite of extensive skin resection in some cases.

Results

On an average of 137 ± 284.2 days (range 19 to 1475 days) OFT was performed after initial cardiac surgery. Mean procedure time was 224.1 ± 41.8 min. (range 170 to 360 min).

Antibiotics were postoperatively applied intravenously following antibiogram and were discontinued after wound healing was clinically complete and inflammatory markers returned to normal.

Thirteen patients (48.1%) were extubated on operative day. Mean postoperative ventilation time was 1.4 ± 2.4 days. Two patients were ventilated for a longer time (4, respectively 13 days) because of respiratory insufficiency. The mean postoperative chest tube drainage measured 302.4 ± 639 ml. In 16 patients (59.3%) drainage was less than 50 ml. In 11 cases (40.7%) a blood transfusion was necessary. A transitory renal insufficiency (creatinine > 1.2 mg/dl) was treated by diuretics in 7 patients (25.9%). The mean duration on intensive care was 4.7 ± 4.4 days (1 to 22 days). Hospital mortality was 7.4% (2 patients). The cause of death in these two cases was sepsis and multi organ failure. Mean follow-up was 23.7 ± 12.5 months (6 to 51 months). One patient (4%) died one year after discharge. During the follow-up period, an abdominal wall hernia occurred in one patient. In one patient (4%) a presternal fistula resection was necessary. Post-operative course was uneventful. There were no other late complications related to OFT.

Discussion

The omental flap has an enormous amount of immunological properties enabling the treatment of situations such as severe DSWI. One of the most important properties is the potential to deliver the vascular endothelial growth factor, a potent angio-genetic substance [7]. Neovascularization around the omental flap is initiated and may stimulate wound healing. Angiogenetic factor were not observed in muscle flaps [8].

Omental flap increases the blood supply in ischemic areas, such as sternum after harvesting of both internal thoracic arteries, leading to increased oxygen and nutrition, with revascularization and stimulation of wound healing. At the same time enhanced blood supply generates increased delivery of antibiotics, and like that eradication of infection.

Furthermore, the amorphous shape of the omental flap is superior to muscle flaps to fill defects more effectively and eliminate dead spaces in the area of implantation, preventing bacterial growth. The pliability of the omental flap allows filling even the most irregular cavities.

By absorbing wound secretion, it eliminates substrates for bacterial growth.

OFT is cost-saving and shortens intensive care unit as well as general hospital stay compared to closed irrigation or open management after muscle transposition, followed by delayed skin grafting.

Obviously, the use of bilateral internal thoracic artery raises the risk of severe therapy resistant DSWI. More than one half of our patients underwent myocardial revascularization by use of left and right internal thoracic artery.

The predominant isolated germ in our patient population was represented by the high pathogenic MRSA. This may explain the high rate of recurrent local infection despite previous therapy consisting on CIT, BPFR and VAT. On the same time this proofs the efficacy of OFT even in presence of MRSA infection.

In all our patients, omental flap transposition (OFT) was performed as ultima ratio after one or more unsuccessful interventions for DSWI. These consisted of CIT, BPFR, VAT or a combination of these procedures. In all cases OFT led to the wound healing. This demonstrates the superiority of OFT compared to other techniques in our opinion.

Possible adverse events of OFT are related to the communication created between pericardial and peritoneal cavity. None of our patients presented spread of intrathoracic infection to the abdomen, or herniation of abdominal organs into the chest.

Harvesting of the gastroepiploic artery with the omental flap doesn't lead in any case to impaired gastro-intestinal function.

There was no failure of the OFT in our patient's population during hospitalization. In all patients wound healing was complete at discharge. One patient returned with evidence of presternal fistula one month after discharge. Resection of the fistula was uneventful. Recurrence of mediastinal infection is possible if debridement and resection of infected tissue is incomplete and if omental flap necrosis occurs. This is the case if torsion of the flap pedicle during transposition is ignored. Recurrence of infection occurs according to literature data in 14 to 22.2% of the cases [9, 10]. Kenzo found the recurrence rate higher if the infection causing organism was MRSA [11]. In our patient with recurrence of the infection the isolated organism was *Staphylococcus aureus*.

Proper timing of surgical intervention for DSWI remains a difficult clinical decision because major reconstructive surgery does not always result in complete wound healing in the presence of active infection [11]. Our opinion is that patients with DSWI are generally in a life threatening situation, especially if prosthetic material is involved. In case of mediastinitis after replacement of ascending aorta or aortic arch with foreign material surgery for mediastinitis should be performed urgent. We had this constellation in only one case and performed OFT with good result immediately after unsuccessful BPFR. If the DSWI occurs after myocardial revascularization, especially after bilateral use of internal thoracic arteries, we usually postponed the intervention until the exudate is reduced markedly and the infection is brought under control. We used in these cases a VAT with good results. Delayed OFT for DSWI may improve survival. Schroeyers reported an in-hospital mortality of 28.1% (9/32 patients) when performing OFT 11 days after the initial operation [12]. We performed OFT on the average of 137 ± 284.2 days (19 - 1475 days) after the initial operation with a hospital mortality of 7.4% (2/27 patients). We have to mention that some patients originated from other hospitals, so that delay of OFT was not our decision, but produced by this circumstance.

Our treatment strategy varies in comparison to other authors to a certain extent. Although we resect extensively infected bone structures, in some patients more than two thirds of the sternal mass, we restore the mechanical integrity of the anterior chest wall. We stabilize the remaining bone structures using a limited number of monofilament sutures. The consequence in some patients is a minimal reduction in the circumference of the inferior chest cage. Some surgeons left the sternum open and closed only the subcutaneous tissue and skin [11]. We are convinced that the continuity of the anterior bony chest wall favorable influences the postoperative respiratory function and allows timely extubation and vice-versa. We were able in all cases to close the skin without the need for skin grafting in all cases. This was possible, because we restored the continuity of the underlying bony structures of the chest wall in all instances.

In our opinion, the omental tissue induces wound healing by creation of adhesions between the flap and surrounding tissue. The direct contact of the flap to the surrounding tissue allows oxygen, nutrition and antibiotics to penetrate. That is the reason why we remove the chest drains as soon as possible, latest on the second postoperative day. Some authors remove the drains after the wound samples are sterile, generally 7 to 10 days after OFT [9]. We don't use any irrigation-suction systems which may avoid the direct contact between omental flap and mediastinal tissue. We believe that aggressive debridement and extensive resection of infected tissue especially bone and cartilage is the key of success for this intervention.

OFT may be difficult to perform in patients with previous abdominal interventions because of intraperitoneal adhesions which impede the flap harvesting. The presence of the omental flap pedicle should not restrict the indication for abdominal surgery if necessary. If needed for the access the pedicle can be divided without consequences if mediastinal infection was eradicated. We have no experience regarding these situations. None of our patients underwent abdominal surgery before or after OFT.

Although our patients with severe, complicated DSWI were very ill patients and OFT was performed as third or fourth intervention, in-hospital mortality was acceptable: 7.4% (2/27). Death in our patients was not related to the OFT procedure. Other authors reported a higher mortality between 14% (1/7) [9] and 28.1% (9/32) [12]. In the experience of Kenzo hemodialysis and ventilatory support at the time of OFT were predictors of in-hospital death [11]. Two of 9 deaths in the patient's population by Schroeyers occurred because of sepsis in presence of local recurrence [12]. Our two patients died of sepsis and multi organ failure on the 35, respectively 41, postoperative day after OFT. In both cases the chest wound was healed. Late mortality was low and there was only one recurrence in our patient's population demonstrating that OFT leads to eradication of DSWI with excellent long term results.

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We hope that this book will serve as a source for fertilizing and evoking new scientific thoughts and experiments in the cardiovascular surgery field.

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VALVULAR PATHOLOGY

Morbidity and mortality after cardiac valve interventions. Retrospectively Study 2003-2010[*)]

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Abstract

Objective: *Morbidity and mortality after cardiac interventions are a new topic in reporting guidelines of AATS and EACTS. The study aim is presentation of morbidity and mortality intraoperatory and early postoperatory in cardiac valve interventions in Cardiovascular Surgery Clinic, University of Medicine and Pharmacy "V. Babes " Timisoara.*

Material and method: *In the period: 01.01.2003-30.10.2010, 2909 cardiac interventions were performed with CPB, 2017 patients men and 892 women.*

Results: *We followed 1256 cases with cardiac valve interventions, 913 cases with simple valve operation and 343 cases with complex valve intervention.*

Discussions: *The general intraoperatory and early postoperatory morbidity in cardiac valve interventions is 29.29% (368 cases). In complex cardiac valve operations is 45.18% (155 cases) and for simple cardiac valve operations is 23.32% (213 cases). The general mortality in cardiac valve interventions is 4.45%, in complex cardiac valve operations is 10.49% and for simple cardiac valve operations is 2.19%.*

Conclusions: *The dates of our study showed that mortality and morbidity, intraoperatory and early postoperatory are higher in patients with complex cardiac valve operations than in simple cardiac valve operations.*

Key words: *mortality, morbidity, simple and complex cardiac valve operations.*

Introduction

Since 1988 there has been tried to elaborate a guide for reporting the mortality and morbidity after valvular interventions and it has been finalized in 1996 through the agreement of international surgical cardio-thoracic societies. This guide establishes a strategy of tracking and analysis of clinical results, morbidity and mortality in valvular patients that have followed a medical, surgical and interventional treatment.

*) **Romanian Journal of Cardiovascular Surgery ■ 2011, vol. 10, no. 2, pp. 97-101**

Purpose of this study

The purpose of this study is to present the immediate intrasurgical and postoperatory mortality and morbidity in the Cardiovascular Surgical Clinic in Timisoara, II-nd department for those patients that have had a surgical valvular intervention in between January 2003 - Octomber 2010.

Material and method

The study has been made in the *II-nd Department of the Cardiovascular Surgical Clinic, IBCV Timisoara*, in between January 2003 - Octomber 2010. In this period of time there have been made 2909 cardiac intervention with a CEC, 1256 of those cases have been valvular interventions (43.17%) for patients between 14-85 years, 861 patients (68.55%) males and 395 patients (31.45%) females.

Patients who underwent valvular interventions were matched by age, ejection fraction, coronary artery disease, diabetes, renal disease, chronic pulmonary obstructive disease, non-elective operation and previous cardiac surgery (table 1).

CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease.

Table 1: Patients characteristics in the study group

All Patients	Number of patients	Percentage
Number of patients	**1,256**	
Mean age (yrs) ± SD	53 ± 8.73	
Male gender	861	68.55%
Age ≥ 80 yrs	41	3.34%
EF ≤ 30%	121	9.63%
CAD	261	20.78%
Diabetes	162	12.89%
Renal disease	138	10.98%
COPB	79	6.28%
PVD	92	7.32%
CHF	158	12.57%
Urgent or emergent operation	103	8.20%
Previous cardiac operation	82	6.52%

Types of simple valvular interventions are describe in (table 2) and valvular interventions associated with CABG and complex valvular operation in (table 3).

Table 2: Types of simple valvular interventions

Cases	Number of patients	Percentage
Aortic valve replacement	367	29.21%
Mitral valve replacement	260	20.70%
Aortic and mitral valves replacement	101	8.04%
Aortic valve replacement and mitral reconstruction	34	2.70%
Mitral valve replacement and tricuspid reconstruction	73	5.81%
Aortic and mitral valves replacement and tricuspid reconstruction	17	1.35%
Mitral valve reconstruction	33	2.62%
Mitral and tricuspid valves reconstruction	11	0.87%
Tricuspid valve reconstruction	6	0.47%

Table 3: Types of valvular interventions associated with CABG and complex valvular operation

Cases	Number of patients	Percentage
Tirone David operation	3	0.23%
Ross operation	7	0.55%
Bentall operation	49	3.90%
Mitral valve replacement and cardiac-tumour	2	0.15%
Mitral valve replacement and DSA closure	11	0.87%
Aortic and mitral valves replacement and DSA closure	4	0.31%
Aortic and mitral valves replacement, LV aneurysm resection and CABG	4	0.31%
Mitral valve replacement, tricuspid reconstruction and CABG	9	0.71%
Aortic and mitral valves replacement and CABG	15	1.19%
Aortic valve replacement and ascendant aorta replacement	15	1.19%
Aortic valve replacement, mitral valve reconstruction and CABG	9	0.71%
Mitral valve reconstruction and CABG	72	5.73%
Mitral valve replacement and CABG	48	3.82%
Aortic valve replacement and CABG	98	7.80%

Results and discussions

Immediate intraoperatory and postoperatory morbidity in 368 cases (29.29%). There has been al large set of complications - arrhythmias (FIA, BAV, ESV): 151 cases, postoperatory bleedings: 82 cases, brain-vascular accidents: 19 cases, pleural complications: 21 cases, kidney insufficiency: 28 cases, post CEC cardio-respiratory insufficiency: 32 cases, encephalopathy post CEC: 25 cases, GI bleedings: 8 cases - infections: 36 cases (table 4).

Table 4: General immediate intraoperatory and postoperatory morbidity

Cases	Number of patients	Percentage
Arythmias (FIA, BAV, ESV)	151	12.02%
Postoperatory bleedings	82	6.52%
Brain-vascular accidents	19	1.51%
Pleural complications	21	1.67%
Kidney insufficiency	28	2.22%
Post CEC cardio-respiratory insufficiency	32	2.54%
Encephalopathy post CEC	25	1.99%
GI bleedings	8	0.63%
Infections	36	2.82%
Hospital mortality	56	4.45%

The morbidity in complex valvular surgeries is 44.89% (154 cases) compared to simple valvular surgeries 23.44% (214 cases). Comparison of intra-operative and postoperative data between simple and complex valvular interventions it is related in table 5.

Table 5: Comparison of intraoperative and postoperative data between simple and complex valvular interventions

	simple valves (n=913)	complex valves (n=343)	*p* value
Arythmias (FIA, BAV, ESV) (%)	12.04%	11.95%	< 0.0001
Postoperatory bleedings (%)	4.92%	10.78%	0.0020
Brain-vascular accidents (%)	0.98%	2.91%	< 0.0001
Pleural complications (%)	1.20%	2.91%	< 0.0001
Kidney insuffiecinecy (%)	1.09%	5.24%	< 0.0001
Post CEC cardio-respiratory insufficiency (%)	1.64%	4.95%	0.0012
Encephalopaty post CEC (%)	1.09%	4.37%	0.0012
GI bleedings (%)	0.43%	1.16%	< 0.0001
Infections (%)	2.19%	4.66%	0.0012
Hospital mortality (%)	5.83%	10.49%	0.0020

The general mortality in valvular interventions is 4.45% (56 deaths/ 1256 surgeries).

The mortality cases in complex valvular interventions are significant higher 10.49% (36 deaths / 343 surgeries) compared to simple valvular surgeries for which it is 2.19% (20 deaths / 913 surgeries).

Conclusion

Immediate intrasurgical and postsurgical complications have a high risk level in case of valvular interventions, increasing by the degree of the surgical intervention and its complexity degree and by multiple pathological associations. In our department the obtained data has shown that the main complications consist in arrhythmias and postsurgical accute bleedings, other complications occur only in reduced number.

The immediate intrasurgical and postsurgical mortality in valvular interventions is also influenced by the complexity of the surgical intervention, so that the obtained data show us a significant difference between complex cases (10.81%) and simple cases (2.47%).

In future we would like to pursue the postsurgical mortality and morbidity on a long term. Thus we hope to be supported by the Ministry in order to develop such programs that involve more medical specializations and data to show the real situation of the postsurgical evolution in cardiac surgery generally and especially in valvular surgery.

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Chirurgie valvulaire après 70 ans: évaluation des facteurs de risque de mortalité hospitalière*)

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Résumé

Objectif: *La chirurgie valvulaire après 70 ans est de plus en plus fréquente en Algérie. Le but de cette étude était d'identifier les facteurs de risque de mortalité hospitalière dans cette population.*

Méthodes: *56 patients d'âge moyen 72 ans (70-81) ont bénéficié d'une chirurgie valvulaire entre 2006 et 2009. 32 patients (57,4%) ont eu un remplacement valvulaire aortique, 17 patients (29,7%) ont eu une chirurgie mitrale et 07 patients (12,9%) ont eu une chirurgie aorto-mitrale. 4 interventions (8%) étaient urgentes. L'Euroscore a été utilisé pour prédire le risque opératoire. L'Euroscore additif moyen était de 9,05 et l'Euroscore logistique moyen de 14,2%.*

Résultats: *La mortalité opératoire était de 3.8%. Les facteurs de risque pré-opératoires étaient: la classe NYHA ≥ III, les réinterventions, un état critique selon l'Euroscore, l'HTAP, la chirurgie mitrale et la chirurgie tricuspide. Les complications post-opératoires étaient: un bas débit (12%), l'arythmie supra-ventriculaire (32,7%), une dysfonction rénale (14,6%), pulmonaires (11%), intestinales (3,5%), l'infection (4%) et la reéxploration chirurgicale (6,5%). Les facteurs de risque post-opératoires de mortalité étaient le bas débit, la dysfonction rénale, les complications gastro-intestinales et la reéxploration chirurgicale.*

Conclusion: *La chirurgie valvulaire après 70 ans est une procédure à bas risque. Nos données sont corrélées avec l'Euroscore.*

Mots-clés: *Chirurgie valvulaire, sujet âgé, mortalité*

Introduction

A l'image des populations des pays industrialisés, en Algérie, la régression de la mortalité dans tous les groupes d'âge, a contribué au vieillissement progressif de la population. La prévalence des pathologies cardio-vasculaires est plus élevée après 70 ans, et peut atteindre 40%.

Depuis quelques années, nous avons constaté une augmentation significative du nombre de patients âgés adressés pour prise en charge chirurgicale. Les progrès récents dans la prise en charge chirurgicale et périopératoire de ces patients ont amélioré les résultats dans ce sous-groupe à risque.

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Le but de cette étude était d'évaluer l'Euroscore et d'identifier les facteurs de risque pré- et post-opératoires de mortalité hospitalière dans ce groupe de patients à risque adressé dans notre institution pour chirurgie valvulaire.

Matériel et méthodes

Patients

Entre janvier 2006 et juin 2009, 56 patients consécutifs âgés de plus de 70 ans ont bénéficié d'une chirurgie valvulaire avec circulation extracorporelle.

Données

Les données concernant les caractéristiques démographiques, le statut préopératoire, les données chirurgicales et les suites opératoires ont été recueillis de manière rétrospective. Les variables étudiées sont listées dans le Tableau 1.

Tableau n°1: variables étudiées

Pré-opératoires	
- âge	- broncho-pneumopathie chronique
- sexe	- insuffisance rénale
- classe NYHA	- FEVG
- angor	- HTAP
- hypertension artérielle systémique	- endocardite infectieuse
- diabète	- coronaropathie associée
- artériopathie périphérique	- type de valvulopathie
- pathologie cérébro-vasculaire	
Intra-opératoires	
- Procédure	
- Réoperation	- Délai (urgence, état critique)
- Durée de circulation extra-corporelle	- Durée de clampage aortique
- Pontages coronariens associés	- Geste sur l'aorte thoracique
Post-opératoires	
- Durée de réanimation	- Nécessité de transfusion
- Bas débit cardiaque	- Ischémie digestive
- Infarctus du myocarde	- Complication pulmonaire
- Fibrillation atriale	- Accident vasculaire cérébral
- Trouble de la conduction	- Insuffisance rénale
	- Infection
	- Réexploration chirurgicale

La définition de variables correspond à leur intituler dans la fiche de calcul de l'Euroscore. Les données du cathétérisme cardiaque incluant les lésions coronaires significatives (>50%), la présence et le degré de la dysfonction valvulaire et la fraction d'éjection ventriculaire gauche (FEVG) ont été rapportées si disponibles. L'atteinte vasculaire périphérique était définie par la présence d'une claudication, d'une occlusion carotidienne ou d'une sténose > 50% et par les antécédents de chirurgie artérielle sur l'aorte abdominale, les vaisseaux du cou ou les membres inférieurs. La notion de pathologie cérébro-vasculaire était définie par les antécédents d'accidents vasculaires cérébraux (AVC), d'accidents ischémiques transitoires (AIT), ou les deux. L'insuffisance rénale était définie par un taux de créatininémie supérieur à 200 µmol/l.

L'hypertension artérielle pulmonaire (HTAP) était analysée par échocardiographie Doppler. La notion d'urgence était défi nie par une intervention réalisée le jour de l'hospitalisation du patient et la présence d'un statut critique selon les critères suivants: tachycardie ou fibrillation ventriculaire ou mort subite récupérée, massage cardiaque préopératoire, intubation et ventilation mécanique avant l'entrée au bloc opératoire, support inotrope préopératoire, insuffisance rénale aiguë (diurèse < 10 ml/h) et présence d'un ballon de contre-pulsion intra-aortique préopératoire.

La technique opératoire était similaire chez tous les patients. Après anesthésie standard, par sternotomie médiane, après canulation aortique et atriale droite, une circulation extracorporelle non pulsatile en hypothermie modérée (32-33°C) était instituée. La protection myocardique était assurée par cardioplégie froide au sang antéro- et rétrograde et glaçage local au sérum froid intermittent.

La mortalité post-opératoire était définie comme la mortalité hospitalière (au bloc opératoire et dans le service quelque soit le délai après l'intervention).

Toutes les complications post-opératoires ont été relevées. Un bas débit cardiaque était défini par un support inotrope dépassant 24 heures. L'infarctus du myocarde (IDM) post-opératoire était défini par une ascension des enzymes cardiaques Troponine I, CPK et leur fraction MB (>50 UI) et des modifications éléctrocardiographiques (apparition d'une onde Q de nécrose). L'AVC était défini par un nouveau déficit focalisé durant plus de 24 heures. Les complications pulmonaires incluaient toutes celles nécessitant une ventilation mécanique prolongée (supérieure à 5 jours). La dysfonction rénale était définie comme une ascension de la créatininémie supérieure à 200 µmol/l ou la nécessité d'une hémo-filtration postopératoire.

Les Euroscores additifs et logistiques étaient calculés pour chaque patient afin de comparer la mortalité prédite par l'Euroscore avec la mortalité observée dans cette population.

Analyse statistique

Les variables continues ont été exprimées par une moyenne ± 1 déviation standard et ont été comparées par *le test de Student*. Les facteurs de risque préopératoires ont été examinés comme prédictifs de complications postopératoires et de mortalité par régression logistique uni variée et multivariée. Un seuil de 0.05 était retenu comme statistiquement significatif.

Résultats

Caractéristiques des patients et données opératoires

Il y avait 25 hommes (44,6%) et 31 femmes (55,4%). L'âge moyen était de 70 ± 2,4 ans (70 à 81 ans). Une coronarographie préopératoire était réalisée chez tous les patients programmés. Les caractéristiques démographiques et les co-morbidités associées sont listées dans le Tableau 2. Les données opératoires sont présentées dans le Tableau 3.

Tableau n°2: Caractéristiques démographiques et comorbidités associées

Variables	N°(%)
Classe NYHA	
➢ I	**4,7**
➢ II	**33,7**
➢ III	**51,0**
➢ IV	**10,6**
Diabète	**10,9**
HTA	**33,0**
Angor instable	**2,2**
Antécédents d'angor	**31,2**
Dysfonction rénale	**23,2**
➢ Créat 130-200 µmol/l	19,5
➢ Créat > 200 µmol/l	3,7
Bronchopneumopathie chr.	**13,9**
Pathologie cérébro-vasculaire	**7,2**
Artériopathie périphérique	**12,9**
Dysfonction VG	**23,2**
➢ FEVG 30-50%	20,4
➢ FEVG < 30%	2,8
Endocardite active	**4,1**
HTAP	**40,3**
➢ PAPs 40-60mmHg	27,5
➢ PAPs >60mmHg	12,8
Coronaropathie	**36,1**

Liste des abréviations:	
NYHA	*New York Heart Association;*
Créat	*créatininémie;*
VG	*ventricule gauche;*
FEVG	*fraction d'éjection ventriculaire gauche;*
PAPs	*pressions artérielles pulmonaires systémiques*

Tableau n°3: Données opératoires

Données opératoires	N°(%)
Délai d'intervention	
➢ Réglée	**90,0**
➢ Urgence	**8,0**
➢ Etat critique	**2,0**
Procédure	
RVAo	**57,0**
Chirurgie mitrale	**29,7**
RVAo + Chirurgie mitrale	**12,9**
Chirurgie tricuspide	**7,1**
PAC associés	**23,0**
Remplacement aorte ascendante	**2,8**
Liste des abréviations:	
RVAo	*remplacement valve aortique*
PAC	*pontages aorto-coronariens*

Le remplacement valvulaire aortique (RVAo) était la procédure la plus fréquente. Le substitut de choix chez ces patients était une bioprothèse. Neuf (16,7%) étaient des reintervention. L'Euroscore additif moyen était de 9,05 (6-23) et l'Euroscore logistique moyen de 14,2% (5,2-76,3).

Complications et mortalité hospitalière

Les complications post-opératoires sont résumées dans le Tableau 4. La survenue d'une arythmie supra ventriculaire était la plus fréquente.

La mortalité hospitalière était de 8% (4 patients), pour une mortalité attendue de 9,05 avec l'Euroscore additif et de 14,2% avec l'Euroscore logistique. Les patients ont été divisés en 3 sous-groupes selon leur Euroscore, et la mortalité a été analysée pour chacun d'entre eux (Tableau 5). Durant la première partie de l'étude (2006-2007) la mortalité hospitalière était de 10,6% pour un Euroscore additif de 8,6, et durant la seconde partie de l'étude (2008-2009), la mortalité hospitalière était de 6,4% pour un Euroscore additif de 9,3. Concernant les reintervention, la mortalité hospitalière était de 13,4%.

Facteurs de risque de mortalité

L'analyse uni variée des facteurs influençant la mortalité hospitalière globale a révélé que les facteurs de risque significatifs préopératoires étaient la classe NYHA III ou IV (P = 0,04), les reintervention (P = 0,02), un état critique selon l'Euroscore (P = 0,03), l'hypertension artérielle pulmonaire (P = 0,01), la chirurgie mitrale (P = 0,02) et la chirurgie tricuspide (P < 0,001). Les facteurs de risque post-opératoires de mortalité étaient le bas débit cardiaque (P < 0,001), la dysfonction rénale (P = 0,01), les complications gastro-intestinales (P = 0,02), la reéxploration chirurgicale (P < 0,001), et le besoin de transfusion sanguine (P = 0,02). Les résultats de l'analyse multivariée sont rapportés dans le Tableau 6.

Discussion

Les femmes représentent la majorité (55,4%), comme dans les autres études concernant les patients âgés, du fait de leur plus longue espérance de vie. Les facteurs de risque préopératoires étaient similaires aux patients plus jeunes exception faite de la proportion de diabète (10,9%), qui reste inférieure du fait de la faible espérance de vie dans ce sous-groupe. Dans notre série la mortalité hospitalière était de 8%, similaire aux résultats rapportés par Akins et al. [2] pour les patients bénéficiant d'un remplacement valvulaire isolé, et moindre que d'autres séries concernant des patients âgés [3, 4].Concernant l'Euroscore, nous avons montré que dans les sous-groupes à faible risque et à risque modéré, l'Euroscore additif donnait une excellente discrimination, et même surestimait légèrement le risque opératoire, comme rapporté par Stoica et al. [5], spécialement dans la seconde période de notre étude. Dans le sous-groupe à haut risque [Euroscore>12], nos résultats montrent que l'Euroscore additif sous estime le risque opératoire, comme rapporté par Jin et al. [6]. Concernant l'Euroscore logistique, il y a une bonne discrimination chez les patients à faible risque, alors qu'il surestime la mortalité opératoire dans les sous-groupes à risque modéré et encore plus dans celui des patients à haut risque (49,3% prévue pour 17,1% observée).

Concernant les reinterventions, Kirsch et al. [7] rapportent une mortalité opératoire de 32% chez 22 patients, alors que la reintervention n'était pas un facteur de risque dans leur précédente étude [4]. Dans notre étude, les reinterventions sont un facteur de risque significatif de mortalité opératoire avec 13,4% de décès. La mortalité opératoire n'est pas supérieure dans les interventions réalisées en urgence, contrairement à d'autres séries [4]. Les facteurs de risque préopératoires étaient la classe NYHA>2 et l'HTAP, comme rapporté par Kirsch et al. [4], la chirurgie mitrale, comme rapporté par Goldsmith et al. [9], et la chirurgie tricuspide. Concernant l'atteinte coronarienne, sa prévalence augmente avec l'âge. Ainsi, l'association pathologie valvulaire-lésions coronariennes est fréquente chez les populations âgées [2]. Un geste de revascularisation myocardique associé n'a pas augmenté la mortalité opératoire dans notre série. En fait plusieurs séries [3,9] ont montré une baisse de la mortalité opératoire quand la chirurgie valvulaire était associée avec une revascularisation myocardique, spécialement à l'aide de l'artère mammaire interne. La réalisation systématique d'une coronarographie préopératoire, la protection myocardique à la fois antéro- et rétrograde [10], et la réalisation de pontages aorto-coronariens en cas de sténose significative (>70%) semblent être bénéfiques pour ces patients.

L'arythmie supra-ventriculaire était la complication la plus fréquente dans notre série (32,7% des patients), mais moindre que dans la série d'Avery [3] où la fibrillation atriale atteignait 55,3% des patients, sans mortalité surajoutée. Un bas débit cardiaque a été observé chez 12% des patients dans notre série avec augmentation de la mortalité, comme montré dans la majorité des études. La dysfonction rénale était un facteur de risque de mortalité hospitalière, comme montré par Akins [2], alors que l'on ne le retrouve pas comme significatif dans d'autres séries [7,8]. Les complications digestives (spécialement l'ischémie mésentérique) sont rares mais associées à une surmortalité chez ces patients fragiles. La nécessité d'une ré-exploration chirurgicale est comprise entre 5,6 et 13% dans la littérature [4,8], couplée à un besoin accru en transfusions sanguines, à un risque plus élevé d'infection, de défaillance pulmonaire et de décès hospitalier. Nos résultats dans ce domaine sont comparables. Malgré des difficultés techniques accrues chez les patients âgés, plusieurs études rapportent un gain fonctionnel certain et une survie à long terme parallèle à celle de la population générale du même âge.

Conclusions

Les résultats de notre étude montrent que la chirurgie valvulaire après 70 ans et sûre et à faible risque. Le taux de mortalité dans la période la plus récente est bas. L'Euroscore additif est corrélé à la mortalité globale, mais surestime le risque dans la période la plus récente de notre étude.

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Mitral valve repair for degenerative mitral regurgitation - Experience of 50 cases - *)

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Abstract

Objectives*: Mitral valve repair for degenerative mitral regurgitation has a better outcome and a lower mortality when compared with mitral replacement. We have evaluated this technique's results at one month, 3 months, 6 months, 12 months and then annually.*

Material and Method: *We have retrospectively analyzed 50 patients (37 male, 13 female) with severe mitral regurgitation who have undergone mitral valve repair between 2007-2011. Twenty-three patients were in functional NYHA class II, 26 were in NYHA class III and one was in acute pulmonary edema. The mean ejection fraction of the left ventricle was 62,64% (±6,58%). Most cases concerned the posterior mitral valve (36 cases), followed by ruptured chordae of the anterior mitral valve (7 cases), Barlow's disease (6 cases) and a mixed mechanism (1 case). Several types of mitral valve repair were used: quadrangular/triangular resection of the P2 segment with sliding of the P1-P3 segments, chordal replacement, Alfieri-type suture etc. Edwards-Carpentier rigid annuloplasty rings were placed in all of the cases.*

Results: *There were no in-hospital deaths and no reinterventions. Thirty-three patients had no residual mitral regurgitation and 17 had minor regurgitation. The left ventricle ejection fraction showed no modification. The follow-up study was 3-55 months; 12 patients were out of study for lack of presentation at periodical evaluation. During this period, the mitral valve function was normal, with no or minor mitral regurgitation. In one case we noticed the progression of initial mitral regurgitation from grade 1 to grade 4 one year after the operation due to deveploment of posterior mitral valve restriction. Eighteen months after the initial operation we reoperated the patient and we performed a mechanical valve replacement.*

Conclusions: *On medium term, mitral valve repair is an effective technique with very low complication rates and mortality.*

Key-words: *Mitral valve repair; Degenerative mitral regurgitation; Short term results*

Rezumat

Obiective: *Plastia de valvă mitrală în insuficiența mitrală degenerativă se asociază cu mortalitate mai mică şi rezultate mai bune decât protezarea mitrală. Am evaluat postoperator rezultatele acestei tehnici la pacienți operați cu plastie de valvă mitrală la intervale de o lună, 3 luni, 6 luni, 12 luni şi apoi anual.*

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Material şi Metodă: *Am analizat retrospectiv 50 de pacienți (37 de bărbați, 13 femei) cu insuficiență mitrală degenerativă severă, operați în perioada 2007-2011. Douăzeci şi trei de pacienți erau în clasa funcțională NYHA II, 26 pacienți erau în clasa NYHA III şi un pacient în edem pulmonar acut. Fracția medie de ejecție a ventriculului stâng a fost de 62,64% (±6,58%). A predominat patologia cuspei posterioare (36 de cazuri), urmată de ruptura cordajelor cuspei anterioare (7 cazuri), boala Barlow (6 cazuri) şi mecanism mixt (1 caz). S-au practicat mai multe tipuri de plastie mitrală, în funcție de etiologie: rezecție cvadrangulară/triunghiulară de scalop P2 şi sliding, neocordaje pe cuspa anterioară, sutură tip Alfieri etc., însoțite în toate cazurile de anuloplastie cu inele rigide Edwards-Carpentier.*

Rezultate: *Nu s-a înregistrat nici un deces intra-/perioperator şi nici o reintervenție de corecție precoce. La externare, 33 de pacienți prezentau regurgitare mitrală reziduală minimă şi 17 pacienți aveau regurgitare uşoară. Fracția de ejecție a ventriculului stâng nu a prezentat modificări. Perioada de* follow-up *a variat între 3 şi 55 de luni; 12 pacienți au ieşit din studiu prin neprezentare la controalele periodice. În această perioadă nu s-a înregistrat nici un deces iar funcția valvei mitrale a rămas în parametri normali, cu menținerea aceluiaşi grad de regurgitare mitrală (minimă sau uşoară). Într-un singur caz, s-a înregistrat o progresie a insuficienței mitrale reziduale până la gradul IV, fiind vorba însă despre un pacient la care s-a asociat un dublu by-pass aorto-coronarian şi care a dezvoltat o restricție de valvă mitrală posterioară în decurs de 12 luni de la momentul efectuării plastiei. La 18 luni postoperator s-a reintervenit şi s-a practicat protezarea valvulară mitrală cu o proteză mecanică.*

Concluzii*: Pe termen mediu, valvuloplastia mitrală este o tehnică eficace, cu o rată redusă a complicațiilor şi cu mortalitate foarte mică.*

Cuvinte-cheie: *Plastie de mitrală; Insuficiență mitrală degenerativă; Rezultate termen mediu*

Introduction

Mitral valve repair is considered the gold standard for the surgical correction of mitral insufficiency. This technique was first introduced in 1959 by Merendino and his colleagues, who made the first postero-medial annuloplasties [1]. In 1969, Carpentier introduces a series of standardized techniques for mitral insufficiency correction [2]. A large number of studies demonstrated that in the case of degenerative mitral regurgitation, mitral valve repair provides a reduced peri-operative mortality rate and longer event-free survival compared with mitral valve replacement [3]. Therefore, mitral valve repair began to be increasingly used as treatment strategy for other etiologies of mitral regurgitation (rheumatic, infectious and ischemic) [4] [5] [6]. Survival to 10 years without reintervention on the mitral valve varies between 72 and 90%. Survival at 20 years for patients with mitral valve repair for degenerative etiology is 48%, similar to normal population with the same age [5]. Thus, whenever feasible, mitral valve repair is preferable to mitral valve replacement [7].

Material and Methods

Patients

We have retrospectively analyzed 50 patients (37 males, 13 females) who have undergone mitral valve repair between 2007-2011 for severe mitral insufficiency (MI) of degenerative, rheumatic and myxomatous etiology, with no other mitral valve associated pathology. Patients with ischemic mitral insufficiency were excluded from the study.

The mean age was 59.63 ± 9.46 years (with values in the range of 37-74 years). On admission, 23 patients were in functional NYHA class II, 26 were in NYHA class III and one was in acute pulmonary edema. All patients were examined by transthoracic echocardiography (TTE) followed by transesophageal ultrasound (TEE). Regarding the severity of mitral insufficiency, all patients had significant MI, mainly fourth degree MI at TEE examination (Figure 1). The mean ejection fraction of the left ventricle was 62.64% (±6.58%).

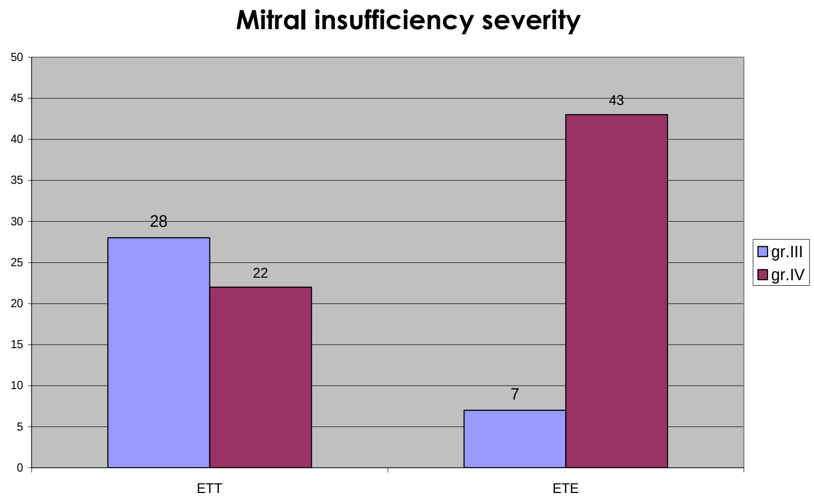

Figure 1:

Mitral insufficiency severity assessment by transthoracic (TTE) and transesophageal ultrasound (TEE)

Associated pathology is summarized in Table 1.

Table 1: Associated comorbidities of the studied patients

Comorbidities	Number of cases (%)
Coronary lesions	**3 (6%)**
Tricuspid insufficiency > gr. III	**7 (14%)**
Pulmonary hypertension	**11 (22%)**
Preexistant chronic atrial fibrillation	**15 (30%) (5 cases farmacologically treated in the postoperative period)**
Ostium secundum type interatrial septal defect	**4 (8%)**
Artherial Hypertension	**12 (24%)**
Dislipidaemia	**14 (28%)**
Diabetes Mellitus	**5 (10%)**

Regarding the mechanism of mitral insufficiency, most cases concerned the *posterior mitral valve* [PMV], accompanied by enlargement of the mitral annulus: 36 cases (72%), of which 28 cases only the P2 scallop was involved, the rest of the cases involving several posterior scallops. Isolated rupture of the anterior mitral valve chordae was found in 7 cases (14%). Barlow disease was present in 6 (12%) patients. One patient had mitral ring enlargement due to the presence of an *interatrial septal defect* [IASD] (Figure 2).

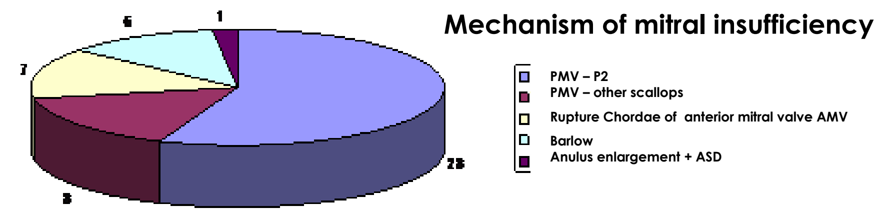

Figure 2: Mechanism of mitral insufficiency

All 50 patients underwent mitral annuloplasty using Edwards-Carpentier rigid annuloplasty rings. Interventions on the cusps and chordae were performed in 48 cases. As associated procedures in 4 cases we performed IASD closing and in 3 cases myocardial revascularization by ***c****oronary* ***a****rtery* ***b****y-pass* ***g****rafting* [CABG]. The mechanism of the mitral insufficiency in these cases was the rupture of the posterior- respectively anterior mitral valve chordae. We also performed a tricuspid annuloplasty for a patient with severe tricuspid insufficiency.

Surgical technique

The surgical approach was by median sternotomy. Patients were **c**onnected to the **e**xtracorporeal **c**irculation [CEC] system through cannulas placed in the ascending aorta, inferior and superior vena cava.

Cardiac arrest in diastole was obtained by anterograde administration of a haemo-potassic cold solution, in the aortic bulb. Patients were kept in normothermy throughout the CEC.

The mitral valve was exposed through left atriothomy.

The chosen surgical procedure depended on the mechanism of the mitral regurgitation. So, in the case of isolated posterior mitral valve involvement we performed quadrangular or triangular resection of the P2 segment with more or less extensive sliding of the P1-P3 segments.

In Barlow disease we performed Alfieri-type mitral annuloplasty (suture A2-P2) and in isolated anterior mitral valve pathology we performed chordal replacement with the implantation of Goretex neo-chordae, or chordae shortening.

In one case we performed papillary muscle splitting with anterior mitral valve shaving.

In Figure 3 (next page), we present the mitral valve repair techniques used.

In all cases, after the mitral valve repair, before performing the left atrioraphy, the mitral valve continence was checked, with serum (Figure 4, next page).

After contractile activity resumption and normal heart function restoration in accurate hemodynamic conditions, trans-esophageal echocardiography examination was performed (TEE).

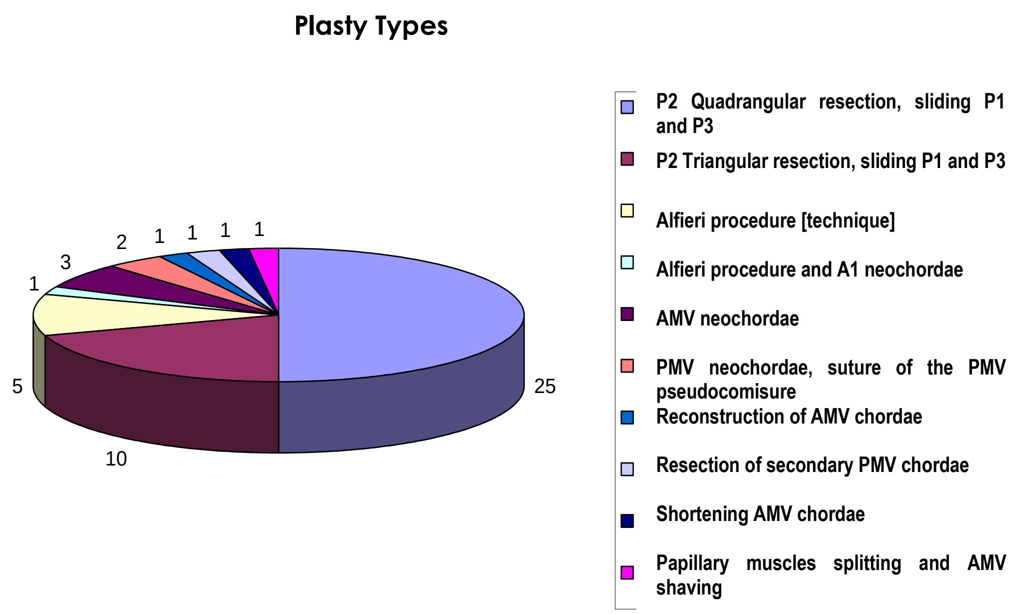

Figure 3: Mitral valve repair techniques performed

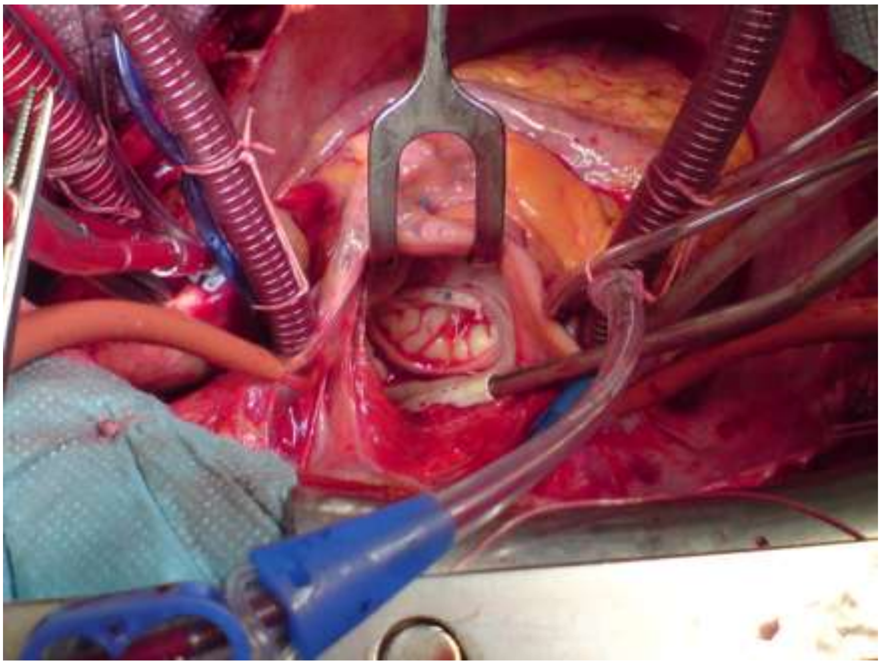

Figure 4: Gore-Tex chordae at A3 level – continent valve – at the serum test

Results

The mean extracorporeal circulation time (CEC) was 85.7 minutes (± 20.07 minutes) and the mean clamping time of the aorta was 62.95 minutes (± 17.6 minutes). There were no cases of re-entering in CEC and no conversions in mitral valve replacement.

The postoperative hemodynamics was stable under minimal pharmacologic support. Forty patients required inotrop positive support in small doses, administered between days 1 and 4 post-operatively; 8 patients required administration of vasoconstrictors.

There were no cases of major organ dysfunction, thromboembolic events or sepsis.

The average ICU stay was 3.5 days.

Trans-thoracic echocardiography performed before discharge showed no mitral regurgitation in 33 cases (66%) and slight regurgitation in the remaining 14 cases (Figure 5).

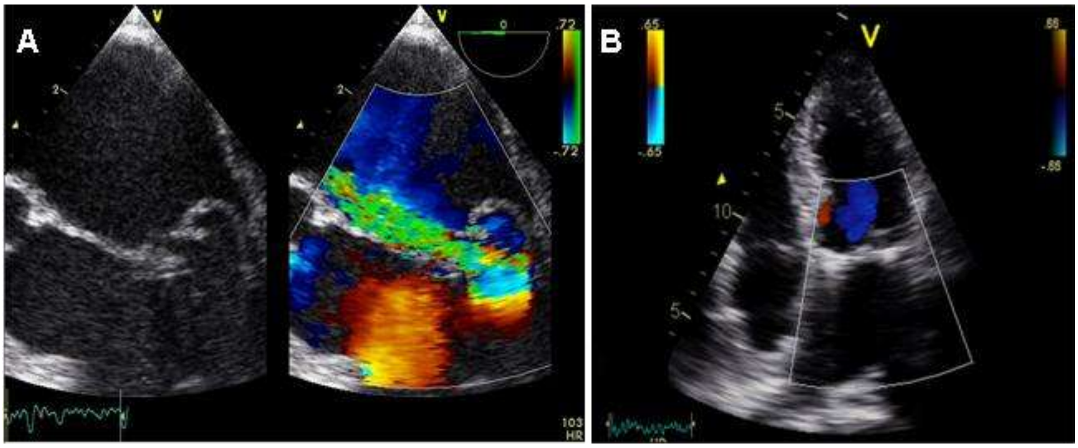

Figure 5. Severe mitral regurgitation with prolapse of the P2 segment - pre-and postoperative images. A. Transesophageal echocardiography, medioesophageal section - long axis. 2D and color Doppler examination. We notice the posterior mitral valve prolapse and flail at the level of the P2 scallop, with severe mitral regurgitation. B. Postoperative image - no residual mitral regurgitation.

The mean postoperative transvalvular gradient was 9.5 mm Hg ± 2.01 mm Hg. Mean mitral valve area was 2.34 cm^2 ± 0.49 cm^2. There were no cases of SAM (systolic anterior motion) of the mitral valve.

The mean postoperative left ventricular ejection fraction, estimated by biplane Simpson method with trans-thoracic ultrasound, was 54.15% ± 5.23%.

The average postoperative hospitalization was 10.2 days.

There were no intraoperative or early postoperative deaths. We had two re-interventions for early postoperative bleeding; there were no re-interventions for mediastinitis, residual mitral regurgitation or mitral stenosis.

All patients were followed by echocardiography at one month post-operatively at 6 and 12 months post-operatively and then annually. The follow-up period ranged between 3 and 48 months. 12 patients were excluded from the study by missing the regular follow-up examinations. During this period there were no deaths and the mitral valve function remained within normal parameters, while maintaining the same degree of regurgitation at consecutive follow-ups (minimal or small) In one case, there was a residual mitral regurgitation that progressed to grade IV, but it must be taken into consideration that it was a patient who previously underwent double aorto-coronary bypass surgery and developed a posterior mitral valve restriction 12 months from the time of the mitral valve repair. At 18 months after the initial intervention we performed a mitral valve replacement using a mechanical valve.

Discutions

The several disadvantages of mitral valve replacement led to an increased interest in the mitral valve repair techniques. Carpentier's concept of a conservative approach of the mitral valve pathology was verified by numerous clinical studies and has proven its validity. Today it is fully accepted that mitral valve repair is an effective treatment of mitral insufficiency with good long-term durability [8].

The complication rate is low and the preservation of the subvalvular apparatus is associated with the conservation of the left ventricular ejection fraction, as was demonstrated in several clinical and experimental trials [9], [10].

The addressed pathology of this conservative intervention is becoming more diversified. Practically, mitral valve repair has become the intervention of choice in the treatment of degenerative and mixomatous mitral valve insufficiency. The standard technique used for PMV prolapse (which is the most common cause of mitral regurgitation), namely quadrangular / triangular resection of the P2 segment, sliding of the P1-P3 segments and annuloplasty is associated with a low mortality and complication rate [9], [11].

AMV prolapse still represents a challenge for the cardiac surgeon, because it requires a more demanding intervention method from a technical standpoint, with less predictable results than PVM repair, namely chordae shortening or replacement. The chordae shortening was often associated with recurrent mitral regurgitation due to their rupture [12]. To resolve these difficulties, David and Frater introduced the synthetic PTFE (Gore-Tex) chordae, a material with superior mechanical strength over time, whose surface is gradually covered by the endothelium without being accompanied by calcium deposits [13] [14]. The results obtained by implantation of neochordae are comparable to those of standard techniques performed at the PMV [15].

Complex mitral valve lesions, such as those found in Barlow's disease or infectious endocarditis are suitable for the Alfieri technique. This new procedure, relatively easy in technical terms, extends the mitral valve repair indication to cases where traditional procedures reach their limits: end-stage cardiomyopathy [16], chronic hemodialysis patients [17] severely calcified mitral ring, limited valve mobility (through ischemic or rheumatic lesions) or erosion on the free edge of the cusps [18]. It can also be used to correct a detected residual mitral regurgitation at intraoperative TEE control during a mitral valve repair intervention [19]. Short and medium term results are satisfactory, with no residual regurgitation or functional mitral stenosis [20] [21]. We used this technique for the 6 cases of Barlow disease and one case of A1 chordae rupture associated with hypertrophic PMV, where we implanted also 2 neochordae on the AMV. Control TEE demonstrated the absence of further modifications at this level.

It can be seen that there is an arsenal of techniques to address degenerative mitral insufficiency. Besides the good results of their use, another advantage is the reduced duration of the aortic clamping and CEC time. These reduced time intervals correlate with low mortality and a better postoperative recovery (short ICU stay period, low pharmacological requirements, reduced complication rate, short hospitalization time) [22]. As mentioned, we had no peri- and postoperative deaths.

Conclusions

On medium term, mitral valve repair is an effective technique with very low complication rates and mortality.

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Facteurs pronostiques de morbi-mortalite de la Chirurgie Valvulaire Redux *)

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Résumé

Objectifs: *la chirurgie valvulaire rédux est de plus en plus fréquente en Algérie. Le but de cette étude était d'identifier les facteurs de risque de morbi-mortalité hospitalière de ce type de chirurgie.*

Methode: *49 patients d'un âge moyen de 51 ans (20-67ans) et avec un sex-ratio de 0.88 ont bénéficié de chirurgie valvulaire rédux entre janvier 2006 et janvier 2009; il s'agissait de chirurgie programmée dans la majorité des cas (89.79%), et dans prés de la moitié des cas (46%) la primo-intervention a été effectuée dans notre service; les causes de ré interventions les plus fréquentes sont les dysfonctions de plastie mitrale, l'expression d'une nouvelle atteinte valvulaire et les désintertions de prothèses mécaniques sur endocardite infectieuse. L'Euroscore a été utilisé pour prédire le risque opératoire.*

Resultats: *80% de nos patients, sont classés dans le groupe dit à risque modéré (score 3-5) avec une mortalité attendue comprise entre 2.90 et 2.94%, nos résultats retrouvent pour ces patients une mortalité à 2.56%. L'étude des résultats post opératoires a objectivé un certain nombre de complications cardiaques (28.5% de bas débit et 37% de troubles du rythme), de complications infectieuses (8% de médiastinites) et de complications neurologiques (6%). Les facteurs de risque de mortalité opératoire retrouvés sont: un geste valvulaire multiple ($p = 0.03$), une fibrillation auriculaire persistante ou apparue en postopératoire ($p = 0.05$) et enfin un âge supérieur à 70 ans ($p = 0.04$).*

Conclusion: *La chirurgie de rédux valvulaire avec geste mono-valvulaire présente une morbi-mortalité opératoire, une survie actuarielle et un bénéfice fonctionnel post-opératoire tout à fait comparables à ceux d'une primo-intervention; Alors que dans la chirurgie de rédux avec geste pluri-valvulaire, la morbi-mortalité opératoire est nettement supérieure, mais la survie actuarielle et le bénéfice fonctionnel sont comparables à ceux d'une primo-intervention.*

Mots-clés: *chirurgie valvulaire, réintervention, morbi-mortalité*

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Introduction

La pathologie valvulaire rédux, cad la réintervention portant sur un geste valvulaire chez un patient déjà opéré une ou plusieurs fois auparavant pour une pathologie valvulaire, est en augmentation constante; elle représente 10% à 15% des patients opérés dans le service.

Ce qui reste vrai c'est que c'est une chirurgie à haut risque de morbi-mortalité (sup. à 5%) non seulement à cause du terrain (multiples tares), mais aussi à cause de la pathologie cardiaque valvulaire (resténose valvulaire, dysfonction de prothèse, désintertion de prothèse sur endocardite, thrombose...).

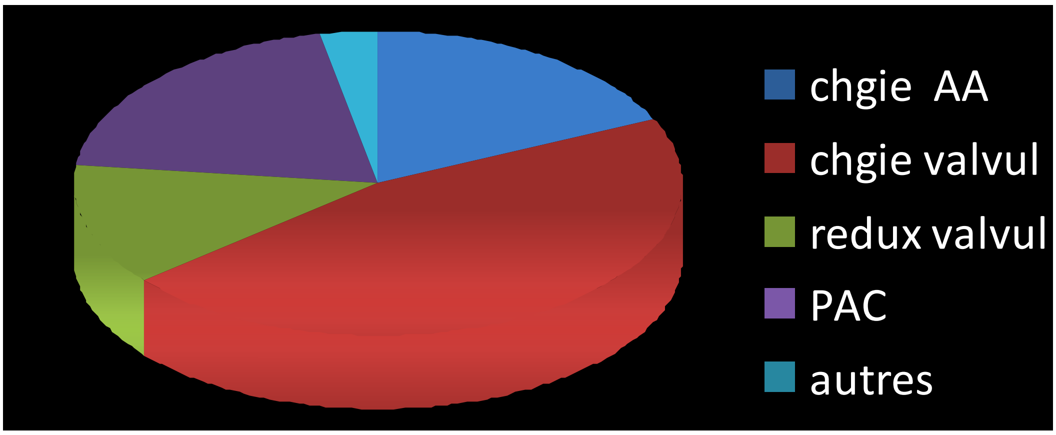
Ce qui change par contre, c'est l'épidémiologie des patients, en effet nous avons affaire à des patients de plus en plus âgés et qui présentent le plus souvent une ou plusieurs tares (diabète, HTA, troubles du rythme, IRF…).

Matériel et méthode

Il s'agit d'une étude rétrospective portant sur une série de 49 patients opérés de janvier 2006 à janvier 2009 dans le service de chirurgie cardio-vasculaire de l'EHS MA.MAOUCHE.

Le sex-ratio est de 0.88 avec une légère prédominance féminine (23 hommes / 26 femmes), l'âge moyen est de 51 ans (extrêmes 20-67 ans), pour le type de chirurgie il s'agit de chirurgie programmée dans 89.79% (seul 05 patients ont été opérés en urgence); enfin pour ce qui est de la provenance des patients il s'agit pour 46% de primo-interventions effectuées dans le service et pour 54% primo-interventions effectuées dans d'autres services en Algérie ou à l'étranger.

Dans cette étude, le critère d'inclusion est de retenir toute réintervention après primo-intervention valvulaire; il s'agit surtout d'une réintervention, mais nous avons recensé néanmoins 04 cas de réinterventions mutiples; le délai de réintervention moyen est de 12 ans (extrêmes 21 jours/26ans).



Les patients présentent de plus en plus souvent une ou plusieurs tares qui peuvent être à l'origine de complications dans les suites post-opératoires et qui allongent la durée d'hospitalisation; en effet prés du tiers des patients présentent une HTA (28%) et/ou un DID (26%), et a présenté un ou plusieurs épisodes d'insuffisance cardiaque gauche, d'OAP, ou d'insuffisance rénale fonctionnelle; plus de la moitié des patients opérés présentait en pré-opératoire des troubles du rythme à type de FA (56%); enfin pour cette série de patients le stade NYHA moyen est de 3.2 ± 0.9.

Pour ce qui est des explorations pré-opératoires, l'indice cardio-thoracique moyen est à 58 ± 5%, l'étude de l'ECG a objectivé 12% de blocs de branche gauche, enfin les données échocardiographiques pré-opératoires ont relevé une fraction d'éjection moyenne à 56 ± 20%, et une pression artérielle pulmonaire systolique moyenne élevée puisqu'elle est à 58 ± 15 mm Hg.

Resultats

Pour ce qui est des causes de réinterventions, nous avons relevé par ordre de fréquence décroissante, les dysfonctions de plastie (qui concernent le plus souvent la valve mitrale), l'expression d'une nouvelle atteinte valvulaire (il s'agit surtout des insuffisances tricuspides négligées lors de la primo-intervention), puis viennent les désintertions de prothèse (dont prés de la moitié sur endocardites infectieuses), les thromboses de prothèses (surtout mitrales) et enfin les dysfonctions de prothèses (surtout aortiques).

L'étude dans le détail des causes de dysfonction de plastie mitrale objective que le geste effectué lors de la primo-intervention consistait par ordre décroissant en une commissurotomie à cœur ouvert, une plastie mitrale avec mise en place d'un anneau de CARPENTIER, et enfin d'une commissurotomie à cœur fermé; nous avons par ailleurs remarqué que les délais moyens de réintervention (pour chacun des gestes effectués en primo-intervention) sont intéressants puisqu'ils sont tous supérieurs à 10 ans.

L'étude des causes de thrombose de valve prothétique mitrale a retrouvé une thrombose précoce à J19 post-opératoire par défaut d'anti-coagulation (patient opéré en urgence dans un tableau d'OAP et de bas débit sévère), deux thromboses sur grossesses de 8 semaines et enfin deux thromboses partielles sur valves prothètiques mécaniques.

Concernant les aspects de technique chirurgicale, la voie d'abord est toujours la sternotomie médiane itérative, la libération des adhérences prudente, la circulation extra-corporelle a été mise en place après canulation artério-veineuse le plus souvent classique.

La canulation artério-veineuse fémoro-fémorale est réservée aux réinterventions multiples, la durée moyenne de CEC est de 70 ± 14 minutes, la durée moyenne de clampage aortique est de 54 ± 15 minutes, enfin la protection myocardique utilisée s'est faite par injection antérograde de solution cardioplégique au sang froid.

La sortie de circulation extra-corporelle s'est révélée difficile dans prés d'un tiers des cas, puisque nous avons du faire face à un bas débit sévère qui a nécessité l'usage de drogues inotropes et même d'une assistance circulatoire.

L'étude des gestes opératoires effectués a révélé qu'en plus du remplacement valvulaire prothétique ou de la plastie valvulaire qui a motivé la rèintervention, nous avons procédé à des interventions de chirurgie combinée (associant remplacement valvulaire aortique et remplacement de l'aorte ascendante), ou à des gestes associés (résection de membrane sous-valvulaire aortique, fermeture de CIV, élargissement de l'anneau aortique…).

Cependant cette chirurgie reste difficile et nous avons eu à déplorer un certain nombre d'incidents per-opératoires tels que des plaies du toit de l'oreillette gauche, des veines cave supérieure ou inférieure, ou de l'anneau mitral; ces plaies ont été réparées sans incident si ce n'est un allongement du temps opératoire.

L'étude des résultats post-opératoires a objectivé un certain nombre de complications cardiaques (28.5% de bas débit, un patient décédé et 37% de troubles du rythme, 2 blocs auriculo-ventriculaires complets qui ont du être appareillés), de complications infectieuses (8% de médiastinites, 2 patients décédés) et de complications neurologiques (6%, 1 AVC massif fatal).

Discussion

La prédiction du risque en pré-opératoire est possible et doit se faire par la détermination statistique des facteurs de risque et par l'utilisation des scores (Euroscore, score Care, score de PARSONNET…) largement validés par de nombreuses études de par le monde.

La détermination statistique des facteurs de risque de survenue d'une médiastinite en post-opératoire a objectivé comme facteur de risque statistiquement significatif, l'obésité (p = 0.03), un diabète insulino-dèpendant (p = 0.025) et la durée opératoire (p = 0.05).

Par ailleurs, La détermination statistique des facteurs de risque de mortalité opératoire a retenu, en analyse univariée, comme facteurs de risque statistiquement significatif, un geste valvulaire multiple (p = 0.03), une fibrillation auriculaire persistante ou apparue en post-opératoire (p = 0.05) et enfin un âge supérieur à 70 ans (p = 0.04).

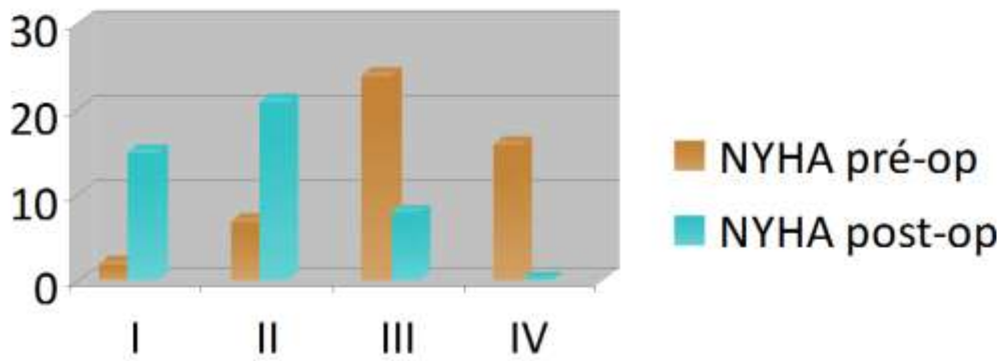
L'analyse multivariée quant à elle, ne retrouve aucun facteur statistiquement significatif de mortalité opératoire.

Dans cette étude, nous avons utilisé L'Euroscore pour la prédiction des risques de mortalité opératoire, ce score validé par de nombreuses études et facile d'utilisation détermine une probabilité directe de mortalité attendue.

80% de nos patients, sont classés dans le groupe dit à risque modéré (score 3-5) avec une mortalité attendue comprise entre 2.90 et 2.94%, nos résultats retrouvent pour ces patients une mortalité à 2.56%.

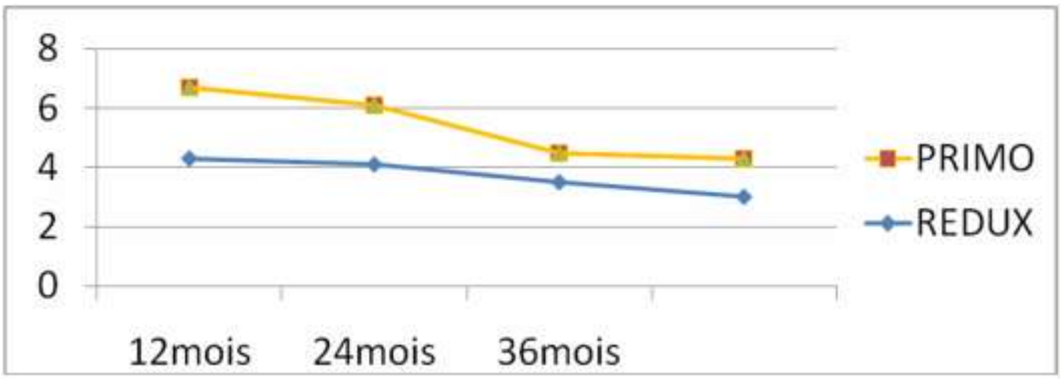
Pour les 20% restants, ils sont classés dans le groupe dit à risque élevé (score supérieur à 6) avec une mortalité attendue comprise entre 10.93 et 11.54%, nos résultats retrouvent pour ces patients une mortalité légèrement supérieure à 15%.

Quant au status fonctionnel en post-opératoire, l'étude démontre clairement un bénéfice fonctionnel certain puisque si en pré-opératoire la majorité des patients sont classés aux stades III et IV de la classification NYHA, en post-opératoire la quasi-totalité des patients sont classés aux stades I et II.

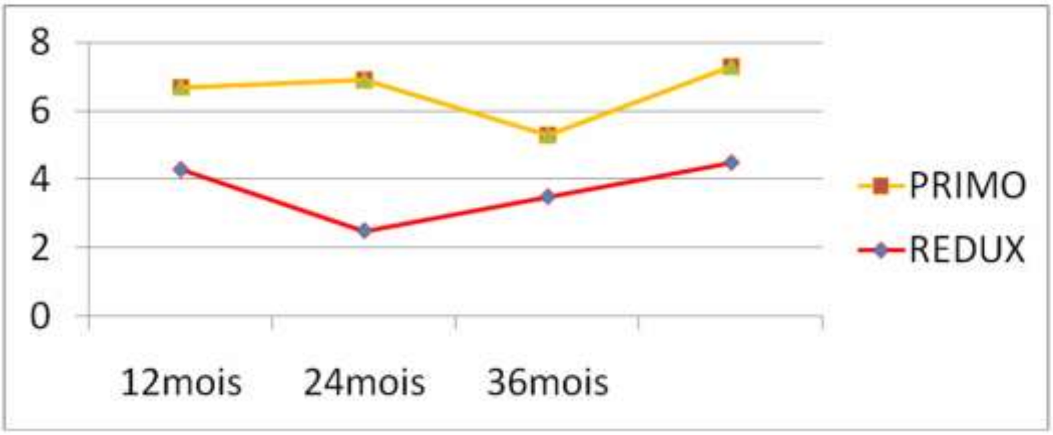


Quant à l'amélioration de la FEVG, sur un délai moyen de 18 mois nous avons revus tous les patients survivants, et l'étude des résultats a pu objectivé une amélioration moyenne de la FEVG de 18 ± 13%; la FEVG moyenne est passée de 56 ± 20% en pré-opératoire à 63 ± 12% en post-opératoire, cela signifie que 73% des patients survivants à l'issue de la période opératoire ont récupéré au moins 5 points de FEVG.

L'étude de la courbe de survie actuarielle à 3 ans des patients qui ont subi une réintervention avec geste mono-valvulaire et celle des patients qui ont bénéficié d'un geste mono-valvulaire en primo-intervention sont tout à fait comparables.



Alors que la comparaison de la courbe de survie actuarielle à 3 ans des patients qui ont subi une réintervention avec geste pluri-valvulaire avec celle des patients qui ont bénéficiés d'un geste pluri-valvulaire en primo-intervention montre des différences notables.



Conclusions

La chirurgie de rédux valvulaire avec geste mono-valvulaire présente une morbi-mortalité opératoire, une survie actuarielle et un bénéfice fonctionnel post-opératoire tout à fait comparables à ceux d'une primo-intervention.

Alors que dans la chirurgie de rédux avec geste pluri-valvulaire, la morbi-mortalité opératoire est nettement supérieure, mais la survie actuarielle et le bénéfice fonctionnel est comparable à ceux d'une primo-intervention.

Enfin, pour améliorer les résultats en terme de morbi-mortalité opératoire, il faut impérativement que la prise en charge chirurgicale soit précoce avant la détérioration du status fonctionnel (NYHA) et de la fonction ventriculaire (FEVG), il faut évaluer les co-morbidités et déterminer les risques de mortalité par l'utilisation des scores, et surtout, il faut améliorer le suivi médical des porteurs de prothèses valvulaires mécaniques.

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The echocardiographyc aspect of mitral valvular prostheses 25 Years after native valve replacement*)

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Abstract

Background. *The echocardiographyc aspect of mitral valvular prosthesis, 20 years after replacement is dominated by a multitude of fixed, mobile, permanent or irreproducible echoes; the purpose of this study is to establish echocardiographyc criteria of these signals which appears more than 25 years later after mechanical mitral valves replacement.*

Matherial and method. *A study of 34 patients with mitral valves replacement (4 patients-Starr-Edwards and 30 pacients-Bjork-Shiley) follow up by echocardiographyc 2D, 3D transthoracic and transesophageal to visualize the periprothetic reproducible echoes.*

Reproducible mobile echo-images, were present at 30 patients, and were represented by echo-images of various sizes to the level of the fixed part of mechanical valves („strands"), left atrial thrombosis, microbubbles, spontaneous contrast in left atrium, others mobile echo images.

The echoes were reproducible (71.4%) but they were not present all at the same patients.

Conclusions. *Echocardiography evaluation of mechanical mitral prosthesis impanted more than 25 years ago, showed mobile echo images to the annular part of prosthesis and to the level of element of sustain to the mobile part. At the mobile part of the mechanical prosthesis echo images were not present by echocardiography.*

Rezumat

Background. *Aspectul ecocardiografic al protezelor valvulare mitrale după ≥25 de ani de la implantare este dominat de diferite ecouri mobile sau fixe, permanente sau nereproductibile şi ne-am propus să analizăm criteriile ecocardiografice de recunoaştere ale acestora la purtătorii de proteze valvulare mitrale mecanice implantate în urmă cu peste 25 de ani.*

Metodă şi rezultate. *Pe un lot de 34 bolnavi cu proteze valvulare mecanice implantate în urmă cu peste 25 de ani, de tipul Starr-Edwards (4 pacienți) şi Bjork-Shiley (30 pacienți), s-a efectuat ecocardiografia 2D, 3D transtoracic (ETT) şi transesofagian (ETE) cu scopul de a obiectiva ecourile reproductibile apărute în spațiul periprotetic.*

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Au fost astfel evidențiate ecouri mobile reproductibile la 30 de pacienți şi au constat în ecouri liniare de mărimi diferite pe elementul de susținere al părții mobile şi la nivelul firelor de sutură, tromboză atrială stângă, contrast spontan în atriul stâng, microbule, alte ecouri mobile.

Dintre modificările ecocardiografice, 71,4% au fost reproductibile şi nu au fost toate întâlnite la acelaşi bolnav.

Concluzii. *Evaluarea ecocardiografică a protezelor mitrale mecanice implantate în urmă cu peste 25 de ani evidențiază ecouri mobile reproductibile situate atât pe inelul protezei cât şi pe componenta de susținere a elementului mobil.*

Funcționalitatea de lungă durată a acestei proteze nu a determinat modificări importante pe elementul mobil evidențiabile ecocardiografic.

Mechanical heart valves (artificial valves, prostheses) have been implanted since the beginning of the 1960s. They have been subject to continuous development and refinement of technical, hemodynamic, and biocompatibility parameters. Mechanical valves can be divided into caged-ball, disc (monodisc), and bileaflet valves [1].

Artificial heart valves (mechanical valves, prostheses) are constructed from three fundamental elements: mobile element (disc, ball), the cage (that holds the mobile element) and the sewing ring, fabricated from various textiles.

25 years ago the most used mechanical valves were the Starr- Edwards and Bjork-Shiley valves.

The Starr-Edwards valve is the best-known caged-ball valve (Figure 1a). In the 1960s and 1970s it was the most-often implanted valve in the world. From a long development line of Starr-Edwards valves, the successful mitral model has been manufactured without any modifications since 1966 [2], as well as the aortic model 1260 since 1968 [3]

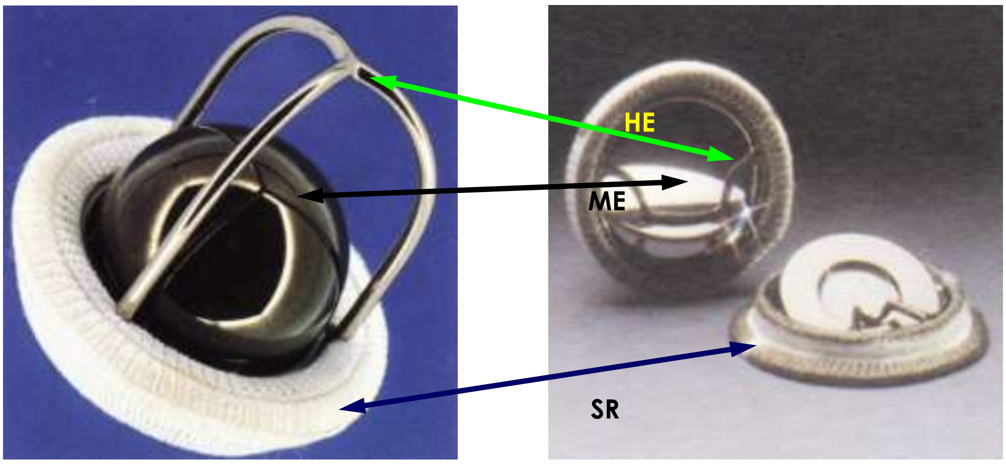


Figure 1a – Caged-ball valve (Starr Edwards)

Figure 1b – Tilting monodisc valve (Björk–Shiley)

HE – holding element, ME – mobile element, SR – sewing ring

The closing component of the valve is a silastic ball, which is held within a stellite alloy cage (opened position). In closed position the ball obturates the metallic ring equipped with a Teflon (DuPont, Wilmington, Del.) fabric sewing ring for implantation.

The more sophisticated tilting monodiscs were the most-often implanted valves in the 1970s and 1980s. In Europe, the most commonly used valves were the Björk–Shiley valves. The first model of this valve was introduced into clinical practice in 1969. It had a flat delrin disc, which tilted up to 60° [4]. The latest Björk-Shiley developmental type, the monostrut (Figure 1b), was introduced into clinical practice in 1982. The disc-housing system was changed and the angle of tilting was increased to 70° [5].

The labeled valve size of the prosthesis is determined by the tissue anulus diameter (TAD) that is common to all types of prostheses. The internal orifice diameter (IOD) of the valve is smaller than the labeled valve size. The whole artificial valve diameter is defined as the external sewing ring diameter (ESRD) (Figure 2).

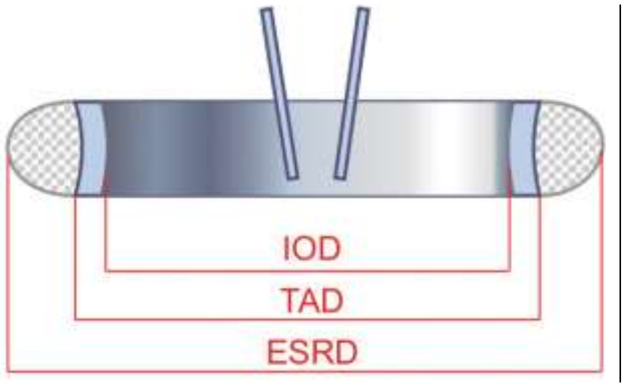


Figure 2 – Valve diameters.

IOD - internal orifice diameter,
TAD - tissue annulus diameter,
ESRD –
external sewing ring diameter [1]

Detailed echocardiographic analysis of mechanical prosthesis implies the identification of each constituent. This correlation is shown in Figure 3 and 4.

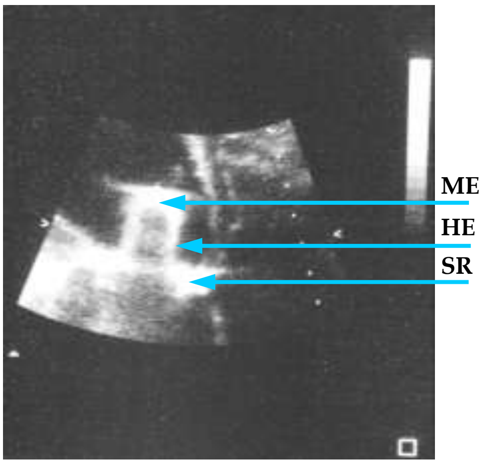


Figure 3 – Echocardiographic identification of the components of the Starr-Edwards prosthesis

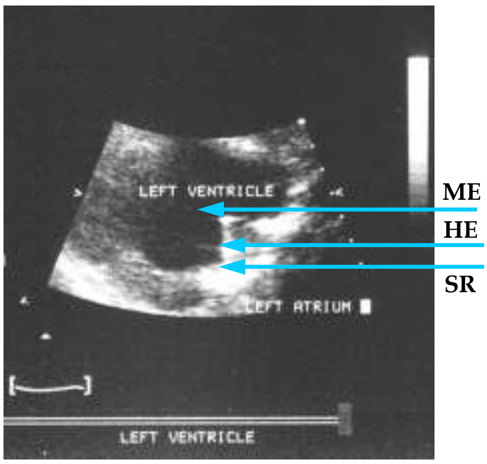


Figure 4 – Echocardiographic identification of the components of the Bjork-Shiley prosthesis

Each type of prosthesis can be identified by auscultation, echocardiography, 2D, 3D transoesophageal or radiological examination.

Generally more principles are considered in assessing the functionality of mechanical prostheses.

Hemodynamically, the most important parameter of both mechanical valves and bioprostheses is their effective orifice area (EOA; Figure 5).

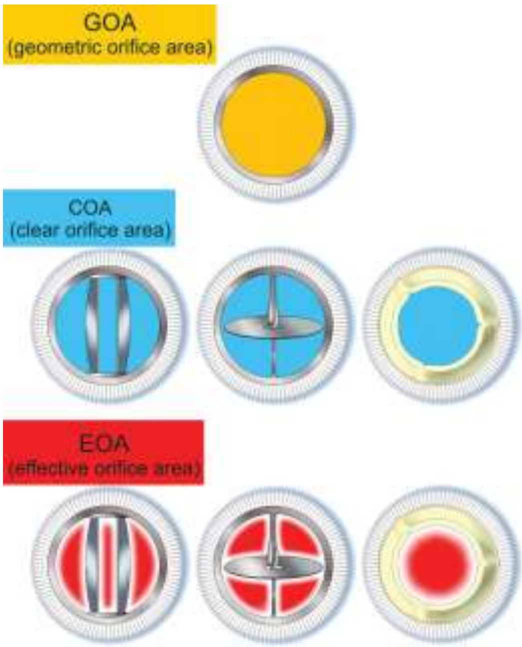


Figure 5: GOA, COA, and EOA of bileafl et valves (left column), tilting monodiscs (center column), and bioprostheses (right column)

Effective orifice area has to be differentiated from geometric orifice area (GOA). Geometric orifice area is the whole inner area of the valve including the area occupied by the opened discs or leaflets, struts, and other mechanisms of the valve. Calculation of the GOA is simple; it is the calculation of the circular area, the radius of which is half of the IOD. By subtracting the area of opening components of the valve from GOA, the so-called clear orifice area (COA) is obtained.

The EOA is that portion of the valve orifice area through which the blood really flows. The EOA is usually one quarter or one third smaller than GOA. The size of EOA and GOA is measured in square centimeters. In a given patient, the most important parameter is the indexed value (IEOA), i.e., EOA related to 1 m^2 of the patient's body surface [1].

The effective orifice area of the prosthetic valves is smaller than that of the bioprosthesis due to the prothetic and sewing ring. The transvalvular gradient is estimated through continuous Doppler after Bernouli's **($\Delta P=4V^2$)** equation. This can be influenced by several factors: the size of the prosthesis fixation ring, transvalvular flow profile, the relative obstruction of the mobile element, presence of intraprosthetic or paraprosthetic regurgitation.

The components of the mechanical prostheses may reflect ultrasound and therefore echocardiography is difficult in the morphological and functional assessment of the prosthesis elements.

Invasive methods are seldom used in the dysfunction assessment of the mechanical prosthesis due to difficulties in crossing the catheter through the prosthesis, thereby noninvasive, echocardiographic examination is particularly important to quantify the function of the mechanical valve.

Materials and methods

We studied mitral valve prosthesis implanted more than 20 years ago with 2D echocardiography, 3D transthoracic and / or transesophageal echocardiography.

The study group included 34 patients with mechanical mitral valveprosthesis. The studied prosthetic valve types were: Bjork-Shiley in 30 patients and Starr-Edwards in 4 patients. Time since the operation ranged from 25 to 34 years (Table I).

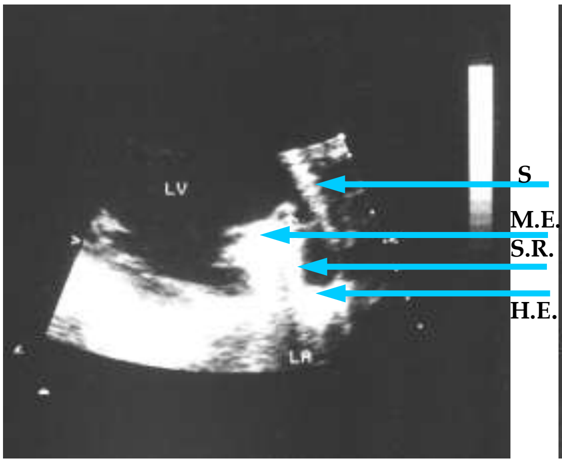
Table I: Valvular prostheses studied, number of patients and the time from mitral valvular replacement

Prosthetic valve type	Nr. of patients	Sex		Postoperator Time (years)
		Male	Female	
Bjork-Shiley	30	12	18	25-34
Starr-Edwards	4	2	2	25-36

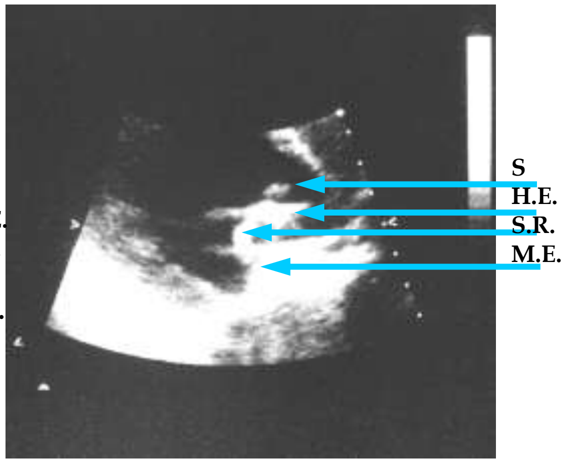
In the performed echocardiographic analysis we used the abnormal echodensities associated to the prosthetic mitral valve: continuous linear echodensity C.L.E (“strands”), microbubbles, spontaneous contrast, suture thread echogenicity, left atrial thrombosis. The definition of these mobile echoes is shown in Table II [6]:

Category	Definition
C.L.E („strand”)	Mobile echo with medium echogenity with a continuous linear aspect, visible intermittently during the cardiac cycle, but at the same place
Microbubbles	Intensely echogenic, discontinuous structures, appearing according to the movement of the mobile component of the prosthesis
Spontaneous contrast	Diffuse moving echoes, like "cigarette smoke", which appear around the fixation ring of the prosthesis in the left atrium
Suture thread	Linear, multiple, spaced echoes, that are in direct relationship with the support ring
Thrombosis	Echodense masses located in the left atrium or in relation to the mitral mechanical prosthesis.

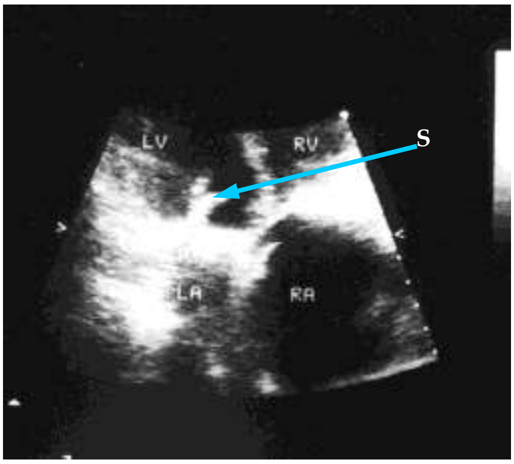
The continuous linear echodensity (CLE) ("strand") is represented by filaments produced by the multiple fibrin layers that start from the constituent elements of the prosthesis. They are mobile and reproducible (Figure 6, 7).



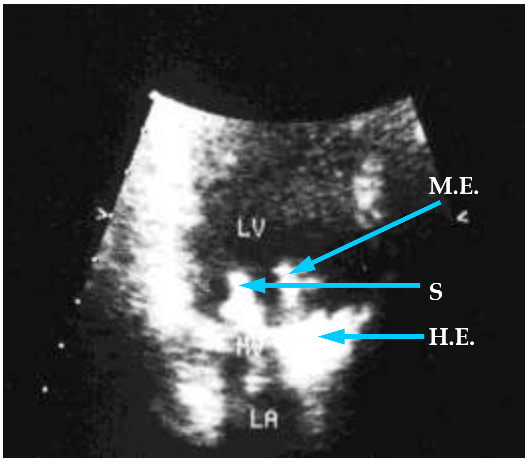
a)
Figure 6a: C.L.E. ("strands") (S) on the Starr-Edwards prosthesis in diastole



b)
Figure 6b: C.L.E ("strand")(S) on the Starr-Edwards prosthesis in systole

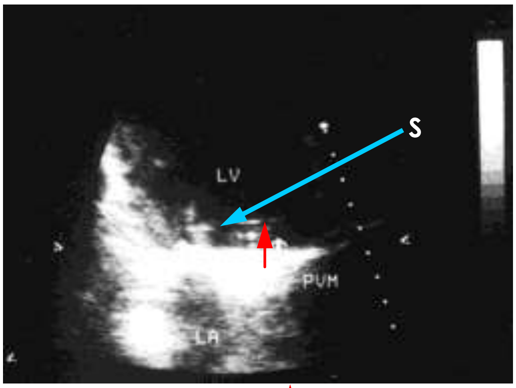


a)
Figure 7a: C.L.E. ("strand") (S) on the Bjork-Shiley prosthesis in systole



b)
Figure 7b: C.L.E ("strands") (S) on the Bjork-Shiley prosthesis in diastole

Microbubbles were found in the vicinity of the mobile element of the prosthesis. They are highly echogenic and are not permanent (Figure 8).



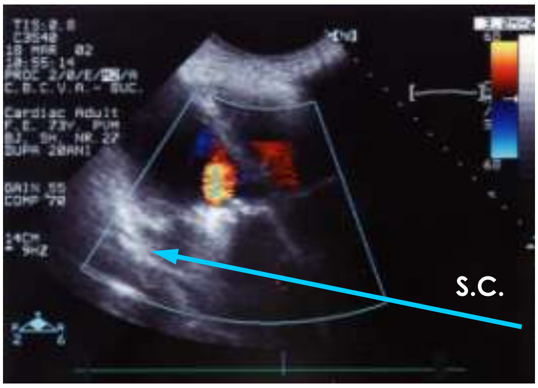
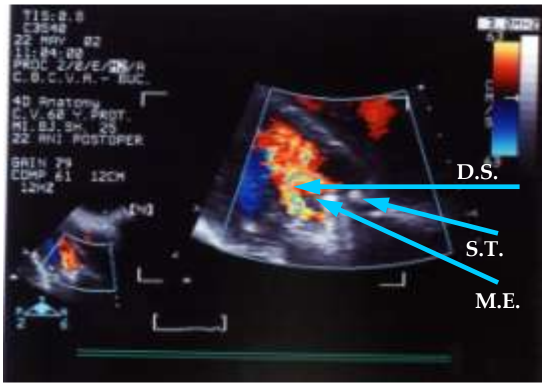


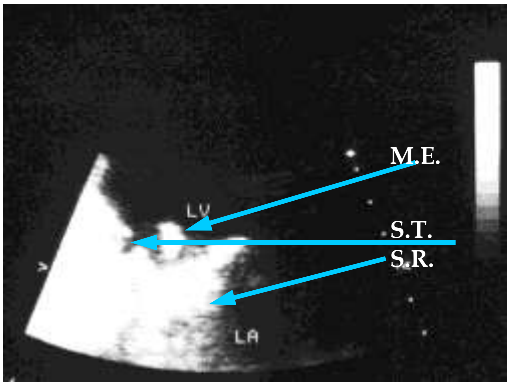
Figure 8: Microbubbles ( ) in the vicinity of the Bjork-Shiley prostheses that presents also C.L.E (S)

Figure 9: Spontaneous contrast (S.C.) at the prosthetic mitral valve with increased size left atrium

Spontaneous contrast, suture threads and LA thrombosis are presented in Figure 9, 10a, 10b, 11.



a)



b)

Figure 10a: Suture threads (S.T.) on the anterior prothetic ring; D.S. = transprothetic blood flow

Figure 10b: Suture threads (S.T.) on the posterior prothetic ring

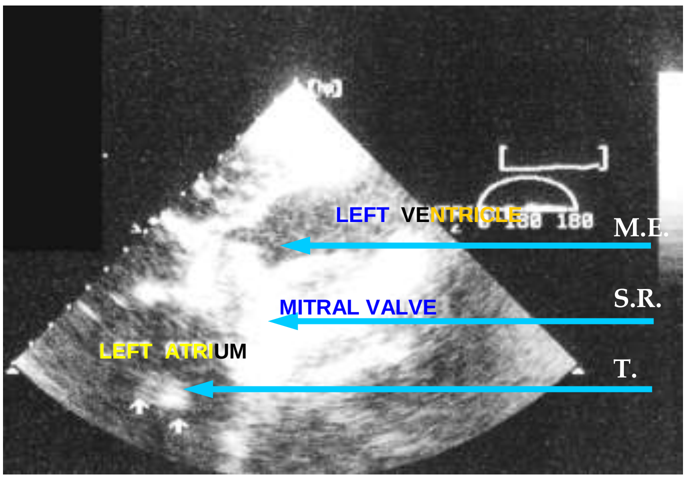


Figure 11: Left atrium thrombosis (T)

Results

In the studied group, the most common echocardiographic changes were C.L.E ("Strands") which is likely explained by the long term function of these prostheses (Table III).

Table III: Frequency of echocardiographic abnormalities

Echocardiographic find	Nr. of patients	Percent
C.L.E „strands”	20	71.4%
Microbubbles	10	35.3%
Spontaneous contrast	6	21.4%
Suture thread	4	14.2%
Other modifications	10	35.3%

Periprosthetic mobile echoes were found in 20 patients (71.4%), the remaining 8 patients in the study group showed no such changes (28.6%), making the physiopathological explanation for these changes more difficult.

Discussion

Our lot is characterized by more than 25 years after valve replacement, its dominant feature being the dynamic normofunction of the mitral valve prosthesis.

We analyzed the Starr-Edwards and Bjork-Shiley valve prostheses because they were more often implanted in our country.

Of the total patients studied, 2 had cerebral embolic events at 4 and 6 years postoperatively, they being neurologically recovered in the present.

Several studies in the literature (7, 8, 9) found correlation between the presence of these echocardiographic changes, in particular CLE (Strands) and cerebral embolic events.

In our study patients had these changes over five years, but no embolic events were highlighted.

Trials (6,10) confirmed the presence of these changes, but did not confirm the causes of these mobile echoes. The diagnosis remains echocardiographic and descriptive only.

The existence of reproductive criteria remains important.

In patients with mitral valve prosthesis thrombosis, who presented previously CLE on echocardiography and who underwent fibrinolytic treatment, after the resolution of the thrombotic phenomenon it could be observed the presence of CLE, which suggests their fibrin structure and recommended designation of "strands" (6).

In our study the most common changes were CLE ("strands") (75.1%). Recent studies on more patients and shorter postoperative period, the frequency of CLE (“strands”) was 26% (7.8). Table IV shows the mobile echo frequency in patients with mitral valve prosthesis in the literature (6).

Table IV: Mobile echo frequency in patients with mitral valve prosthesis

Ecographycal abnormality	Prevalence
C.L.E "strands"	13-67%
Microbubbles	0-50%
Spontaneous contrast	7-53%
Suture threads	0-37%
Other multiple echoes	27-80%

Conclusions

The presence of mobile echoes in patients with mitral valve prosthesis after more than 25 years after surgery is not an important pathological element, but must be monitored to determine the exact risk of embolization and their modification over time.

In the analyzed casuistry the mechanic prostheses were normofunctional and the patients had no embolic events during the studied period.

Diagnostic criteria are not established by consensus and their clinical importance is not evident. We mention that 4 patients in the study group underwent CABG and 6 patients underwent PCI with stent implantation under the conditions of the normofunctioning mitral valve prosthesis.

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Protheses mecaniques ou prothese biologique pour le remplacement valvulaire? *)

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Prothèse mécanique ou prothèse valvulaire? Cette question agite la communauté cardiologique depuis des lustres. Les malades concernés recherchent sur internet les informations récentes qui leur permettront de faire le bon choix ou feront confiance à leur cardiologue pour prendre la décision. Les Sociétés savantes, américaines et européennes ont emis des recommandations assez claires pour les patients les plus âgés mais qui laissent la décision au cardiologue pour les patients les plus jeunes. Dans cette grande confusion, une observation s'impose: le nombre des bioprothèses implantées est croissant, au dépend des valve mécaniques dans la plupart des pays développés. Par contre dans les pays émergents, la valve mécanique reste la valve la plus implantée, la bioprothèse restant un choix exceptionnel qui concerne moins de 10% des opérés.

Une mise au point sur la question est d'autant plus intéressante que des innovations technologiques importantes sont apparues, que les aspirations des malades ont beaucoup changé, que l'objectif même du traitement s'est, à la suite des observations précédentes beaucoup modifié.

Les innovations technologiques sont très importantes dans le domaine des bioprothèses, beaucoup moins importantes dans le domaine des prothèses mécaniques.

Les prothèses biologiques ont beaucoup évolué au cours des trente dernières années. Le moteur de l'amélioration a été la compréhension du mode de dysfonction des prothèses tissulaires qu'elles soient d'origine porcine ou d'origine bovine. Tout tissu, après son implantation, est le site d'une infiltration plasmatique responsable de déposition de fibrine, de macrophages. L'activation de l'inflammation locale, le rôle des élastases, aboutit à une atteinte de la matrice extracellulaire, à une infiltration lipidique. Lié à ce phénomène, des calcifications intra-tissulaires ou superficielles apparaissent. Le traitement par le glutaraldéhyde qui a pour but de stabiliser les tissus aggrave le pénomène de calcification par la fixation de calcium sur les sites libres du glutaraldéhyde. Le résultat de cette cascade d'évènement est la fragilisation du tissu et sa calcification. La distribution des forces qui s'exercent sur les valvules explique la localisation des sites de déchirure du tissu fragilisé, là où le stress est maximum, au sommet des picots du stent.

Ces observations ont conduit à revoir le mode de fixation du tissu, avec pour objectif de réduire le risque des calcifications (optimisation de la fixation par le glutaraldéhyde, agents anti-calcification comme l'éthanol, l'acide amino oléique), la configuration et la

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flexibilité des stents pour améliorer la distribution du stress sur les valvules, le montage est des valvules sur le stent (valve intra ou supra annulaire). Le développement ultime de ces évolutions est la valve sans stent qui reproduit en fait l'homogreffe.

La conséquence de toutes ces innovations est l'allongement considérable de la durabilité des bioprothèses récentes, mais aussi l'amélioration de leurs performances mécaniques. Nous sommes en 2010 très loin des notions que nous avions au début des années 90, notions qui se sont ancrées dans la tête des médecins cardiologues et des patients: le taux de liberté de toute dysfonction est passé de moins de 50% à 10 ans pour les premières bioprothèses à plus de 95% à 20 ans chez les sujets âgés de plus de 65 ans, 75% à 20 ans pour les sujets plus jeunes, en cas de valve de deuxième génération (comme la Hancok II) en position aortique. Cet allongement de la durée de vie des bioprothèses de troisième génération (comme la Mosaic ou l'Epic) devrait être encore plus marqué: ces dernières valves bénéficient d'un traitement anti-calcification très prometteur.

Dans le même temps, peu de progrès ont été réalisés dans le domaine des valves mécaniques et du traitement anticoagulant qu'elles imposent. Le design des prothèses à ailettes a peu évolué. Les tentatives de traitement de la surface de carbone (ForceField de ATS) ne sont pas disponibles cliniquement. Le seul vrai progrès dans l'attente des anti-coagulants anti X oraux, est le self monitoring de l'INR par le patient lui-même: le taux de prothrombine est plus stable, l'INR peut être abaissé modérément réduisant d'autant le risque hémorragique.

La comparaison des performances cliniques des deux catégories de valve à long terme est intéressante: le taux de survie de la population tout âge confondu est égal dans le groupe des patients porteurs de valves mécaniques et dans celui des patients porteurs des valves biologiques de première génération. Le taux d'évènements liés à la valve est sur 20 ans équivalent. La seule différence est la nature de ces évènements: accident hémorragique chez les porteurs de valves mécaniques, dysfonction de la prothèse en cas de bioprothèse. Rappelons la gravité totalement différente des deux complications: la première peut être rapidement létale, la seconde étant facilement corrigée par une ré-intervention au risque faible. Le résultat de ces études comparatives doit être pris avec une grande réserve: les bioprothèses utilisées aujourd'hui présentent des performances très supérieures à celles qui ont permis l'étude entreprise il y a plus de vingt ans. Une bonne étude comparative des prothèses actuellement utilisées reste donc à faire!

Cette étude comparative des performances respectives de chaque prothèse a convaincu les grandes sociétés savantes: qu'elles soient américaines ou européennes, les sociétés savantes ont émis des recommandations précises. Au-delà d'un âge de 65 ans, les patients reçoivent une prothèse biologique, sachant que la durée de vie de la prothèse dépasse à cet âge l'espérance de vie du patient. Chez les patients de moins de 65 ans, l'utilisation des bioprothèses est raisonnable chez les patients en rythme sinusal et la recommandation est double: le médecin doit parler au malade des risques de l'anti-coagulation et de la ré-intervention; il doit prendre en compte dans ses recommandations au patient du mode de vie de celui-ci.

Il est intéressant de noter à cet égard que les aspirations des patients les plus jeunes ont évolué. Au sacro saint allongement à tout prix de la durée de vie, les malades préfèrent aujourd'hui la qualité de vie. Il est peu discutable que la qualité de vie des patients porteurs de bioprothèse est très supérieure à celle des patients porteurs de prothèses mécaniques. Silencieuses, les bioprothèses se font totalement oublier d'autant plus que le patient ne connait pas la contrainte de l'anti-coagulation. Cette observation explique que de nombreux patients préfèrent aujourd'hui le confort de la valve biologique.

Un élément nouveau est apparu récemment: la ré-intervention aprés dysfonctionnement d'une valve biologique n'est plus synonyme d'opération chirurgicale. L'avènement des prothèses implantables par voie percutanée change ainsi le raisonnement lors du choix de la première prothèse. Il y a tout lieu de penser que les progrès très rapides observés au cours des cinq dernières années vont s'amplifier et que dans les dix ans qui viennent ce nouveau concept de la valve dans la valve sera largement validé.

Au total, l'avenir est indiscutablement aux valves biologiques. Les observations scientifiques faites jusqu'à ce jour, qui donnent un certain avantage aux bio-prothèses, l'evolution de la demande des malades pour plus de confort, les perspectives de développement des valves trans-catheter concourent à amplifier le tendance actuelle.

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Illustrations

Figure 1: le risqué à long terme des valves mécaniques est lié au développement du pannus, facteur favorisant de dysfonctionnement mécanique et d'accident thrombo-embolique

Valve SJM après 16 ans: noter la pousse de pannus sous valvulaire.

Fig. 2: le risque à long terme des valves en tissu est essentiellement la dysfonction primaire de la valve par calcification et /ou déchirure d'une cusp. Cette complication, souvent d'apparition rapidement progressive laisse au patient le temps de retourner vers le chirurgien et de bénéficier d'une ré-intervention dont le risque est voisin de celui de la première implantation:

Valve CE Péricarde après 9 ans: noter les incrustations calcaires et la déchirure d'une cusp au sommet d'un picot, là où le stress est maximum.

Dispositif universel d'annuloplastie: résultats à moyen terme de l'évaluation clinique initiale *)

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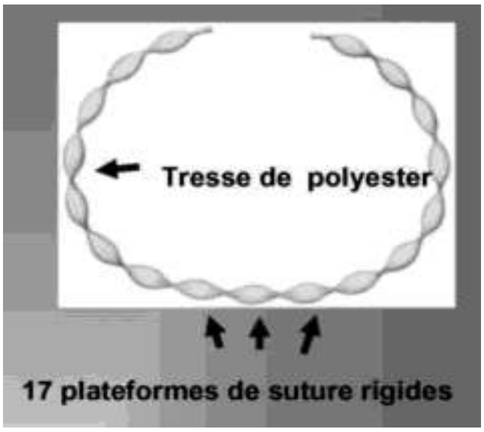
Le dispositif Universel d'annuloplastie est composé de 17 éléments rigides, ou plateformes de suture, de forme ovale unis entre eux par une tresse procurant un ensemble globalement flexible. Les 17 éléments rigides sont en polyester moulé (5,5 mm de long x 3 mm de large et 1,2 mm de haut) imprégné de bismuth pour être radio-opaque. Une tresse de polyester unit les plateformes en laissant un espace de 2 mm flexible entre 2 plateformes. La zone entre les plateformes est thermo-soudée pour éviter l'effilochage de la tresse au niveau de la zone de section des plateformes non utilisées.

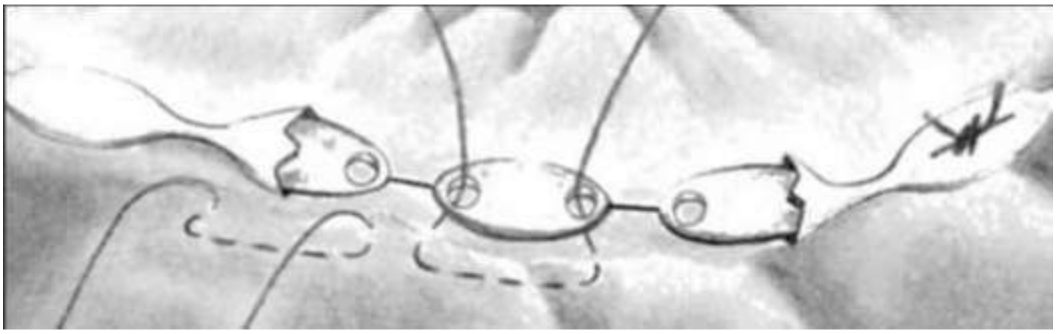
L'implantation commence par un premier point en U au niveau du milieu de la partie postérieure de l'anneau.

Le nombre total de points de fixation nécessaire est déterminé par le mesureur. Les points sont répartis de façon régulière de part et d'autre du premier point, sur le reste de l'anneau.

Après passage des sutures dans l'anneau universel, les plateformes inutiles sont réséquées au niveau des zones thermo-soudées.



*) Romanian Journal of Cardiovascular Surgery ■ 2008, vol. 7, no. 2, pp. 104-106

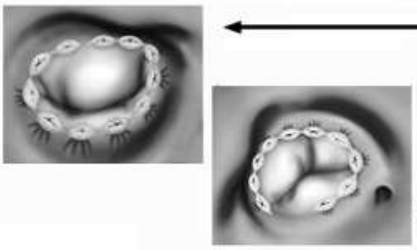
Objectifs

Le but de l'étude était d'évaluer à moyen terme les résultats des insertions initiales de cet anneau en position mitrale et tricuspide.

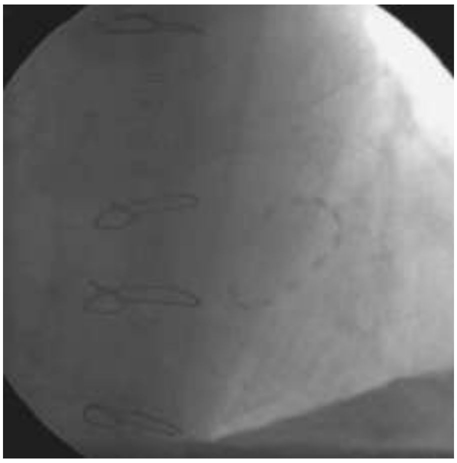
Méthodes

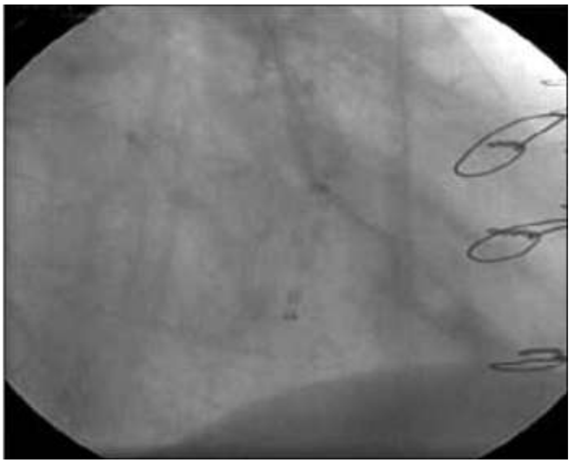
En 2004 ce nouveau dispositif a été implanté chez 9 patients. Sept implantations ont été faites chez des patients porteurs de diverses pathologies mitrales, trois associées à des valvuloplasties pour des pathologies dégénératives et quatre pour des annuloplasties isolées pour des cardiopathies ischémiques, une myocardiopathie ou des insuffisances mitrales fonctionnelles chez deux patients dont un coronarien avec une cardiopathie dilatée. Deux implantations tricuspides ont été faites pour des insuffisances tricuspides fonctionnelles.

Tous les patients ont eu une échographie trans-oesophagienne peropératoire et une échographie trans-thoracique avant de quitter l'hôpital. Huit patients ont bénéficié d'une échographie à moyen terme après 14 à 30 mois et un patient a été exploré en fluoroscopie.



Mitrale	**Dégénérative**	**Valvuloplastie**	**3**
	Ischémique	**Annuloplastie isolée**	**1**
	Cardiomyopathie		**1**
	IM fonctionnelle (dont un coronarien)		**2**
Tricuspide	**IT fonctionnelle**	**Annuloplastie**	**2**
Total			**9**





Résultats

• Il n'y a pas eu de mortalité hospitalière.
• Tous les patients avaient une valve continente en fin de procédure sur le contrôle échographique transoesophagien et sur l'échographie trans- thoracique à la sortie du patient.
• Les 2 patients coronariens sont décédés, l'un à 4 mois de défaillance multiviscérale chez un patient à très mauvaise fonction ventriculaire gauche avec une IM fonctionnelle, et l'autre à 2 ans d'une mort subite.
• Les 7 autres patients sont toujours en vie après plus de 3 ans avec un statut NYHA entre I et II et sans insuffisance mitrale ou tricuspide

Conclusions

• L'expérience clinique initiale de cet anneau universel a été bonne en terme de sécurité et d'efficacité.
• Les résultats à moyen terme (3 ans) des implantations tricuspides et mitrales sont encourageants.
• La conception et le design de cet anneau permettent d'envisager son utilisation pour des annuloplasties aortiques ainsi que pour des abords vidéo chirurgicaux ou robotiques des réparations tricuspides ou mitrales.

The On-X Prosthetic Heart Valve*)

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Bileaflet heart valves have been widely used for more then 15 years demonstrating the quality of the principle.

A low rate of thrombotic complications and structural failure could be demonstrated for the St. Jude Medical and the Carbomedics prosthesis. However, patients with mechanical valves are still of risk of thromboembolic and hemorrhagic complications.

Functional stenosis and closure related regurgitation remain a technical challenge compared to native heart valves. First implanted in September 1996, the On-X prosthesis heart valve was designed to optimized bileaflet pyrolytic carbon valve performance. Design feature of the valve were intended to address existing deficiencies of mechanical valve: inadequate hemodynamics in small aortic size, hemolytic anemia, tissue interference or excessive pannus overgrowth and thrombotic complications.

This design features are: pure pyrolytic carbon, inlet flare, natural length to diameter ratio, fully opening leaflets, stasis free hinge, reduced closing contact velocity, full annulus support and guarding the leaflet motion.

The inlet flare natural length, fully opening leaflets and the maximized use of the annulus while maintaining support all provide for improved hemodynamics. Annulus support and leaflet guarding address tissue interference and pannus overgrowth. The reduced turbulence from improved hemodynamics, pure pyrolytic carbon, reduced closing contact velocity and smooth back flow patterns through the stasis free hinges act to reduce hemolysis. All of these features combine to address the reduction of thrombotic complications.

To start, we use the best material available for mechanical heart valves, On-X carbon. On-X carbon was developed for critical implant applications involving long-term blood contact. Not only is it totally free of the silicon-carbide inclusions found in other valves' carbon, it is also stronger and smoother. The purity and surface finish of On-X carbon ensure maximum bio-compatibility of the valve (U.S. Patents Nos. 5,284,676; 5,514,410; and 5,667,061) (figure 1-5).

On-X is modeled after the natural human valve, which is long and contoured with a similar ratio of length-to-diameter. The On-X design uses this optimal length for reducing turbulence and lowering pressure gradients. It also allows a reduction in leaflet excursion, which means that reverse flow is reduced.

Full length naturally provides benefits like annulus maintenance and leaflet guards. The On-X orifice length is so effective that future designs may never revert to short valves (U.S. Patent No. 5,127,532) (figure 6).

*) **Romanian Journal of Cardiovascular Surgery ▪ 2003, vol. 2, no. 1, pp. 74-80**

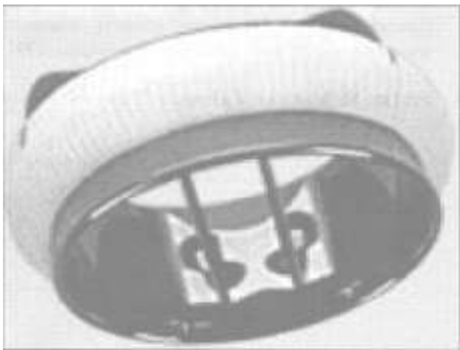


Figure 1: The first substantial design improvement in decades, On-X valves achieve the lowest pressure gradients and least blood damage of all mechanical valves. This is especially beneficial for recipients of smaller aortic valves.

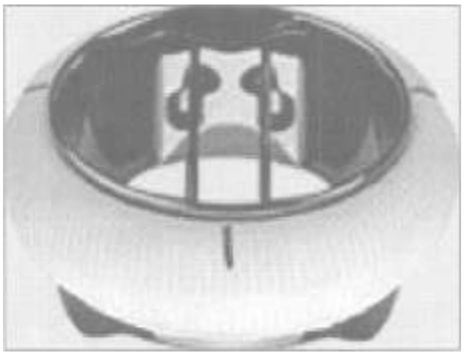
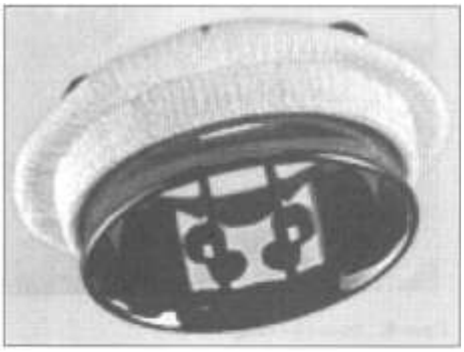


Figure 2: The On-X mitral valve's unique leaflet guards provide unmatched protection from interference by retained chordae tendineae



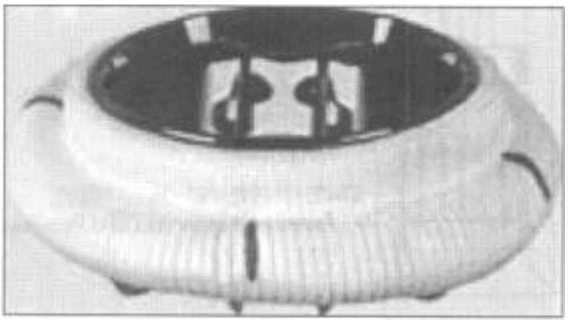


Figure 3: These are On-X valves with the more flexible ConformX cuff option. In the aortic position the cuff provides improved conformability to the narrow annulus. In the mitral position a single valve fits annuli between 25 and 33 mm.

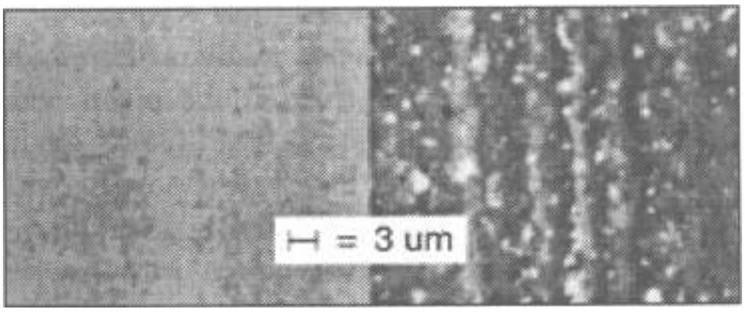


Figure 4: Pure On-X Carbon

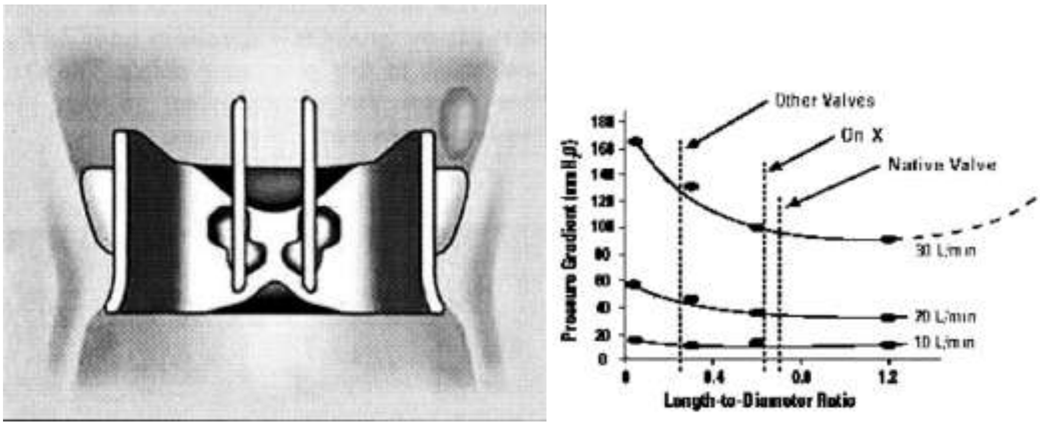


Figure 5: Natural Length

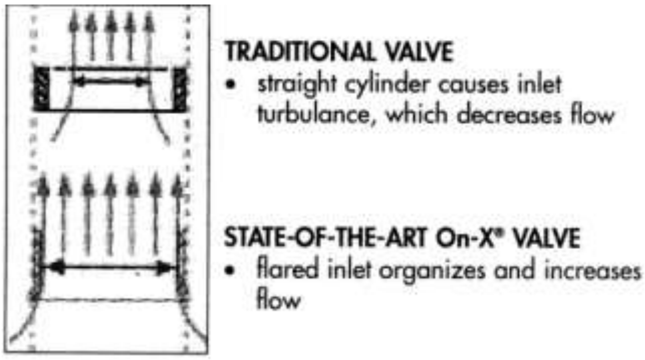


Figure 6: Inlet Flare

On-X is the first mechanical heart valve to successfully incorporate a flared inlet, a well-known fluid dynamic principle for producing smooth, organized flow with reduced turbulence. The smoother flow pattern produces a greater volume of flow, comparable to that of a larger orifice. The On-X flow volume can be equivalent to that of a traditional valve sized 2 mm larger (U.S. Patent No. 5,772,694), figure 7.

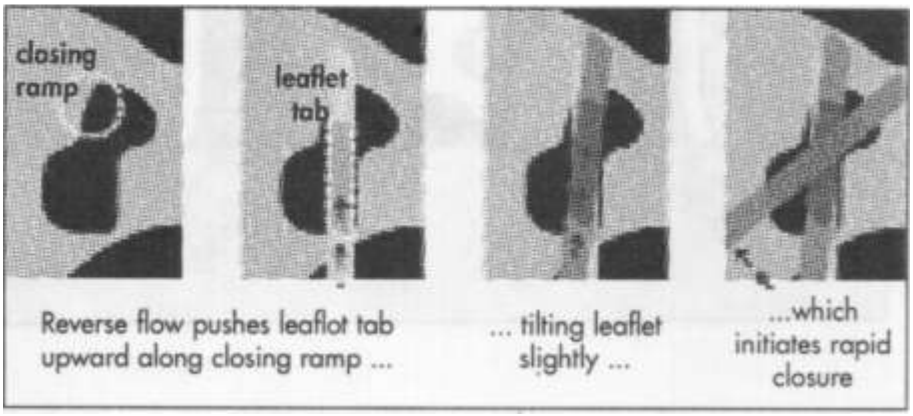


Figure 7: Leaflets that can open fully

With other valves, leaflets lack the freedom to align with the flow; instead, they must stop short of the fully open position to ensure that they will close reliably with backflow. This can increase obstruction and turbulence. On-X is the only mechanical valve with leaflets that are free to open fully yet still close reliably. The key to leaflet freedom is the On-X "actuated pivot" design that slightly tilts the leaflets just as flow reverses to start the leaflets toward closure. The result: reduced turbulence and increased flow (U.S. Patent Nos. 5,545,126 and 5,641,324).

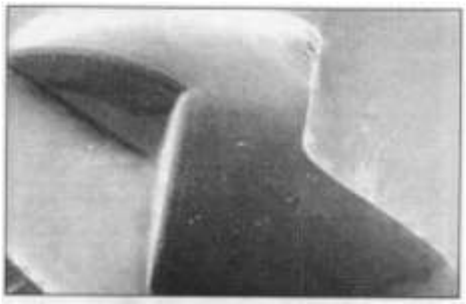


Figure 8: Stasis-Free Design

In a mechanical valve, pivots are the site of greatest risk for thrombosis (clotting) because of their tendency to cause stasis (flow stagnation). To minimize the risk of stasis and resultant thrombosis, On-X provides backflow through the pivots when the valve is closed. Because the On-X closing volume is small, a larger backflow is possible without increasing total regurgitant flow relative to other valves. The stasis-free pivot design with smooth, blended contours is one reason the thrombosis rate is so low for the On-X valve.

Figure 9: Soft landing closure

The On-X valve has leaflets with "soft landing" because of two important design features. First, the leaflet contacts the orifice at two points instead of one. These two points are closer to the pivots so that closing velocity is reduced. Secondly, the two-point landing distributes the closing impulse so that the impact is glancing rather than direct. The soft landing minimizes blood damage, as well as noise and cavitation potentials (U.S. Patent No. 6,096,075).

Short valves are vulnerable to annulus shrinkage and tissue in-growth (pannus) that can compromise valve function. The length and flare of the On-X valve provide unprecedented protection from these impairments on both the inflow and outflow sides.

The leaflet guards on the On-X valve extend the orifice to form an effective barrier which protects the leaflet motion from impingement by tissue. This is particularly important in the mitral position when chordae tendinae are preserved. On-X is the only valve with leaflet guards that offer this degree of protection.

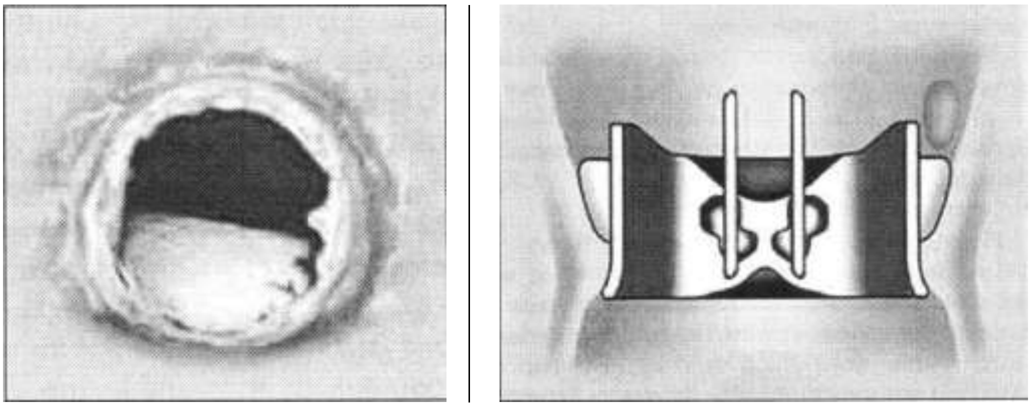


Figure 10: Annulus Maintenance

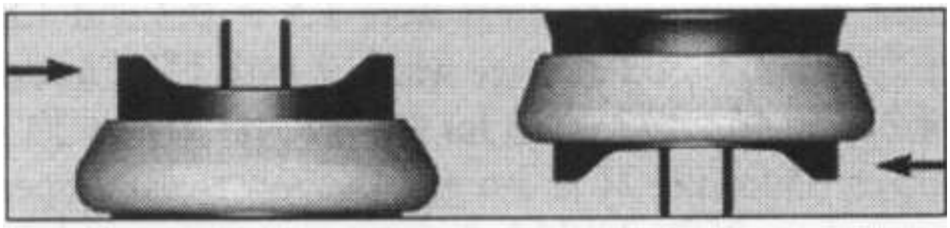


Figure 11: Leaflet Guards

Multi center clinical trials were conducted in Europe and North America to evaluate the performance of the On-X bileaflet heart valve prosthesis (Medical Carbon Research Institute, Austin, TX).

A study was performed by Reinhard Moidl et al. (Department of Cardiothoracic Surgery, University of Vienna, Vienna, Austria) on 532 patients who underwent valve implantation, 303 aortic valve replacement (AVR) and 229 mitral valve replacement (MVR), at 20 centers from September 1996 to July 2001. The study followed the guidelines of the AATS/STS. Mean follow-up was 23 months (total 1024 patient-years; maximum 5 years). Probability analysis was performed to show the equivalence of the populations.

Patients and results were found to be similar and poolable. Freedom from adverse events at 2 years in the study was as follows: thromboembolism, 96.0% for AVR patients and 96.3% for MVR; thrombosis, 100% for AVR and 100% for MVR; bleeding events, 96.6% for AVR and 95.7% for MVR; and overall mortality, 95.2% for AVR and 92.4% for MVR. Median lactate dehydrogenate levels were in the normal range for AVR and MVR patients at all intervals. At 1 year, AVR echocardiographic results for the 19 to 25 valves, respectively, ranged from 1.5 to 2.8 cm^2 for effective orifice area and 9.2 to 4.7 mm Hg for mean gradient, and MVR effective orifice area by pressure half-time was 2.8 cm^2 and mean gradient was 4.2 mm Hg.

A clinical trial of the performance of the On-X Prosthetic Heart Valve, particularly in the small aortic root, was conducted at 11 centers in Europe. From September 1996 to January 2000, 184 aortic valves were implanted, including 17 19mm and 35 21mm valves. All patients were followed with a mean of 11 months. Hemodynamic values were measured at discharge and 1 year, and blood studies were done at each visit. Clinical outcome was evaluated by NYHA classification. Mean pressure gradient for the valve at discharge was 12.6 ± 4.7 and 9.0 ± 5.3 mmHg for 19 and 21mm valves, while their effective orifice areas were 1.5 ± 0.2 and 1.8 ± 0.4 cm^2. Blood damage was low with LDH levels of 214 ± 46 - 196 ± 33 for size 19 and 212 ± 33 -215 ± 33 for size 21 at 3-6 months and 1 year (upper normal = 250). NYHA improvement occurred in 75% of patients. The early performance of the On-X valve in the small aortic root is exceptional. (A. Haverich, and the *Multicenter Investigators Medizinische Hochschule Hannover,* Hannover, Germany)

Mechanical valves are known to produce chronic, subclinical hemolysis in most patients. Generally, haptoglobin is reduced to below normal in most patients, while lactate dehydrogenase (LDH) is increased to as much as 200% above the upper normal, sometimes resulting in anemia. The study was designed to investigate the clinical hemolysis of the On-X Prosthetic Heart Valve in a multicenter experience with a standard protocol and a single laboratory.

Results

At 3-6 months and at 1 year, the average values for hematocrit, hemoglobin, red cell count and reticulocyte count all were about in the middle of the normal range regardless of valve position or size. Statistically significant increases in red cell count and decreases in reticulocyte count occurred in both AVR and MVR. These changes had no clinical importance, but do indicate that a tendency toward anemia is not occurring in these patients. At 3-6 months, haptoglobin was reduced to below normal in 86% of both AVR and MVR patients. This finding was repeated at 1 year and is statistically significant. LDH rose significantly at 3-6 months postoperatively, but did not change from then to 1 year (see table 1). The mean value of LDH postoperatively in AVR is only 228 (91% of upper normal 250) and 246 (98% of upper normal) at 3-6 months and 1 year, respectively. In MVR the respective means are 271 (108% of upper normal) and 265 (106% of upper normal).

These results indicate that the On-X valve provides lower levels of chronic hemolysis in the immediate and late postoperative period especially compared to reports of LDH elevations as high as 200% of upper normal, and demonstrate that the valve is safe and effective (Examination of Hemolytic Potential with the On-X® Prosthetic Heart Valve - Dietrich Birnbaum, Axel Laczkovics, Martin Heidt, Hellmut Oelert, Gunther Laufer, Hans Greve, Jose L. Pomar, Friedrich Mohr, Axel Haverich, Dieter Regensburger).

For aortic valves mean and peak DP were low and analysis of variance (ANOVA) showed a significant decrease as annulus diameter increased, while EOA increased significantly with valve size (p < 0.001) (see table 1). The mean and peak DP for all mitral valves sizes were similar, with the mean ranging from 4.4 to 4.7 mmHg (no statistically significant difference by ANOVA). This was also true for mitral EOA with a range of 2.0 to 2.3 cm^2.

Table 1

	19 mm $n = 12$ mean (std)	**21 mm** $n = 22$ mean (std)	**23 mm** $n = 38$ mean (std)	**25 mm** $n = 21$ mean (std)	**27/29 mm** $n = 16$ mean (std dev)
Peak DP	24.8 (9.0)	16.3 (6.3)	14.6 (7.1)	13.6 (8.8)	11.0 (5.5)
Mean DP	12.7 (5.0)	9.0 (3.3)	8.0 (3.9)	7.0 (4.8)	5.6 (2.8)
EOA	1.5 (0.2)	1.8 (0.4)	2.3 (0.7)	2.6 (1.0)	2.8 (0.5)

The initial postoperative results show favorable hemodynamic performance for this new design bileaflet valve. (The On-X® Prosthetic Heart Valve: *Update of the Early Postoperative Echocardiograpic Hemodynamics* - John Chambers, John Ely, *MCRI Multicenter Clinical Investigators*).

Changes in left ventricular mass were then examined by valve size and by valve lesion leading to replacement (i.e., stenosis, regurgitation or mixed disease). Paired t-tests were used to determine significance within groups and analysis of variance (ANOVA) was used to examine differences between groups.

In an average time to follow-up of 7.7 months, left ventricular mass was reduced significantly in all size valves, except the 19 mm. It was also reduced significantly in all disease states. Left ventricular mass was directly related to valve size. The change in ventricular mass postoperatively did not relate to valves size. Disease condition did not affect left ventricular mass.

So, reduction of left ventricular mass occurs in all valve sizes by 7.7 months after surgery and statistically significant in size 21 mm and above. This may be reflected by improvement in functional status including NYHA classification.

(The On-X® Prosthetic Heart Valve: Evidence of Left Ventricular Mass Regression in Aortic Valve Replacement by Postoperative Echocardiograpic Examination John Chambers, John Ely, MCRI Multicenter Clinical Investigators).

Comment: As with all mechanical valves a major concern is the long term need for anticoagulation and a thrombogenic potential associated with these valves. Clinical studies of such valves rightly focus on thromboembolism, thrombosis and bleeding rates. Patients must be maintained on permanent anticoagulation therapy. The sum of the embolic and bleeding events produce a freedom of this events at 2 years of 92.6% ± 1.2% AVR and 92% ± 1.4% MVR. Comparable results were reported by Horstkotte & Korfer for both Bjork Shiley and St. Jude Medical Valves.

For prosthetic endocarditis Pomar & Miro noted that the percentage of persons developing this complication can be as high as 3% in the first 9 months. Wilson and colleges in a review of literature reported total endocarditis between 1% and 3.9%.

In the studies about On-X valve the liniarezed rate for endocarditis was 0.5% patients-years for AVR and 0.9% patients-years for MVR.

Gersh et all noted a time related decrease in rates for thromboembolic complications after the first year.

Grunkemeier et al report paravalvular leak in mechanical valves ranging from 0 to 2.8% patient-years. In the experience with On-X valves the linearized rates for paravalvular leak were 0.50% patient-years for AVR and 0.72% patient-years for MVR.

The overall survival at 2 years was 95.1% ± 1.5% for AVR and 92.4% ± 2% for MVR and total freedom for valve related morbidity and mortality was 88.4% ± 2.1% for AVR and 88 ± 2.5% for MVR, similar to the early experience with other heart valves reported in many articles (Fiore et al and Burkhardt et al).

The hemodynamic results compare favorable to those reports by Wong et al in a review of the literature. Typically aortic bileaflet mechanical valves at 19 mm have EOAs of 0.9 to 1 scm in comparison to On-X which have EOA of 1.56 scm at one year.

The on-X valve performed satisfactorily in the first 5 year period in isolated valve replacement. Longer term follow-up is needed to establish the expected rates for late valve related events as well as the long term clinical efficacy of the valve.

In part because of the improved hemodynamics, the valve is expected to have low thromboembolic rates that appear to justify further studies at reduced anticoagulant levels especially in AVR patients in sinus rhythm.

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Mitral stenosis from anatomy to therapeutical decision*)

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Abstract

Mitral valve stenosis covers a large spectrum of pathological modifications and involves both the elements of the valve as well as adjacent structures. In the Western world, older patients come nowadays to the examining physician or to the surgeon raising more complex and complicated issues regarding both the diagnosis and the surgical therapy.

A thorough knowledge of the normal anatomy of the mitral valve and respectively, of the pathological modifications that characterize the stenosis are of utmost importance, especially due to the fact that new anatomical and physiological elements are continuously added and that the classical concept of mitral valve stenosis has new significances. In the present study, the authors have gathered data from wet-lab sessions and from the specimens collection at the Institute of Pathology at Niguarda Hospital Milan, Italy - focusing on the normal anatomy (with practical echographic and surgical applications) and on the pathological lesions that characterize the mitral valve stenosis.

Dissections have been performed on 30 adult hearts of both sexes, belonging to patients deceased of non-cardiac pathology. In these, the normal anatomy has been reviewed with a critical approach. Macroscopic examination of the lesions has been performed on 25 explanted mitral valve specimens. The macroscopic and microscopic examination of heart specimens with mitral stenosis completed the study. An integration of the data obtained, was made by comparing wet-lab data with clinical and echographic details, especially regarding the most debated topics of mitral stenosis nowadays.

The authors demonstrate thus the interdependence of the various structures that constitute the so-called "Mitral Valvar Complex" *and which includes: the valve leaflets, the chordae, the papillary muscles, the atrial and ventricular myocardium, the atrial and ventricular endocardium, the mitral-aortic continuity, "the annulus", the fibrous skeleton of the heart - aiming towards a better systematization and offering a more comprehensive approach to the echographist as well as to the surgeon.*

The pathological aspects of the disease are presented from simple, incipient lesions, towards the late, complicated ones while focusing not only on the mitral valvar apparatus but on the involvement of adjacent structures too. This latter aspect represents a real challenge for the cardiologist, as well as for the surgeon. A critical review of the therapeutically modalities and their indications is performed. The work has an important iconographical aspect, comprising new and unparalleled images.

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Background

The mitral stenosis, as a pathological entity, comprises a wide spectrum of modifications that affect both the elements of the mitral valve as well as adjacent structures (1). In various areas of the world the rheumatic mitral stenosis still represents a challenge for the national health care systems; in the European countries the picture has changed as we encounter the mitral stenosis in older patients, with associated pathologies, thus representing a real challenge for both the cardiologist and the surgeon, either in making the diagnosis or regarding the therapy. The thorough knowledge of the normal anatomy of the mitral valve and respectively, of the pathological modifications that characterize the stenosis, is of utmost importance and especially as new anatomical and physiological details are continuously added and the very concept of mitral stenosis is being invested with new significances (2).

In the case of such an old disease what has actually changed today is represented by the modalities of evaluation, including techniques with an important anatomical weight as the echography or magnetic resonance (MRI) (3).

The increasing number of cardiac surgery patients has demonstrated more than ever, that a unitary language between the various categories of specialists is necessary to be established and the fact that many details of the disease regard larger categories of specialists, as the area of interest gets well beyond the cath lab and comprises cardiologists, echographists and even the general practitioners. The various angles of vision should comprise a common denominator anyway, when dealing with such a complex disease.

The cardiologist has a "mediated" vision of the heart while using the imaging techniques. A permanent feed-back with anatomy is necessary for all the categories of specialists mentioned above (and not least, for the surgeon too), especially as anatomy demonstrates new dimensions today.

Thus, the very concept of "mitral valve" or "mitral valvar apparatus" has lost its primordial limited sphere being included in the larger concept of "mitral valvar complex" (4) nowadays. Beside the "classical" elements already described (leaflets, chordae, papillary muscles, annulus), the mitral complex also includes: the left ventricular myocardium, the left atrial myocardium, the atrial and ventricular endocardium (actually continuous with each other at level of the valve), the fibrous skeleton of the heart and the mitro-aortic continuity (figure 1).

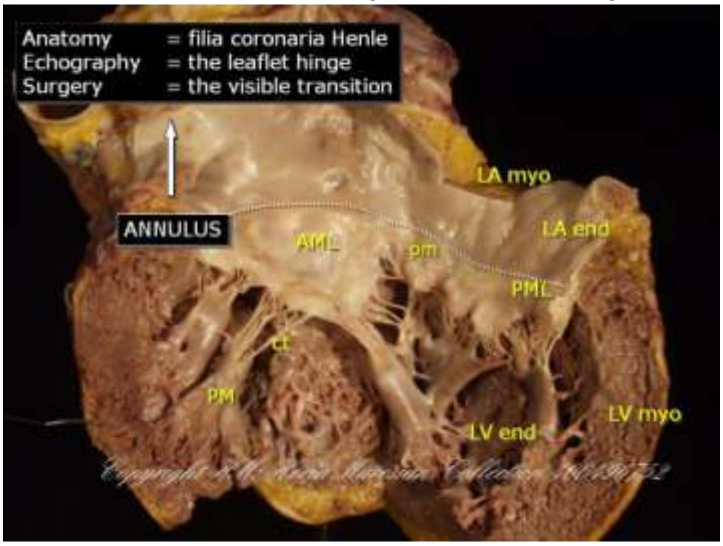


Figure 1

The authors have thus chosen as a paradigm the mitral stenosis - by no means a new pathological entity, but which demonstrates new aspects today - and have performed a complete analysis and characterization of this disease, with the aim of being useful to every physician who evaluates and treats patients with mitral stenosis.

Methods

A number of 30 adult human hearts have been dissected, in order to perform a critical review of the normal anatomy of the mitral valve. The heart specimens belonged to non-cardiopathic patients, of both sexes. Hearts were fixed in formalin (by immersion and injection of the coronaries) prior to dissection. Macro- and micro-dissection techniques have been used. Specimen preparation and photography have been performed by a cardiac surgeon (HM) at The Institute of Pathology Niguarda Hospital.

The pathological study included the examination and photographic recording of 25 explanted stenotic mitral valves (operation specimens); these have been carefully analyzed by a cardiac surgeon (HM).

The remainder pathological study consisted of the gross and microscopic examination of heart specimens belonging to the collection of The Institute of Pathology as well as their photographic recording - all being performed by a pathologist with special expertise in cardiovascular pathology (EB).

The correlation with the functional anatomy, echography and medico-surgical pathology has been performed by a cardiologist echographist having a special training in the surgical field (GC).

A review of the medical literature has also been added.

A cross-specialistical critical dialogue was established between the authors and the most important topics have been selected. The results have been expressed as data regarding the normal anatomy, the definition and severity of mitral stenosis, the etiology of the disease, the therapeutical armamentarium. The authors have focused on the less known or more debated aspects of mitral stenosis bringing into attention answers or possible solutions to the practical questions issued nowadays.

Results

a. The normal anatomy

The review of the normal anatomy of the mitral valvar complex brings into attention some important details.

The normal function of the mitral valve depends on the coordinated action of all the elements that belong to the valvar complex (4).

The coaptation of the valve leaflets takes place "under" the plane of the annulus (i.e. towards the apex). The leaflets do not meet exactly at level of the rough zones, but more towards their free margin.

By joining the coaptation point with the bases of the leaflets in correspondence to the annulus, a triangular zone can be thus obtained ("the mitral triangle"). The presence of this triangle and its dimensions, strictly correlate with the elastic proprieties of the subvalvar apparatus and especially the chordae. Thus, the prolapsing mitral leaflets will show a flattened or even "a negative" triangle.

The leaflets are not interrupted at level of the commissures (5), these latter ones are but the thinner and narrower parts of the valve, with less chordal support; all these structural details can explain the earlier involvement of the commissures in the rheumatic process.

The anterior leaflet (together with the papillary muscles) partially separates the left ventricular inflow from the outflow compartment. The posterior part of the mitral valve corresponding to the posterior leaflet and posterior annulus, dynamically changes shape and dimensions during the cardiac cycle, both during the ventricular and atrial systole.

The "annulus" although being a subject of debate (6), is an important diagnostic landmark. The anatomist recognizes as "annulus" the circumferentially-oriented fibro-elastic tracts at level of the atrio-ventricular junction ("*the filia coronaria*", described by Henle). The echographist localizes the annulus in correspondence to the leaflet hinge. The surgeon identifies it where the whitish hue of the leaflet, changes to light brown (the part corresponding to the endocardium-covered left atrial muscle). It is obvious that the annulus as described above, has slightly different meanings and each category of specialist must take into account the obvious difference.

The number of chordae (7) is generally of 25 (cf. Appendix 1); their length is of about 23±4 mm (cf. Appendix 2). In rheumatic mitral stenosis, by chordal thickening and fusion, the number and their length will decrease.

The interdependence between the posterior left ventricular wall and the mitral valve (8) is best illustrated while taking a look at the origin of the posterior papillary group and respectively, at the origin of the basal chordae (figure 2).

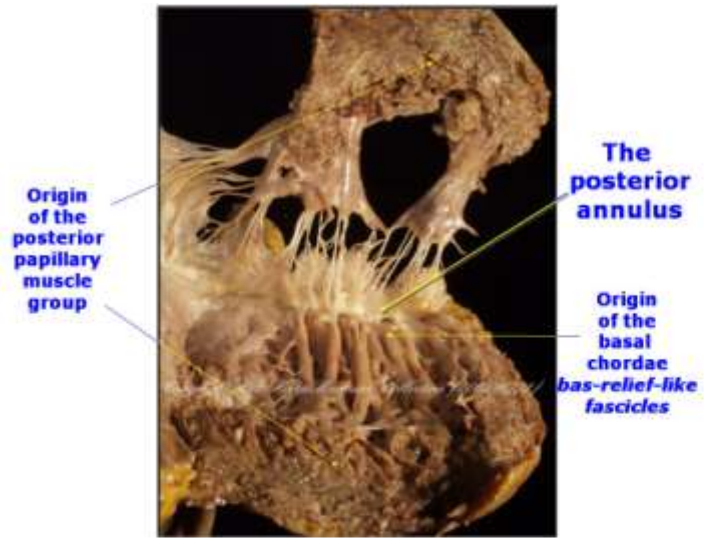


Figure 2

Lots of examples from pathology regarding the ischemic dysfunction of the posterior papillary group and the ruptures of the posterior leaflet, confirm this point of view. The posterior annulus bears considerable stress especially under pathologic conditions (9). The calcifications of the posterior annulus and wall are illustrative (figure 3, next page).

In the degenerative processes involving the fibrous skeleton of the heart, the relationship of the mitral valve with the membranous septum and with the cranial part of the muscular interventricular septum, explain the extension of the calcify process towards these structures and the resultant heart block (10, 11) (figure 4, next page).

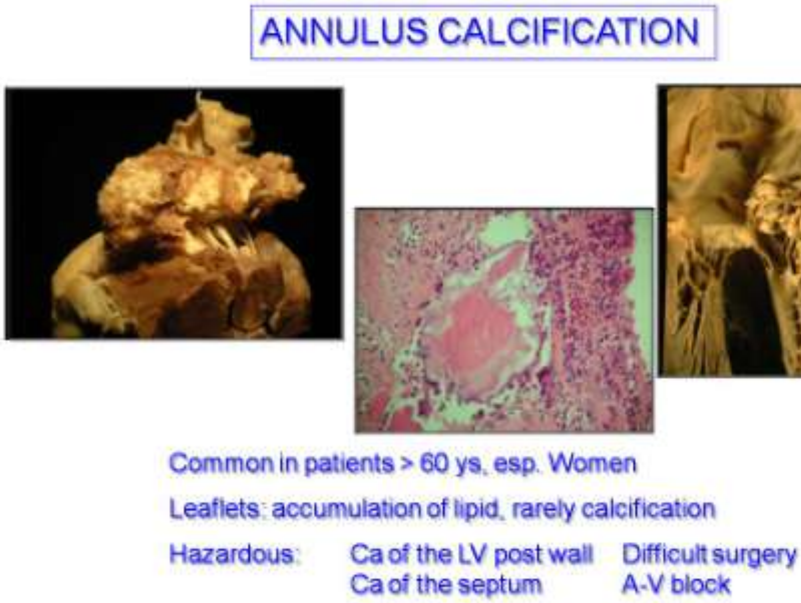


Figure 3

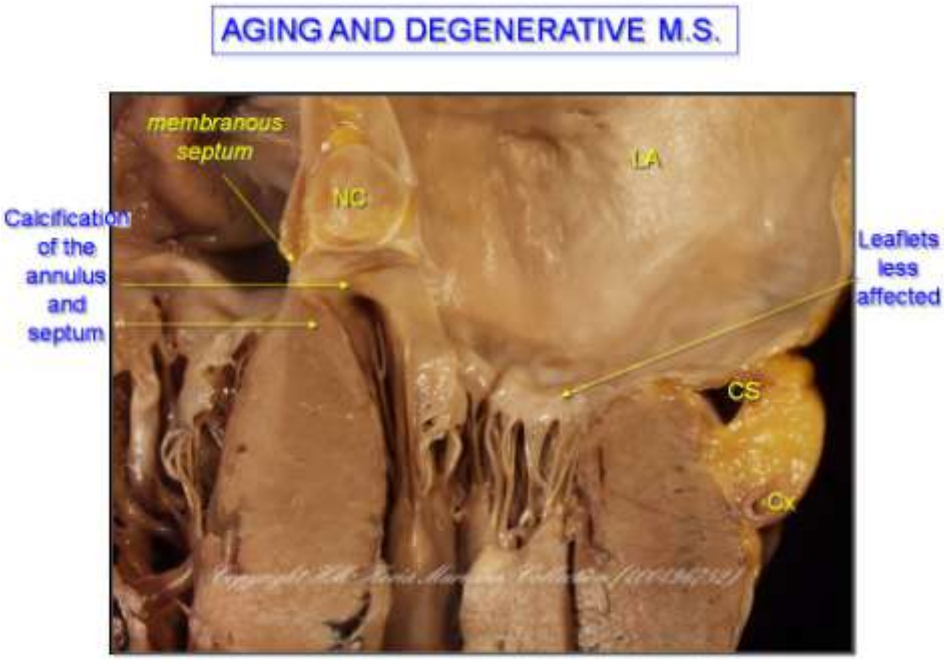
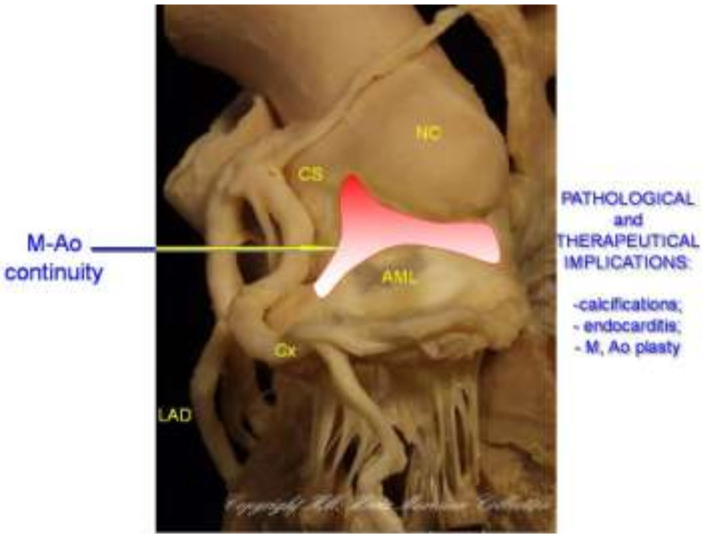


Figure 4

The posterior left ventricular wall represents the area of myocardium most dependent on the coronary typology and anastomoses. The apex of the papillary muscles represents the most distal coronary territory. Stenoses of the coronary arteries, even subclinical otherwise, can produce ischemic phenomena at these levels (12, 13, 14).

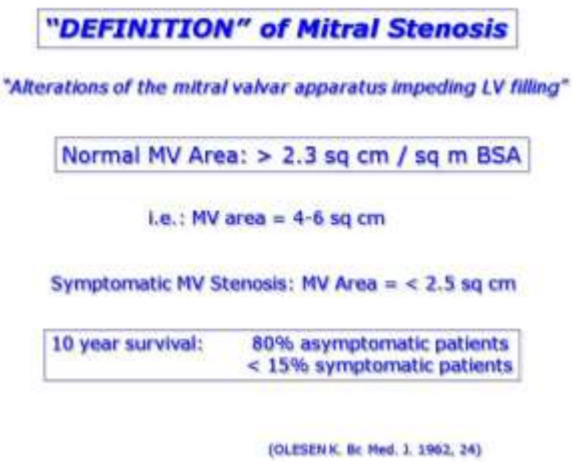


The mitro-aortic continuity is represented by the pentagonally-shaped area in correspondence with the left and non-coronary sinuses of the aorta (15) (figure 5); this area is also frequently involved in pathology (e.g. calcifications, endocarditis). Reconstructions are generally difficult to perform.

Figure 5

From the histological point of view, the leaflets are constituted by a fibrous, dense collagen core (the fibrosa) closer to the ventricular side (facing the chamber with higher pressure). The middle part is constituted by looser connective tissue (the spongiosa). Towards the atrium, a variable quantity of elastic tissue is present. Both the atrial and the ventricular aspects are lined by endocardium. Leaflets are avascular structures (except some areas towards the basal zone, where small amounts of muscular tissue can penetrate). The disappearance of this layered leaflet structure and the presence of neovascularization are characteristic for the ongoing rheumatic process.

b. Mitral stenosis: definition and criteria of severity



Mitral stenosis is represented by all the factors which impede the normal diastolic filling of the left ventricle. The definition implies the criteria "area" and respectively "pressure gradient" FIGURE AII data regarding the area, should be referred as to the patient's BSA (figure 6).

Figure 6

In some cases, atrial myxoma can cause genuine mitral stenoses. After various surgical procedures (edge-to-edge or other types of plasty) the measurement of valvar area and pressure gradient, can reveal various degrees of stenosis.

The use of criteria of severity of the stenosis, allows the definition of three degrees (see table).

SEVERITY OF MITRAL STENOSIS

SEVERITY	area [cm^2]	gradient
• Mild MS	1.6-2.0 0.9-1.5/m^2 BSA	< 7
• Moderate MS	1.1-1.5 0.6-0.9/m^2 BSA	7-15
• Severe MS	≤ 1.0 ≤ 0.6/m^2 BSA	> 15

(J.Oh-1999 The Echo Manual, Graves & Co)

Further details are needed and used by the cardiologist and surgeon when choosing the therapeutical decision and especially the presence of commissural fusion, calcifications the status of the chordae etc. The greater part of such details is offered by the ultrasound examination nowadays.

The permanent feed-back with anatomy offers newer and more precise data regarding the advantages and limits of each diagnostic procedure.

The anatomical and respectively the functional mitral orifices (16, 17, 18), must be considered as distinct entities; their measurement follows derived calculations as for example, PHT.

Currently, the therapeutical decision emerges by measuring the planimetric (anatomical) area of the medium gradient and the indirect determination of the functional area (other evaluation methods as the PISA or the continuity equation are more time-consuming and are used mostly for research purposes).

The intraoperative assessment is eventually performed by the surgeon, under direct vision or by sizing the valvar aperture (using his own finger or a sizer). The pathologist appreciates better the stenosis without opening the valvar annulus.

c. The etiology of mitral stenosis nowadays

In spite of the fact that the greater part of mitral stenoses are still of the acquired type, the congenital forms must also be taken into account. These are better and earlier diagnosed, and not the least, they can be more successfully treated, today. From the numerous morbid entities that comprise the congenital mitral valve disease, those manifesting predominantly with stenosis. A clear distinction should be made between some congenital lesions and the anatomical variations.

In the case of the acquired forms, the rheumatic stenosis gives way, little-by-little to the calcific-degenerative forms, characteristic to patients in older age, with significant associated diseases and which ultimately raise difficult diagnostic and therapeutical problems. Annular calcifications and heart blocks appear more frequently in women age 60 and above.

The rheumatic mitral stenosis is encountered in older patients. As the interval between the rheumatic process and the symptomatic disease covers many decades, the Aschoff body is absent in the European populations. The diagnosis is made by the gross appearance of the valve. Another important issue is the following: in the presence of aortic rheumatic stenosis, the mitral valve will undoubtedly show anatomical alterations (not necessarily accompanied by functional modifications), an important detail to be taken into account regarding the therapeutical decision.

The acquired forms demonstrate evolving lesions, the initial insult being followed by progressive scarring and superimposed jet-lesions. The valve becomes eventually highly-damaged and totally unfunctional, rendering surgery more difficult. Even though initially in some forms, the valve leaflets are not predominantly affected, they can become the site of endocarditis or thrombosis (19). Embolic phenomena can complicate the course of the disease.

The anterior mitral leaflet can apparently bulge towards the left atrium during the ventricular systole due to the ventricular remodelling that follows the calcification process; by asymmetrical apposition of the leaflets, the valve becomes insufficient.

The stenosis produced by the presence of myxoma is more-readily diagnosed nowadays. Some particular forms of myxoma can also be encountered.

A distinct chapter is represented by the post-surgical mitral stenosis as after various plasties perfomed for adult pathology (posterior annular plasty Radovanovic', Paneth or the edge-to-edge technique) or for congenital lesions (AV canal defects repair).

The percutaneous mitral plasty can result inefficient (unopened stenosis) or it can be complicated by atypical ruptures of the valve and consequent insufficiency. The surgical plasties can result incomplete (residual insufficiency) or leading to a genuine post-surgical mitral stenosis.

Knowledge and quantification of these details and data are of utmost importance (20, 21).

d. The percutaneous mitral plasty

It is indicated in the infant and adolescent, where a good opening of the valve can be expected, without important alterations of the subvalvar apparatus. There is a steep ratio between the valvar area and the pressure gradient, for areas less than 1 cm^2; this explains the beneficial effect of the percutaneous plasty in these cases, with the lowering of the left atrial pressure, the augmentation of the cardiac output, the reduction of the pulmonary vascular resistance. Restenosis may appear at a 3-6 months interval but anyway less than in the case of the percutaneous aortic valve plasty.

The potential candidates for the percutaneous plasty are chosen nowadays by echographic criteria and the ideal ones demonstrate a Wilkins score less than 8 (22 - 27).

e. The surgical plasty

There is less experience in the case of mitral stenosis (as compared with the insufficiency). The already-known techniques are: commissurotomy, chordal and papillary splitting, decalcification.

The ideal indication for a god surgical plasty is the following: younger patient with isolated mitral stenosis, with no calcifications or women in child-bearing age.

With respect to the rheumatic mitral stenosis, the greater part of the authors prefers the valvar substitution.

We would like to draw attention to the phenomenon of "doming of the anterior mitral leaflet", which is the consequence of predominantly periorificial fibrosis with a relatively lesser involvement of the remainder of the leaflet. The pressure gradient at level of the left atrium represents the functional cause of the doming. The presence of the doming represents a positive criterion for the plasty.

The plasty of the rheumatic mitral stenosis is addressed to the anterior mitral leaflet: it can be mobilized by commissurotomy, by splitting and even enlarged with a patch. The valve becomes a mono-cuspid valve eventually.

A variety of procedures are added (28) in case of atriomegaly or in the presence of atrial fibrillation (ablation or the Cox maze technique). In spite of a reduced follow-up the benefice is obvious in case of younger patients or potential mothers.

Chordal rupture in case of rheumatic stenosis is not suited for repair, transpositions etc. The concomitant involvement of the aortic valve and the necessity of an aortic replacement, usually contraindicates the mitral plasty.

Final remarks

Although the rheumatic mitral stenosis is frequently encountered, place is gradually taken by the degenerative lesions, as life expectancy augments in the general population.

The surgery of the mitral valve must be seen as a prophylactic measure in face of the risk of cardiac failure; the therapeutical decision (surgery vs. percutaneous plasty) and the timing of the procedure are based on data of functional anatomy as revealed by echography.

The surgical planning aiming towards either the valvar replacement or plasty is also based on criteria of functional anatomy certified intraoperatively by the direct examination of the valve. In the case of surgical plasty, mortality is generally lower compared with valvar replacement but one should take into account the fact that mortality in case of failed plasty and redo is significantly higher. Thus the intraoperative evaluation as performed by the surgeon and respectively by the echografist (TEE) represents a very important decisional moment looking both at the immediate evolution as well as to the late fate of the patient.

The collaboration and the sound communication between the various specialists (cardiologist, surgeon, pathologist, diagnostic imaging specialist) are of utmost importance not only regarding the choice of the best therapeutical approach but also in perspective, in order to develop new criteria for the diagnosis and therapy of mitral stenosis.

The selection of the patients - potential candidates for the various therapeutical procedures is performed nowadays outside the cath lab, in the midst of the cardiology and internal medicine network; this means that the details regarding the clinical anatomy of the mitral valve have a decisional utility on a larger scale.

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Appendix 1: Mitral valve. The chordae tendineae

By their mode of inseriton, four main types of chordae can be distinguished:

[1] commissural chordae insert into and define the commissures (between the anterior and posterior chordae).
[2] rough zone chordae insert into the ventricular aspect of the distal rough portion of the anterior and posterior leaflet. They typically split into three branches (secondary chordae) before inserting into the leaflet. Generally two of the anterior leaflet rough zone chordae are thicker than the others and are called strut chordae.
[3] cleft chordae are inserted into and define the clefts between the scallops of the posterior leaflet.
[4] basal chordae are single strands that arise from the posterior left ventricular wall and insert into the basal zone of the posterior mitral leaflet.

SITE OF INSERTION	TYPES OF CHORDAE	LENGTH (cm)	THICKNESS (mm)
ANTERIOR LEAFLET	Rough zone chordae	1.75 ± 0.25	0.84 ± 0.28
	Strut chordae	1.86 ± 0.43	1.24 ± 0.51
POSTERIOR LEAFLET	Rough zone chordae	1.40 ± 0.08	0.65 ± 0.24
	Basal chordae	0.84 ± 0.21	0.40 ± 0.29
	Cleft chordae	1.30 ± 0.18	0.78 ± 0.15
COMMISSURAL AREAS	Anterolateral comm. eh.	1.2 ± 0.31	0.70 ± 0.20
	Posteromedial comm. eh.	1.4 ± 0.40	1.0 ± 0.30

On the average, 25 chordae insert into the mitral valve. There is no significant difference in the total number between the two sexes. Of the 25 chordae, 9 pass to the anterior leaflet (7 rough zone chordae and 2 strut chordae), 14 to the posterior leaflet (10 rough zone chordae, 2 cleft chordae and 2 basal chordae)

From **Lam JHC, Ranganathan N, Wigle ED, Silver MD** - *Morphology of the human mitral valve. I. Chordae tendineae: A new classification*. Circulation, 1970; 41:449:458.

Appendix 2: Distance between mitral annulus and papillary muscles

In normal hearts, the annulo-papillary muscle distances of the mitral apparatus are similar in 2-, 4-, 8-, and 10-o'clock positions and correlate with the mitral annular diameter. Distance is approximately 23.5 ±4 mm.

From **Sakai T, Okita Y, Yuichi U et al**. - *Distance between mitral annulus and papillary muscles: Anatomic study in normal.* J. Thorac Cardiovasc Surg 1999; 118:636-641.

The assessment of mitral regurgitation in surgical aortic stenosis*)

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Abstract

We performed an ecocardiographic study on 209 patients in order to assess the frequency, mechanisms of production, degree and implications of mitral regurgitation in surgical aortic stenosis. The study also included the patients with associated mitral valve lesions or coronary artery disease. We found that approximately one third of the patients with surgical aortic stenosis had significant mitral regurgitation, mitral annular calcification being one of its main etiologic mechanisms. Significant *mitral regurgitation was found to be a supplemental risk factor for increased perioperative mortality and morbidity in patients with surgical aortic stenosis*

Introduction

A number of determinants influence the outcome of patients with surgical aortic stenosis. Mitral regurgitation appears to be one of them. We intended to assess the frequency and mechanisms of production of the mitral regurgitation in aortic stenosis, to establish the relationship between the degree of mitral regurgitation and the severity of the aortic valvular lesion and to evaluate the consequences on operative mortality and morbidity.

Materials and Methods

Our study included 209 patients with aortic stenosis of different etiologies operated in the Cardiovascular Surgery Clinic of the "C.C. Iliescu" Institute of Cardiovascular Disease between January 1st 1996 and December 31st 1998. 30% of the patients were women and 70% men. The mean age of our patients was 43.3 years (6 to 75 years). We also included in our study the patients with associated mitral valve lesions or associated coronary disease (figure 1).

*) **Romanian Journal of Cardiovascular Surgery ■ 2003, vol. 2, no. 2, pp. 89-91**

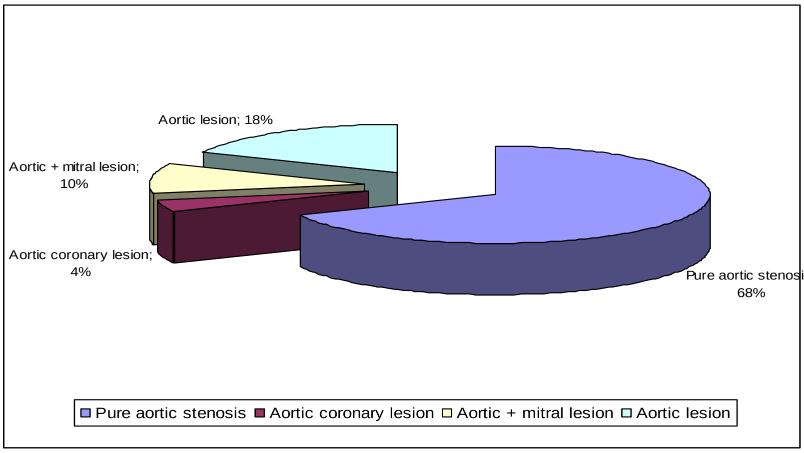

Figure 1: Patients-in-study structure upon type of valvular lesion

The following echocardiographic parameters were measured:

1. Left ventricular remodeling parameters
   - LV (systolic and diastolic), LA, RA and RV size
   - IV septum and LV lateral wall thickness
   - LV mass
   - End-systolic and end-diastolic LV volumes
2. Aortic lesion severity parameters
   - LV/Ao pressure gradient
   - Degree of aortic regurgitation
   - LV end-diastolic diameter
3. LV performance parameters
   - Ejection and shortening fraction (EF and SF)
   - LV wall motion

We also assessed the degree and mechanisms of production of the mitral regurgitation associated with the aortic valvular lesion. We calculated the following parameters: the degree of mitral regurgitation, the thickness of the regurgitant flow and the ratio between this and the left atrium surface, the mitral annulus diameter and degree of calcification and the morphology of the mitral valve.

The statistic analysis of the results used simple and multivariate linear regression analysis, calculation of the correlation coefficient and of the odds ratio. We used the Epi Info, Systat and SPSS programs.

Results

1. The incidence of mitral regurgitation in patients with surgical aortic stenosis was 36% (p = 0.0000001). The main mechanism of production was found to be mitral annular calcification (55% of cases) (figure 2).

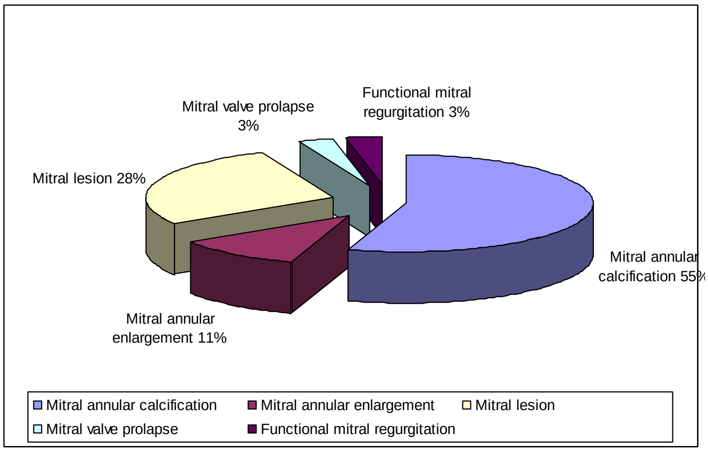

Figure 2:
The mechanisms of production of mitral regurgitation in patients with surgical aortic stenosis

2. In 28% of cases the mitral regurgitation was due to a cuspal lesion while in 11% of cases it was due to mitral annular enlargement. Mitral valve prolapse and functional mitral regurgitation were rare causes (each accounting for 3% of the cases) of mitral regurgitation in our study.

3. The degree of mitral regurgitation correlates well with the left ventricular remodeling parameters: interventricular septal thickness (r = 0.006), LV mass (r = 0.04), LV end-diastolic parameter (r = 0.09) and LV posterior wall thickness (r = 0.15). It also correlates well with the left ventricular performance parameters (ejection fraction and shortening fraction, with r = 0.11 and 0.06, respectively) and patient age (r = 0.09) (fig. 3).

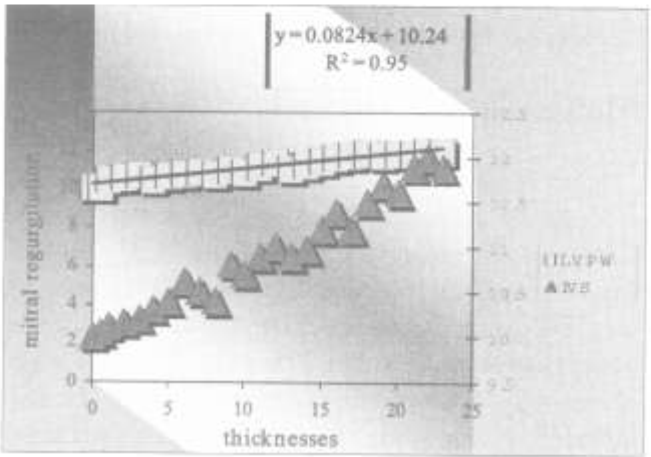

Figure 3:
Correlation between degree of mitral insufficiency and LV remodeling parameters (IVS, LVPW)

4. The degree of mitral regurgitation does not correlate in our study with the aortic lesion severity assessed by measurement of the LV/Aorta pressure gradient and degree of aortic regurgitation.

5. A mitral regurgitation of more than second degree in severity was predictive for increased perioperative mortality and morbidity. Its presence increased the perioperative mortality threefold (12% compared with 3.8%) and the Intensive Care Unit stay 1.5-fold compared with lesser degree mitral regurgitation (figure 4).

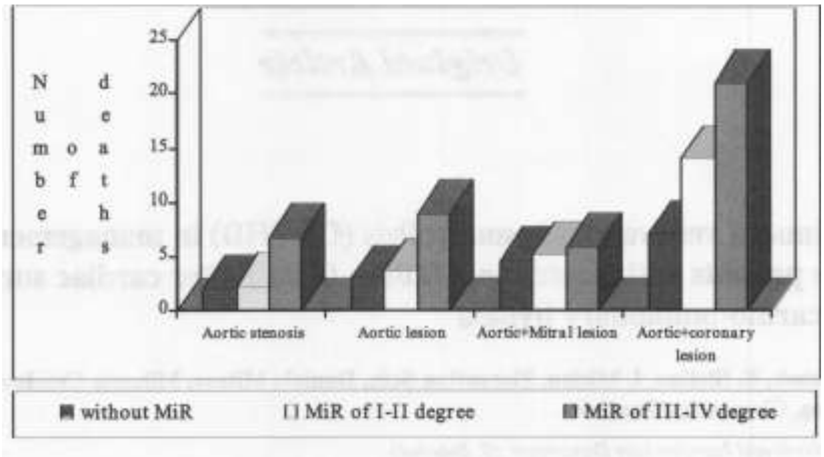

Figure 4: The relationship between mortality and degree of mitral regurgitation

Conclusions

1. Approximately one third of patients with surgical aortic stenosis have hemodynamically significant mitral regurgitation. Mitral annular calcification is one of its main etiologic mechanisms.

2. The degree of mitral regurgitation in surgical aortic stenosis is influenced by patient age, LV remodeling parameters and LV performance parameters but nor by the severity of the aortic lesion.

3. Hemodynamically significant mitral regurgitation is a supplemental risk factor for increased perioperative mortality and morbidity in patients with surgical aortic stenosis.

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Robotic da Vinci mitral valve repair - technique description combined with femoral cannulation (step-by-step guidelines)*)

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Abstract

Mitral valve repair is a standardized technique by median sternotomy with conventional cardiopulmonary perfusion. Minimal access is demonstrated to improve the patient outcomes and has huge economic benefits. A guideline steps in Robotic Mitral Valve Repair are described in the paper below using the da Vinci Robotic System combined with Femoral Cannulation. The advantage of using the Robot consists in extreme precision of the surgical act, by scaling and enhancing the surgeon's movement at the tip of the robotic articulated instruments while maintaining a less invasive approach through minimal port incisions.

Rezumat

Plastia de valvă mitrală reprezintă o tehnică bine standardizată, practicându-se prin sternotomie şi by-pass cardio-pulmonar convențional. Accesul minim-invaziv a demonstrat o recuperare mult mai rapidă a pacienților cu un beneficiu economic enorm. În lucrarea de față, descriem un Guideline al Plastiei de Valvă Mitrală Robotice asociind şi tehnica canulării periferice femorale. Avantajul utilizării robotului constă în extrema precizie chirurgicală transmisă la vârful instrumentelor robotice articulate prin demultiplicarea gestului chirurgical de către computer, totodată menținându-se caracterul minim invaziv al intervenției.

Introduction

The mitral valve operations have been performed by median sternotomy with conventional cardio-pulmonary perfusion. In 1995, surgeons began to focus on the benefits of smaller sternal incisions and short cardiopulmonary perfusion times. Cohn and colleagues [1], Cosgrove and colleagues [2], and Navia and Cosgrove [3] demonstrated that minimal access operations for both mitral and aortic valves improved patient outcomes and had economic benefits. These reports led others to investigate less invasive techniques for performing valvular heart operations. In 1996, Carpentier's group [4] performed the first videoscopic mitral valve repair through a right thoracotomy using cold fibrillatory arrest.

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Then, Mohr and his group [6] performed a similar operation using three-dimensional camera guidance displayed through a head-mounted monitor. New peripheral cannulation techniques were developed and widely used, along with intraaortic occlusive balloons. Then surgeons at East Carolina University developed cross clamps that enabled central aortic occlusion without the use of intraaortic balloons [7].

The first robotic assistant with cardiac operations was Aesop (Computer Motion, Santa Barbara, CA), which allowed surgeons to control endoscopes without having to communicate through a human assistant [8]. In a 1998 report, Falk and Mohr [9] described robot-assisted minimally invasive or "solo" mitral valve repairs done in 8 patients.

Time, overall hospital lengths of stay and costs were significantly reduced. Over the last few years computerized surgical robotic systems have been developed. The da Vinci (Intuitive Surgical, Inc, Sunnyvale, CA) surgical robot have assisted the surgeon's work using tele-manipulation through a master-slave (console-effector) activation principle with a three dimensional intracardiac camera.

In 1998, Carpentier [13] and Mohr [14] serially performed the first mitral valve repairs using the da Vinci. Later, Lange's group in Munich and colleagues [15] performed the first closed chest endoscopic mitral valve repair. In May 2000, under the first Food and Drug Administration (FDA) robotic investigational device protocol Chitwood group repaired a mitral valve using the da Vinci surgical system [15].

This paper describes a step by step guideline in performing the Mitral Valve Repair using the da Vinci System.

Steps of the Robotic Mitral Valve Repair (Guidelines)

1. Patient positioning and preparation

Figure 1: Right Groin cannulation

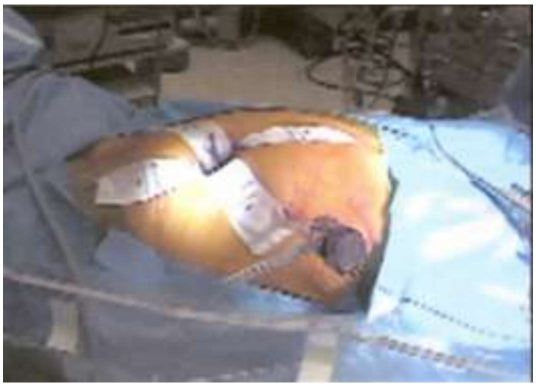
The patient is positioned at the right edge of the operating table with a positioning pad under the right mid-thorax. The table rotation of 30° provides the chest exposure. Single left lung ventilation is employed.

The Mitral Valve condition is studied by TEE *[Trans-Esophgeal Echography]*.

The right femoral anatomy is exposed and the femoral vessels are prepared for peripheral canulation (figure 1).

A percutaneous internal jugular vein cannula is placed for additional venous drainage. At this point, the da Vinci System is positioned at patient's left side for docking.

2. Working incisions and port placement



The Camera port is placed (figure 2) in the 4th intercostal space, medial to anterior axillary line. The CO2 insufflation is initiated through this port. The atrial retractor rod is inserted through the 3rd intercostal space lateral to sternum.

Figure 2: Port placement

A 2.5 cm lateral working incision is performed in the 4th intercostal space, slightly medial to anterior axillary line.

The cardiac sump suction inserted laterally in 5th intercostal space.

The right da Vinci® port is placed in the 5th intercostal space, just above the anterior axillary line while the left da Vinci port is placed in the 2nd intercostal space, 3 cm medial to anterior axillary line.

The triangular da Vinci port positioning maximizes mitral valve access and minimizes external interference.

A small heartport port in thoracotomy allows heart access without rib spreading.

The da Vinci Surgical Cart is now positioned at table, the instrument arms being docked to ports.

3. Aortic Cross-Clamping and Antegrade Cardioplegia Delivery

The EndoWrist Resano Forceps tip-closing design enables delicate tissue grasping during pericardiotomy using EndoWrist Permanent Cautery Spatula.

All pericardial stay sutures are applied with EndoWrist Large Needle Drivers.

The femoral venous and arterial cannulae is placed under TEE guidance. The CPB is now initiated.

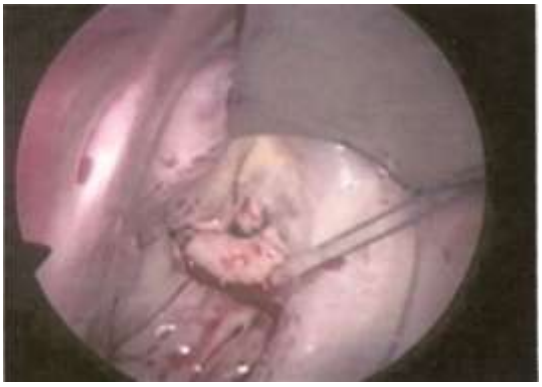
Figure 3: Surgeon's position at the console

The Endoaortic balloon is inserted for cross clamping. The correct balloon placement is confirmed with ultrasound imaging.

Cardiac arrest is achieved by inflating the endoaortic balloon and delivering antegrade cardioplegic solution.

A 3D visualization of aorta and surrounding anatomy allows endoscopic confirmation of correct balloon placement.

4. Left atriotomy and mitral valve exposure (figure 4)



The interatrial groove is dissected and freed from the fatty tissue. A 3 cm left atriotomy is made anterior to the superior pulmonary veins.

The EndoWrist Curved Scissors narrow cutting profile provides clean cut of the atrium while the EndoWrist Resano Forceps are designed for safe tissue grasping without atrial edge tearing.

Figure 4: Mitral Valve Exposure

The atrial retractor blade is inserted through the working port and attached to the retractor rod. The retractor blade is inserted and the interatrial septum is elevated to achieve mitral valve exposure. The atrial retractor is fixed in place with external mounting assembly.

5. Mitral valve repair (figure 5)

Figure 5: Mitral valve repair

The da Vinci® System enables enhanced 3D view of the annulus, leaflets and subvalvular apparatus for unparalleled precision.

The EndoWrist® Articutated Scissors' design provides visualization that can enable precise valve tissue sculpting.

The EndoWrist Resano Forceps' atraumatic jaw design allows for delicate valve-leaflet handling without slippage.

Figure 6: Leflet approximation

Unparalleled precision, dexterity and visualization facilitate complex mitral valve reconstructions.

Leaflet approximations (fig. 6) are performed applying suture and U-Clip™ repair devices with EndoWrist Large Needle Drivers.

Reinforcing annuloplasty bands (figure 7) are secured using larger size U-Clip repair devices. The da Vinci MVR offers patients the benefits of a minimally invasive procedure while providing the surgeon the control of an open-chest procedure.

Figure 7: Annuloplasty band

6. Left atrium closure and decannulation (figure 8)

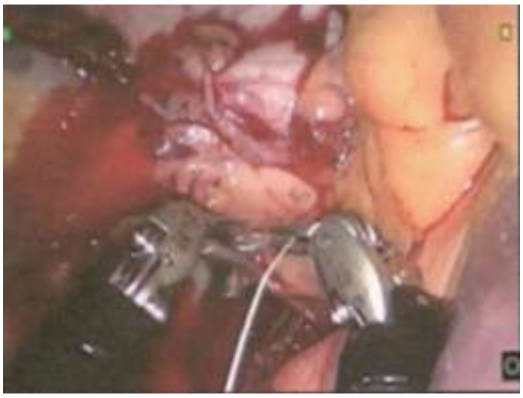


Figure 8: Left atrium closure

After completing the repair the atrium retractor is removed. Left atrium closure (figure 8) is performed with EndoWrist instrumentation, running a double layer suture line (Goretex 4-0).

The heart is de-aired before complete atriotomy closure.

Deflating the endoaortic balloon terminates aortic cross-clamping.

The patient is weaned from CPB and decannulated.

The da Vinci Surgical System is undocked from its ports and moved out from the Operating table.

7. Quality control and post-operative care (figure 9)

Both lungs are now ventilated.

Ports and working incisions are now closed by using standard suture techniques.

The da Vinci ports are used for chest tube drainage. Post-repair mitral valve performance is assessed intraoperatively with TEE.

Post-operative pain management is accomplished using local anesthetic injections or a pain pump system.

Figure 9. Post-operative cicatrices

Conclusions

The Mitral Valve Repair performed with the aid of the da Vinci Surgical System is now a standardized technique.

This procedure offers all the advantages of an open technique, combining also the advantages of the minimally invasive access.

By enhancing any surgeon's movement at the robot's console, the dexterity and precision are of extreme accuracy at the tip of robotic instruments which are placed inside the patient.

Femoral cannulation enables safe and minimal invasive CPB.

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La chirurgie de la valve mitrale associée au pontage aorto-coronarien chez les malades avec dysfonction de ventricule gauche - implications pronostiques*)

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Résumé

But: *Le but de l'étude est d'évaluer le pronostic chez les patients avec dysfonction de ventricule gauche chez lesquels on pratique la revascularisation myocardique chirurgicale et une intervention sur la valve mitrale simultanément.*

Matériel et méthode: *97 patients (72% hommes, âge moyen 63,6±6) avec dysfonction systolique de VS (FEVS <35%) partagés en 2 groupes: le groupe A formé de 47 patients qui ont subi un pontage aorto-coronarien (40 sans régurgitation mitrale et 7 patients avec régurgitation mitrale modérée), le groupe B formé de 50 patients qui ont subi un pontage aorto-coronarien et une intervention sur la valve mitrale (remplacement mitral chez 38 patients et annuloplastie mitrale chez 12 patients). L'analyse statistique a utilisé les programmes SPSS et SYSTAT pour la régression linière simple et multivariée, le calcul du coefficient de corrélation et du risque relatif.*

Résultats: ***1.*** *Le taux des complications post-opératoires et la mortalité ont été significativement plus grands chez les patients du groupe B par rapport à ceux du groupe A (38,2% et 12,7%, respectivement 29,1% et 6,9%,* p < *0,0001).* **2.** *La FEVG et la classe NYHA (valeurs moyennes) se sont améliorées dans les deux groupes.* **3.** *La mortalité à moyen terme chez les patients avec insuffisance mitrale sans correction chirurgicale a été de manière significative plus grande (18,9% par rapport à 12,7%). L'insuffisance mitrale est un facteur de risque important pour un pronostic défavorable et augmente la mortalité à long terme (RR = 7,2,* p < *0,01).* **4.** *L'annuloplastie mitrale détermine une mortalité inférieure à moyen terme par rapport au remplacement valvulaire mitrale (9,3% versus 15,8%,* p < *0,01).*

Conclusions: ***1.*** *La chirurgie de la valve mitrale associée (simultanément) au pontage aorto-coronarien chez les patients avec dysfonction de ventricule gauche est une alternative chirurgicale qui implique une mortalité opératoire acceptable et permet une amélioration clinique significative.* **2.** *La régurgitation mitrale est un facteur de prédiction important pour une évolution défavorable à long terme.* **3.** *L'annuloplastie mitrale a un meilleur pronostic et un taux plus réduit de complications par rapport au remplacement mitrale.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2002, vol. 1, no. 1, pp. 7-12**

Abstract

Postoperative Evolution in Mitral Valve Surgery associated to Coronary Artery Bypass Grafting in Patients with Left Ventricular Systolic Dysfunction

Aim: *The aim of the study was to evaluate the prognosis in mitral valve surgery with simultaneous coronary artery bypass grafting with left ventricular systolic dysfunction.*

Material and method: *97 patients (72% male, mean age 63.6+6) with LV systolic dysfunction (LVEF<35%), divided into 2 groups: group A-47 patients who underwent CABG (40 patients without mitral regurgitation and 7 patients with moderate mitral regurgitation), group B- 50 patients with moderate mitral regurgitation), group B- 50 patients who underwent CABG and mitral valve surgery (38 patients with mitral valve replacement sty). Statistical analysis used SPSS and SYSTAT programmes for simple linear and multivariate regression, correlation coefficient and relative risk calculation.*

Results: ***1.*** *Periooperative complications and mortality were significantly higher (p < 0.0001) in group B (38.2% respectively) 12.7 in group B and 29.1% respectively 6.9% in group A).* **2.** *The mean LVEF and NYHA class were improved in both groups.* **3.** *Medium term mortality rate in patients with mitral regurgitation without surgical correction was significantly higher (18.9% vs 12 .7%, p < 0.0001), mitral regurgitation is an important risk factor which predicts a poor prognosis and increases the long term mortality (RR = 7.2, p < 0.01).* **4.** *Mitral annuloplasty leads to a lower mortality on medium term compared to mitral valve replacement (9.3% vs 15.8%, p < 0.01).*

Conclusions: *1. Mitral valve surgery with simultaneous CABG in patients with LV systolic dysfunction and mitral regurgitation is a surgical alternative which determines an acceptable operative mortality and clinical improvement. 2. Mitral regurgitation is an important predictor for unfavorable evolution on long term prognosis.3. Mitral annuloplasty has a better prognosis and avoids the complications related to valvular replacement.*

Introduction

La chirurgie de la valve mitrale associée au pontage aorto-coronarien chez les patients avec dysfonction systolique de ventricule gauche s'est avérée avoir un taux de mortalité grand, ces patients présentant un risque opératoire accru.

Le but de l'étude a été d'évaluer, d'un côté, le pronostic à court, moyen et long terme des patients soumis à l'intervention chirurgicale de fixation d'une prothèse mitrale simultanément au pontage aorto-coronarien chez les patients avec dysfonction systolique de ventricule gauche et, de l'autre, tester la régurgitation mitrale en tant que facteur de risque.

Matériel et méthode

Ont été pris à l'étude 97 patients avec sténoses coronariennes importantes et dysfonction systolique de ventricule gauche (définie conformément à la fraction d'éjection du ventricule gauche au-dessus de la valeur de 35%), qui ont été soumis à l'opération de pontage aorto-coronarien et ont été suivis de manière prospective à l'Institut de Maladies Cardio-vasculaires "*Prof. Dr. C.C. Iliescu*" pendant une année.

La majorité des patients pris à l'étude ont été des hommes (72%), avec un âge moyen de 63,6 ± 6 ans et ont été évalués par échocardiographie en pré- et en post-opératoire à 10 jours, un mois, 3 mois, 6 mois et un an.

Les critères d'exclusion ont été les suivants: infarctus myocardique aigu, anévrisme de ventricule gauche, lésions valvulaires aortiques ou tricuspidiennes associées, co-morbidités (diabète sucré, insuffisance rénale).

En fonction du procédé chirurgical, le lot a été divisé en deux groupes:

1. **Le groupe A:** 47 patients ayant subi un pontage aorto-coronarien (40 patients sans insuffisance mitrale et 7 patients avec insuffisance mitrale modérée);
2. **Le groupe B:** 50 patients ayant subi une opération simultanée de pontage aorto-coronarien et de fixation de prothèse valvulaire mitrale (38 patients avec fixation de prothèse valvulaire mitrale et 12 patients avec annuloplastie mitrale).

Les deux groupes ont été comparables du point de vue des paramètres cliniques et paracliniques et du nombre moyen de greffes per patient.

L'analyse statistique a été faite en utilisant les programmes SYSTAT et SPSS pour la régression linière univariée et la logistique multivariée, pour le calcul du coefficient de corrélation et du risque relatif. On a utilisé les courbes de survie Kaplan-Meier pour l'analyse de survie.

Résultats

1. Les complications postopératoires cardiovasculaires et le taux de mortalité précoce postopératoire ont été significativement plus grands chez les patients soumis au pontage aorto-coronarien (61%, respectivement 34-2%) que chez ceux auxquels on a pratiqué simultanément le pontage aorto-coronarien et la chirurgie de valve mitrale (23,75% respectivement 11,25%). Dans la figure 1 est présentée la distribution des complications cardiovasculaires postopératoires chez les patients avec cardiomyopathie ischémique en fonction du procédé chirurgical. Les courbes de survie générées pour ces patients à un an en post-opératoire sont représentées graphiquement dans la figure 2. On observe un taux plus grand de survie chez les patients soumis à seule l'intervention pour pontage aorto-coronarien.

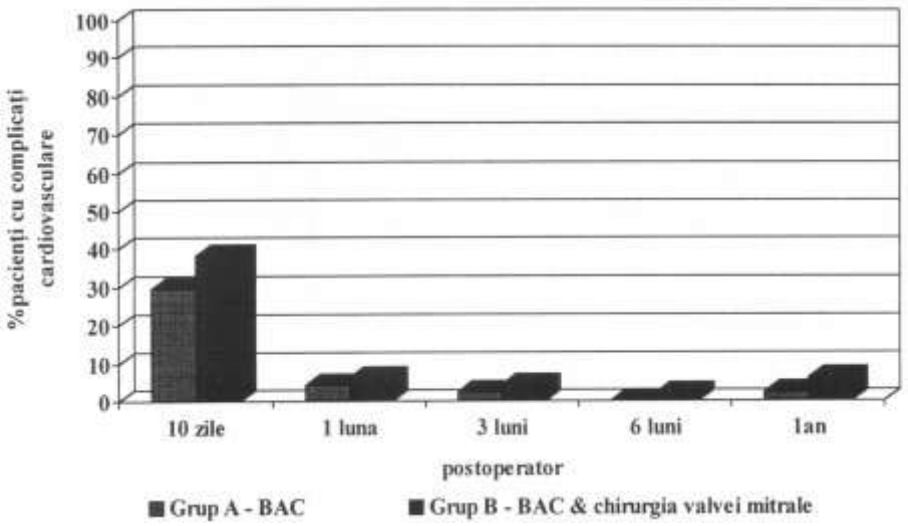

Figure 1: Complications cardiovasculaires postopératoires chez les patients avec cardiomyopathie ischémique en fonction du procédé chirurgicale.

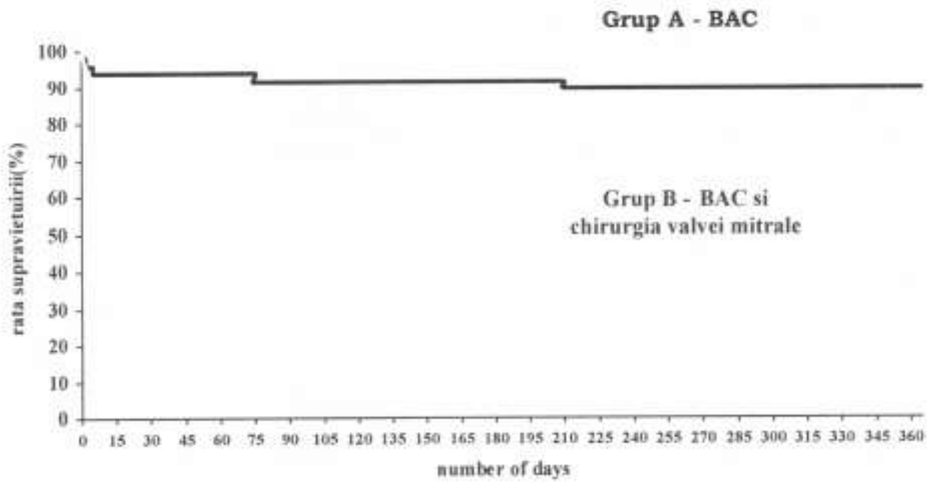

Figure 2: Les courbes de survie à 1 an en post-opératoire en fonction du procédé chirurgical.

2. La classe NYHA d'insuffisance cardiaque (comme il est montré dans la figure 3) s'est améliorée et la fraction d'éjection du ventricule gauche est accrue (figure 4) sans qu'une différence significativement statistique entre les deux groupes existe. La croissance plus lente de la fraction d'éjection du ventricule gauche postopératoire chez les patients soumis à l'intervention pour pontage aorto-coronarien associé à la chirurgie de la valve mitrale est due à la surestimation de cette valeur en préopératoire à cause de la régurgitation mitrale.

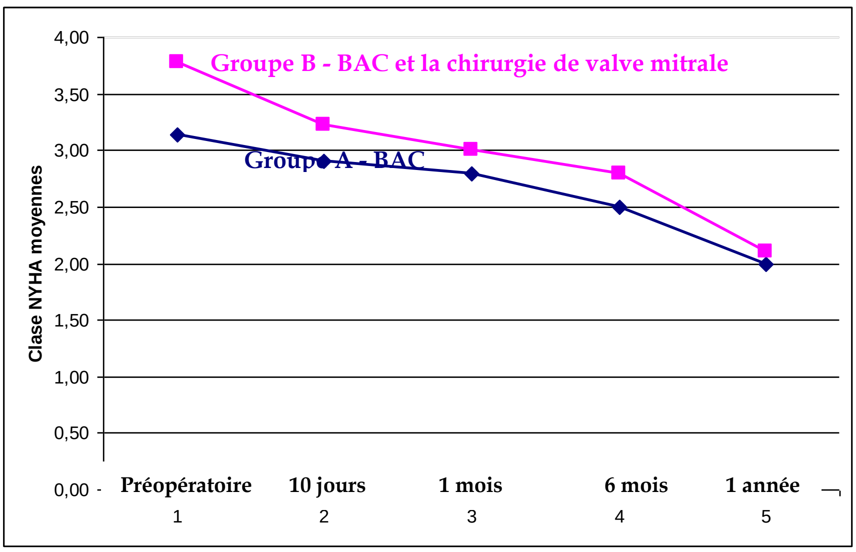

Figure 3: L'évolution postopératoire de la Classe NYHA d'insuffisance cardiaque

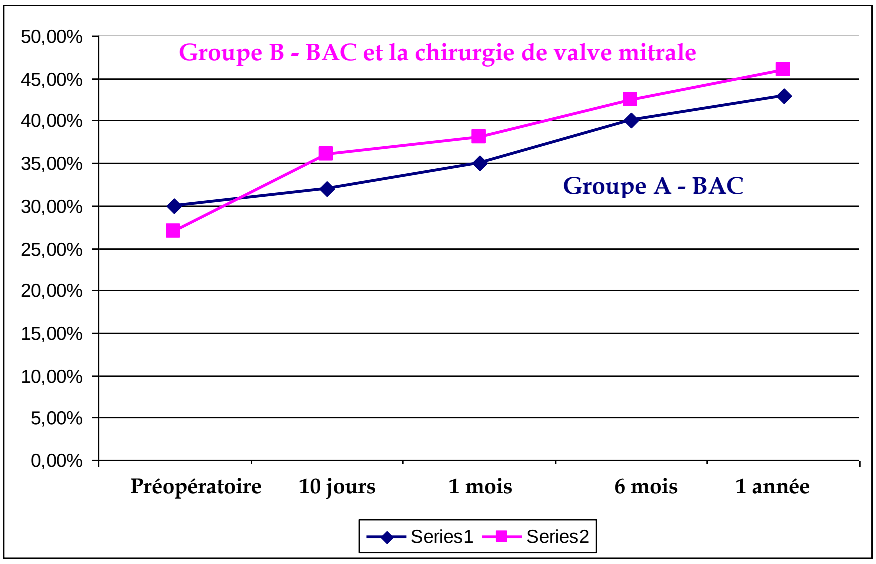

Figure 4: L'évolution postopératoire de la fraction d'éjection

3. La mortalité à moyen terme chez les patients avec insuffisance mitrale non corrigée chirurgicalement a été significativement plus grande (18,9% par rapport à 12,7%, $p < 0{,}0001$). L'annuloplastie mitrale a déterminé une mortalité plus grande à moyen terme par rapport à la prothésation valvulaire mitrale (9,3% vs 5,8%, $p < 0{,}01$). Dans la figure 5 sont présentées les courbes de survie générées pour une période d'un an en post-opératoire en fonction du procédé chirurgical utilisé pour le traitement de l'insuffisance mitrale associée au pontage aorto-coronarien et le degré de la régurgitation mitrale restante.

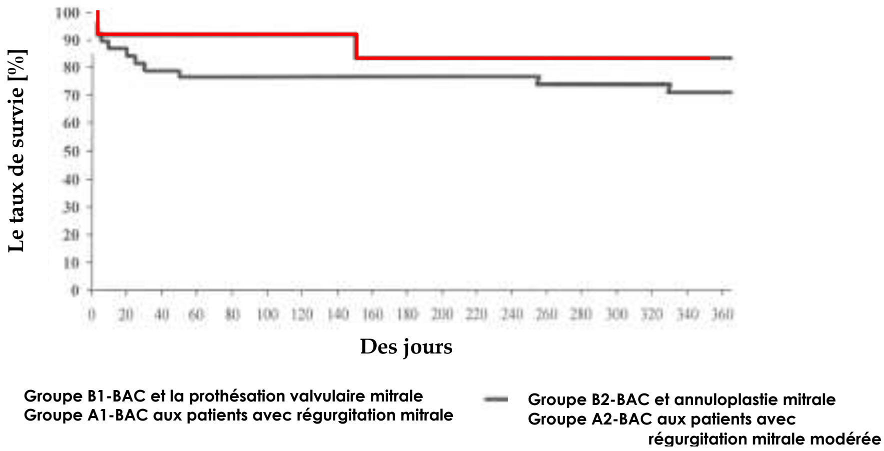

Figure 5: Les courbes de survie à 1 an en post-opératoire en fonction du procédé chirurgical utilisé pour le traitement de l'insuffisance mitrale associée au BAC et le degré de la régurgitation mitrale restante

4. La présence de la régurgitation mitrale, bien que modérée, est un facteur de risque important qui prévoit un pronostic plus réservé et la croissance à long terme de la mortalité (*RR* = 7,2, *p* < 0,01).

La régression multivariée a identifié en tant que prédicteurs indépendants pour la mortalité périopératoire les paramètres suivants: la présence de la régurgitation mitrale, le temps de décélération de l'onde E < 150 ms, la fraction d'éjection du ventricule gauche < 20%, l'index du volume télé-diastolique du ventricule gauche > 100 ml/m². Les risques relatifs de décès après 10 jours en post-opératoire (représentés dans la figure 6) et un mois post-opératoire (représenté dans la figure 7) - calculés pour les paramètres ci-haut énémérés, chez les patients avec dysfonction systolique de ventricule gauche - ont montré que la régurgitation mitrale et l'index du volume télé-diastolique du ventricule gauche accroissent le risque de décès.

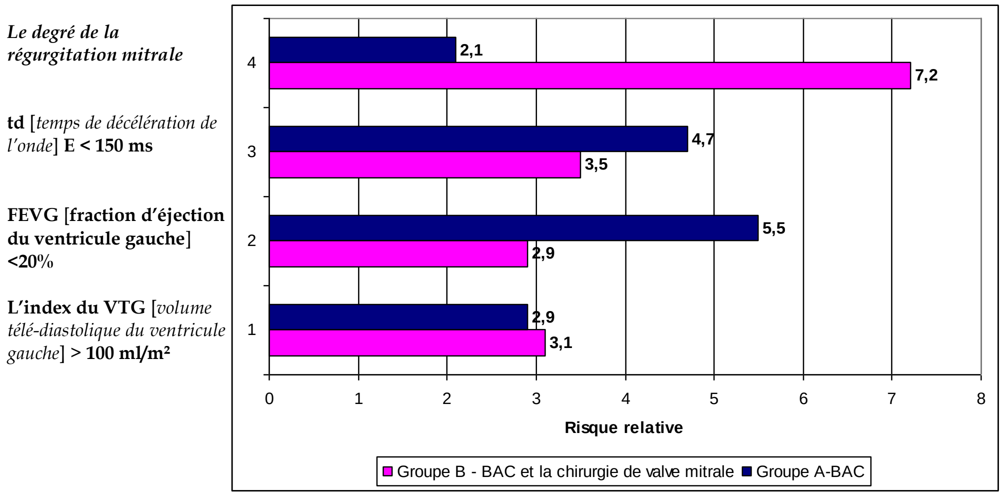

Figure 6: Le risque relatif de décès à 10 jours en post-opératoire chez les patients avec dysfonction systolique de VG

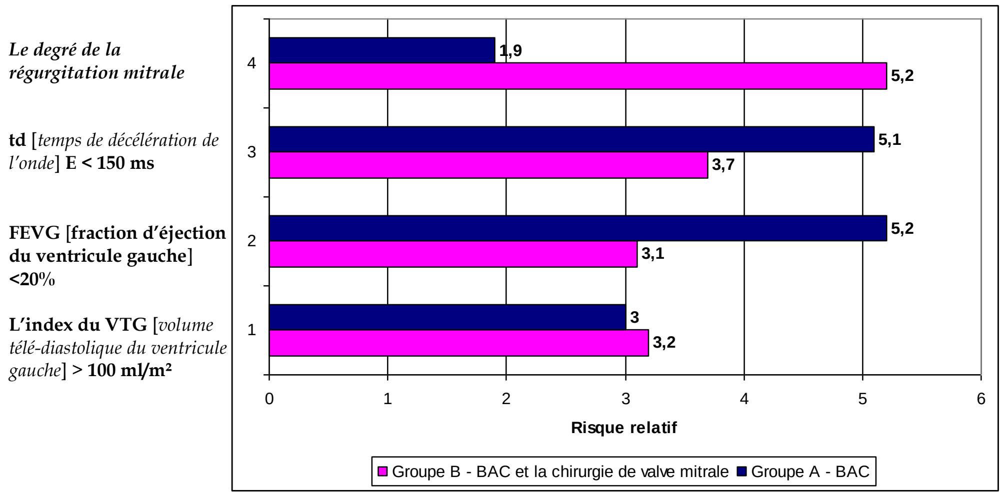

Figure 7: Le risque relatif de décès à un mois en post-opératoire chez les patients avec dysfonction systolique de VG.

Conclusions

1. La chirurgie de la valve mitrale effectuée simultanément avec le pontage aorto-coronarien chez les patients avec dysfonction systolique du ventricule gauche et régurgitation mitrale sévère jusqu'à modérée doit être prise en considération comme méthode de traitement alternative qui présente une mortalité périopératoire acceptable et une amélioration évidente de la symptomatologie clinique.
2. Les techniques opératoires simples comme l'annuloplastie mitrale ont un pronostic meilleur et évitent les complications liées à la prothèse valvulaire. La régurgitation mitrale bien que modérée, corrigée ou non, est un prédicteur important pour l'évolution défavorable à long terme chez ces patients.
3. La présence de la régurgitation mitrale, le modèle restrictif de remplissage diastolique, une fraction d'éjection très réduite et un indice du volume télé-diastolique de remplissage du ventricule gauche > 100 m² ont été identifiés comme prédicteurs indépendants pour la mortalité périopératoire chez ces patients.

Pulmonary Hypertension - an additional risk factor of postoperative evolution in patients with aortic stenosis and left ventricular systolic dysfunction undergoing aortic valve replacement*)

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Abstract

Aim: *The aim ofthe study is to assess the involvement of pulmonary hypertension in patients with aortic stenosis and left ventricular systolic dysfunction.*

Material and method: *109 patients (53% male, mean age 65 ± 8) with aortic stenosis and left ventricular systolic dysfunction (LVEF<40%, in sinusal rhythm), undergoing aortic valve replacement. There were 76 patients without PHT (mean pulmonary artery pressure <30mmHg) and 33 patients with PHT. Statistical analysis used SPSS and SYSTAT programmes for simple linear and multivariate regression, calculation of relative risk.*

Results*: Multivariate logistic regression was identified as independent predictors for PHT presence in those patients cardiac frequency > 80/min (RR = 6), E/A >2 (RR = 12), E wave deceleration time <120 (RR = 9), second degree mitral regurgitation (RR = 9). In this pattern, the prediction of HTP occurrence was mode with 80% sensitivity and 85% specificity. Perioperative mortality and postoperative cardiovascular complications were similar in both groups.*

Conclusions: *1.Pulmonary hypertension in patients with aortic stenosis and left ventricular dysfunction occurs more frequently in patients with LV restrictive pattern of diastolic filling and secondary mitral regurgitation. This does not depend on aortic stenosis severity parameters. 2. Relevant predictors for PHT occurrence were cardiac frequency, mitral inflow parameters and moderate mitral regurgitation presence. 3. PHT presence is not an additional risk factor for immediate postoperative evolution in these patients.*

Introduction

Long term prognosis in patients with aortic stenosis and left ventricular systolic dysfunction, who added pulmonary hypertension is worst than in those with normal pulmonary artery pressure.

Previous studies have not evaluated the influence of pulmonary hypertension on postoperative course in these patients.

*) **Romanian Journal of Cardiovascular Surgery ■ 2002, vol. 1, no. 1, pp. 27-30**

Aim of the study

1. Assessment of the predictive factors for the development of the pulmonary hypertension in patients with aortic stenosis and left ventricular systolic dysfunction with surgical indication.

2. Evaluation of the pulmonary hypertension involvement as additional perioperative risk factors in patients with aortic stenosis and left ventricular (LV) systolic dysfunction, who underwent aortic valve replacement.

Material and methods

The study encompassed 109 patients: 53% male, mean age 65 ± 8years, with aortic stenosis and LV systolic dysfunction (defined as left ventricular ejection fraction - LVEF<40%, appreciated by echocardiography volumetric method), undergoing aortic valve replacement. AII patients were in sinusal rhythm.

The exclusion criteria were: atria fibrillation, aortic valve insufficiency, acute myocardial infarction, coronary lesions, associated mitral or tricuspid lesions, comorbidities (diabetes mellitus, renal failure).

Depending on pulmonary artery pressure, there were identified 2 groups:

1. Group of patients without pulmonary hypertension - 76 patients (mean pulmonary artery pressure < 30mmHg);
2. Group of patients with pulmonary hypertension - 33 patients (mean pulmonary artery pressure > 30mmHg).

Both groups were comparable regarding mean age, gender and risk factors.

Statistical analysis used SYSTAT and SPSS programs for: simple linear and multivariate logistic regression analysis, calculation of the relative risk.

Results

The differences between the two groups were displayed in table 1. There were noticed significantly differences from the left ventricular ejection fraction, left atrium dimensions, cardiac rate, mitral valve E/A and mean mitral regurgitation degree.

Table 1: Characteristics of the groups

Characteristic	Group of patients without pulmonary hypertension	Group B	*p*-value
LV-Ao gradient	60 ± 4.3	59 ± 3.8	Ns
LVEF (%)	34 ± 5.2	31 ± 4.8	0.010
LV mass index (g/m2)	156+12.1	172 ± 13.2	Ns
LA (mm)	45 ± 6.1	51 ± 5.2	0.030
Cardiac rate (b/min)	70 ± 10	79 ± 9.8	0.001
Mitral valve E/A	0.7 ± 00.1	1.4+0.1	0.001
E wave deceleration time	190 ± 12	157 ± 11.7	Ns
Mean mitral regurgitation degree	0.7 ± 00.1	1.5 ± 0.2	0.005

Multivariate logistic regression analysis has identified as independent predictors for pulmonary hypertension, the presence in these patients of the following parameters:

- cardiac rate >80 b/min (RR = 6);
- E wave/A wave velocity ratio > 2 (RR = 12);
- E wave deceleration time < 120ms (RR = 9);
- Associated second degree mitral regurgitation (RR = 9).

Relative risks for the occurrence of the pulmonary hypertension in patients with aortic stenosis and LV systolic dysfunction are shown in the figure 1.

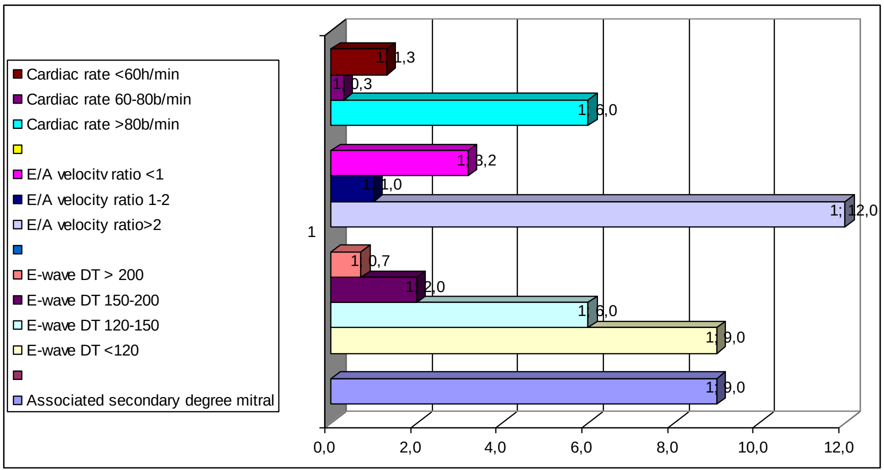


Figure 1: Relative Risks for the Occurence of PHT in Patients with Aortic Stenosis and LV Systolic Dysfunction

In this pattern the prediction of the pulmonary hypertension occurrence was made with a sensitivity of 80% and a specificity of 85%.

Postoperative cardiovascular complications and perioperative mortality were similar in both groups as in the figure 2, which show the relative risks for cardiovascular complications and early postoperative death depending on the presence of pulmonary hypertension.

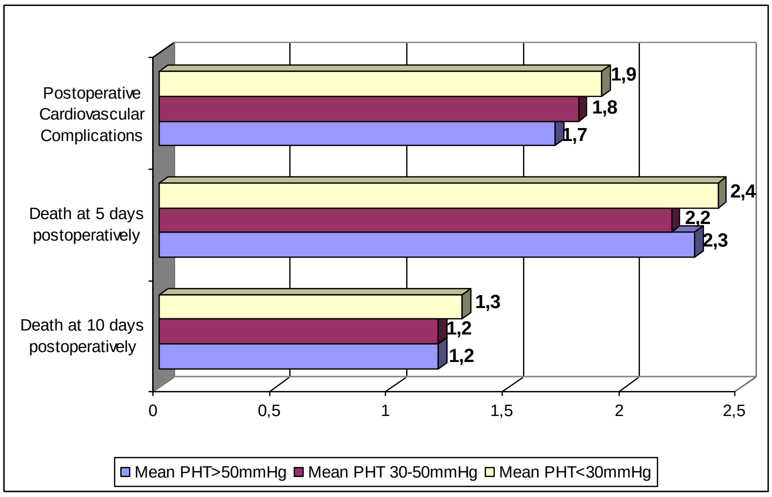


Figure 2: Relative Risk for Cardiovascular Complications and Early Postoperative Death by the Presence of PHT

Postoperative cardiovascular complications (figure 3) and early mortality rate (figure 4) were significantly higher in patients with left ventricular end diastolic volume index > 100ml/m² (55% respectively 40%), regardless the presence of pulmonary hypertension.

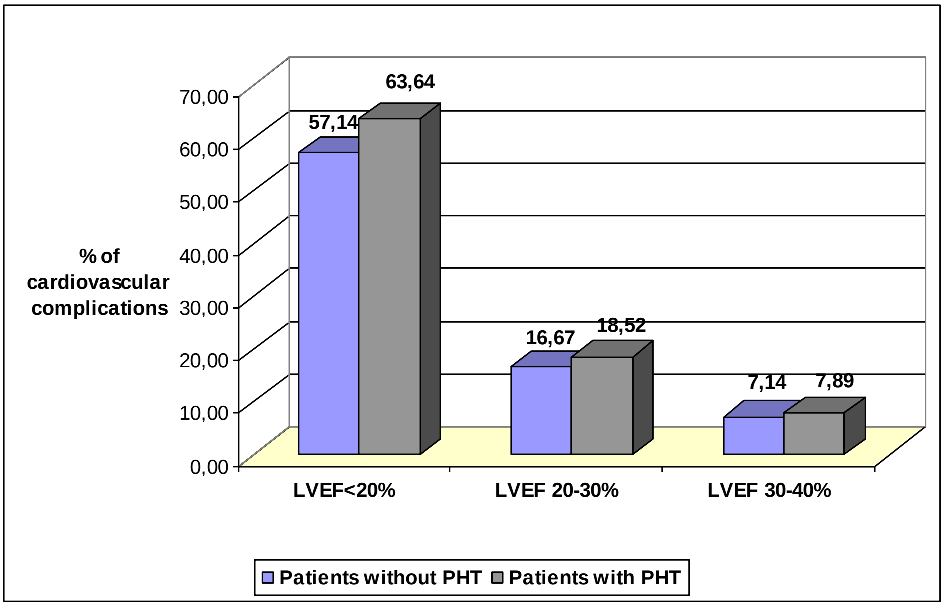


Figure 3: Postoperative complications Postoperative cardiovascular complications depending on LVEF and presence of PHT

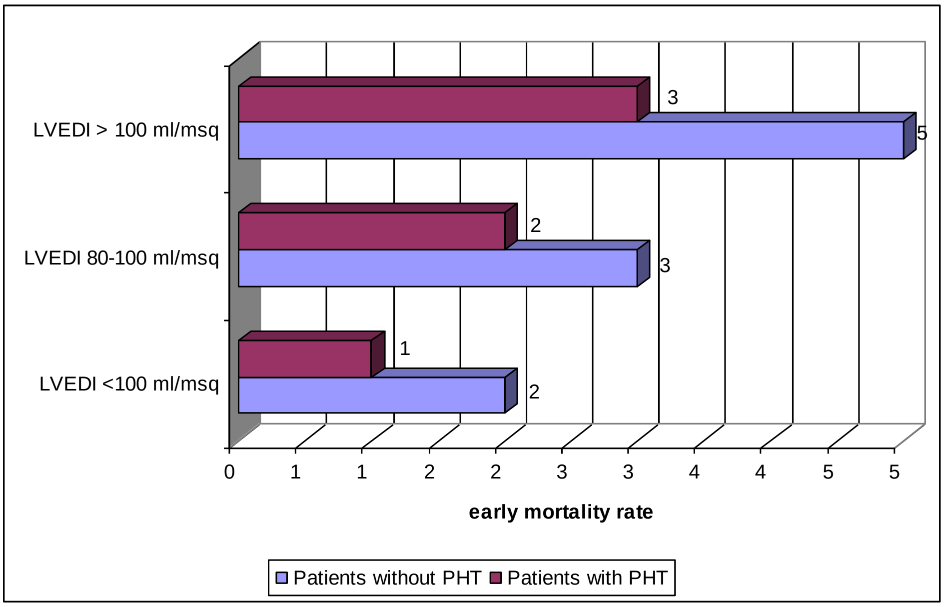
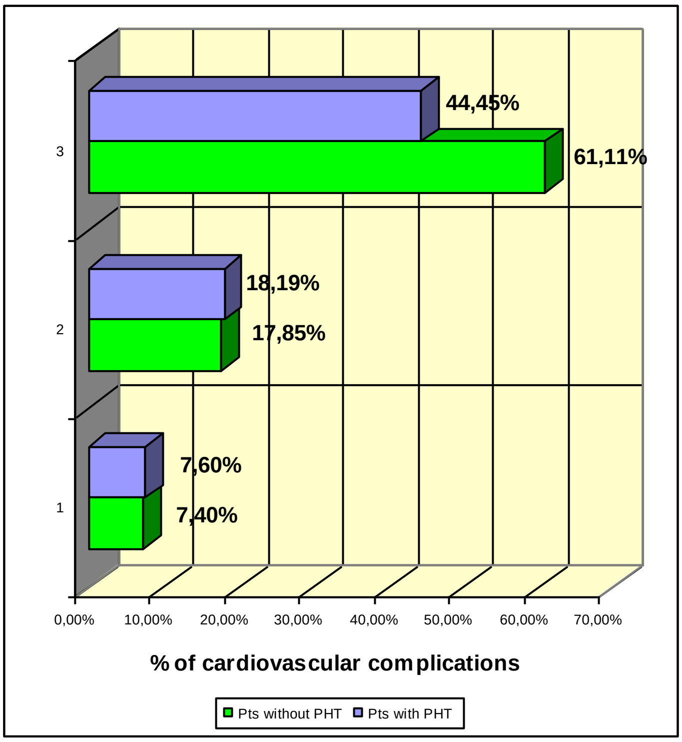


Figure 4: Early Mortality Rate by the LV End Diastolic Volume Index



Postoperative cardiovascular complications and early mortality rate (figure 5) were significantly higher in patients with LVEF < 20% (61.11% respectively 44.45%).

Figure 5: Postoperative cardiovascular complications and early mortality rate depending on LV end diastolic volume-index

Discussion

1. Pulmonary hypertension in surgical aortic stenosis and LV dysfunction occurs more frequently in patients with LV restrictive pattern of diastolic filling and secondary mitral regurgitation. The presence of pulmonary hypertension does not depend on aortic stenosis severity parameters.

2. Relevant independent predictors for pulmonary hypertension occurrence were cardiac rate, LV diastolic filling pattern and the presence of secondary moderate mitral regurgitation.

3. Pulmonary hypertension presence is not an additional risk factor for immediate postoperative evolution in patients with surgical aortic stenosis and LV systolic dysfunction.

4. LVEF < 20% and left ventricular end diastolic volume index > 100 ml/m^2 increase twice the early postoperative morbidity and mortality.

Ventricular systolic dysfunction in patients suffering mitral and aortic valve replacement - its relationship with postoperative evolution and prognosis*)

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Abstract

Purpose: *The assessment of the specific features of the postoperative evolution of the LV performance parameters in patients with LV systolic dysfunction suffering mitral or aortic valve replacement in relation to the type of operation.*

Materials and methods: *182 patients with LV systolic dysfunction undergoing mitral valve replacement (92 patients - group A) or aortic valve replacement (92 patients - group B). The two groups were matched in regard to sex, age and associated pathology. The patients were assessed clinically and by means of cardiac ultrasound at 10 days, 30 days 1 month and 6 months from the operation. The statistical analysis included the calculation of the correlation coefficient and simple liniary and multivariate regression analysis. We used the SYSTAT and SPSS programs.*

Results: *1. The perioperative mortality was significantly higher in group A. The highest mortality was scored in the group suffering mitral replacement for acute mitral regurgitation. 2. The LVEF increased postoperatively (at 1 month) in patients in group B but not in patients in group A. 3. Decrease in LV chamber size appeared postoperatively after aortic valve replacement earlier than after mitral replacement. 4. A LV end diastolic diameter >57 mm in aortic stenosis and >65 mm in aortic regurgitation was correlated with an unfavorable course after aortic replacement ($r = 0.78$, $p < 0.001$). The LV size did not alter the postoperative course in case of mitral valve replacement. 5. Percentual increase in LVEF was correlated with age ($r = 0.78$, $p < 0.001$), LVED diameter and volume ($r = 0.81$ and 0.79, respectively, $p < 0.0001$), and functional NYHA class ($r = 0.79$, $p < 0.005$).*

Conclusions: 1. *LV systolic dysfunction has a more favourable outcome (perioperative mortality, postoperative LVEF increase and decrease of LV chamber size) in patients suffering aortic replacement compared with those suffering mitral replacement. 2. Age is an independent predictor of the LV remodelling pattern after mitral and aortic replacement. 3. The LV end-diastolic diameter >57 mm for aortic stenosis and >65 mm for aortic regurgitation is predictive for an unfavourable outcome in patients with aortic valve replacement independent of the preoperative LVEF.*

Keywords: *valvular replacement, prognostic factors, echographic assessment.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2003, vol. 2, no. 1, pp. 5-8**

Background

Valvular heart disease poses an important load on the ventricular work. Chronic as well as acute volume and/or pressure overload more or less progressively alters the ventricular performance. In parallel, the natural history and prognosis worsens. There is generally no non-interventional effective therapy for organic valvular heart disease. Obviously, the results of surgical treatment depend upon the preoperative status of the patient. Unfortunately many patients present at operation after severe left ventricular impairment has occurred. It is not always easy to appreciate in how far the functional impairment of the left ventricular function will influence the postoperative outcome or in how far the ventricle will recover postoperatively.

Purpose

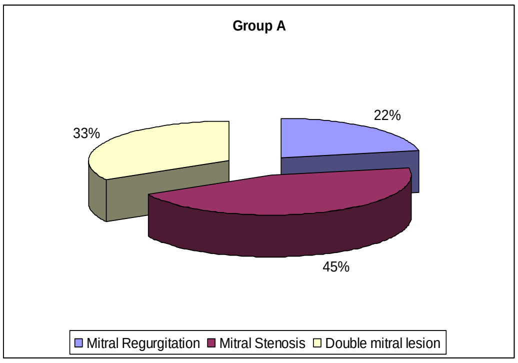
The assessment of the specific features of the postoperative evolution of the LV performance parameters in patients with LV systolic dysfunction suffering mitral or aortic valve replacement in relation to the type of operation.

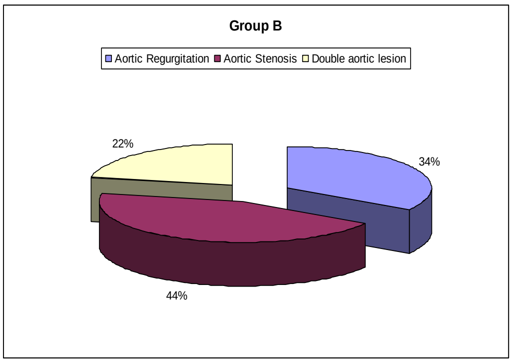
Materials and methods

We performed a study on 182 patients with LV systolic dysfunction undergoing mitral valve replacement (91 patients group A) or aortic valve replacement (91 patients - group B). The two groups were matched in regard to sex, age and associated pathology.

In group A, 45% of patients were operated for mitral stenosis, 33% for associated mitral stenosis and regurgitation and 22% for mitral regurgitation.

In group B, 34% of patients were operated for aortic regurgitation, 44% for aortic stenosis and 22% for associated aortic stenosis and regurgitation (figure 1).





Left ventricular systolic dysfunction was defined by a left ventricular ejection fraction of less than 40% calculated by cardiac ultrasound using the volume method. We excluded from our study patients with multivalvular disease and patients suffering simultaneously CABG.

The valvular prostheses used for mitral or aortic valve replacement were of the bi-leaflet type. The patients were assessed clinically and by means of cardiac ultrasound at

10 days, 30 days 1 month and 6 months from the operation. The statistical analysis included the calculation of the correlation coefficient and simple liniary and multivariate regression analysis. We used the SYSTAT and SPSS programs.

Results

1. The perioperative mortality was significantly higher in patients with left ventricular dysfunction suffering mitral replacement than in patients with left ventricular dysfunction suffering aortic replacement. The highest mortality was scored in the group suffering mitral replacement for acute mitral regurgitation (figure 2).

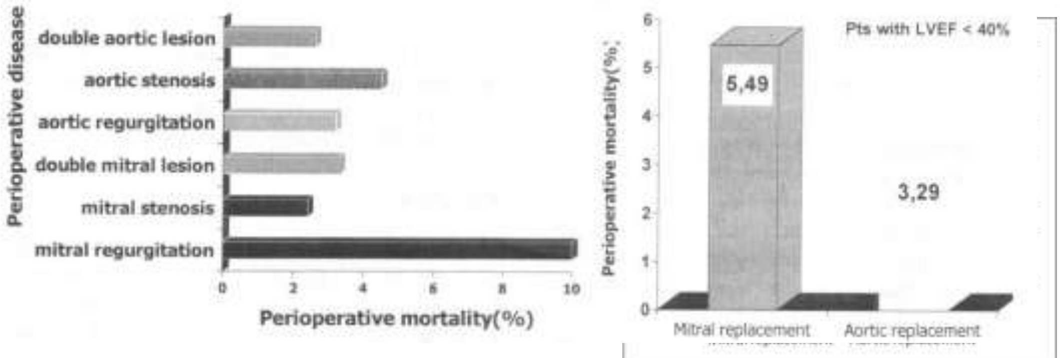


Figure 2

2. The LVEF increased postoperatively (at 1 month) in patients with aortic replacement and especially in those patients operated for aortic stenosis but not in patients suffering mitral replacement. In patients with mitral replacement the left ventricular ejection fraction did not improve or increased rather insignificantly postoperatively (figure 3).

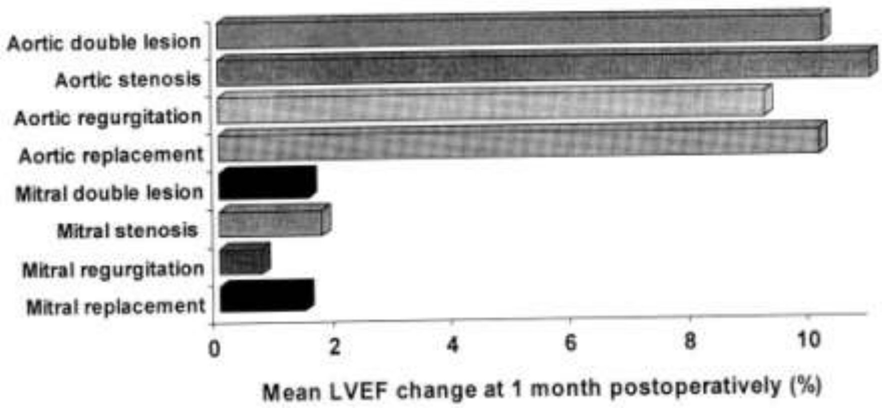


Figure 3

3. Left ventricular remodeling with decrease in LV chamber size appeared postoperatively after aortic valve replacement earlier than after mitral replacement. This was the case especially in patients operated for aortic regurgitation ($p < 0.005$) (figure 4).

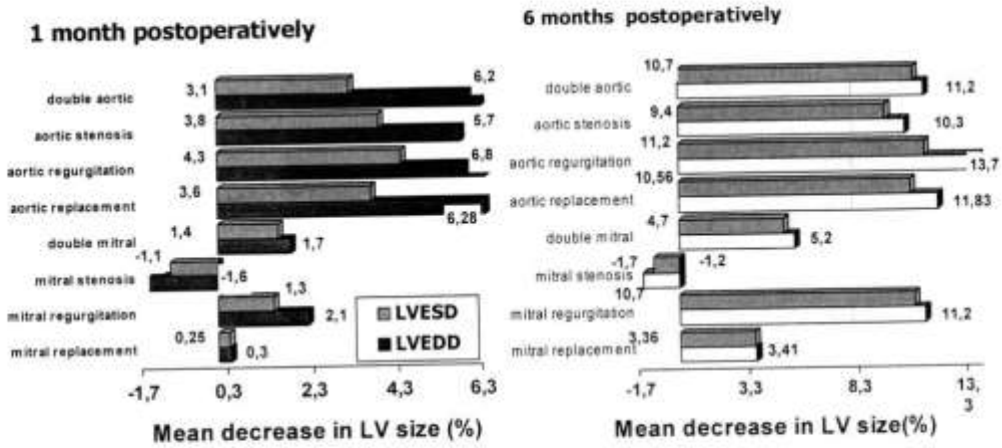


Figure 4

4. A LV end diastolic diameter > 57 mm in aortic stenosis and > 65 mm in aortic regurgitation was correlated with an unfavourable course after aortic replacement (r = 0.78, p < 0.001). The LV size did not alter the postoperative course in case of mitral valve replacement (figure 5).

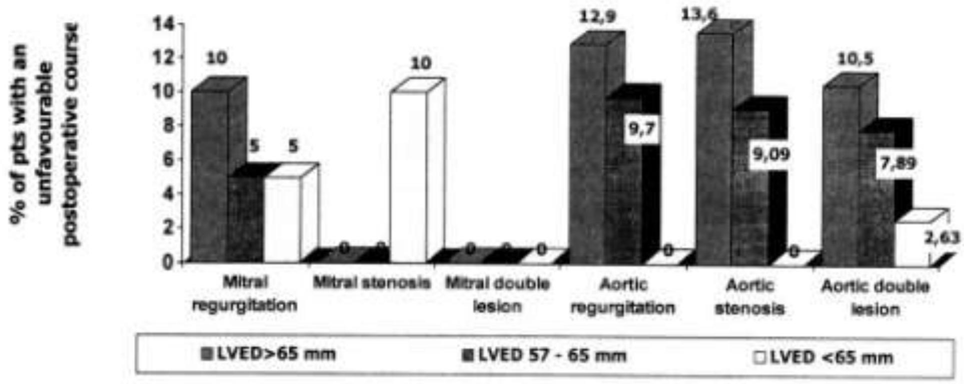


Figure 5

5. The univariate regression analyis of the clinical and echocardiographic parameters showed that the percentage increase in LVEF was correlated with age (r = 0.78, p < 0.001), LVED diameter and volume (r = 0.81 and 0.79, respectively, p < 0.0001), and functional NYHA class (r = 0.79, p < 0.005) (figure 6).

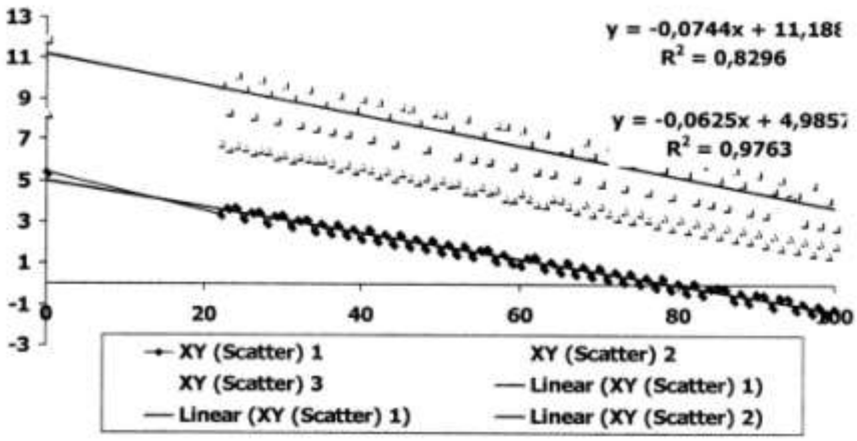


Figure 6

Conclusions

[1] LV systolic dysfunction has a more favorable outcome (perioperative mortality, postoperative LVEF increase and decrease of LV chamber size) in patients suffering aortic replacement compared with those suffering mitral replacement.

[2] Age is an independent predictor of the LV remodeling pattern after mitral and aortic replacement.

[3] The LV end-diastolic diameter > 57 mm for aortic stenosis and > 65 mm for aortic regurgitation is predictive for an unfavorable outcome in patients with aortic valve replacement independent of the preoperative LVEF.

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Atrial tachyarrhythmias after valve replacement for aortic stenosis*)

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Abstract

One hundred and eighteen patients undergoing aortic valve replacement for aortic stenosis were analyzed to determine the incidence and predisposing factors to postoperative atrial tachyarrhythmias. Univariate and multivariate analyses were performed on a number of clinical, hemodynamic, radiographic, electrocardiographic, operative and postoperative variables. 47 patients (40%) experienced atrial tachyarrhythmias at a median 3 days after surgery (70% atrial fibrillation, 22% atrial flutter and 6% jonctional tachycardia). Preoperative descriptors associated with an increased prevalence of atrial tachyarrhythmias were age 70 years or older ($p < 0.02$), mitral regurgitation ($p < 0.002$), history of paroxismal atrial fibrillation ($p < 0.03$), or antiarrhythmic therapy ($p < 0.006$), diabetes mellitus ($p < 0.01$), and elevated pulmonary systolic, mean, and capillary wedge pressures ($p < 0.02$, $p < 0.07$, $p < 0.005$). Postoperative descriptors were prolonged respirator therapy ($p < 0.001$), use of catecholamines ($p < 0.01$) or vasodilators ($p < 0.05$), and prolonged stay in the ICU ($p < 0.04$). Multivariate analysis of these 12 variables showed advanced age, diabetes mellitus, and prolonged respirator use to be independently associated with atrial tachycardias and to predict them with a sensitivity of 62% and a specificity of 77%. Anticipation of atrial arrhythmias in patients with specific clinical descriptors may be used to guide prophylactic therapy.

Key words: *aortic valve replacement, aortic stenosis, tachycardia, atrial fibrillation*

Background

Atrial tachyarrythmias are a frequent, potentially serious complication after thoracotomy or cardiac surgery. Impaired function of valve prostheses at high heart rates increases the morbidity of tachycardia in such patients.

Prophylactic anti-arrhythmic therapy has been proposed, but concerns of efficacy and safety suggest selective use. Unfortunately, not much data are available to provide basis for selective prescription of anti-arrhythmic drugs after aortic valvular surgery.

*) **Romanian Journal of Cardiovascular Surgery ■ 2004, vol. 3, no. 1, pp. 27–30**

In our study we analyzed patients undergoing aortic valve replacement for aortic stenosis (1) to determine the prevalence of postoperative atrial tachycardias, (2) to systematically examine a large number of clinical predictors as possible risk factors, and (3) to develop a profile of those patients at greatest risk for postoperative arrhythmias in whom prophylactic use of antiarrhythmic therapy might be used most effectively.

Methods

118 patients suffering aortic valve replacement between 01 January 1998 and 31 December 2001 were reviewed. Patients with aortic valve gradients less than 25 mm Hg, chronic atrial fibrillation, and simultaneous mitral valve surgery were excluded, and those undergoing all other additional cardiac procedures such as coronary artery bypass grafting, aneurysmectomy, and resection of the ascending aorta were included. The study population consisted of 118 patients with aortic stenosis at risk for postoperative atrial arrhythmias. Ninety (76%) were men, and the average age was 62 ± 13 years (range 16 to 87). Seventy-seven (65%) were taking digoxin preoperatively and 19 (16%) were taking beta-blockers.

All surgical procedures included cardiopulmonary bypass with systemic hypothermia and multiple doses of cold potassium cardioplegis solution. Seventy-seven patients received mechanical prostheses while 41 received porcine heterograft valves. Prophylactic postoperative digoxin or beta-blockade was not used. All patients underwent continuous electrocardiographic monitoring while in the surgical intensive care unit (at least 48 h), and many were monitored also thereafter.

Arrhythmias are defined as any atrial tachycardia (rate >100/min) with a supraventricular nonsynus mechanism, including atrial fibrillation, atrial flutter, and ectopic atrial tachycardias, occurring after admission to the surgical intensive care unit. All arrhythmias were of a duration long enough to confirm diagnosis by 12 lead electrocardiogram in all cases and often by intra-atrial recordings with temporary implanted electrodes.

The following preoperative clinical, hemodynamic, radiographic, electrocardiographic, intraoperative, and immediate postoperative variables were reviewed to determine those individually predictive or protective of postoperative atrial tachycardias: clinical - age, NYHA class, hypertension, previous myocardial infarction, previous heart surgery, renal disease, pulmonary disease, cerebrovascular disease, diabetes mellitus, hepatic disease; medications - digoxin, vasodilators, anticoagulants, beta-blockers, diuretics, antiarrhythmics; operative - CABG, aortic valve prosthesis type, pump time, aortic clamping time, use of IABP, additional procedures, intraoperative myocardial infarction; postoperative - catecholamine use, vasodilator use, prolonged respirator use, cerebrovascular accident, wound infection, emergency thoracotomy, abnormal mental status, excessive bleeding, acute renal failure, intensive care unit stay, pericarditis, endocarditis, hospital mortality, late mortality; electrocardiograms - Q-wave scar, first degree atrioventricular block, left atrial abnormality, QRS voltage for left ventriclular hypertrophy, QRS duration >0.09 ms, left axis deviation, repolarization abnormalities, bundle branch block, permanent pacemaker, paroxysmal atrial fibrillation; roentgenogram - cardiothoracic ratio; hemodynamics -pulmonary vascular resistance, left ventriculogram, presence of CAD, presence of aortic regurgitation, severity of aortic regurgitation, cardiac output, ejection fraction, aortic valve gradient, aortic valve gradient, aortic valve area, left ventricular end-diastolic pressure, mitral regurgitation, arteriovenous oxygen difference, pulmonary arterial systolic, mean, and capillary wedge pressures.

Statistical analysis was performed with the *chi-squared test* or unpaired *t-test*. Multivariate analysis used stepwise logistic regression to determine the simultaneous significance of several variables.

Results

Forty seven patients (40%) had atrial tachyarrhythmias at a median of 3 days after surgery (mean 3.3 ± 2.0 days, range 1 to 9). In the 32 patients in whom intracardiac recordings were performed for the determination of the mechanism of tachycardia, 23 (72%) had atrial fibrillation, seven had atrial flutter (22%), and two (6%) had junctional tachycardia. In the remaining patients, available data were insufficient to identify the mechanism of tachycardia.

Clinical variables associated with an increased risk of atrial tachyarrhythmias were age 70 years or older ($p < 0.02$), history of diabetes mellitus ($p < 0.01$), paroxysmal atrial fibrillation ($p < 0.03$), and antiarrhythmic drug therapy ($p < 0.006$).

Variables not associated with an increased prevalence of arrhythmias were sex; previous cardiac surgery; previous myocardiac infarction; NYHA symptom class; history of hypertension, renal, hepatic, pulmonary, or cerebrovascular disease; and treatment with digoxin, nitrates, vasodilators, oral anticoagulants, beta-blockers, diuretics. No variable was associated with a decreased prevalence of arrhythmias.

Analysis of electrocardiograms revealed no significant associations between arrhythmia and any criterion for left ventricular hypertrophy, including *P*-wave abnormality, or history of conduction disturbances, or the presence of a myocardial scar. Similarly, there was no association between atrial tachycardias and the cardiothoracic ratio measured on chest roentgenogram. Hemodynamic variables associated with an increased risk of atrial arrhythmia were greater elevations in pulmonary arterial systolic, mean, or capillary wedge pressures ($p < 0.02$, $p < 0.07$, $p < 0.005$, respectively). The presence of mitral regurgitation (1+ or greater) was associated with increased risk ($p < 0.002$), although the angiographic or echographic severity was not. Variables unrelated to the prevalence of arrhythmia were left ventricular systolic and end-diastolic pressures, cardiac output, arteriovenous oxygen differences, pulmonary vascular resistances, abnormal left ventriculogram, ejection fraction, the presence or severity of coronary artery disease or aortic regurgitation, and aortic valve pressure gradient or estimated valve area.

No operative variables were associated with the occurrence of atrial tachycardia. This included pump and aortic cross-clamp times, type and annulus size of aortic prosthesis inserted, performance of CABG or other additional operative procedures, intraoperative myocardial infarction, or use of the IABP.

Because arrhythmias occurred up to 9 days after surgery, events of the immediate postoperative period could have predictive importance. Descriptors related to an increased prevalence of atrial arrhythmia were mechanical ventilation beyond 48 h after surgery ($p < 0.001$) or need for inotropic support or vasodilators for more than 12 h ($p <$

0.01, $p < 0.05$). Lengthy of stay in the ICU was grater in those with atrial tachycardia (mean 5.5 ± 9.8 days) than in those without (mean 2.4 ± 1.4 - $p < 0.04$). Events unrelated to atrial tachyarrhythmia were hospital mortality, acute renal failure, reoperation for excessive bleeding, emergency thoracotomy, abnormal mental status, cerebrovascular accident, and sternal or wound infection. Subsequent events unrelated to arrhythmia included postpericardiotomy syndrome, prosthetic endocarditis and late mortality.

Logistic regression or multivariate analysis was applied to all 12 variables significantly associated with atrial tachyarrhythmia. Only those patients with complete data sets for these variables were included, reducing the study population to 108 patients. Examination of preoperative variables showed age and mitral regurgitation to be closely related, as were diabetes and antiarrhythmic therapy. Similarly, prolonged respirator use was related to pulmonary arterial pressures, postoperative use of pressors, catecholamines, and vasodilators, and length of stay in the ICU (all $p < 0.05$). The strongest predictor of each of these groups excluded the other variables from the regression model.

The preoperative and postoperative variables proving to be significant were respirator use greater than 48 h ($p < 0.01$), diabetes mellitus ($p < 0.02$), and age 70 years or older ($p < 0.03$). This model had a sensitivity of 62%, a specificity of 77%, and was 71% correct. Although the overall p value was highly significant ($p < 0.0001$) the correlation was only modest, with a coefficient of 0.346.

Discutions

Atrial tachyarrhythmias occur frequently after cardiac or thoracic surgical procedures. The prevalence after CABG ranges from 15.2% to 38%. Although addressed by fewer studies, atrial arrhythmias after valvular surgery have been reported to occur in from 4.6% to 53% of patients. Because the incidence of arrhythmias is highly dependent on the methods used for their detection it may be difficult to compare results between institutions. However, our finding of 40% prevalence is considerably higher than the average found after CABG in most studies, although the type and timing of arrhythmias are similar. Extensive examination of potentially associated preoperative and perioperatiove characteristics shows postoperative atrial arrhythmias to be multifactorial and enables formulation of a demographic profile of patients at greatest risk. Advanced age in particular, is a strongly associated descriptor and is related to the presence of several other significant variables. Most investigators have found age to be unrelated to the development of arrhythmia. However, the number of elderly patients in these studies is generally small. Our results may be explained by the larger group of elderly patients examined (60 patients aged 65 years or older) and by the higher proportion of these patients (51%) in the study population.

The association of mitral regurgitation and increased pulmonary arterial and capillary wedge pressures with postoperative atrial arrhythmias is not surprising. However, the lack of associations between arrhythmias and pulmonary vascular resistance, LV end diastolic pressure, the severity of mitral regurgitation and ECG left atrial abnormality underscores the complexity of arrhythmia production, and the limitations of our knowledge of their pathogenesis. The association between arrhythmia and the complicated perioperative course but not preoperative pulmonary disease or heart failure indicates the importance of perioperative events.

The mechanism of atrial fibrillation and flutter is unclear, although characteristics of reentry such as slowed conduction, atrial premature depolarization, and abnormal refractoriness seem to be important to arrhythmia production. Other studies confirmed the importance of asynchronous atrial activity as a predictor of arrhythmia after CABG surgery. Our observation that paroxismal atrial fibrillation and preoperative antiarrhythmic drug use increased the incidence of atrial tachyarrhythmia supports the importance of a preexisting electrophysiologic abnormality as an etiologic factor of early postoperative arrhythmia.

The association between atrial tachyarrhythmia and diabetes mellitus noted in our study may be related to microangiopathic ischemia, to autonomic dysfunction, or even to primary nonischemic myocardial disease.

Although description of the population at risk for arrhythmia is of great clinical usefulness, the lack of association between use of beta-blockers or descriptors of ischemia and atrial arrhytmias is also important. These results are in conflict with postulated mechanisms of arrhythmia production such as adrenergic hypersensitivity caused by beta-blocker withdrawal or inadequate atrial or ventricular preservation.

Analysis of variables by logistic regression determines the relative strengths of their association with atrial tachyarrhythmias and creates a statistically significant profile with moderate sensitivity and specificity with a small number of variables. Although additional underline descriptors may be of value, this profile helps to determine prophylactic therapy. Our data indicate that elderly patients or those with diabetes mellitus, elevated pulmonary arterial pressures, history of arrhythmias, or a complicated postoperative course are at increased risk of postoperative atrial arrhythmias. Because potential benefit may outweigh the risks, prophylactic digitalis and/or beta-blockers should be strongly considered in these patients.

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Mitral valve replacement for severe mitral regurgitation caused by Libman-Sacks endocarditis*)

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Paper presented at the "XI Annual meeting of the Danubian Forum for Cardiac Suregry", May 27-29, 2005, Rivierea Holiday Club, Varna, Bulgaria

Abstract

We present a Caucasian 22 years, female with long SLE evolution, which developed on the last months cardiac symptoms, diagnosed by clinic examination and echocardiography being a Libman-Sachs endocarditis, unusual large vegetation and mitral regurgitation III degree. She was operated for the high risk of embolisation and due to severe mitral regurgitation, receiving a mechanical valve. Postoperative evolution was uneventful and the patient discharged at home one week later.

Key words: *Libman-Sachs endocarditis, mitral valve replacement*

Rezumat

Prezentăm cazul unei femei caucaziene, de 22 de ani, SLE cu evoluție îndelungată care a prezentat în ultimele luni simptome cardiace care au dus la diagnosticarea prin examinari clinice şi ecocardiografice a unei endocardite Libman-Sachs, cu vegetații neobişnuit de mari şi regurgitare mitrală de gradul III. Pacienta a fost operată datorită riscului mare de embolie şi datorită regurgitării mitrale severe, implantându-i-se o valvă mecanică. Evoluția postoperatorie a fost simplă, necomplicată, şi pacienta a fost externată o săptămână mai târziu.

Cuvinte cheie: *endocardita Libman-Sachs, înlocuire valvulară mitrală*

Introduction

Libman-Sachs Endocarditis complicating SLE has been reported to due hemodinamically significant mitral regurgitation necessitating valve replacement. This case report describes a young woman with severe mitral regurgitation and massive vegetation on the anterior leaflet. She was successful operated by mitral valve replacement.

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Case report

We described a 22 years old, female with diagnosis of, systemic lupus erythematosus (SLE), since 1994, Libmann-Sachs enocarditis with mitral regurgitation 3rd degree, secondary pulmonary hypertension, detected on July 2004, after an emergency hospital admission for acute pulmonary edema.

Clinical examination revealed an afebrile, normotensive slender woman with pallor and dependant edema. Auscultation revealed S3 gallop and 4/6 pansystolic murmur of mitral regurgitation. Pericardial rub was absent; symptomatic with acute pulmonary edema, chest discomfort, mild exertion dyspnea, fatigue and high risk of embolisation. No previous history of fever. Cardiac failure class II NYHA; treated with antibiotics, diuretics, steroid and non steroid anti-inflammatory therapy.

The ECG showed sinus rhythm, heart rate 120 beats/min, LV hypertrophy, ST elevation in V2-V4. Chest X-ray revealed moderate enhancement of the pulmonary vascular design, mild pleuresia. Echocardiography: – mode M: LA 4.6 cm, EDD 3.5cm, ESD 2.1 cm, RV 2.5 cm, EF-72%, thickened mitral leaflets, reduced mobility, moderate mitral stenosis, mean gradient 17 mm Hg, maximal gradient 28 mmHg, mitral area 1.44 sq cm, but 3rd degree mitral regurgitation, echodense mass of 2.2 cm attached to the anterior mitral leaflet (Fig. 1), mild tricuspid regurgitation, systolic pulmonary pressure of 43 mm Hg. Coronary angiography: showed normal coronary arteries.

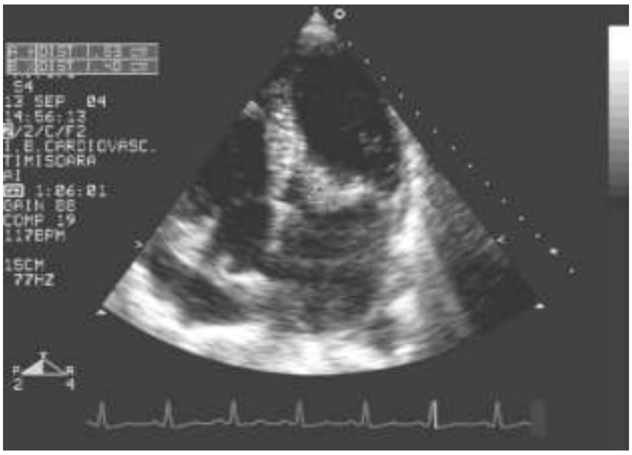

Figure 1: Transthoracic echocardiography showing a large vegetation on the anterior leaflet of mitral valve

She was operated (Oct 27, 2004) by median sternotomy approach, using bicaval cannulation, ante-grade and retrograde cardioplegia and the mitral valve, with a huge vegetation on the anterior leaflet (Figure 2), was replaced by a St. Jude mechanical valve 27 mm. Postoperative evolution and follow-up was uneventful. Macroscopic and microscopic examination of the valves revealed no active endocarditis.

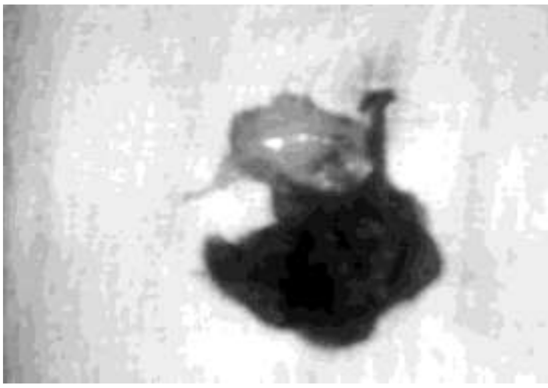

Figure 2: The anterior mitral leaflet with large vegetation

Comment

Systemic lupus erythematosus is a multisystem disorder with cardiac manifestations in about 50% of cases. Cardiovascular disease is the major cause of mortality and morbidity in systemic lupus erythematosus (8). All the cardiac structures: pericardium, myocardium, valves, coronary arteries can be involved.

Valvular manifestation in patients SLE, early described by Libman-Sachs, in 1924, the non-infectious verrucous valvular endocarditis, is the most prevalent and outcome important form of cardiac involvement. In some situations, leads to regurgitation of one, rare two valves and less frequently to stenosis (2). The mitral valve is most commonly affected, followed by aortic valve.

The most frequent abnormal findings is thickening of the valve, followed by vegetative lesions that usually are sessile and no more than 3-4 mm diameter (10). Our patient was diagnosed with SLE, in special kidney manifestations, ten years ago. She had a large vegetation on the anterior leaflet and the histopathology examination revealed valvular leaflet fibrosis, with extensive area of hyalinization and calcification, also necrotic material in vegetation but not active endocarditis.

The increase of mitral valve insufficiency associated with systemic lupus erythematosus (SLE) seems to be related to the treatment with corticosteroids (1). Corticosteroids heal Libman-Sacks endocarditis, but thereby they lead to fibrotic, retracted leaflet tissue and thus to severe valvular dysfunction.

Also, there is an increased incidence of atherosclerotic heart disease in SLE, including in premenopausal women. Coronary artery disease remains a major cause of mortality and morbidity with SLE (4). Coronary angiography was considered necessary for coronary artery disease exclusion, despite the age, also in our patient.

The best management, with immunosuppressive therapy and to wait for the vegetation regression could expose the patient to a high risk of embolism (5), more-over the patient remains with a severe regurgitation.

The surgical intervention to be considered as a feasible treatment without major risk in patients with compensated organ function (1, 7). If surgery is necessary, replacement with a mechanical valve may be better than with a bioprosthesis (3).

In conclusion, mechanical valve replacement is the best choice for the patient with SLE endocarditis, hemodinamically significant valve modification and high risk of embolism.

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Right ventricular outflow tract reconstruction using pericardic valved conduit – a 3 year retrospective study in Mures Transplant and Cardiovascular Disease Institute*)

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Abstract

Objective: *To assess the performance of the valved conduit used for tract reconstruction in right ventricular (RV) outflow stenosis or athresia.*

Methods: *A retrospective study of 7 consecutive right ventricular to pulmonary artery-conduit implants patients between January 2006 and April 2009 was performed. The majority of cases 3 - were with pulmonary atresia/VSD, one with Fallot's tetralogy one with truncus arteriosus with ventricular septal defect, one with single ventricle type right ventricle and one with complete atrioventricular septal defect with double outlet left ventricle and great vessels transposition. At all the cases we have performed conduit implantation and supplementary repair techniques. Echocardiography was performed for a median follow-up of 14 months.*

Results: *Median age at implantation was 13 months and median weight was 7.8 kg. Six patients were < 10 kg at the time of surgery. Early mortality was 14% (n = 1). One reintervention was performed in one patient at 4 years after surgery. Acquired distal conduit stenosis at the suture line was the commonest indication for conduit-specific reintervention and was associated with the small size of the conduit.*

Conclusions: *The pericardial valved conduit is widely applicable to RVOT reconstruction with satisfactory mid-term results.*

Key-words: *valved conduit, right ventricle, pulmonary artery*

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Rezumat

Scop: *Studiul performanțelor conductelor valvulate în tehnicile de reonstrucție a tractului de ejecție al ventriculului drept.*

Material şi metodă: *urmărirea postoperatorie a 7 pacienți operați în cadrul IBCVT în perioada ianuarie 2006-aprilie 2009. Dintre aceştia, 3 pacienți au prezentat atrezie pulmonară şi defect septal ventricular şi câte un caz cu tetralogie Fallot, trunchi arterial tip II, ventricul unic tip VD şi arc aortic întrerupt, canal atrioventricular comun şi VS cu cale dubla de ieşire şi vase mari transpuse. La toți pacienții, în paralel cu implantarea de conduct valvulat, s-au practicat şi tehnici chirurgicale complementare.*

Rezultate: *vârsta medie a pacienților a fost de 13 luni, iar greutatea medie de 7,8 kg. Mortalitatea imediată postoperatorie a fost de 14% (1 caz). La un singur caz s-a reintervenit la 4 ani postoperator (stenoză linie de sutură distală la un conduct de dimensiuni mici).*

Discutii: *Utilizarea de conducte valvulate în stenozele/obstrucțiile de tract de ejecție al ventriculului drept au rezultate satisfăcătoare pe termen mediu.*

Cuvinte-cheie: *conducte valvulate, ventricul drept, artera pulmonară*

Introduction

It is 40 years since Ross and Somerville reported the successful use of human tissue graft valves, which broadened the scope for a possible durable conduit for right ventricular outflow tract reconstruction. A variety of prosthetic conduits have since developed, although homografts continue to be regarded as the most reliable option. The most used conduit is heterologus pericardial conduit, because it is made with low costs. The alternative possibility is to use homologous conduit or jugular bovine conduit (Contegra) [4]. However, the pericardial conduit is a conduit with good pliability, but they have an important inconvenience – early/medium calcification and degeneration, particularly in very young patients [6]. The objective of this study was to assess the performance of pericardial valved conduit particularly referring to younger age at time of implantation.

Materials and methods

This is a prospective study of 7 cases of valved conduits used in right ventricle outflow tract reconstruction between January 2006 and April 2009 at Transplant and Cardiovascular Disease Institute. The majority of cases 3 were with diagnosed pulmonary atresia/VSD (43%), one with Fallot's Tetralogy (14%), one with truncus arteriosus with ventricular septal defect, one with single ventricle type right ventricle and one with complete atrioventricular septal defect with double outlet left ventricle and transposed great vessels (Table 1).

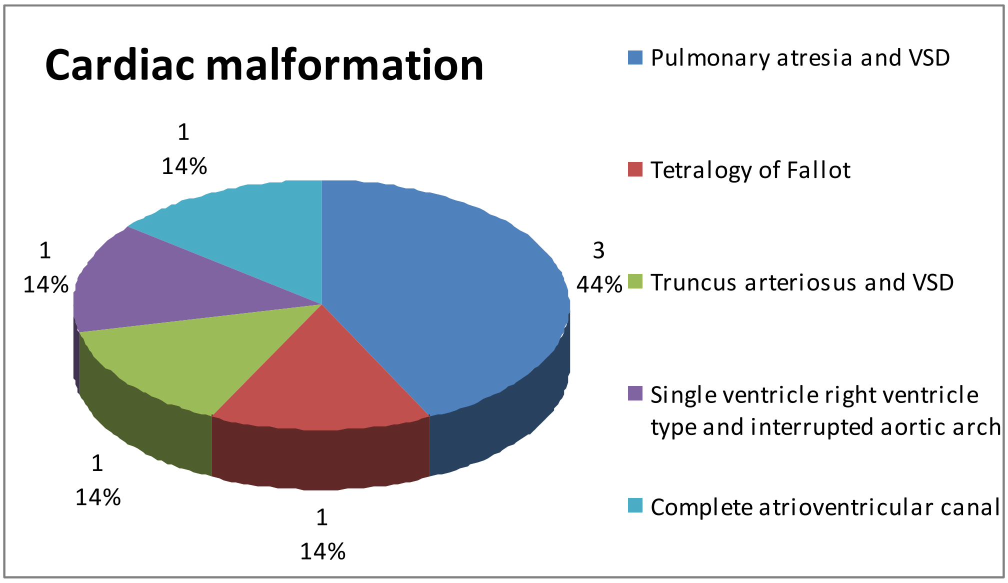


Table 1

All the children presented patent ductus arteriosus. The most common diagnosed method was echocardiography, only the patient with Truncus arteriosus needed cardiac catheterization for pulmonary hypertension evaluation. New techniques are figured by 3D tomography reconstruction (Figures 1-3).

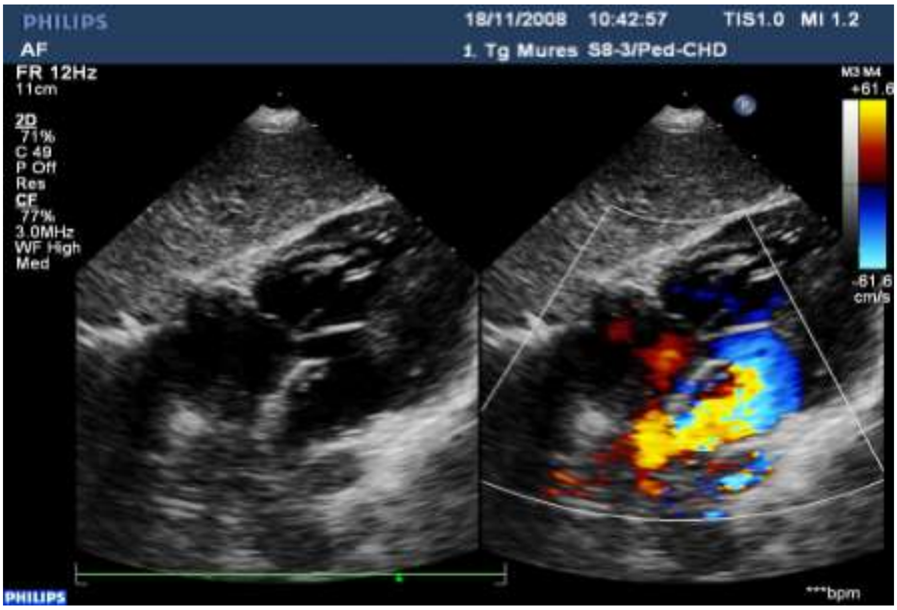


Figure 1: Echographic image in Tetralogy of Fallot

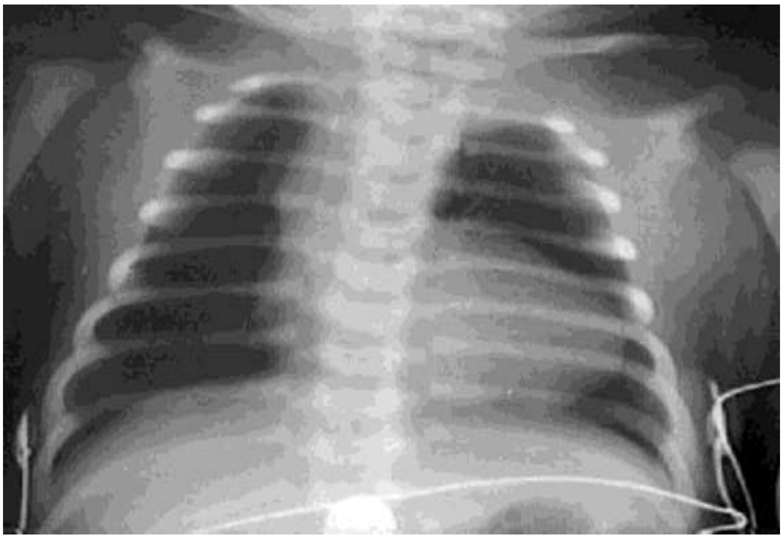


Figure 2: Chest radiography in tetralogy of Fallot (Coeur en sabot)

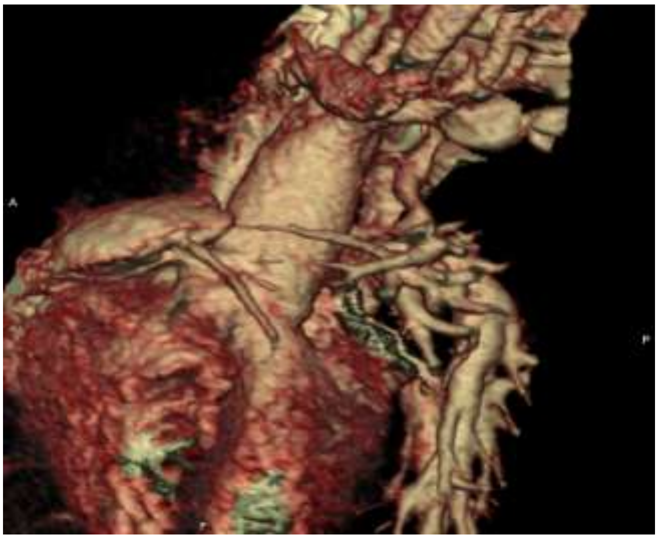


Figure 3: 3D reconstruction in Tetralogy of Falot (angio CT)

Results and Conclusions

Median age at implantation was 13 months (a range between 6-32 months) and median weight was 7.8 kg (a range between 5.5-14 kg). Six (86%) patients were < 10 kg at the time of surgery. At all the cases we perform conduit replacements and additional repair techniques. All the heterologous pericardial valved conduit were realized by our specialists in our research laboratory. The grafts have been treated with buffered glutaraldehyde without either additional anticalcification or antithrombogenic preparation (Figure 4).

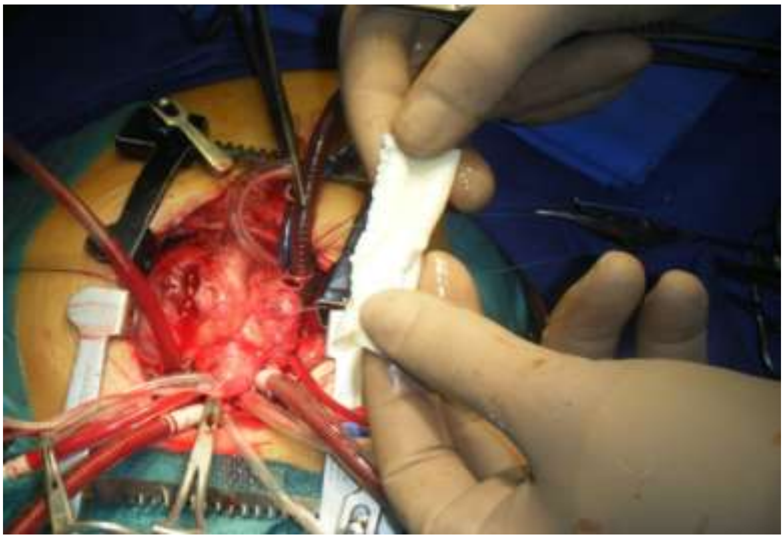
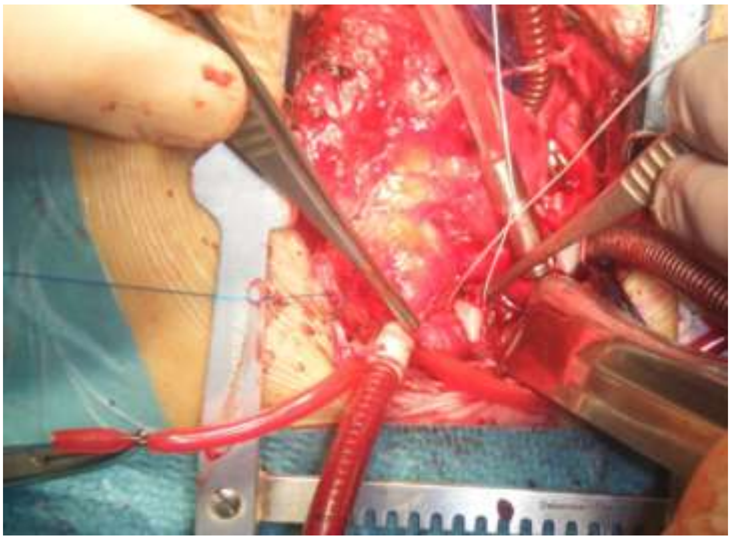


Figure 4: Intraoperator aspect – a valved conduit made by our research team

At one patient with pulmonary atresia and VSD we performed in a first step a modified Blalock-Taussig shunt. The surgical technique used to implant the pericardial valved conduit was in moderate hypothermic cardiopulmonary bypass and aortic cross-clamping, with intermittent doses of cold blood or crystalloid cardioplegia for myocardial protection.

The lenght of cardiopulmonary by-pass was between 64 and 127 minutes (mean of 81 min) and the aorta cross clamping time was between 41 and 92 minutes (mean of 66 min). The conduit was rinsed in physiological saline water.

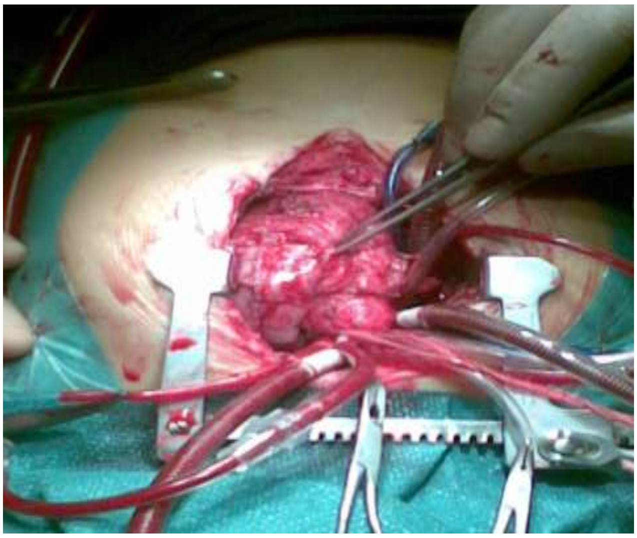


The opening in the native pulmonary arteries was extended if necessary to at least the same diameter as the chosen conduit. At the patient with modified Blalock-Taussig shunt, we have performed the shunt take-down before starting the cardiopulmonary by-pass (Figure 5).

Figure 5: Intraoperator aspect

At one case, we have performed an enlargement plasty of both pulmonary branches. At first, the distal anastomosis was performed using 6/0 continuous running polypropylene sutures with an everting technique (Figure 6).

Figure 6: Intraoperator image – distal suture of the valved conduit



The proximal suture line (at the ventriculotomy site) was performed with a layer of continuous 5/0 or 6/0 polypropylene suture (depending on the conduit size) reinforced with interrupted pledgetted sutures at the heel of the anastomosis (Figure 7).

Figure 7: Intraoperator aspect – final result after valved conduit implantation

All the children were left with the sternum open, with a pericardial membrane, for 24-48 few days, to avoid sternal conduit compression. Early mortality was 14% (*n* = 1).

The recovery in cardiac intensive room had a mean value of 7, 6 days with a range between 5 and 11 days. The children were discharged from the hospital at a median time of 14 days after the operation. Actuarial survival was 100% and all the children have freedom from reintervention at 4 years after the operation. Some studies recommend anticoagulant or Aspirin utilization, to haste the endothelialisation of the graft in a low pressure system. In some cases, we used Aspirin therapy for a few months after the operation.

We follow the patients at 1, 3, 6, 12 month after the operation and annually thereafter. At this time, all the children are free of unexpected evolution of the pericardial valved conduit. The valved conduits are free of stenosis (only in 1 case have a moderate stenosis of distal suture line), conduit dilatation and/or valvular regurgitation, conduit endocardithis or trombosys.

At ecocardiography of the children who was operated 3 and 4 years ago, we observe incipient calcification and degeneration of the pericardial valved conduit. The international studies showed us that the pericardial conduit presents severe calcification after a mean time of 8 years (Figure 8), (Figure 9).

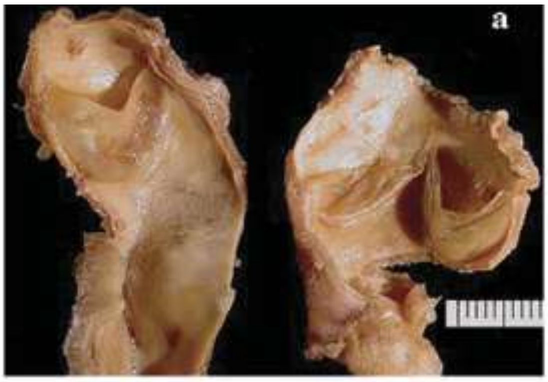


Figure 8: Explanted valved conduit

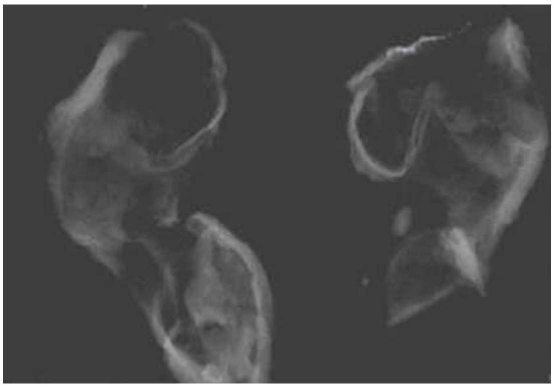


Figure 9: Radioscopic image of explanted valved conduit

Short and mid-term results showed minimal transvalvular pressure gradients and good hemodynamic functional performance according to other available conduits. All the small children are in good clinical status and low clinical symptoms.

Discussions

The heterologous valved conduit could be an attractive option with small costs for right ventricular outflow tract reconstruction particularly in smaller patients. [3, 4, 5, 6] Excellent tissue handling, haemostasis, versatility and off-the-shelf availability are the main advantages [4, 6]. However, there is a low incidence of conduit-related complications, the commonest being the stenosis at the distal suture line during follow-up only at the smaller-sized conduits (12 and 14 mm). High pressure in the conduit can lead to aneurismal dilatation and secondary valvar regurgitation [4]. However, there is also a small unpredictable risk of conduit dilatation that is unrelated to pressure and also of thrombosis in the valve sinuses, neither of which appear to be clinically important but remain a cause for concern and will need further evaluation. The role of aspirin and antithrombotic therapy needs to be evaluated.

It must be taken into account that a child is more sensitive than adults, and cardiac surgery has a major psychological impact. It is necessary to choose always the most favorable surgical maneuver to prevent the reintervention and to ensure the comfort of a child's life at a high level. [1, 2]

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The Ross operation: anatomy and surgical technique*)

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Introduction

The available options for patients with aortic valve disease, who require surgery, are the following:

- the valve repair. It represents an option in carefully selected patients with aortic regurgitation or stenosis in whom the valve is not calcified. Long-term results are limited at the present time;
- the valve replacement. There are four main types of valvar substitutes: mechanical, biopstostheses, allo(homo)graft, autograft (Ross technique).

The choice for a particular type of prosthesis is influenced by several inter-related factors: patient's age, associated pathologies (coronary disease, mitral valve disease, atrial fibrillation), the surgeon's and the center's experience with implantation of a prosthesis, the preference of the referring cardiologist, attending surgeon and the patient.

The decision for a particular type of prosthesis is made rather arbitrarily (1).

Guidelines were developed for the management of patients with valvar disease, in order to improve the effectiveness of care, optimize patient outcomes. But only general criteria for valve selection are given (2).

The perfect aortic valve substitute is easy to implant, has excellent hemodynamics, lifelong durability, no risk for thrombosis or thromboembolism, bleeding, non-structural valve deterioration, endocarditis. The ideal valvar substitute still doesn't exist.

Although implantation of autografts and allografts is technically more challenging there are major advantages over mechanical prostheses and stented bioprostheses with regard to hemaodynamic profile, endocarditis and thromboembolic event rates. As disadvantages /limits, both autografts and allografts have a limited durability (3, 4, 5, 6, 7). Ross described the first replacement of the aortic valve with an allograft, in 1962 (8). Ross was also among the first to describe the use of the pulmonary autograft in aortic position (9, 10). Indications have changed during time: while initially these reflected the continuous search for a feasible valvar substitute, nowadays, indications point toward young patients, women in childbearing age, endocarditis patients, small aortic annulus.

The major drawbacks of this procedure are the following:

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- a monovalvar pathology is transformed in a bivalvar one;
- reimplantation of the coronaries (both technically more challenging and with potential hazards);
- long procedure, longer cardiopulmonary bypass times and cross-clamping times;
- performed in few centers, by few surgeons (11); technically more challenging;
- contraindicated in case of Marfan syndrome or rheumatic aortic disease (these contraindications can be either relative or absolute); limited, in case of pathology of the pulmonary valve;
- difficult excision in case of redo operations;
- redo operations more often necessary for the degenerescence of the homograft in pulmonary position;
- relative short follow-up and different patient groups among various centers;
- dilatation of the autograft.

While one of the major advantages of the use of the pulmonary autograft in aortic position is represented by its alleged propensity to grow (12, 13, 14), a major concern is represented by its dilatation (15, 16, 17, 18). Several available options would theoretically minimize this risk, though these will limit the growing potential of the autograft.

The dilatation of the autograft, has as a consequence, not only the well-known aortic insufficiency but it can also produce distortion of the coronaries with secondary ischemia (that might appear even at several months after the operation) (19).

Dilatation of the autograft can be explained by the histological differences either between the aorta and pulmonary trunk or between the bicuspid and normal aorta (18), as well as by associated pathologies as Marfan syndrome, rheumatic disease, hypertension, longer autografts or a supra-annular implantation (20).

After its introduction as a subcoronary valvar substitute, the pulmonary autograft can be used nowadays in the following ways: subcoronary, subcoronary with non-coronary sinus wall retained, cylinder and respectively, root (21). The potential solutions for avoiding the dilatation of the autograft are: the use of the inclusion technique or subcoronary (22), the reinforcement of the autograft, banding the sinotubular junction, reinforcement of the aortic annulus, the use of shorter autografts.

While talking about the Ross procedure one would open another important chapter and would bring into discussion the topic of allograft use and degenerescence (and calcification), because the allograft (homograft) in pulmonary position will degenerate usually earlier and will need special attention (23, 24). Allografts in pulmonary position develop mostly stenosis. One opinion quite diffused nowadays is that some disadvantages related to the allograft stenosis can be prevented or cured by the percutaneous technique - but this doesn't take into account the fate of the right ventricle: postponing the allograft replacement can be "comfortable" for the surgeon and quite "tempting" for the patient, while both would overlook the risk of right ventricular failure (25). There has also been advocated the use of oversized allografts and tissue-engineered heart valves (26).

The Ross procedure seems to show even more selected indications, while taking into account all the previous details.

In the light of all the afore mentioned details, it is obvious that the Ross procedure, in order to be widely accepted and performed, must pass "the exam" of analyses of larger series of patients and of the long-term results and concomitantly, surgeons should become more acquainted with this procedure.

Materials and Methods

The present work concentrates on the anatomical details and on the surgical technique demonstrating the procedure as currently performed in the *Cardiac Department at the San Donato Hospital Milan, Italy* where more than 150 patients have been operated so far. The anatomical study was performed at the *Institute of Pathology at Niguarda Hospital Milan.*

Ten formalin-fixed and five fresh adult hearts from non-cardiopathic patients were dissected in order to show the pattern of coronary distribution and with special emphasis on the vascularization of the pulmonary infundibulum. The anatomical landmarks of the latter have also been thoroughly depicted and special attention was given to "the cleavage plane" between the pulmonary trunk and the aorta (and left ventricular outflow tract) and to the size and course of the first septal branch of the LAD. No special measurements of the aortic and pulmonary annuli was performed, because of the evident biases introduced by the post mortem changes and/or fixation in formalin; the echo measurements "in vivo" are the most reliable.

A review of the operative statistics from the *San Donato Cardiac Surgery Department* was performed on 141 patients and the main steps of the Ross procedure were illustrated and discussed. Some technical innovations are presented.

Anatomy

The region of the pulmonary infundibulum and the pulmonary trunk have presented a major interest mostly for the pediatric cardiac surgeon, so far, being invested with new significances for the surgeon who treats adult pathology only recently.

The pulmonary valve is quite separate from the remainder three ones (aortic and atrioventricular valves) and there is no element belonging to the fibrous skeleton of the heart at this level as there is no real "pulmonary annulus". The pulmonary valvar cusps take off directly at level of the right ventricular outflow tract myocardium. There is no macroscopically distinguishable fibrous "tendon" or "ligament" connecting the aorta with the pulmonary trunk ("the tendon of the infundibulum" - Tandler). A clear dissection can be performed between the two major arteries and some degrees of separation can thus be obtained, although, towards the pulmonary infundibular posterior wall, the ventricular myocardium is much thinner. Some surgeons thus suggest "to err" towards the aorta and not towards the pulmonary while dissecting the infundibulum. This separation can not proceed too much in an apical direction, because the apparent cleavage plane quickly disappears, with the risk of opening either the right or left ventricle (Figure 1).

Many variations regarding the vascularization of the pulmonary infrundibulum have been described so far (27, 28, 29). More recently another study (30) has shown that the pulmonary infundibulum receives four arterial pedicles two of which anterior and respectively, two posterior (Figure 1 and 2).

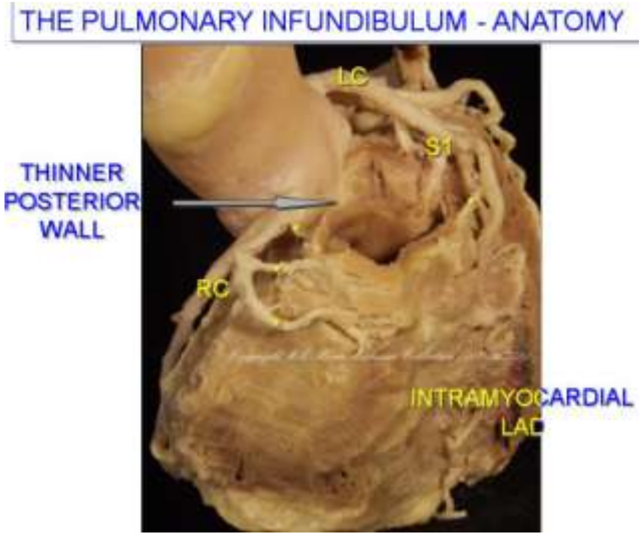


Figure 1: The pulmonary infundibulum - anatomy
*** = *Arterial pedicles to the infundibulum*** *[copyright©Horia Muresian]*

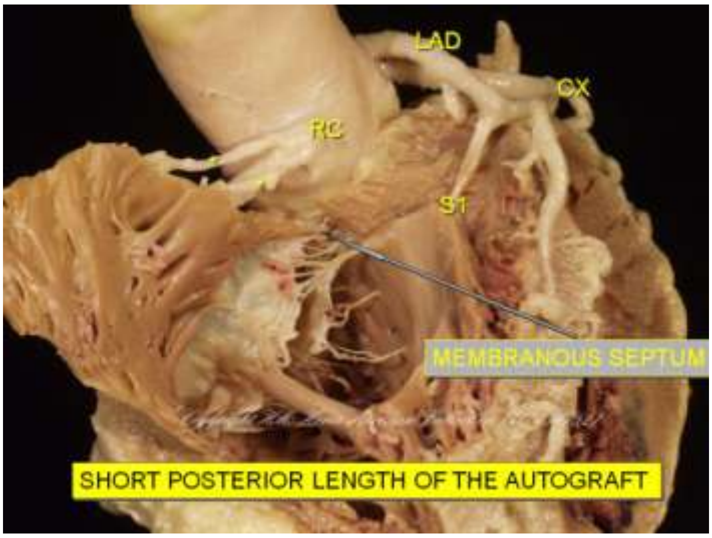


Figure 2: Anatomy *[copyright©Horia Muresian]*

The right pedicles are usually more conspicuous. They take origin at level of the right coronary, right sinus of the aorta, either separately or as a common trunk that soon divides in anterior and respectively, posterior branches.

The left pedicles take origin at level of the common trunk (rarely) of LAD (more frequently). In very rare cases, the posterior left pedicle can have origin at level of the left aortic sinus. A clear distinction should be made between the first septal and the left posterior infundibular pedicle.

The pedicles anastomose intramyocardially both at anterior and posterior level. These anastomoses represent important collateral pathways. The first septal contributes with minor branches at the vascularization of the infundibulum. The first septal branch can be dissected and its injury avoided, with careful dissection (vide infra). The pedicles can be visualized during the coronary angiogram (Figure 3).

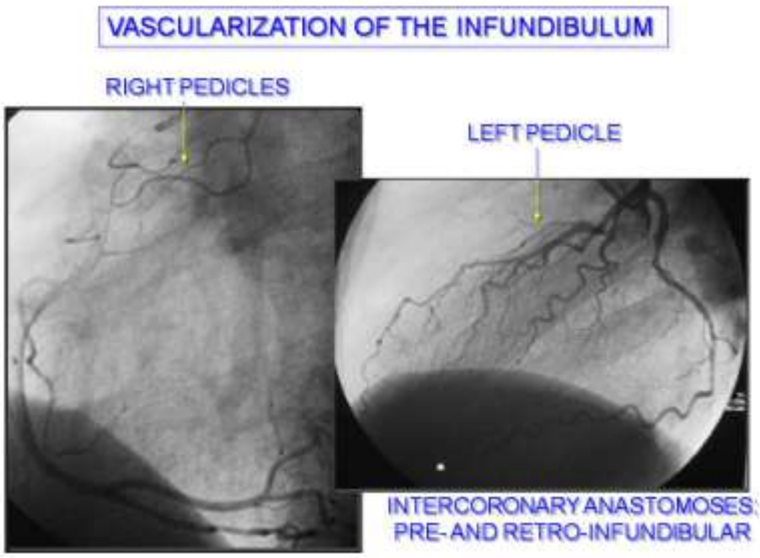


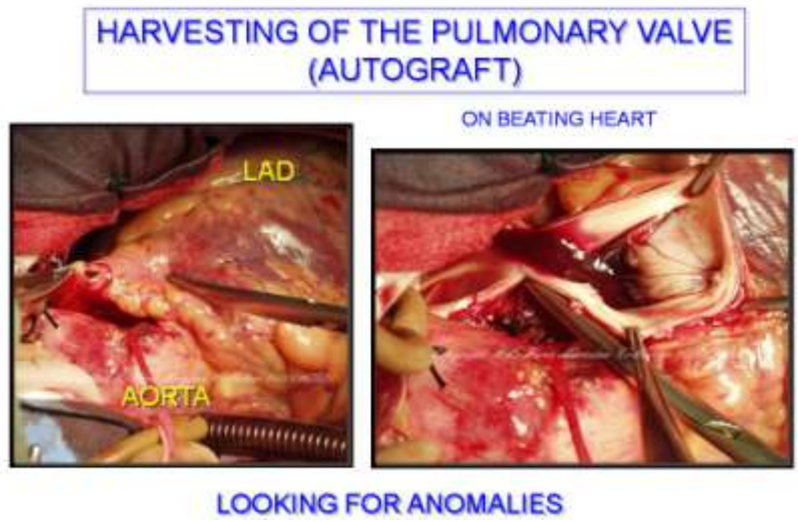
Figure 3: Angiographic aspect

Surgery

Some surgeons prefer to open first the aorta, to inspect the valve, annulus, LVOT to check for the suitability for this particular operation, and only afterwards, to proceed toward the Ross operation; this implies longer cross-clamp times. In the San Donato experience, a major part of the operation is being performed on beating heart while relying more on the preoperative echographic data. Pericardium is opened widely including at its cranial level, in order to have as much aorta at hand as well as the pulmonary bifurcation. Strips of autologous pericardium are harvested; these will serve to reinforce the proximal aortic suture and respectively, the posterior aspect of the autograft. Pericardium is used fresh (unfixed).

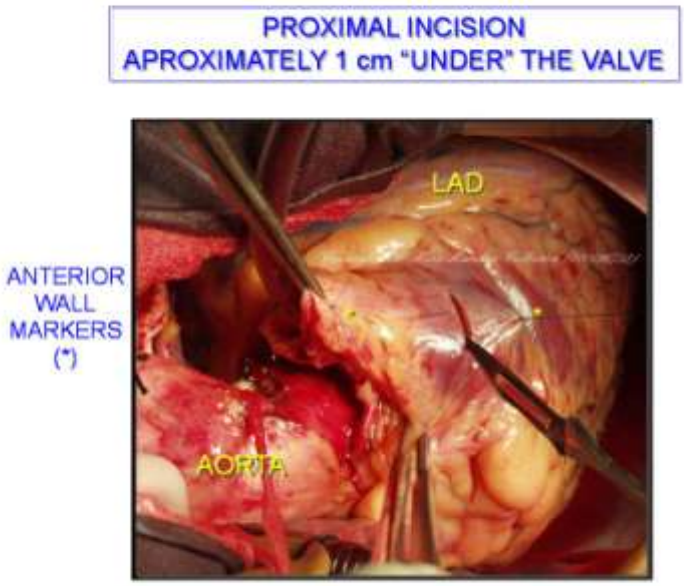
The aortic root is carefully dissected around and a degree of separation from the pulmonary trunk is thus obtained. Special attention is given to the left coronary artery, LAD. Stay-sutures are placed at the level of the anterior aortic and respectively anterior pulmonary walls (serving as future reference points). After regular heparinization, distal ascending aorta is cannulated (a little higher than usual in order to allow a more comfortable clamping of the aorta). A double-stage right atrial cannula is inserted in the regular manner. Double caval cannulation is performed only when a Ross-Konno operation is envisaged. Cardiopulmonary bypass is started. LV vent is introduced at level of the superior right pulmonary vein or a pump sucker can be inserted at the level of the pulmonary bifurcation after its trans-section.

On beating heart



The pulmonary trunk is transversely opened just proximal to its bifurcation (Figure 4).

Figure 4: Harvesting of the pulmonary valve (autograft) [*copyright©Horia Muresian*]



The pulmonary valve is inspected for any variations or anomalies. If feasible, the harvesting of the autograft will start at this point, detaching first the trunk from the bifurcation and then, performing an incision at the level of the anterior wall of the infundibulum, approximately at 5-6 mm "under" the valve (a right-angled clamp can be passed from above, through the valve - in order to be sure to cut well under the level of the pulmonary cusps) (Figure 5).

Figure 5: Proximal incision aproximately 1 cm "UNDER" the valve
*** = *Anterior wall markers*** [*copyright©Horia Muresian*]

Incision and dissection proceed on the left aspect of the pulmonary trunk and infundibulum with special care of not injuring the LAD and its first septal branch. The left pedicles of the pulmonary infundibulum can be cut at this point and bleeding can be confusing for the surgeon. In this case, the remainder of the dissection should be performed with the aorta cross-clamped (Figure 6). Some surgeons prefer to dissect deliberately the LAD in order to obtain an easy identification of it and the first septal. This is a good maneuver although care should be given to the great cardiac vein.

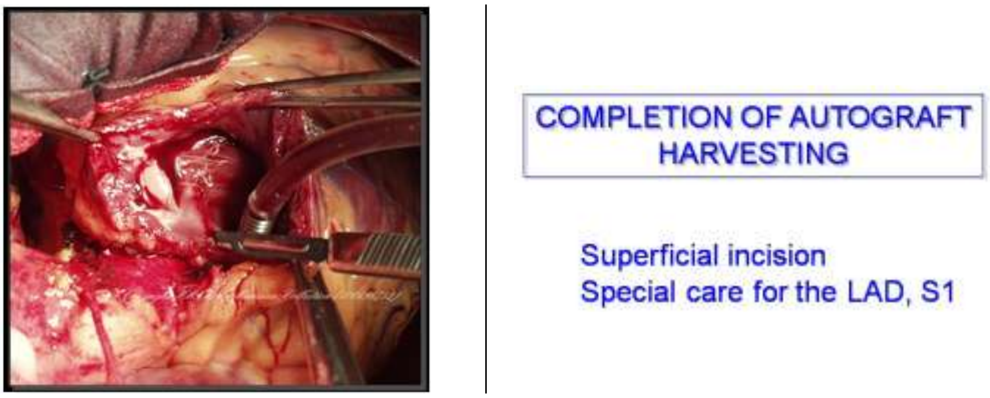
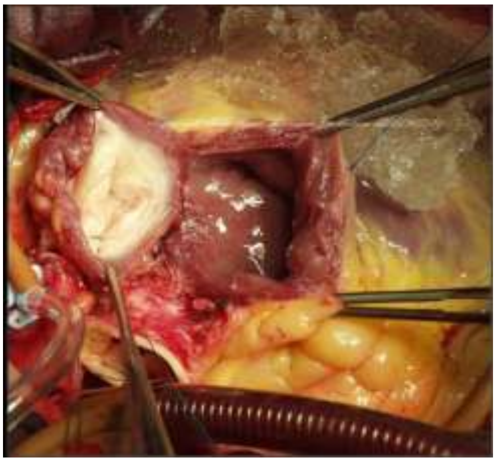
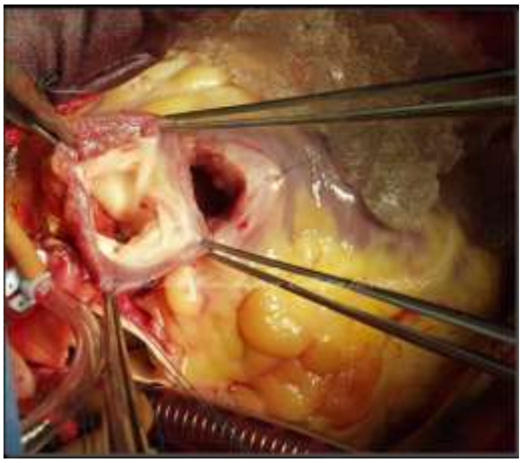


Figure 6: Completion of autograft harvesting *[copyright©Horia Muresian]*



Superficial incision



Special care for the LAD, S1

The dissection and separation between the aorta and pulmonary trunk (and infundibulum) can proceed at this moment, from the right aspect. The last part to be dissected is the adjacent walls of the aorta and pulmonary trunks. As stated before, the surgeon should "err" towards the aorta and a greater part of this dissection can be performed bluntly. When uncertain and when tissues and "cleavage planes" are not so clearly defined, the remainder of the dissection is performed after cross-clamping the aorta. The posterior wall of the infundibulum is dissected from the inside, performing first a superficial incision with the knife. Afterwards, the surgeon tries to get into the same "cleavage" plane that he previously dissected from above. Again, this part can be accomplished with the aorta cross-clamped if difficult.

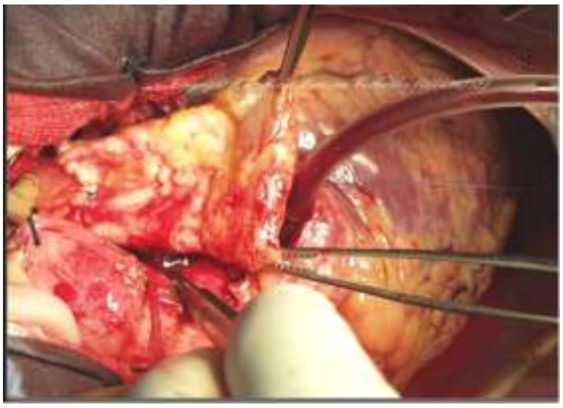
In the mean time, the homograft is rinsed and prepared by an assistant (careful inspection, trimming of muscle in excess, lengthening with preserved pericardium sized with a Hegar probe, etc.). The pulmonary will accept practically any homograft size if the patient is beyond childhood (21); over sizing is even recommended in children (who otherwise, will "outgrow" the homograft).

The distal pulmonary anastomosis is now performed (i.e. at the level of the pulmonary bifurcation). Care must be taken in order to have clear reference points on the homograft and the recipient's heart in order to avoid the twisting of the homograft (easily-deformable).

If the harvesting of the autograft has been superficial incision Spécial care for the LAD, S1 completed on beating heart, careful hemostasis especially at level of the septum must be performed (with electrocautery and sometimes surgical glue) (Figure 7).

Figure 7: Performing the distal anastomosis on beating heart *[copyright©Horia Muresian]*

Superficial incision



Special care for the LAD, S1

The autograft is inspected, prepared in a similar manner and kept either in saline or in the pericardial well. The posterior wall of the autograft is being reinforced with the pericardial sheath; pericardium is fixed to the autograft, with a few stay sutures and RFG glue and kept on a Hegar sizer (Figure 8, next page).

We believe that a circumferential reinforcement of the autograft will preclude its normal function (reinforcement will impede the dilatation of the sinuses while the cusps are prone to earlier degeneration). Reinforcement can be obtained using a PTFA patch, too.

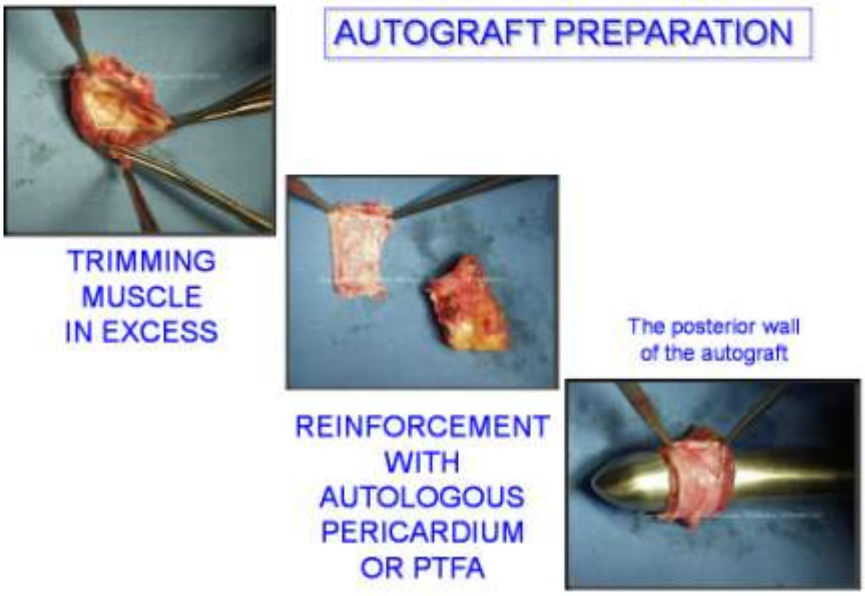


Figure 8: Autograft preparation *[copyright©Horia Muresian]*

With the aorta cross-clamped

The operation takes place under moderate hypothermia. Antegrade cold blood or crystaloid cardioplegia is administered in the aortic bulb and selectively in the two coronary ostia. Aorta is cut transversely distal to the commissures (approximately 1 cm. "above" the right coronary ostium). The root technique is used in most of the cases at the San Donato Cardiac Surgery Center (as well as at international level).

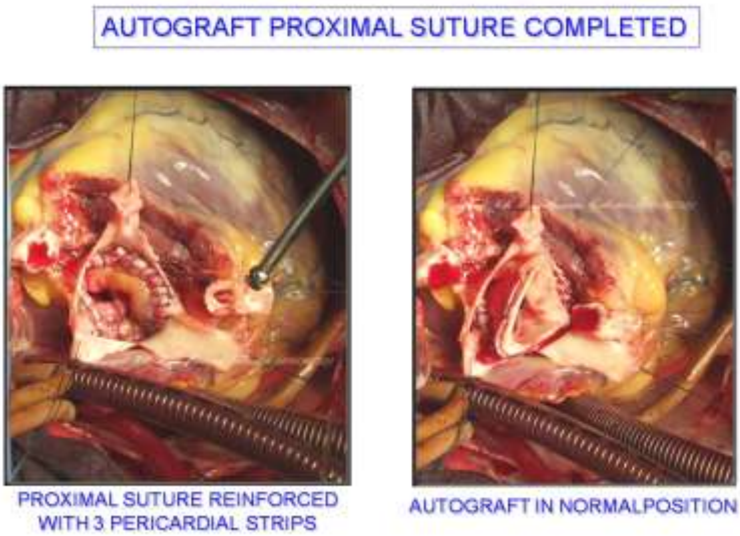


Figure 9: Autograft proximal suture *[copyright©Horia Muresian]*

After the excision of the valve, calibration is performed using a Hegar sizer. Large coronary buttons are tailored (diameter of 6-7 mm). Stay sutures (Prolene 6-0) are used to avoid twisting and any displacement of the ostia. The proximal anastomosis is performed using three strips of autologuous pericaridum as a butress. Separate non-pledgetted single sutures are used (Figure 9).

After the completion of the proximal aortic anastomosis (i.e. anastomosis of the autograft on the distal LVOT), the autograft is again checked with saline "in situ".

A stab incision and the punch are used to perform holes for the coronary ostia. The left coronary is re-implanted first. Coronary buttons can be retailored but these can be preferably kept at their initial size. In this technique, a special attention must be given to the re-implantation of the left coronary because, the autograft has a double layer at its posterior aspect (pericardium + autograft wall proper). The anastomosis is inspected from the inside and additional stiches are put if necessary. No glue is used at this point. The right coronary is re-implanted next. In other surgeons' experience, the right coronary is re-implanted after the completion of the aortic distal anastomosis and distension of the aortic bulb with cardioplegia. In the San Donato technique, the right coronary is re-implanted before performing the distal anastomosis. The autograft is simply distended using a Hegar sizer and the site of re-implantation can be thus easily located (Figure 10).

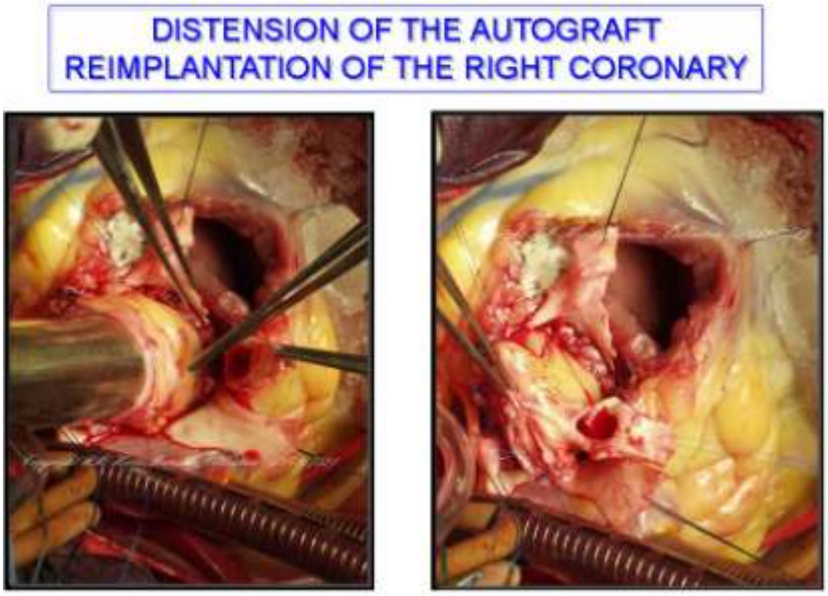


Figure 10: Distension of the autograft reimplantation of the right coronary
[copyright©Horia Muresian]

Another advantage is that the anastomosis can be checked from the inside after completion. If the autograft is inserted on the distal LVOT (and not higher), the right coronary won't be pulled at all.

The distal aortic anastomosis follows. Usually, the autograft has a suitable length and it doesn't require additional lengthening. Two continuous Prolene sutures are used for each half of the anastomosis.

The posterior proximal anastomosis of the homograft on the RVOT is also performed while the aorta still cross-clamped, with special care of not injuring the LAD and the first septal. More superficial bites are recommended at this point (Figure 11, next page).

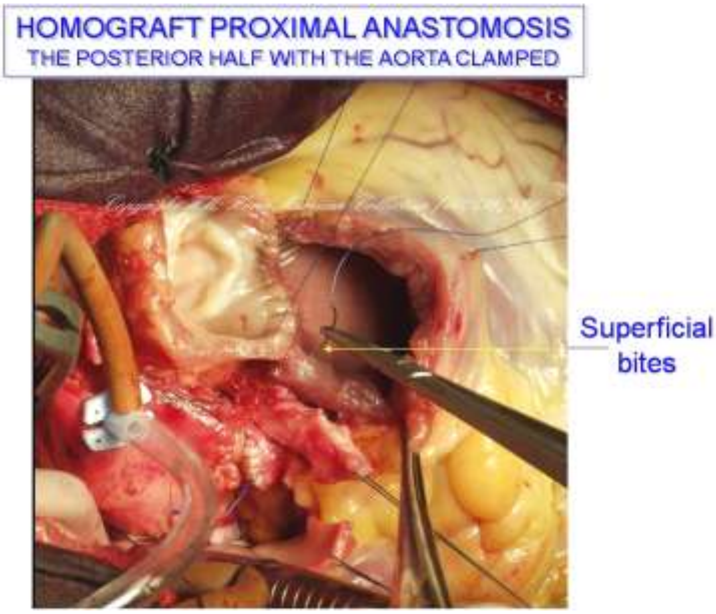


Figure 11: Homograft proximal anastomosis the posterior half with the aorta clamped

Again, two continuous Prolene sutures are used for each half on the anastomosis (posterior and respectively anterior).

At this point, the aorta is declamped and the anterior aspect of the homograft proximal anastomosis in performed (a pump sucker can be left in place until the completion of the anastomosis).

Heart is de-aired in the regular manner, defibrillated, etc. A thorough checking of the hemostasis follows. Transesophageal echocardiography and ECG monitoring are of particular use at this point. Aortic remnant tissue is sutured to the autograft and used to reinforce the anterior aspect of the latter.

The remainder steps of the operation are performed in the usual manner.

The improvement in technique resulted in shorter bypass and cross-clamp times.

Bypass times have diminished, from 183 min. to 155 min. Aortic cross-clamp times diminished from 138 min. to 110 min. (31).

Discussion

The Ross procedure represents a valid option especially for some categories of patients. Technical difficulties, lack of long-term follow-up, problems related to the degenerescence of the homograft in pulmonary position represent the main limiting factors in what regards the large-scale use of this technique.

This paper illustrates how this procedure is used in a center with a large experience in the field, where numerous pediatric and adult heart procedures are performed and where the Ross operation has gained little-by-little its place in the therapeutical armamentarium. This shows not only that the Ross operation is technically feasible, but also that it can become the technique of choice in selected categories of patients, especially in children, younger patients, women in childbearing age, people with contraindications for the anticoagulant therapy and not the least, endocarditis patients. Improvement in technique and careful selection of the patients has led to a decreased morbidity and mortality. Pediatric patients represent 38% in the San Donato series. There were no deaths (early and late). The patients' stay both in the ICU and in-hospital, are comparable to the remainder of the procedures (Tables 1, 2, 3).

Table 1: Operative statistics, San Donato Center

No. of pts.	141
Age (yrs)	19 ± 18 (6 m - 59 y)
Pediatric pts.	52 (38%)
NYHA	II-III

Ross operation Operative Statistics: Aug.1994 - Aug 2002

Table 2: Ross operation - early results

• Death	0
• Bleeding (reop)	3 (2.6%)
• Transient myocardial ischemia	4 (3.6%)
• Mechanical ventilation	18 h (6-30)
• Mean hospital stay	14 d (10-20)

Ross operation Early results (115 pts)

Table 3: Ross operation - Mid-Term results

• Deaths	0	
• Redo	2	1 Ao-P fistula 1 Heart transplant
• NYHA	3	1.2 ($p < 0.0001$)

Ross operation Mid-term results 94/115 pts (96%)

Mean follow-up = 42 months (1-76)

Some technical innovations as the reinforcement of the posterior wall of the autograft, the implantation of the autograft at the level of the distal LVOT (an not on the "aortic annulus"), the reinforcement of the proximal anastomosis of the aorta, the use of larger-size homografts, the completion of several surgical maneuvers on beating heart - these all have contributed to the achievement of better results.

Follow-up is still limited in time (at 42 months average), but intermediate-term results seem promising.

A thorough anatomical study and a continuous review and reappraisal of the "basic" morphological notions, coupled with wet-lab sessions - are absolutely necessary for the surgeon in order to improve his/her manual skill and in order to obtain a more comprehensive mental image regarding this procedure.

Final remarks

New studies are and will be added, especially in the following directions as new questions and doubts arise:

- what are exactly the structural modifications of the aortic wall in case of bicuspid aortic valves and their functional relevance, especially those which will limit the results of such a procedure, with time?;
- the same, in case of Marfan syndrome or rheumatic heart disease;
- what are the main differences between the aortic and respectively, the pulmonary root and what is the faith of the autograft after more than 10 years? What will be the hemodynamic profile of these autografts by then?
- is there a real growing potential of the autograft or only an adaptation?
- in the very young patient, is there any place for aortic percutaneous valvotomy in order to post-pone the surgical correction?
- will there be a place for the newly-invented tissue-engineered heart valves?
- what is the place of treated aortic homografts in pediatric patients?
- is the root replacement the technique of choice when performing the Ross operation, especially looking toward the dilatation of the autograft?
- are the technical improvements as presented today, the best surgical solutions?

As any procedure, the Ross operation will need some more time in order to gain its wide acceptance. Probably, it will never represent "the surgical panacea" regarding the aortic valve replacement, but in the mean time, it must be part of the surgeon's armamentarium and used, when indicated. In this respect any statistic, experience and opinion are worthwhile to be presented, discussed and critically reviewed.

The surgeon has an important role in the development of such researches and regarding his/her contribution for answering these questions. Nonetheless, the new imaging techniques will help even more as these will demonstrate the morphological and functional parameters of the valves during the follow up and will contribute to improve our understanding and knowledge in the field.

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Early and Mid-Term Results of the Ross Operation using Complete Aortic Root Technique*)

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Abstract

Background. *The autograft operation introduced in 1967 by D. Ross, as a scalloped subcoronary implant, a better alternative for aortic valve replacement in young patients, have been recently modified to a complete aortic root technique. We introduced this operation two years ago and the aim of our study is to assess operative technique, early complication, patient-related factors of survival, autograft and homograft function over time.*

Material and method. *From May 2000 through September 2002, 25 consecutive patients (means age, 26 years; range 3 to 49 years) underwent replacement their pathologic aortic valve by a pulmonary autograft, receiving a cryopreserved homograft in pulmonary position, using complete aortic root replacement technique exclusively and Bioglue® application. Transesophagian echocardiography was the method used for all the patients, preoperatively, intraoperative and serial after operation (at discharge, 3, 6, 12 and 24 months) with the purpose of measuring aortic and pulmonary annulus, evaluating transvalvular gradient and both valve function, evolution of muscular mass regression and studying the LV function.*

Results. *There were no deaths early or late after operation, no bleeding or other major complications. The patients remained in mean 24 hours in intensive care unit and were discharged after mean six days. Early postoperative TEE has shown no regurgitation or minimal incompetence of autograft in some cases. The result remained stable after 6 months with recovery of LV function approximately 10% and the muscular mass reduction has been decreased.*

Conclusion. *The Ross operation is a very appealing choose in young patients avoiding mechanical valve with their burdens and gives excellent early and mid-term results, no mortality (or low) and no morbidity. However, we are looking for the autograft and homograft function over time, in special dilatation of autograft and homograft stenosis.*

Key words: *Ross operation, complete aortic root technique, Bioglue®.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2003, vol. 2, no. 1, pp. 33-38.**

Introduction

The Ross operation first introduced as a scalloped subcoronary implant with the results of more than 5095 patients operated and reported with a survival rate of 65% at 25 years and freedom of autograft and homograft reoperation over 80% at 25 years regained the interest of many surgeons (28). Very attractive is this operation for the young, active people with aortic valve disease, for children with anticipated growth (3), female getting pregnant and on the case of aortic valve endocarditis (17).

We initiated our experience some years ago at Vienna's University with more than hundred patients operated and extended this technique of complete aortic root replacement at Innsbruck Cardiac Surgery Department. Moreover we are using our standard of the annular reduction and Bioglue® application around the autograft in order to get a better long-term stability of the autograft. On these papers we are reporting our early and mid-term results of more than 30 patients undergoing this modification.

Material and methods

Between May 2002 and September 2002 at the University Department of Cardiac Surgery Innsbruck, 25 patients underwent a Ross operation. From this, 23 were male (92%) and 2 female (8%), mean age 27.76 ± 13.31 years, the range between 3 and 49 years old.

Etiology of aortic valve pathology is presented in Table 1 and associated co-morbidities in Table 2. All the patients were operated elective and monitoring intraoperative by TEE.

Table 1: Etiology of the Aortic Valve Disease

Etiology of Aortic Valve Pathology	No.	%
Congenital/bicuspid valve	18	72%
Aortic stenosis insufficiency	2	8%
Endocarditis	2	8%
Degenerative myxomatous	1	4%
Rheumatic	1	4%
Biologic aortic valve degeneration	1	4%

Table 2: Associated commorbidity of the patients underwent a Ross operation

Associated pathology	No.	%
Mitral insufficency	7	28%
Arterial Hypertension	7	28%
Dilatation of the Ascending Aorta (>3,5 cm)	5	20%
LV Function reduced (EF< 50%)	4	16%
Dilative Cardiomiopathy	3	12%
LV decompensation	2	8%
Status post cerebral stroke	2	8%

Atrial Fibrillation	2	8%
Hyperlipidemie	2	8%
Smoking	2	8%
Alchool abuse	2	8%
Diabetes mellitus Typ I	1	4%
Colitis ulcerosa	1	4%
MELAS Syndrom	1	4%
RCA ostiumm stenose	1	4%
Kay-Whooler Mitral Valve Reconstruction	1	4%
Hepatitis	1	4%

The pulmonary homografts were provided in 15 patients (60%) cryopreserved from different Austrian Valve Bank, in 9 (36%), cryopreserved from Cryolife® (Georgia, USA) and in one case (4%) fresh antibiotique conserved.

In 5 (20%) patients was performed an annulus reduction in order to get a surface area normal size. The mean CPB was 180.7 ± 84.5 min, and aortic clamp 126.7 ± 57.3 min.

Postoperative infection prophylaxis was assured in 16 (64%) patients using Teicoplanin (Targocig®) for 5 days. In one patient we founded from aortic valve examination a coagulaso-negative Sptaphyloccocus Vancomycin sensitive.

All the patients were investigate intraoperative by 2-D TEE (Sequoia 512, Accuson, California, USA) for autograft competence and the after at the discharged, 3, 6, 12 months later completely reporting, autograft insufficiency, homograft function, LV muscle mass and function.

For all the patients we used our standard aortic root technique and Bioglue® application as the following description.

The Surgical Technique

The operation is performed on moderate hypothermic cardiopulmonary bypass (CPB) at 28°C, using bicaval cannulation for better exposure and venous drainage. Cardiac protection is assured by antegrade cardioplegia delivered direct in coronary orifices and then after retrograde by coronary sinus catheter each 20 minute, 200 ml of St. Thomas II solution or Buckberg solution in very compromised left ventricle function. Also, topical ice is additionally used. An apex vent is inserted for LV. Trans-esophagian echocardiography is routinely used. Ascending aorta, aortic root and pulmonary artery are extensively mobilized before aortic clamp for anatomic reason. CPB is started and aorta is clamped. A transverse incision is performed 1 cm above right coronary artery origin and completed posterior. Aortic root is inspected and aortic valve resects. The aortic annulus is sizing according with a normal value after body surface area reporting. Then pulmonary artery is transacted distally before bifurcation, the valve is inspected for three leaflets shape, competence or any splitting and autograft completed harvesting by a curve clamp inserted through the pulmonary valve 3-4 mm distally in right ventricle outflow tract.

During this time a tester 2 mm diameter is inserted in left main coronary artery to prevent damage of LAD (Figure l). Also a special care should be paid for the posterior aspect of autograft preparing to prevent the first septal branches lesion, using a sharp blade dissection. A meticulously hemostasis of the pulmonary artery "bed", should be achieved by thermocauter, additional Prolene 7/0 suture and Bioglue® application.

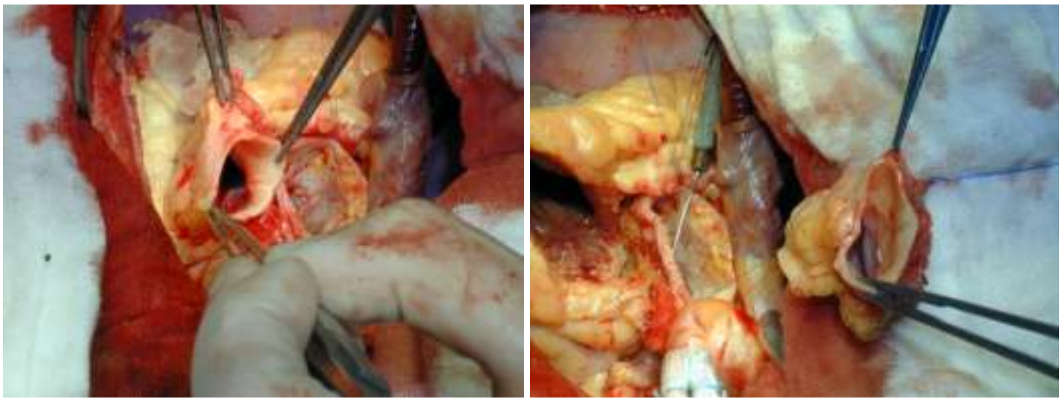

Figure 1: Intraoperative view, showing aortic root prepared and autograft harvesting
(Department of Cardiac Surgery, Innsbruck, Oct, 2001, Op team: G. Laufer, M. Gaspar)

A preselected pulmonary homograft is prepared in this time after a special protocol on a close table. The coronary artery ostium "on button " technique are mobilized . If the annulus is dilated according with body surface area, we routinely performed a annulus reduction using a commissural suture. In all the patients operated we used only total aortic root technique implantation using three suture Prolene 4/0 from each commissural in running technique with the autograft inverted in LV. Then the left coronary artery and right coronary artery ostium were implanted using Prolene 6/0, running suture. The cryopreserved pulmonary homograft is then used for the right ventricle outflow tract reconstruction. The distal ascending aorta anastomosis completed this technique before declamping and application of Bioglue® around the autograft" new aortic root", in order to prevent the dilatation. However, our initial experience and limited follow-up don't permit to come into any conclusion regarding the superiority of this Glue application or not.

Results

There were no deaths early or late after operation, no bleeding or another major complication. The patients remain in mean two days (range: 2 - 6 days) in intensive care unit and were discharged after mean 10 days (range: 6-21 days). Prospective serial transesophageal echocardiographic measurements of the diameters (mm) of the aortic annulus (AA), sinus Valsalva (SV), sinotubular junction (ST), LV function, muscle mass-index were acquired.

Autograft function

From 16 patients examined after one year, 2 patients (12.5%) had improved their intraoperative grade I aortic insufficiency to null; 9 (53.33%) patients remained stabile with trivial aortic regurgitation (one remained stabile but with grade II, insufficiency) and 5 patients (33.33%) remained with grade I insufficiency.

Dilatation of the autograft

We examined on 2-D, TEE, 13 patients at 3 and 6 months later for autograft dimension and founded a significant dilatation of the sinus of Valsalva but not clinic resonance (32.85 ± 4.93after 3-6 months vs. 30.54 ± 7.50 at effort; $p = 0.0001$). The annulus remained stabile (22.62 ± 62 after 3-6 mo vs. 22.69 ± 5.39 at effort; $p = 0.006$) and the same sinotubular junction (25.15 ± 4.12 after 3-6 mo vs. 26.31 ± 3.43 at effort; $p = 0.067$). At one year dilatation is also significant but without clinical expression; aortic annulus (23.25 ± 4.56 after one year vs. 22.50 ± 5.54 after 3-6 mo; $p = 0.002$); sinus Valsalva (33.18 ± 4.85 after one year vs. 32.27 ± after 3-6 mo; $p = 0.0001$), the same sinotubular junction (28.40 ± 4.65 after one year vs. 26.50 ± 3.75 after 3-6 mo; $p = 0.025$) (Table 3).

Table 3: Aortic Valve Insufficiency after Ross Operation

Pat. N	After Operation	After 12 Months	Difference
1	Grad 1	Grad 1	0
2	Grad 0	Grad 0	0
3	Grad 1	Grad 1	0
4	Grad 0	Grad 0	0
5	Grad 0	Gradl	1
6	Grad 0	Grad 0	0
7	Grad 2	Grad 2	0
8	Grad 0	Grad 1	1
9	Grad 1	Grad 1	0
10	Grad 1	Grad 0	-1
11	Grad 0	Grad 1	1
12	Grad 0	Grad 1	1
13	Grad 1	Grad 1	0
14	Grad 1	Grad 1	0
15	Grad 1	Grad 0	-1
16	Grad 1	Grad 2	1

Pulmonary Homograft Function

We examined 12 patients at one year for homo-graft regurgitation and founded; 2 patients (16%) improved from grad I to null, for 7 patients (58.3%) remained stabile (trivial insufficiency), for 2 patients founded grade II. For three patients (12%) also we founded a transvalvular gradient between 18 and 66 mmHg maximal. We are still following this patients.

Reduction of the LV muscle-mass/index (g/m^2)

Using TEE examination and Simpson modified formula, we assessed for 10 patients the LV muscle mass before and after operation. At 3-6 months was noted a significant reduction of the LV muscle-mass (107.85 ± 32.02 vs. 144.48 ± 98.60 before operation; $p = 0.547$). And later at one year is even more significant (113.45 ± 52.36 vs. 125.80 ± 54.72

after 3-6 mo; p = 0.002). This showed the reduction of LV wall-stress after aortic valve replacement and improving of LV ejection fraction up to 5-10% after 6-12 months postoperative.

Discussion

We are still looking for the best solution of the aortic valve surgery. After years of criticism regarding the Ross operation "from one sick valve, two", early degeneration of both autograft and homograft, the publication of the long term results, 20 years for 339 patients operated almost all by scalloped sub-coronary implantation technique, with 80% survival, 85% freedom from valve re-operation, 70% freedom from valve related complication, resurfaced the interest for this procedure (1). Even more after pulmonary autograft replacement of the aortic valve as a root replacement (1988) and annular correction the results steadily improved.

The advantages of Ross operation are well recognized (2, 6, 8, 9), however two major problems are rising concerning the autograft dilatation and homograft stenosis and need for re-operation. The operative mortality and morbidity is very low, the same like for a aortic valve or even less. The International Ross Registry (28), for 5095 patients (August 2002), the operative mortality was 3,5%, survival rate 68% at 25 years (Figure 2) freedom from autograft re-operation 82% and freedom from homo-graft reoperation 84% after 25 years.

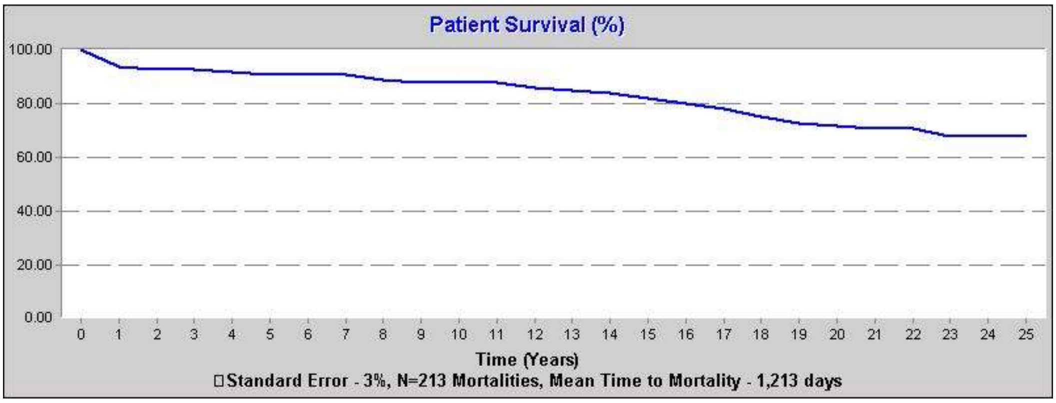

Figure 2: Mortality after Ross operation for 5095 patients *after Ross International Register* (28)

In our lot we had no mortality, no major complication and no reintervention at two years. In three patients we met an increased gradient over homograft and light sinus Valsalva dilatation but not clinical significant. Further investigation will be performed. What we do to avoid this autograft dilatation is annular correction for all the patients with annular dilatation and using external fixation with Bioglue®, reinforcement around the autograft.

The Ross operation seems to be an ideal option for children, in order to avoid anticoagulant therapy and to assure the growth of the aortic root with the patient. Elkins and all (3), in ten years of practice have been performed over 150 Ross operation for children, with very good results, 97.3% survival a1 eight years, 90% ± 4% freedom from reoperation for autograft dysfunction and 94%±3% freedom from reoperation for homograft obstruction at 8 years follow-up.

We had operated 6/25 (24%) children between 3 years up to 12 years old without mortality oi morbidity. Simon and all (12), Vienna Group, demonstrated for 30 children at the follow-up mean 4.3 ± 2.6 years on serial echocardiography studies growth of the pulmonary autograft concomitant to somatic rate. Also the hemodynamic performance at rest and exercise were physiological in the majority of patients.

Simon and all, followed 107 patients for 2.5 years (range: 10 months – 8.3 years) and founded in 11 patients (10.2%) a sinus Valsalva up to 4.2 mm. Free time for aortic dilatation is 62% at one year, 48% at five years and 45% at seven years. Maximal grad was II/III, but without reoperation at eight years maximal follow-up (18).

At least three category of patients remained better choice for a Ross operation aortic valve endocarditis, children and young women which are getting pregnant.

Conclusion

The Ross operation is a very appealing choose in young patients avoiding mechanical valve with their burdens and gives excellent early and mid-term results, no mortality (or low) and no morbidity. However, we are looking for the autograft and homograft function over time, in special dilatation of autograft and homograft stenosis after our special policy of regular annular correction and Bioglue® application.

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Part 6.

VASCULAR PATHOLPGY OF THE SUPERIOR AND INFERIOR AORTIC SYSTEM

Treatment of acute traumatic aortic rupture*)

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Abstract

Objectives*:* *Blunt traumatic thoracic aortic rupture is a life-threatening surgical emergency associated with high mortality and morbidity. The recent development of endovascular stent-graft prostheses offers a potentially less invasive alternative to open chest surgery, especially in patients with associated injuries. We sought to compare the results of conventional surgical repair and endovascular treatment of traumatic aortic rupture in a single center.*

Methods*:* *From January 2005 to July 2011, 7 patients with acute blunt traumatic aortic rupture underwent treatment at our institution. All patients had a lesion limited to the isthmus, and associated injuries. Initial management included fluid resuscitation, treatment of other severe associated lesions, and strict monitoring of blood pressure. Five patients (5 male; mean age, 35.2 years) underwent surgical repair, all patients with graft interposition. One patient was operated upon without cardiopulmonary bypass. Four patients were operated on with cardiopulmonary support (left bypass with extracorporeal circulation, n = 4). The delay between trauma and surgery was mean 4.2 days (range, 0-21 days). Two patients (1 men, 1 woman; mean age, 24 years) underwent endovascular treatment with commercially available devices Relay W (Bolton Medical, Sunrise, FL, USA) (n = 2). In one patient the left subclavian artery was intentionally partial covered with the device. The delay between trauma and endovascular treatment was 5.8 days (range, 5-8 days).*

Results*:* *Early mortality after 30 days in the surgical group was 40% (2 of 5 patients). The most common cause of death in the surgical group was brain death in severe traumatic patients. Two surgical complications occurred in 2 patients: renal insufficiency (n = 1), paraplegia (n = 2) and coma 3-4 degree. In the endovascular group successful stent-graft deployment was achieved in all patients, with no conversion to open repair. No patient died and no procedure-related complications, including paraplegia, occurred in this group. Control computed tomography scans obtained within 21 days after endovascular treatment showed exclusion of pseudoaneurysm in all cases. Length of follow-up for endovascular treatment ranged from 8 to 30 months (mean, 12.1 months). Computed tomography scans obtained 3 months after endovascular treatment showed complete disappearance of pseudoaneurysm in all patients.*

Conclusion*:* *In the treatment of blunt traumatic thoracic aortic rupture, the immediate outcome in patients who receive endovascular stent grafts appears to be at least as good as observed*

*) **Romanian Journal of Cardiovascular Surgery ■ 2011, vol. 10, no. 2, pp. 129-136**

after conventional surgical repair. Long-term follow-up is necessary to assess long-term effectiveness of such management.

Key-words: *Traumatic aortic rupture; Conventional surgery; Endovascular stent graft*

Introduction

Traumatic thoracic aortic rupture is a life-threatening surgical emergency and is often fatal in the first hours after injury. Surviving patients frequently have other associated injuries to various organs such as the head, abdomen, pelvis, or the extremities. Without appropriate treatment, 30% of survivors who reach the hospital die within the first 6h. Standard surgical procedure requires aortic cross-clamping and the use of cardiopulmonary bypass or other arterial shunt techniques for distal perfusion to prevent ischemic, neurological, and visceral complications. Post- operative morbidity remains high and the mortality rate ranges from 15% to 28%. This poor outcome after surgical repair seems to be related to the other associated injuries that may be present in patients with polytrauma. However, the necessity of systemic heparinization as required by circulatory assistance increases the risk for fatal hemorrhage, particularly in patients with cranio-cerebral trauma. Surgical repair with a delay between trauma and treatment, allowing the patient to recover first from other major injuries, has been advocated to improve the outcome of early conventional surgical treatment. However, even in an apparently stable situation, approximately 2-5% of patients experience further rupture within the first week after the trauma. Endovascular stent grafting is a less invasive treatment for descending aortic pathologies and may be considered an alternative treatment option to conventional surgical repair. The advantages of endovascular treatment over conventional surgical repair of acute traumatic aortic rupture include the avoidance of thoracotomy and systemic heparinization. Therefore reduced perioperative morbidity and mortality rates can be expected. The purpose of this retrospective study was to compare the results of conventional surgical repair and endovascular treatment of traumatic aortic rupture in a single center, to better define the role of stent grafts in management of traumatic aortic rupture.

Patients and methods

Between January 2005 and July 2011, 7 patients with acute traumatic rupture of the descending aorta received treatment at our institution. All patients had sustained a violent traumatic injury involving sudden deceleration (2 falls from great height, 5 road accidents) within 3-6 days before treatment. The group included 1 female patient and 6 male patients aged 21 to 68 years (mean, 35.2 years). All patients had associated injuries in various organs: at least two additional severe lesions, including lung contusion and/ or serial rib fractures with reduced respiratory function, cranio-cerebral lesions, abdominal visceral lacerations, and multiple extremity or pelvic fractures. Two patients were admitted to our institution after emergency surgery for life-threatening non-aortic injury such as head injury; abdominal trauma with spleen or liver rupture; or fixation of pelvic, spinal, or extremity fractures. In all patients the diagnosis of traumatic rupture was made at computed tomography (MS-CT) of the aorta when they were admitted to the emergency department. CT was usually indicated because of the severity of the traumatic injury, the clinical signs, or findings on chest x-ray studies (Figure 1). We progressively changed the way our group manages traumatic rupture of the descending aorta during the study period. At the beginning of the study all patients underwent surgical therapy and those in whom thoracotomy or circulatory assistance was contraindicated underwent delayed surgery after treatment of the associated injuries. The development of aortic stent grafts has enabled us to accelerate management in these patients and to treat in a less invasive manner immediately after diagnosis.

Figure 1: Computed tomography scan shows acute contained rupture of aortic isthmus.

Therapeutic strategy

The majority of patients had been intubated on admission (3 patients in the surgical group and 2 patients in the endovascular group). We aimed to perform surgical or endovascular repair soon after admission, unless severe associated injuries or complications restricted this policy. In 2 patients treatment was delayed for more than 7 days after trauma due to severe pulmonary contusion in two and severe head injury in one. All patients were monitored on the intensive care unit with continuous monitoring of arterial and central venous pressure, renal function, and other hemodynamic and clinical parameters. Hypertension was prevented with deep sedation and treated, if necessary, with nitrates, calcium-blocking drugs.

Surgical group and conventional surgical technique

In our study, 5 patients underwent conventional surgical repair of the traumatic aortic rupture (Figure 2, next page).

All patients were treated within mean 4.2 days (range, 0-21 days); in 2 of them emergency surgery was performed within 24 h after the trauma (in 2 patients within 6-12 h). Except for one patient who was operated on without cardiopulmonary bypass, in all patients, femoro-femoral bypass was established with systemic heparinization.

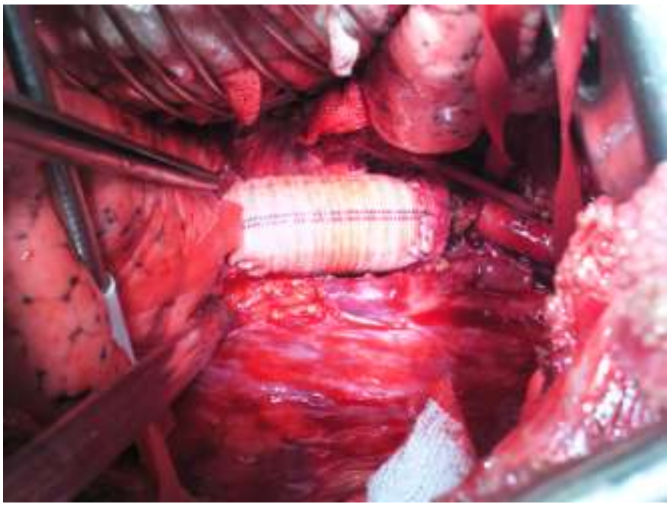

Figure 2: Conventional surgical repair of the traumatic aortic rupture with graft interposition

The thoracic aorta was approached through a posterolateral thoracotomy, with an incision in the fourth or fifth left intercostal space.

The aorta proximal and distal to the injured segment was dissected and isolated circumferentially and was clamped between the left common carotid artery and the left subclavian artery or distal from the left subclavian artery in all 5 patients. In all patients (100%), the aorta was repaired with graft interposition. After weaning from bypass, heparin was reversed with protamine sulphate.

Endovascular stent-graft group and treatment technique

We started thoracic endovascular stent grafting in 2008. We performed endovascular stent grafting in patients with acute traumatic aortic rupture as a less invasive option for urgent or emergency treatment. In the last 3 years, 2 patients were treated with endovascular stent grafting. We implanted only one commercially available thoracic stent grafts: the Relay W (Bolton Medical, Sunrise, FL, USA) (n = 2). In all patients, the rupture was located near or distal to the origin of the left subclavian artery. The diameter of the stent graft was oversized by 10-20% in relation to the diameter of the native aorta, to achieve a satisfactory tight seal. The endovascular stent grafts used were 26-28 mm in diameter and 120-150 mm in length.

All procedures were performed with the patient under general anesthesia, tracheal intubation, and mechanical ventilation. Patients were placed in the dorsal decubitus position, one common femoral artery, was exposed by a small groin incision. An angiography catheter was introduced by the Seldinger method either through the main access artery or separately from the contralateral groin percutaneously or from the surgically exposed right brachial artery. A maximal dose of 5000 IU of heparin was administered i.v. An initial aortogram was taken from a left, anterior oblique view to visualize the aortic arch anatomy and to determine the best position in which to deploy the stent graft. The angiography catheter was then advanced up to the ascending aorta under fluoroscopic guidance and replaced by a 260-cm long 0.035-inch ultra-stiff guide wire). The delivery system was positioned at the desired level and the stent graft deployed under fluoroscopic guidance at a mean arterial pressure of less than 70 mmHg to avoid downstream migration of the stent graft during deployment. Next, an endovascular balloon was inflated to obtain optimal shape and sealing of the implanted stent into the normal wall of the aorta. A final aortography was performed to demonstrate stent-graft localization and to ensure that the false aneurysm had been properly excluded. After removal of the introducer delivery system, the femoral artery was closed with a transverse 6-0 prolene suture.

Postoperatively, the patients were referred back to the trauma centers for further treatment of the associated injuries. Chest X-ray and spiral CT angiography scan were performed before discharge and seen by our team. Follow-up was obtained by office visits, hospital reports, telephone interviews with patients, families and home physicians, and inquiries of local population registries. However, CT scans in the follow-up period were only available in 1 of the 2 patients treated with endovascular stent grafts.

Results

In all patients the aortic rupture was located in the isthmus. In the surgical group, 9 patients were operated on within 24 hours of the traumatic injury. Two patients underwent delayed surgery 4 days and 21 days, respectively, after the initial injury, because of severe orthopedic injuries in 1 patient and extradural hematoma in the other patient. The mean interval before surgery was 2.6 days (range, 0-21 days). In the group treated with stent grafting, 6 patients had delayed treatment and 3 patients were treated within 24 hours of the traumatic injury. Treatment was delayed in 6 patients because of associated injuries and because the stent graft was not available. The mean interval before stent-graft placement was 17.8 days (range, 1-68 days). All data for the patients who underwent surgery and those who received endovascular treatment are provided in Table I and Table II respectively.

Table I. Data on 5 patients with traumatic rupture of the thoracic aorta treated by surgery

Age and Gender	Comorbidity and associated lesions	Time of repair	Mechanical circulatory support	Repair	Outcome
M 68 yrs	None	Delayed (21 days)	Yes	Graft interposition	Alive
M 21 yrs	mesenteric rupture Frontal lobe hematoma	Delayed (1 day)	No	Graft interposition	Die after 8 days
M 33 yrs	none	Delayed (3 days)	Yes	Graft interposition	Alive
M 28 yrs	none	Immediate	Yes	Graft interposition	Die after 30 days
M 27 yrs	Spleen contusion, L4-L5 spinal fracture	Immediate	Yes	Graft interposition	Alive

Table II. Data on 2 patients with traumatic rupture of the thoracic aorta treated by stent-graft

Age and Gender	Comorbidity and associated lesions	Time of repair	Device diameter/length (mm)	Outcome
M 21yrs	hepatic lobe rupture, right lung contusion, rib fractures, right hemothorax	Delayed 8 days	Relay W 26/1155	Alive
F28yrs	Left femoral fracture Temporo-occipital fracture Bilateral hemothorax	Delayed 4 days	Relay W 26/150	Alive

Surgical group

Five patients were operated, four with circulatory assistance and one without. The damaged portion of the aorta was replaced with a prosthetic graft in all patients. The 30-day mortality was 40% (2 of 5 patients) in patients who underwent surgical repair. The causes of death were severe brain injuries, which deteriorated after the aortic repair in two patients and postoperatively paraplegia, severe acutrenal failure (dialysis), massive cerebral edema, septic shock, grade IV coma in one patient.

Endovascular group

A right femoral approach was used in all the procedures. The mean diameter of the aorta proximal from the rupture was 26.5 mm (range, 26-28 mm), and distal from the rupture was 24 mm (range, 23-25 mm). The distance between the posterior edge of the left subclavian artery and the rupture was, on average, 12.5 mm (range, 10-14 mm). We used the Relay W (Bolton Medical, Sunrise, FL, USA) stent graft in all patients. Mean diameter of the stent grafts was 27.3 mm (range, 26-28 mm). Mean length of the stent grafts was 152.5 mm (range, 150-155 mm). In all patients a single stent graft was deployed to cover the rupture. We partially covered the ostium of the left subclavian artery in 1 patient, because of insufficient length of the neck (10 mm, respectively), with no clinical effect. No patient died after endovascular treatment. No complications occurred during the procedure in this group, and, more important, no patients had paraplegia as a result of the endovascular repair, no did we have to convert to open surgery.

Follow-up

Mean follow-up in all patients was 18.3 months (range, 1-62 months). In the surgical group 2 patientswere lost to follow-up 3 months after surgical treatment. For the mean duration of follow-up of 25 months (range, 2-68 months) there were no complications. In the stent-graft group no patients were lost to follow-up. Mean duration of follow-up was 20.5 months (range, 8-32 months). On CT scans at 3 months follow-up the aortic rupture had completely healed, and no change occurred during the subsequent follow-up period (Figure 3, next page). No damage to the stent-graft materials was detected. The one patient with partial coverage of the ostium of the left subclavian artery reported no symptoms.

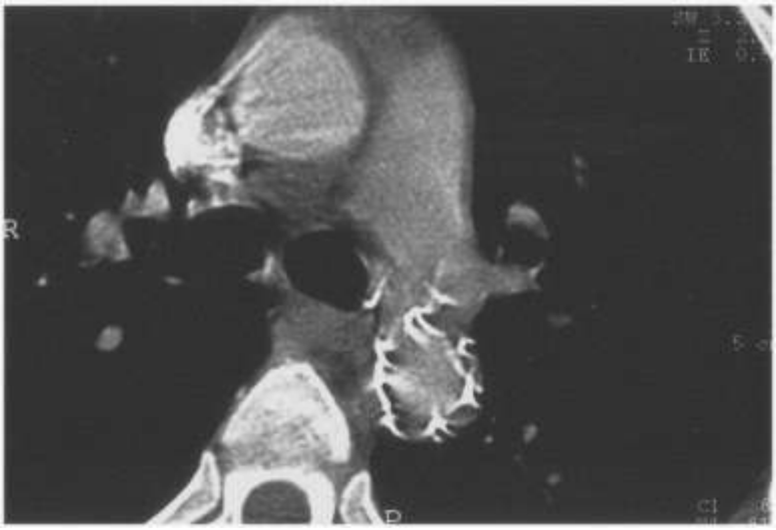

Figure 3: Computed tomography scan obtained at 3-month follow-up demonstrates complete healing of the aortic wall

Discussion

We undertook a retrospective analysis of 7 patients who underwent treatment of traumatic rupture of the descending aorta. Five patients underwent surgery, and in 2 patients an aortic stent graft was placed. In the surgical group 2 patients died in 30 days after surgical repair, for an operative mortality rate of 40%; one of the patients in this group had postoperative paraplegia. In the stent-graft group no patient died, and none had postoperative paraplegia. The overall mortality rate for the study was 28.57%.Acute rupture of the thoracic aorta as the result of blunt chest trauma is a highly lethal condition. Immediate death occurs in up to 85% of cases before the hospital is reached. The etiology, patient status at the time of the treatment, and associated injuries are mainly responsible for the poor prognosis of the survivors after the trauma. Despite advances in surgical techniques and management in recent years, immediate surgical repair, including thoracotomy, one-lung ventilation, and use of cardiopulmonary bypass, is associated with a high morbidity and mortality rate. There is general agreement concerning the necessity of surgery in acute traumatic aortic rupture, but the timing of repair is still a matter of controversy. Under discussion are, in particular, the treatment of patients' extrathoracic and craniocerebral injuries or lung contusion and the fear of possible aggravation of intracranial, intra-abdominal, and pelvic bleeding through heparinization during surgery for the aortic rupture. By virtue of these considerations, the concept of delayed elective treatment of the rupture has been developed. In-hospital mortality rates increase from 32% on the first day, to 61% within the first week, and 74% after 2 weeks. In a recent review of the literature, the surgical mortality rate ranged between 8% and 15%, whether or not circulatory assistance was used to maintain satisfactory perfusion pressure in the aorta distal from the clamp. Risk factors that explain the increase in postoperative mortality include severity of the associated traumatic lesions, preoperative shock (only 25% of which was related to aortic rupture), and cardiac risk factors. Paraplegia was the main complication of surgical treatment. When aortic repair was achieved without circulatory assistance, the postoperative paraplegia rate can be as high as 19%, and this risk increases significantly when the aorta is clamped for more than 30 minutes.

With circulatory assistance, this rate remains at about 2%. Surgery is sometimes contraindicated if the patient has serious multiple traumatic injuries for which circulatory assistance and thoracotomy are contraindicated. In these situations, as long as the rupture remains contained and there is no pseudo-coarctation, surgical repair can be delayed until the patient's status has improved and is compatible with major surgery, provided the patient's arterial pressure is strictly monitored and controlled. The satisfactory results obtained with this type of surgical management have led some authors to systematically propose delayed surgery. Although this attitude is justified by objective data,it is not entirely risk-free, inasmuch as 4% of patients awaiting surgery die of a ruptured aorta, usually within 1 week of the traumatic injury. Rousseau et al. have transferred the concept of delayed elective treatment to endovascular repair as well. In this study, however, endovascular repair was performed immediately after trauma or as early as possible. Langanay et al. reported 20% of 50 patients with delayed surgical treatment between 6 and 60 days because of late diagnosis or coexisting life-threatening lesions without further aortic rupture or sudden death. Four different surgical techniques have been described for the repair of an aortic isthmus rupture: clamp and sew, repair with distal perfusion by means of a Gott shunt, left heart bypass, and femoro-femoral full cardiopulmonary bypass. The question of which of the four methods should be used for an acute traumatic aortic rupture has been discussed extensively during the last 20 years. In 1994 von Oppel published a meta-analysis of all English-language publications between 1972 and 1992 concerning this question. A total of 985 patients who were operated upon with one of the three methods of distal perfusion had a paraplegia rate of 6.1% compared with 19.2% of the 443 patients who had direct clamping. A summary of studies on this issue published in the later period between 1995 and 1999 revealed similar results. We especially refer to a large prospective multi-center study of the American Association for the Surgery of Trauma (AAST) directed by Fabian, in which 206 patients treated within 30 months were studied. The rate of mortality was similar in the two groups (16.0% vs 17.3%).The influence of systemic heparinization on mortality and the risk of hemorrhage in such multiple-injured patients, particularly in patients with coexisting brain or pulmonary contusion, remain unclear because no separate analysis has been made for different forms of distal perfusion. Recently the emergence of endovascular treatment has enabled us to find solutions to some of the controversies in the debate on surgical management. By nature, endovascular treatment is less invasive than standard surgery, and is associated with decreased mortality and morbidity, as the results of our study demonstrate. There is no need for thoracotomy, and this reduces morbidity related to single-lung ventilation in patients who often have lung contusions and fractured ribs. The absence of circulatory assistance, and thus of high systemic doses of heparin, limits the hemorrhagic complications of the procedure. It also helps to avert onset of a systemic inflammatory response, which can have a deleterious effect if it is amplified by an underlying trauma-related inflammatory status. Placement of a stent graft does not require aortic cross-clamping, which reduces the distal risk for visceral and medullary ischemic complications. The potential risk for medullary ischemia remains if the intercostal arteries opposite the stent graft are occluded, but it is limited in that rarely does the spinal artery arise from the aortic isthmus. To our knowledge, this complication has not been reported in the literature, but similar to ours, these studies included a small number of patients, and it is difficult to make a reliable comparison with larger surgical series. With respect to the delay between the traumatic event and surgery, again stent-graft treatment shows a considerable advantage. It can be performed before or immediately after treatment of other life-threatening injuries and in patients for whom conventional surgery is contraindicated, because the procedure is short and has little physiologic effect. Successful endovascular treatment in these cases depends partly on strict evaluation of the patient's anatomic features, as in treatment of aneurysms of the abdominal aorta. The length of the healthy remaining portion of the aorta proximal from the rupture must measure at least 15 mm to achieve a satisfactory seal and to exclude the false aneurysm. If need be, we do not hesitate to cover the left subclavian artery to lengthen the proximal neck, as we did in 1 of our patients. When the left subclavian artery must be covered, it rarely causes upper limb ischemia; thus transposition of the subclavian artery into the carotid artery before thoracic stent-graft implantation is not mandatory. On the basis of this approach, endovascular treatment has not been contraindicated in any of our patients, and we did not observe any type I endoleaks in this series. The 3-month follow-up CT scan showed complete healing of the aortic wall, without any residual pseudoaneurysm. This retrospective study shows that endovascular treatment is a safe method for repair of traumatic rupture of the descending thoracic aorta, with immediate and short-term results that are at least comparable with those of standard surgery. In the future, prospective studies will confirm these data, which must be considered with all due reservations for the moment, because there were only a few patients in each group. However, the preliminary results are interesting because they are comparable with those in the literature, that is, low postoperative mortality, no neurologic complications, and stability of the results over the short term. Although some authors reserve endovascular treatment for patients in whom standard surgery is contraindicated, one might raise the issue of extending the stent-graft indication to all patients with traumatic injury who have rupture of the thoracic aorta, even the most favorable cases for surgical treatment, that is, those with no associated injuries. If the stent graft were to deteriorate during follow-up, a possible solution would be elective endovascular or surgical conversion in a far safer setting. Studies must be carried out to determine the precise place of endovascular treatment in management of acute rupture of the thoracic aorta. Taking into account the small number of patients who received treatment in each center, even a multicenter randomized study comparing the 2 treatment methods is illusory.

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Recurrent Rupture of Abdominal Aneurysm - Important Anticipation*)

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Abstract

In this case report we present a patient who experienced the ruptured AAA twice in two years and survived them both due to minimally invasive nature of the EVAR, but at the same time suffered from the shortcuts of this treatment and its complications.

The rupture of previously stented abdominal aneurysm is a well known and published phenomenon. On the other hand re-rupture after previous EVAR for rupture is mentioned only scarcely. This devastating event is a new entity of the endovascular era and deserves to be discussed with specific conceptual and technical considerations that should be mentioned.

Introduction

Protecting patients with abdominal aortic aneurysms (AAA) from rupture and aneurysm associated death by completely excluding the aneurysmal sac from circulation is the main goal of surgical repair. In open surgical repair it is achieved by opening of the aneurysmal sac and replacement of the arterial wall with a vascular prosthesis. Endovascular repair (EVAR) is assumed to achieve the same goal by complete sealing in proximal and distal neck(s) of the vessel, providing device fixation with exclusion of aneurysmal sac and supplying adequate prograde blood flow.

Several large trials have shown multiple benefits with EVAR compared to open surgery in elective repair of AAA[1-3].

A three-fold reduction in mortality coupled with a shorter length of hospital stay and operation time has increased the popularity of EVAR. Considerably reduced physiological impact of EVAR encouraged its introduction in emergent cases of ruptured AAA (rAAA). Since the first report by Yusuf[4] in 1994, multiple series and two prospective studies[5,6] have reported the results of EVAR for ruptured AAA (EVRAR) with decreased perioperative mortality and morbidity. This finding was substantiated by recent meta-analysis in systematic review by Rayt et al[7].

A protocol for treating rAAA's by endovascular means was initiated in our hospital in 2004. Since then, every patient has been screened for endovascular eligibility and offered a stent-graft repair unless the patient was anatomically unsuitable or considered to be moribund for any intervention at all.

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The patient we present in this case report is special because he underscores advantages and disadvantages of endovascular era: he experienced the rAAA twice in two years and survived them both due to minimally invasive nature of the repair, but at the same time suffered from the shortcuts of this treatment and its complications.

Case report

The patient, age 68, was seen first on February 2007 in emergency room after syncope at home. The EMS referred him to the hospital while he was awake and hypotensive. No remarkable medical history besides stable ischemic heart disease after CABG in 1993 and dyslipidemia were mentioned. In ER the FAST was performed by general surgeon and free blood with suspected AAA was found. The vascular surgeon was immediately involved, the protocol of hypotensive resuscitation instituted and the patient taken to the CT. On CT a 9 cm infrarenal AAA with retroperitoneal bleeding was found **(Figure 1)** and the patient was taken to the operating theatre immediately.

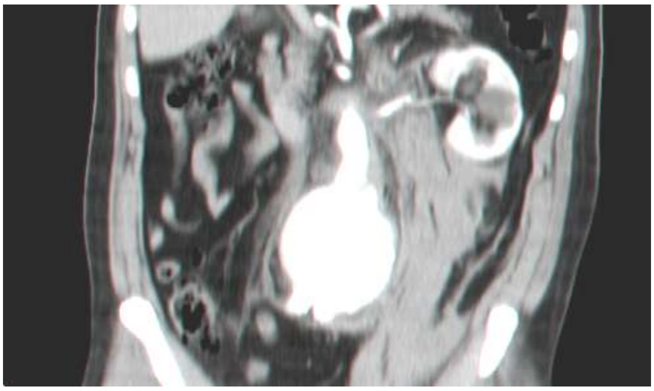


Figure 1: Huge aneurysm with rupture and retroperitoneal hematoma on presentation.

The EVAR of two piece AUI Talent configuration was planned and a device introduced through the right iliac artery. After aortography and marking of the renal arteries on the screen an unnoticed C-arm displacement of several centimeters led to low graft deployment. An additional thoracic Talent graft was used to extend the graft proximally to its proper subrenal position and suprarenal fixation and the distal extension was deployed successfully. The left common iliac artery was occluded by occluder. Completion angiography proved complete exclusion of the aneurysm and femoro-femoral bypass was constructed. The patient improved remarkably fast: his ICU stay was only 1 day, there were no any postoperative complications and hospitalization length was 8 days. His first CT follow up a week later showed a proper graft positioning without any endoleaks **(Figure 2).** Whole graft configuration was seen on 3-dimensional reconstruction **(Figure 3).**

His ambulatory follow up CT at 12 months showed no migration or endoleaks with aneurysmal sac shrinkage to 6.4 cm with some bowing of the graft which was assumed to be insignificant **(Figure 4).** The patient didn't appear to the next follow up.

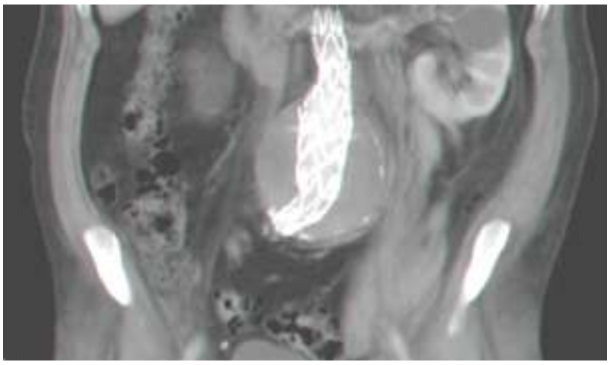


Figure 2: Post deployment CT with complete exclusion of aneurismal sac and residual hematoma. The thoracic Talent with suprarenal fixation and low sitting erroneously deployed abdominal Talent are seen.

Figure 3: Final graft configuration.

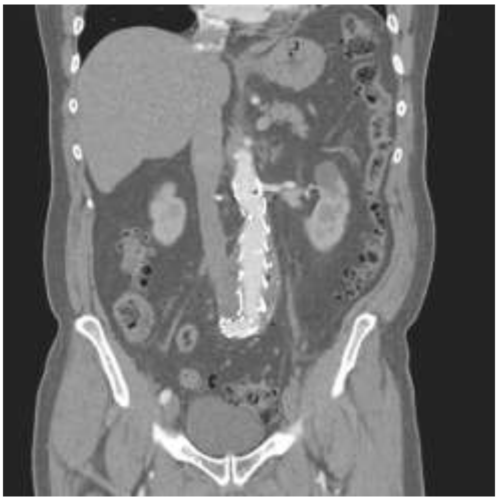
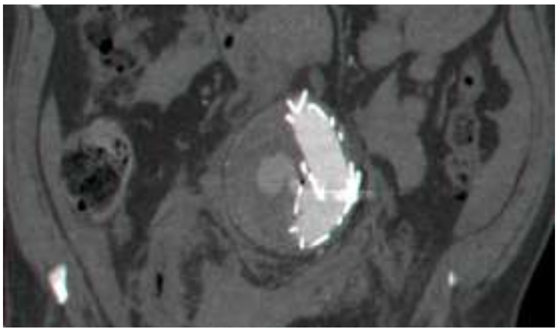


Figure 4: The endograft is in place on 1 year follow up CT with shrinkage of the aneurysm and no leak. The bowing of the graft is seen in its lower part.

Two years after index operation, on January 2009, the patient arrived again to the emergency room, this time with low intensity lower abdominal pain. He was respiratory and hemodynamicaly normal, had small inguinal hernia on his right, no palpable masses on his abdominal exam and normal pulses. On CT angiography a bowing of the body of the graft with type 3 endoleak between main body and extension was noted.



The patient was admitted to vascular department and scheduled for bridging graft repair on the next operating list. The same night the pain reappeared and the patient became hypotensive. He was taken to the CT angiography again and a leaking aneurysm with large retroperitoneal hematoma proved to be the cause **(Figure 5).**

Figure 5: Type 3 endoleak and retroperitoneal hematoma of the second rupture.

The patient was taken to the OR. As a first stage a left transbrachial aortic balloon was introduced and inflated in supraceliac position. While the patient was resuscitated and remained hypotensively stable the right iliac artery proximally to the femoro-femoral bypass anastomosis was exposed, the device introduced and bridging Talent thoracic stent graft deployed. No anticoagulation was used due to the aneurysmal leak. The balloon was exchanged for pig tail catheter and aortography performed. The graft appeared to be full of thrombus **(Figure 6).** Intravenous 5000 IU Heparin were given. Thrombectomy applying aortic balloon and Fogarty 6 F was performed with good result and complete exclusion of the sac on repeat angiography **(Figure 7).**

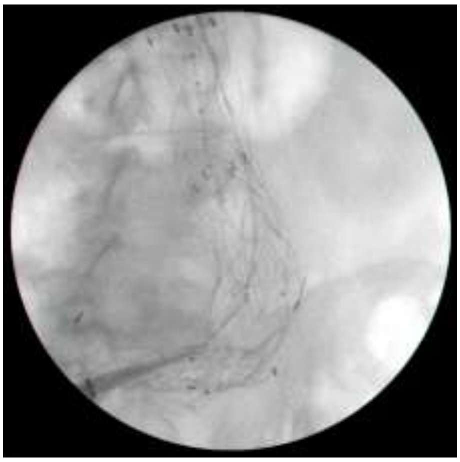


Figure 6: Angiography after bridging graft deployment. The dilator of device is still in place and no contrast progression is seen. The graft appeared to be full of fresh thrombus.

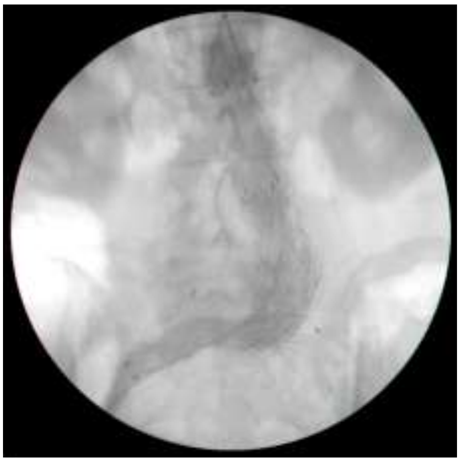


Figure 7: Postthrombectomy angiography. The runoff is still closed and the contrast progression is very slow.

The arteriotomy was closed and blood flow reestablished: this time the femoro-femoral graft was occluded with thrombus. Thrombectomy was performed through incision over the graft. At this time the patient was hypotensive, hypothermic and severely acidotic. It was decided to bail out without completion arteriography. Arteriotomy of the brachial artery was closed and the patient was referred to ICU, where he was rewarmed and resuscitated for several hours when the pulseless ischemic left hand and ischemic left leg were found on examination.

The patient was taken back to the OR for thrombectomies and fasciotomies with good result on completion angiography. The patient had a long but successful recovery without renal or intestinal ischemic complications. On discharge he had a partial left drop foot but was otherwise happy and completely functional. His next follow–up CT-angiography showed normal stent graft position and no leaks **(Figure 8).**

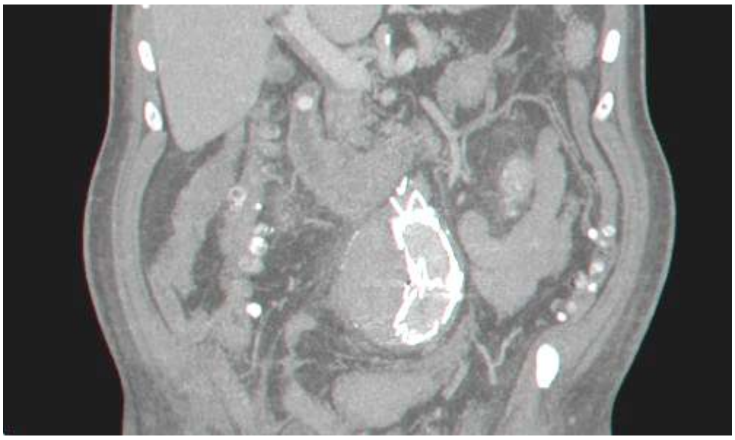


Figure 8: 1-month follow-up CT after bridging graft deployment. No endoleak is seen.

Discussion

The rupture of previously stented abdominal aneurysm is a well known and published phenomenon[8] and it was even claimed to have a better survival than in previously untreated aneurysms[9]. Re-rupture after previous EVAR for rupture is mentioned only scarcely (8 cases in recent meta-analysis of post-EVAR ruptured AAA[8]). This devastating event deserves to be discussed with specific conceptual and technical considerations that should be mentioned.

The first one is a simple fact that in sense of pathology, at least at this stage of stent graft technology, the EVAR is a palliative and not a curative treatment. The ruptured aneurysm, though excluded, stays in place with the defected and ruptured arterial wall and in case of a technical break down the presentation is immediately dramatic. If the patient with previously ruptured and stented aneurysm develops a leak with repressurization of the previously torn sac there is no place for delays and the treatment should be emergent and aggressive. Rupture after EVRAR treatment stays a rupture.

There is a debate in the literature regarding the rate and mode of the follow up after EVAR. Based on the mentioned concept we strongly advocate very strict follow up protocol after EVRAR.

The point of experienced and around the clock availability of the endovascular staff involved in the treatment of ruptured aneurysms cannot be exaggerated. The error in initial deployment of the graft in our patient is a direct consequence of an inexperienced member of the radiology team who moved the C-arm after marking the renal arteries. In cases of rupture, when the patient is actively bleeding and the time is critical, it is crucial that every member understands the procedure and the order of actions.

The issue of the configuration of the deployed stent graft is debatable. AUI configuration has several immediate advantages: the planning is fast and simple and a rather small emergency EVAR kit can suffice a large population. Centers without immediate supply can provide care on the spot with a relatively small stock of grafts. The procedure is less complicated and the occasional time consuming opposite limb catheterization is not required. This shortens the time to exclusion, achieving faster hemodynamic stability by bleeding cessation, which is a primary purpose of the procedure. The reconstructive part of the procedure is performed when the bleeding has stopped.

But there is a payoff: the total procedure including the crossover bypass lasts longer and the synthetic extraanatomic graft has the potential for occlusive and infectious complications. The AUI configuration is seemingly less stable compared to bifurcated stent grafts. In large aneurysms without external support the stent graft seems to be more prudent to bowing and migration, and the multimodular graft is more prone to disintegration, as was in our patient.

The other less noticed short cut of AUI device is that it excludes iliac approach on the opposite side and makes approach to the femoro-iliac segment more technically demanding, time consuming and prone to thrombotic complications.

Occlusion of the ipsilateral iliac artery by the device itself leads to total bilateral flow cessation. In our case of recurrent rupture, when heparin administration was withheld, at least in first stages of the procedure, it caused thrombosis of the whole arterial tree from aorta to both legs via femoro-femoral graft, necessitating thrombectomy with considerable prolongation of the procedure and reoperation next day with repeated thrombectomy, fasciotomy, myectomy and consequent significant postischemic morbidity.

It seems to us, that in these unfortunate cases where the rupture occurs with AUI construction already in place, the heparin should be administered just before the introduction of the device into the artery. After deployment is completed the device should be withdrawn and arteriotomy closed immediately, possibly by perstring suture performed before the device introduction, to open the only runoff available to prevent an unfortunate sequence of events we had with our patient.

The supraceliac balloon occlusion can be life saving and there are two principle ways to its application: through the femoral or brachial arteries. In case the patient is after previous AUI procedure you actually have only one route - through the brachial artery, which is traumatic, considering the large diameter of the aortic balloon. It proved true in our patient, who had immediate major complication of the brachial artery thrombosis, ischemia of the arm, necessary reintervention, fasciotomy and long convalescence. In our opinion the route should be femoral and shaft supported whenever possible and the brachial route used only when time is critical and no other route available. After the balloon is withdrawn arteriography should be performed to reveal any significant intimal injury and arteriotomy closed scrupulously to prevent late thrombosis and ischemic damage.

In this manuscript we report the case of double rupture of aortic aneurysm treated by EVAR in both cases and tried to stress several points relevant to this rare but unfortunately predictable event. With continuous increase in the proportion of patients treated with EVRAR worldwide it is inevitable that we will see more and more patients with recurrent ruptures with different stent grafts in different configurations and with novel problems.

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Factors influencing the outcome among 38 consecutive cases with ruptured infrarenal aortic aneurysms. Experience in one single center from Romania[*)]

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Abstract

AAA represents a common pathologic condition, with an estimated incidence between 30‰ and 66‰ in various studies, increasing in the last three decades. Unfortunately, the mortality rate in ruptured AAAs had also increase. Therefore it is important to identify and treat them before they become a surgical emergency. The aim of this study was to determine the variables that could interfere with the surgical outcome of patients with AAA and with the perioperative morbidity and mortality rates.

Material and Method: *In this study were included 94 consecutive patients with AAA, who underwent elective repair or emergency repair for ruptured AAA, in the Cluj-Napoca Cardiovascular Surgery Clinic between January 2003 and December 2008. The mean age of the studied patients was 68.64 ± 6.27 years (range: 49 - 84 years), of which 11 (12%) were females and 83 (88%) were males. The mean hospital stay was 14.36 ± 7.63 days (range: 0.3 - 39 days). The mean aneurysm diameter measured intraoperatively, was 7.4 ± 1.85 cm (range: 4 - 13 cm). The symptoms and clinical findings at admission were as it follows: in the case of ruptured AAAs, the main findings were low arterial blood pressure in 22 patients (78.6%) and abdominal pain in 18 patients (64.3%), the lumbar pain and the pulsatile abdominal mass were found in 14 patients (50%), while in the patients who underwent elective surgery the predominant signs were the pulsatile abdominal mass in 38 patients (67.8%) and abdominal pain in 34 patients (60.7%).*

Results: *Three types of interventions were performed: tubular graft interposition, aorto-biliac bypass and aorto-bifemoral bypass. The perioperative mortality in the elective repair group was 8.93% (5 / 56), while the perioperative mortality in the emergency repair group was 39.47% (15 / 38).*

Conclusions: *Ruptured AAA or AAA in imminence of rupture continues to represent a condition associated with substantial risks and high mortality; however its rate is decreasing in the last decades, mainly due to an increase in professional performances. It is therefore necessary the selective screening and the elective repair for the improvement of infrarenal AAA patients' survival rate.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2009, vol. 8, no. 1-2, pp. 30-36**

Introduction

The infrarenal AAAs represent the most frequent arterial aneurysms, with a multifactorial etiology in which the degenerative alterations of the arterial wall seem to have the predominant role. They affect mostly the male patients with a history of smoking and hypertension. Although the prevalence of AAA is high, the risk of rupture and the consequent mortality rate is underestimated.

Our aim was to determine the factors that influence the postoperative outcomes in AAAs and the perioperative morbidity and mortality rates: the demographics of the patients, the associated diseases (hypertension, COPD, renal dysfunction, peripheral arterial disease), the clinical signs at presentation (abdominal or lumbar pain, hypovolemic shock, pulsatile abdominal mass), the AAA diameter, and the serum creatinine levels at presentation. The preoperative imaging studies were the abdominal US, CT scanning, and angiography (in elective cases associated with renal disease or peripheral occlusive arterial disease). The operative treatment (tubular graft interposition, aorto-biiliac bypass or aorto-bifemoral bypass) was evaluated by the operatory moment, the approach of the aorta (transabdominally or through the retroperitoneal space), and the perioperative complications and mortality causes.

Patient Population and Methods

A retrospective study was undertaken of all the 94 patients with infrarenal AAA, who underwent elective repair or emergency repair for ruptured AAA, in the *Cluj-Napoca Cardiovascular Surgery Clinic* between January 2003 and December 2008. The data were collected from the hospital inpatient inquiry system and the operative registers.

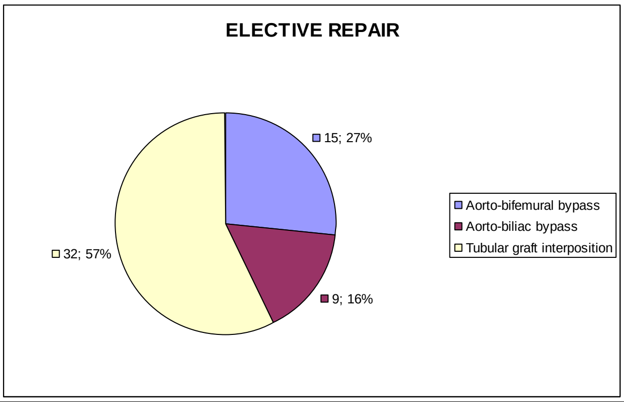
The main objective was to quantify the connection degree between the comorbidities and the postoperative complications respectively, with the perioperative mortality risk. We also compared the postoperative outcomes and mortality rates in patients who underwent elective repair with those that underwent emergency repair.

Elective Repair

Fifty-nine percent (n = 56) of the study population had elective AAA repair. The mean age was 68 ± 4.46 years (range 49-84 years), by which 87.5% (49/56) were males and 12.5% (7/56) were females. The mean hospital stay was 16.5 ± 4.3 days (range 6-38 days). The serum creatinine level at presentation varied between 0.6 and 2.35 mg/dl, with a mean of 1.18 mg/dl, and the mean AAA diameter was 6.9 ± 1.26 cm (range 4-13 cm). The clinical signs at presentation most frequently encountered were the pulsatile abdominal mass (67.8%) and abdominal pain (60.7%), while the most frequent comorbidities were hypertension (78.57%), other cardiac diseases (55.35%), and peripheral arterial disease (35.71%). The operative management was by conventional open repair, using the trans-abdominal method. Postoperatively most patients have had no complications (35/56), but in the others 21 patients the main complications were at the surgical wound level (11/56), and only 1.8% of patients presented cardiac or respiratory failure. The most frequent cause of perioperative mortality in this population group was cardiac failure (3/56), followed by renal failure and mesenteric ischemia, each encountered in 1 case. The perioperative mortality rate was almost nine percent of the patients (5/56).

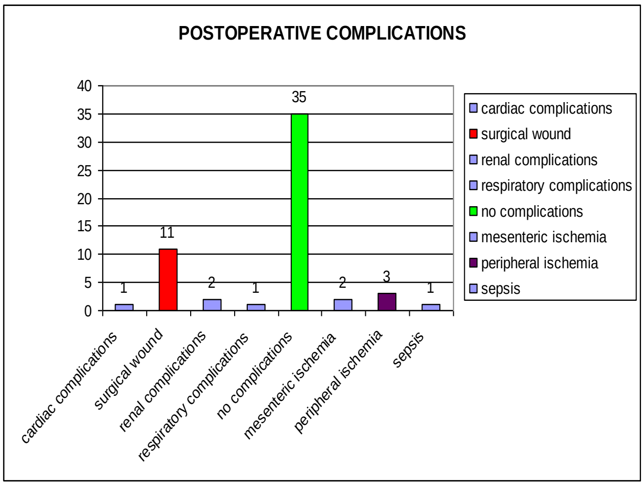
Surgical Techniques

Elective repair	Pacients No	%
Aorto-bifemural bypass	15	27%
Aorto-biliac bypass	9	16%
Tubular graft interposition	32	57%
Total	56	100%

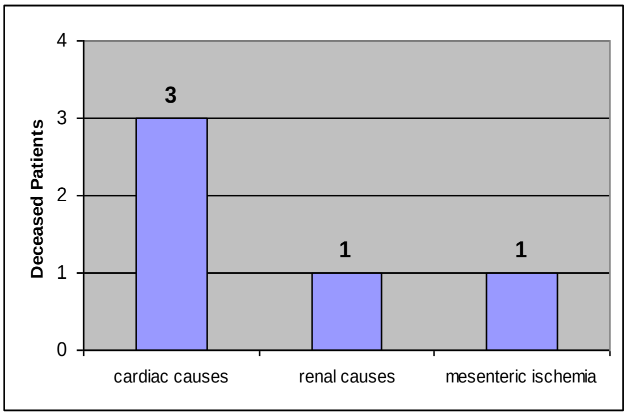


Postoperative Complications

Postoperative Complications	Pacients No	%
cardiac complications	1	1,79%
surgical wound	11	19,65%
renal complications	2	3,57%
respiratory complications	1	1,79%
no complications	35	62,50%
mesenteric ischemia	2	3,57%
peripheral ischemia	3	5,34%
sepsis	1	1,79%
Total	56	100,00%



Perioperative Mortality:

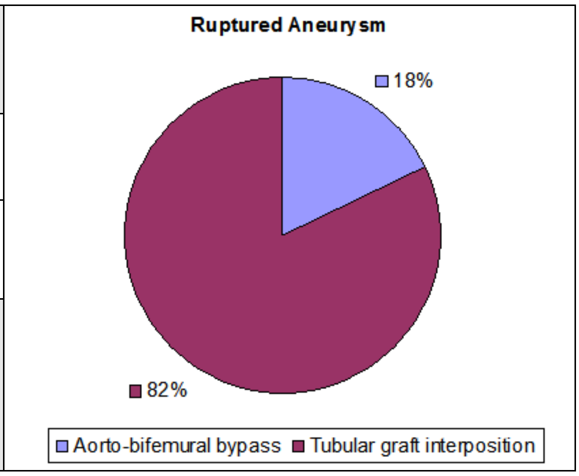


Emergency Repair

Forty-one percent (n = 38) of the study population patients had emergency repair. Only 7 of these patients (18.42%) were previously known and followed up for AAA, and all had initial emergent presentation. Their mean age was 68.5 ± 5.58 years (range 52 - 83 years), by which 89.57% (34/38) were males and 10.53% (4/38) were females. The mean hospital stay was 11.2 ± 5.8 days (range 0.3 - 39 days). The serum creatinine level at presentation varied between 0.73 and 8.78 mg/dl, with a mean of 2.30 mg/dl, and the mean AAA diameter was 8.2 ± 1.37 cm (range 4.5 - 13 cm). The most frequent clinical signs at presentation were the hypovlemic shock (hypotension) (78.6%) and abdominal pain (64.3%), the abdominal pulsatile mass being detected in 50% of patients, while the most frequent comorbidities were hypertension (60.52%), other cardiac diseases (55.26%), and peripheral arterial disease (18.42%). The operative management was by conventional open repair, using the transabdominal method. Postoperatively the main complications were at the surgical wound level (6/38), cardiac complications (6/38) and mesenteric ischemia (6/38) and only 4 patients presented renal dysfunction; also the sepsis and respiratory failure appeared in 2.6% of patients. The most frequent causes of perioperative mortality in this population group were renal failure (5/38) and mesenteric ischemia (5/38), followed by MSOF (3/38) and cardiac failure in 2 cases. The perioperative mortality rate was almost forty percent (15/38).

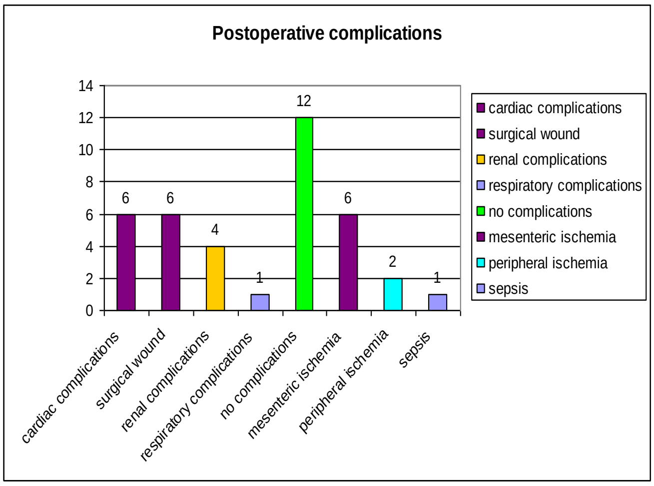
Surgical Techniques

Ruptured Aneurysm	Pacients No	%
Aorto-bifemural bypass	7	18%
Tubular graft interposition	31	82%
Total	38	100%

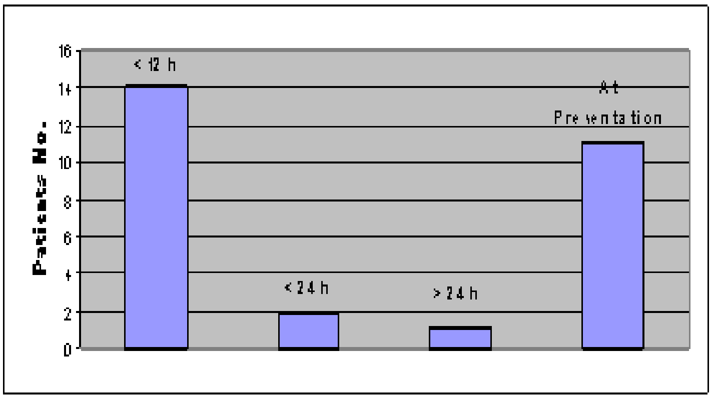


Postoperative Complications

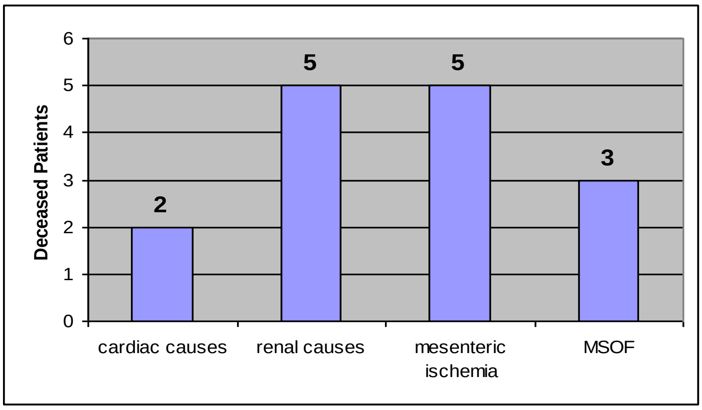
Postoperative Complications	Pacients No	%
cardiac complications	6	15,79
surgical wound	6	15,79
renal complications	4	10,51
respiratory complications	1	2,63
no complications	12	31,60
mesenteric ischemia	6	15,79
peripheral ischemia	2	5,26
sepsis	1	2,63
Total	38	100,00%



Operatory Moment:



Perioperative Mortality:



Statistical Analysis

Statistical analysis was done using the Chi-square and the Student t-test for qualitative variables, and the correlation coefficient between numerical data. Statistical significance was taken as $p < 0.05$.

Results

Patient Characteristics

Characteristic	*Elective Repair* (n = 56)	*Emergency Repair* (n = 38)
Mean Age (years)	68 ± 4.46	68.5 ± 5.58
Males	49 (87.5%)	34 (89.47%)
Mean Hospital Stay (days)	16.5 ± 4.3	11.2 ± 5.8
Mean AAA Diameter (cm)	6.9 ± 1.26	8.2 ± 1.37
Mean Serum Creatinine (mg/dl)	1.18	2.30
Comorbidities	44 (78.57%)	23 (60.52%)
Postoperative Complications	21 (37.50%)	26 (68.42%)
Perioperative Mortality	5 (08.93%)	15 (39.47%)

The mean hospital stay for emergency repair was statistically significant lower than for the elective repair group (*t-Test*), with a ***p*** value of 0.001. In the emergency repair group of patients the mean serum creatinine level at admission was significantly higher than in the elective group (*t-Test:* ***p* = 0.0003**).

t-Test: Two-Sample Assuming Unequal Variances

Hospital Stay	*Elective Repair*	*Emergency Repair*
Mean	16.517857	11.192105
Variance	35.563312	76.245612
Observations	**56**	**38**
Hypothesized Mean Difference	0	
df	60	
***t* Stat**	3.2768289	
P(T ≤ t) one-tail	0.0008739	
***t* Critical one-tail**	1.6706489	
P(T ≤ t) two-tail	**0.0017478**	
***t* Critical two-tail**	2.0002978	

t-Test: Two-Sample Assuming Unequal Variances

Serum Creatinine	*Elective Repair*	*Emergency Repair*

Mean	1.18	2.30526316
Variance	0.15471273	3.06330669
Observations	**56**	**38**
Hypothesized Mean Difference	0	
df	40	
t Stat	-3.897027	
P(T ≤ t) one-tail	0.00018106	
t Critical one-tail	1.68385101	
P(T ≤ t) two-tail	0.00036212	
t Critical two-tail	2.02107537	

t-Test: Two-Sample Assuming Equal Variances

Aneurysm Size	*Elective Repair*	*Emergency Repair*
Mean	6.892857143	8.171052632
Variance	3.106493506	2.990220484
Observations	**56**	**38**
Pooled Variance	3.05973153	
Hypothesized Mean Difference	0	
df	92	
t Stat	-3.476782352	
P(T ≤ t) one-tail	0.000388304	
t Critical one-tail	1.661585397	
P(T ≤ t) two-tail	0.000776609	
t Critical two-tail	1.986086272	

There was a significant statistical difference in mean aneurysm diameter between the elective repair and the emergency repair group (p = 0.0007).

Comorbidities

The connection between the frequency of comorbidities and the postoperative complications and the mortality rate respectively (*Chi-square* test) in the emergency repair group showed no statistical difference (p = 0.563 and 0.443 respectively).

Postoperative Complications

In the emergency repair group there was a significant statistical difference in the correlation between the perioperative mortality rate and the presence of associated diseases (Chi-square test), with a p value of 0.0096.

Also the correlation between the frequency of postoperative complications and patient age or hospital stay respectively was statistically moderate, with C_s = 0.5 and 0.44 respectively; there was no signifficant correlation between the hospital stay and the patients age, in the emergency repair group (C_p = 0.12).

Perioperative (30-Day) Mortality

The 30-day mortality in the emergency operative group (39%) was almost four-times higher than in the elective operative group (9%) (p = 0.0003), showing a significant difference between the two patient populations.

Discussion

Many studies have determined that some preoperative, intraoperative, and postoperative patient variables could predict mortality for the AAA open repair. Some of the most commonly cited variables include age, gender, elevated serum creatinine, congestive heart failure, chronic pulmonary obstructive disease, hypotension, cardiac arrest, and syncope(1). Elderly patients with AAA in emergency presentation with hipovolemic shock status or cardiorespiratory arrest present an increased risc for perioperative morbidity and mortality and should be evaluated in order to establish the indication for endovascular repair. The endovascular repair has been widely accepted for the elective treatment of AAA. There is also a growing body of evidence supporting the successful application of this technique to patients with ruptured AAA(1), but our center has very little experience in applying it, especially to patients with ruptured AAA. This is due to numerous reasons, including surgeon preference and the speed of open repair with acceptable results.

Between the two groups of patients we found significant difference in serum creatinine levels at admission (higher for emergency repair group - p = 0.0003); also the mean hospital stay was lower for the patients presenting with ruptured AAA, maybe due to the higher frequency of major postoperative complications which lead to higher mortality rates.

The study showed an increased incidence of associated cardiac diseases and hypertension both in the elective repair group (55.35% and 78.57%) and in the emergency repair group (55.26% and 60.52%); still there was no evidence of a significant correlation with the frequency of perioperative comorbidities or 30-day mortality rate (p = 0.563 and 0.443).

Postoperative complications were predominantly cardiac (15.78%), renal (10.52%) and ischemic – especially mesenteric ischemia (21.05%) in the emergency repair group while in the elective repair group the most frequent complication was at the surgical wound level (19.64%). There is a statistically moderate correlation between the postoperative complications frequency and the patients' age and hospital stay respectively (0.5 and 0.44).

Although relatively high, the overall perioperative mortality rate in elective repair group was significantly lower (8.93 %) than in the emergency repair group (39.47%) (p = 0.0003), with a statistically significant connection with the presence of postoperative complications in the emergency repair for ruptured AAA (p value = 0.009). In light of decreasing elective operative mortality rates, early recognition of likely rupture might further identify those patients for whom the surgical management of AAA would be beneficial. Among the variables potentially linked with rupture are gender, aneurysm size, and preexisting cardiovascular disease (especially hypertension)(13). The conventional thinking is that the risk of rupture is most related with the maximum AAA diameter. Comparing the average aneurysm size in the elective group with that of the aneurysms of the emergency group we found that there is a significant difference in the average size (p = 0.0007). Thus, selective screening and elective surgical repair is necessary in order to improve the survival rate for the patients with infrarenal AAA.

In **conclusion**, we believe that the ruptured AAA continues to represent a condition associated with considerable risks and high mortality rates, even if those are decreasing in the past decades, especially due to an increase in professional performances. The decision of when, or whether to electively operate on high-risk patients will ultimately depend on the risk of surgery compared with the risk of nonoperative management or alternative procedures(13). However, to estimate the risk of elective AAA repair it is necessary not only to identify what constitutes "high risk" but also to understand the natural postoperative history with short- and long-term outcomes.

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Risk factors for early death in aortic dissection. IBCV Timisoara experience*)

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Abstract

Obiectiv. *Studiu retrospectiv al rezultatelor tratamentului disecției acute de aortă în perioada ianuarie 2000- ianuarie 2011 în Institutul de Boli Cardiovasculare Timişoara, precum şi identificarea factorilor de risc pentru mortalitatea precoce.*

Material si metodă. *Au fost incluşi 85 de pacienți operați în această perioadă. Vârsta medie a fost de 54,35 ± 13.33 ani (14-78.5 ani). Sexul preponderent a fost cel masculin (69.41%). Marea majoritate a pacienților au fost hipertensivi (86.75%). Ceilalți factori de risc pentru boala aterosclerotică au fost reprezentați de diabet zaharat (49.41%), hiperlipoproteinemii (57.65%), obezitate (40%), fumat (65%). Cinci pacienți au prezentat sindrom Marfan (6.17%). Diametrul aortei a fost de 5.96± 1.48 cm, iar poarta de intrare primară a fost în aorta ascendentă (80.49%) sau în crosa aortei (19.51%).*

Rezultate. *Operația a constat în înlocuirea aortei ascendente (54.12%), eventual asociată cu alte proceduri, sau în înlocuirea valvei aortice, a rădăcinii aortei şi a aortei ascendente (operatie Bentall) în 45.88% din cazuri. Timpul de clampaj a fost de 124.89±52.87 minute iar cel de CEC de 197.20±85.10 minute. Mortalitatea intraspitalicească a fost de 29,71% (25/85), iar cea intraoperatorie de 12.94% (11/85). Analiza uni- şi multivariată folosind regresia logistică a permis identificarea nivelului creatininei la internare, precum şi timpul de circulație extracorporeală ca fiind factorii de risc independentă capabili să influențeze semnificativ mortalitatea precoce.*

Concluzii. *Tratamentul chirurgical al disecției de aortă este grevat de o mortalitate importantă, care însă a fost redusă semnificativ în ultimii ani. Cunoaşterea factorilor de risc pentru mortalitatea precoce are importanta prognostică.*

Introduction

The surgical treatment of aortic dissection continues to have high early mortality rates, in spite of the technical advances in surgery and intensive care. The incidence of this severe pathology is rising [1], but this fact may be due to more accurate and timely diagnosis, a consequence of the widespread use of computer-tomography (CT) in

*) **Romanian Journal of Cardiovascular Surgery ■ 2011, vol. 10, no. 2, pp. 137-144**

secondary medical units. This has also leaded to an extension of the classic double-lumen definition of aortic dissection to include intramural hematoma or penetrating aortic ulcer [2].

The prevalence of acute aortic dissection in the general population seems to be on the rise, one study in Sweden having reported a rate of 16 cases per 100.000 inhabitants yearly [3]. The natural history of untreated acute aortic dissection is dire: 40% die immediately and of those who survive the acute episode 1% will expire every hour [4].

The contemporary era results of the surgical treatment have been collected in the International Registry of Acute Aortic Dissection, the in-hospital mortality being 25% [5], however high-volume centers seem to have better outcomes with early deaths around 10% [6].

This paper intends to present the results of our team in the treatment of aortic dissection and to identify risk factors for early (<30 days) mortality.

Patient Population and Methods

The hospital records of all patients operated upon in our department from January 1st 2000 until April 1st 2011 were reviewed. We identified 85 patients who had surgery for aortic dissection. The dissection was considered acute if symptoms developed less than 24 h before admission otherwise it was classified as being chronic. Most of the patients were male (69.41%) with a mean age of 54.35±13.33 years, with the youngest patient in our series being thirteen years old.

Surgical technique

Peripheral arterial cannulation (femoral or right axillary) was performed prior to entering the chest in most stable patients. If the patient was in cardiac tamponade we performed first a median sternotomy with partial pericardial decompression and once a stable hemodynamic state was achieved went on to perform peripheral arterial cannulation. The right common femoral artery was exposed and directly cannulated in a standard fashion. Axillary cannulation involved exposing the right axillary artery in its second segment after detaching the great pectoral muscle from its clavicular insertion and dividing the lesser pectoral muscle. The axillary artery was either directly or via an 8 mm Dacron graft (anastomosed end-to-side at this level) cannulated, according to the surgeon's preference and anatomic characteristics of the patient. Venous return was obtained via the right atrium. A left ventricular venting catheter was inserted through the right superior pulmonary vein. The coronary sinus was indirectly cannulated through the right atrial wall. Once cardiopulmonary bypass was established we cooled down the patient to 25 degrees (after 2003) or to 18 degrees (2000-2003). The supra-aortic trunks were exposed and encircled. The aorta was cross-clamped and the heart arrested. Visual inspection was performed of the interior of the aorta, looking for the primary entry tear, the extension of the dissection, the state of the aortic root and valve. Extensive resection of the ascending aorta/aortic root was performed by detaching it from the surrounding structures. If an aortic root replacement/sparing procedure was deemed necessary we performed mobilization of the coronary ostia. The proximal anastomosis was performed first by external felt-reinforced 4-0 Polypropylene sutures. Once the patient reached the desired temperature, we performed either total circulatory arrest in deep hypothermia or systemic circulatory arrest with retrograde (before 2005) or antegrade cerebral perfusion (after 2005). The aortic cross was visually inspected for any additional entry tears. If present, we performed partial/total arch replacement.

If arch replacement was deemed unnecessary there were two methods for constructing the distal anastomosis, according to the surgeon's preference. The first involved applying again the crossclamp, reestablishing the bypass and warming-up the patient while performing the distal anastomosis on the clamped aorta. The other consisted of manufacturing the distal suture line while under circulatory arrest and cerebral protection.

Statistical analysis

Results for continuous variables are expressed as mean ± standard deviation. Results for categorical variables are expressed as number (percent). The Student *t* test for independent samples was used to determine statistically significant differences between the 2 groups for the continuous variables. The χ^2 test was used to determine statistically significant group differences for the categorical variables. Stepwise logistic regression was used to select the predictor variables for the outcomes surgical mortality. Statistical calculations were performed by means of Stata version 11.2 (Stata Corporation, College Station, Tx, USA).

Results

Uncontrolled arterial hypertension was found in almost all patients (86.75%) and was the most common atherosclerosis-related risk factor. Most of our patients (76.47%) were admitted and operated upon as an emergency, defined as a time-frame of less than 24h between admission and surgery, while 40% presented with cardiogenic shock, due mainly to cardiac tamponade.

Limb or end-organ ischemia was found in 14.12% of cases on admission. The symptom of acute chest pain motivated the physicians in the original referral units to give loading-dose antiplatelet medication (300 mg clopidogrel) to these patients in 14.12% of cases, which resulted in severe bleeding. The mean ascending aortic size was 5.96±1.48 cm and was accompanied by severe aortic regurgitation in 40.74% of cases (Figure 1).

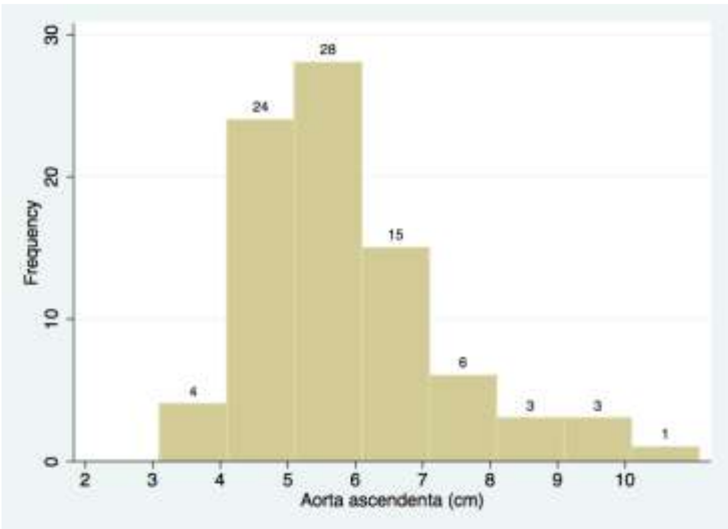

Figure 1: Diameter of the ascending aorta in our cohort.

The primary entry tear was located in the ascending aorta most of the time (80.49%) (Figure 2), aortic arch (9.76%) or descending aorta (2.44%). Six cases (7.06%) were intramural hematomas of the ascending aorta.

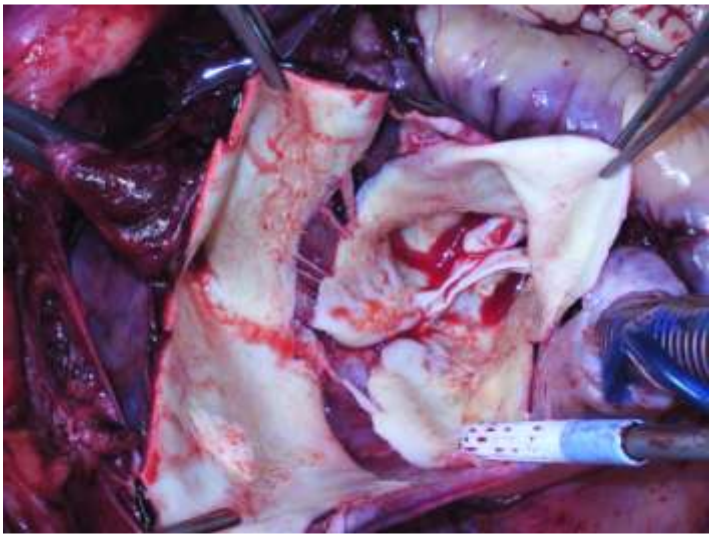

Figure 2: Large entry tear located just above the sinotubular junction and extending into the right commissure.

Simple replacement of the ascending aorta with or without including the concavity of the aortic arch in the repair was the most used surgical technique (48.23%). Ascending aorta and aortic root replacement was performed in 45.88% of cases, most of the time with concomitant aortic valve replacement (Bentall procedure) - in one patient we performed aortic valve-sparing aortic root reimplantation procedure (David I procedure) (Figure 3).

Figure 3: Aortic valve reimplantation technique (Tirone-David I) in a patient with anulo-aortic ectasia, severe aortic regurgitation and Type A aortic dissection.

Five patients who had the primary tear within the aortic arch benefitted from ascending aorta and total arch replacement (5.88%), with patch-reimplantation of the supraaortic trunks in the Dacron graft (4/5) (Figure 4) or by means of a total arch replacement graft (1/5) (Figure 5). Aortic cross clamp time was 124.89±52.87 min, while bypass time was 197.2±85.1 minutes.

Figure 4: Total arch replacement and patch reimplantation of the supraaortic vessels. The entry site was located in the antero-inferior aortic arch, extending three-quarters circumferentially and between the common carotid and left subclavian artery. The ascending aorta was replaced during the cooling phase by another 30mm Dacron graft.

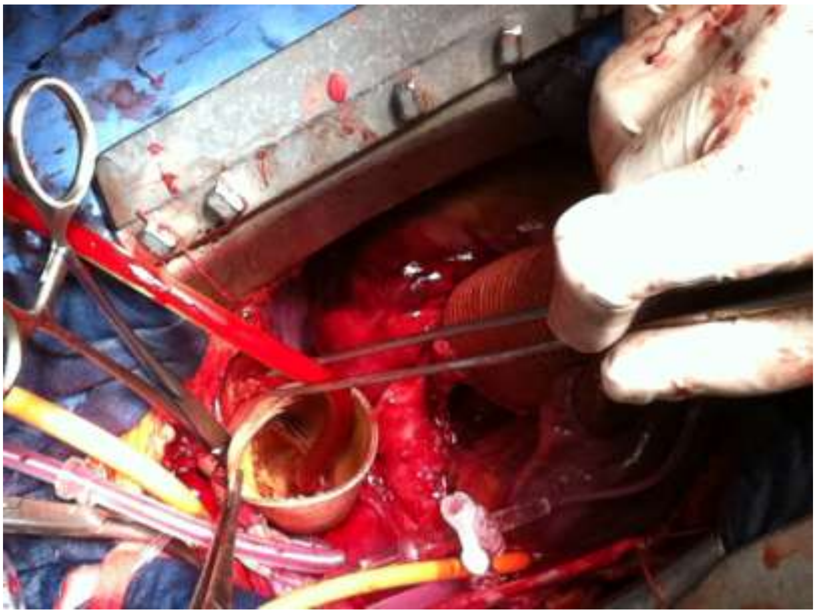

Figure 5: Operative view in a patient with severe aortic stenosis on a bicuspid aortic valve and Type A aortic dissection with malperfusion of the supraaortic trunks. Aortic valve replacement as well as ascending aorta and total arch replacement with a bifurcated graft was performed.

We employed circulatory arrest for the distal anastomosis in almost half of the patients in our cohort (44.71%) for 41.83±22.08 minutes (Figure **6**). Cerebral protection was by deep hypothermia alone (*n* = 9), deep hypothermia with retrograde cerebral perfusion (*n* = 8) and moderate hypothermia and anetegrade cerebral perfusion (*n* = 21), since 2006.

Concomitant procedures performed at the same time as the repair/replacement of the ascending aorta/aortic root included: coronary bypass grafts (*n* = 5) aortic valve repair (*n* = 3) aortic valve replacement (*n* = 1), mitral valve repair (*n* = 1), femoro-femoral bypass (*n* = 1) and balloon embolectomy (*n* = 1).

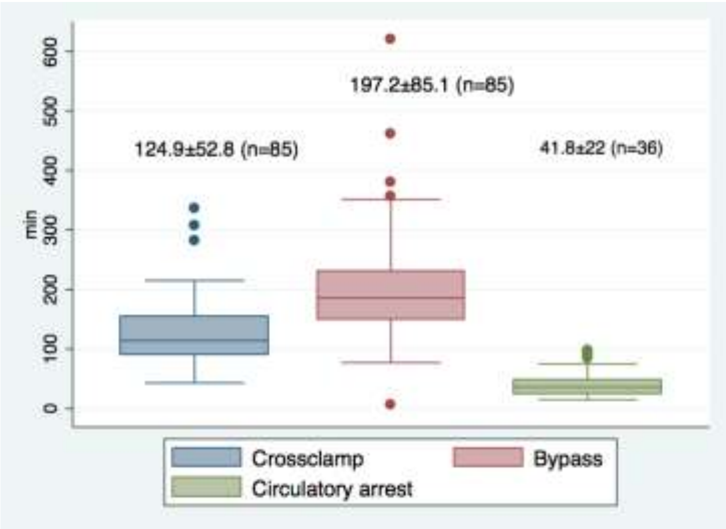

Figure 6: Mean aortic crossclamp and bypass time in our cohort.

Early mortality (<30 days) was 29.41%, of which 12.94% were operative deaths. There were fewer deaths in patients who did not experience a circulatory arrest time (*p* =0.008). Other variables that influenced early mortality are depicted in Table **1**.

Table 1: Other variables that influenced early mortality

Variable	*p*
Circulatory arrest	*p* = 0.008
Acute dissection	*p* = 0.005
Aortic cross-clamp time	*p* = 0.035
Bypass time	*p* = 0.003
Serum creatinine	*p* = 0.001
Blood Glucose level	*p* = 0.004
Shock upon admission	*p* = 0.001
Emergency	*p* = 0.049
Arterial hypertension	*p* = 0.017

Multivariate analysis using the logistic regression model, in which all factors significant or marginally significant (*p* <0.2) in the univariate analysis were taken into account, allowed the identification of the *cardiopulmonary bypass time* (*p* = 0.043, OR=1.03, per minute, 95% CI 1.00-1.06) and *serum creatinine* level (*p* = 0.018, OR = 13.46, 95% CI 1.55-116.68) as the independent variables capable of having a significant impact on early survival.

Mean ICU stay for patients who survived the first 24h after the procedure was 6.63±7.21 days (range 2-35). The most common postoperative complication was bleeding, which resulted in the need for 19 surgical revisions (22.35%). This was particularly true in patients in whom the thoracic pain (although without ischemic changes on the rest ECG in most patients) led, in the primary admission unit, to the suspicion of acute coronary syndrome and the administration of a loading dose of 300 mg clopidogrel - those patients experienced severe bleeding diatheses with repeated surgical revisions and/or cardiac tamponade. Postoperative comorbidities included bronchopneumonia (18.92%), sepsis (14.86%), cerebrovascular accident (14.86%), acute renal failure (14.86%), cardiac tamponade (9.46%), and hepatic failure (6.76%). If we exclude the patients who expired at the end of the surgical procedure, the highest correlation coefficient (Spearman's rho) with early death occurred with postoperative acute renal failure (r = 0.67) - all other complications r <0.55.

Discussion

Better understanding of the physiology of aortic dissection has allowed tailoring the surgical technique to improve outcomes [7, 8]. It is well established nowadays the need to secure antegrade arterial access before entering the chest – the right axillary artery has become the cannulation site of choice due to it being rarely involved in the dissection process [9]. In our series this attitude depended on the hemodynamic stability of the patient: when this was compromised we first performed a partial drainage of the pericardial cavity. Femoral cannulation doesn't offer certainty with regard to the perfused lumen, which can lead to end-organ malperfusion during cardiopulmonary bypass. Interestingly, in our series there was no improvement in outcome when the right axillary artery was used (Fisher's p = 1.00), but this may be due to our sample size and the characteristics of our study cohort.

The introduction of antegrade cerebral perfusion has improved neurologic outcomes and allowed surgeons to expand into performing more complex surgery on the aortic arch [10, 11]. Of our five patients with total arch replacements, four had antegrade cerebral perfusion (two expired) and one retrograde cerebral protection (he died). It must be said, however, that the anatomy and the preoperative injury of the brain may play a role in the neurologic outcomes.

We have since standardized on using the antegrade, anatomic technique for affording protection to the brain during arch procedures.

Bleeding remains the most frequent complication of this type of surgery, due to the frailty of the dissected tissues, the long suture lines and the coagulopathy inherent to this pathology [7]. This may be exacerbated in patients who are mistakenly diagnosed with an acute coronary syndrome and were given loading dose clopidogrel. Bleeding may lead to surgical revisions, a higher need for blood products and tamponade. This in turn, may lead to or worsen an acute renal failure (in patients with pre-op tamponade), which is the independent variable most strongly linked to early death in our cohort, as well as other studies [12]. Management of the bleeding diathesis remains a cornerstone for a favorable outcome, particularly in the specific conditions which exist in our country: the local blood banks do not deliver platelet-related products after noon, cell-saver kits are rare and surgical sealing products expensive and not always available.

In spite of these shortcomings, our results are in line with the International Registry of Aortic Dissection Database, the global mortality in our series (29.41%) similar with that from a pool of 18 cardiac surgery units worldwide, 25.1% [5]. However, we firmly believe that our results could be improved upon with better coordination, attention to detail and better supply of surgical materials.

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Acute Type A Aortic Dissection 7 Years after Aortic Valve Replacement*)

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Abstract

We report a case of a 41-year-old man, with a previous history of aortic valve replacement for bicuspid aortic valve. The patient was admitted to our institution for evaluation of a severe, constant, tearing anterior chest pain radiated to the neck with suspicion of acute aortic dissection. A multidetector computed tomography scan of thorax and abdomen demonstrated a dissection starting 5 mm above the origin of the left coronary artery extending to the proximity of the innominate artery. The dissection was classified as Stanford type A. We performed an emergency composite graft replacement of the mechanical aortic valve, aortic root and ascending aorta, with re-implantation of the coronary arteries into the graft (Bentall procedure).

Keywords: *Aortic Valve Replacement, ascendant aortic dissection, Bentall procedure*

Introduction

Acute aortic dissection (AAD) type A (Stanford) is a medical emergency with a high mortality rate, rising by approximately 1% per hour[1]. Complications such as aortic rupture, cardiac tamponade and acute aortic regurgitation require immediate surgical intervention. The perioperative mortality rate for patients with aortic dissections ranges from 5 to 10% and may approach 70% in cases with complications [2].

It usually presents with severe chest pain of sudden onset. Pain can be described as ripping, tearing, stabbing or sharp in character. It can migrate as the dissection extends down to the aorta (17%). Less common signs and symptoms are related to organ hypoperfusion and include peripheral ischemic syndromes (19%), syncope (13%), myocardial infarction (13%), heart failure (8.8%), and neurological symptoms (6.1%) [1]. Because of such heterogeneous clinical presentations, many cases remain incorrectly diagnosed. Approximately one-third of patients ultimately diagnosed with AAD have another initial diagnosis. The true incidence of AAD is therefore difficult to determine, but is estimated to be 5–20/1,000,000 [1].

Replacement of the aortic valve (AV), root and ascending aorta with a composite graft carrying a mechanical valvular prosthesis is one of the most used treatment option especially if the aortic root is severely impaired.

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Case presentation

We present a case of a 41 year old man who developed Stanford type A dissection 7 years after aortic valve replacement (AVR) for congenital bicuspid aortic valve (BAV). The ascending aortic diameter was 46 mm at the time of AVR for wich a spiral aortic reconstruction was also performed.

He was emergently admitted to our department because of strong, tearing chest pain with sudden onset, radiating to the neck, with a suspicion of acute aortic dissection. Physical examination in the intensive care unit showed: stable haemodynamics, blood pressure 140/85 mmHg; pulse 84 beats/minute. No pulse deficit of radial artery was observed. The performed electrocardiogram showed right ventricular hypertrophy. Laboratory workup revealed increased C reactive protein. Chest X-ray showed widened mediastinum and aneurysm of aorta with abnormal contour.

Transesophageal echocardiography revealed moderate aortic regurgitation, a dilated aortic root and ascending aorta and an acute aortic dissection with an entry tear staring 10 mm above the previously implanted functional mechanical valve. The ascending aorta was dilated and dissected with a large intramural heamatoma of the antero-lateral wall, compressing on the right cardiac chambers. It also revealed a dilated right ventricle and a second degree tricuspid valve insufficiency.EF-50%.

Contrast enhanced computed tomography showed an aortic root and ascending aorta dilatation, with a maximum diameter of 6.7 cm. It demonstrated a type A aortic dissection with false and true lumen, with an intimal flap arising 5mm above the origin of the left coronary artery extending to the proximity but not involving the innominate artery (Figure 1, 2). There was no evidence of aortic rupture.

Figure 1: Aortic root and ascending aorta dilatation, with a maximum diameter of 6.7 cm

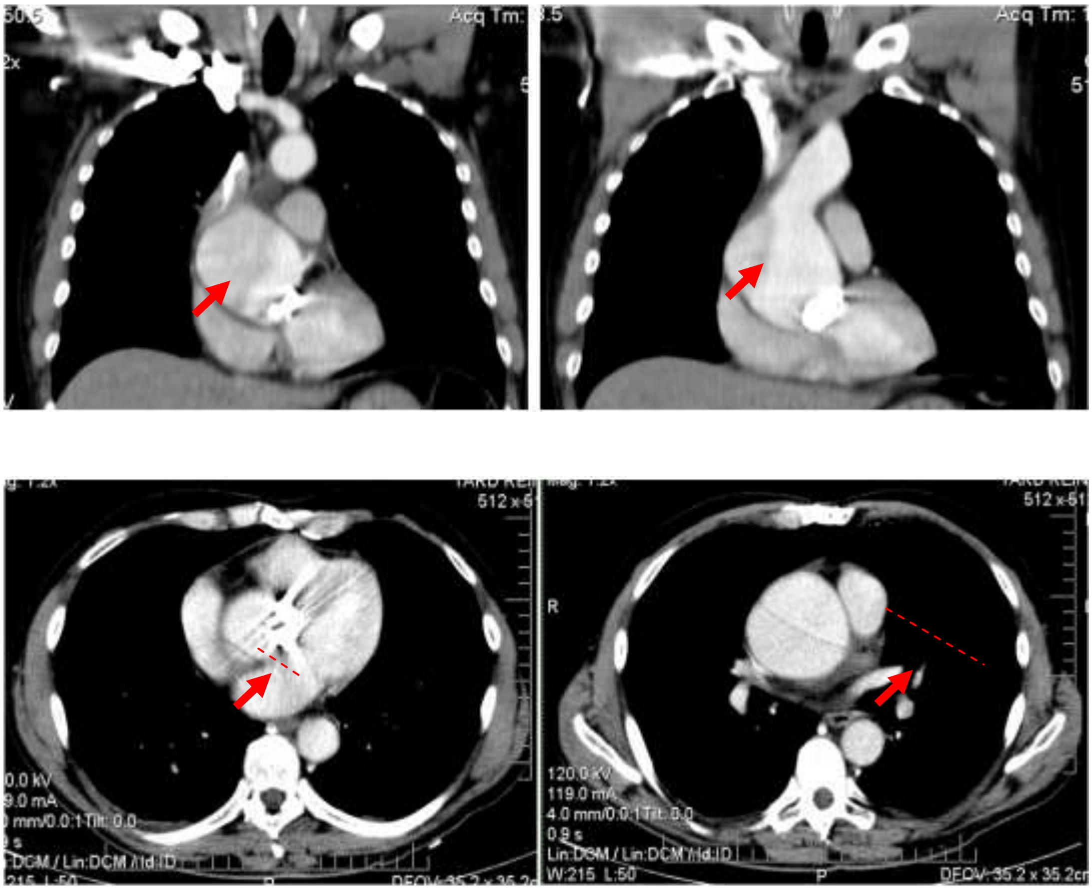

Figure 2: Type A aortic dissection with false and true lumen, with an intimal flap arising 10mm above the previously implanted mechanical valve

Emergency surgery was performed under general anaesthesia and hypothermic circulatory arrest. The intraoperative examination of the aorta confirmed the imagistic findings. The aorta was dilated and blue in color, presenting an intramural haematoma (Figure 3a, next page).

We performed a classic Bentall procedure consisting of composite graft replacement of the previously implanted mechanical valve, aortic root and ascending aorta, with re-implantation of the coronary arteries into the graft. (Figure 3 b, c, d, next page). The procedure was performed with a No. 25 mechanical valved conduit.

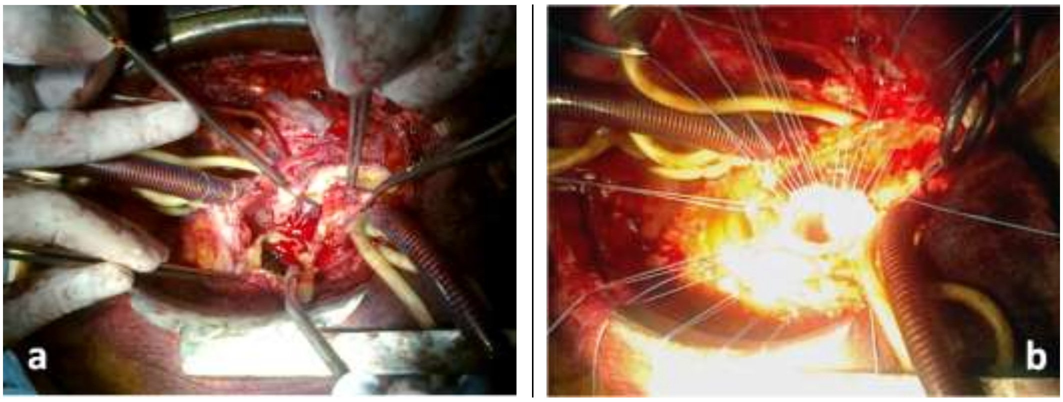

Figure 3 a,b: Intraoperatory aspect of the ascending aorta aneurysm and the exposed aortic prosthesis. Excision and replacement of the aortic prosthesis with a St. Jude Nr.25 valved conduit

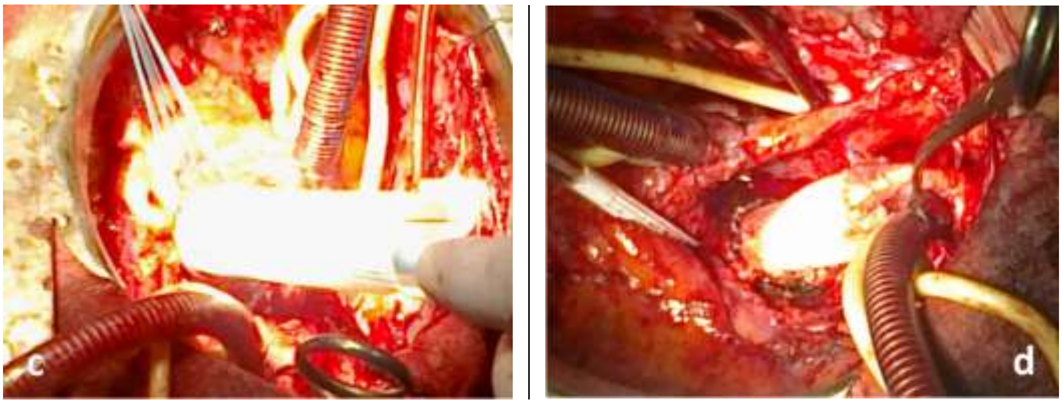

Figure 3 c, d: Proximal anasthomosis and completed procedure, with the reimplantation of the right and left coronary arteries

There were no postoperative complications. The patient was discharged on the 14-th postoperative day.

Discussion

Congenital bicuspid aortic valve (BAV) is known to be a predisposing factor for aortic aneurysms and dissection because of intrinsic weakness of the aortic wall [3]. Isolated aortic valve replacement in this case, without the correction of the aortic dilatation most probably will result in early or late dissection at this level. More so, previous aortic valve replacement (AVR) without aortic dilatation is also considered to be an independent risk factor for aortic dissection. Type A aortic dissection develops in 0,6% of patients late after aortic valve replacement, and 13% of patients with type A aortic dissection have a history of AVR [4].

A randomised, prospective study analysed the long-term survival after Bentall procedure in 206 patients with bicuspid aortic valve. The results showed that long-term survival was 93% after 5 years and 89% after 10 years. The discharged patients enjoyed survival equivalent to a normal age- and gender- matched population and superior to survival reported for a series of patients with aortic valve replacement alone [5].

In the unfortunate case of aortic type A dissection occurring after previous cardiac intervention, emergency surgical correction consisting of aortic valve, aortic root and ascending aorta replacement proved to be safe and effective. A randomised single centre study evaluated the outcome after repair for acute spontaneous type A dissection in 114 patients of which 11 underwent previous cardiac surgery [6].The results showed that the survival at five and eight years for redo compared to first-time surgery was 68±3.63% vs. 81±5.34% and 51±3.8% vs. 61±5.4%, respectively (P=0.365) [6].

In conclusion, acute type A aortic dissection repair in patients with previous cardiac surgery has an acceptable mortality and comparable long-term outcome to first-time surgery.

Even if the reintervention has acceptable outcomes, in the case of patients initially diagnosed with BAV/aortic regurgitation combined with fragile and thinned aortic walls we recommend concomitant aortic valve and ascending aorta replacement in order to prevent future aortic complications.

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EVAR for AAA treatment*)

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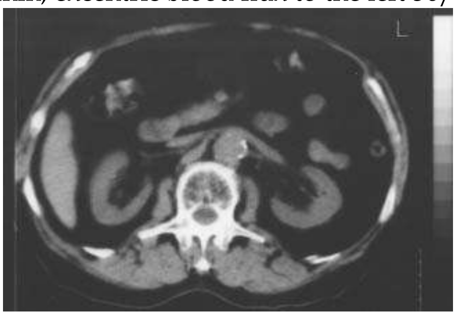
Case presentation

A 74 years old patient, with no important personal or hereditary health issues, is admitted in our ward, after a routine check up to a primary medical facility, suspected of an abdominal aorta aneurism.

Clinical examination shows the presence of a middle abdomen tumor, with elastic consistence, almost painful at physical examination, systolic expanded. The patient excludes any symptoms, perhaps a moderate fatigue and a non-continuous abdominal discomfort, but he admits the pulsatility of the tumor for aproximaly an entire year.

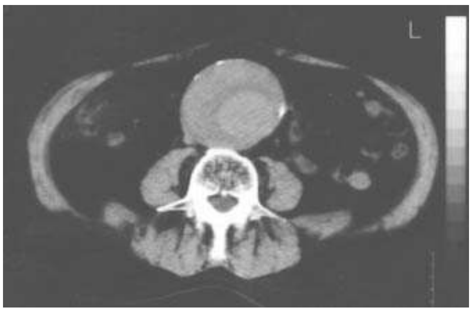
The ecographic exam shows a subrenal abdominal aorta aneurism with maximum diameter 80 mm.

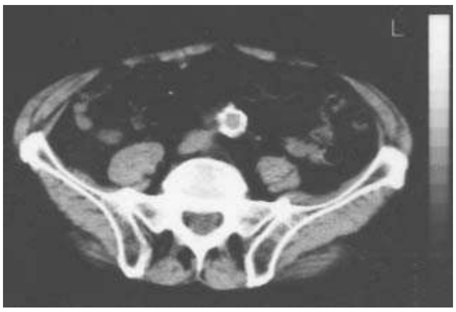
CT scan indicates a huge prolonged infrarenal aneurism of the abdominal aorta, with important parietal calcifications, cranial diameter 26/29 mm, medial diameter 75/76 mm, excentric blood flux to the left 36/39 mm, parietal thrombus 30 mm.



The upper limit of the aneurism is 30 mm below the origin of the left renal artery, the lower limit is 10mm above aorta bifurcation. The iliac and femoral arteries are within normal limits, with important parietal calcifications but no important stenosis (figure 1).

Figure 1: Abdominal CT-scan





*) Romanian Journal of Cardiovascular Surgery - 2007, vol. 6, no. 4, pp.203-206

Having the possibility for endovascular treatment, spiral CT was necessary for a better analysis of dimensions and shape of aneurism. The results were similarly with plain CT scan (figure 2).

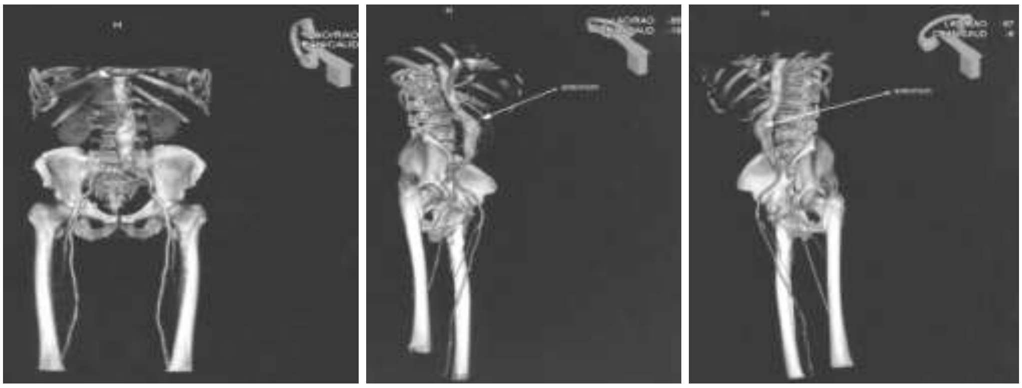


Figure 2: Abdominal multislice CT

Having these results we've decided for the endovascular resection of the aneurism, using as stent graft the endovascular Anaconda (Vascutek) system. This system has 3 segments (one for the aorta, two for the iliac arteries) (figures 3, 4).

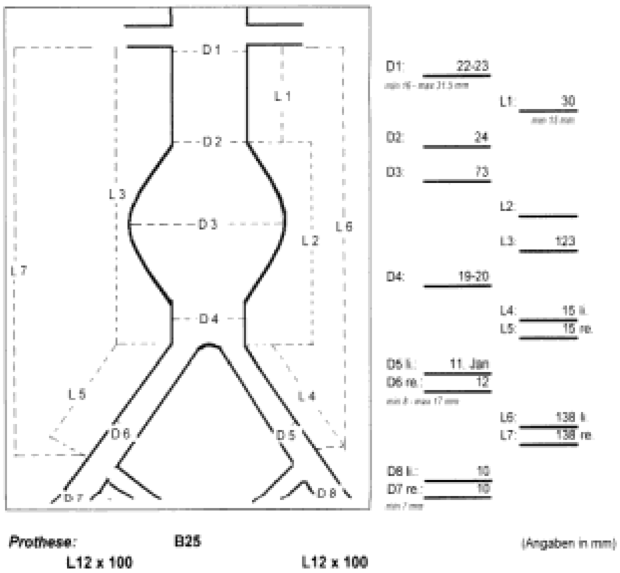


Figure 3: Measurements for endovascular treatment

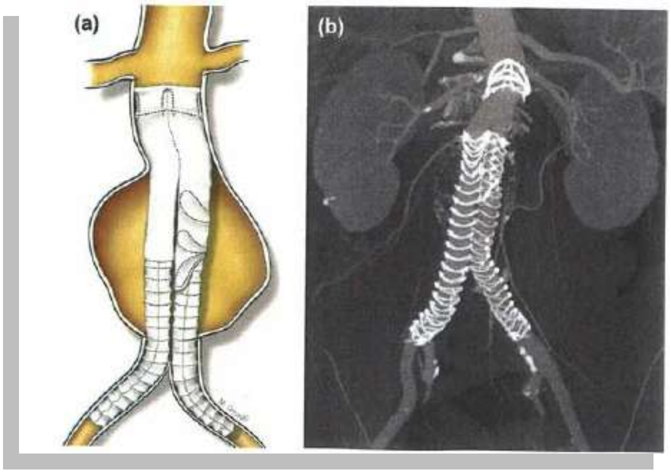


Figure 4: Anaconda endograft for infrarenal abdominal aortic aneurysm therapy

Under peridural anesthesia, we have exposed the common femoral arteries bilaterally and their branches and isolate them, we have controlled the hemostasis to the punction points, with pockets created with monophilament 4-0 sutures, securized with tourniquets. After a control angiography, who also indicates the exact position of renal arteries, we introduce through right femoral artery the first aortic segment and we fix it to the upper limit of aneurism. Later we connect the two iliac segments through the two bilateral femoral arteries (figures 5, 6, 7).

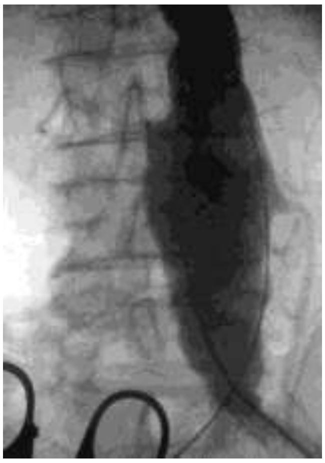


Figure 5: Angiography at the beginning of the procedure

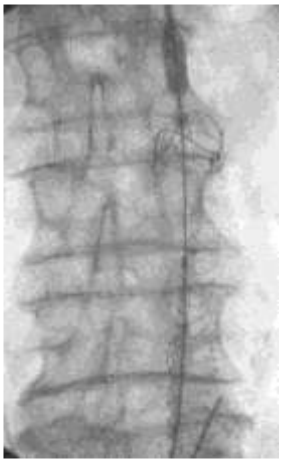


Figure 6: The main body of the stent

Figure 7: The two iliac segments of Anaconda system

The final arteriography shows the correct position of the endoprosthesis, with no type I endoleak and normal aorto-bifemoral blood flux. In the end of the procedure we close the pockets with no important blood leaking and no vascular stenosis. After 48 h we eliminate the drainage. Antiagregation and flux therapy is introduced: Aspenter 75 mg/day and Pentoxiretard 400 mg, 2 times/day.

72h after the intervention the patient is leaving the hospital with good blood circulation to the inferior members (distal pulses present similar to those before the procedure). 4 weeks after the intervention the patient will be reexamed with CT scan.

Conclusions

The endovascular prosthesis is a modern alternative to the classical surgery for the therapy of abdominal aorta aneurisms. There are limits of this procedure: dimensions of the aneurism, the caliber of vessels we want to use, preexistence of ilio-femoral occlusive disease. The benefits of this therapy (less perioperation stress, rapid recovery, cure of patients who can not be treated with classical surgery) are balanced by some disadvantages (highly costs, perioperational risks such as endoleak which makes necessary to convert to open surgery, exact preestimation of the lesions for a compatible prosthesis, exposure to high radiation doses, exposure to radiocontrast substances).

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Abdominal aortic aneurisms treatment – new devices for endovascular treatment*)

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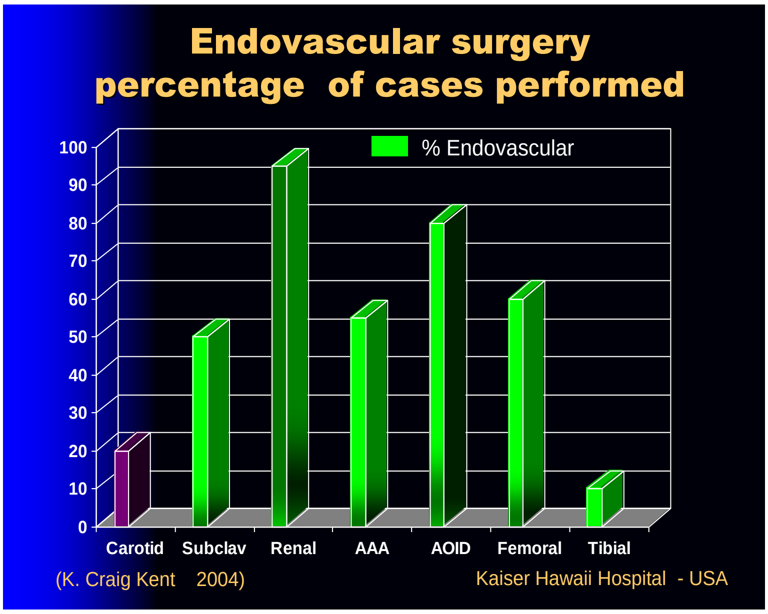
EVAR (*endovascular aortic repair*) offers an important new alternative to open surgical procedures. Reported mortality rates after EVAR are between 0 and 5%.

Long term reports are not available, but mid term follow-up of EVAR reveals an incidence of re-interventions between 10 and 20% and a rate of late rupture of between 0.5 and 1.5%/year (8, 9). The percentage of endovascular repair for AAA in Kaiser Hawaii Hospital-USA was in 2004 - 50% of the surgical activity (Table 1).

Table 1: the most used devices in clinical practice.



*) Romanian Journal of Cardiovascular Surgery - 2008, vol. 7, no. 4, pp. 235-241

In order to evaluate this new method, there are registries for Evar (retrospective): RETA, UK, 1996; Eurostar, 1996; the lifeline registry, USA, 1998. There are also randomized, controlled, multicentered trials: Evar1, 1999; Evar2, initiated also in 1999 and Dream, 2000. The diagnostic and patient selection is very important: we use Echo2D+Doppler, SpiralCT+/-3D reconstruction and angiography.

Endoleaks and graft failure continue to be challenges technological innovations must solve. Until solutions for these problems are found, Evar remains an imperfect long-term treatment and requires regular life-long graft surveillance. Based on the available evidence, Evar is an appropriate treatment for selected patients, especially those at high risk for open surgical repair. The benefits of this therapy (less perioperation stress, rapid recovery, cure of patients who cannot be treated with classical surgery) are balanced by some disadvantages (highly costs, perioperational risks such as endoleak, wich makes necessary to convert to open surgery, exact pre-estimation of the lesions for a compatible prosthesis, exposure to high radiation doses, exposure to radiocontrast substances).

There are limits of this procedure: dimensions of the aneurism, the caliber of vessels we want to use, preexistence of ilio-femoral occlusive disease. Table 2 shows the devices the most used in clinical practice. Figure 1 shows the endografts configuration.

Table 2

Endograft characteristics

Device	Material	Configu ration	Deployment	Fixation	Aortic graft diameters	Iliac graft diameters	Supra-renal stent
Zenith (cook)	Polyester	Modular	Self-expanding	Compression-fit and barbs	22-36	8-24	Yes
Talent (Medtronic)	Polyester	Modular	Self-expanding	Compression-fit	24-34	8-24	Yes
Excluder (Gore)	ePTFE	Modular	Self-expanding	Compression-fit and anchors	23/26/28.5	12-14.5	No
Anaconda (Terumo)	Twilleave	Modular	Self-expanding	Compression-fit and hooks	19.5-34	9-18	No
Powerlink (Edwards Lifescineces)	ePTFE	Uni-piece	Self-expanding	Compression-fit	25/28	16	*Optional*

The Endologix Powerlink system is a one piece bifurcated graft composed of PTFE supported by nitinol. The one-piece design eliminates the risk of endoleaks seen at attachment sites in modular devices.

In addition, the frame is composed of a self-expanding non nitinol wire, which eliminates the need for sutures to hold individual stents in place.

The graft is a thin-walled PTFE, which may allow for downsizing of the delivery system. The PTFE fabric is sewn to the stents only at the proximal and the distal ends of the device. This allows the fabric to move off the endoskeleton (1).

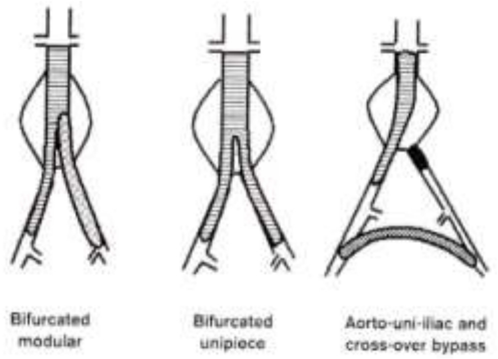


Figure 1

Figure 2: Powerlink® system with infrarenal extension and iliac extension.

Having the possibility for endovascular treatment, spiral CT was necessary for a better analysis of dimensions and shape of aneurisms. The results were similarly with plain CT scan (Figure 3).

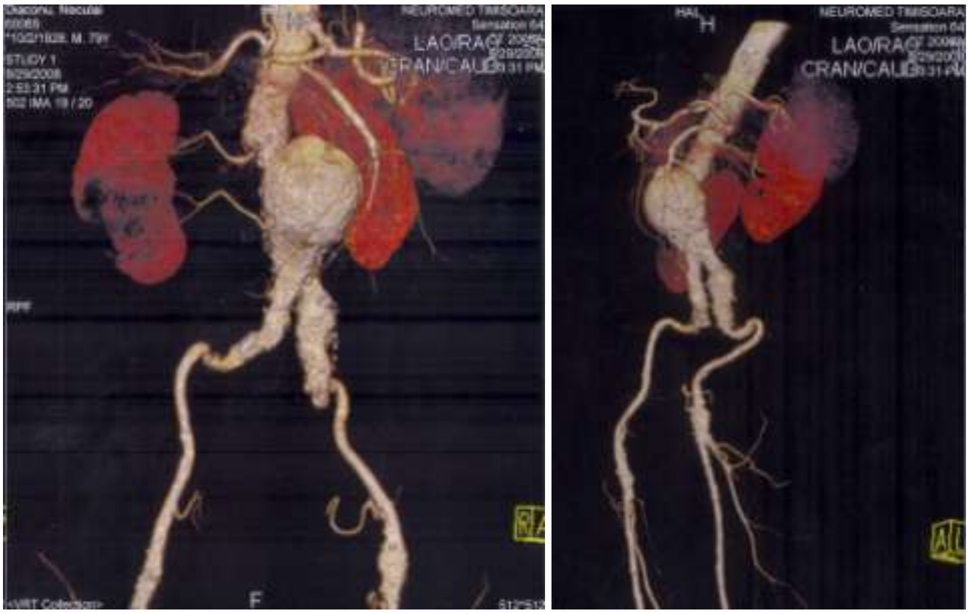


Figure 3: Abdominal multislice CTof a subrenal AAA with bilateral iliac extensions.

Having these results we've decided for the endovascular resection of the aneurism, using as stent graft the endovascular Powerlink® endoprosthesis from endologix (Figure 4, 5).

Under peridural anesthesia, we have exposed the commune femoral arteries bilaterally and their branches and isolate them, we have controled the hemostasis to the punction points, with pockets created with monophilament 4-0 sutures, securized with tourniquets.

After a control angiography, who also indicates the exact position of renal arteries, we introduce through left femoral artery the endoprosthesis and we fix it to the bifurcation of the aorta. Later we connect the aortic extension, just under the origin of the renal arteries (Figure 6, 7, 8). This is done in order to avoid neck dilatation with type one endoleak and distal migration.

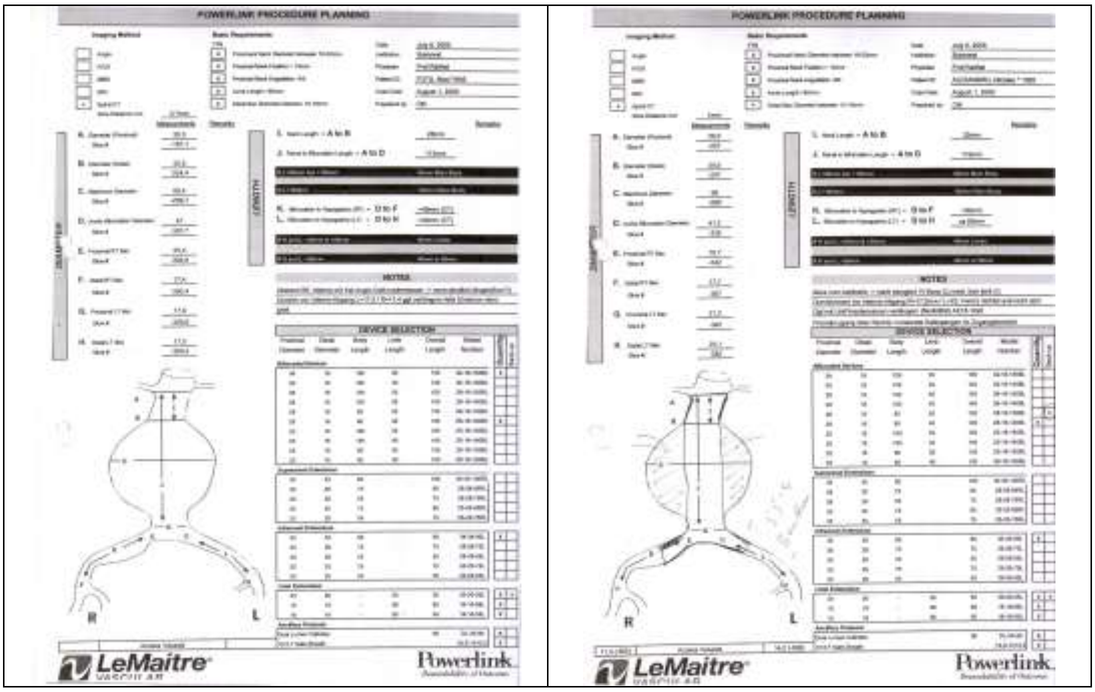


Figure 4: Measurements for endovascular treatment.

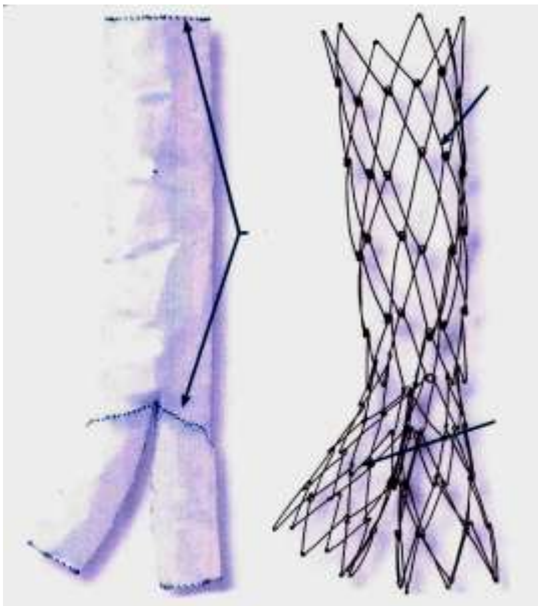


Figure 5: Endologix endograft for infrarenal abdominal aortic aneurysm therapy.

Figure 6: The proximal extension.

Figure 7: The main body of the stent

Figure 8: The two iliac segments of Powerlink® system

The final arteriography shows the correct position of the endoprosthesis, with no type I endoleak and normal aorto-bifemoral blood flux. In the end of the procedure we close the pockets with no important blood leaking and no vascular stenosis.

After 48h we eliminate the drainage. Antiagregation and flux therapy is introduced: Aspenter 75mg/day and Pentoxiretard 400mg, 2 times/day.

72h after the intervention the patients are leaving the hospital with good blood circulation to the inferior members (distal pulses present similar to those before the procedure). 4 weeks after the intervention the patients will be reexamined with CT scan (Figure 9, next page).

Conclusions

The endovascular treatment is a modern alternative to the classical surgery for the therapy of abdominal aorta aneurisms. Multislice CT is the imaging modality of choice when assessing patient suitability. A relatively high proportion of cases (up to 80 %) will be anatomically suitable for EVAR. Using a range of systems will allow the best option to be used for each case.

Figure 9: CT scan at one month – no endoleaks.

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Endoluminal stent graft for the thoracic aortic lesions: The EndoFit System*)

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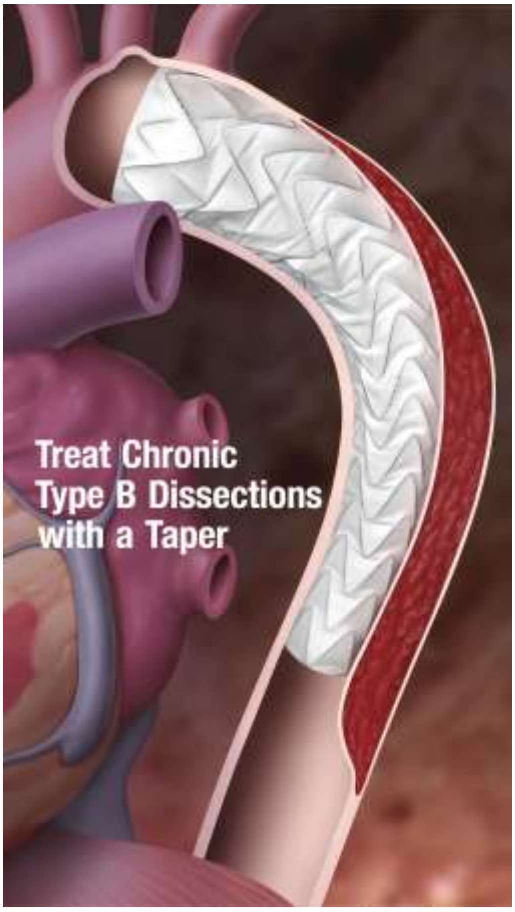

Experience: Nürnberg South Hospital initiated thoracic endovascular aneurysm repair (TEVAR) since 1995, and totally we have 202 cases of TEVAR by the end of 2006. Regarding the devices, our experience includes all the CE-approved and FDA-approved devices available on the German market: Gore TAG, Medtronic Talent, Cook TX2 and LeMaitre Vascular EndoFit. Regarding LeMaitre Vascular EndoFit, we have 52 cases in total since Dec. 2005. Among the 52 cases of thoracic aortic lesions treated with EndoFit, 27 cases were thoracic atherosclerotic aneurysm (TAA) and 25 cases were thoracic aortic dissection (aneurysm) (TAD), there were 40 males and 12 females, the mean age of TAA and TAD patients were 69.3 years old and 66.7 years old respectively. The mean maximal diameter of TAA was 6.8 cm, and the mean maximal diameter of TAD was 5.8 cm. 40 cases were elective therapy and 12 cases were emergent treatment for ruptured or pending ruptured lesions (7 cases of TAA and 5 cases of TAD). For the locations of the aortic lesions, 28 cases involved or very close to the supra-arch vessel(s) or the ascending aorta, 15 cases located in the descending aorta and 9

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cases involved visceral arteries (type IV thoraco-abdominal aortic aneurysm). For the challenging aortic aneurysm involving or very close to the vessels, for a total of 37 cases we performed six different kinds of debranching techniques before TEVA to gain sufficient proximal or distal landing zone for the stent graft and to preserve the target organ blood perfusion. All the cases were carried out in the OR with supervision of a mobile DSA. We prefer 15-20% and 10-15% oversizing of the stent graft for the corresponding diameter of TAA and TAD respectively. And for chronic TAD and debranched type IV thoraco-abdominal aortic aneurysm, we prefer tapered stent-graft. If the stent graft should be implanted proximal to the brachiocephalic truck after debranching, we prefer cartridge loaded stent graft to prevent perforation of the left ventricle and disturbance of the aortic valve.

Our intra-operative results demonstrated 100% of technical success (52/52). Averagely 1.8 (1-3) stent grafts were implanted for each patient. 13 cases had taped stent graft. There were 4 cases of intra-operative proximal endoleak and all of them were remedied by proximal cuff or PTA. One emergent case died on table because of aneurysm rupture and another died on table because of heart arrest. During the 1 week to 1 year follow-up, there was 1 case suffered from paraplegia that had infrarenal AAA tubing before TEVAR, there was 0 case of post-TEVAR rupture. There was one case suffered from proximal endoleak and was cured by proximal cuff.

Clinical comments: Analysis of the current data suggests that the use of LeMaitre Vascular EnodFit stent graft system in TEVAR proved safe and effective. The delivery system is flexible for passing through kinking iliac artery and kinking aortic arch, both the straight and tapered stent grafts provide multiple size choice for either diameter or length. The ePTFE lined inside and outside stent graft proved flexible and easy to deploy. The cartridge loaded stent grafts can be implanted several times via the staying introducer with only one time insertion of the delivery system. Furthermore, the cartridge loaded system is optional for supra-arch debranched thoracic lesions, which can avoid interference of the aortic valve and perforation of the left ventricle.

Developments in Postinterventional Surveillance of EVAR for AAA*)

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Abstract

The present paper proposed to gather and underline the new developments and evidence at hand in the management of abdominal aortic aneurysms (AAA), focusing especially on the endovascular treatment (EVAR) and the surveillance of EVAR performed for AAA. The intention was to identify the existing controversies, identify a problem and give way to new research possibilities in this direction.

Key-words: *abdominal aortic aneurysm, EVAR, postinterventional surveillance, contrast-enhanced ultrasound, contrast CT, endoproshtesis*

The management of infrarenal abdominal aortic aneurysms (AAA) has changed radically over the last decades since the introduction of the endovascular treatment by Juan Parodi in 1992. Applied with caution and scepticism in the past, due to the lack of long-term results, today is gaining ground given the new solid evidence at hand. A study published in November 2011 identifies the rate of endovascular treatment for AAA in different countries during 2005-2009 **(Figure 1)**, whose prospective data were included in the VASCUNET database [1].

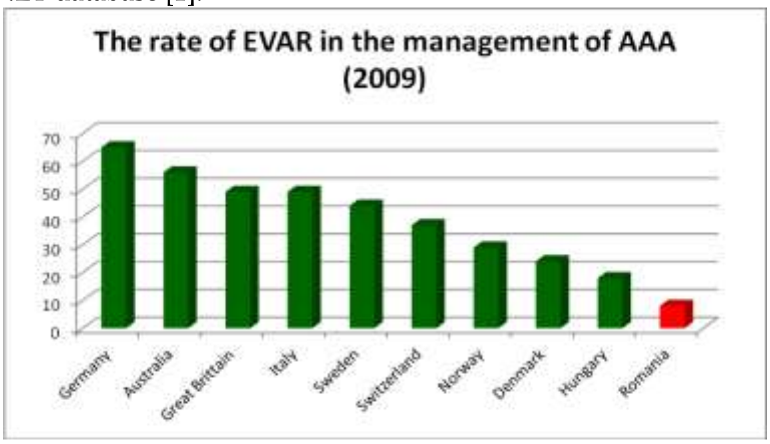

Figure 1: The rate of EVAR in the management of AAA in different counties, between 2005 and 2009 [1]

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The study shows a rapid and extensive implementation of the endovascular treatment, with the advent of studies with favourable results in this direction. The endovascular treatment rate in Romania was illustrated for comparative purposes.

EVAR, in addition to the advantage of being a minimally invasive method and as such preferred by the patients, has many proven benefits compared with traditional open surgery: low rate of peri- and postoperative mortality and morbidity, shorter hospital stay, significantly reduced intraoperative blood loss and faster recovery [2, 3, 4].

Results of several controlled, randomized studies are published today, which highlight the many benefits of this minimally invasive treatment, stressing also its shortcomings and controversies.

The first short-term results of the endovascular treatment appeared after EVAR1 (England), EVAR 2 (England) and DREAM (Netherland) trials, randomising patients diagnosed with infrarenal abdominal aortic aneurysm ≥ 5.5 cm for endovascular (EVAR) or open surgical treatment consisting of an aorto-bifemoral by-pass.[2,5]. EVAR 1 and DREAM trial showed a 2.5 fold reduction in postoperative mortality in the favour of EVAR: 4.6% for open surgery and 1.2% for EVAR (DREAM trial), 4.7% vs. 1.7% (EVAR 1 trial). A recently published trial, the OVER trial (Open versus Endovascular Repair) reported a perioperative mortality of 0.5% for EVAR [6]. The higher peri- and postoperative mortality in older studies might be explained by the use of first-generation endoprostheses, prostheses that have undergone many changes until present, being constantly improved. Currently IV-th generation endoprostheses are available on the market.

The above mentioned studies included infrarenal abdominal aortic aneurysms ≥ 5.5 cm in diameter with a well established reason. The Clinical Practice Guidelines of the European Society for Vascular Surgery on the management of AAA, published in April 2011 sets out a series of recommendations in all aspects of diagnosis and management strategies of AAA (Figure 2, 3 – next page) [7].

There is a consensus that in the case of small aneurysms, with a diameter between 3.0-3.9 cm, the risk of rupture in negligible. Therefore, these aneurysms do not require surgery, supervision by Doppler Ultrasound at regular intervals being sufficient. The management of the AAA with a diameter between 4.0-5.5 was determined by two multicenter, randomised, controlled studies, that compared the natural evolution of these aneurysms versus early intervention: UK Small Aneurysm Trial (UKSAT) and American Aneurysm Detection and Management Study (ADAM) respectively [8, 9] and a smaller study, that compared endovascular treatment versus surveillance, the CAESAR study [10]. The PIVOTAL study including aneurysms with diameters between 4.0-5.0 cm compared the endovascular treatment versus Doppler Ultrasound surveillance [11].

Medium-term results of these studies did not indicate a statistically significant difference in terms of overall mortality at 5 years, the results being similar in the long-term, at 12 years [8, 12]. The rupture rate of the aneurysms was 1% in the surveillance group and the overall mortality rate was 5.6% in the early intervention group.

The results of the above mentioned large studies, UKSAT and ADAM were recently included in the COCHRANE study, that underlines the safety and through this the benefits of the Doppler ultrasound surveillance of the AAA with a diameter between 4.0 and 5.5 cm [13].

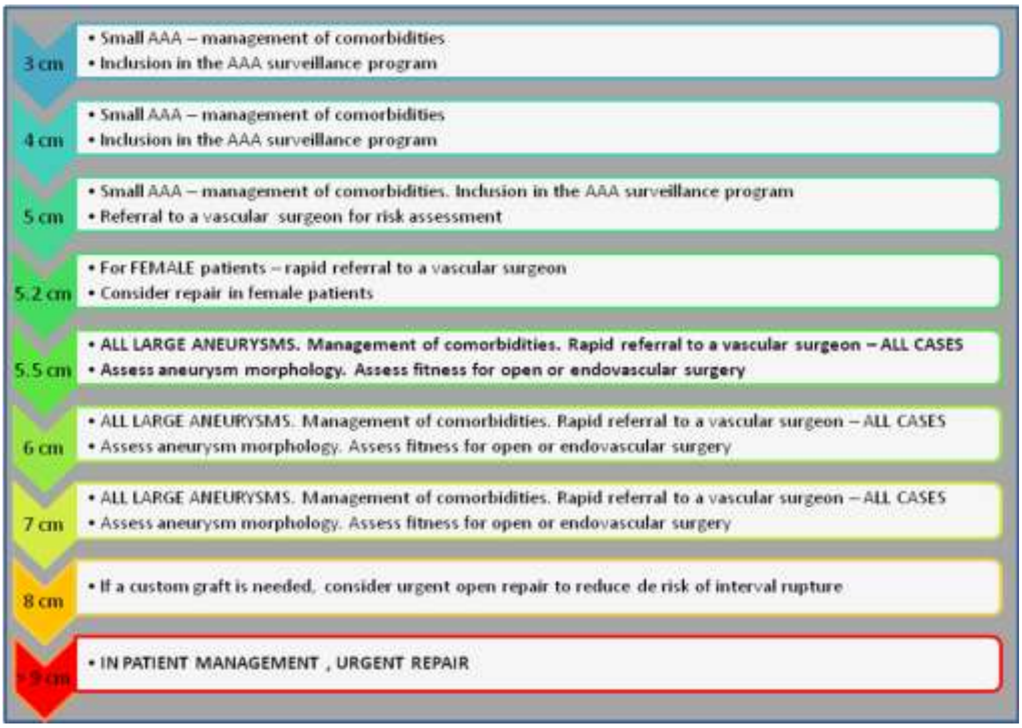

Figure 2: Management strategy of AAA according to the size of the aneurysm
(modified after F.L. Moll et Al. [7])

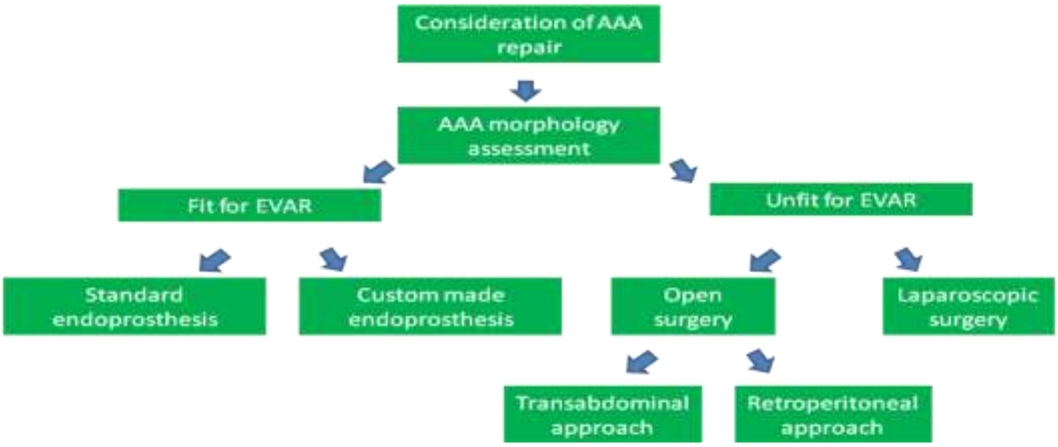

Figure 3: Management of large aneurysms, with a diameter ≥5,5 cm
(modified after F.L.Moll et Al. [7])

A conduct of Doppler Ultrasound surveillance of small aneurysms (4.0-5.5 cm) is safe and recommended for asymptomatic aneurysms. If the aneurysm reaches the 5.5 cm diameter limit, measured by Doppler ultrasound (in male patients), it becomes symptomatic or there is an annual diameter increase of >1cm/year, the patient must be immediately referred for further investigation to the specialised vascular surgery department.

As highlighted, the diameter of the AAA establishes the moment for intervention, but this criteria alone is not enough to establish the indication for the endovascular treatment of the AAA. With new treatment methods new complications occur, requiring further investigations in order to assess the feasibility of the AAA for EVAR. The morphological criteria of the AAA are the ones that can establish or exclude the indication of EVAR. The failure to comply with these criteria, requested also in the instruction manuals of the endoprostheses currently on the market may lead to the increase of the peri- and postoperative complication, reintervention and post-EVAR mortality rate. The minimum requirements in terms of AAA morphology are listed in Table1.

Table 1: Minimal morphological requirements of the AAA for EVAR
(modified after F.L. Moll et Al. [7])

PROXIMAL AORTIC NECK
• Neck diameter >17 mm, < 32 mm
• Angle between the suprarenal aorta and the juxtarenal aorta < 60°
• Neck length >10 mm
• Neck thrombus covering <50% of the proximal neck circumference
• Neck calcification <50% of the proximal neck circumference
AORTIC BIFURCATION
• Aortic bifurcation diameter >20 mm (in case of a bifurcated graft)
ILIAC ARTERIES
• Iliac luminal diameter > 7 mm
• Iliac neck length >15 mm
• Iliac neck diameter <22 mm

The postoperative surveillance of patients with AAA treated by EVAR

There is no controversy about the short-term benefit of EVAR to open surgery, opinions being divided and reserved as the long-term benefits are concerned.

The real benefit of the AAA treatment depends on the impact on the long-term survival of the patients.

The absence of complications such as aneurysm rupture (due to the emergence of endoleaks), infection, aorto-enteric fistula formation or migration of the endoprosthesis should be considered as an indicator of sustainability and long-term therapeutic success of EVAR.

Despite careful selection of patients with AAA considering and respecting the morphological suitability criteria, the choice of appropriate endoprosthesis, operator experience, specific complications can still occur, underlining the necessity of life-long surveillance of the treated patients.

The results of several randomized, controlled studies show a significant post procedural complication rate up to 8 years post EVAR [14, 15]. A recent study considered mandatory a life-long surveillance after EVAR, in order to identify the complications and to plan a possible reintervention [16].

Incomplete aneurysm exclusion with the persistence of blood flow in the aneurysm sac outside the endoprosthesis, defined and described under the term "endoleak" in 1998 by White et al. [17] is the most common complication of EVAR occurring in 10-45% of cases [18]. It is a severe complication because it leads to the repressurization of the aneurysm sac and consequent aneurysm rupture. White differentiated early endoleaks, occurring within 30 days post-EVAR and late endoleaks occurring later than 30 days in the surveillance period. Schlosser et al. [19] showed that endoleaks are the main cause of postinterventional aneurysm rupture, being responsible for 160 out of a total of 235 ruptures of the AAA after EVAR. This result reinforces the need of long term surveillance with an imaging method that can effectively and safely identify this complication.

Four types of endoleak were described Table 2 [17, 20].

Table 2: Classification of endoleaks (modified after F.L. Moll et Al. [7])

Endoleak (Type)	Source of perigraft flow
I.	**Attachment site defects of the endoprosthesis**
A	Proximal end of the stentgraft
B	Distal end of the stentgraft
C	Iliac extension
Endoleak (Type)	**Source of perigraft flow**
II.	**Persistent backflow from patent aortic branches**
A	Simple: from one patent branch
B	Complex: two or more patent branches
III.	**Stentgraft defect – junctional leak, modular disconnect or fabric holes**
IV.	**Stentgraft fabric porosity <30 days after placement**
Endotension	**AAA enlargement with increased intrasac pressure after EVAR without visualized endoleak on delayed contrast CTA**

The most common and discussed is the type 2 endoleak, caused by retrograde flow from aortic side branches into the aneurysm sac, outside the endoprosthesis, such as the inferior mesenteric artery, lumbar arteries or accessory renal arteries. The identification and treatment of this type of endoleak is currently the subject of numerous debates. They may have a benign evolution, with gradual decrease of the aneurysmal sac or may also lead in some cases to pressurization and rupture. Their identification with the currently used imaging methods is frequently hampered by a small retrograde blood flow that is below detection [20].

Another complication of the endovascular treatment is the migration of the endoprosthesis. It is identified as a dislocation of the endoprosthesis with > 10 mm considering the anatomic landmarks established at the time of the intervention. This complication was observed using most of the endoprosthesis types available on the market. Studies that examined the incidence of endoprosthesis migration defined it as a late complication occurring more than 24 months after surgery [21]. The complication may be asymptomatic, being identified at the regular follow-up intervals with different imaging modalities, but it represents a significant risk of late rupture. Several predisposing factors have been identified that can be responsible for the migration: inadequate aneurysm and aneurysm neck morphology (short, <15 mm, angulated neck), faulty technique in the initial fixation of the endoprosthesis, late aneurysm neck dilatation.

In order to avoid this complication new endoprostheses were developed, such as the PowerLink (Endologix, CA, USA) endoprosthesis (Figure 4), accomplished on the principle of "anatomic fixation". Unibody endoprosthesis with two iliac extensions, that when positioned and deployed rests on the iliac bifurcation thus preventing the caudal migration of the device.

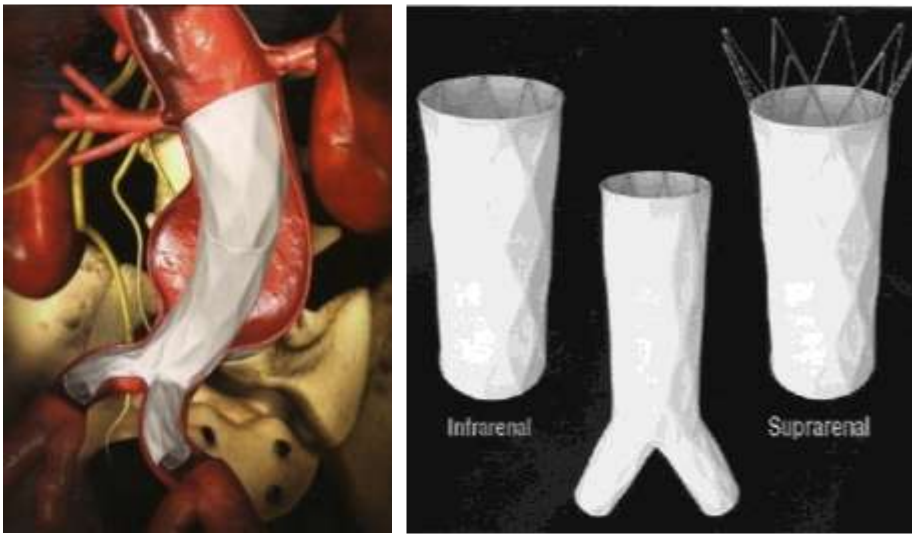

Figure 4: PowerLink Endoprosthesis (Endologix, CA, USA)

Postinterventional imaging methods for the follow-up of EVAR for AAA

During the last years, multiple studies have focused on establishing a protocol of postoperative surveillance of patients with AAA treated by EVAR, without reaching a consensus in this regard [22, 23, 24, 25].

The ideal imaging method should meet several requirements: to be cheap, repeatable, widely available, safe, non-invasive and accurate.

Several imaging methods are available in the current practice for the follow-up of EVAR: Native and Contrast Enhanced Computer Tomography (CT), Colour Doppler Ultrasound (US), Contrast Enhanced Ultrasound, Plain radiography, Angiography and Nuclear Magnetic Resonance (NMR). All have their benefits and limitations.

Iodine Contrast Enhanced CT

The “Gold Standard” imaging method used in current practice for the follow-up of patients with AAA treated by EVAR is Contrast Enhanced CT. The high resolution images and data obtained with this method make it possible to measure with great accuracy the dimensions of the excluded aneurysm sac.

Some studies show that CT with contrast can detect endoleaks with a higher sensitivity (Se) and specificity (Sp) that conventional angiography.

Identification of all type endoleaks:

- Contrast-enhanced CT examination: Se 92%, Sp 90%
- Angiography: Se 63%, Sp 77%

Given the fact, that in the case of endoleaks the blood flow intensity varies, they can be detected at different time intervals after the injection of the iodine contrast. For this reason a multiphase CT protocol was recommended, with image acquisition prior to contrast administration, immediately after contrast administration in the arterial phase and in the delayed postcontrast phase. The recorded precontrast images can be useful in differentiating the aortic wall calcifications from intraluminal thrombus or endoleak, thereby reducing the number of false positive results.

Concerns regarding this protocol refer to the high dose of radiation involved, the nephrotoxicity of the administrated iodinated contrast [26] and the high cost of the method.

The radiation dose calculated for one examination is around 15 mSv, although this value may change depending on the device used. The patients included in the follow-up program, assessed at 30 days, 3 months, 6 months and then annually have an accumulated exposure of 50-100 mSv, a dose that has been identified as presenting high risk for cancer [27]. Limiting the exposure to ionizing radiation by reducing the examination numbers or by replacing the CT examination with other imaging modalities would decrease this risk.

Another study evaluated the risk of developing nephropathy due to the repeatedly administered contrast agent. The results showed an incidence of 11% for renal injury and a mortality of 0.6% after repeated CT examinations.

Another disadvantage of the CT examination is that although the examination may reveal the presence of the endoleak, it often fails to specify its type and exact source of the persistent blood flow. For this reason Contrast-enhanced CT cannot be applied as an unique method of surveillance of patients with AAA treated by EVAR.

Colour Doppler Ultrasound

Ultrasound imaging is a method commonly used in the screening of abdominal aortic aneurysms. Some investigators have stressed the importance and usefulness of this method in the postinterventional surveillance of patients with AAA treated by EVAR. It has the advantage of being widely available, safe, cost effective and well tolerated by the patients. The disadvantages of the method include the low quality of the obtained images in obese patients and investigator dependence. Another drawback is that the follow-up protocols vary from one institution to another and from one examiner to the other influencing the reported global results. Numerous studies concluded that there is an urgent need to standardise the US examination technique in order to reduce the variability in the quality of the examination.

Colour Doppler US failed to demonstrate superiority over CT, but in some cases proved equal to it. It is able to detect all known complications of EVAR, particularly the controversial endoleaks. Of course there remains the problem of variations between examination protocols, techniques and diagnostic criteria used. The reported sensitivity of the US examination in the literature varies between 25% and 100%. For the detected endoleaks, Doppler US examination can provide a far better level of characterization than other imaging techniques using spectral Doppler analysis. The type II endoleaks with bidirectional flow, low flow and speed are of interest in this respect. Most of these endoleaks are detected by US examination but not by CT or angiography.

A recent meta-analysis of Mirza et Al. [25] including 21 studies that compared Contrast CT examination with Colour Doppler Ultrasound (DUS) and Contrast-enhanced Ultrasound (CEUS) reported for DUS a sensitivity and specificity in detecting all type endoleaks of 77% and 94% respectively.

Another limitation of the US examination is the inability to provide information about the status and the position of the endoprosthesis. For this reason neither DUS can be considered as a unique method for postinterventional surveillance of patients with AAA treated by EVAR.

Contrast-enhanced Ultrasound

The introduction of Contrast-enhanced Ultrasound examination in the EVAR surveillance raised once again the hope for the possibility to replace the Contrast CT, but there is not enough evidence available in order to establish a clear surveillance protocol. The advantage over the Contrast CT is that the contrast agent used for the US examination is not nephrotoxic and its repeated use does not pose a risk to the patient.

In some cases the accuracy of CEUS in detecting endoleaks proved to be superior to CT examination and NMR examination also.

The results of the meta-analysis of Mirza et al. [25] showed a sensitivity and specificity in the detection of endoleaks of 98% and 88% respectively.

The limitation of CEUS are the same as for DUS.

Nuclear Magnetic Resonance Imaging (NMR)

NMR is a non-invasive imaging method based on intravenous injection of gadolinium chelates (0.1 mmol/kg). The imaging performance of this method depends largely on the metallic composition of the stent-graft used. Several studies, including patients with nitinol or elgiloy stent-grafts, resulted a sensitivity and specificity of NMR at least equal to that of Contrast CT examination. The identification of type II endoleaks with NMR has a Se of 100% and a Sp of 82% according to recent studies [28].

Regarding the disadvantages, beyond the limitations presented by the metallic composition of the stent-graft, we have to mention the absolute contraindications of the NMR examination, such as the presence of previously implanted metal devices: Pace-makers, mechanical heart valves, intraocular ferromagnetic foreign bodies, vascular clips placed at different levels (ex. Aorto-coronary by-pass with the great saphenous vein or internal mammary artery).

There are also a few technical limitations such as poor visualization of the calcified aortic wall and difficulty in the exact measuring of the aneurysm diameter due to the surrounding fat.

Plain radiography

Even with so many advanced imaging modalities at hand, plain radiography remains a useful technique for postinterventional surveillance of EVAR. X-ray is considered by some authors to be superior to CT in providing information about the conformation and possible migration or deformation of the endoprosthesis [29].

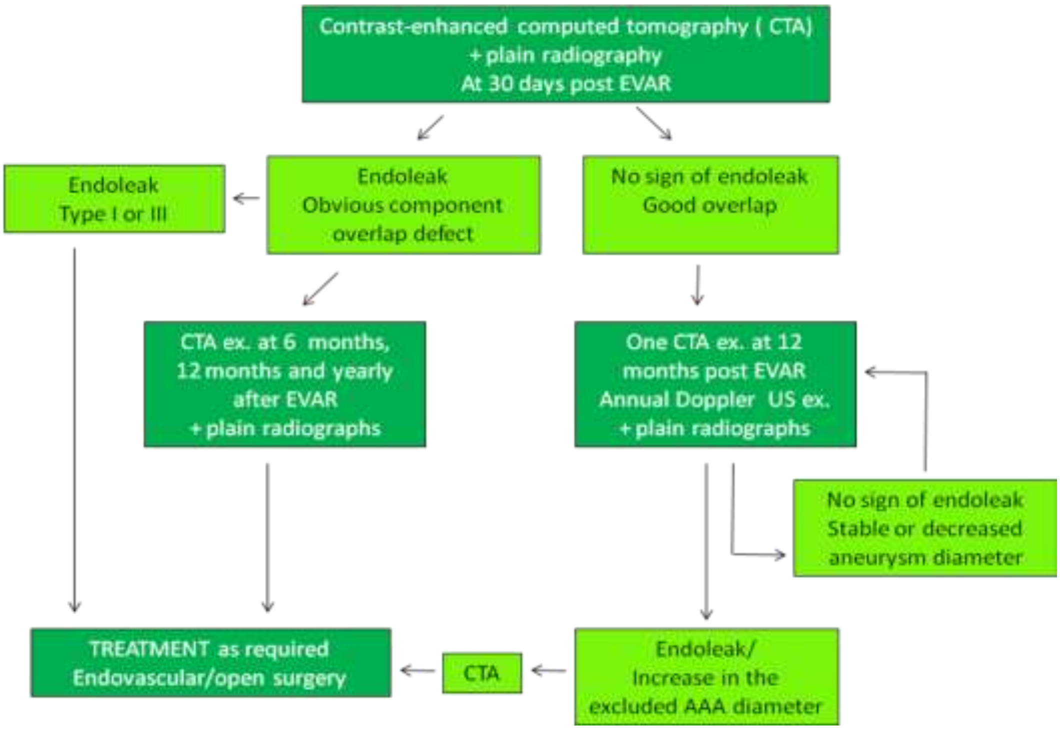

Figure 5: Simplified surveillance protocol of patients with AAA treated by EVAR
(modified after F.L. Moll et Al. [7])

The antero-posterior and latero-lateral incidence can accurately detect migration and component separation and the oblique incidence is useful in detecting wire fractures of the stent-graft.

The disadvantage of the X-ray is that it provides no information regarding the excluded aneurysm sac size, failing also to identify the possible endoleaks.

Based on the evidence currently available the European Society for Vascular Surgery issued a guideline, consisting of a set of recommendations for the management of AAA, along with postinterventional follow-up recommendations for patients with AAA treated by EVAR [7].

The final conclusion of this guideline is that there is still a need for further research in this direction, a need to optimise the use of DUS, CEUS and CT by establishing a safe and effective, standardized surveillance protocol of patients with AAA treated by EVAR.

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Thoracic and thoraco-abdominal aortic aneurysms repair without mortality in high risk patients*)

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Abstract

Objective: *to evaluate our results of open surgery of lower thoracic aorta in high risk patients.*

Methods: *Between 1986-2005, 16 patients underwent replacement of the descending or thoraco-abdominal aorta; two patients carry out twice at 2 years interval. Five patients were women. The mean age of the patients was 57 years (range 29-83 years). The adjuncts used in this patients included perioperative cerebrospinal fluid drainage, temporary passive shunt for thoracic aneurysm, normovolemic hemodilution, cell-saver, full cardiac monitoring including trans-oesophageal echography, -blocker. Intercostal arteries were implanted when possible in distal or proximal anastomosis. There were 4 operative repairs for type II, -2 for type III and 12 types IV for thoraco-abdominal aneurysm, Crawford classification. Two patients had prior aortic repair (one AAA and one thoraco-abdominal aneurysm type IV). Thirty-day follow-up was complete for all the patients. Concurrent medical problems included chronic obstructive lung disease in 7, inferior right lobectomie in 1 patient, a history of coronary artery disease in 5 patients, renal insufficiency (creatinemie= 39mg/l) in 2 patients, HTA for all the patients, neoplasm 2 patients. Visceral arteries were reimplantet in 14 patients (82%) and renal arteries in 13 patients (76%). Fast track anaesthesia was used for all patients.*

Results: *early mortality was 0%. 1 patient (emergency case with mycotic aneurysm) had a paraparesis. Transitory renal failure occurred in 2 patients (11%). Intubation after surgery - 0 patients. Reoperation for postoperative bleeding: 0%.*

Conclusions: *thoraco-abdominal and thoracic aneurysm surgery can be accomplished with low mortality and morbidity using a uniform approach of modern adjuncts and precise anaesthetics and operative management.*

Introduction

Results of thoraco-abdominal aneurysm surgery have improved over the last two decades. Nevertheless, patients undergoing this kind of surgery still represent a significant challenge for all physicians and medical personnel involved in their care. Postoperative complications including spinal cord injury, renal failure, respiratory insufficiency, bleeding and cardiac failure continue to be a major problem. We have used

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the adjunct that has included cerebrospinal fluid drainage, temporary passive shunt, and moderate hypothermia.

The aim of this analysis was to define a uniform approach during repairs of the thoraco-abdominal aorta.

Material and methods

This study was designed as a single team experience, a retrospective approach.

Patients

Between 1986 and 2005, 16 patients underwent replacement of the descending or thoraco-abdominal aorta; two patients carry out twice at 2 years interval. Five patients were women. The mean age of the patients was 57 years (range 29-83 years).

Table 1: Preoperative, intraoperative variables used in the analysis

N° of patients	**16**
Total operations	**18**
Mortality	**0**
Average age	**57 years** (range 29 – 83)
Female	**5**
Male	**11**
Inferior right lobectomie	**1**
TAA II (Thorecoabdominal aneurysm type II)	**4**
TAA III (Thorecoabdominal aneurysm type III)	**2**
TAA IV (Thorecoabdominal aneurysm type IV)	**10**
Inferior right lobectomie	**1**
COPD (Chronic obstructive pulmonary disease)	**7**
HTA (Arterial hypertension)	**16**
CAD (Coronary artery disease)	**5**
ICA reimplant (Intercostal arteries reimplant)	**2**
Visceral arteries reimplant	**16**
Renal Dysfunction	**2**
Prior AAA	**1**
Prior TAA	**1**
Neoplasm history	**2**

In this study we analyzed the preoperative characteristics including age, gender, hypertension, chronic obstructive pulmonary disease, renal failure, coronary artery disease, and neoplasm history and aneurysm extent. Repair was considered elective when the patient underwent scheduled admission to the hospital for treatment of the aneurismal process. Intra-operative data included aortic cross clamp time, intercostals artery reattachment, and the adjunct used. Adjunct use referred to the combined use of cerebrospinal fluid drainage, passive shunt, and moderate passive hypothermia. Postoperative neurological deficit was defined as paraplegia or paraparesis related to spinal cod ischemia or infarction. Preoperative renal dysfunction was defined as having a serum creatinine greater than 2.0 mg/%, a previous history of renal failure or insufficiency.

All patients are monitored as per our protocol of this kind of procedure including: ECG, pulse oxymeter, temperature probes, hemodilution, selective intubation, a invasive radial artery, cell-sever, transesophageal echography (TEE). Heparin was administrated 50 UI/Kg before clamping.

Volume management of aortic de-clamping was made by anticipating major volume shifts while clamping and de-clamping and used vasopressors. Cerebrospinal fluid pressure is maintained below 10 mmHg throughout the surgery and 3 days postoperatively, using a lumbar drain placed percutaneously in the third or fourth lumbar space immediately prior to surgery. To minimize the ischemic time to spinal cord, viscera and kidneys, we use sequential cross-clamping technique. Other adjunctive measures include the use of visceral and renal perfusion with crystalloid solution to lower the renal temperature. To achieves distal aortic perfusion we used in two cases passive shunt with prosthesis Goretex N°12.

Surgical procedure

The surgical procedure was previsiously reported and therefore only roughly be summarized here. (3, 4) A left sided thoraco-phreno-laparatomy following preparation of the aorta was the standard approach. We prefer circumferential division of the diaphragm through its muscular portion, leaving a few centimeters attached laterally to the chest wall and complete exposure of the thoraco-abdominal aorta (13). We used in two patients a partial bypass between the proximal and distal aorta. Balloon catheters were used routinely to control back bleeding during the procedure. Visceral and intercostals patches were reimplanted to a small opening in the graft using a continuous suture. Revascularization of the left renal artery often involved a separate bypass. The aneurysm sac was closed over the completed repair, to the extend allowed by the anatomy. We use staged aortic cross clamping, repair with sealed grafts from proximal to distal.

Major postoperative complications were recorded. Bleeding was defined as postoperative blood loss requiring re-operation. Respiratory failure was defined as patient requiring respiratory support after extubation.

Thirty-day follow-up was complete for all the patients.

Cerebral Spinal Fluid Drainage: the perfusion pressure of the spinal cord is defined as the difference between the anterior spinal artery pressure and the cerebrospinal fluid (CSF) pressure (or venous pressure, whichever is greater). Aortic cross-clamping induces a decrease of distal aortic pressure and there-fore in a lower anterior spinal artery pressure. Volume shifts and proximal hypertension lead to increased CSF pressure. As result of these changes, spinal artery blood flow is decreased and the patient is consequently a higher risk for paraplegia. CSF drainage has been associated with greater spinal cord perfusion pressure, increased spinal cord blood flow, diminished reperfusion hyperemia, and decreased incidence of neurological injuries (2).

Results

The 30 day survival rate was 100%. The incidence of neurological deficit was 5.5% (1 of 18). Paraplegia was in thoraco-abdominal aortic replacement in a patient with mycotic aneurysm.

Table 2: Intraoperative variables used in the analysis

Clampage Time	**32 (range 28-37)**
Passive shunt	**2**
Adjunct: cerebral spinal fluid drainage	**18**
Fast Track	**18**
Auto transfusion	**18**
Cell-sever	**18**
Blood Loss	**2100ml (range 600-3500)**
Etiology	**Degenerative 17; Mycotic 1**
Dialysis	**0**
Reoperation for bleeding	**0**
Reintubation	**0**
N° Neurologic deficit	**1**
Mortality	**0**

Discussions

Few years ago surgical results of TAA aneurysm repair were less satisfactory than are today. A downward trend in complications rates and mortality is generally observed. The introduction of several adjuncts is probably associated with this decrease.

In our series we notice a low of the incidence of paraplegia and paraparesis (1 patient). Our current strategy to prevent spinal damage in elective patients consists of the use cerebral spinal fluid drainage (CSFD), moderate permissive hypothermia (32°C), liberal reattachment of intercostals and /or lumbar arteries (especially those between T8 and L2). This multimodality approach is based on findings of other surgeons with a vast experience and is supported by own results (3, 4, 6).

We do not identify preoperatively the artery of Adamkiewicz by angiography any more. Furthermore we think that this identification does not prevent spinal cord problems (1). It is not a surprise to us that a previous chronic dissection is a protecting factor against spinal cord deficit because in these patient categories more intercostals arteries are patent. As a consequence of our strategy, there are reimplanted in a higher number as compared to patients with atherosclerotic aneurysms (5). This necessitates underlayed protective interventions such as the immediate drainage of spinal fluid and accelerated reimplantation and reperfusion of intercostal/lumbar vessels. Coselli described a reduction of paraplegia from 13 to 2.6% in thoraco-abdominal aneurysm repair using these adjuncts (11). When comparing our rate of paraplegia of 5% during the recent years with the results of Coselli it has taken into account that in our series there were only 18 TAA repairs.

The incidence of respiratory failure seems particularly high and the mortality associated with this complication was significant in the TAA. We prefer a circumferential division of the diaphragm through its muscular portion, leaving a few centimeters attached laterally to the chest wall. However, radial division of the diaphragm will irrevocably paralyze the left hemidiaphragm and contributes to postoperative respiratory compromise. Very important for fast-track and pulmonary function is volume management by anticipating major volume shifts while clamping or declamping.

Pulmonary pressures may not represent a good volume indicator. Black flow of hypoxemic blood loaded with CO2 and acid compounds increases after release of the clamp and may result in pulmonary vasoconstriction. In anticipation of acute pulmonary vasoconstriction, we initiated hyperventilation a few minutes prior to unclamping.

Cardiac complications are among the most common causes leading to an increase of the mortality. All patients have an accurate assessment of the cardiac function to guide appropriate preoperative preparation. Very important is the management of sequential aortic cross-clamping.

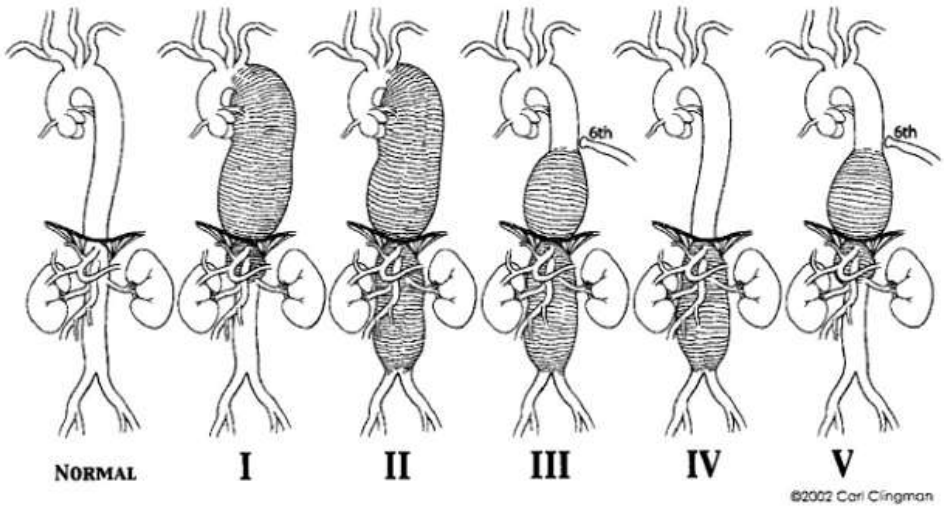

Figure 1: Normal thoraco-abdominal aorta and aneurysm classification.
Extent I, *distal to the left subclavian artery to above the renal arteries.*
Extent II, *distal to the left subclavian artery to below the renal arteries.*
Extent III, *from the sixth intercostal space to below the renal arteries.*
Extent IV, *from the twelfth intercostal space to below the renal arteries (total abdominal aortic aneurysm).*
Extent V, *below the sixth intercostal space to just above the renal arteries.*

The degree of hemodynamic stress will vary depending the patients condition, the type of TAA aneurysm (*classification of Crawford I-IV*), the etiology of the TAAA, the location of the aortic cross-clamp, the volume status of the patient, and the surgical technique used (only clamp, partial or complete shunt, bypass). The anesthesiologist has to take all above into consideration and anticipate upcoming changes. The different techniques will require different approaches regarding volume management and pharmacological treatment, including vasoconstrictors prior to declamping (7).

Peroperative hemorrhage can occur from technical mishaps and from dilutional coagulopathy caused by excessive blood turnover, and previously were an important source of early mortality. Coselli documented that blood and plasma transfusions increased with use of partial cardiopulmonary bypass. We use a low dose of heparin, selective bypass, and very strictly control of the blood turnover. Regardless of whether the mechanism of coagulopathic bleeding is hepatic ischemia, clinical observations suggest that minimizing mesenteric ischemia is critical in avoiding coagulopathic bleeding (8, 9, 12).

The technique of reconstruction of the intercostals vessels is using of a long beveled suture line in a region of a proximal or distal aortic anastomosis, when it is possible. Since we have the protective effect of cerebral spinal fluid drainage, there is no urgency to re-establish intercostal blood flow. Another technique is an inclusion button anastomosis, when the anatomy of the region imposes this approach.

Perioperative renal insufficiency increased five-fold the operative mortality(14). The most important maneuver to minimizing the risk of postoperative renal failure is minimizing renal ischemic time. We use a sequential clamping technique so that the renal arteries can be perfused during construction of the proximal aortic anastomosis and selective hypothermic renal artery perfusion. The most common method of visceral/renal reconstruction, which has been applied in the majority of our cases, is a single inclusion button to encompass the origins of the celiac, superior mesenteric, and right renal arteries. Just prior to completion of this suture line, backbleeding and patency of the celiac, superior mesenteric and right renal arteries are verified. Reconstruction of the left renal artery is accomplished with a separate sidearm graft.

This study must be viewed with certain limitations. This report is a retrospective analysis and must accept its inherent limitations. Our analysis of survival emphasized the importance of selective operative repair and the group is composed only 18 operations.

In conclusion, repair of TAA aneurysm is a complex procedure, which requires use of adjuncts that attempt to minimize postoperative organ dysfunction. A uniform method to repair this complex aneurysm should include spinal drainage, passive shunt, intercostal revascularization, permissive hypothermia, modest heparinization, and complete repair. This approach is associated with good outcomes for all electives cases.

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Subrenal aortic aneurisms: open surgical treatment vs endovascular*)

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EVAR (*endovascular aneurysm repair*) offers an important new alternative to open surgical procedures. This method was introduced by Parodi in the early 1990s, with a device composed by a Dacron graft and a Palmaz stent. Since the first use, the endovascular treatment of AAA has greatly expanded, and more than 50000 devices have now been implanted (9). This technique is curently being evaluated in several multi-center randomised trials in Europe and the USA.

However, the current treatment for AAA remains the transabdominal open surgical approach and replacement of the aneurysmal aorta by a prosthesis. Open repair involves a large laparatomy incision, cross-clamping of the aorta for at least 30 min. and a period of postischemic reperfusion.All of these procedures contribute to the 4-12% elective mortality rate in patients undergoing open repair (5). In addition, many patients with aneurysms are elderly with significant comorbidities, wich may preclude open repair.

What are the advantages of EVAR?

The procedure is less invasive; it has lower perioperative and medium term mortality. It reduces operating time, blood transfusions, intensive care requirements and length of hospital stay. Reported mortality rates after Evar are between 0 and 5% (5).

There are also disadvantages: reintervention rate for Evar are significantely higher than for open repair. Long term reports are not available, but mid term follow-up of Evar reveals an incidence of re-interventions between 10 and 20% and a rate of late rupture of between 0, 5 and 1, 5%/year (9). The percentage of endovascular repair for AAA in Kaiser Hawaii Hospital-USA was in 2004 - 50% of the surgical activity (Figure 1) (3).

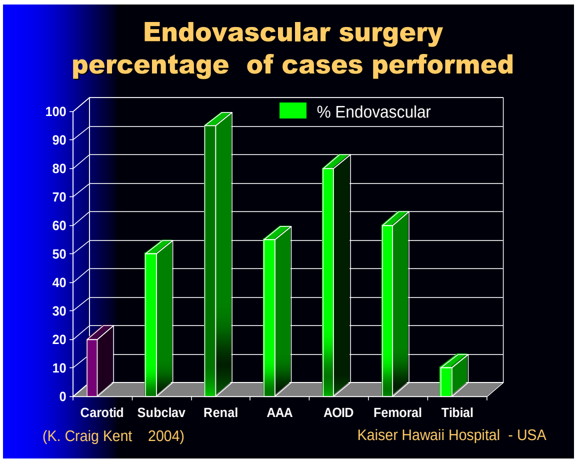

Figure 1

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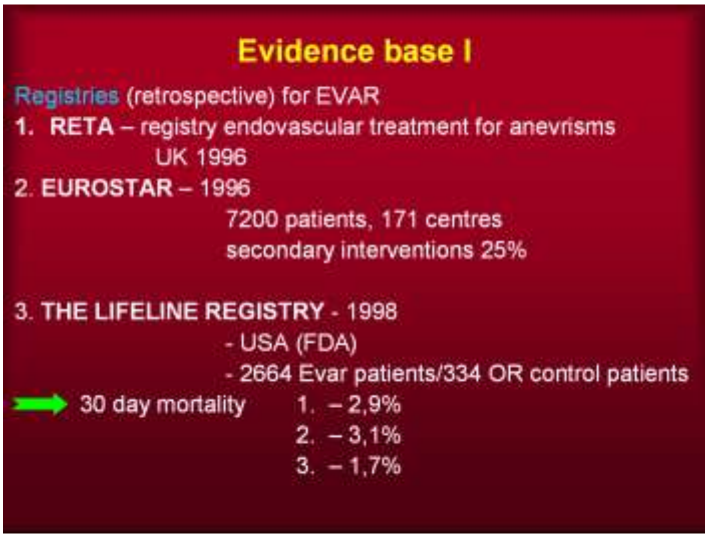
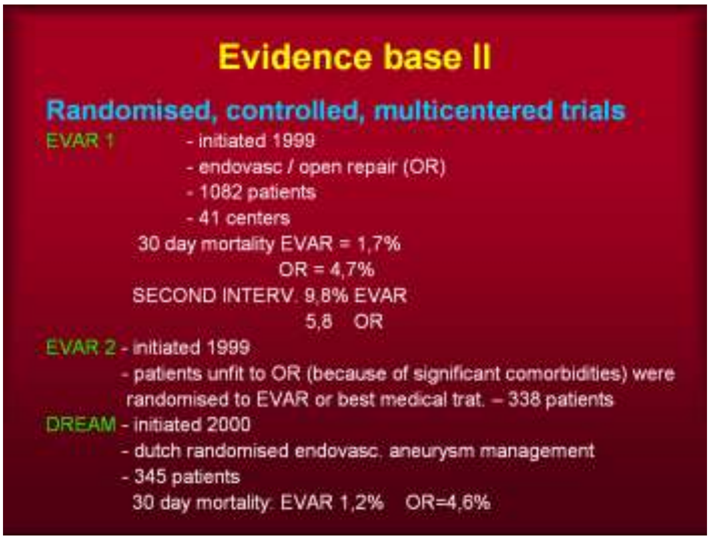
*) **Romanian Journal of Cardiovascular Surgery ■ 2007, vol. 6, no. 2, pp. 98-100**



In order to evaluate this new method, there are registries for Evar (retrospective): RETA, UK, 1996, Eurostar, 1996, The lifeline registry, USA, 1998 (figure 2).

Figure 2



There are also randomized, controlled, multicentered trials: Evar1, 1999, Evar2, initiated also in 1999 and Dream, 2000 (figure 3).

Figure 3

The diagnostic and patient selection is very important: we use Echo2D + Doppler, SpiralCT ± 3D recostruction and angiography. Not all patients with an AAA are suitable for endovascular repair. Pre-procedural assessment must reject unsuitable patients, identify potential difficulties and allow selection of an appropriate stent-graft.

The main criteria for patient selection apply to anatomical details of the vascular tree between the renal arteries and the external iliac artery. With endovascular repair the anatomic configuration of the infrarenal aorta must be known to a high degree of accuracy.

Figure 4 shows different types of aorto-iliac aneurysms and their possibility of treatment.

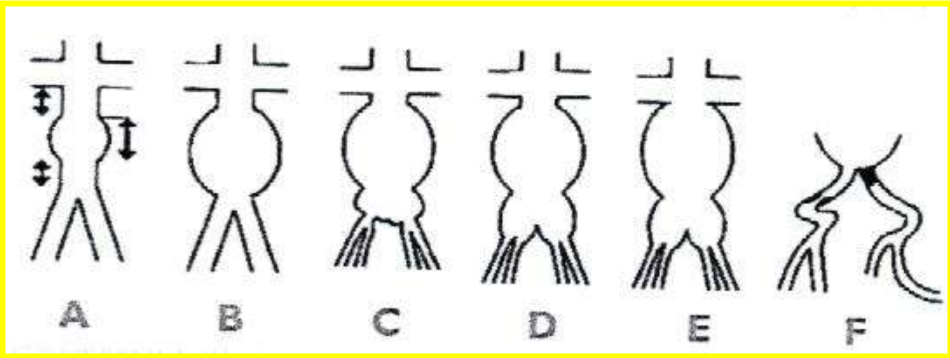
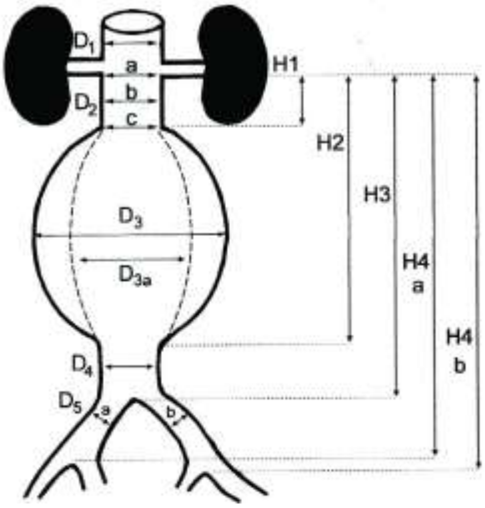


Figure 4

A. A superior and inferior neck of more than 1.5 cm - the possibility of endovascular repair by a straight prosthesis (Ao - aortic tube).
B. B.A. superior neck of 1.5 cm, but without inferior neck, suitable for endovascular treatment by bifurcated graft ao-bi-iliac.
C. A superior neck of 1.5 cm, aneurysms of the common iliac arteries, with 1.5 cm of inferior neck - endovascular treatment by bifurcated graft ao-bi-iliac
D. A superior neck of 1.5 cm, without inferior neck at the level of iliac bifurcations - the possibility of endovascular treatment by regressive Ao-uni-iliac graft and and femoro-femural crossover graft, with the exclusion of the contralateral common iliac artery.
E. No proximal neck-contraindication of endovascular treatment
F. Iliac tortuosities and stenosis or occlusions of iliac arteries are contraindications of endovascular treatment.



Regardless of which kind of stentgraft is to be used, a similar series of measurements must be obtained for each patient (figure 5).

Figure 5

Figure 6 shows the morphology of the proximal neck. This is very important because the occurred problems are at the origin of the type one endoleaks. Endoleaks and graft failure continue to be challenges technological innovations must solve. Until solutions for these problems are found, Evar remains an imperfect long-term treatment and requires regular life-long graft surveillance. Based on the available evidence, Evar is an appropriate treatment for selected patients, especially those at high risk for open surgical repair.

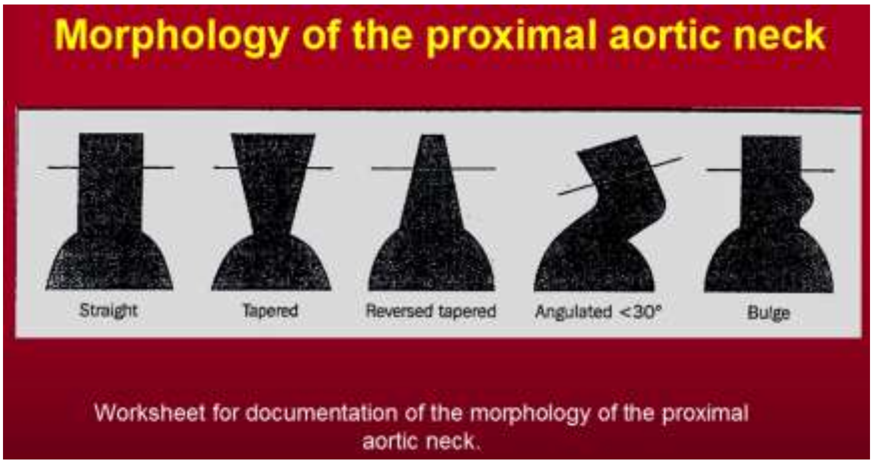


Figure 6

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Advantages of combined anaesthesia - continuous epidural and general anaesthesia - in abdominal aorta surgery*)

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Introduction

There is growing evidence that epidural anesthesia (EA) techniques may improve outcome in selected cases. EA has been shown to blunt the "stress response" to surgery, to decrease intraoperative blood loss, the incidence of postoperative tromboembolic events, and the morbidity and mortality in high-risk surgical patients. In addition, continuous epidural technique (CET) can be used to extend analgesia into the postoperative period (1).

Aim of the study: To compare per operative morbidity, mortality and postoperative analgesia using general anesthesia (GA) or CET + GA /light sedation.

Method

We retrospectively studied 300 patients with abdominal aorta surgery between Jan. 2001 - Jul. 2004. Emergencies with shock were excluded. The patients were assigned to 2 groups:

- Group A (120 patients): with GA alone.
- Group B (102 patients): CET with GA or superficial sedation

The GA technique used was a classic one: induction with Fentanyl 5 mg/KgBW, Midazolam 0.1 mg/ KgBW and Pavulon 0.1 mg/KgBW; maintenance with Isoflurane, Fentanyl, Pavulon as nedded.

EA was induced with 30 ml 0.5% Bupivacaine at the vertebral level L1- L2 or L2-L3 After 40min-1 hour we test the efficiency of analgesia with the patient awake at the time of skin incision and add an infusion of 8-10 ml/h 0.25% Bupivacaine; when needed, is induced a GA or, in retro peritoneal abord of the abdominal aorta, a superficial sedation (Propofol 0.52 mg/KgBW/h). Hypotension secondary to epidural block was treated with vasoconstrictor support: long term infusion of epinephrine (40-80 ng/ KgBW/min).

The hypothermia was avoided by using external warming devices.

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We used CET to extend analgesia into the postoperative period (2-3 days) with a continuous infusion of 0,125% Bupivacaine + Fentanyl 4 mcg/ mL (8-12 ml/h). The GA patients received morphine for postoperative analgesia: 0.05-0.07mg/KgBW/4H. The same dose of morphine was used for CET patients with inadequate analgesia.

Monitoring was the same in both groups:

1. Arterial blood pressure (invasive measurement): the radial artery remains the most popular site for cannulation, because of its accessibility and the presence of collateral blood supply.
2. Central venous pressure - the right internal jugular vein is the preferential site for cannulation.
3. Arterial pulmonary pressure, capillary wedge pressure, cardiac output, cardiac index and derived hemodynamic variables in some special cases.
4. Pulse rate and oxygen saturation of hemoglobin with pulse oximetter.
5. Continuous display of electrocardiogram with ST segment analysis.
6. Central core temperature with thermocouple placed into the rectum
7. Multiple expired gas analysis and parameters of ventilation if the patient was intubated.
8. Diuresis.

The end points were:

1. the mortality
2. the morbidity:
    a. Pulmonary complications: acute lung injury (ALI), acute respiratory distress syndrome (ARDS), bronchopneumonia, atelectasia
    b. Myocardial ischemic events: acute myocardial infarction, arrhythmias
    c. Systemic inflammatory response syndrome (fulfilling the criteria ACCP/SCCM Consensus Committee)
    d. Bowel activity
3. The length of stay in the intensive care unit (ICU)
4. The pain relief (measured by the amount of morphine needed)
5. Early extubation (defined as the extubation during the first postoperative six hours) The statistical analysis was performed using t-test or chi-test, as appropriate. A p value < 0.05 was considered statistically significant.

Results

There are no demographic statistically significant differences between the two groups and no differences of pathology (abdominal aorta aneurisms, occlusive aortic and iliac disease) or surgical technique (see Table 1).

The results printed in Table 2 show a lower incidence of the peroperative morbidity and mortality and a better postoperative analgesia.

- Mortality was higher in group A (perioperatively 2%, in the first week 5% and 3% after).
- The per operative myocardial ischemic events were lower in group B:
    • the acute myocardial infarction (group A = 7%, group B = 1%);

- the cardiac arrhythmias (A = 7%, B = 3%).

- The postoperative pulmonary complications were:
  - acute respiratory distress syndrome (A = 5% B=0%)
  - acute lung injury (A = 5%. B = 2%)
  - pneumonia (A = 15%, B = 4%),
  - hypoxemia secondary to basal athelectasia (A = 5%, B = 4%).

Table 1: Demographic data

Demographic data	Group A	Group B	*p*
Sex (%) M/F	86% / 14%	84.3% / 15.7%	$p < 0.05$
Age (mean)	63.4	64.8	$p < 0.01$

Table 2: Per operative morbidity, mortality and postoperative analgesia

End points	Group A	Group B	*p*
Per operative myocardial ischemic events (%)	14	4	< 0.01
Early extubation (%)	20	100	< 0.01
Postoperative pulmonary complications (%)	30	10	< 0.03
SIRS (%) 30	15	< 0.03	
Early bowel activity (hours)	84 ± 12	36 ± 16	< 0.01
Mortality 10%	1	< 0.001	
ICU (days)	10 ± 2	2 ± 0,5	< 0.01
Morphine (mean ±SD), (mg/24h)	22.7±10	5±1	< 0.001

While in group B the patients were extubated at the end of the surgery (90%) or postoperatively during the first hour (10%), in group A only 20% of the patients were extubated in the first 6 h.

- The systemic inflammatory response syndrome (SIRS) occurred in a lower percent in group B (15% versus 30%in group A) without significant organ system dysfunction.

- The patients in group B had an earlier bowel activity (in the first postoperative day) compared to group A (the third day).

- In group B only six patients (6%) experienced inadequate pain relief, needing supplemental i.v. morphine.

Discussions

It is well known that the vascular patients have a high incidence of concomitant coronary and/or carotidal pathology, are hypertensive or have cardiac insufficiency and that the aortic abdominal surgery is a very "stressing" surgical procedure; the acute myocardial infarction with cardiogenic shock is the main cause for early peroperative mortality.

The effect of epidural anesthesia is a sympathetic blockade which reduces the ventricular preload and afterload, the heart rate and the myocardial 02 consumption; it indirectly reduces the peroperative myocardial ischemic events (2). It produces a "preemptive" analgesia with a lower incidence of postoperative SIRS.

CET with a larger dose of bupivacaine produces efficient intraoperative analgesia without adverse or toxic effects. For this reason, a lighter general anesthesia or even a superficial sedation is needed, with lower cardio-vascular adverse effects.

Treatment of hypotension secondary to epidural block must be aimed at the root causes: decreased cardiac output, decreased peripheral resistance, or both. Drugs with alpha and beta-adrenergic activity have been shown to be superior for correcting the cardiovascular derangements produced by epidural anesthesia (3). We obtained excellent results using a continuous infusion of epinephrine without adverse effects.

The patients with CET and superficial GA are extubated at the end of surgery or in the first hour after admission in ICU because they have analgesia, a low blood drug concentration and are not hypothermic (efficient warming during surgery).

This early extubation, with a lower incidence of SIRS and an efficient postoperative analgesia reduces the incidence and the gravity of postoperative pulmonary complications that occur more frequently in GA patients with postoperative morphine analgesia.

The gastrointestinal effects of epidural analgesia are largely the result of sympathetic blockade and unopposed parasympathetic activity.

This results in increased secretions, sphincter relaxation, bowel contractions and an earlier bowel activity.

Conclusions

Combined anesthesia (continuous epidural + general anesthesia) and continuous postoperative epidural analgesia decrease the incidence of per operative morbidity and mortality and improve outcome in high - risk surgical vascular patients.

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The use of the superior mesenteric artery as inflow in a case of celiac frunk occlusion associated with a double pancreaticoduodenal artery aneurysm*)

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Abstract

Pancreatico-duodenal artery aneurysm is rare but a very important cause of retroperitoneal bleeding, in some circumstances being a life-threatening disease. Also, it could be considered as a differential diagnosis for liver or pancreatic tumors. This article presents the surgical management of a 61-year-old woman with double pancreatico-duodenal arteries aneurysms and reviews the available literature at this moment concerning this subject.

Key words: *pancreaticoduodenal artery aneurysm, revascularization of celiac axis, splanchnic artery aneurysm.*

Résumé

L'anévrisme de l'artère pancreato-duodenale est rare, mais il est une cause importante de l'hémorragie retroperitoneale, étant dans certaines conditions une maladie qui menace la vie. Également, il pourrait être considère comme un diagnostic différentiel pour les tumeurs du foie ou du pancréas. Cet ouvrage présente l'approche chirurgicale dans le cas d'une femme âgée de 61 ans avec anévrismes des deux artères pancreato-duodenales et passe en revue la littérature dont on dispose a présent concernant ce sujet.

Mots clefs: *anévrisme de l'artère pancreato-duodenale, revascularisation de l'axe coeliaque, anévrisme de l'artère splanchnique.*

A 61-years-old normostenic woman with history of hypertension for almost 20 years, presented for approximately 1 year upper abdominal discomfort and pain unrelated to meals.

At physical examination she presented a pulsatile mass of 6 cm in diameter with murmur at auscultation.

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Echographic and CT evaluation at another hospital revealed the suspicion about two pancreatic tumors or pancreatic pseudocysts and scleroatrophic cholecyst with gallbladder calculus. The principal biliary duct was unobstructed.

For a more precise evaluation of the tumors relationships with splanchnic vessels, the patient underwent transfemoral angiography that revealed two pancreatico-duodenal artery aneurysms (one of 6 cm in diameter at the postero-superior pancreatico-duodenal artery and another of 2 cm in diameter at the antero-inferior pancreatico-duodenal artery) and occlusion of celiac trunk. The other abdominal vessels were normal.

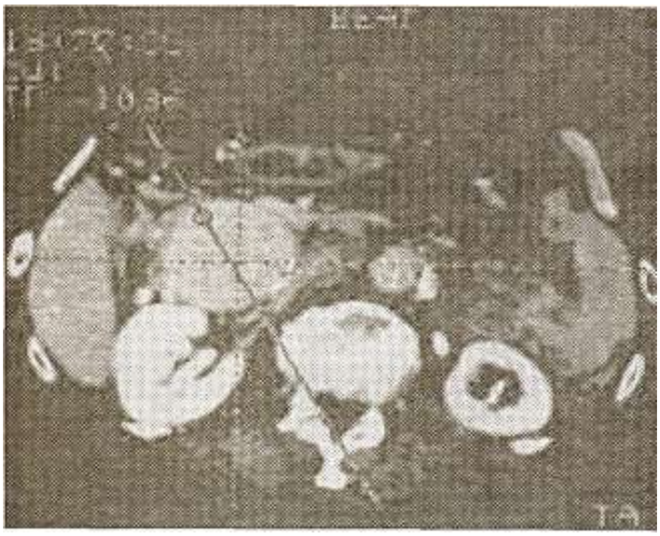

Figure 1 - Preoperative abdominal CT

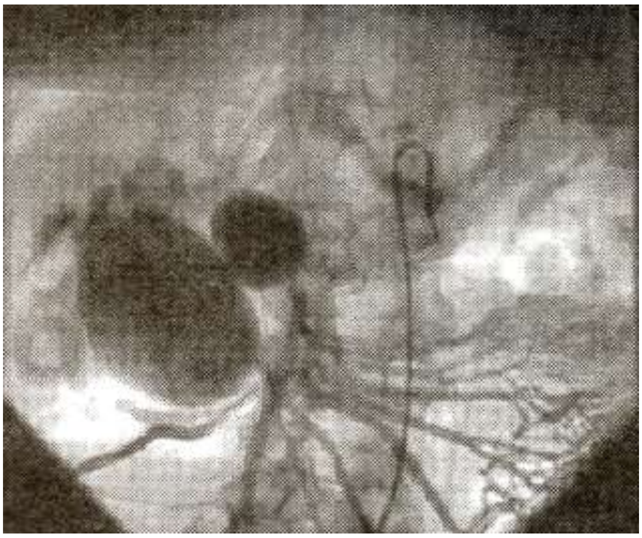

Figure 2: Preoperative arteriogram

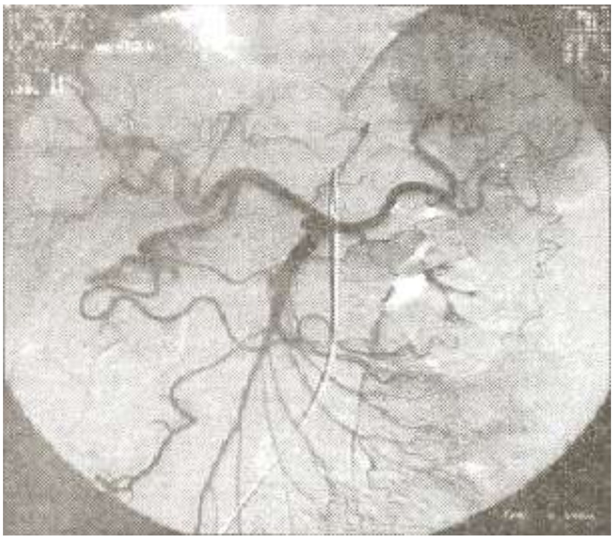

Figure 3: Postoperative angiogram

After this finding, the patient was admitted to our department for surgical management. Intra-operatively we found cholecysto-duodenal adhesion with a cholecysto-duodenal fistula in formation, scleroatrophic gallbladder with one gallstone of 4 cm in diameter and an intense process of perivisceritis, a pulsatile mass of 6 cm in diameter posterior to the pancreatic head and second segment of duodenum, and a pulsatile mass of 2 cm in diameter antero-inferior to uncus of pancreas.

After section of gastro-colic ligament, we arrived at the celiac trunk which has a fibrous and non-pulsatile origin. The pancreas showed a normal aspect.

The superior mesenteric artery was very pulsatile and has almost 1 cm in diameter.

We performed the exclusion of aneurysms by section between ligations of gastro-duodenal artery at its origin from hepatic artery, of postero-superior pancreatico-duodenal artery at its emergence from the 6 cm aneurysm and of antero-inferior pancreatico-duodenal artery at its entrance and emergence from the 2 cm aneurysm.

After this, we set free the celiac trunk by section of the left gastric artery and we reimplanted the celiac trunk in the superior mesenteric artery at the origin of the mesentery. This method was used because the superior mesenteric artery was very well developed and could supply the celiac trunk. But the main advantage of this method is that revascularization of the celiac trunk could be done without clamping the suprarenal aorta.

We also closed the 'in formation' cholecysto-duodenal fistula by anterograde cholecystectomy and transverse duodenoraphy.

Postoperative evolution was positive; the patient left the hospital 13 days later with no complication and no abdominal discomfort.

Discussion

Pancreatico-duodenal artery aneurysm has a very low incidence, since the year 2000 less than 100 cases were reported. This is a life-threatening disease because pancreatico-duodenal artery aneurysm has a propensity to rupture [1] and when it is ruptured it leads to catastrophic retroperitoneal bleeding very hard manageable and with high mortality rate (49.1%) [2].

The exact etiology of this disease is unknown. There are many theories but none is certain.

One observed that pancreatico-duodenal artery aneurysm is frequently associated with stenosis or occlusion of celiac trunk of various etiologies [3]. The most common cause of obstruction of the celiac trunk seems to be atherosclerosis [4], but new theories conclude that compression of the median arcuate ligament of the diaphragm was found to be responsible for this stenosis.

In our case this supposition seems rather probable, because our patient used to practice in her youth for approximately 5 years parachute landing; the repeated severe compression on the celiac trunk made by the median arcuate ligament of the diaphragm during the landing probably caused lesions on the celiac trunk walls that could lead to stenosis and occlusion. On the other hand atherosclerosis is improbable because the angiogram of the other arteries was normal.

So the obstruction of the celiac axis can cause a hyperdynamic flow through pancreatico-duodenal arteries which could lead to pancreatico-duodenal artery aneurysm [4].

Also pancreatico-duodenal artery erosion owing to acute or chronic pancreatitis could lead to aneurysm of this vessel [5].

Other rare causes of the pancreatico-duodenal artery aneurysm are: mid-aortic dysplastic syndrome [6], rheumatoid vasculitis [7] and mycotic aneurysm. The last four causes can be excluded in our case. Hypertension [6] could be another possible etiology.

The clinical presentation of a patient with pancreatico-duodenal artery aneurysm can vary from no symptom to abdominal discomfort, malaise, anorexia, vomiting, severe abdominal pain, jaundice, severe diarrhoea bloody or non-bloody, weight loss and finally shock [8], [9]. This symptomatology is determined by the associated processes (acute or chronic pancreatitis, acute or chronic cholecystitis), by the sizes of the aneurysm and its relations with the surrounding tissues and organs (compression of the common bile duct, compression of ampulla of Vater, stenosis of duodenum).

The compression of common bile duct can lead to mechanical icterus, the compression of the cystic duct could obstruct the evacuation of bile and can lead to gall stone formation. This process can advance towards formation of a cholecysto-duodenal fistula (like in our case) or towards any other complication of chronic cholecystitis [10].

The suspicion of diagnosis can be made on the ground of B mode ultrasonography, computed tomography or RMN, but without color-coded Duplex Doppler ultrasonography and angiography (that remains the gold standard for the diagnosis visceral artery aneurysm) [10] the correct diagnosis could not be made.

That is why the pancreatico-duodenal artery aneurysm must be included in the differential diagnosis of liver or pancreatic tumors and all patients detected with these processes must be further examined by color coded Duplex Doppler ultrasonography, angiography or intravenous digital subtraction angiography (IVDSA).

Once detected, patients with pancreatico-duodenal artery aneurysm need immediate treatment because of the high risk rupture of the aneurysm.

Methods of treatment are various and depend on the associated lesions, technical support of the hospital where the patient is treated, and, last but not least, on the preferences and the experience of the medical team.

In uncomplicated cases with no associated lesions intravascular transcatheter embolectomy with steel coils or glue is the first method of choice. Also, in emergencies, as a first step in managing such patients in stabilizing of the situation and for a temporary hemostasis one could try these methods. But in cases with associated lesions when revascularization of the celiac axis is necessary surgery is the best choice.

Conclusions

Pancreaticoduodenal artery aneurysm is a high-risk affection submitted to suspicion in every case of pancreatic or hepatic tumors. The treatment must be promptly made by a highly trained medical team formed by invasive angiologist, general and vascular surgeons.

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Surgical treatment of ruptured common iliac artery aneurysm*)

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Abstract

Aneurysmal degeneration of the iliac artery is extremely rare. When symptomatic is followed by major complications: thrombosis, distal embolia, rupture, dissection. Surgery is the only treatment of a ruptured aneurysm, saving the life of the patient.

Aim: *To present a case with ruptured common iliac artery aneurysm successfuly surgical treated.*

Material and method: *A 66 years male with ruptured common iliac artery transferred in our Department 9 days after the diagnostic was mode.*

Results: *A complex anamnestic, clinic and paraclinic re-evaluation is made imposing the aneurysm excision, left lower limb arterial reconstruction and removal of the retroperitoneal haemorrhagic effusion. Postoperative favorable evolution registered is confirmed by computed tomography. We were confronted with some particular aspects of this case implying: the precipitated diagnosis by the rupture of the aneurysm, the 9 days period of time elapsed between the diagnosis and the surgical treatment and the post-operative resorbtion of the preoperative retroperitoneal haemorrhagic infiltrate.*

Conclusions: *We present the case of a patient with ruptured common iliac artery, a rare but extremely severe disease, successfully treated after 9 days from its rupture. Diagnostic cooperation and multi-specialty treatment decisively contribute to obtain such a good result.*

Key words: *1. Common iliac artery; 2. Ruptured aneurysm*

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Rezumat

Tratamentul chirurgical al anevrismului de artera iliacă comună rupt.

Degenerarea anevrismală a arterei iliace este extrem de rară; atunci când devine simptomatică este urmată de complicații majore: tromboză, embolie distală, ruptură, disecție. Singurul tratament al anevrismului rupt este cel chirurgical, acesta salvând viața pacientului.

Scop: *prezentarea unui caz cu anevrism de arteră iliacă comună rupt tratat chirurgical cu succes.*

Material şi metodă: *un pacient în vârstă de 66 ani cu anevrism de arteră iliacă comună rupt transferat în Secția noastră la 9 zile după diagnostic.*

Rezultate: *reevaluarea complexă anamnestică, clinică şi paraclinică impune excizia anevrismului cu reconstrucția arterială la nivelul membrului inferior stâng şi evacuarea hematomului retroperitoneal. Evoluția postoperatorie, confirmata prin tomografie computerizată, a fost favorabilă. Ne-am confruntat cu câteva aspecte particulare la acest caz: diagnosticul precipitat de ruptura anevrismului, intervalul de timp de 9 zile scurs între diagnostic şi admiterea în spital şi resorbția postoperatorie a infiltratului hemoragie preoperator.*

Concluzii: *Prezentăm cazul unui pacient cu anevrism de arteră iliacă comună rupt, afecțiune rară, dar extrem de severă, tratat cu succes la 9 zile după ruptură. Cooperarea diagnostică şi terapeutică au contribuit decisiv la obținerea acestui rezultat.*

Cuvinte cheie: *1. Artera iliacă comuna; 2. Anevrism rupt*

Arterial aneurysms have been treated surgically for at least a thousand years. Many of the procedures used in the past have been abandoned, but others, such as proximal ligation, still have a place in the management of arterial aneurysms. Excision with reconstruction was performed by Lexer in 1907 and by Pringle in 1918; an ilio-femoral aneurysm was excised and replaced by a venous graft. Antilus, great greek doctor (around 300) makes the difference between traumatic and spontaneous aneurysms; he has clinical and therapeutic knowledge.

Arterial aneurysm is in most cases the result of a degenerative disease of the arterial wall, mainly atherosclerosis. Atherosclerosis is the modern civilization disease being responsible of several millions deaths per year. The diagnostic and treatment of atherosclerotic patient is a difficult task because it affects all organs and systems of the body. Such a patient is consulted by neurologist, cardiologist and surgeon at least; the psychiatrist and psychologist are often implicated.

Atherosclerotic disease of the arteries consists in stenosis and thrombosis on one side and aneurysm and elongation on the other side; a degenerative process implicates all layers of the arterial wall.

The symptoms of arterial aneurysm are the result of thrombosis, distal embolia, rupture and adiacent structures compression. By an unknown reason aneurysmal degeneration of the profunda femoris and iliac arteries is extremely rare.

Atheroslerotic iliac arterie aneury has slow expansion and induces diffuse local pain associated with distal pain (adiacent nerve compression), oedema (adiacent vein compression) or hydronephrosis (adiacent ureter compression).

Investigation consists of Biplane Echography and Angiography and Computed Tomography allowing precise location and arterial bed evaluation; intraluminal thrombosis may obliterate the presence of the aneurysm.

Symptomatic aneurysm is followed by major complications: thrombosis, distal embolia, rupture, dissection. Rupture results in pain, shock and abdominal pulsatile tumor; Computed Tomography is imposed. Rupture risk increases with the diameter of the aneurysm (Laplace law) and the blood pressure; it is well known that parietal tension is higher in the proximal region of a bifurcation.

Aim

To present a case with ruptured common iliac artery aneurysm successfully surgical treated in the *Department of Vascular Surgery of the "Prof. Dr. CC. Iliescu" Cardio-Vascular Disease Institute, Bucharest.*

Material and method

VD, 66 years old male, from a rural region, is admitted in the Emergency Department of the Vrancea County Hospital for abdominal pain after intens physical effort, loss of consciouneess and abdominal tumor in the left lumbar and iliac regions; he is known with systemic hypertension with intermittent treatment. Abdominal puncture reveals fresh blood. A median laparotomy is performed, supposing a splenic rupture and a left giant retroperitoneal haemorrhagic effusion is found. It follows the recovery after the haemorrhagic and operatory shock in the Intensive Care Unit, where vital functions are maintained. Abdominal Echography and Computed Tomography reveal ruptured left common iliac artery aneurysm, retroperitoneal haemorrhagic accumulation, ureterohydronephrosis, bilateral pleural effusion, bilateral posterior segment of the inferior pulmonary lobe condensation and hepatomegalia (Figure 1).

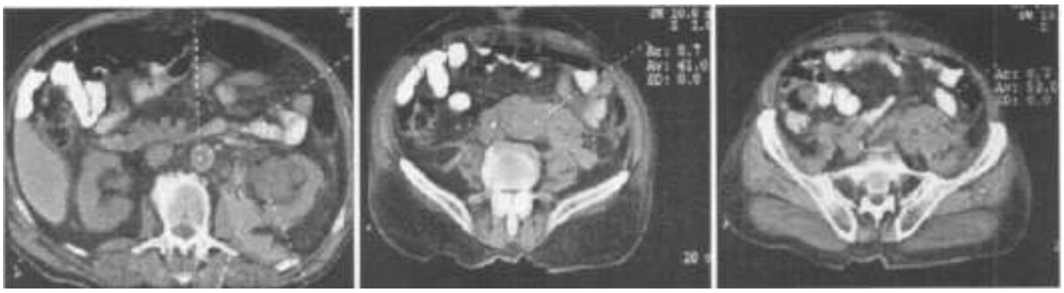


Figure 1. Pre-operative Computed Tomography

The patient is transferred in our Department, where he remains for 21 days, 9 days after the onset of the rupture for further investigations and surgical treatment.

Results

At the admittance, the patient is pale, with icteric skin and sclerae, diffuse abdominal pain, non-pulsating abdominal tumor in the left lumbar and iliac regions, lower limb distal equal present pulsations of the peripheral arteries, sinusal rhythm, 88/', blood pressure 140/80mmHg. Cardiac transthoracic echography is in normal range. Abdominal ecography confirms the lesions. Aortic angiography: ascending and thoracic descending Aorta is normal; abdominal Aortic kinking; right common iliac artery kinking; left common iliac artery aneurysm; bilateral normal femoral, popliteal and infrapopliteal arteries (Figure 2). Hb: 12.5 mg/L, Ht:37%, Glucose 103 mg/L, Ureea:53 mg/L, Creatinin: 0.77 mg/L, K: 4.35 mmol/L, APTT :25.3", AP:63%, INR:1.43, F:690 mg/dL.

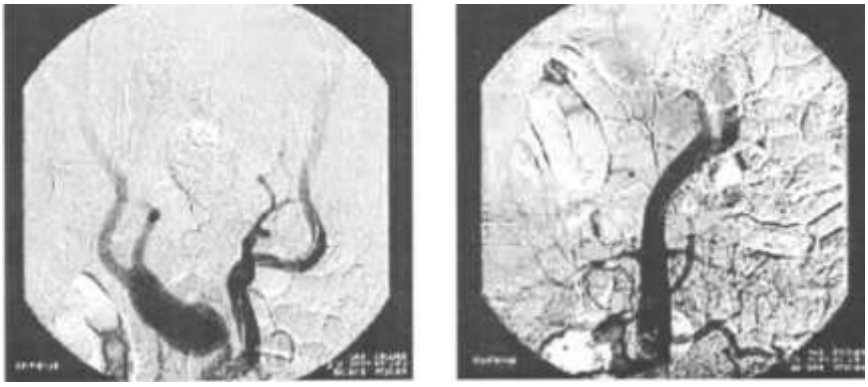


Figure 2: Pre-operative Angiogram

A complex anamnestic, clinic and paraclinic re-evaluation reveals the following diagnosis: Systemic atheromatosis, left common iliac artery aneurysm with 9 days old rupture, massive retroperitoneal haemorrhagic mass in the left lumbar and iliac regions, left ureterohydronephrosis, oliguria, icter, right inguinal hernia, bilateral inferior pneumonia, bilateral pleural effusion, recovered haemorrhagic and postoperative shock.

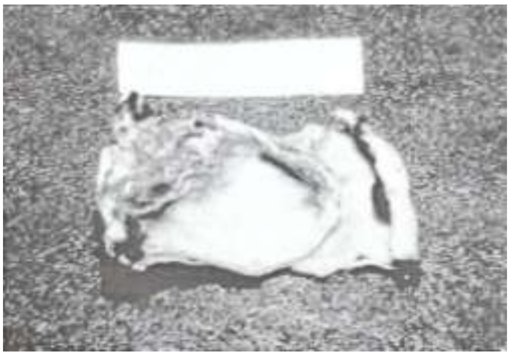
The following operation is done: aneurysm excision, left lower limb arterial reconstruction with Impra nr. 8 (ePTFE) graft interposition between the left common iliac artery origin and the left common femoral artery, removal of the retroperitoneal haemorrhagic effusion, multiple drainage (Figure 3-8).

Figure 3

Figure 4

Figure 5

Figures 3-5: Intra-operative Aspect



Figures 6-7: Macroscopic Aspect

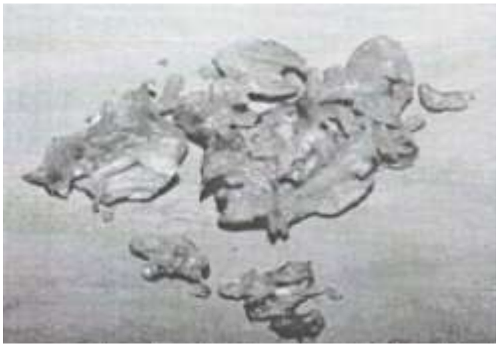


Figure 8: Aneurysmal content

The wall of the excised iliac artery presents dystrophic atherosclerotic lesions with intra- and extra-cellular lipidic deposits in the intima and media, substitutive fibrosis, colagen fibres replacing the elastic fibres, thickened intima with vasa of neoformation, calcifications, ruptures of the lamina elastica interna, adventiceal inflamatory infiltrate (Figure 9-10).

Figure 9: Microscopic Aspect. 1. Van Gieson stain 100X: Aneurysm of common iliac artery with tear in retroperiotoneal space; the aneurysmal wall with sclerous remaniation with intra- and extra-haemorrhage and necrosis aria

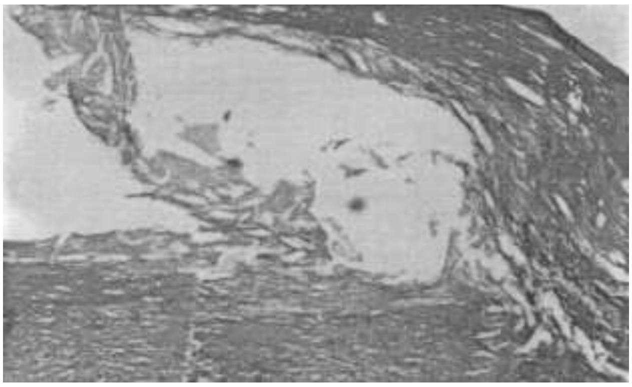
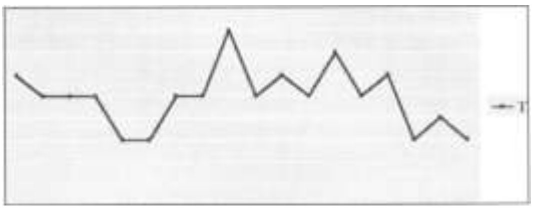


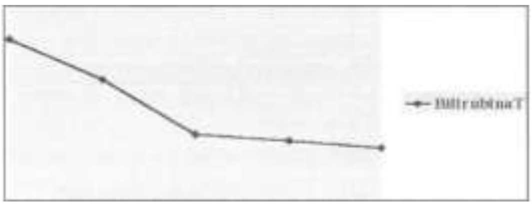
Figure 10: Microscopic Aspect. 2. Van Gieson stain 400X: Fibrosclerous wall with large tear and lymphocyti inflamatory inflitrate; haemorrhagic aria and cholesterol chirystals from atheroma

Postoperative care: maintenance of an adequate blood pressure, blood transfusion, ionic intravenous infusion, Captopril 12.5 mg b.i.d., Metoprolol 25 mg b.i.d., intravenous diuretic, Furosemid 20 mg o.i.d., intravenous antibiotic infusion in accordance with the antibiogram, Tienam 500 mg q.i.d., Amikacina 500 mg o.i.d., anticoagulant therapy, subcutaneous Clexane 0.4 ml o.i.d. in the first 72 hours and oral anticoagulant: Trombostop 2 mg o.i.d.

The patient is hypertermic within a period of time between the 9-th and the 14-th days (Graphic 1). Seric Total Bilirubin (Graphic 2) shows a decreasing curve from the 5-th to the 17-th postoperative day (5.77 to 1.90 mg/L).



Graphic 1: Post-operative Temperature Curve



Graphic 2: Post-operative Total Bilirubin Curve

Postoperative Computed Tomography shows a residual fluid accumulation in the left psoas muscle extended in the proximal segment of the prosthesis. Minimal bilateral pleural effusion reduced grade of left hydronepohrosis as compared to the preoperative image (Figure 11).

Figure 11: Post-operative Computed Tomography

Discussions

Isolated aneurysmal degeneration of the iliac arteries is extremely rare and clinical diagnosis is difficult; when symptomatic it is followed by major complications: thrombosis, distal embolia, rupture, dissection. Not infrequently small fusiform or saccular dilatations of the iliac arteries accompany an abdominal aortic aneurysm.

Incidence: 0.03% of necropsies; 70/100 000 males and 2/100 000 females admitted in the hospital/year; sex ratio is 5-16/1, males/females. It implies both sides in 50% of cases, the common iliac artery in 10-30% of cases. The most frequent age in the surgical series is 65-75 years.

Isolated iliac artery aneurysm is either asymptomatic and due to its pelvic localisation has a not very well defined evolution and in most cases an impossible objective detection, or has various clinical expressions as: hematuria, ureteral obstruction, iliac vein thrombosis, colic obstruction, pelvic limb neurological imparement. The aneurysm often contains atheromatous ulcers covered by mural thrombi with consequent thinning and destruction of the media, prime sites for the formation of atheroemboli that lodge in the vessels of the lower extremities.

It as high rate of mortality: under 5% in the elective surgery (under 3 cm diameter and low risk patients), 25-57% in ruptured cases operated in emergency.

The diagnosis was precipitated by the rupture of the aneurysm in our case; a carefully retrospective anamnesis revealed the presence of a diffuse abdominal pain for several months before the rupture, interpreted as of neurological etiology, our patient being a physical worker.

The onset of the symptoms after an intens physical effort, in the absence of immediate possibility to perform an echographic, angiographic or computed tomographic examination concluded to a misleading diagnosis. Median laparotomy revealed the left giant retroperitoneal haemorrhagic mass of another origin that first estimated.

During the period of 9 days that follows in the Intensive Care Unit, appropriate investigation is done and a correct and quasi-complete diagnosis is made. The patient is transferred in our Department for the appropriate treatment.

Supplementary investigation (angiography) is performed in order to estimate the distal vascular bed and to establish the correct surgical strategy. Intraoperative exploration and postoperative microscopic examination confirmed the diagnosis.

The extension of the aneurysm imposed a distal anastomosis of the graft on the common femoral artery and the ligation of the bifurcation of the common iliac artery. Postoperative period is marked by the resorbtion of the preoperative retroperitoneal haemorrhagic infiltrate.

Reviewing the literature we found some special indications, contraindications, preoperative, anaesthetic and post-operative measures in the surgical treatment of an abdominal artery aneurysm.

Surgical techniques

Unilateral location and limited extension allows the retroperitoneal approach while bilateral location and large diameter or long extent imposes transperitoneal approach through a large mid-line incision. Aorto-iliac excision of the aneurysm and Aorto-iliac artery reconstruction by the insertion of a prosthetic graft (Dacron, PTFE) is the surgical treatment of choice of the aneurysm.

The thrombus and, if possible, the atherosclerotic intima is removed from within the aneurysm.

Bleeding from patent vessels must be controlled with mattress or figure-of-8 stiches of 2/0 sutures. Atherosclerotic plaques must be debrided away before attempting to suture these vessels. Percutaneous treatment with endovascular prosthesis has limited indications and experience.

Indications

Most arterial aneurysms should be treated surgically. The reason for this are that medical measures are without effect, that the aneurysm itself often produces severe symptoms, and a variety of complications may arrise. Among these may be listed rupture, thrombosis, peripheral embolisation, dissection and pressure on surrounding structures; many patients may live for years after an aneurysm has been diagnosed, but the usual cause of death is the rupture of the aneurysm.

Contra-indications

Ischemic heart disease, if severe, may be a contra-indication to major surgery of this type. Another contra-indication is gross multiplicity of the aneurysm and arterial reconstruction operation is possible when there is an adequate lumen to the arterial tree distal to the aneurysm. Surgical treatment is the only treatment of a ruptured aneurysm, saving the life of the patient.

Pre-operative preparation

Whenever possible, infection should be controlled before the operation. Prophylactic antibiotics are administered if a plastic graft is to be inserted. In most patients blood transfusion is required and arrangement should be made for this in adequate amounts. AII patients should have full preoperative assessment of their cardiovascular system. The patient should enter the operating room well hydrated; this can be accomplished by giving 1-2 liters of intravenous fluids during the 12 hours prior to operation.

Anaesthesia

General Anaesthesia with an endotracheal tube is usually satisfactory. However, when the aneurysm has leaked recently or ruptures, the anesthetic presents a special problem, because of grave risk of further severe haemorrhage when the muscles of the abdominal wall are relaxed by the anesthetic. Anaesthesia is induced without relaxants, the surgeon makes the abdominal incision down to peritoneum, relaxants are given and the surgeon immediately opens the peritoneum and rapidly gains control of the Aorta proximal to the sac of the aneurysm.

Post-operative care

It is essential to maintain an adequate blood pressure to prevent clotting in the transplant or at another site such as the coronary arteries by continuing the blood transfusion if indicated and sometimes the intravenous infusion of positive inotropic agents at a rate sufficient to maintain the blood pressure at its pre-operative level; the blood pressure should be recorded at half-hourly intervals until it is stable.

Anticoagulants are dangerous in the immediate postoperative period and should be avoided if possible during the first 72 hours; even with meticulous control lesion bleeding can occur. On the other hand, long-term oral anticoagulant therapy is recommended in some patients after the first 72 hours.

Paralitic ileus follows nearly every transperitoneal arterial reconstruction and should be treated by gastric aspiration by means of an indwelling tube plus intravenous fluid and electrolyte replacement until intestinal mobility has been re-established. The patient is nursed flat until the blood pressure is stable; after this most patients can be allowed to sit in a chair by the second postoperative day. Sacral pressure sores are best prevented by careful cushioning with thick foam rubber pads during the operation and careful nursing afterwards. Oliguria should be controlled by a pre-operative water load plus adequate hydration during and after the procedure.

Conclusions

We present the case of a patient with ruptured common iliac artery, a rare but extremely severe disease, successfully treated after 9 days from its rupture. Diagnostic cooperation and multispeciality treatment decisively contribute to obtain such a good result.

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Aortoiliac occlusive disease with superficial femoral aneurysm[*)]

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Abstract

A 60-year old man, heavy smoker, alcohol consumer, hypertensive was admitted in the hospital for rest pain in both calf and claudicative pain in both thigh and minor interdigital ischemic lesions to the right foot. Physical examination shows pallor on elevation, rubor on dependency, shiny atrophic skin in distal limbs and feet, absence of femoral pulses. The resting ECG echocardiography and lab test seems to be normal. Vascular Doppler echography discovered both superficial femoral aneurysms with thrombosis. Arteriography indicated multilevel lesions with terminal aortic occlusion and calcified aortic walls, critical stenosis to both iliac arteries, superficial femoral occlusion, permeable profunda and good outflow tract. The patient has been operated by a direct anatomic surgical reconstruction (aortobifemoral by-pass). Postoperatory the evolution was good, pulse volume recordings with better amplitude than preoperative tracings. Arteriosclerotic occlusive disease is a common cause of lower extremity ischemic symptoms. In the majority of patients occlusive lesions are multiphocal including lower abdominal aorta, both iliac arteries and frequently the infrainguinal arterial tree. A careful clinical examination supplemented with vascular laboratory dynamic data, good artheriographics must be done before proceeding with aortic reconstructive surgery.

Key Words: *occlusive arterial disease, femoral aneurysms, surgical treatment*

Case report

We present here a case of a 60 year old patient, heavy smoker, hypertensive in treatment with antihypertensive pills and aspirin with history of proximal claudication symptoms in the distribution of thigh, hip, and buttocks musculature. He was admitted in the hospital with rest pain.

The clinical examination, lab test (abnormal serum lipid levels) cardiological examination, thoracic radiography, non-invasive examinations technique and arteriography showed the anatomical distribution of occlusive disease in aorto-iliac segmental distal vessels (figures 1, 2 – next page). Doppler echographic examination showed two femoral aneurysms 4/7 cm versus 5/8 cm with partial thrombosis.

Based on clinical and paraclinical examination the patient was prepared for surgical aortic reconstruction. On the day before surgery, the patient was restricted to a liquid diet and mechanical bowel preparation. The routine lab test, coagulation parameters

*) **Romanian Journal of Cardiovascular Surgery, 2007, vol. 6, no. 3, pp. 127-130**

hematocrit, complete blood count, platelet count and prothrombine time has been performed. The aspirin has not been stopped before surgery.

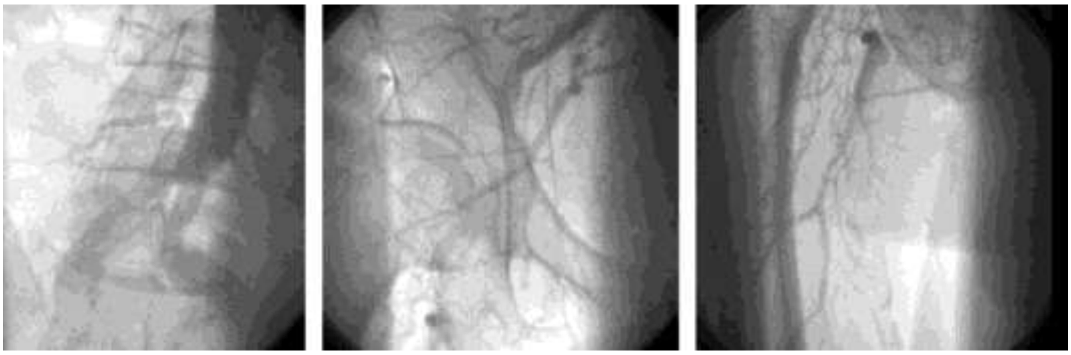


Figure 1: Arteriography of the right side showing occlusion of the external iliac artery and occlusion of the superficial femoral artery

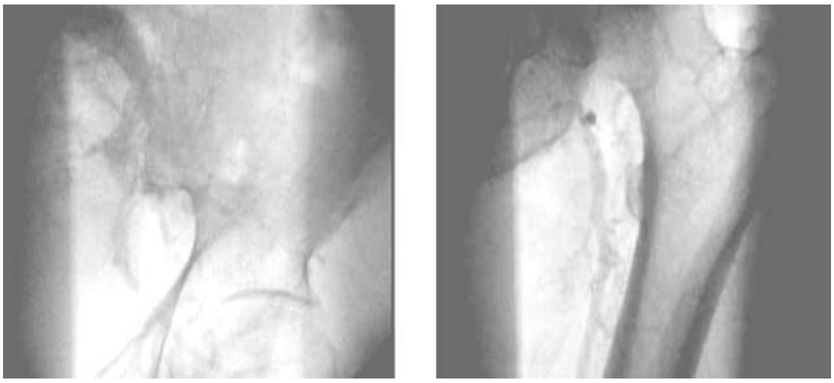


Figure 2: Arteriography of the left side showing occlusion of the external iliac artery and occlusion of the superficial femoral artery

The technique used was the standard one, aortobifemoral by-pass under general anesthesia and peridural catheter, prophylactic parenteral antibiotics was routinely given. The exposure of the aorta was performed transperitoneal (Figure 3).

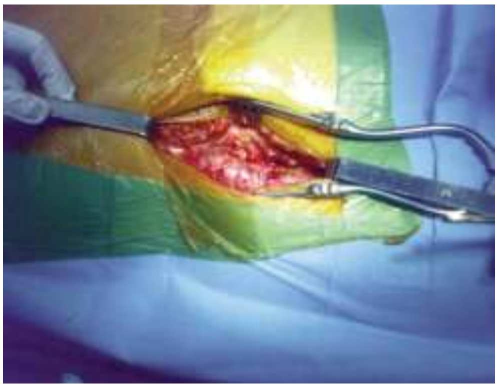
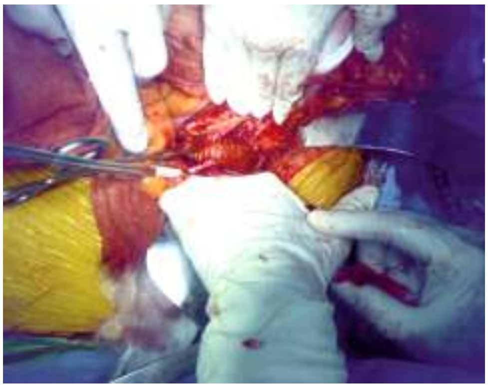


Figure 3a) Femoral aneurysms left

Figure 3b) Femoral aneurysms right side



The proximal anastomosis end-to-side, was placed high in the infrarenal abdominal aorta, relatively close to the renal arteries in the area less involved by the occlusive process. It has been used total clamp of the aorta. The suture procedure was difficult because of the calcified aortic walls. The inferior mesenteric artery has been reimplanted in to the body of the graft (Figure 4).

Figure 4: Aortic anastomosis with inferior mesenteric artery reimplantation

The distal anastomosis of the aortic graft has been constructed at the level of the profunda artery because of the large thrombosis superficial femoral aneurysm. The arteriotomy was extended down to the produnda femoris artery beyond the orifice where the outflow was adequate (Figure 5). The aneurysm has been excluded by ligation and suture (Figure 6).

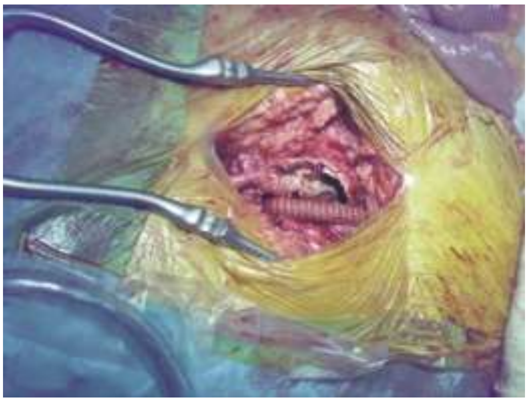


Figure 5a) Distal anastomosis to profunda femoralis arteries left

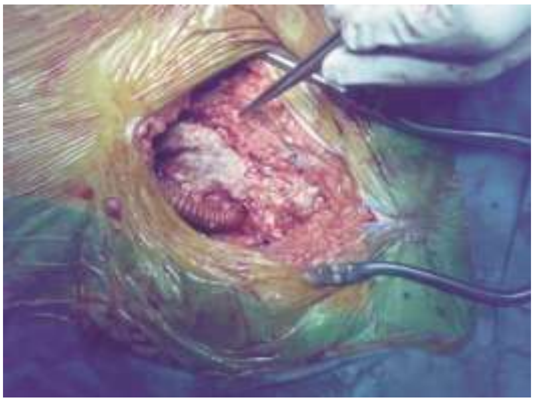


Figure 5b) Distal anastomosis to profunda femoralis arteries right

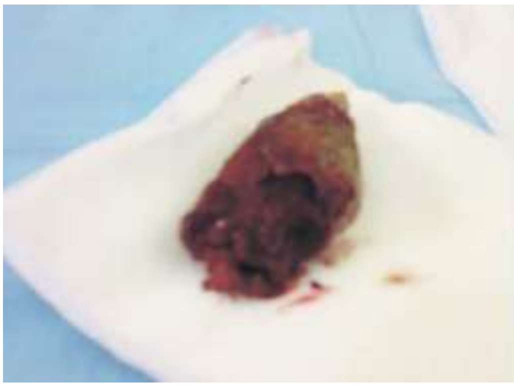


Figure 6a) Intra-aneurysmal thrombus on the left side

Figure 6b) Intra-aneurysmal thrombus on the right side

After the aortic by pass was performed, the posterior parietal peritoneum was closed. The graft used was a bifurcated Dacron graft coated with collagen and silver to reduce the risk infections. The closure has been performed after drainage of the Douglas recess and both femoral. Postoperator was administrated antibiotics for infection prophylaxis (ceftriaxone and gentamicyn), antithrombotic therapy, vasodilator drugs, heparin. Early postoperator the patient suffered lymphoragy to both femoral sides treated with bed rest, moderate leg elevation, antibiotics, antiinflamatory. The culture obtained from the fluid was sterile. The patient has been discharged from the hospital after 14 days. The evolution was good at 1 month after surgery, with good improve of claudication distance, relieves rest pain and healing minor ischemic lesions.

Conclusions

The case combined occlusive disease with large atherosclerotic aneurysms at high risk of rupture and predisposition for thrombosis or distal embolization.

Even with several levels of disease, successful correction of hemodynamic impairment in the aortoiliac inflow system often satisfactory clinical relief of ischemic symptoms.

Lymphorrhea and lymphocele formations are more common following the extended groin incision associated with profunda artery dissection.

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Ruptured popliteal artery aneurysm. Case report*)

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Abstract

We present a case of a popliteal artery aneurysm in a 55 years old male, who presented with right thigh and popliteal region pain, and a pulsatile mass in the popliteal fossa. Angiography and angio CT revealed a popliteal artery aneurysm, which was subsequently resected and bypassed. The popliteal vein was found thrombosed and the long saphenous vein was therefore spared

Popliteal aneurysms are the most frequent aneurysms found in the lower limbs. They are found in about 1% of the adult population and are infrequent in females. They are associated with the presence of contralateral aneurysm in 30-50% of cases and with abdominal aortic aneurysms in 30-60%. Their main complication is arterial ischemia secondary to the thrombosis of the aneurysm, although it can also be presented in the form of compression symptoms or distal embolization. Spontaneous rupture is an uncommon complication and it is associated with arterial diameters of > 4 cm. The amputation rate associated with ruptured popliteal aneurysms is 25% [1].

Case report

A 55-years old male patient presented to our department complaining of pain and swelling in the right popliteal fossa. The medical history revealed a prior left femoro-tibial by-pass using the ipsilateral long saphenous vein (LSV), intervention made for multiple aneurysms along the superficial femoral and popliteal artery, which caused ischemic symptoms due to distal embolization. He also underwent PTA for a right external iliac critical stenosis in February 2010.

Figure 1: Ruptured popliteal aneurysm clinical presentation

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The physical examination showed inflammation in the popliteal fossa with a pulsatile mass causing considerable increase in its diameter. All peripheral pulses were palpable.

Urgent duplex scanning was performed, showing a giant 8.5/12.5 cm, partially thrombosed aneurysm of the right popliteal artery.

We performed an angiography that confirmed the diagnosis of true popliteal artery aneurysm, revealing also an infra-renal abdominal aortic aneurysm with a diameter of 4.3 cm and several other smaller aneurysms along the hypogastric arteries.

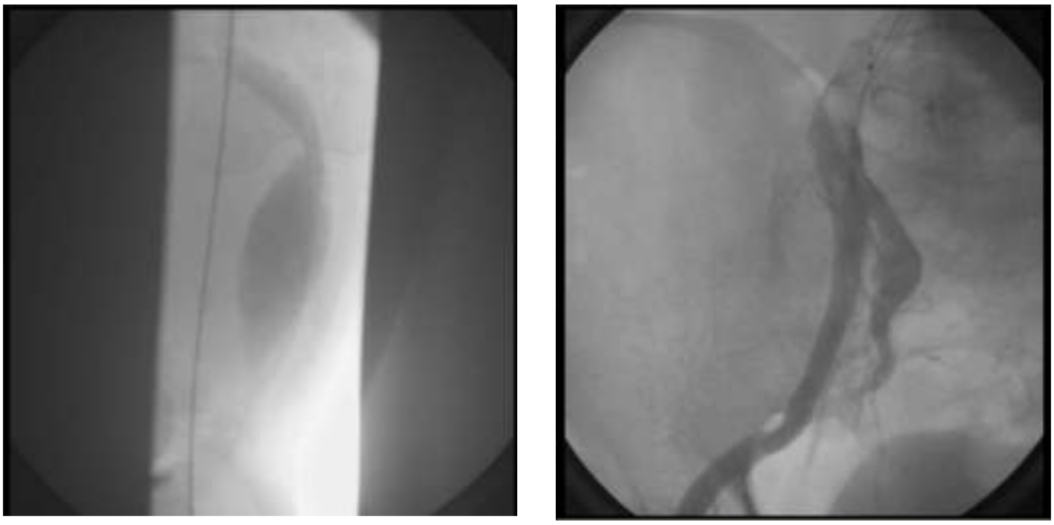

Figure 2:
a) arteriography of the aneurysm before rupture **b) hypogastric artery aneurysm**

Three days after his admission the patient reported sudden pain in the popliteal fossa with an increase of the limb diameter. An emergency CT-angiography was performed, which confirmed the rupture of the popliteal aneurysm.

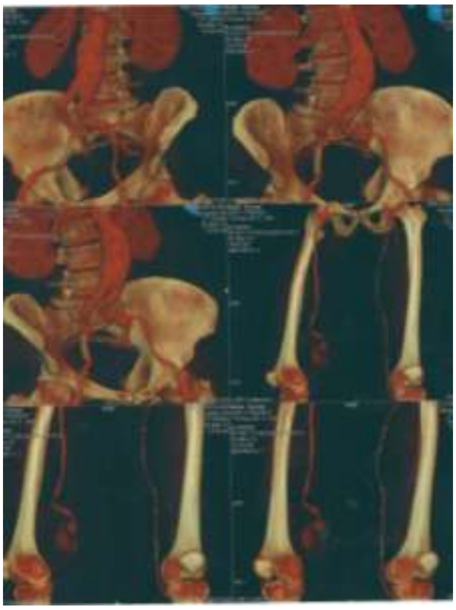

Figure 3: CT-angiography image of the ruptured popliteal aneurysm, and abdominal aorta aneurysm

Urgent surgical intervention consisting of femoro-popliteal by-pass and aneurysm excision was decided upon.

At the time of the operation, dissection posterior to the aneurysm revealed an adherent, thrombosed popliteal vein. As it was likely that long saphenous vein (LSV) was now a significant channel for venous return, it was not used for bypass. Instead a below-knee femoro-popliteal bypass was performed using polytetrafluoroethylene (PTFE) prosthesis. Because of its massive size and the initial dissection needed for distal control, we resected the aneurysm completely.

Figure 4: Intraoperatory aspect of the aneurysm before excision

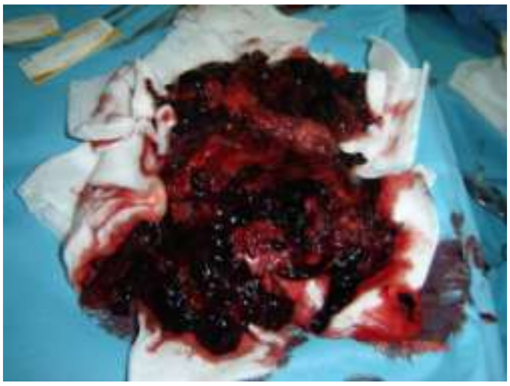

Figure 5: Aspect of the evacuated thrombus

Figure 6: Intraoperatory aspect of the opened and evacuated aneurysm

Figure 7: Distal anasthomosis of the PTFE graft

The patient had an uneventful postoperative course, apart from a mild oedema, and regained ambulatory function of the extremity. The control duplex scanning reported good patency of the graft. The patient was discharged from the hospital with antithrombotic and antibiotic treatment (ciprofloxacin) for 2 weeks.

He was also included in a follow-up program to assess the development of the 4.3 cm abdominal aortic aneurysm, and the multiple, bilateral, small hypogastric artery aneurysms. The follow-up of the revascularization technique (1 month, 6 months and then annually) through duplex scanning is important, not only for the early detection of potential graft problems, but also to verify the complete exclusion of the aneurysm and to avoid potential problems related to leakages [1].

Discussion

After the aorto-iliac system, the popliteal artery is the most common site of aneurysm formation. The ratio of popliteal to aortic aneurysms is estimated to be 1:10 to 1:20, and 5% to 10% of those with aortic aneurysms have popliteal aneurysms. Associated aneurysms are common. Approximately 50% of patients have bilateral popliteal aneurysms, one third has aortic aneurysms, and one fourth has femoral aneurysms. The incidence of extrapopliteal aneurysms is highest among those with bilateral popliteal aneurysms; up to 78% of such patients have aortic aneurysms. These patients continue to develop other, remote aneurysms, and new aneurysms have been documented in 6% of treated patients at 1 year and 49% at 10 years, illustrating the need for lifelong surveillance.

Popliteal aneurysms classically manifest in several ways. In about one half of affected patients, they manifest with limb ischemia from thrombosis (around 32%) or embolization (around 20%). Approximately 37% of the aneurysms are asymptomatic and are detected by palpation or ultra-sonographic examination. Popliteal aneurysms can also manifest with symptoms from compression of adjacent structures (around 10%), notably nerve (causing paresthesias or other deficits) or vein (leading to deep venous thrombosis). By contrast rupture is rare, with an overall incidence of 2.1%.

Unfortunately, no reports describing rupture documents the size of the aneurysm. It may be that the relatively thigh bony and musculo-fascial relations of the popliteal artery offer some degree of protection [2].

Conclusions

Popliteal artery aneurysms are limb threatening because of their potential to cause embolism, thrombosis, and, uncommonly, rupture. Their timely diagnosis before complications is a relevant clinical issue. For instance, elective repair of a popliteal aneurysm results in substantially better outcomes than revascularization for acute aneurysmal thrombosis or delayed revascularization for chronic limb ischemia resulting from repeated subclinical embolism.

Ultrasonography or CT angiography are the radiological investigations of choice. A CT angiography is still the gold standard test for diagnosing ruptured popliteal aneurysms. It is recommended to perform a preoperative arteriogram to assess the run-off and rule out distal embolization [1].

When contemplating exclusion bypass for such operations, it would be useful to have an ultrasound scan of the venous system to allow appropriate preoperative planning in term of conduit formation [3].

The 14% incidence of popliteal artery aneurysm among men with aortic aneurysm suggests that routine Doppler ultrasound scanning should be considered as a screening test in male patient with AAA.

The etiology of femoral and popliteal aneurysms probably involves the interaction of a genetic alteration that predisposes to the loss of the arterial wall integrity following local forces such as repeated flexion of the arteries at the hip and knee. The familial as well as genetic bases of these lesions remain unresolved at the present time [2].

Definition of the genetic basis for aneurysms, aortic or peripheral, will hopefully be aided by the complete mapping of the human genome, which will form the basis for determining if gene functions exists that interact to produce these diseases.

Unfortunately, the clinical relevance of these lower extremity aneurysms discovered in association with AAAs is ill defined at present, and there remains a need for a prospective natural history study to establish their actual significance [4].

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Popliteal artery aneurysm diagnosed after revision of total knee replacement*)

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Introduction

The aneurysm of the popliteal artery is second in incidence after aneurysm of the abdominal aorta, being responsible of almost 4% of total peripheral vascular diseases. Its reputation as "a silent killer of the leg circulation" is justified by the fact that eventual amputation of the affected limbs has been noted in over one-half of the patients with untreated popliteal aneurysm. Popliteal arterial aneurysms have a male predominance. Common risk factors include smoking, hypertension and atherosclerosis.[3,4]. True popliteal artery aneurysms are mostly of atherosclerotic origin. The possible modes of clinical presentation make the condition an interesting one because it may produce a variety of symptoms or may be completely asymptomatic. The aneurysm may be asymptomatic although the patient may have noticed its presence behind the knee, as a pulsatile or solid mass. If it is thrombosed, symptoms may still be absent because of a well developed collateral circulation or because the patient exercises so little that he gets no intermittent claudication. When symptoms develop they are the result of acute or chronic ischaemia of the lower leg and foot after thrombosis of the aneurysm or distal embolic event. Acute rupture or infections are rare complications.

Failure to consider this condition may result in a late diagnosis and the start of an inappropriate management plan [3, 4].

Due to the fact that in one third of the cases patients are asymptomatic, its presence can be easily overseen especially if the patient has a well known history of gonarthrosis or other knee involving pathology. Existing data in the literature concerning the association of aneurysm and revision of total knee replacements are rare.

In this paper, we present a particular case of unknown popliteal artery aneurysm discovered after revision of total knee.

Case report

A 78-year old man was presented to our cardiovascular surgery department, with critical ischemia signs and high risk of limb loss. He was previously admitted for a redo total knee replacement after a posttraumatic degradation with various deviation and limited flexion of preexisted total knee (TKR) prosthesis. The injury resulted in a varus

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and flexum deformity of 30º. The redo intervention was made one year after the injury, which succeeded to correct the lower limb axis. The patient presented arteriosclerosis with this chronic deviation in varus and flexum. The correction of the axis of pelvic limb was restored by this revision.

Figure 1: Traumatic deformity, varus 30°, fexum 30°

Figure 2: Intraoperatory aspect of the correction

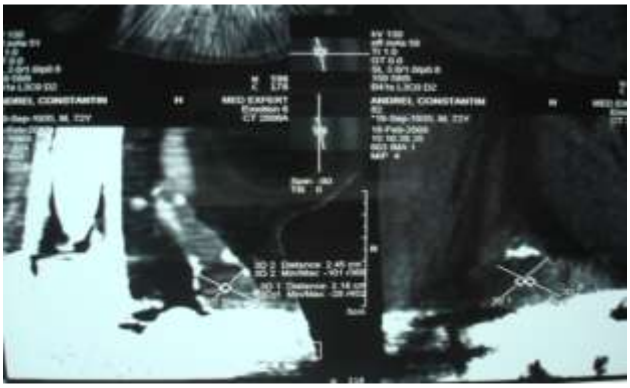

Figure 3: Angio-IRM aspect of the popliteal aneurysm.

Figure 4: Echographic aspect of the popliteal aneurysm.

Two weeks after the revision of TKR occult ischemia signs were presented. Clinical examination revealed marmorated, cyanotics and cold skin over the lower leg associated with knee hyperextension. These signs were also presented when the penthoxiphilin infusion was stopped.

Three weeks after the redo TKR, being on conservative treatment, patient claimed a suddent change in the pain patern with worsening of leg ischemia signs. At the moment of clinical examination patient presented with signs of irreversible leg ischemia.

The clinical diagnosis of popliteal artery aneurysm was confirmed by echo Doppler and angio-MRI examination (2.4 cm in axial diameter).

At 6 hours after the onset of critical ischemia sings, under peridural anesthesia we performed an above-knee popliteal- below-knee popliteal arterial bypass with proximal and distal aneurysm ligation, using a silver-coated Dacron vascular graft.

Figure 5. Schematic illustration of the knee deformity and popliteal artery aneurysm.

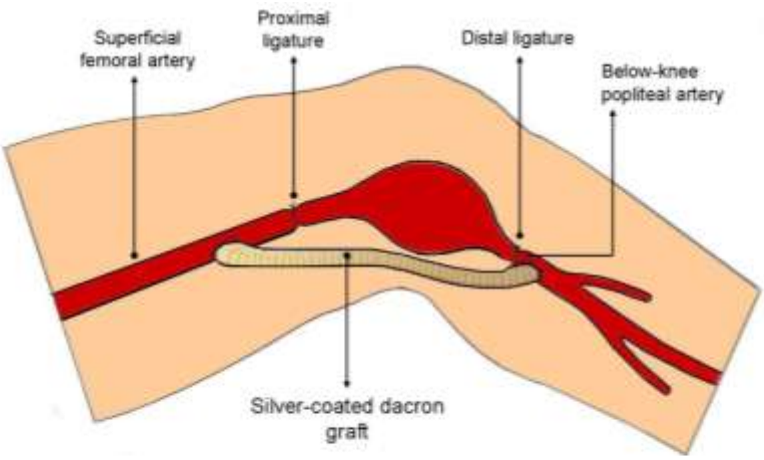

Figure 6. Typical popliteal artery bypass graft with aneurysm exclusion [1].

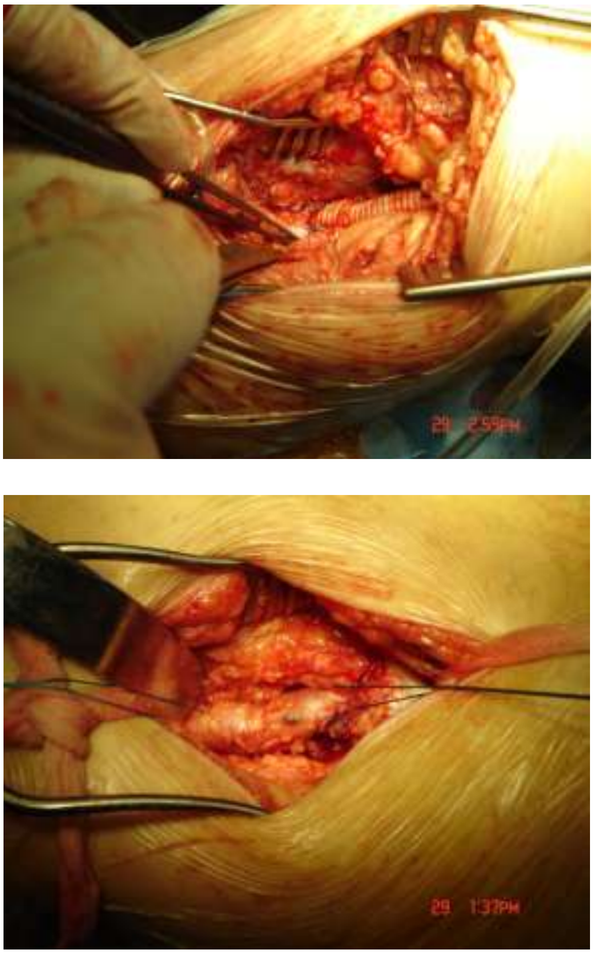

Figure 7: Intraoperatory aspects of the popliteal artery bybass with aneurysm ligation.

Figure 8: Postoperative aspect, 4 months after intervention

Conclusions

In old patients with systemic arteriosclerosis and arthritic knee we must not ignore the possibility of popliteal artery aneurysm presence. A meticulous clinical and imagistic exam must be performed. When the ischemic signs are obvious the vascular intervention must be performed immediately.

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Femoral anastomotic pseudoaneurysms*)

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Abstract

Introduction: *The authors present their clinical experience in the diagnosis and treatment of femoral anastomotic pseudo-aneurysms over a period of 7 years.*

Material and methods: *In a report of 180 aorto-bi (uni) femoral bypasses, 4 anastamotic pseudoaneurysms of the femoral artery were registered. All of these four pseudoaneurysms were unilateral (even when they were bilateral femoral anastomosis). In a single case symptomatology was of peripheral embolic phenomenon, while the rest presented with rapidly growing aneurysms with compression of contiguous structures, which lead to surgical intervention.*

Results: *In two cases a simple interposition with a synthetic knitted graft (Dacron) was performed, and the rest of the cases required complete reconstruction of the femoral bifurcation, utilizing two synthetic (Dacron) prosthesis (femoro-femoral interposition with re-implantation of the profunda femoris artery utilizing another synthetic prosthesis).*

Conclusions: *Results obtained in all the four cases were favorable with complete recovery within a week of surgery.*

ANASTOMOTIC ANEURYSM

Introduction

Anastomotic aneurysms are mentioned as being a frequent complication in medical literature; in our clinical experience we encountered four such cases from which we shall preset the first case due to its particular postoperative evolution.

Material and methods

Patient A.I, *64 years of age, who underwent successive aorto-femoral (unilateral) bypasses and further required after a period of two years surgical re-intervention - an aorto-bi-femoral bypass with uni-lateral femoro-popliteal extension on the left side. Post-operative evolution was favorable with evident improvement, onset of claudication at 5-600 m from 20.*

Specialist consultation was addressed 3 years after surgery, patient presenting with a palpable pulsatile tumoral mass (figure 1) situated in the region of Scarpa's triangle, at the site of the femoral anastomosis, and another one situated internally somewhere in the Hunter's canal. The tumoral mass (figure 2) presented all the signs of a pseudoaneurysm (mass expanding on systole, situated over an anatomic region that corresponds to an artery).

*) **Romanian Journal of Cardiovascular Surgery ■ 2006, vol. 5, no. 1, pp. 33-37**

Figure 1: Tumoral mass: Situated in Scarpa's triangle at the level of the anastomosis between the graft and the profunda femoris artery, the second on the length of the extension

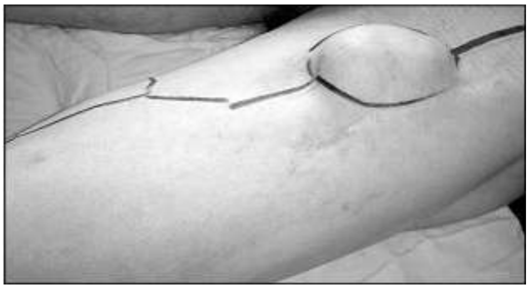

Figure 2: Pseudo-aneurysm of the femoro-popliteal graft

The patient was admitted in surgical ward with complains of pain associated with local compression in the region of the first tumoral mass in Scarpa's triangle - imaging explorations and surgical intervention succeeded rapidly. Careful surveillance using vascular echo-doppler and angio-MRI identified the presence of two fusiform dilatations at the level of the femoro-popliteal bypass (Figure 3).

Figure 3: Image angio-MRI Pseudoaneurysm of the femoro-popliteal prosthesis

Open surgical repair included careful dissection, followed by the obtaining of proximal control of the graft above the tumoral dilatation and the longitudinal incision of the tumoral mass, which concluded the presence of a pseudoaneurysm, with complete disruption of the suture line between the femoro-popliteal and the aorto-femoral bypass. The femoro-popliteal bypass was completely disrupted and was incorporated in a thick fibrous layer, formed over the period of 3 years which maintained it in place (figures 4-5). A new prosthetic graft was re-implanted over the left arm of the aorto-bifemoral graft (figures 4-5). Unfortunately we were unable to dissect the distal tumoral mass, being collapsed due to clampage, and did not have sufficient data concerning its nature (synthetic material fracture?).

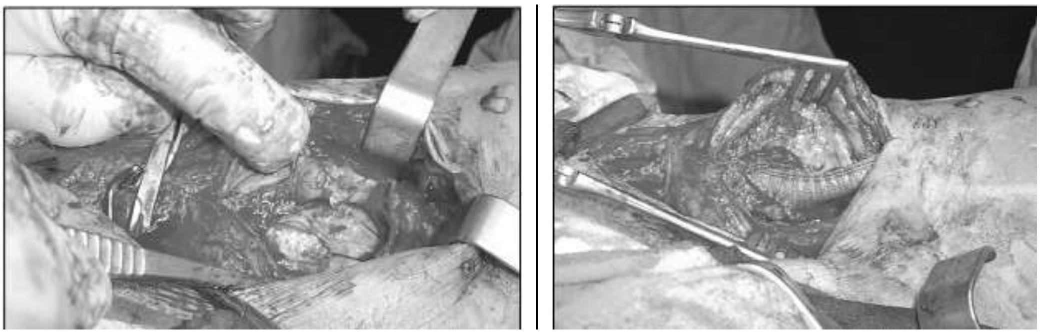

Figure 4, 5: Reimplantation of a new graft on the left arm of the aorto-bi-femoral bypass

The results were favorable, even though the proximal graft was anastamosed with the native graft in termino-terminal position (fig 6-7). The cause of the degeneration of the anastomosis and the development of the pseudoaneurysm was related with the suturing material and the texture of the graft.

Figure 6-7: Image angio-MRI postoperative which evidentiates the 2 anastomosis (proximal and distal) and the permeability of the conduit after intervention

Cases 2, 3 and 4 *presented with a pseudo-aneurysm on one side; two cases involved aorto-bi-femoral bypass, while the fourth was an aorto-uni-femoral bypass after rupture of a right iliac artery aneurysm.*

Time interval after the last intervention was 12 years, 5 years, 4 years and 3 years respectively.

A single case presented with peripheral sub-acute ischemia 48 hours after onset, but did not necessitate emergency surgical intervention.

The rest of the three cases reported at regular follow up, and surgical indications were stabilized according to the growth of the tumoral mass and local simptomatology associated with compression.

Having encountered in the first case two pulsatile masses, we explored the rest of the cases using, angio-MRI and Doppler, the region with the tumoral mass as well as the abdominal proximal anastomosis for any eventual proximal anastomotic pseudoaneurysms (figure 8 and figure 9).

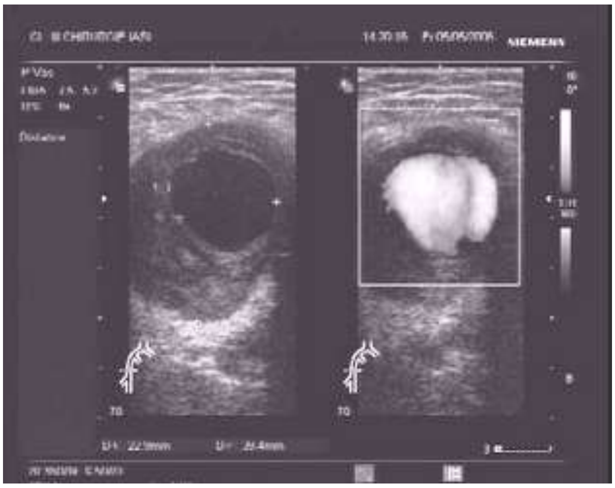

Figure 8: Image Doppler of a pseudoaneurysm with diameter (22.9mm). We can observe the presence of excentric fibrin thrombi that reduces the lumen

Figure 9: Image Doppler at the level of the inguinal ligament where we can observe the prosthesis, emergence of the pseudoaneurysm, retrograd flux in the iliac artery

In all the other cases, no other proximal pseudo-aneurysms were identified; the prosthetic grafts were well incapsulated within surrounding tissue. Patients did not present signs of infection (local or general otherwise).

Surgical intervention

Such surgical re-interventions must be carried out by an experienced vascular surgeon. Access to the anastomotic aneurysm should start proximally, under the inguinal, but may be prolonged over it, in order to successfully gain proximal control (synthetic graft as well as the native artery - external iliac artery being permeable in 2 cases). Dissection should be carried using dissection scissors, as well as surgical blade no. 15, which having a rounded tip allows for debridgement of the thick fibrous periprostetic tissue without vascular trauma; continuous aspiration is necessary. After gaining proximal control, the next step should include encircling the superficial femoral and *profunda femoris* artery. When required, reconstruction of the femoral bifurcation must be carried out.

Results

In 2 cases interposition of an 8mm knitted synthetic graft was performed (prosteto-femoral) (figure 10), while in the rest of the cases reconstruction of the femoral bifurcation was required (figure 11).

Post operative evolution was favorable in all the cases, with patients being discharged within 7 days of surgical intervention.

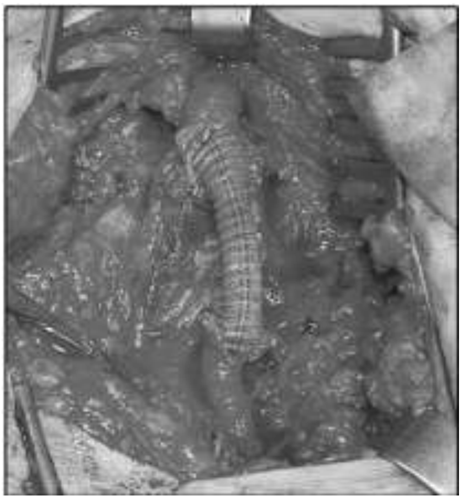

Figure 10: Interposition prosteto-femoral superficial with Dacron graft

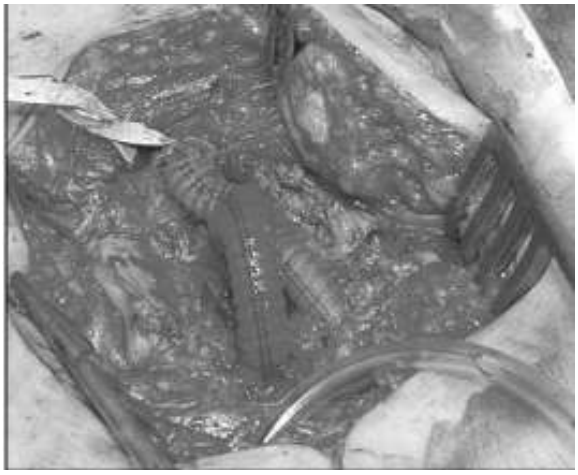

Figure 11: Reconstruction of the femoral bifurcation with graft (Dacron)

Discussions

The incidence of pseudoaneurysms varies between 1 and 5% (Rutherford), and the most common site being the femoral anastomosis. In a report from Emory University, of 41 patients who had femoral pseudo-aneurysms after aorto-bifemoral grafting, 7 % had bilateral aneurysms and 17% had proximal anastomotic aneurysms. Due to this reason, imagistic investigation should always include control for any proximal pseudoaneurysms, and the confirmation of the diagnosis (echo-Doppler, angio-MRI).

The rate of thrombosis for aneurysms less than 5 cm is 17%, while for those over 5 cm is 5% (1, 7). Occurrence of rupture for aneurysms less than 5 cm is 1.6%, while for those 5 cm in diameter is 16% (1, 7).

Factors that contribute to the pathogenesis of anastomotic aneurysms are suture line disruption, arterial wall failure, technical error (taking inadequate bites of graft and arterial tissue during suturing), excessive tension on the graft, thromb-endarterectomy and graft infection (which is the most severe) (8).

We consider that in the first case (patient with 2 pseudoaneurysms), the suture material utilized lacked brittle quality. In rest of the three cases the factor which determined the occurrence of the pseudo-aneurysms was endarterectomy of the common femoral artery during the initial intervention.

Even though arteriography is an ideal method for precise data (situation of the tumoral mass, distal vascular bed) is an unsuitable due to the high risk graft infection. Ultrasonography associated with Doppler (Duplex), should be the first choice investigation to offer data about the proximal anastomosis and distal vascular bed, tumoral mass, fibrin thrombus. Angio-MRI (figure 3) is a useful tool but often does not offer data in excess of duplex even when performed by competent technician.

Open surgical repair is the only treatment for anastomotic pseudoaneurysms and the indications for operation are dictated by the following complications – peripheral emboli with acute ischemia, rupture with bleeding, acute thrombosis. Urgent surgical intervention is indicated when there is rapid dimensional enlargement or infection of the synthetic prosthesis.

Surgical re-intervention of the femoral bifurcation is an important test for the vascular surgeon, having to pass across layers of scarred, fibrous tissue, evidently difficult to dissect. The usage of surgical blade no.15 is called upon many a time to identify vascular structures, and with continuous aspiration, dissection should performed carefully in order as not to damage vascular and nervous structures in the inguinal region.

In the case of venous or arterial trauma during dissection, hemostasis should be performed followed by proximal and distal control. Surgical repair includes identification of the proximal and distal vascular elements (native arteries – iliac, superficial femoral and profunda femoris – and graft), partial resection of the aneurism and interposition of a graft (synthetic or autologous depending from case to case) (6). Cultures obtained intra-operatively (figure 12 and figure 13) are essential for evaluating the case in its integrity. In all the 4 cases, such cultures obtained intra-operatively were negative.

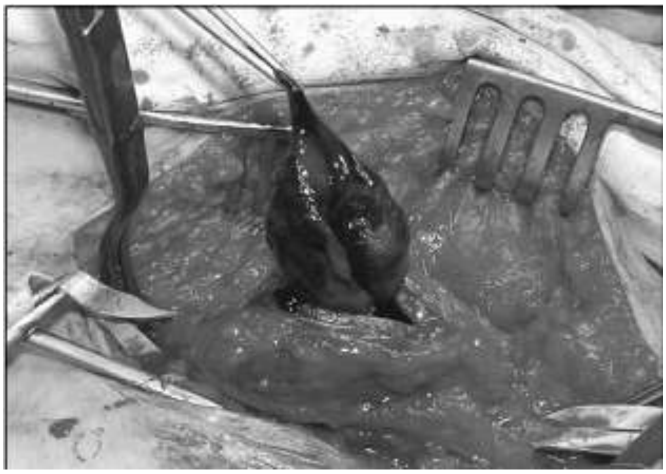

Figure 12: Proximal and distal control, vessel loop on iliac graft, profunda femoris artery, femoral superficial artery, and incision of the pseudoaneurysm

Figure 13: Fibrin clot extracted in its totality

Conclusions

All the 4 cases were elective operations. A single case presented with peripheral ischemia due to distal micro emboli requiring surgery the next day. The rest of the cases presented as an expanding pseudo-tumoral masses, symptoms associated with local compression. Pre and post operative exploration using angio-MRI was performed in one case, while in the rest of the cases echo Doppler was considered as being sufficient. Evaluation of the proximal anastomosis is absolutely necessary; the approach in the case of an aortic pseudoaneurysm is much more complex, and changes the outlook of the entire case. Vascular techniques in the revascularization of an extremity are not difficult and form the basic techniques in vascular surgery. We would like to confess that in spite of mobilization of the pseudoaneurysm during dissection, we did not have any cases of acute ischemia through embolization of a fibrin clot, but advise the clampage of the superficial femoral and profunda femoris artery before mobilization of the pseudo aneurysm. Distal control utilizing Fogarty catheter is recommended and is often necessary.

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Current devices and access sites available in the peripheral endovascular interventions for the vascular practitioner: a short review*)

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Abstract

The authors are presenting a succinct overview concerning the common devices and access possibilities currently encountered in the endovascular interventional field, updated and serviceable in an institutional multidisciplinary program.

Key words: *endovascular, trans-catheter devices, percutaneous vascular access.*

Introduction and historical perspectives

Endovascular interventions had became become an indispensable part of the current therapeutic arsenal in peripheral revascularizations. Since the first percutaneous catheter-based techniques were pioneered by Dotter and Grunzig over 40 years ago (1, 2), many other approaches using low profile balloons, stents, endoprothesis, excimer laser recanalization, cutting balloons, radiations or ultrasound imaging for more complex pathologies and lesions were thereafter developed. In the recent years, new advances regarding adjuvant pharmacologic agents, the drug-coated stents, subintimal angioplasty, excisional atherectomy, cryoplasty and the brachytherapy have showed promising results in the treatment of the multilevel arterial disease and in preventing recurrent stenotic lesions after angioplasty and stenting. These latest, are reputed to hamper the long term benefits of endo-luminal techniques in about one fourth of cases (3, 4).

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It is in the author's whish to consider in this topic a succinct overview of the common devices and access possibilities useful to conceive in a potential institutional endovascular program.

Basic skills and patients selection

A large body of literature points at present-days, the increasing interest allowed to endoluminal procedures devoted to stenotic or occlusive vascular lesions, aneurysms, traumatic and arterio-venous pathologies, gene therapy etc.

Although little is known about the long term durability of these techniques, their wide utility and confined aggressiveness have brought a major impact in the training and the general practice of the contemporary vascular interventionist (5).

In the current practice, percutaneous vascular access and radiological imaging techniques are noticeable elements in the common catheter-based practice. From the surgeon's point of view, most interventions are achievable in the operating room, using a portable C-arm fluoroscopic unit, with adequate surgical table adapted for connective procedures. New models of roentgeno-graphic C-arm units provided with digital storage disk, "road mapping" and able to create "freeze-frame" techniques and high quality definition imaging are however requested in the modern endovascular units. Although most surgeons are probably already familiar with these requirements (the practice of central venous access catheters and/or vena caval filters placements), the training with a fluoroscopy-based indirect monitoring and the subsequent "under the wire" manipulations, are probably few mandatory new skills necessary to be possessed. Some of these habits are similar to those needed in performing laparoscopic-techniques, thus working on virtual images away from the operative field.

A probably important point to consider in planning an effective endovascular service, is to create an "endovascular team", establishing an agreement among the different involved participants (vascular surgeon, interventional radiologist, cardiologist etc.). Practically, this could also focus on their optimal contribution, the location of the procedures and the follow-up of the patients.

Current contemporary opinions are also stipulating the usefulness for the endovascular specialist or correspondent team, to assume a complementary therapeutic approach between the "trans-catheter" and the open surgical techniques, with a convergent issue in each given case (7).

The decision to perform a "classical" surgical versus endovascular or combined revascularization and the assessment of the maximal benefit and risks for each therapeutic option depends undoubtedly on a rigorous patient’s selection. Multiple factors need to be evaluated in order to make a proper indication including:

a) the characteristic of each presentation concerning the anatomical type and the level of the lesions. Thereafter, a contributory concern is represented by the *Trans-Atlantic Inter-Society Consensus* (the TASC classification) (8), Table 1, 2, 3 – next page)

b) the clinical presentation (claudication, versus critical ischemia);

c) the potentially associated diseases: coronaropathy, diabetes, renal insufficiency, smoking, obesity etc.;

d) the life expectancy: the survival rate at 5 years was evaluated at 50% in subjects with peripheral arterial disease (PAD) and ankle-brachial index (ABI) at less than 0,5, besides those patients presenting critical limb ischemia (CLI) (9, 10);

e) the ambulatory autonomy;

f) the individual technical points: local sepsis, fresh thrombosis, unaffected autologous vein, calcifications, multilevel disease etc.

g) the independent consent of the person.

Table 1: The TASC Classification of the Iliac Artery angiographic Lesions

TASC – CLASSIFICATION OF ILIAC LESIONS
TASC – A. ILIAC LESIONS
Single Stenosis of CIA or EIA (Unilateral or bilateral) < 3 cm
TASC – B. ILIAC LESIONS
Single Iliac Stenosis of 3-10 cm, not involving the CFA
Two Iliac Stenosis < 5 cm, not involving the CFA
Unilateral CIA Occlusion
TASC – C. ILIAC LESIONS
Bilateral CIA or EIA Stenosis of 5-10 cm, not involving the CFA
Unilateral EIA Occlusion, not involving the CFA
Unilateral EIA Stenosis extending into the CFA
Bilateral CIA Occlusions
TASC – D. ILIAC LESIONS
Extensive Stenosis > 10 cm of the CIA, EIA and CFA
Unilateral occlusions of the CIA and EIA
Bilateral EIA Occlusions
Iliac Stenosis concomitant to Aortic or Iliac Aneurysms

Table 2: The TASC Classification of the Superficial Femoral and Popliteal Artery angiographic Lesions

TASC – CLASSIFICATION OF THE SUPERFICIAL FEMORAL AND POPLITEAL ARTERY LESIONS
TASC – A. FEMOROPOPLITEAL LESIONS
Single, focal Stenosis < 3 cm
TASC – B. FEMOROPOPLITEAL LESIONS
Single SFA Stenosis of 3-10 cm
Heavily Calcified or Multiple Stenoses < 3 cm
TASC – C. FEMOROPOPLITEAL LESIONS
Single Stenosis or Occlusion > 5 cm
Multiple Stenosis of 3-5 cm
TASC – D. FEMOROPOPLITEAL LESIONS
Occlusion of the entire SFA
Occlusion of the SFA and the Popliteal Artery

Table 3: The TASC Classification of the Tibial Artery Lesions

TASC – CLASSIFICATION OF TIBIAL ARTERY LESIONS
TASC – A. TIBIAL LESIONS
Single Stenosis < 1 cm
TASC – B. TIBIAL LESIONS
Multiple focal Stenoses, each < 1 cm
TASC – C. TIBIAL LESIONS
Stenosis of 1-4 cm
Short Occlusions of < 2 cm
TASC – D. TIBIAL LESIONS
Diffuse Stenoses of > 4 cm
Occlusions of > 2 cm

Patients with CLI (rest painor gangrene according to the stage III and IV of Fontaine or grades II and III, category 4, 5 and 6 in conformity with the Rutherford classification), are typically subjects of a multilevel disease and often require staged endovascular approaches or combined surgical by-pass and angioplasty (11).

In their recommendations, the TASC Working Group (8) suggests the endoluminal treatment as a clear indication for type A iliac and femoropopliteal lesions and surgery for the type D arterial disease, respectively. Recent results available from increasing clinical experience, are proposing endovascular approaches much more frequently and often like the first line of interventions in larger types of lesions (12). This aspect reflects perhaps the extended progresses in endovascular technology and experience (12).

In TASC-B lesions, the percutaneous transluminal angioplasty (PTA) has become the priority method of treatment based on level V and II of evidence (13). Although for infrainguinal TASC-D lesions, there is yet no proven benefit for other satisfactory revascularization than the conventional femoro-popliteal or femoro-distal bypass (14), a number of authors suggests (also for some aspects of type C presentations) the endovascular approach, as "the first line" of treatment (14). Several factors are supporting this reasoning: the large applicability of endoluminal treatment, the lower perioperative morbidity and mortality and the respect for a potential unaffected "second line" surgical solution.

Nevertheless, the evolving trans-catheter techniques with improving devices and enhanced skills, are playing an essential role in the future therapeutic orientations.

Basic instrumentation for endovascular procedures

A succinct overview of the principal endoluminal instruments currently available for the interventional specialist could be attempted in the followings, without itemize the whole commercial variety of products disposable at present, which is beyond the purpose of this paper.

Sheaths and Catheters

They are disposable in a diversity of forms and materials (teflon, polyurethane, polyethylene etc.). Sheaths can stabilize the vascular access, allowing endoluminal manipulations with less blood loss and arterial damage. A majority of the procedures can be performed via a 4 to 6F diameter and 11 cm-length sheaths. Longer and flexible sheaths are advantageous for the contra-lateral limb access (Figure 1) and for the renal, visceral or supra-aortic trunks entrance. Catheters with different standard preformed shapes and sizes are useful in the diagnosis, the access and the post-procedural evaluation of the target lesions. Some flexible catheters with slipping coating in combination with glide-wires, could ensure a good trackability and represent a very operative combination in crossing tortuous arteries and sharp angled bifurcations (Figure 2). They provide also good support for fibrinolytic therapy and endovascular measurements and spotting by their tips and optional radiopaque markers.

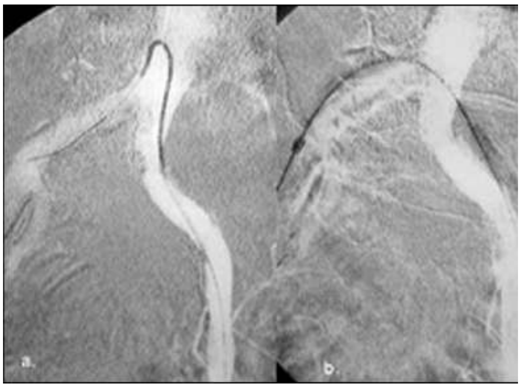


Figure 1: The contra-lateral inferior limb access, using the "cross-over" technique

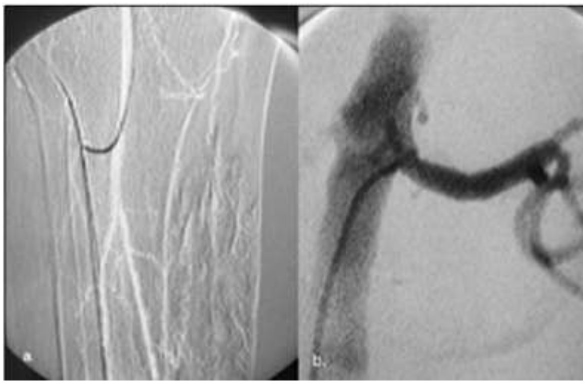


Figure 2: An example of endovascular catheterization in an occluded anterior tibial artery (a), respectively in a left renal artery (b), allowed by right angled and slipping coated catheters

A new generation of catheters with flexible tip, allowing difficult vascular accesses (Venture, St. Jude Medical) has been recently developed.

Guidewires are containing a stiff inner core and a flexible outer coil. Different types of wires are commonly used according to the different stages of the intervention: standard-wires, glide-wires, exchange-wires or stiff-wires. Therefore, the stiffness and the frictional resistance are two important features to take into account in choosing the optimal device. Classically, the 0.035 inches wires allow the majority of accesses to the target lesions. Glide-wires provide difficult passage in tortuous or thrombosed arterial segments and are also helpful in new interventional conditions like the extraluminal recanalizations of long arterial occlusions (subintimal angioplasty). They should not be used like support in the initial arterial access since the coating could be torn by the entry needle. An important technical point for the practitioner is to keep the wire stable once the lesion has been crossed, allowing a permanent control of the trans-catheter manipulations during the entire procedure. Inasmuch smaller guide-wires (from 0.014 to 0.018 in.) yield access of smaller balloons, stents and laser devices in tiny vessels like the tibial trunks, these wires are however delicate and care must be taken to avoid deformations.

Balloons are representing an important category of "endo-tools". The "Angioplasty effect" which is responsible of the balloon inflation, delineates in fact a complex local mechanical outcome with controlled injury of the vessel wall, including focal plaque fracture, adventitial stretching and limited dissection. The global result is expressed by an enlargement of the "circulating section area" of the vessel. Available in a coaxial or monorail-type design, the balloons present different shaft sizes, diameters, profiles, length and construction materials (nylon, propylene or polyethylene). They could be compliant, with utility in the endovascular control of hemostasis, non-compliant with constant intended shape even at different pressures of inflation (current utilization in PTA) or semi-compliant (a combination of both).

Hence, some notable technical conditions must be pointed out:

a) large balloons require less pressure to perform substantial radial force, conversely small-diameter balloons need higher pressure to be effective;

b) the optimal inflation pressure often represents the lowest pressure able to make the stenotic indentation disappear;

c) the optimal diameter size of the balloon is equal to the native artery with the lowest possible length (it is generally recommended to avoid exposure of the healthy tissue which could enhance additional hyperplasia);

d) the stenosis best suited for angioplasty is a concentric lesion located at 5mm or more from the nearest bifurcation;

e) the time for inflation is variable. Probably short inflations are less traumatic and thereafter with decreased risk of further intimal hyperplasia. It has been showed that 180 seconds instead 30 seconds inflation time, are diminishing the probability of dissection and residual stenoses in PTA (15) but does not affect significantly the long term patency of the treated vessel (16).

Angioplasty can also be performed with special balloons provided with blades or the "cutting balloons". These seem to be specifically useful in calcified stenoses, myointimal hyperplasic or ostial lesions, in-stent or vein graft restenoses (17, 18). The Figure 3, shows a case of revascularization using cutting balloons in calcified tibial artery stenoses of a diabetic patient.

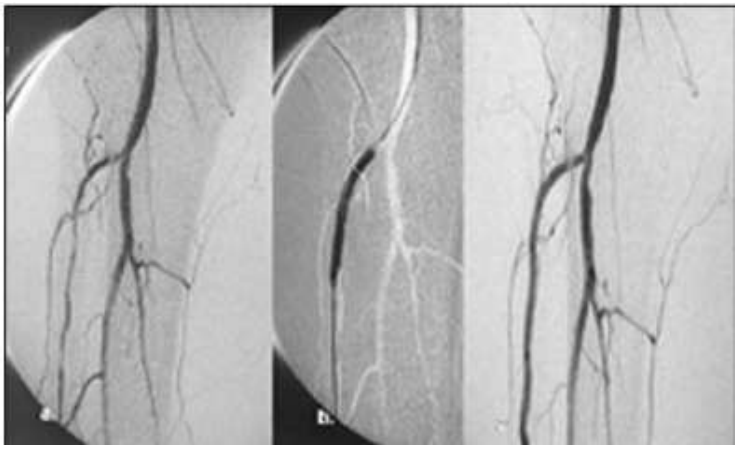


Figure 3: Endoluminal revascularization for multilevel tibial disease using the "cutting balloons" (Boston Scientific co.) in calcified stenoses of a diabetic patient

Another type of PTA is represented by the intentional extraluminal recanalization or the "Subintimal Angioplasty" (SA). This technique allows revascularization of extensive occluded arterial segments longer than 3 cm (TASC-C and D lesions), creating an intentional dissection channel (Figure 4) frequently devoid of calcifications. It is less aggressive than the conventional bypass and reproducible. The method seems to be beneficial especially in fragile patients with critical limb ischemia (CLI) (19), where open classical repair could enhance a noteworthy challenge. Likewise, in case of technical failure, SA does not preclude consequent bypass surgery (19, 20). However despite modest mid- and long-term patency, this technique allows a better immediate tissue perfusion and optimizes limb salvage in this contingent of generally "high-risk" surgical patients (19-20).

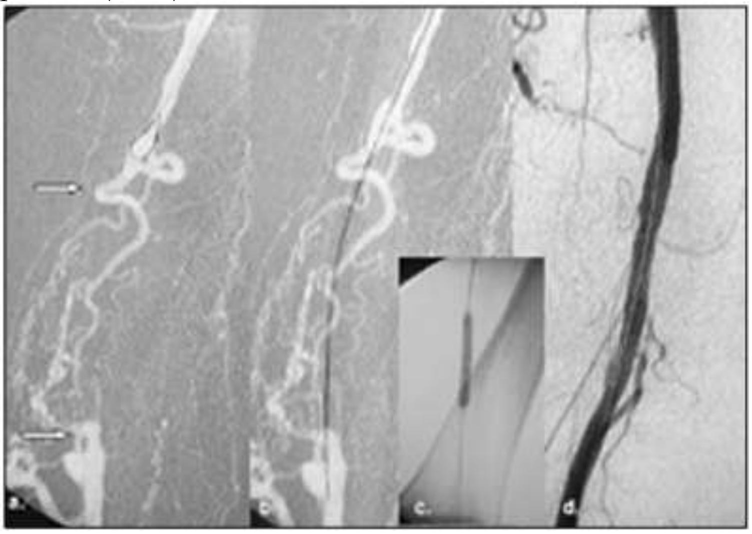


Figure 4: Recanalization of an occluded superficial femoral artery by "Subintimal Angioplasty": a) Initiation of the proximal subintimal channel by the loop of the glide-wire; b) The achievement of the new extraluminal way and the "re-entry" in the native artery at the popliteal level; c) Complementary angioplasty to improve the flow through the reopened passage; d) The final angiographic result

Stents and endoprosthesis

The "stenting effect" consists in a remodeling of the vascular lumen in a more desirable configuration without excluding the atherosclerotic plaque. Two types of currently available stents are worthy of comment: the balloon-expandable (BE) stents (stain-less-steel construction) and the self-expanding (SE) stents (made from stainless-steel or nitinol, which is a metal alloy provided with thermal memory that expands at the normal body temperature).

The BE stents allow placement with high degree of accuracy in the target arterial lesions, with recommended deep location (low risk of mechanical impact and deformity). They are also helpful in the treatment of ostial or eccentric lesions and should be used only with non-compliant balloons (Figure 5). The SE stents excel by their flexibility and are easy to deploy in the cross-over technique on the contra-lateral limb lesions. Therefore, other advantages of their elastic properties are the possible placement in superficial located artery with high risk of traumatic deformity, in tortuous or mechanical twist exposed arterial segments and through the diseased vessels of different native diameter (Figure 6).

Figure 5: Angiography showing bilateral subocclusive ostial renal artery stenoses (a – arrows). Synchronuous angioplasty and stenting of the right (b), followed by the left (c) renal arteries

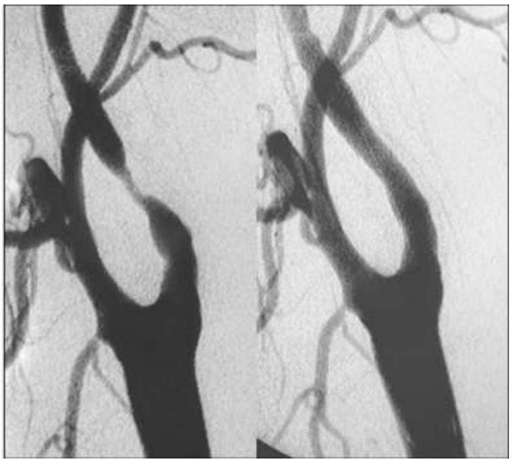


Figure 6: Filter protected carotid stenting using a nitinol stent (Precise, Cordis Inc.) covering the internal carotid lesion, but also the initial part of the common carotid artery

Current situations when stenting is needed include (21):

a) inadvertent dissection during PTA,

b) inadequate "angioplasty effect" (residual stenosis greater than 30% on angiography or systolic pressure gradient superior or equal to 5mm Hg),

c) "elastic recoil" after PTA in eccentric lesions,

d) localized ulcerative plaques with embolic symptoms and

e) totally occluded artery, where simple PTA have showed disappointing results (embolic events and poor long-term patency (22)).

Recent information suggests that for TASC type A and B presentations, selective stenting in iliac and femoropopliteal lesions is equivalent to primary stenting and that PTA should be tented first in these focal lesions (23, 24). Although lacking for evidence provided by randomized trials, for TASC-C and D iliac disease also for the external iliac lesions (25), direct stenting seems to be advisable. Despite promising mid-term data regarding the nitinol stents, the late restenosis (after 1-2 years) and the stent fracture rate (noted in the treatment of long lesions situated in "risk zones" with high dynamic forces), represent clear long-term limitations. Specifically for the femoropopliteal segment it appears to be a growing consensus to avoid primary unvarying stenting, in keeping this alternative as a provisional late resort only after sub-optimal angioplasty (26). Concerning the below-knee lesions, although surgery remains the "gold-standard" treatment in terms of patency and hemodynamic success, many recent data from the literature suggest that endovascular therapy should be considered as the "first-line" approach, because it is safe, less aggressive and with fewer major complications than surgery (27).

Hoping to improve their patency by diminishing the risk of myointimal hyperplasia, other variant of stents have been proposed. The coated stents which contain non-biodegradable polymers (polyurethane, silicone, cellulose etc.), loaded drugs (heparin, hirudin, glycoprotein IIb/IIIa) or antiproliferative agents (drud-eluting stents with sirolimus, angiopeptin) and also the radioactive stents are equally yet under clinical evaluation.

The Biodegradable Stents represent in addition a new promising therapeutic alternative. The complete absorption of these devices after two months confers a probable significant decrease in intimal hyperplasia (28). Larger randomized studies are thus needed to state their applicability and long-term results.

Endoprothesis or covered stents comprehend a classical stent covered with Dacron or polytetrafluo- roethylene (PTFE). Their large utility have been demonstrated in the treatment of the aorto-iliac aneurysmal pathology (Figure 7) but also in the endovascular approach of dissections, traumatic arterial perforation or false aneurysms, arterio-venous fistulas, popliteal aneurysms and recanalization of thrombosed arterial segments. It has been shown in this later category, that beyond the iliac branches, the endoprothesis diameter (inferior to 7mm) and the length of the occluded zone (superior to 10 cm) seem to play an important role in the post-operative permeability (29).

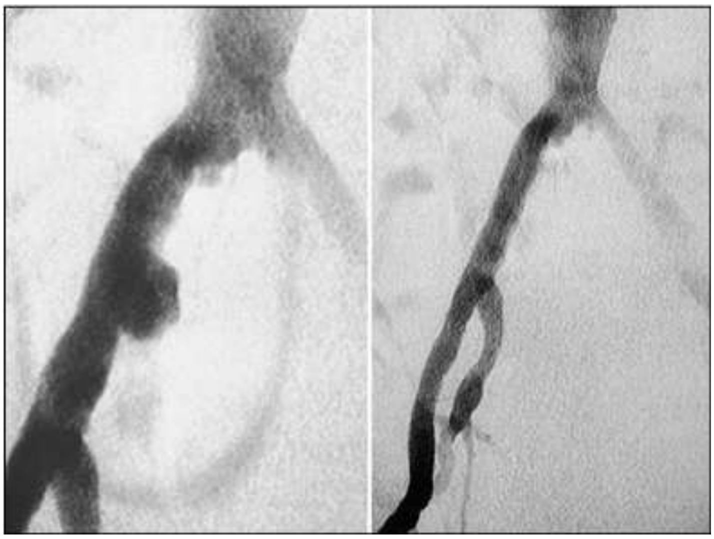


Figure 7: A right common iliac artery aneurysm excluded by a retrograde femoral placed endoprothesis (Viabahn, Gore-Tex Inc.)

Laser light energy and excisional atherectomy devices, are other methods used for peripheral revascularizations. Excimer laser recanalization is an alternative technique to treat total chronic occlusions. Laser-assisted angioplasty has the ability to degrade molecular links by photochemical means therefore, in the thrombus-dominant lesions, the new channel is little larger than the laser-catheter itself, whereas in atherosclerotic-dominant occlusions the new lumen has an identical shape as the leading catheter. Succeeding PTA or stenting are often required to complete the final hemodynamic result.

Endoluminal excisional atherectomy uses rotational or unidirectional devices, that avoids the baro-trauma which invariably occurs after PTA. This technique that showed a recent renewed fervour, excise plaque with either spinning or focally applied cutting blades. The longer operative time, the noticeable distal embolic risk, the larger sheaths demanded and the need of frequent association to PTA, are some noted limitations of the method despite encouraging 6 months and midterm results (31, 32).

Endovascular thrombectomy and thrombolysis are other useful ways to approach thrombus dominant occlusions. Recent thrombus is easier to treat than the ancient, more adherent thrombotic lesions. Nevertheless, a rigorous patient selection for thrombolysis which carries an undeniable risk of bleeding is thus mandatory (33).

Endovascular Cryoplasty consists in a combination of angioplasty coupled to a system that delivers simultaneous cold thermal energy to the arterial wall.

Following this method, it has been experimentally shown a concomitant induction of apoptosis in smooth muscle cells that participate in the restenosis process (34). Albeit the technical success and immediate results which seems promising with acceptable late arteriographic patency (35), further prospective studies are thereafter needed to state its efficacy.

Intravascular Ultrasound imaging catheters (IVUS) provide cross-sectional diagnostic information and corresponding assessment of the efficacy of intraluminal interventions. The morphologic differentiation of the lesions, the accurate definition of the luminal dimensions and pathologies (such intimal flaps and dissections) and the precision of the estimations (i.e. stent deployment) (36), are important features of this class of instruments with recognized qualities.

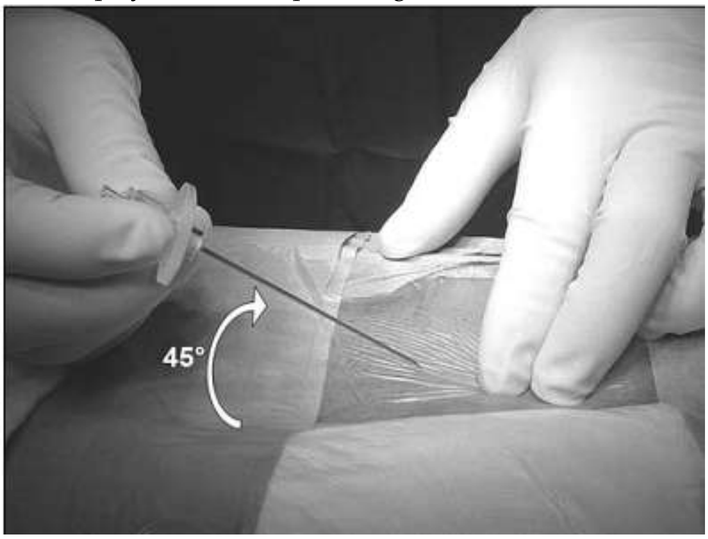
Complementary endovascular devices are also used in the trans-catheter techniques. Among them, the Cerebral Protection Devices (CPD) is conceived to reduce the incidence of intracranial embolic events during carotid artery stenting (CAS). There are roughly three principal groups of CPD under clinical investigation such as filters, distal single balloon occlusion and double balloon occlusion with reversal-flow or aspiration systems. CAS is an evolving technique, and contemporary published clinical experience seems to indicate that the use of CPDs, provides a possible beneficial postoperative outcome (37-38). However, currently available CPDs have specific technical limitations, and the level – I evidence concerning their utility has not yet been stated (39-40).

Endovascular *Arterial Closure Devices* (ACD), as hemostatic agents after withdrawal of the trans-catheter instrumentation, are yet also gaining a heightening utilization. They are reputed to provide expeditious hemostasis and early ambulation of the patients, in keeping uninterrupted the anticoagulant therapy. Several types of this kind of equipment were developed such as the mechanical compression (Femostop), the collagen disk system which serves as an "intra-luminal anchor" (Angioseal), the external arterial wall sealing (Duett) and the percutaneous endo-suture method (Perclose). Although the ACD have documented a significant reduction in time for the postoperative hemostasis and discharge of the patients, their global superiority compared to the manual compression is controversial and none of these devices has been proven to reduce the major local complications (large pseudo-aneurysm and retro-peritoneal hematoma) (41-42). Local sepsis and arterial occlusion are rare but notable drawbacks additionally encountered with ACD systems (43).

Percutaneous accesses for endovascular techniques

Vascular access imply a complementary and flexible concept which gather the dominant percutaneous way, jointly with elective surgical minimal-invasive options and represents an other influential step in planning the future intervention.

The patient's anatomical conformation, the pre-operative assessment and the type of lesions, play thereafter a prevailing decisional role in the subsequent therapeutic approach.



Appropriate skin disinfection and draping are mandatory. It is important to keep a constant palpation of the arterial pulse to guide the direction of the needle. The arterial puncture should be done by a single stick, holding a constant 45° angle of the needle (Figure 8).

Figure 8: Percutaneous arterial puncture in keeping the needle at 45° inclination from the skin plane

Although the double wall arterial puncture has a current widespread utilization, the single anterior wall stick presents the advantages to be befitting when closure devices are used to conclude the intervention or when unplanned fibrinolytic therapy is requisite. Percutaneous arterial access could be difficult in strengthless pulse arteries, when local calcifications or remote lesions are diminishing the blood flow. In these instances, a doppler guided needle, an upstream injection of contrast media, a puncture focusing on the linear calcifications (Figure 9) or a small superficial skin incision could be helpful.

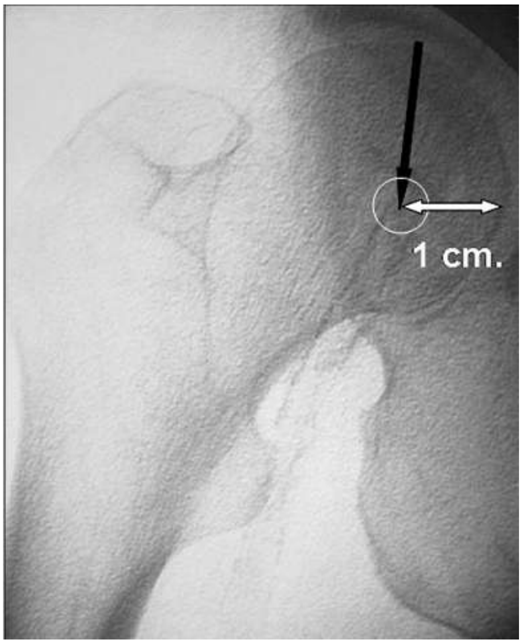


Figure 9: Targeting the common femoral artery under fluoroscopic guidance in the groin: the adventicial calcifications and the orientation of the tip of the needle at 1 cm lateral from the most medial border of the femoral circumference, could be helpful markers

The groin access in the Common Femoral Artery (CFA) is the prevailing technique for the majority of the trans-catheter diagnostic and interventional procedures. It provides a convenient ante-, or retro-grade flow control. In some patients with particular body habitus (i.e. obesity) or associated pathologies (i.e. groin hernias), the arterial puncture can be fastidious (Figure 10). Bony marks of the femoral head could help in these situations by targeting the tip of the needle 1 cm lateral from the most medial border of the femoral circumference (Figure 9).

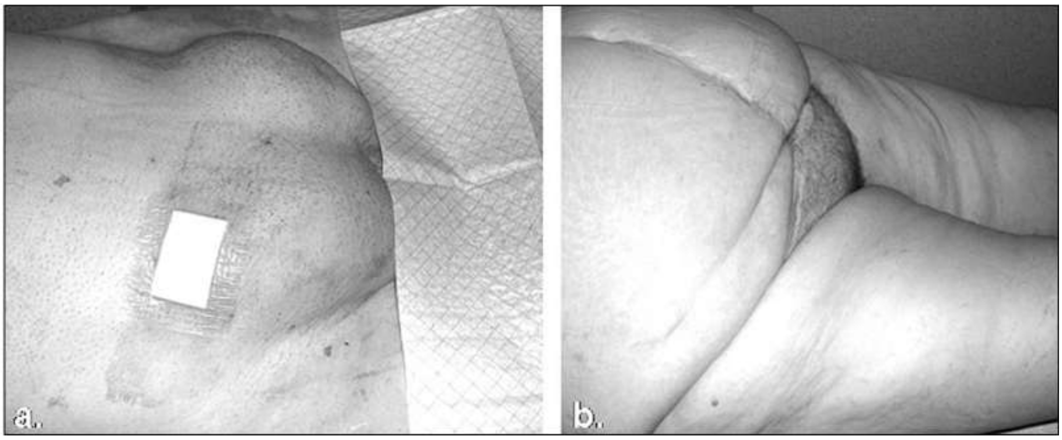


Figure 10: Difficult situations encountered in the femoral percutaneous access such as the presence of the groin hernias (a) and obesity (b)

Beside the visceral and the supra-aortic trunks approach, the retro-grade femoral access provides contra-lateral iliac and femoral vessels entrance (the cross-over technique), to treat lesions of the opposite limb by different recanalization procedures (Figure 10) or by fibrinolytic therapy. The ante-grade femoral access is more technical demanding. Often, a test of a sparing contrast injection is recommended to ensure the exact location of the profonda femoris artery, which can be sometimes inadvertently punctured (Figure 11, next page). It is in the author's belief, that this accustomed attitude is prudent and serviceable before the introduction of the guidewire.

Inasmuch fibrinolysis is not projected, this way enable also extremely distal access to reach the tibial or pedal arterial trunks lesions, where catheter manipulations could be difficult to achieve by the contra-lateral femoral access (Figure 12, next page).

The percutaneous trans-popliteal access: warrants in a retro-grade way, a favourable approach to the ipsilateral iliac artery disease, when the femoral cross-over is not feasible and also for "junction lesions" situated between the CFA and the *superficial femoral artery* (SFA) (44-45). It seems to be also convenient and safe in treating flush occlusions of the SFA by retrograde subintimal angioplasty (45-46).

Brachial artery access was described to be fitted in treating carotid stenosis (47) or other supra-aortic trunks lesions. This path could be useful particularly for CAS, when unfavourable "bovine" type or other "hostile" aortic arch anatomy is documented. Another possible indication is represented by the coexisting aorto-iliac atherosclerotic disease, which hampers the efficacy of the common femoral access. Additional axillary, radial or even subclavian artery (48) percutaneous puncture and accesses were furthermore detailed. These could be more serviceable to treat lesions in the thoracic aorta, the brachiocephalic vessels and also those renal or visceral arteries that emerge in an acute angle (less than 60°) from the abdominal aorta.

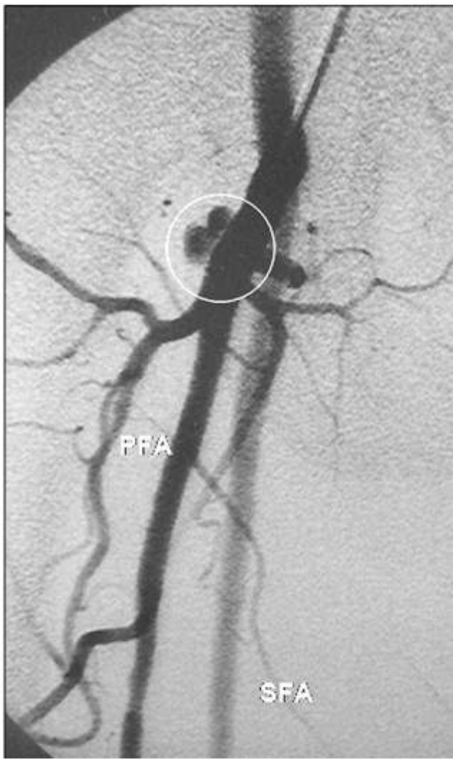


Figure 11: Fluoroscopic control after antegrade femoral puncture is advisable, in order to exclude an eventually inadvertent access in the profonda femoral artery

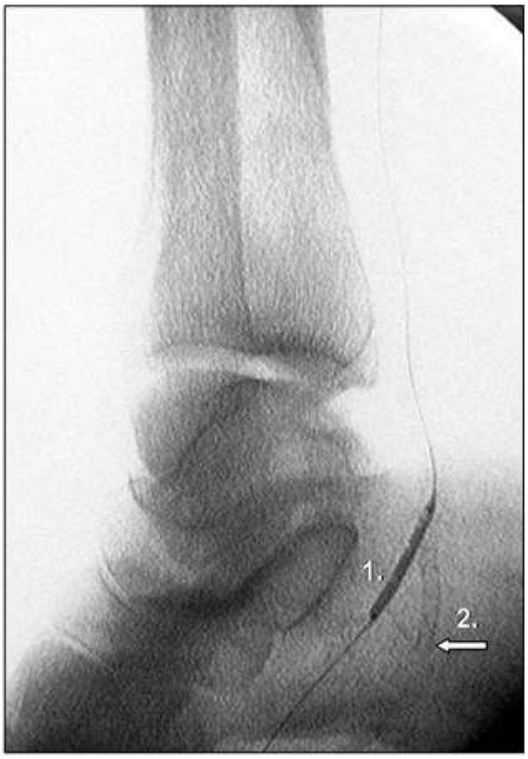


Figure 12: Angioplasty of the distal tibial and plantar vessels (1), allowed by the antegrade ipsi-lateral femoral path; note the heavy arterial calcifications (2), often confronted in the multi-level ischemic disease of the diabetic patients

Finally, taking in account that the aorto-iliac occlusive and aneurysmal disease are not so rare features observed in these poly-vascular patients, some contemporary reports promote in addition the minimally invasive trans-cervical approach for protected CAS, which has been showed encouraging preliminary results using different types of CPD (49-51).

Overall, it should be mentioned that nowadays, new advances in devices and access possibilities that at the first glance did not appear to be revolutionary, have in reality a non-negligible influence on how these relatively new procedures are successfully carried out in the vascular field (52).

Conclusions

Endovascular techniques have showed an impressive evolution over the last several decades. The development of imaging and new interventional technologies in catheters, balloons, cryoplasty, subintimal angioplasty, stents, laser light, atherectomy and all the other derivative devices and associated pharmacotherapies, are bearing new concepts and therapeutic strategies for the vascular surgeon which became more involved in a field of interdisciplinary interest. New possibilities to treat complex lesions are thereafter appearing that only a few years ago would have been managed by surgical means. Consequently, new challenges and debates are also emerging, that engage the ability of the new interventional specialists.

It is perhaps the goal of this topic to enhance a brief discussion focusing on the current catheter-based contemporary technologies, whose evolution will probably continue to remodel our specialty frontiers and the future approach to the vascular pathology.

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Interventional treatment with autoexpandable stents in ileofemoral arterial diseases*)

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The importance of peripheral arterial diseases is revealed by statistical data collected during Framing-ham study, which showed a frequency of arterial diseases equal to the one of stable angina. According to this study, annual incidence of PAOB was 26/10.000 in men and 12/10.000 in women, and one third of these cases were located in aortoiliac arteries (10).

The traditional treatment of these patients was the surgical bypass, but, as we all know, surgical bypass at this level is frequently associated with a high risk. Analyzing the studies published from 1957 till 1997, an operative mortality of 3.3% and a general mortality of 8.3% were recorded for aortoiliac bypass surgery.

An alternative therapy for these cases is the interventional treatment, which is a less invasive procedure, with an immediate success rate of 95%, and good long term results comparable to surgery (analysis of recorded data showing a 5 year patency of 80-90%) (18).

The unresolved issues in iliac interventions, which are still subject to debate between interventionist and vascular surgeons, include the following:

- surgery versus endovascular treatment in complex lesions;
- primary versus secondary stetting and the role of lesion morphology in selecting between the two alternatives;
- the importance of maintaining the patency of hypogastric arteries during the intervention;
- the role of thrombolysis;
- the choice of stent from different types available on the market;
- the appropriate length of stent;
- the access (contralateral, ipsilateral, axillary).

According to international trials, there is no statistical significant difference between surgical and interventional treatment regarding the long term patency. In these circumstances, the reasons to choose interventional treatment could be: it is less expensive, it decreases the duration of stay in hospital, it does not require general anesthesia, and complications are less frequent and less severe (1, 7).

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History

The interventional treatment was introduced for the first time by Charles Dotter, the father of interventional therapy, and Judkins, who performed the first PTA in 1964, using coaxial catheters in femuro-popliteeal arteries, and in 1973, Gruntzing introduced for the first time the PTA ballon catheter and performed the first PTA using this balloon catheter. Streptokinase was discovered by Tillet and Garner in 1933, and was first time used in peripheral arteries by Dotter in 1974, which administrated Streptokinase in low dose local, intra-arterial, describing a good result with repermeabilisation of arterial bed in 70% of cases. In 1985 Simpson introduced rotablation aterectomy, and in 1969 Dotter performed the first arterial stent implant in a dog, procedure which was extended to humans in 1987 by Sigwart, who performed the first stent implant in iliac artery in a men.

In Romania, first angioplasties were performed in our clinic in 1978, in subclavian artery, renal artery and in one case it was performed in aortic coarctation. In 1989, in Bucharest this method was introduced in the cardiac catheterisation laboratory by Prof. Fotiade, and from 1984 this procedure was currently used in the Cardiology Clinic of Targu-Mures, with a continuous growing number of cases treated each year.

If we analyze the data from registries, we note that while the number of surgical treated cases increased from 24/100,000 inhabitants in 1979 to 65/100,000 inhabitants in 1989, the number of interventional increased from 1/1,000,000 cases in 1979 to 32/100,000 cases in 1989, showing a much more pronounced tendency to increase (figure 1).

Unfortunately, despite the increased number of treated cases and the technology progress, the number of limb amputation remains constant (30 cases/100,000) inhabitants) (3).

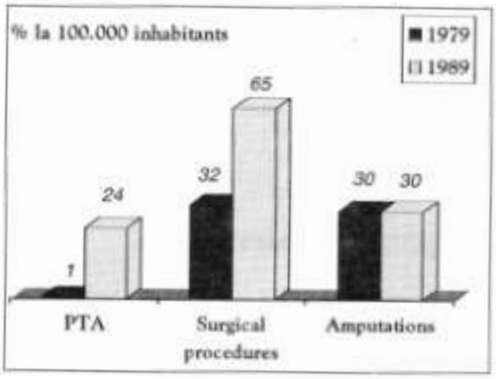

Figure 1: Methods of treatment in peripheral arterial diseases - tendencies from 1979 to 1990.

The role and place of interventional treatment of PAOB begun to be recognized and accepted in 1984, when the Council of for Scientific Affairs of the American Medical Association stated: "Angioplasty is an alternative of surgical by-pass". Also in 1984, the *Health and Public Committee of the American College of Physicians* declared that PTA requires less medical assistance that the surgical bypass. In 1999, the role of interventional treatment was also accepted by the surgeons, in an article published by Bequemin et al in Journal of Vascular Surgery: "*Surgical iliac PTA with selective stetting: long term results*" concluding: "*the angioplasty is the elected treatment in localized iliac lesions*".

These days there is a great debate about who should perform these interventional procedures: the cardiologist, the radiologist, the angiologist or the vascular surgeon? The proportion is different in different countries of Europe (figure 2, next page). In our opinion, the cardiologist should be responsible for these interventional procedures, knowing how to prevent and to treat possible complications that could occur, but the most important fact is the good collaboration in a team which includes all these specialties (8).

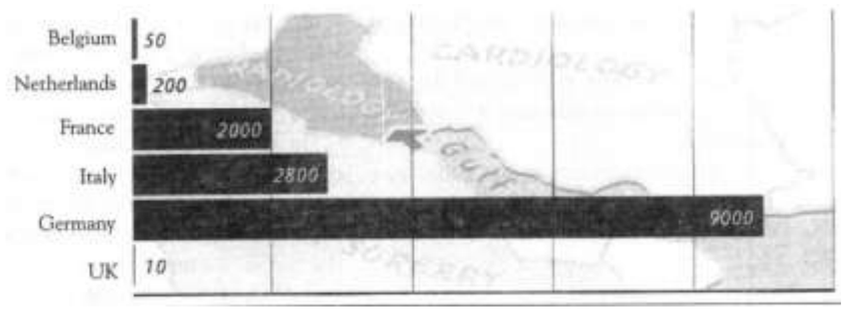

Figure 2: Interventional procedures performed by cardiologists in different European countries in 2000

Among the possibilities of interventional treatment in peripheral arteries, the most important which we apply in our clinic are: percutaneous transluminal angioplasty, intraarterial stent implant, laser angioplasty and intraarterial thrombolysis, some of them performed with IVUS control.

Indications for interventional treatment

Interventional treatment is recommended especially in cases of short, isolated stenosis of great vessels (iliofemoral arteries). During the last years, indications for interventional treatment were expanded to more difficult and complex cases, due to the advances in technology of endoluminal treatment products.

The indications of interventional treatment on iliofemoral arteries, according to AHA guidelines published in 1994, are listed in table 1. Still, these indications are nowadays expanded to different situations, such as: long occlusions of superficial femoral artery, PTA in absence of surgical bypass possibilities, or in association with surgical bypass, in cases of bypass stenosis, or limb salvage angioplasty (14).

Table 1: Indications for interventional treatment in peripheral arterial diseases in ilio-femoral segment

1. Iliac angioplasty	
Category 1	• Stenosis is less than 3 cm in length and concentric and noncalcified.
Category 2	• Stenosis is 3 to 5 cm in length • Calcified or eccentric and less than 3 cm in length.
Category 3	• Stenosis is 5 to 10 cm in length • Occlusion is less than 5 cm in length after thrombolytic therapy with chronic symptoms.
Category 4	• Stenosis is greater than 10 cm in length • Occlusion is greater than 5 cm in length, after thrombolytic therapy and with chronic symptoms • Extensive bilateral aortoiliac atherosclerotic disease, • Iliac stenosis in a patient with abdominal aortic aneurysm or another lesion requiring aortic or iliac surgery

2. Femoral angioplasty	
Category 1	• Single stenosis up to 5 cm in length that is not at the superficial femoral origin or distal portion of the popliteal artery, • Single occlusion up to 3 cm in length not involving the superficial femoral origin or distal portion of the popliteal artery.
Category 2	• Single stenosis 5 to 10 cm in length, not involving the distal popliteal artery, • Single occlusion 3 to 10 cm in length, not involving the distal popliteal artery, • Heavily calcified stenosis up to 5 cm • Multiple lesions, each less than 3 cm, either stenosis or occlusions, • Single or multiple lesions where there is no continuous tibial runoff to improve inflow for distal surgical bypass.
Category 3	• Single occlusion 3 to 10 cm in length, involving the distal popliteal artery, • Multiple focal lesions, each 3 to 5 cm (may be heavily calcified), • Single lesion, either stenosis or occlusion, with a length of more than 10 cm.
Category 4	• Complete common and/or superficial femoral occlusions, • Complete popliteal and proximal trifurcation occlusions, • Severe diffuse disease with multiple lesions and no intervening normal vascular segments.

Definition of categories

Category 1. Lesions for which percutaneous transluminal angioplasty alone is the procedure of choice. Treatment of these lesions will result in a high technical success rate and will generally result in complete relief of symptoms or normalization of pressure gradients.

Category 2. Lesions well suited for percutaneous transluminal angioplasty. Treatment of these lesions will result in complete relief or significant improvement in symptoms, pulses, or pressure gradients. This category includes lesions that will be treated by procedures to be followed by surgical bypass to treat multilevel vascular disease.

Category 3. Lesions that may be treated with percutaneous therapy, but because of disease extent, location, or severity have a significantly lower chance of initial technical success or long-term benefit than if treated with surgical bypass. However, percutaneous transluminal angioplasty may be performed, generally because of patient risk factors or because of lack of suitable bypass material.

Category 4. Extensive vascular disease, for which percutaneous therapy has a very limited role because of low technical success rate or poor long-term benefit. In very-high-risk patients, or in those for whom no surgical procedure is applicable, percutaneous transluminal angioplasty may have some place (4).

In conclusion, the elected indications for interventional treatment are: isolated stenosis of great vessels (iliac arteries), multiple, bilatella iliac stenosis, isolated stenosis on a superficial femoral artery, and iliac grefon stenosis. Severe stenosis should be treated immediately to prevent the risk of thrombus formation and total occlusion (5). Other indications are:

- segmental occlusions of superficial femoral arteries, with length less than 10 cm,
- recent femuropopliteeal thrombosis, with length less than 10 cm, with good outflow
- short stenosis or occlusions, less than 5 cm, at infrapopliteeal vessels
- in absence of surgical possibilities, or in association with surgical procedures
- in bypass stenosis
- for limb salvage

Contraindications for interventional treatment

Among the contraindications for interventional treatment, the most important are:

- long iliac occlusions, because of the risk for perforation,
- stenosis located near or in contact with an aneurism,
- extended femoropopliteeal occlusion,
- coagulation disturbances.

1. Percutaneous transluminal angioplasty

Definition

Percutaneous transluminal angioplasty represents a controlled dilatation of an arterial aterosclerotic stenosis or occlusion, using a balloon catheter introduced intraarterial until the lesion level, using a percutaneous approach and under fluoroscopic control. Different types of approach could be used for this procedure: for lesions located at femoral arteries and bellow, ipsilateral approach is recommended, and for lesions located on iliac arteries, contralateral or axilar approach, because of the need to have antegrade flow (figure 3) (16).

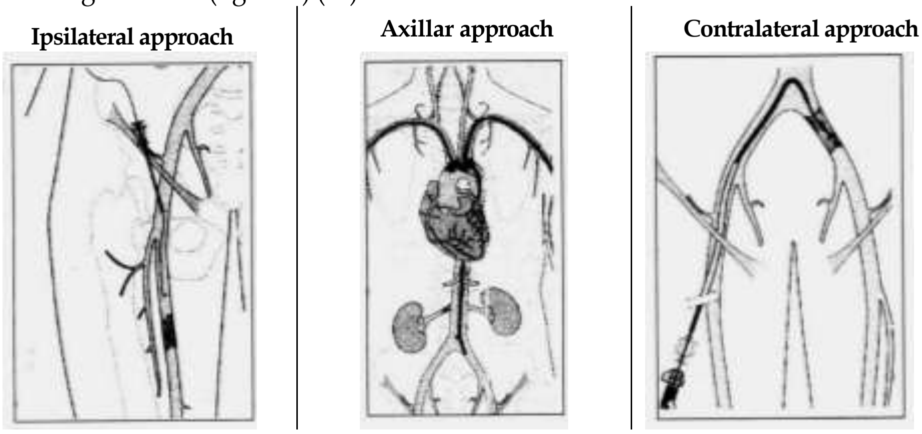

Figure 3: Different types of approach used in PTA

Acute closure immediately after angioplasty is usually caused by dissection, spasm, or embolism and frequently is complicated by thrombosis. It occurs in 1% to 4% of peripheral angioplasties. Spasm is now aggressively pretreated and treated, with calcium channel blockers and nitroglycerin, as in the thrombosis itself with heparin and thrombolytic agents. Stents may represent the best treatment for dissection, which is the major cause of immediate postangioplasty closure. Another acute problem is elastic recoil, which usually results only in a poor angioplasty result with a significant gradient. Again, vascular stetting appears to be the treatment of choice (12, 19).

One of the most limitating factors which have a negative impact on the results of PTA is the restenosis, which is recorded in a significant percent in the long term follow-up of these patients.

Early restenosis, the most common type of restenosis, most frequently occurs from 1-2 months to 1 year after angioplasty and is an intimal proliferative response. It also occurs after vascular surgery and is not specific to angioplasty. Among the factors which lead to restenosis is the elastic recoil of the arterial wall after angioplasty, the negative remodeling of the vessel, and the neointimal hyperplasia, which are more pronounced in diabetic patients (figures 4-5) (11, 16).

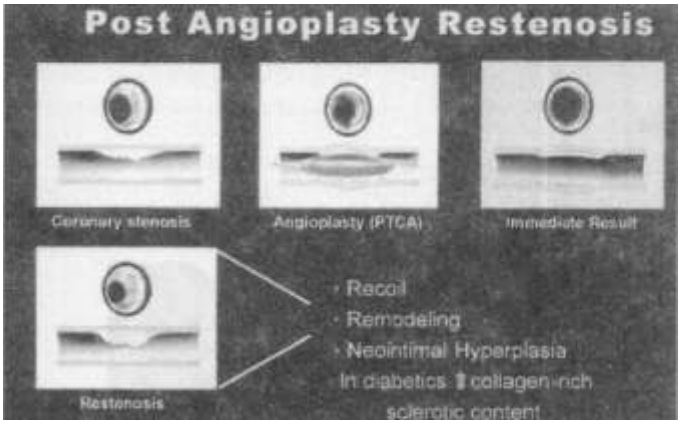

Figure 4:
Restenosis after PTA

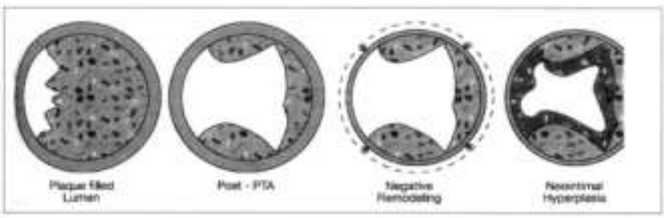

Figure 5:
Neointimal hyperplasia after PTA

For all these cases, vascular stents were introduced as an adjuvant therapy for arterial diseases, which significantly improved the long-term results of interventional treatment.

2. Vascular stenting

Definition

Vascular stetting represents implantation of an endoluminal scheleton at the level of an arterial lesion treated with angioplasty, compressing the subintimal layer and keeping the vessel open and intact, with laminal flow (figures 6-7).

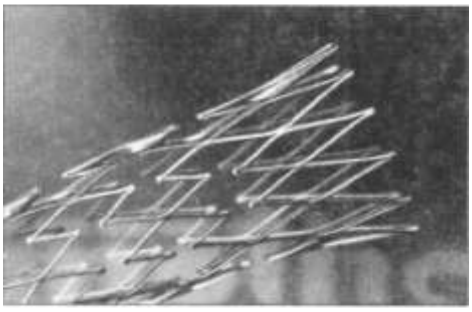

Figure 6: Autoexpandable vascular stent

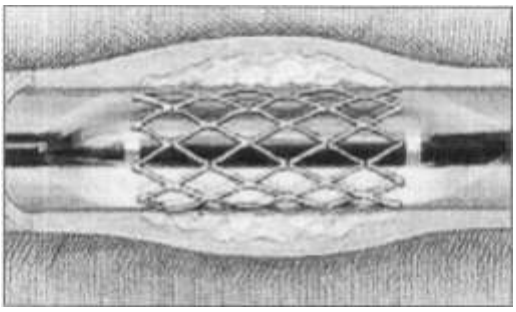

Figure 7: Premounted balloon expandable stent

A stent is a wire mesh tube used to prop open an artery that's recently been cleared using angioplasty. The stent stays in the artery permanently, holds it open, improves blood flow to the muscle and relieves symptoms (13, 16).

Stent-grafts are special stents covered with prosthetic materials at the exterior or interior, used to create a new lumen in cases of arterial aneurism (figures 8-9).

Figure 8: Exterior stent-graft

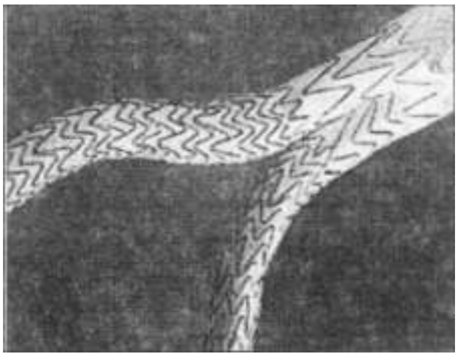

Figure 9: Interior stent-graft

Indications of peripheral stetting

1. Post angioplasty dissection - to prevent acute occlusion
2. Residual stenosis post PTA (> 50%) - it is frequently associated with occlusion
3. Occlusion (after inefficient PTA)
4. Long lesions (> 10 cm) - to prevent remodeling
5. Critical ischemia - stents associated with PTA assure a better outflow, leading to a more rapid healing of ulcers
6. Severe vascular lesions, with embolic potential - stents isolates the atheroma
7. Recurrent lesions, if the results of PTA are not satisfactory

Results of arterial stenting

A meta-analysis performed by Bosch in 1997, comparing the results of different interventional methods on iliac arteries, included 6 studies of PTA on 1.300 patients and 8 stent studies on 816 patients. The results of this meta-analysis showed significantly better results in cases were stetting was associated, with a primary success rate of 95% using stents compared with 91% using only PTA (figure 10), and a 4 year patency of 75% versus 62% in iliac stenosis and 60% compared to 51% in iliac occlusions (figure 11) (17).

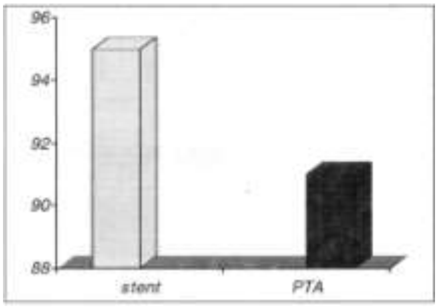

Figure 10: Primary success

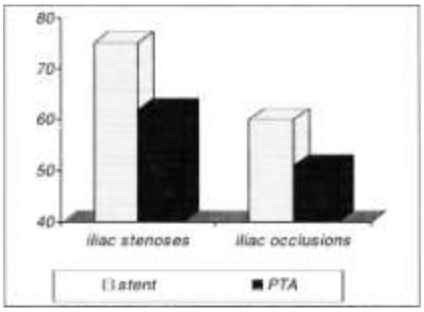

Figure 11: 4 year permeability after interventional treatment

BIAS study was performed in 2001 by the British Society of Interventional Radiology, on 1.135 patients which underwent iliac angioplasty with or without stent implant. Patients were examined and treated using a very strict protocol and they underwent interventional or surgical procedures according to very strict indications. This study showed better results obtained with stent implant comparing with PTA without stent. The percentage of patients with no residual stenosis was 45% in the PTA group and 80% in the stent group, while the percentage of patients with residual stenosis < 30% was 45% in the PTA group and 15% in the stent group, and the percentage of patients with > 30% residual stenosis was 10% in the PTA group and 5% in the stent group (figure 12) (6, 15).

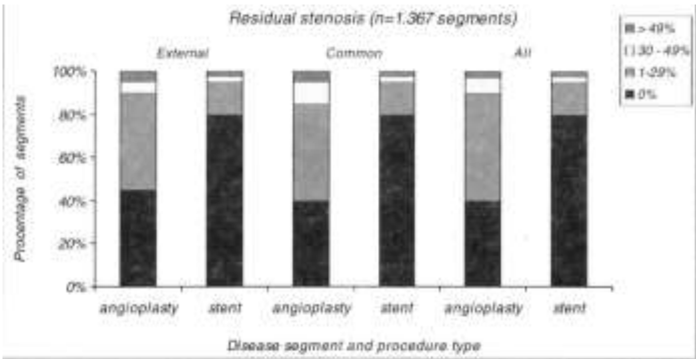

Figure 12: Results of interventional treatment - percent of residual stenosis

Regarding the lesion length, it was demonstrated that the long term patency at 4 years was 85% when the stented segment was < 10 cm, and 50% when the stented segment was > 10 cm (9).

Types of peripheral stents

Two major types are used in present: premounted on balloons and autoexpandable stents.

[1] Premounted stents are stents premounted on a balloon, and are used especially for short, calcified, ostial lesions.

[2] Autoexpandable stents are self expanding stent, ideal for long, noncalcified lesions.

The autoexpandable stent was introduced in 1994. An example is the Memotherm stent, from nitinol, a special alloy formed by nickel and titanium in proportion of 50-50%, with thermic memory, which has the property to expand at a preconfigured shape and dimension in contact with human blood (at 35.5 C degree) (figure 13-14).

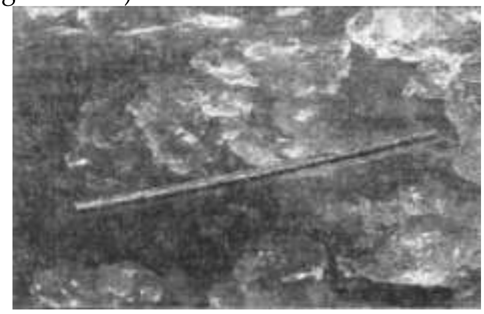

Figure 13: Nitinol stent not expande, at low temperature

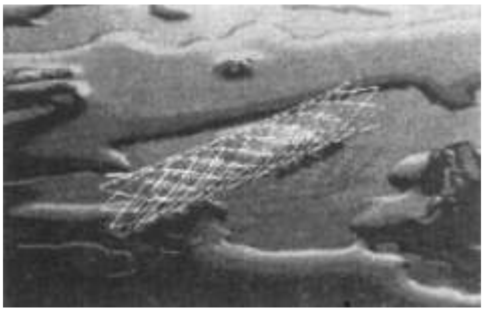

Figure 14: Nitinol expanded stent-body temperature

This shape is preconfigured and is in the memory of the stent, who will try to maintain it and to return to this shape even after a distortion. Different types of auto-expandable stents, with different sizes, can be used in the iliofemoal arteries (table 2).

Table 2: Nitinol stents that can be used in the SFA

Stent type	diameter (mm)	length [mm]	Source
SMART	20/30/40/60/80/120	5-12	Cordis, J &J
SelfX	44/68/80	6,7,8	Jomed
Dynalink	28/35/56	5-10	Guidant
Memotherm	20/30/40/60/80/100/120	6-12	C.R. Bard
Protege	20/30/40/60/80	6- 10	Sulzer Medica
Symphony	20/23/40/60	6-14	Boston Scientific
IntraCoil	40/60	4-7	IntraTherapeutics

The advantages of nitinol stents are: shape memory effect, flexibility (figure 15), good biocompatibility, enhanced radial force, good radiopacity, and MRI compatibility. The recent stents have radiopaque markers at the both sides (figure 16) (2).

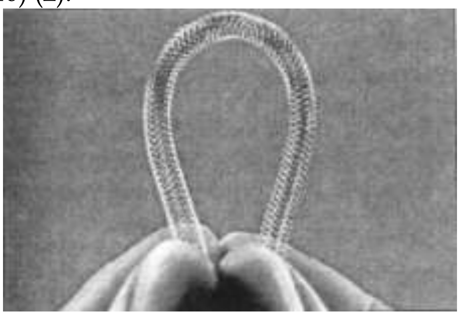

Figure 15: flexibility of a nitinol stent

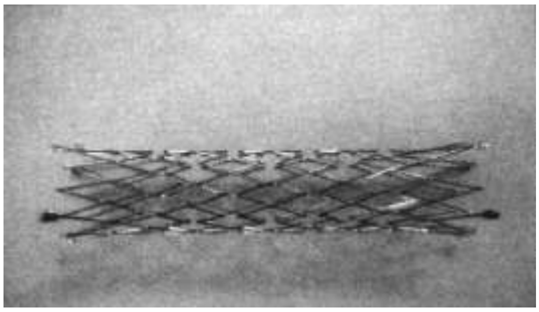

Figure 16: The new Luminexx stent (C.R.Bard) with radioopaque markers)

In the Paris Course of Revascularization in 1997 was presented a very good long term patency after implant of Memotherm vascular stents, with 1 year rate of 90% and 2 year rate of 80% on iliac artery and 1 year rate of 80% a 2 year rate of 75% on femoral artery (16). The long term results of stent implants are also negative affected by in stent restenosis, in many cases caused by the neointimal hyperplasia, especially in diabetic (figure 17). The therapy for these cases is the laser angioplasty.

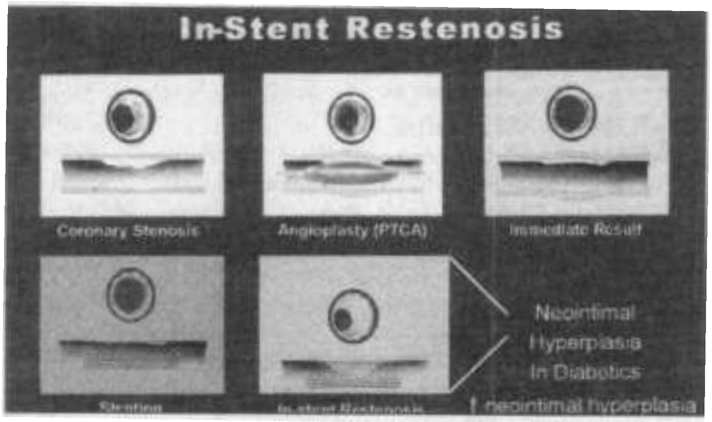

Figure 17: In stent restenosis

3. *Laser angioplasty*

Laser angioplasty is used especially for the treatment of total occlusions or severe stenosis, and for in stent restenosis. It uses argon laser energy, which dissolves the aterosclerotic plaque, creating a channel in the vessels which will be afterwards completed with balloon angioplasty (figures 18-19).

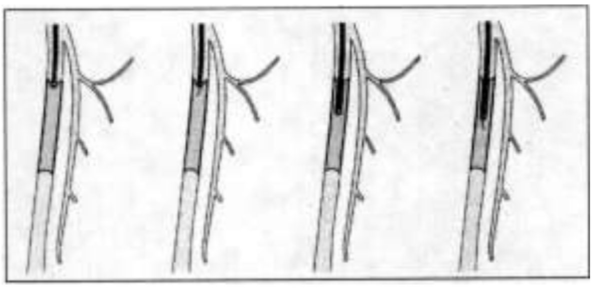

Figure 18: Laser angioplasty on femoral artery

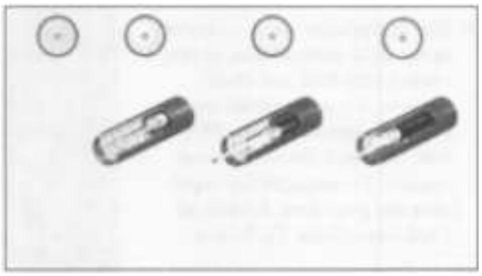

Figure 19: Laser angioplasty: principle

Laser angioplasty is a technique that opens arteries blocked by plaque. Plaque is the build-up of cholesterol and other fatty substances in an artery's inner lining. A thin, flexible catheter with a laser at its tip is inserted into an artery. Then it's advanced through the artery to the blockage. When the laser is in position, it emits pulsating beams of light, which vaporize the plaque. This procedure has been used alone and with balloon angioplasty. The first laser device (the "eximer laser") for opening arteries was approved by the Food and Drug Administration in 1992. It's used in many major U.S. medical centers (16).

In a study published in 2002, Scheinert et al reported an immediate success of 90.5% and a 1 year permeability of 75.1% using laser angioplasty in total occlusions.

Among the complications of laser angioplasty there are mentioned: reclusion in 1%, perforation in 2.2%, distal embolization in 3.9% of cases (16).

Casuistry of Cardiology Clinic from University Hospital Targu-Mures

In a period of 13 years, in the Cardiology Clinic from University Hospital Targu-Mures were examined a total number of 6.032 patients suffering from peripheral obstructive arterial diseases. Invasive diagnosis performed in our clinic consisted in aortography in 634 cases and peripheral arteriography in 1.794. Interventional treatment consisted in percutaneous transluminal angioplasty (1.075 procedures), intraarterial thrombolysis (197 procedures), laser angioplasty (54 procedures) and stent implant (41 cases).

In the last 2 years in our clinic was inaugurated the new laboratory of interventional cardiology, and starting with this moment the number of procedures performed significantly increased, and new procedures were introduced in the algorhythm of interventional treatment, such as stent implant and laser angioplasty. For instance, from the total number of 1.075 PTA, 591 were performed in the last 2 years. Peripheral stetting was introduced in our clinic in 2001 and since than 41 implants was performed; laser angioplasty was introduced in June 2002, and since than 54 procedures were performed. Axillary approach was also introduced in 2001 and it was applied in 49 cases.

Results

We recorded a 76.5% success rate using only PTA for repermeabilisation of the arteries. Association of intraarterial thrombolysis increased the success rate to 91%. Using laser angioplasty and stent implantation, the success rate achieved was 100%.

In conclusion, interventional treatment is an important alternative in the complex algorhythm of treatment in PAOB. Intraarterial stetting significantly improves the immediate and the long term results of interventional treatment, and autoexpandable stents with thermic memory shows superior results. Laser angioplasty is an adjuvant method which significantly improves the results of interventional treatment in long occlusions or in stent occlusions. In all these methods, a very important role plays the good cooperation of the team formed by cardiologist, angiologist and vascular surgeon.

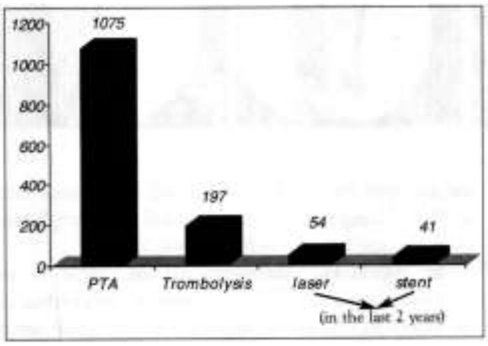

Figure 20: Casuistry of Cardiology Clinic Targu-Mures in 13 years

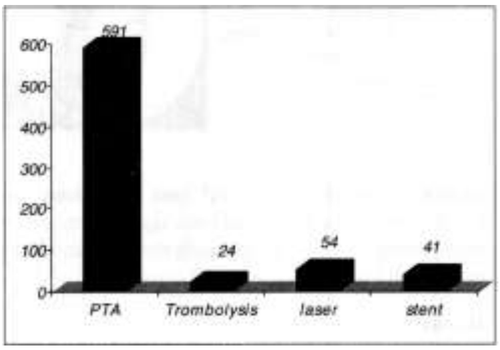

Figure 21: Casuistry of Cardiology Clinic Targu-Mures in the last 2 years

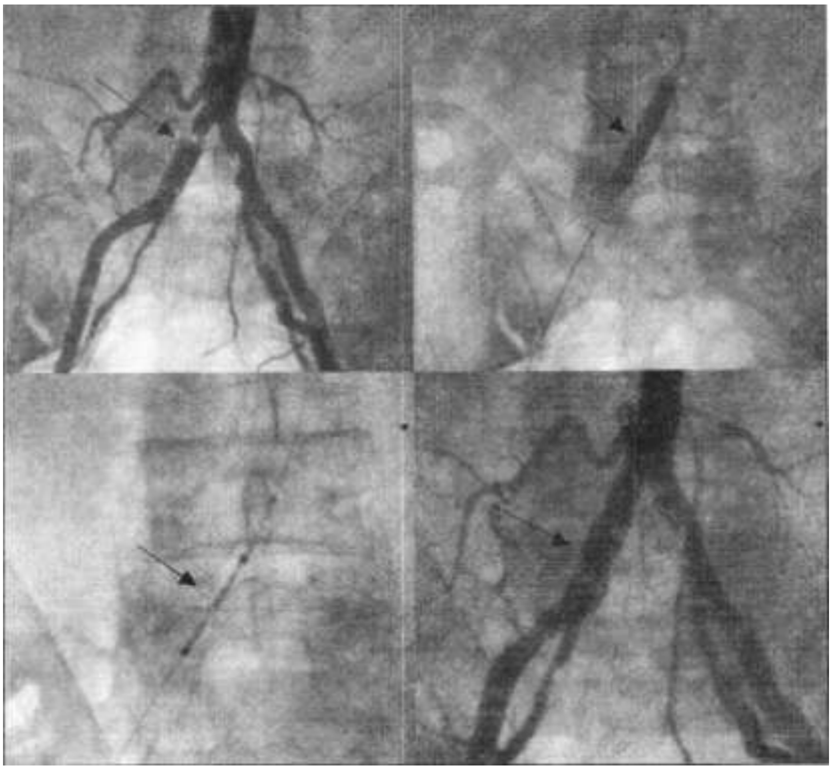

Figure 22: Iliac angioplasty: short occlusion at the right common iliac artery, treated with PAT and stent implant.

A - angiographic aspect before the procedure.

B - PTA with balloon inflated.

C - stent implant.

D - angiographic aspect after the procedure.

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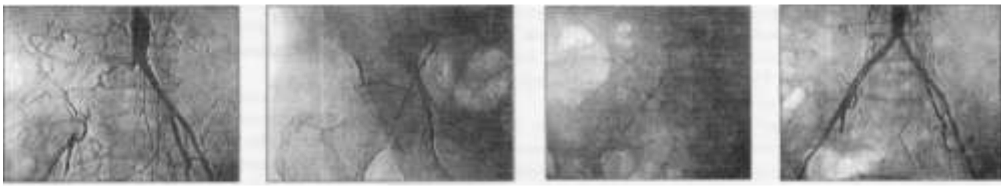

Figure 23: Iliac laser angioplasty completed with balloon angioplasty.
A - angiographic aspect before the procedure.
B, C - laser angioplasty,
D - angiographic aspect after the procedure *[Archive of Cardiology Clinic Tg. Mures]*

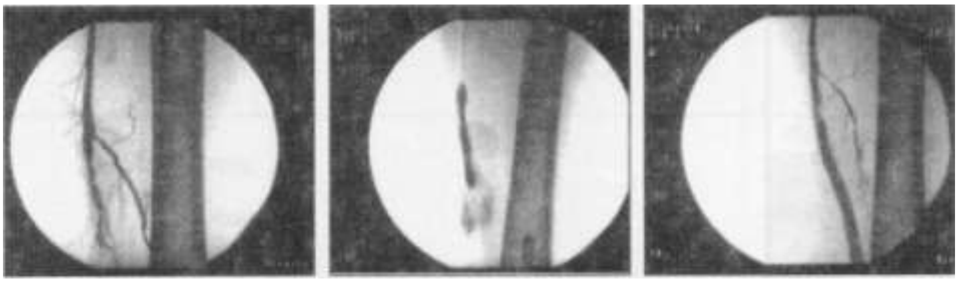

Figure 24: Angioplasty of an occluded femoral stent.
A - Stent occluded,
B - Balloon angioplasty, C - angiographic control

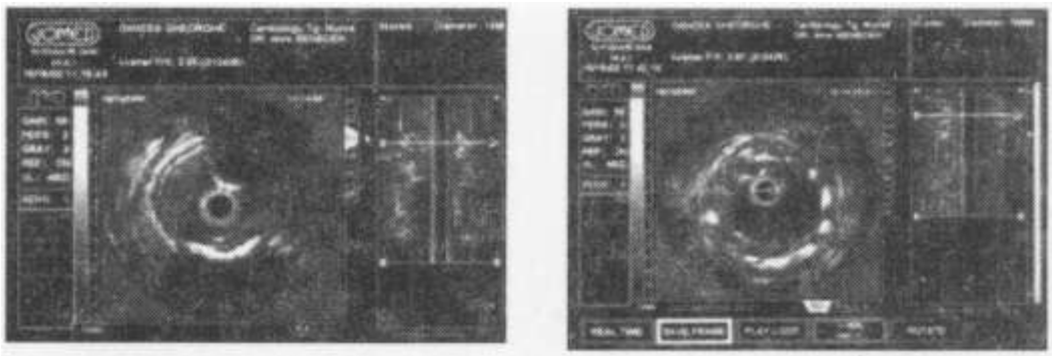

Figure 25: IVUS controll of an occuded stent:
A - atherosclerotic plaques above the origin of the stent,
B - Free lument in the stent

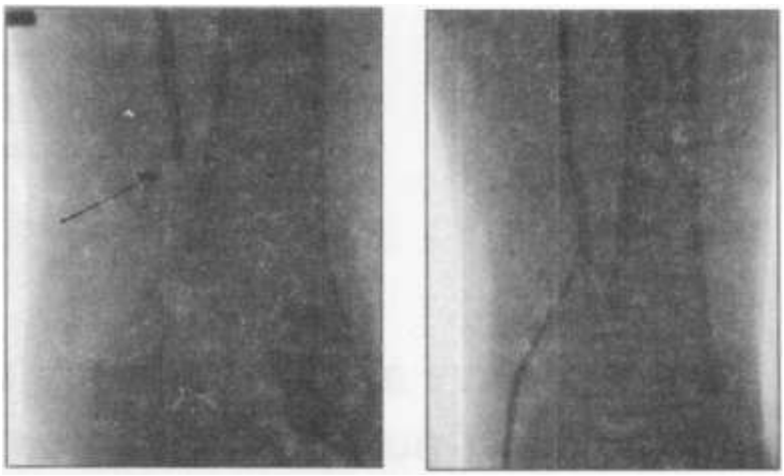

Figure 26: Angioplasty of occluded bypass graft.
A - occlusion of bypass graft, B - result after angioplasty

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Interventional reconstruction of aortoiliac bifurcation in total occlusions of terminal aorta*)

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Abstract

Background: *The importance of interventional procedures in the complex treatment of peripheral arterial diseases is continuously increasing. In the current practice of our clinic, association of balloon angioplasty, laser angioplasty and arterial stenting in reconstruction of iliac arteries led in the last years to superior results, these methods being proved as an alternative to surgical interventions in iliac lesions. In this article, we present several cases of laser angioplasty in the treatment of occlusions located in the terminal abdominal aorta.*

Methods: *In 4 patients (3 male, 1 female) with occlusions of terminal aorta interventional treatment (peripheral transluminal angioplasty, laser angioplasty and stenting) was performed. Two cases presented total occlusion of terminal aorta, without any visualization of iliac arteries, and 2 cases presented occlusion of one aortoiliac axis, starting from terminal aorta.*

Results: *In all cases, complete repermeabilisation of aortoiliac axes was achieved, without complications. In all patients we recorded a significant improvement of symptomatology, and arterial Doppler showed an increase of Doppler ankle/brachial index in average from 0.4 up to 0.95. No complications were recorded so far.*

Conclusion: *extension of classical indications of interventional treatment for balloon and laser angioplasty to occlusions located in terminal aorta is possible when the procedure is performed by an experienced team. Interventional techniques, having a superior applicability in practice, good results, low complication rates, and decreasing the hospitalization times, could be applied in the future to a larger extend, targeting also aortic occlusions.*

Keywords: *angioplasty, laser, aorta*

Rezumat

Introducere: *Importanța procedurilor intervenționale în tratamentul complex al bolilor arteriale periferice este în creştere. În practica curentă a clinicii noastre asocierea angioplastiei cu balon, angioplastiei cu laser şi a stentării în reconstrucția arterelor iliace a determinat rezultate superioare în ultimii ani. Aceste metode s-au dovedit a fi alternative la intervențiile chirurgicale asupra leziunilor arteriale iliace. În acesastă lucrare prezentăm câteva cazuri de angioplastie cu laser în tratamentul ocluziilor localizate în aorta abdominală terminală.*

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Metode: *La 4 pacienți (3 bărbați şi o femeie) cu ocluzii de aortă terminală s-a realizat tratamentul intervențional constând în angioplastie periferică transluminală, angioplestie cu laser şi stentare. Două cazuri au prezentat ocluzia completă a aortei terminale fără vizualizarea arterelor iliace iar două cazuri au prezentat ocluzia unui singur ax aortoiliac începând de la nivelul aortei terminale.*

Rezultate: *În toate cazurile a fost obținută repermeabilizarea completă a axurilor aortoiliace fără complicații. La toți pacienții am înregistrat o ameliorare semnificativă a simptomatologiei iar examenul Doppler arterial a indicat o creştere a indicelui gleznă/braț în medie cu 0,4 până la 0,95. Până în momentul actual nu s-au înregistrat complicații.*

Concluzie: *Este posibilă extinderea indicațiilor clasice de tratament intervențional (angioplestie cu balon şi laser) şi la ocluziile localizate la nivelul aortei terminale atunci când procedura este realizată de o echipă experimentată. Tehnicile intervenționale, care au o aplicabilitate practică superioară, rezultate bune, rate reduse de complicații şi durate reduse de spitalizare, ar putea fi aplicate în viitor într-o arie mai largă, țintind inclusiv ocluziile aortice.*

Cuvinte cheie: *angioplastie, laser, aorta*

Background

The place and importance of interventional procedures in the complex treatment of peripheral arterial diseases is continuously increasing (1, 2). Due to the superior results achieved using interventional techniques (angioplasty, stenting), they became the procedure of choice in many complex lesions which were considered in the past as an exclusive indication for surgery (3).

For instance, in present we see a continuous expanding of classical indications, from the short and limited stenosis, located on great vessels (4), to more and more complex lesions (5). Such an extension could be considered angioplasty for aortic occlusions, a high risk and complex intervention (6, 7).

Regarding the procedure type, it is unanimously recognized the place of classical balloon angioplasty and arterial stenting in ileofemoral lesions (8). In contrast, there is a marked reticence regarding laser angioplasty in iliac lesions, because of the associated risk of perforation of iliac arterial wall with laser and its consequences (9, 10). For the same reason, laser angioplasty on aortic occlusions was not performed by now by even experienced teams of interventional angiologists (11, 12).

A significant progress in this field was the introduction of vascular stent-grafts, which offer, in case of arterial wall perforation, the possibility of immediate cessation of bleeding after implanted by the interventionist operator, covering the perforation at the site of the lesion. As a consequence, having the stent-graft available, the interventionist could perform such a high-risk procedure, because the possible complication – retroperitoneal bleeding – can be easily corrected by an experienced team (13, 14).

In the current practice of our clinic, association of balloon angioplasty, laser angioplasty and arterial stenting in reconstruction of iliac arteries led in the last years to superior results, these methods being proved as an alternative to surgical interventions in iliac lesions.

In this article, we present several cases of laser angioplasty in the treatment of occlusions located in the terminal abdominal aorta, trying to prove that the classical indications of interventional treatment could be extended to aortic and aortoiliac occlusions.

Methods

In this study we included 4 patients (3 male, 1 female) with occlusions of terminal aorta, in whom we performed interventional treatment (peripheral transluminal angioplasty, laser angioplasty and stenting). Two cases presented total occlusion of terminal aorta, without any visualization of iliac arteries, and 2 cases presented occlusion of one aortoiliac axis, starting from terminal aorta.

All patients received aspirin 75 mg/day, clopidogrel (300 mg loading dose 3 days before intervention and than 75 mg/day), and atorvastatin minimum 2 weeks before intervention. Preprocedure in all patients' blood group and Rh was determined, and transfusion units were prepared in stand-by.

During procedure, 5.000 UI heparin was administrated on the arterial sheath. In all cases we used axillar approach, from the left axillar artery. After placing a 7F introducer sheath in the left axillar artery, we introduced and advanced a nitinol guidewire in the aorta, which penetrated and crossed the lesion, and the guidewire was advanced until the origin of common femoral artery. A laser catheter was advanced over the wire, until the origin of external iliac artery. Laser energy was applied, starting from the aorta, from the starting point of occlusion, with 45 pulse/min, and the laser catheter was advanced gradually over the wire during lasing.

The procedure was repeated several times, repeatedly withdrawing and advancing the laser catheter, with saline flush after each lasing.

After lasing, through the new created channel, a 10 mm diameter and 8-12 cm length balloon angioplasty catheter was introduced, and balloon was inflated repeatedly from the terminal aorta to the level of external iliac artery, and autoexpandable nitinointraarterial stents (Luminexx) were implanted.

During procedure, blood pressure and arterial pulse were invasive monitored consinuously, and coagulation times and hematocrit were determined.

Results

In all cases, complete repermeabilisation of aortoiliac axes was achieved, without complications. In the 2 cases with complete occlusions of terminal aorta, reconstruction of one aortoiliac axis was performed, in the ischemic leg with more pronounced ischemic symptoms (Figure 1, 2), reconstruction of the second aortoilic axis being scheduled in a second procedure. In the 2 cases with occlusion of one aortoilic axis, from emergency of common iliac artery, complete reconstruction of aortoilic bifurcation was achieved (Figure 3, 4).

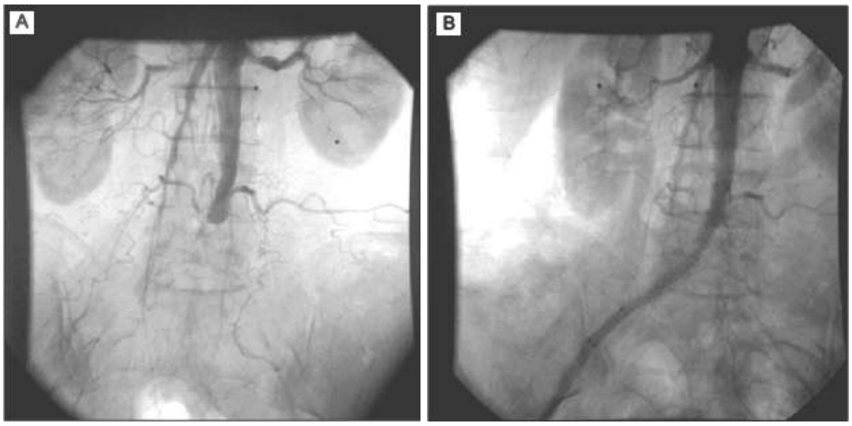

Figure 1: Aortic angioplasty: reconstruction of right aortoiliac axis. A) Total occlusion of terminal aorta. B) Reconstruction of right aortoilic axis, with laser angioplasty and stenting

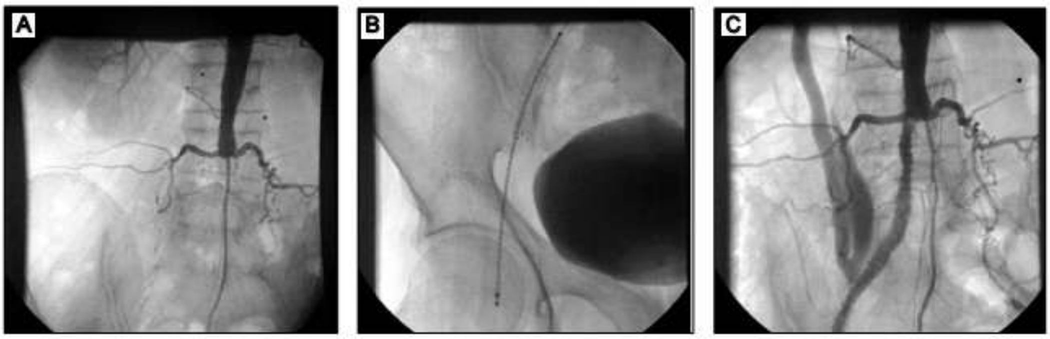

Figure 2: Aortic agioplasty: reconstruction of right aortoiliac axis. A) Total occlusion of terminal aorta. Well developed collateral circulation starting immediate before the occlusion. B) Crossing the lesion with the guidewire and laser and placing an iliac stent. C) Postprocedure: reconstruction of right aortoiliac axis

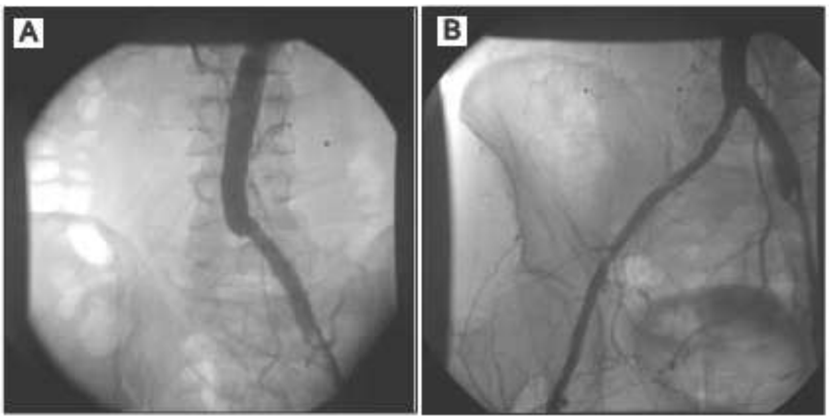

Figure 3: Right aortoiliac angioplasty. A) Occlusion at the emergence of right common iliac artery. B) Complete reconstruction of aortoiliac bifurcation and iliac stenting

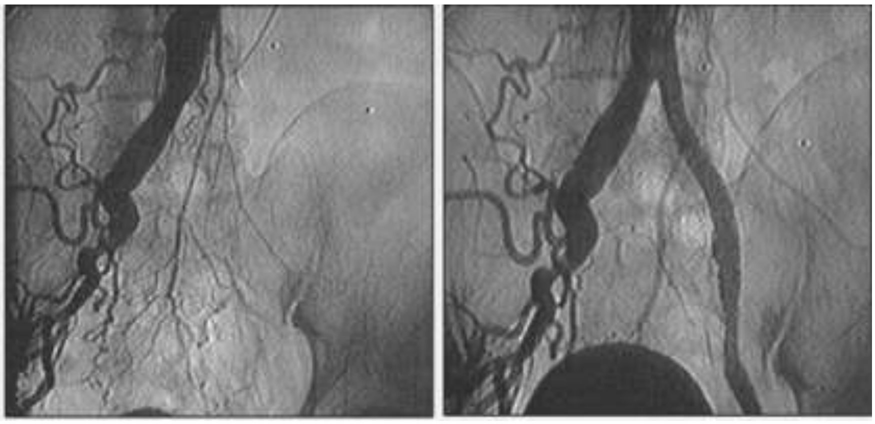

Figure 4: Left aortoiliac angioplasty.
A) Occlusion at the origin of left iliac common artery.
B) Complete reconstruction of aortoiliac bifurcation with laser angioplasty and stent implant

In all patients we recorded a significant improvement of symptomatology, and arterial Doppler showed an increase of Doppler ankle/brachial index in average from 0.4 up to 0.95.

No complications were recorded so far.

Conclusion

In conclusion, extension of classical indications of interventional treatment for balloon and laser angioplasty to occlusions located in terminal aorta is possible when the procedure is performed by an experienced team, having the possibilities of urgent and adequate intervention in case of emergency.

Interventional techniques, having a superior applicability in practice, good results, low complication rates, and decreasing the hospitalization times, could be applied in the future to a larger extend, targeting also aortic occlusions.

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Hybrid approach for the treatment of multilevel arteriosclerotic occlusive disease. Case report*)

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1. Background

Patients with lower extremity ischemic symptoms secondary to multilevel arteriosclerotic occlusive disease represent a frequent and challenging problem for the vascular surgeon.

In the setting of concomitant iliac and infrainguinal atherosclerotic occlusive disease limb salvage or clinical improvement may require surgical reconstructions to correct both inflow and outflow levels of disease. The main concern is that such extensive procedures may result in unacceptably high morbidity and mortality rates in these typically high-risk patients.

With the rapid development of endovascular techniques, the management strategy of patients with multilevel atherosclerotic arterial occlusive disease is also evolving.

The release of the TransAtlantic Inter-Society Consensus (TASC) statement on treatment of peripheral vascular disease in 2000 and then TASC II in 2006 allowed stratification by length and morphology of lesions and reinforced the concept of treating short focal stenoses via endovascular approach and using surgical revascularization for long-segment occlusions [2].

In this consideration for limited iliac stenotic lesions (< 3 cm) iliac artery stenting is a means whereby multiple bypass operations can be avoided in such patients.

Therefore, the assessment of the patient's general condition and anatomy of the diseased segments become central in deciding which approach is warranted.

The technical and initial clinical success of PTA of iliac stenosis exceeds 90% in all reports in the literature. This figure approaches 100% for focal iliac lesions [1].

2. Case report

A 72 years old female patient presented to our department complaining of left pedal, severe, sharp, shooting rest pain that typically occurred at night. Partial relief was obtained by the dependent position, whereas elevation and cold increased the severity of the pain. The walking capacity was very severely impaired.

The physical examination showed discoloration and dependant hyperemia of the foot, ankle and foot edema, muscle and subcutaneous tissue atrophy of the left calf.

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Peripheral pulses of the left lower limb were absent at all levels (femoral, popliteal, posterior tibial and pedal)

Risk factors included the presence of hypertension, coronary artery disease, hyperlipidemia and former tobacco use.

The patient presented with the recent results of a CT-angiogram that made possible a precise evaluation of the localization and anatomy of the diseased arterial segments. It evidentiated a focal (< 3 cm), 90% right external iliac artery stenosis, a left external iliac artery occlusion that extended to the superficial femoral artery (SFA) and another SFA occlusion in it's distal segment.

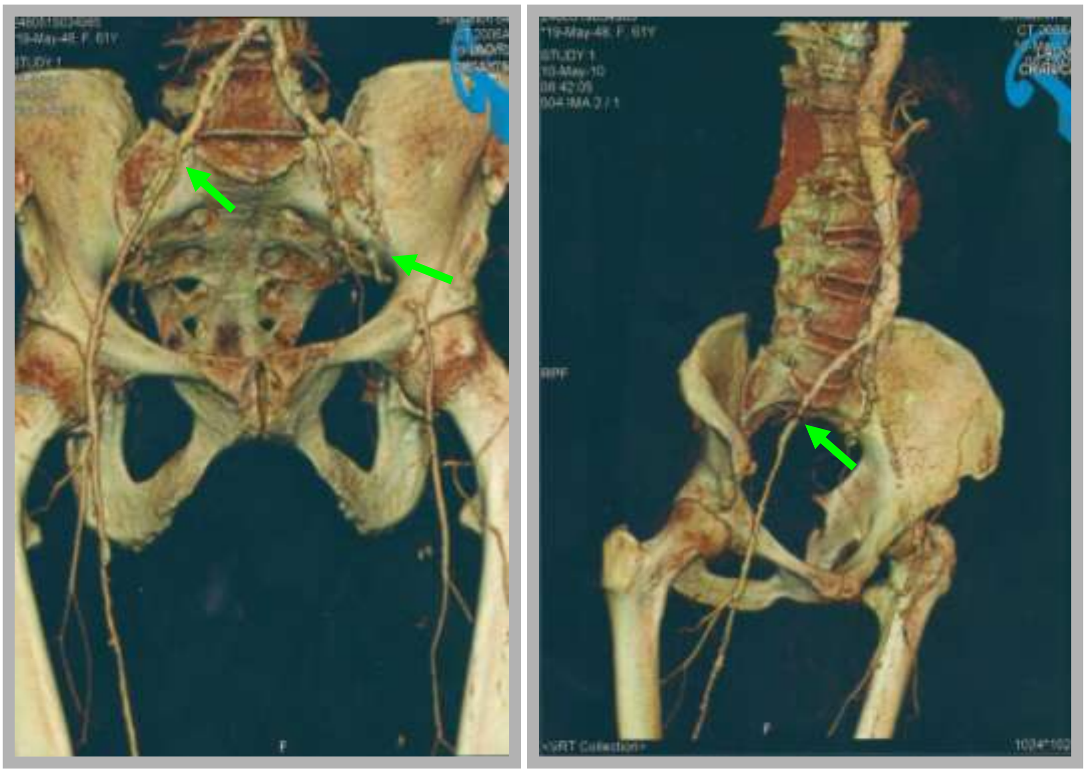

Figure 1: CT-angiogram that reveals a focal (< 3 cm), 90% right external iliac artery stenosis and a left external iliac artery occlusion that extends to the superficial femoral artery (SFA)

The treatment strategy was established based on the TASC II recommendations. We treated the focal right external iliac stenosis by endovascular balloon angioplasty (PTA) and stent placement after which we performed a sequential femoro-femoral and femoro-popliteal by-pass surgery to treat the significant occlusive disease in the contralateral iliac and superficial femoral artery. Inflow for this crossover graft was based on the dilated and stented right iliac artery.

The endovascular procedure was performed in the angiography suite of our center by an interventional radiologist. The preoperatory arteriography performed by means of an ipsi-lateral femoral approach revealed a 1 cm long 90% right external iliac stenosis.

The endovascular repair consisted in PTA followed by a self expandable nitinol stent placement. A completion contrast injection was performed to assure a satisfactory morphologic result of PTA and stenting.

Figure 2 – CT-angiogram that reveal a distal SFA occlusion

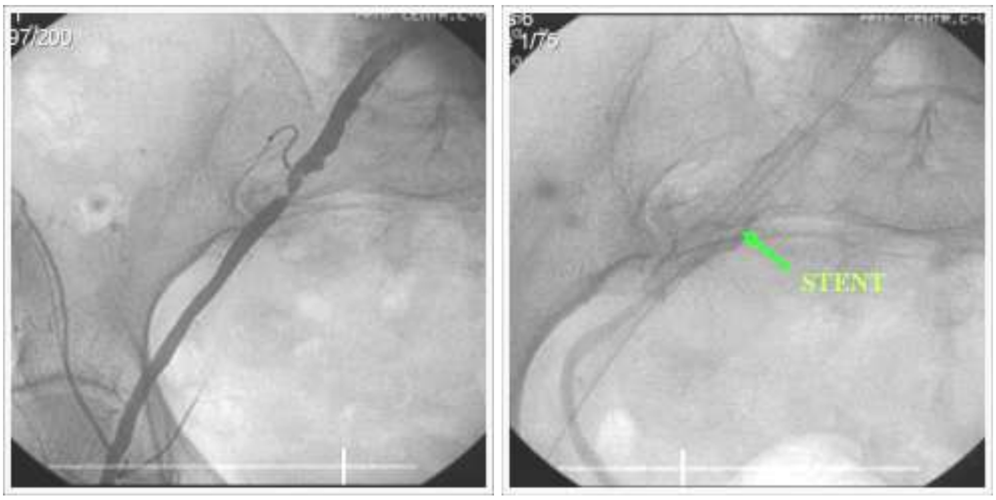

Figure 3, 4: Angiographic image of the right iliac stenosis and stent placement

Figure 5: Completion angiography showing the restoration of normal blood flow.

The operative procedures were carried out immediately after the endovascular intervention on the right external iliac artery, in the operating room.

A sequential right-to-left 8 mm ringed PTFE femoro-femoral crossover and a left femoro-popliteal proximal by-pass with reversed great saphenous vein was performed in order to treat the left external iliac and SFA occlusions.

The technical success of the procedure was proven by the presence of a palpable pulse distal to the surgical reconstruction, at the left posterior-tibial artery, along with the amelioration of the simtomatology. The patient had an uneventful postoperative course and was discharged 4 days after surgery with anticoagulant, antiaggregant and antibiotic treatment.

3. Discussions

The endovascular treatment of iliac occlusive disease has evolved over the last two decades. Balloon angioplasty and stent technology, along with endovascular techniques and imaging, have improved significantly. This has led to the preferential treatment of iliac stenoses via endovascular means with high technical success rates and low morbidity. This is mirrored by the decreasing number of aortobifemoral grafts performed over the past decade as more patients undergo endovascular treatment.

Iliac PTA/stenting has high rates of patency, and, more importantly, there is a significant improvement in functional outcome for the individual patient [2].

Becker et al. found 5-year patency rate of 72% in an analysis of 2697 cases from the literature, noting a better patency of 79% in claudicants [3]. Rutherford and Durham found a similar 5-year patency of 70%.A recent study reported a primary patency of 74% (primary assisted patency of 81%) 8 years after stent placement suggesting durability of patency of iliac artery stenting [4]. Factors negatively affecting the patency of such interventions include quality of run off vessels, severity of ischemia and length of diseased segments. Female gender has also been suggested to decrease patency of external iliac artery stents.

Infrainguinal bypass procedures need to arise from a patent and uncompromised inflow artery although the actual level (common femoral artery versus superficial femoral or popliteal artery) does not correlate with patency. If the infrainguinal bypass is constructed following an inflow procedure, patency is improved by making the proximal anastomosis to a native artery (in the case of iliac stenting) rather than the inflow graft (usually limb of aortobifemoral bypass) [5].

Regarding the material used for the infrainguinal by-passes, the five-year assisted patency rates in grafts constructed with vein approach 60% and those constructed with prosthetic material are usually less than 35% [1].

Figure 6: Surgical interventions performed

4. Conclusions

The treatment of iliac artery occlusion can be accomplished via endovascular means with little morbidity and with acceptable patency and limb salvage rates. The TASC stratification is an important tool in allowing us to assess the extent of lesion morphology, but extensive lesions do not preclude successful endovascular treatment. The fate of the limb is dictated by the infra-inguinal disease that is often present in patients with complex iliac occlusions. We believe that endovascular attempts should be exhausted before attempting open surgical repair of iliac occlusions.

We must await further studies and experiences before a more aggressive application of PTA / stenting as first intention treatment of more widespread iliac disease (TASC **B**, TASC **C)** before an infra-inguinal surgery.

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Robotically assisted aorto-femoral bypass grafting technique*)

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Abstract

The da Vinci™ Surgical Robot (Intuitive Surgical Inc., Sunnyvale, CA, USA) is a computer-enhanced surgery device that helps to surpass some of traditional laparoscopic instruments limitations. Our work was performed to assess the safety and feasibility of robotically assisted aorto-femoral bypass grafting (AF) in order to describe the technique. The aortic dissection is performed laparoscopically, with the patient in a modified right lateral position. The proximal anastomosis is completed with the da Vinci™ system by a remote surgeon, positioned at a distance from the patient. The role of the assistant at the patient's side is especially to expose, to perform haemostasis and to maintain traction on the running sutures performed by the robot. No robot-related complications were noted. Robotically assisted anastomoses are possible by its unique ability to combine conventional laparoscopic surgery with stereoscopic 3D magnification and ultra-precise suturing techniques due to the flexibility of the robotic wristed instruments using different motion scaling of surgeon hand movements. In addition, prior training in laparoscopic aortic surgery is not necessary for surgeons to obtain the level required for suturing. Further clinical trials are needed to explore the clinical potential and value of robotically assisted AF.

Keywords: *laparoscopic, robot, vascular*

Introduction and Technique

Vascular surgical technology has progressively evolved in the direction of minimally invasive procedures for the treatment of aorto-iliac occlusive diseases. According to TASC, endovascular surgery is the treatment of choice for Type A focal lesions and the most currently utilized for type B and C lesions although evidence of superiority over conventional surgery is still lacking (1). Aorto-femoral grafting is considered as the gold standard treatment of diffuse aorto-iliac lesions (type D) (2). For this procedure, a 5-year patency of 90% in case of claudication, of 87.5% in case of critical ischemia has been described with combined morbidity/mortality greater than 10% (3).

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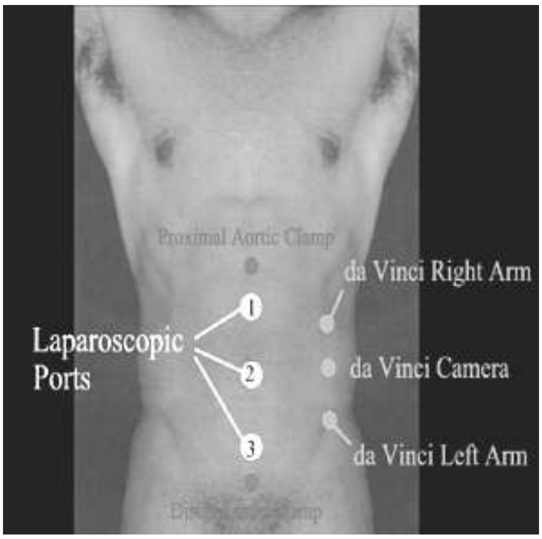
Local and systemic post-operative complications derive mostly from the large exposure of the aorta either trans- or retroperitoneally. To reduce the surgical trauma, laparoscopic aortic surgery has been proposed by Dion in 1993 (4). From that time, there have been an increasing number of reports describing different techniques of laparoscopic aortic surgery ranging from laparoscopically assisted procedures with minilaparatomy (5, 6, 7) or with hand port (8, 9) to totally laparoscopic (10, 11).

However, the surgeon has to face a large number of technique related challenges for the realization of laparoscopic aortic surgery:

1) laparoscopic surgery is limited by an unnatural operating field due to the unnatural manipulation of the instruments i.e. inversion of response to hand action in combination with 2-D visualization.

2) Once the aortic dissection is complete, performing an aorto-prosthetic anastomosis is exceedingly difficult to accomplish with currently available endoscopic instruments and requires a huge amount of training. The quest for a high-tech device that can transfer the natural movements of wrist and fingers of the surgeon to the operating field, using laparoscopic access has raised the interest of investigators to implement robotic technology in surgical practice. The da Vinci™ Surgical System (Intuitive Surgical Inc., Sunnyvale, CA) is a computer-enhanced telemanipulator that may help to overcome some of the limitations of traditional laparoscopic instruments. This work was performed to assess the safety and feasibility of robotically assisted aorto-femoral bypass grafting (AF).

Under general anaesthesia the aortic dissection is performed laparoscopically with the patient in a right lateral decubitus position according to the method described by Coggia et al. (12). Carbon dioxide pneumoperitoneum is established through a small incision performed on the anterior axillary line at 10 cm below the costal margin.



A 10 mm - trocar is introduced at this site to allow the introduction of a 30-degree endoscope. Two other trocars are inserted on the anterior axillary line 5 cm above and below the endoscope in order to allow the insertion of a grasping forceps and laparoscopic scissors. Two or three other ports are inserted on the linea alba and used for another grasping forceps and the suction device (figure 1).

Figure 1: Robotic and laparoscopic port placement for a robotic aorto-femoral bypass

A left retrocolic dissection is then performed until the left renal vein is found after cephalad dissection of the aorta. Due to the lateral position of the patient, the gravity drop of the left mesococolon acts as small bowel retractor. The site of aortic cross clamping is dissected as well as the inferior mesenteric artery. The femoral arteries are dissected according to the conventional manner. The conventional prosthesis is inserted through a port. After systemic heparinization, the infrarenal aorta is percutaneously cross-clamped with two laparoscopic Clamps (Xomed-MicroFrance, Saint-Aubain le Monial, France).

The da Vinci™ Surgical System is comprised of the following: a surgeon console with an integrated 3D display stereo viewer, a surgical cart with a camera arm and two instrument arms as well as a vision cart (figure 2).

Figure 2: The da Vinci™ Surgical System: surgeon console, three arms surgical cart and the vision cart

The surgical cart is positioned at the left side of the patient, next to the surgical table, partially within the sterile field and locked in position. This unit consists of three robotic arms: two instrument arms for endowrist™ technology instrument control and one for 3D stereoscopic camera positioning. The 7mm instruments and the 0° laparoscope are introduced through trocars by the assistant who stays within the sterile field during the procedure and controls additional instruments, exposure, hemostasis and maintains traction on the running sutures performed by the robot. Seated at the console, the surgeon operates using two masters positioned directly under a magnified 3D display of the operative field. The surgeon rests his head between head sensors on either side of the view port in order to see the 3D display in the stereo viewer. Instrument tips viewed in the display are aligned with the masters to ensure natural and predictable instrument movements. The hand/eye orientation and natural operative feel found in open surgery is maintained for the surgeon. A full range of instruments is provided to support the surgeon while operating. The da Vinci™ system places instrument movements under the direct, real time, and control of the surgeon by employing a kinematic – or joint movement - structure allowing the surgeon to use open surgery techniques at the console. These open surgery techniques are instantly converted into minimally invasive surgery movements at the surgical site. The da Vinci™ System electronics allow the use of motion scaling of surgeon hands movements. Motion scaling reduces hand movements to correspondingly smaller Instrument tip movements in the surgical field. Several settings allow surgeons to optimize scaling for different clinical steps. Natural tremor of the surgeon's hand is eliminated through electronic filtering which ensures stable and predictable Instrument control. Instruments – EndoWrist™ technology – have a total of 7 seven degrees of freedom, two more at the tip than traditional laparoscopic instruments. Tip articulations mimic the up/down and side-to-side flexibility of the human wrist. These articulations extend the surgeon's minimally invasive surgery capabilities to a new level. This enables the surgeon to perform complex, reconstructive surgery as aorto-prosthetic anastomosis through incisions less than 1 cm in length. Each instrument has a specific surgical mission such as clamping, suturing and tissue manipulation. Quick-release levers speed instrument changes during surgical procedures.

The proximal anastomoses are attempted with the help of the da Vinci™ System by a remote surgeon using either 4-0 Prolene suture or CV 4 Gore-Tex sutures. Two large needle drivers instruments with Endowrist TM technology are used, both attached to the robotics arms (figure 3).

Figure 3: Robotic Arms with Endowristed Instruments attached and 3D endoscope. Patient's side view

A 20-cm long double-armed suture is fixed at the prosthesis heel with a U-stitch before inserting it through a trocar. The first running suture is started posteriorly then ran to the right side of the arteriotomy. A second suture ran from the left side. Once the anastomosis completed, both sutures are tied anteriorly. Each limb of the graft is tunnelled into the femoral regions using vascular clamps. The distal femoral anastomoses are performed conventionally.

Conclusion

Laparoscopic surgery is an emerging method that could supplement the excellent 5-year patency rates of more than 90% after AF bypass with the advantage of videoendoscopic approach i.e. reduction of patient pain and trauma, faster recovery times and lower healthcare costs. However, it remains a very challenging procedure that falls victim to a difficult learning curve particularly for performing anastomoses. Contrary to GE surgeons, vascular surgeons do not have the minimal laparoscopic training skills. This may explain why initial procedures are generally more time consuming and have a higher complication rate.

Nevertheless, robotic surgery transfers to the laparoscopic instruments surgeon's natural dexterity and precision. Robotic surgery have already been used extensively in minimally invasive procedures across a broad range of disciplines including general surgery, (13) gynaecology, (14) urology (15) and cardiac surgery (16, 17, 18). In this paper, we described the technique of the aorto-femoral grafting using a surgical robot based on a 5 patient experience world's first performed at our institution. We have noticed that robotic surgery helped by the Da Vinci does not require a prior training in laparoscopic surgery to obtain the level required for suturing. Unlike standard laparoscopic surgery where the surgeon's hand movements are counterintuitive, the da Vinci System provides natural hand-eye coordination, and as a result, removes a significant barrier to learning and performing minimal invasive surgery. In addition, as remote surgery, this technology has potential use in cases involving a high risk of patient-to-professional or professional-to-patient virus transmission.

Robotic compared to conventional laparoscopic surgery has a prohibitive cost and has the same limitations: the absence of tactile feedback on which surgical skill and decision making are strongly involved. For example, the absence of feedback can be deleterious when manipulating the Prolene sutures. This is the reason why we moved to the Gore-Tex sutures that are much less prone to breakage during grasping. The robotic system may overcome the absence of touch by enhancing the precision of suturing using the stereoscopic magnification, the ultraflexibility of the robotic wristed instruments and the stability of the system.

Another robotic surgery fundamental aspect is its compatibility within the standard room environment. There are also internal space limitations. In some patient, we can see an external conflict between robotic arms that may lead to procedure alteration. The da Vinci set-up takes 30 minutes while changing instruments necessitate 30 seconds. The instruments can be autoclavable and have 10 uses. The instruments are attached to fix arms and can be manipulated by the surgeon sitting at the console. Moving the table may require some complex manoeuvres as actioning the set-up joint release buttons of all three arms. However, the ergonomic environment of surgeon console permits to eliminate work-related injuries by fully supporting the body.

Our preliminary experience demonstrates that robotically assisted anastomoses are possible and can minimize some of the difficulties and limitations associated with laparoscopic aorto-bifemoral by-pass. Precision of surgical technique is a significant advantage. Several problems became evident, as cumbersome devices, interferences between the robotic arms and poor tactile feedback. Reducing these drawbacks should expand the use of robotic surgery in vascular surgery. However, minimally invasive surgery has entered now a new era by the introduction of the robotic surgery systems, which will offer to the patient the benefits of endoscopic surgery, while surgeons regain the dexterity they experience in open surgery.

Instrument Check List

Atraumatic Forcep Graspers (Intuitive Surgical, Inc.) Monopolar Cautery Hook (Intuitive Surgical, Inc.) Two large needle drivers (Intuitive Surgical, Inc.) Round Tip Scissors (Intuitive Surgical, Inc.) O degree endoscope (Intuitive Surgical, Inc.) Wide angle (60o FOV) camera head (Intuitive Surgical, Inc.) Conventional suction/irrigation device Conventional laparoscopic forceps Conventional laparoscopic scissors.

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Unusual Treatment Strategy for a Well-Known Complication of Peripheral Open Arterial Reconstructions*)

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Abstract

Restenosis of arteries and grafts after revascularization interventions represent difficult management decisions and real technical challenges that the vascular surgeons need to face.

We present a case of a 59 year old male patient with multilevel arterial disease for which he underwent a complex open arterial reconstruction two years ago. He presents with 80% restenosis at the proximal anasthomosis on the external iliac artery. Our option was the endovascular treatment by placing a stent from the external-iliac artery into the Dacron prosthesis. Six months after the intervention, the patient is free of symptoms with patent bypasses evidentiated on Echo Doppler examination.

Introduction

As we approach the second century of modern vascular surgical practice, one hundred years after Alexis Carrel's pioneering work on arterial and graft anastomoses, the narrowing, or restenosis, of arteries and grafts after intervention to improve blood flow continues to provide vascular surgeons with technical challenges and difficult management decisions [1]

Greater than 20% of all interventions fail because of restenosis. Failure occurs early due to technical problems and later (1-12 months) because of injury-induced scarring [2]. At much later periods (> 12 months), failure results from the underlying atherosclerotic process. Although restenosis occurs within the context of atherosclerosis, the clinical features of atherosclerosis and restenosis are different [3]. Atherosclerosis is a multifactorial, inflammatory disease that develops slowly, usually taking decades, while restenosis results from the wound healing response to arterial injury and occurs within months.

We present a case of iliac restenosis after initial synchronous ilio-femoral and femoro-popliteal reconstruction, treated by endovascular stenting.

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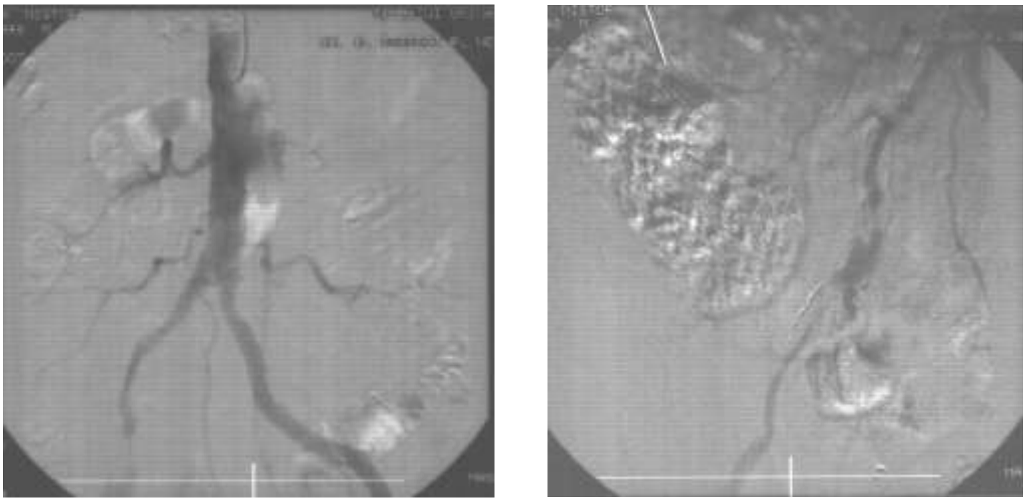
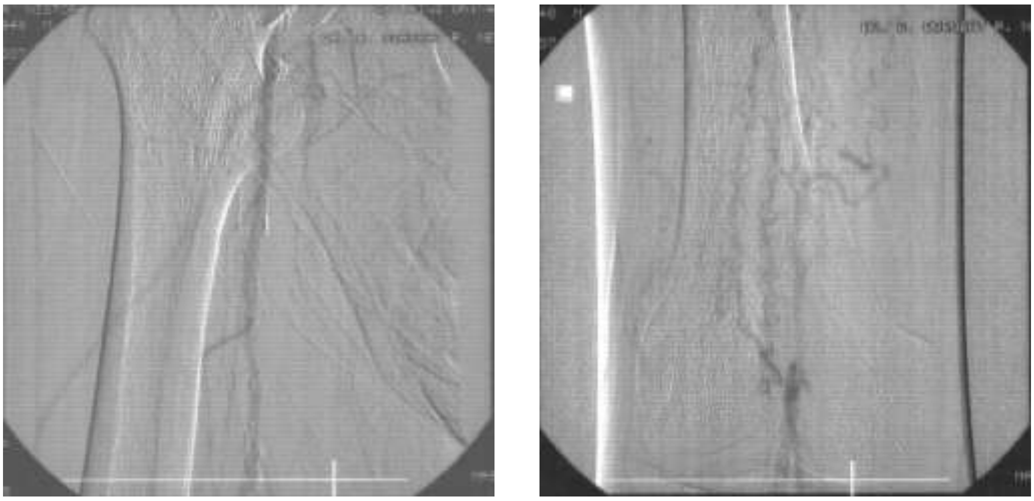
Case presentation

A 59 year old male patient with significant co-morbidities, a medical history of ischemic heart disease, hypertension and dyslipidemia presented to our department complaining of buttock claudication. The median pain-free walking distance was as low as 20 m. This is a patient who presented 2 years ago with critical limb ischemia, complaining of severe right pedal rest pain. The performed angiogram revealed a 90% extensive common femoral artery stenosis and superficial femoral occlusion in the distal segment followed by popliteal artery stenosis **(Figure 1 a, b, c, d).**



a) b)

Figure 1a, b: Common femoral artery subocclusion



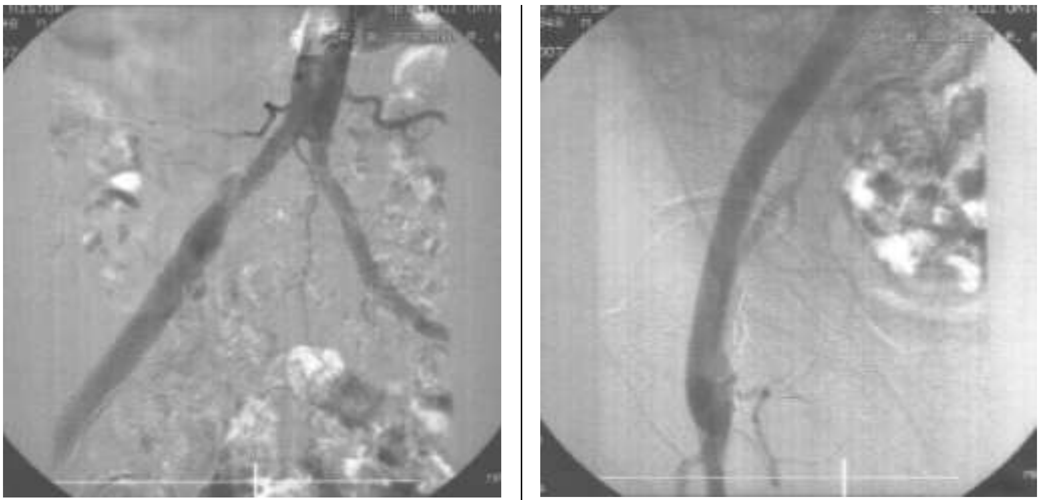
c) d)

Figure 1c, d: Superficial femoral artery occlusion in the distal segment and popliteal artery stenosis

We performed a sequential external-iliac- superficial femoral by-pass with an 8mm Dacron graft and a prosthetico-distal popliteal by-pass using the ipsilateral great saphenous vein **(Figure 2 a, b, c, d, e).**

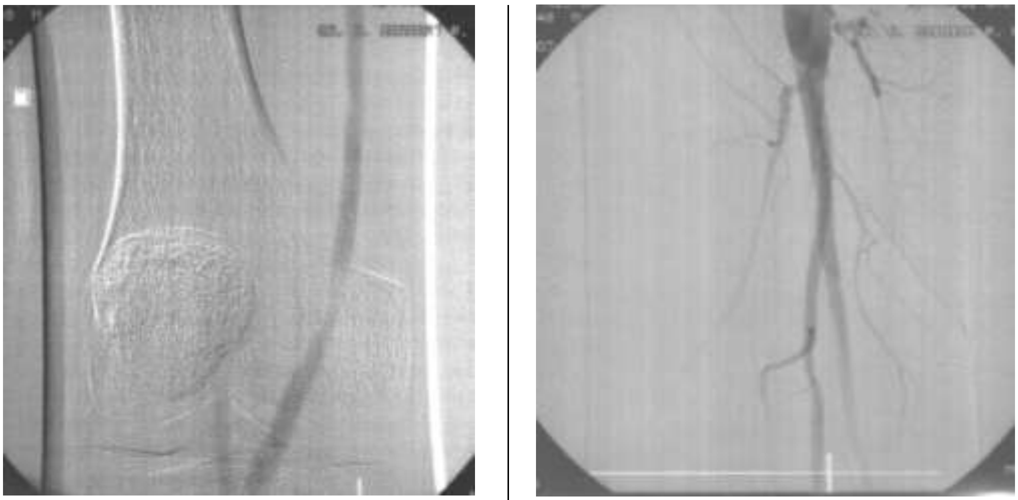
On his latest presentation 6 months ago a lower extremity angiographic examination evidentiated an 80% stenosis localized at the proximal anastomosis of the Dacron graft **(Figure 2b),** on the external iliac artery, and patent by-passes despite the decreased inflow **(Figure 2 d, e**).

Figure 2a: Schematic representation of the sequential external iliac – superficial femoral and prosthetico-distal popliteal by-pass



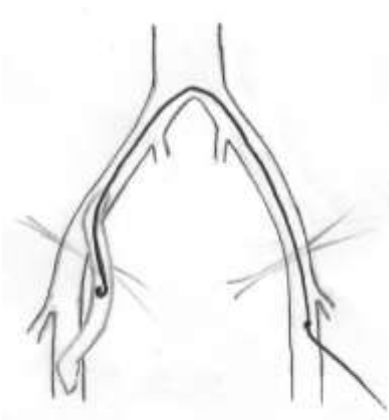
b) c)

Figure 2b, c: Angiographic aspect of the ilio-femoral by-pass with Dacron 8mm prosthesis with 80% stenosis localized at the proximal anastomosis



d) e)

Figure 2d, e: Angiographic aspect of the prosthetico-distal by-pass with GSV



The scar in the groin, compromised lymph drainage and the presence of synthetic material from the previous operation excluded the possibility of surgical exposure and reconstruction considering the high risk of wound and graft infection. In this case the percutaneous transluminal angioplasty (PTA) and stent deployment through the contralateral femoral artery and crossover manoeuvre **(Figure 3)** offered a reliable option for sufficient revascularization of the iliac artery and consecutive limb salvage.

Figure 3: Contralateral femoral artery approach

The endovascular repair consisted in a PTA followed by a self expandable nitinol stent deployed from the external iliac artery into the proximal portion of the Dacron graft (Figure 4, next page).

Completion angiogram was performed to ensure the successful revascularization of the external iliac and peripheral arteries.

The postoperative course was uneventful with discharge on day 3.

The patient was set in a clinical surveillance programme with lifestyle and atherosclerotic risk factor modification, as well as in a follow-up programme which included clinical examinations and duplex ultrasound examination at 1 and 3 months, now being in the 6-th month after the endovascular intervention.

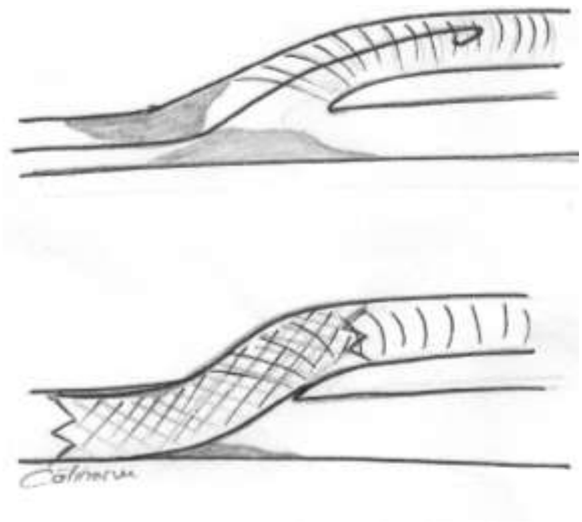


Figure 4: Stent deployment in the external iliac artery and proximal segment of the Dacron graft.

The post-interventional treatment included aggressive lipid control as well as double anti-platelet agents (acetylsalicylic acid 100 mg and clopidogrel 75 mg daily). The duplex ultrasound examination performed at 6 months after the procedure confirmed the patency of both inflow and outflow reconstructions, the patient being free of ischemic symptoms.

Discussion

All forms of arterial reconstruction involve vessel wall injury and repair of the injury by cells from adjacent normal tissues. Intimal hyperplasia is the hallmark of this healing process, often resulting in significant luminal narrowing that predisposes the repair to failure.

Since intimal hyperplasia affects 15–30% of all arterial interventions, strategies to control this injury response would have significant clinical impact [4].

Arterial and venous autografts remain the materials of choice to replace diseased or damaged blood vessels. However, because of their limited supply, there is an increasing need to develop arterial substitutes that are durable, are readily incorporated by host tissues, possess a non- or hypothrombogenic flow surface, have compliance characteristics that closely approximate the native vessel, are resistant to infection, and are easily sutured [5,6]. Although none of the currently available prostheses manifests all of the desired characteristics of the ideal arterial replacement, large-diameter Dacron grafts used to replace the abdominal aorta have proved adequate, with 5-year cumulative patency rates of 85–90% (7–10). Late patency rates of 74 and 70% at 10 and 15 years, respectively, have been reported by Nevelsteen et al. [9]. Unfortunately, the longevity of small-diameter prosthetic grafts (8 mm in internal diameter or less) is limited by the development of anastomotic intimal hyperplasia and consequent thrombosis of the grafts. When small diameter prosthetic grafts such as those fabricated from PTFE or Dacron are placed above the knee, cumulative patency rates range from 37.9 to 71%; below the knee, they range from 30 to 57% [10, 11].

It is estimated that approximately one-third of patients will require additional surgery related to their bypass graft within 2 years of the initial procedure. Furthermore, the risk of reoperation is increased substantially by the progression of ischemic heart disease and other associated atherosclerotic risk factors in these patients. Reoperative mortality rates of up to 5% and major limb loss rates of 20% have been reported. As a consequence, patients in whom complications related to their grafts develop may be unable to withstand the secondary operations needed to replace them.

The morbidity and expense of further treatment for restenosis is considerable, since adjuvant therapies to prevent luminal renarrowing are only now being realized in the limited context of stent angioplasty with drug coated stents. The ultimate goal of research in this area is to develop pharmacological strategies to modify vascular scarring so that zones of injury are repaired without luminal narrowing.

Conclusion

In the case of severe limb ischaemia in patients with a history of multiple vascular reconstructions in the ipsilateral groin, the surgical exposure of the femoral and iliac artery is not only technically demanding but also has an unfavorable prognosis. In these cases endovascular interventions offer a reliable and safe approach at least in the short and medium term.

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Descending Thoracic Aorta-to-Bilateral Femoral Artery Bypass*)

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Abstract

Background. *Arterial revascularization of the lower limbs by way of bypass from the descending aorta to the femoral system provides successful perfusion in case of a heavily-diseased abdominal aorta or of a hostile abdomen. The descending aorta allows a good inflow and the vessel usually has a parietal structure of a higher quality. The author presents his personal experience in a series of 13 patients with descending aorta-to-bilateral femoral artery bypass (DTAFA).*

Materials and methods. *A series of 13 patients with a mean age of 63,6 years underwent DTAFA bypass over a period of 6 years. The main operative indications consisted of heavily diseased aortas (including extensive calcifications), previous abdominal and vascular procedures. The series consisted mostly of male patients (92.3%) with aorto-iliac occlusion and associated infrainguinal disease.*

Results. *Perioperative mortality was 0. Graft patency is 100% during a follow up period ranging from 6 years to 6 months. One patient underwent splenectomy for splenic rupture while another patient needed femoro-popliteal extension of the graft.*

Conclusions. *DTAFA bypass grafts represent a sound alternative to axilo-femoral bypass in case of heavily diseased abdominal aortas and/or hostile abdomens. Due to the good inflow, to the better parietal quality of the thoracic aorta and to the anatomical course of the graft, DTAFA represents a durable method even in cases with infrainguinal arterial disease.*

Key-words: *Descending thoracic aorta; aorto-iliac occlusive disease, arterial bypass; aortic graft infection*

Introduction

Descending thoracic aorta-to-femoral artery bypass (DTAFA) represents a sound and durable substitute in cases in which aorto-bifemoral or axillo-bifemoral bypass does not represent an option [**1**]. The major impediment to a standard revascularization of the lower limbs is represented by a hostile abdomen (radiation, previous extensive surgery,

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retroperitoneal fibrosis, extensive scarring of the abdominal wall and visceral adhesions), previous vascular procedures (or surgical attempts), poor quality of the aortic wall (heavy and extensive calcifications, friable wall, juxta-renal calcifications and calcifications extending to the origin of the renal arteries, "high" obstruction of the abdominal aorta).

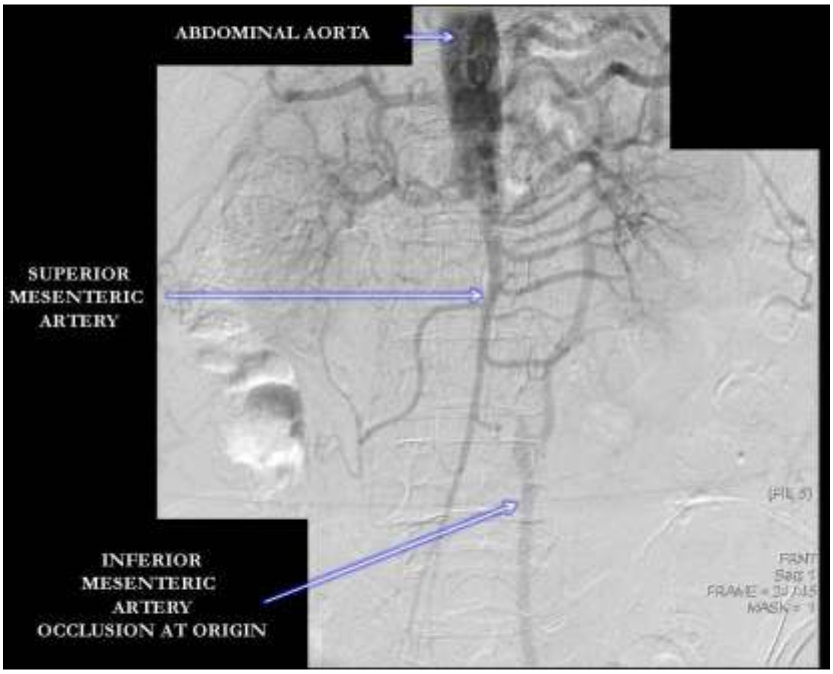

Figure 1: Preoperative angiogram depicting a "high" thrombosis of the abdominal aorta. The renal arteries and upper lumbar arteries are still patent. The superior mesenteric artery and its main branches – is visible. The inferior mesenteric artery is occluded at its origin, being filled through collateral circulation from the superior mesenteric artery.

However, this type of surgical procedure is not contemplated by all authorities and vascular centers in spite of its obvious advantages and long-term results [**2-7**]. The author presents his personal experience with a series of 13 patients who underwent DTAFA.

Materials and methods

A number of 13 consecutive patients underwent DTAFA bypass grafting, over a 6 year period (from 2006 to 2011).Male sex was predominant (92.3%) **TABLE 1** Patient age ranged from 52 to 78 years, with a mean age of 62.6 (**TABLE 1**). Among age groups, it is noticeable the number of younger patients (in the age group 51-55. **TABLE 1**)

Table 1: Patient demographics

SEX	NUMBER	%
Male	12	92.3
Female	1	7.7
TOTAL	**13**	**100%**

AGE GROUP (YEARS)	NUMBER	%	NOTES
51-55	4*	30.7	*1 female patient
56-60	1	7.7	
61-70	1	7.7	
66-70	3	23.1	
71 -75	3	23/1	
76-80	1	7.7	
TOTAL	**13**	**100%**	

The severity of ischemia upon admission in the hospital, is presented in **Table 2**

TABLE 2: Severity of ischemia

MAJOR COMPLAINT / CLINICAL SIGN	NUMBER	%
Foot and/or leg gangrene	4	30.7
Rest pain (intractable)	3	23.1
Disabling claudication (< 10 m)	6	46.2
TOTAL	**13**	**100%**

All patients suffered advanced or disabling ischemia. In 4 patients, the DTAFA grafting represented ***a limb-saving procedure***. All patients had notable associated diseases **table 3**.

TABLE 3: Associated diseases

ASSOCIATED DISEASE	NUMBER	%
Arterial hypertension	13	100
COLD* / Heavy smoking	13	100
Infrainguinal occlusive arterial disease	12	92.3
Diabetes	4	30.7
Renal artery stenosis	3	23.1
Incisional hernia (previous surgical attempt)	2	15.4
Stroke	1	7.7
Cerebrovascular insufficiency without stroke	1	7.7
Chronic renal failure	1	7.7

*** COLD =** *Chronic* ***O****bstructive* ***L****ung* ***D****isease*

Special notes*:*

- *ALL patients had high blood pressure and chronic obstructive lung disease.*
- *Except one patient, all had infrainguinal occlusive arterial disease, hence the distal anastomosis was performed on the deep femoral arteries.*
- *In spite of a younger age, all patients were at higher perioperative risk, while accumulating more than one associated disease.*

The main indications for choosing the descending aorta as inflow (the donor vessel), are presented in **Table 4**.

Table 4: Major indications for choosing the descending aorta as inflow

MAJOR INDICATION	NUMBER	%
Heavily calcified aorta and previous surgical attempt	7	53.8
Heavily calcified aorta and NO previous surgical attempt	2	15.4
Previous extensive abdominal surgery ("hostile abdomen")	2	15.4
Horseshoe kidney	1	7.7
Infected abdominal aortic graft	1	7.7
TOTAL	**13**	**100%**

Most of the patients had previous surgical attempt for performing a standard abdominal aorta-to-bifemoral bypass (performed in other centers). Two such patients had incisional hernias needing repair as a separate surgical procedure after performing the DTAFA. In the remainder two patients with a pre-operative diagnosis of heavily-calcified aorta (**figure 2**), we also performed an intraoperative control of the abdominal aorta just in case of finding a suitable segment for clamping and anastomosis.

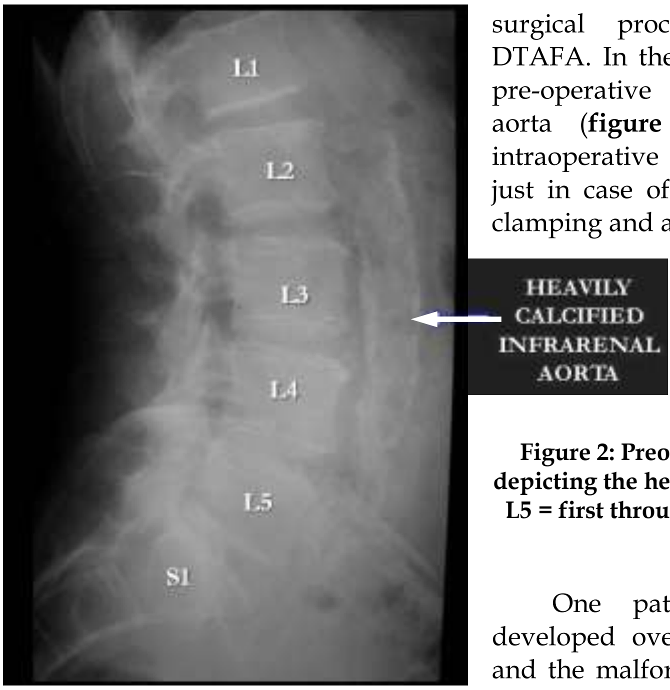

Figure 2: Preoperative simple abdominal x-ray, depicting the heavily-calcified abdominal aorta. L1-L5 = first through fifth lumbar vertebra. S1 = first sacral vertebra.

One patient had horseshoe kidney, developed over the inferior abdominal aorta and the malformed kidney received numerous separate renal branches from the abdominal aorta.

The patient with infected graft, had an aorto-femoral bypass which was subsequently removed. After complete sterilization, the patient underwent a DTAFA grafting.

Surgical technique. All patients had a preoperative check-up consisting of cardiological clearance (ECG, echocardiogram), spirometry, chest x-ray, angiogram. All patients had selective intubation and left lung deflation + epidural analgesia. A lateral thoracotomy in the left seventh interspace allowed a good exposure of the descending aorta after cutting the pulmonary ligament and aided by a gentle traction of the left hemidiaphragm. The mediastinal pleura was longitudinally incised and suspended with 2 pairs of stay sutures. This minimized the need for pericardial traction. There was no need for a circumferential dissection of the supradiaphragmatic aorta. The aorta was exposed up to the level of the left pulmonary hilum and a proper segment was chosen. Lateral clamping of the aorta eliminated the risk of paraplegia or visceral ischemia [**8**]. A 8 mm Dacron graft was anastomosed to the descending thoracic aorta after being tunneled through the diaphragm, allowing a better orientation of the graft and of the proximal anastomosis. Separate incisions were made at femoral level and the left abdominal wall, and the graft was tunneled through the retroperitoneal space in anatomical position. An "*ad hoc*" bifurcation was constructed in such a way that the bifurcation of the graft was superposed on the natural aortic bifurcation. The two femoral branches passed slightly lateral to the iliac and femoral vessels on their way to the deep femoral arteries.

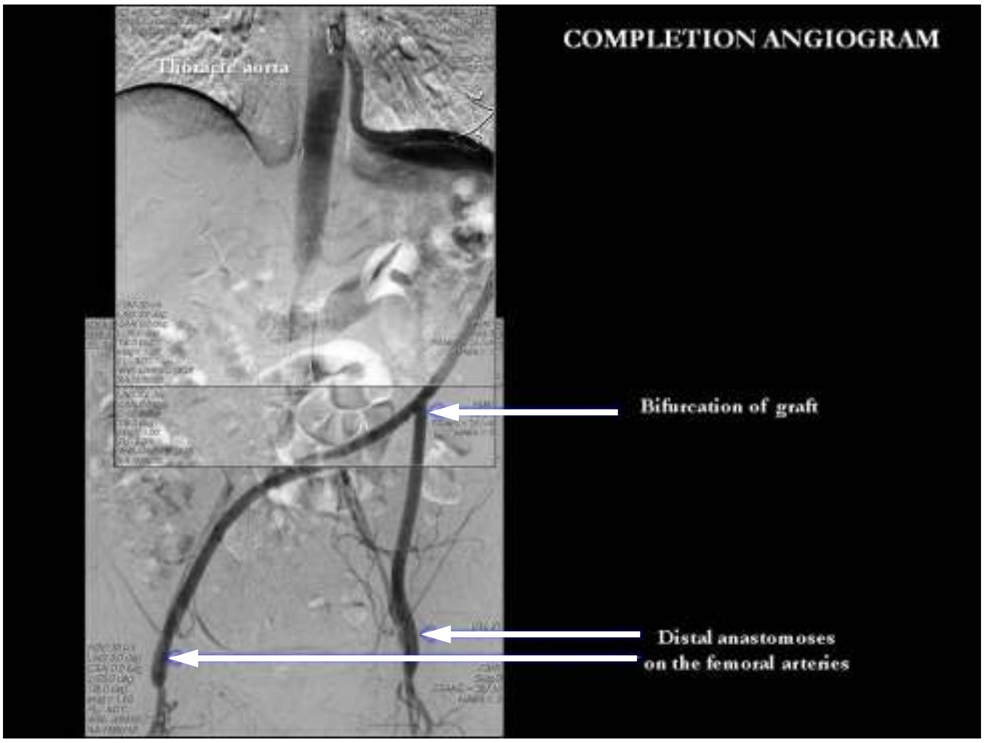

Figure 3: Completion angiogram, depicting the descending thoracic aorta-to-bilateral femoral artery bypass. The "*ad hoc*" bifurcation is visible, as well as the general disposition of the graft.

Results

There was no mortality in the group of patients.

Splenic rupture in one patient required splenectomy. Rupture was not produced when tunneling the graft through the diaphragm but due to a forceful retraction of the left hemidiaphragm.

There were no other notable complications in this group of patients. Pulmonary function was not affected by the left thoracotomy approach. Epidural analgesia provided a good and rapid respiratory function after extubation.

The ICU stay was 48 hours. All patients were extubated in the operation room. Chest drainage was removed on the third postoperative day. In-hospital stay was 7-10 days.

All patients had a good evolution. Ischemia resolved, even in patients having occlusion of the superficial femoral arteries. In 4 patients, who had foot of leg gangrene, necrectomy was concomitantly performed.

During a follow up ranging from 6 years to 6 months, the graft patency was 100%. One patient required extension of the graft, through a unilateral femoral-to-popliteal bypass at 2 years after the DTAFA.

Conclusions

Descending thoracic aorta-to-bilateral deep femoral artery was successfully performed in 13 patients as alternative to conventional arterial revascularization. The surgical procedure appears more demanding both for the anesthesiologist and for the surgical team. In spite of this aspect, the thoracic aorta offers a good inflow and in most cases, a better quality of the arterial wall. The procedure appears to be durable and with few complications. This particular group of patients had numerous associated diseases, including extensive peripheral vascular occlusive disease. The construction of a bifurcated graft and placement in an anatomical position contributed to the good results in patients with more distal arterial lesions. The outcome and quality of life are comparable to the conventional aorto-bifemoral bypass [**9**]

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The vein graft - what do we know about it today?*)

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In 1968 Favaloro performed the replacement of a diseased segment of a coronary artery using a saphenous vein graft. One year later he performed an aorto-coronary bypass using the same saphenous graft introducing on large scale this technique. Since then coronary artery-by-pass grafting using vein grafts has been evolving as a standard technique for the treatment of coronary artery disease. Despite the early enthusiasm concerning the use of vein grafts it soon became obvious that coronary artery bypass grafting only offered a palliation for an evolving process that also implies the accelerated involvement of the grafts themselves.

Unfortunately, except for the synthetic grafts that are only exceptionally used for coronary artery bypass grafting, strong evidence showed that vein grafts are the most prone to degeneration among all grafts used. It is assumed that between 10 to 15% of all vein grafts are non-functional at one year from the operation. There is evidence to show that as many as 10% of the vein grafts are occluded as soon as 30 days from the intervention. After the first postoperative year the yearly occlusion rate is 1-2% for the following 5 years and of as much as 4%/year for the period between 6 and 10 years from the operation. An average patency rate of around 50% at 10 years is obtained consecutively. Unfortunately among the patent vein grafts, at ten years about one half is in good condition while the rest show single or multiple stenosis of a higher or lower grade.

The high failure rate that is encountered at the level of vein grafts brought those in the spotlight of research media. It was soon shown that early failure of vein grafts is due to two biologic processes: thrombosis and neointimal hyparplasia (the latter also known as subintimal hyperplasia). On a longer term the vein is affected by an accelerated process of atherosclerosis that is responsible for most of the cases of late failure.

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Vein graft thrombosis

Vein graft thrombosis appears mainly as a consequence of an endothelial lesion that makes the contact of blood with the thrombogenic sub-endothelial layer possible. Endothelial lesions with basal membrane exposure or thrombosis that is produced even throughout the harvesting process predispose to early thrombosis of the vein graft.

Thrombotic occlusion of the vein graft appears, as stated earlier, in as much as 12% of all vein grafts in the first 30 days from the operation. A series of factors certainly play an important role in the etiology of graft thrombosis. One of these factors is the time elapsed from harvesting to reinsertion in the bloodflow (arterial in this instance). This time is also known as ischemic time. The thrombosis rate increases slowly with time in the first 60 minutes of ischemic time. After that the increase is more abrupt. The influence of the length of ischemic time on the probability of vein graft thrombosis is also obviously affected by the conditions of vein storage during this period.

Vascular tissue reperfusion with oxygenated blood is associated with leukocyte aggregates accumulation at the site of hypoxic endothelial damage. There is a local release as various cytotoxic substances as are oxygen free radicals, prostanoids (leukotrienes, thromboxane) and proteases. Neutrophyle adherence is mediated by cell membrane receptors whose expression is induced by the ischemia-reperfusion process. The adhesion and activation of neutrophyle leukocytes induces not only ongoing endothelial damage but can also activate the coagulation cascade directly.

The surgical act in itself and the cardiopulmonary bypass in particular induce a series of alterations of the fluid-coagulation balance. On one side the marked increase in fibrinogen levels encountered during CPB has a procoagulant effect, but on the other the decrease in platelet count and the prolongation of coagulation times act anticoagulant. Numerous vasoactive substances are released in response to the extensive surgical intervention. These substances act on the endothelium and vessel wall of the vein graft. The saphenous vein graft is very sensitive at the action of circulating vasoconstrictors as is endothelin I. This is the case especially when the vein graft is denuded of its adventitial layer. Thrombin acts also as a vasoconstrictor on the vein graft. The vasoconstricting effect of thrombin depends on the integrity of the venous endothelium. An intact endothelium can counterbalance the vasoconstrictive effect of thrombin. More so, the action of thrombin on several receptors that are expressed on intact endothelial cells may induce vasodilatation. Vein spasm is a strong promoter of thrombosis. It is obvious that the main factor on which the development or not of thrombosis depends is the integrity of the venous endothelium.

Neointimal hyperplasia (NIH)

NIH is defined as an accumulation of smooth muscle cells and intercellular matrix at the level of the venous intima. This is tha main pathologic process that affects the vein graft in the first postoperative year. Virtually all veins that are inserted into the arterial bloodstream develop some level of wall thickening in the first 4 to 6 weeks from implantation. This is a response that is common to all cavitary organs whose intraluminal pressure is increased and represents the tendency toward a compensatory decrease of the wall tension.

NIH has in its center the migration and accelerated proliferation of smooth muscle cells. In the normal vessel wall the proliferation rate of smooth muscle cell is very low. This rate increases very much in response to certain stimuli among which are endothelial lesions and increase in vessel wall tension. The migration of smooth muscle cells supposes their detachment from local tissue matrix and breaking of the adjacent intercellular junctions. This process implies the expression and release of matrix metalloproteases and of their natural inhibitors. The balance between metalloproteases and their inhibitors may be of key importance.

NIH only rarely determines significant stenosis to limit the blood flow through the graft. It generates though a rough aspect of the interior of the vessel wall that promotes by a multitude of mechanisms among which the turbulent blood flow itself an accelerated process of atherosclerosis. Atherosclerosis is the process that is responsible for the gradual failure of most of the vein grafts in time.

The thickening of the intima produced by the migration of smooth muscle cells at this level and by deposition of extracellular matrix, both processes characteristic for NIH, is probably closely associated with wide denudation and destruction of the endothelium. NIH has been associated with excessive distension of the vein, the degree of spasm and with the use of certain vasodilators during vein preparation. In experimental studies on animals the denudation of the endothelium is followed by platelet adhesion. The platelets are progressively replaced by a new endothelial covering that starts at the periphery. The growth and regeneration of the endothelium is stimulated by a series of growth factors among which are the plateled derived growth factor (PDGF), TGF-b and epidermal growth factor. These growth factors do not only stimulate endothelial cells to proliferate but also act on other cells present in the vessel wall as the smooth muscle cell and the fibroblast. In fact, the smooth muscle cell and the fibroblast appear to be two distinct evolutive phases of the same cell line: the myofibroblast. The migration of the myofibroblast toward the intima is favored. The vein wall lesions also determine the release of other strong mitogenic factors as the fibroblastic growth factor and the PDGF-like growth factor. These factors induce mitosis by activation of a specific cellular sequence that implies a family of regulatory proteins - the cyclin dependent kinases (CDK). CDK's act at the level of certain cellular oncogenes. Their derepression activates DNA synthesis and the consecutive evolution of the cells from phase G to phase S and M of the cell cycle. It appears that the process of NIH is induced by endothelial damage.

There is scientific proof that suggests the involvement of matrix metalloproteinases in the process of NIH. These enzymes find themselves in the center of the degradation/deposition of tissue matrix. It was formerly shown that the use of metalloproteinase inhibitors in human saphenous vein cell culture may inhibit or significantly decrease the deposition of intercellular matrix. These data suggest that these substances may play a role in the future in the prevention of alterations that appear in the vein grafts in time.

Recent studies show that perivascular fibroblasts may play a role in the development of NIH. This perivascular fibroblast appears to pass the vessel wall media and transform into smooth muscle cells at intimal level. The analysis of the proteins that build up the cytoskeleton of myofibroblasts that are involved in the development of NIH in human vein grafts used in CABG (harvested at the time of redo cardiac surgery) indicate strong resemblance to those of the perivascular fibroblasts. Actual proof is not very strong as it is mainly based on extrapolation and comparison with a porcine experimental model.

Nitric oxide (NO) and vein grafts

NO, also known as endothelial derived growth factor (EDRF), is a mediator with a very short half-life of about 5 seconds. NO is produced in the process of conversion of L-arginin to citrulin. This reaction is catalyzed by the enzyme nitric oxide synthase (NOS). NOS is present in several isoforms that can be schematically drawn into two categories: constitutive NOS (normally present in various tissues and producing NO at a constant rate) and inducible NOS. Inducible NOS is synthesized in large amounts under the influence of more or less specific stimuli.

NO has a series of effects on cells that he acts on. These effects are cytoprotective on the one side but can also be cytotoxic. From the first category, of cytoprotective agents, are the neutralization of oxygen free radicals, the inhibition of release of prostanoids as PGE2 and PGF2a, the depression of endothelial cell activation (including the decrease of the expression of adhesion molecules that reflect in decrease of neutrophyle and platelet adhesion), direct inhibition of neutrophyle function and the modulation of cytokine release. Cytotoxic effects of NO are represented by inhibition of protein synthesis, increase in lipid peroxidation (generating highly active radicals as - ONOOH) and inhibition of acute phase proteins. The actions of NO are due to the stimulation of the soluble phase fraction of the enzyme guanilate cyclase that produces a very active second messenger - cyclic GMP (cGMP). cGMP produces vasodilatation and smooth muscle relaxation. Other mechanisms of action of NO are also involved. Among these are the inhibition of CDK's, the inhibition of threonine phosphorilation, the inhibition of certain kinases and the decrease of the expression on cyclin. All these mechanism have as a main consequence an antimitogenic effect on the myofibroblastic cell line.

The damage produced by the ischemia-reperfusion phenomenon at the level of the endothelium induces a marked decrease of both forms of NOS (constitutive and inducible) and consequently a decrease in the concentration of NO. There is also a reduced sensitivity of the vein wall at the action of NO agonists as acetylcholine and bradikinin. Hence the biological effects of NO are severely affected by traumatic lesions caused by vein manipulation before and during its insertion as a bypass graft. Though, NO synthesis increases transiently during reperfusion following transitory ischemia. It is not yet clear what the effect of increased wall stress on NO releases. There is evidence that NO opposes to the effects of increased wall stress represented by smooth muscle cell and fibroblast migration and matrix deposition. NO inhibits both these processes. It has been shown that the treatment of the harvested veins with L-arginin induces a reduction in NIH. More precisely, increased levels of NO are associated with a lower level of NIH.

In vessels severely affected by atherosclerosis the production of NO is much reduced. It is not very clear what the sequence of events and the mechanism of the relationship between atherosclerosis and decreased NO synthesis. *Hypercholesterolemiant* diets induce alterations of some cellular functions that are mediated by specific receptors. They also induce interactions between oxidized low density lipoproteins (LDL) and NO. Arginin administration decreases or even abolishes the vascular dysfunction in hypercholesterolemic patients. Meanwhile smoking is associated with a decrease of NO activity at the level of the vessel wall. The increased susceptibility of the vessel wall at the action of endothelin I that is encountered in smokers can be possibly explained by this mechanism. An increased susceptibility to smoking could be explained by NOS polimorphysm. It has been shown that patients with particular NOS isoforms are especially prone to the development of atheroslerosis if they smoke. Conversely, premenopausal women that smoke have a better resistance to atherosclerosis as compared to men of similar age. It may be that increased basal estrogen levels induce a higher level of basal NO production.

The role of cell adhesion molecules

Cell adhesion molecules are membrane receptors that recognize as a ligand surface proteins present on other cells facilitating intercellular interactions, matrix proteins allowing anchoring of specific cells in different locations or circulating proteins enabling the extraction of these circulating proteins from the adjacent environment. The main classes of cell adhesion molecules are the selectins, integrins and the immunoglobulin supergene family.

Selectins are proteins that conditions of lack of a specific stimulus are stored in cytoplasmic granules. Specific stimulation induces exposure of these proteins on the cell surface. Selectins bind specific ligands that are represented by receptors on the leukocyte surface. Selectin exposure on the outer cell surface (that takes place as a result of the action of TNFa or IL1, that is as a result of tissue injury) is the first step of leukocyte adhesion.

Integrins are membrane receptors that represent the main mechanism of anchoring of cells to extracellular matrix. They posess the capacity of deep structural and conformational changes that depend on the state of the specific cell. These conformational changes are responsible for the variable affinity of integrins for various ligands. Proteins from the integrin family are responsible for the adhesion of platelets or leukocytes to the sub-endothelial space in case of endothelial denudation. Integrins recognize as ligands fibronectin, collagen, laminin, etc. Integrins also bind specific circulating proteins as fibrinogen.

Receptors from the immunoglobulin supergene family are responsible for cooperation of homotypic cells (cells of the same type) but also of heterotypic cells (cells of a different type as are endothelial cells and leukocytes). This class of cell adhesion molecules comprises receptors such as VCAM (*vascular cell adhesion molecule*), ICAM (*intecellular adhesion molecule*), PECAM (*platelet-endothelial cell adhesion molecule*), LFA (*leukocyte function associated*). The interaction between these receptors lies in the center of various cellular activation/ translocation processes as is leukocyte diapedesis and cellular activation during the immune response.

An increase in cell adhesion molecule expression at the level of endothelial cell membrane is encountered in the case of NIH but most of all in the presence of atherosclerosis. An increase in the expression of cell adhesion molecules favours the development of atherosclerosis by means of the tisular sequestration of leukocytes that become loaden with lipids as foamy cells. Foamy cells are a very active source of cytokines and growth factors that promote neointimal proliferation. That is, as leukocytes accumulate within the vessel wall they continue to further and further stimulate the activation and migration of myofibroblasts towards the intima and the proliferation of these latter cells.

Another factor involved in the increase of adhesion molecules expression is increased wall tension. The wall tension can be increased basically in two manners. First, as is the case in uncontrolled distension of the vein during preparing, the wall tension is increased statically but with high pressure. Second, as is the case with the vein grafts inserted in the systemic arterial flow, the wall tension may be increased in a pulsatile manner. The increase of wall stress stimulates the expression of ICAM 1 and VCAM 1 and inhibits the expression of thrombomodulin. These molecular changes can be counterbalanced at least in part by decreasing the wall stress. This has been experimentally performed by wrapping the vein in an external tube graft in a noncompressive manner, as external compression damages the adventitial layer and represents in itself a strong stimulus for proliferation. External wrapping increases wall thickness decreasing wall stress according to Laplace's law and may be associated with a reduced incidence of NIH at least on short term.

Techniques of prevention of vein graft failure

Techniques to prevent vein graft failure are addressed both to the intraoperative period and to the postoperative period.

Intraoperative prevention of vein graft failure concerns the harvesting technique and the technique of preservation of the vein before its insertion in the systemic arterial flow. It comprises also techniques to prevent or minimize lesions produced by the arterial flow at high pressure and reperfusion. This type of prevention of vein graft lesions is known as primary prevention.

Secondary prevention is addressed to the period after the operation on short or long term. Secondary prevention measures, unfortunately not very numerous, have as a theoretical substrate the thought that the vein graft will suffer in any case a more or less pronounced process of NIH and atherosclerosis. Early diagnosis of these lesions, before symptoms reoccur, is of great clinical significance while methods of altering the natural course are evolving.

Primary (intraoperative) prevention of vein graft failure

A good, clean surgical technique is essential for the minimum possible damage to the harvested vein. The main objective is the preservation of the venous endothelium. This is the thought that the surgeon has to constantly keep in mind. There are many available methods to reach this task.

Papaverine infiltration along the course of the vein that is about to be harvested preceding the skin incision has more than a single reasons for being performed. Papaverine prevents vein graft spasm (spasm that may induce damage to the endothelium by disruption of intercellular junctions among endothelial cells and denudation of the subendothelial layer) and decreases endothelial susceptibility to damage produced by high pressure dilatation.

A good surgical technique implies a non-touch strategy. Direct touch of the vein by means of surgical instruments or the hand is prohibited. Only adventitia and perivenous tissue may be grasped and by this means careful mobilization of the vein and dissection of side branches before their ligation is possible.

A continuous skin incision allows a more expeditious vein harvesting. It, too, allows a good "direct vision" of the vein throughout the procedure decreasing the risk of vein damage. Serial short incisions prolong the duration of harvesting and increase the risk of vein damage in the hands of an unexperienced surgeon. Both techniques have a low rate of wound complications. Endoscopic harvesting offers the advantage of a very appreciated cosmetic result while the handling of the vein is very gentle.

After isolation the vein is filled with fluid and gently dilated. It is essential that the distention of the vein is performed with low pressure. As pressure measurement during vein dilatation is only exceptionally used, the good common sense of the surgeon is of great importance. The distension pressure should ideally be lower than 100 mm Hg. At pressures above 150 mm Hg endothelial lesions are produced. The severity of the endothelial lesions is directly associated with the intraluminal distension pressure. It has to be kept in mind that a syringe may easily generate pressures of 600 and even 800 mm Hg.

Other controversies regard the composition of the solution used for vein distension, flushing and preservation before insertion in the systemic arterial tree. It is almost unanimously accepted that simple crystalloid solutions (as normal saline, Ringer's lactate) are not adequate for endothelial preservation. Heparinized blood (with or without the addition of papaverine) is definitely superior. However, preservation of the harvested vein in blood-containing solutions implies the possible activation of platelets, leukocytes and other enzymatic systems with a certain deleterious effect on the endothelium. It has been shown that damage to the endothelium that is produced during harvesting and preservation persist a relatively long period of time or even is irreversible. A series of more complex solutions (colloidal solutions) have proved to be superior and more advantageous for vein graft preservation. Such solutions are the Krebs-Henseleit, Plasma-Lyte, Harmann and others. The University of Wisconsin solution that is currently used in organ preservation for organ transplantation is particularly indicated for vein graft preservation. It has been proven that the use of this solution is followed by a good preservation of the normal function of the vein wall myofibroblasts and of their response to various vasoactive agents such as Acetylcholine. Given the fact that the vasodilating effect of such agents is mediated by the endothelium and its integrity is essential for it, it appears that the use of such colloid solutions offers good advantages. There are, though, conflicting results in this regard, too. Some studies show an abnormally powerful response to vasoconstricting agents such as serotonin.

The temperature at which the veins are kept after harvesting also plays a central role in the preservation of the endothelial integrity. Low temperatures (below 20°C and especially around 4°C) induce severe damage to the endothelium and are therefore contraindicated. Cooling produces lesions to the cytoskeleton of the endothelial cells and subsequent cell death. Approximatively 20% of the endothelial cells of a vein graft die after 90 minutes of preservation at 4°C as compared to only 4% for a similar period of preservation at 20°C.

Vasoactive mediators released during cardiopulmonary bypass may, too, induce alterations at the level of the vein graft wall. It has been proven that these mediators produce an increased expression of adhesion molecules on the endothelial cell membrane. This process favors platelet and leukocyte adherence and their deleterious effects. It may be that off-pump coronary artery surgery has a positive effect on vein grafts by a reduction of the inflammatory response that is induced by the surgical procedure, although data on this topic are conflicting.

An interesting approach is the wrapping of the vein graft in a non-compressive prosthetic material. The rationale of such an approach is the increase in wall thickness and a consecutive reduction in wall stress according to the law of Laplace. The reduction in wall stress may be of cornerstone importance in the prevention of neointimal hyperplasia as increased wall stress is one of the main factors initiating this particular pathologic response of the vein wall. The early works on this topic reported disappointing results with an unacceptable high graft failure rate. It is now assumed that these early results were due to compressive wrapping of the graft with consecutive adventitial and perivenous tissue damage and inflammation. Recent works suggest that non-compressive wrapping using ePTFE may indeed increase at least mid-term patency, a good healing of the prosthetic material being necessary for attaining such results. More large scale studies are needed for the confirmation of the utility of this approach, recent reports being encouraging.

Secondary (postoperative) prevention of vein graft failure

Antiplatelet therapy has been used for many years in patients suffering coronary artery bypass grafting. Therapy with aspirin or dipiridamole started immediately postoperatively (in the first postoperative 24 hours) decreases the early thrombotic graft occlusion rate. Therefore, early postoperative aspirin administration (at 6 hours from admission in the intensive care unit) is recommended. There is though no proven effect of aspirin or dipiridamole on the development of neointimal hyperplasia or athero-sclerosis. It may be that newer antiplatelet agents (such as the IIb/IIIa protein inhibitors) will offer long term benefits regarding long term graft patency given their improving effect on the results of PTCA and stenting.

Among the tries to limit the process of neointimal hyperplasia, process that is centered on cell activation, multiplication and migration, there is also the use of therapeutical approaches that are specific to the treatment of neoplastic disease. Brachitherapy (local radiation therapy) was tried especially in experimental models and less so in the human patient. Vein grafts treated by means of brachitherapy may improve their patency rate but may as well develop fibroproliferative lesions. Photodynamic therapy using lutetium meto-texan as photosensitizing agent has the advantage of fixing of the photosensitizant in atheromatous plaques and it being activated by far red light. There are yet no studies to assess the efficacy of these new therapeutic approaches.

The use of antimitotic drugs with specific action on myofibroblasts was also tried. Not one of the substances used and that eventually proved to be effective in animal models showed any efficacy in the human patient. There was no degree of decrease of the long term failure rate of the vein grafts.

Much interest is gathered by gene therapy. This form of therapy consists in insertion of nucleic acid fragments in specific cells of the vein graft, whose activation is able to block or at least slow the activation and progression to a mitotic phase of the respective cells. The introduction of ex-vivo genetic material may be performed by means of plasmide incorporation and direct injection into the cell, by use of liposomes or by use of viral vectors. The technique using viral vectors seems to be the most effective and is hence the most used method. The most frequently used viral virus is an adenovirus that can be generated in high titers, has a high capacity of genetic material insertion and is relatively easy to use. It has the ability to infect as well cells that are in the proliferation process as well as cells that are not dividing in a non-pathologic manner. The main shortcoming is that adenoviruses infect non-selectively all cell types and can hence induce non-selectively mutations that are hard to control or predict. Genes that antagonize the expression of cell division promoters may be introduced. An example is the inhibition of cyclin or various cyclin dependent kinases. It was proven that such a therapy inhibits neointimal hyperplasia after bolloon induced endothelial lesions in experimental models.

Other techniques that will possibly prove useful in the future with regard to neointimal hyperplasia prevention are the administration of a retinoblastoma-specific modified protein that selectively inhibits mitosis by antagonizing a cell mitosis promoting factor (E2F factor), of competitive inhibitors of cyclin dependent kinases or of a hybrid proteic inhibitor of plasmin, plasmin being a strong promoter of cell migration.

Another technique resides on the transfer of the gene coding the nitric oxyde synthase at the level of the vein graft endothelium. A significant decrease of the thickness of the intima as compared to the media was noted in experimental models where this gene was successfully transferred by means of an adenoviral vector.

Conclusions

The vein graft is still one of the most commonly used grafts in revascularization surgery and especially in coronary artery bypass grafting. Unfortunately long term patency of vein grafts is not especially good, they being exposed to thrombosis, neointimal hyperplasia and accelerated atherosclerosis, each of which being specific to a certain period of the graft lifetable. The central element upon which the patency of the vein graft depends is the venous endothelium. Its damage promotes a cascade of events that include the generation of mediators of inflammation, the expression of specific membrane receptors, transformations, migrations and eel division. The biology of this particular cascade of events is now better understood. This better understading allows for new approaches to prevent especially neointimal hyperplasia. These new approaches tend to influence cell migration, cell proliferation, matrix production, neoangiogenesis and other alike biological processes. At the present time the results of such new approaches are still under debate and sometimes nonconvincing, but in the future it will be among them where efficient techniques of improvement of vein graft patency will be chosen.

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L'utilisation de la prothèse en polytetrafluoroethylene PTFE-DISTAFLO dans la chirurgie artérielle reconstructrice distale*)

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Comme connu, les meilleurs résultats dans la chirurgie artérielle femoro-poplite et des troncs jambiers sont obtenus en utilisant comme greffon la veine saphène interne.

Si les veines des membres inférieurs sont non utilisables (maladie variqueuse, diamètre inférieur à 3,5 mm), ou manquent (chirurgie antérieure) on utilise les greffons prothétiques. Pour la chirurgie de l'artère poplitée distale et les troncs jambiers, des auteurs comme Taylor, Miller et Cormier ont propose de mettre un segment veineux entre l'artère réceptrice et la prothèse. Les avantages de cette technique sont:

- amélioration de la perméabilité du pontage en baissant le risque de sténose au niveau de la pointe de l'anastomose
- baisse de l'hyperplasie myointimale (qui représente 20-30% d'occlusion de la prothèse) [10]

D'entre eux, les plus utilisées sont:

- le patch veineux de Taylor et
- le collier de Miller

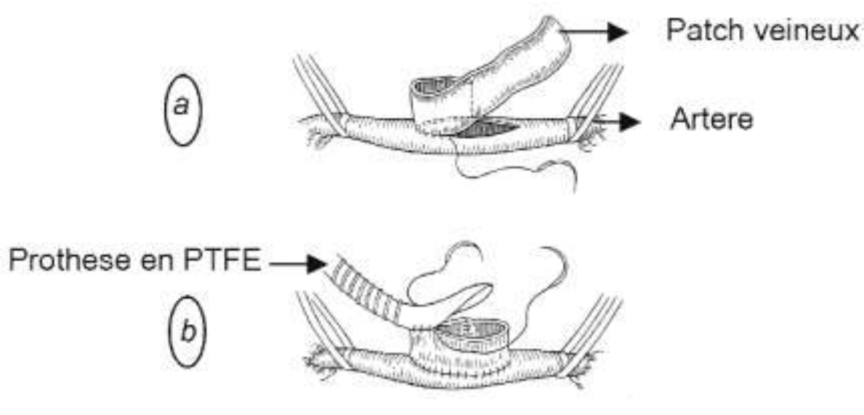

Figure 1: La technique de Miller

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Les avantages du matériel prothétique sont: la rapidité de l'intervention, la réduction des complications cutanés et des séquelles neurologiques périphériques lies a la prelevation de la veine et la rapidité de l'intégration socioprofessionnelle.

La Figure 2 montre la perméabilité des pontages femoro-popliteo jambiers. En suprapoplite, la perméabilité est similaire avec ou sans collier.

Localisation de l'anastomose distale	**Perméabilité primaire (%)**		**Auteur (année)**
	1-ere année	**2-eme année**	
Suprapoplite PTFE	83,9	69,6	Stonebridge (U.K)
Infrapoplite:			
- collier	84	69	F. Cormier (1999)
- sans collier	66	38	Raptis, Miller (1995)
- veine saphene interne		80	Harris (U.K.)

Figure 2: La perméabilité des pontages femoro-popliteo jambiers

En infrapoplite, la perméabilité primaire des pontages avec collier se rapproche de la perméabilité des pontages veineux.

L'hyperplasie myointimale limite le succès de tout type de reconstruction artérielle, à moyen ou long temps, a cause de la thrombose du greffon (Figure 3).

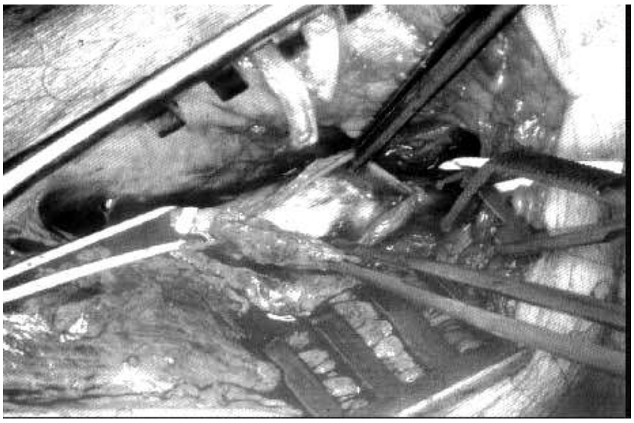


Figure 3: Image intraoperatoire montrant l'hyperplasie myointimale

La localisation d'élection de la hyperplasie myointimale est **l'anastomose distale:** le talon et la pointe de l'anastomose, mais également le talon de l'artère réceptrice.

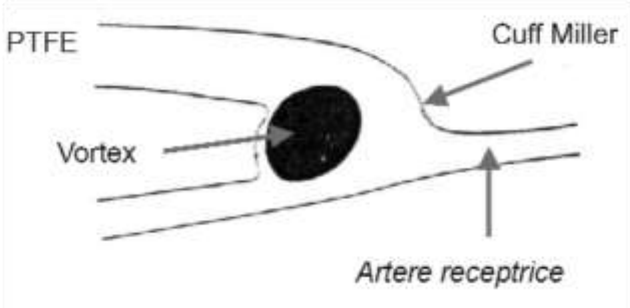
Cela est bien connu aujourd'hui que les prothèses vasculaires, notamment les PTFE font stimuler la prolifération myointimale.

Les caractéristiques de ce phénomène sont: la prolifération et la migration de cellules musculaires lises (mediée par l'endothélium), l'augmentation de la production de la matrice extracellulaire, qui ont comme effet la diminution du lumen du vaisseau avec la diminution du flux sanguin et finalement la thrombose du vaisseau [1].

P. Harris et l'équipe de l'Université de Liverpool ont étudie l'hémodynamique de l'anastomose avec le collier [1, 8]. Dans le cas de l'anastomose termino-latérale le flux sanguin est laminaire. Néanmoins il y a des zones de répartition du flux (talon et pointe de l'anastomose) qui sont associes avec des faibles forces de cisaillement.

Il y a aussi un point statique de stagnation du sang au talon de l'anastomose, (sur l'artère native); zone ou le flux se divise en proximal et distal. Ce point, associe avec des faibles forces de cisaillement correspond a la formation ultérieure de l'hyperplasie myointimale.

Dans le cas de l'anastomose avec le collier les régions avec des forces de cisaillement faibles sont localise au niveau du collier, donc loin de l'artère réceptrice.



Dans ce cas, du point de vue hémodynamique, est essential l'existence du "vortex" (flux rotatif antihoraire). Il apparaît au moment de la pointe de la systole, et il est complètement dissipe a l'arrive du nouveau cycle sanguin (Figure 4) [1].

Figure 4: L'hémodynamique de l'anastomose avec collier

Le caractère hémodynamique de l'anastomose est détermine par la géométrie de l'anastomose et non par le matériel de l'anastomose. C'est la premise pour produire une prothèse avec un collier idéal. Les caractéristiques de l'anastomose préforme synthétique sont les suivants:

- géométrie reproductible;
- que la portion distale de la prothèse soit suffisamment résistent;
- l'existence du "vortex" au plan hémodynamique dans l'anastomose;
- sans zones de faibles forces de cisaillement au niveau de l'artère de réceptrice.

Matériel et Méthode

Entre août 1998 et mars 2001, sur un lot de 164 malades opères (revascularisation femoro-popliteo-jambiere), sur une période de suivi de 12 moins, nous avons utilisée le collier de Miller dans 21 cas et la prothèse Distaflo (avec anastomose préformée) dans 5 cas. La Figure 5 montre la répartition des malades par groups d'age; la Figure 6 montre la répartition par sexe; L'étiologie a été dans la majorité des cas athero-sclérotique (Figure 7). Les facteurs de risque ont été l'hypertension artérielle (49,1% des cas), dislipidemies (25,5%) et diabète (32,1%) (Figure 8).

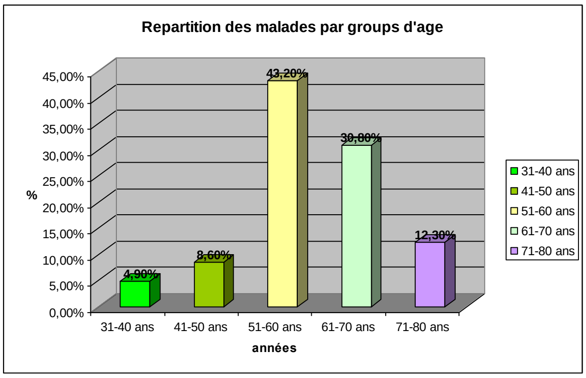


Figure 5: La répartition des malades par groups d'age

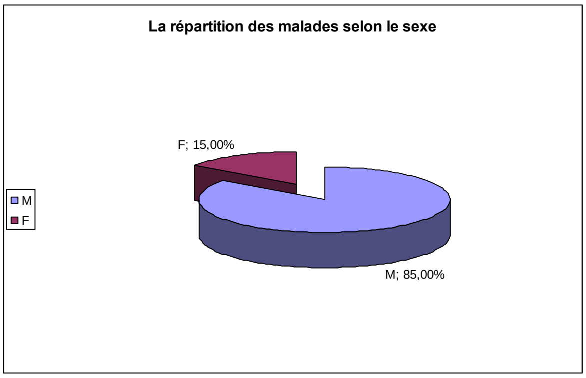


Figure 6: La répartition des malades selon le sexe

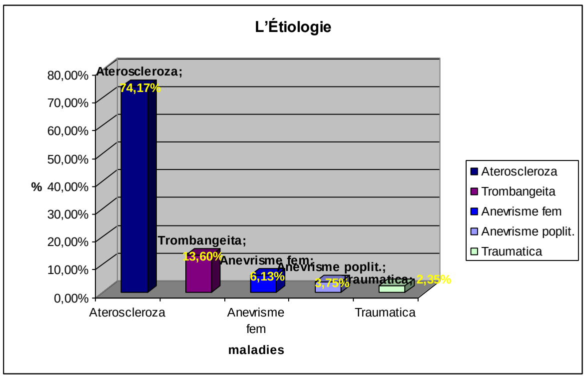


Figure 7: L'Étiologie

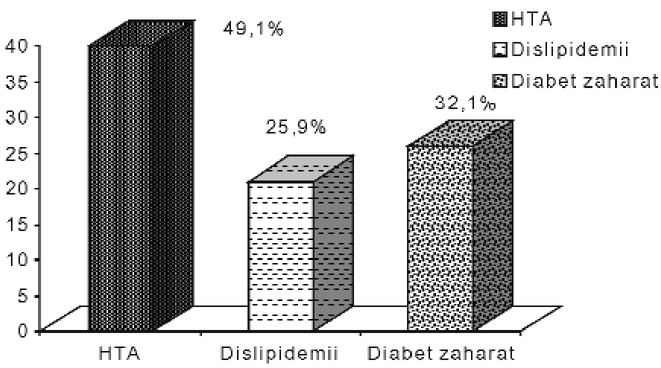


Figure 8: Facteurs de risque

Figure 9 et 10 montres deux images intraoperationes pendant l'exécution de l'anastomose distale avec la prothèse Distaflo.

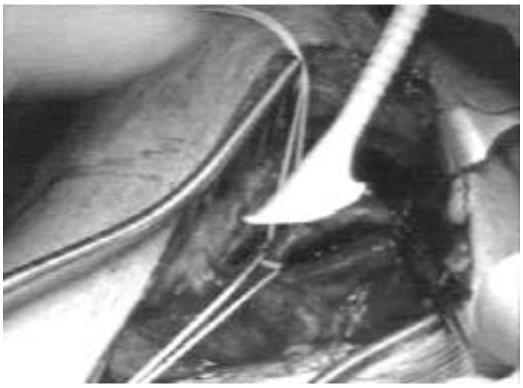


Figure 9

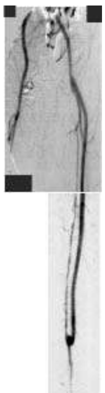
Figure 10

La localisation des pontages a été la suivante:

- *femoro-poplite* - *54,3%*
  - proximale - 32,1%
  - distale - 22,2%
- *ilio-poplite* - *4,9%*
- *poplite proximale-distale* - *7,4%*
- *pontage sur les troncs jambiers* - *18,5%*
- *extra-anatomique:*
  - femoro-femoral - 13,5%
  - femoro-poplite contralaterale - 1,2%

Comme matériel du greffon nous avons utilisé:

- *veine saphène interne o inverse* - *25,9%*
  - in situ - 8,6%
- *terom* - *10,4%*
- *PTFE (IMPRA, ATRIUM)* - *18,5%*
- *PTFE carbone (IMPRA)* - *3,7%*
- *Composite* - *1,2%*
- *Dacron:*
  - Sulzer Vascutek - 21,3%
  - B. Braun - 6,7%
- *PTFE Distaflo* - *3%*



L'indication chirurgicale a été mise secondairement à l'examen clinique, l'écho Doppler et l'artériographie, avec le bilan des autres localisations artérielles-coronaires, carotides, viscères abdominaux.

Le contrôle postopératoire a été fait de manière systématiques par l'écho Doppler et dans quelque cas par l'artériographie (Figure 11). Figure 11 montres l'artériographie de contrôle d'une revascularisation en PTFE avec collier.

Figure 11: Contrôle postopératoire d'une revascularisation en PTFE avec "cuff"

Résultats

La perméabilité primaire des pontages utilisant le collier veineux ou la prothèse Distaflo a été:

- un mois – 96%
- six mois – 92%

L'étude est préliminaire et nécessite un suivi pour une période plus longue.

Conclusions

Dans les dernières années on assiste en chirurgie vasculaire à une évolution technique considérable, en élargissant les indications opératoires aux lésions artérielles très distales, en ischémie critique.

Les résultats cliniques ont été encourageants en utilisant les prothèses (PTFE en spécial), mais en utilisant un artifice veineux pour l'anastomose distale ou la prothèse Distaflo. Ces résultats devrons être confirmés par des études a moyen long terme.

La géométrie de l'anastomose et non le matériel utilise est le facteur déterminant de l'inhibition de la hyperplasie myointimale, donc dans l'augmentation de la perméabilité des pontages.

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Arterial reconstructions using a "St. Mary's Boot" vein-cuff for lower limb ischemia*)

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It has been shown that autologous veins are the material of choice for infrainguinal and especially infrageniculate arterial reconstructions (1).

In the absence of saphenous vein due to previous use, too small diameter (2) or diffuse varicosity, a prosthetic graft may be used. *Polytetrafluoroethylene* (PTFE) and polyester (Dacron) grafts have been applied for limb salvage at the level of infrageniculate arteries with or without adjunctive procedures in order to improve graft patency. The main purpose of adjunctive procedures with prosthetic grafts is to diminish the most frequent cause of graft failure: myointimal hyperplasia (3).

In this article, a technical description of the different procedures is followed by a report of our results with one of the adjunctive procedures.

Causes of prosthetic graft failures

Myointimal hyperplasia (MIH) is one of major of graft failure, especially in cases involving prosthetic material. It develops preferentially at the level of the distal anastomosis both in the graft and on the floor of the recipient artery. Arteries with a diameter of 1 or 2 mm are prone to early occlusion due to the process of MIH. Hyperplasia is a non-specific reaction which rapidly develops after surgery and can occur following all kinds of arterial intimal damage. The intensity of MIH is far more apparent in association with direct contact between a prosthesis and a recipient artery as compared to venous-arterial interface, probably due to interaction between the graft and blood elements, platelets in particular.

Another reason for the development of MIH is the limited compliance of the graft which is not in harmony with the compliance of the recipient artery. It has been shown that prosthetic grafts are prone to occlusion if the blood reaches the critical thrombotic threshold level, due to the higher thrombogenicity as compared to native blood vessels. If grafts are connected to vessels with a high flow resistance, the risk of occlusion is obviously increased.

The attempts to impregnate prosthetic grafts with heparine focus on minimizing these complications and aim at reaching the same wall characteristics as autogenous veins, which accept considerably lower ranges of blood flow without thrombosing.

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Kinking of prosthetic grafts, especially at the level of the knee, constitutes another cause of graft failure. Composite grafts (prosthesis-vein) and external support of synthetic grafts decrease the occurrence of these failures.

Adjunctive procedures with prosthetic grafts

Composite PTFE - vein graft

This technique overcomes the problems at the distal anastomosis, but the data suggest that MIH occurs between the PTFE and vein. Since this is an oblique end-to-end anastomosis between the PTFE and vein there is no capacious conduit to accommodate the inevitable MIH, which might explain why these grafts are little better than PTFE alone in the experience of most surgeons.

Linton patch

Conceived before the process of MIH was known, it consists of a venous patch on the recipient artery (4).The patch has to be large enough to allow the prosthetic graft to be anastomosed to the patch, thereby avoiding direct contact between the prosthetics and the artery. Because of their small diameter it is often technically difficult to perform a Linton patch on crural arteries. Furthermore, the distance between PTFE-vein anastomosis and vein-artery anastomosis is extremely small.

Taylor patch

This technique combines a long distal anastomosis with an interposition of a lozenge-shaped venous patch onto the toe of the anastomosis (5); it is rather difficult to perform on an artery of 1 or 2 mm and does not prevent the prosthesis-artery contact. When an anastomosis is performed to a crural vessel, the proximal flow into the calf arteries and collaterals is an essential component of success, and if this back flow is low the peripheral resistance may increase sufficiently for the graft to fall.

Arterio-venous fistula

The creation of an arterio-venous at the level of the distal anastomosis is a procedure to prevent prosthetic graft thrombosis by lowering the peripheral resistance. The aim of a fistula is to increase the flow in the graft beyond the thrombotic threshold. The technique of Dardik (6), which is the most commonly applied method, consists of creating a common posterior wall by anastomosing the adjacent walls of the recipient artery and a commitant vein, thus forming a common ostium to which the prosthetic graft is anastomosed. It is also possible to combine an arteriovenous fistula and a vein-cuff, carrying the advantage to decrease the MIH and to diminish the peripheral resistance (7).

Miller cuff

Initially described by Siegman (8), this technique was largely used and published by Miller (first important series in 1984) (9). It consists of a venous cuff which is circumferentially sutured to the arteriotomy with subsequent end-to-end anastomosis with the prosthetic graft. The Miller cuff has a poor anatomic profile and the bulbous vein cuff can cause severe turbulence due to the distensibility of the vein.

"St. Mary's boot" vein cuff

This technique, described by Tyrrell and Wolfe, aims to incorporate the advantages of the Taylor patch and Miller cuff (10, 11).

A segment of vein is used to form a long interposition boot between PTFE and artery. A 5-6 cm length of vein is harvested from a suitable site (frequently it is necessary to use arm vein if all other available vein has been previously used). This segment of vein is then slit down its longitudinal axis to yield a venous rectangular sheet. The far edge of the venous sheet is then draped around the arteriotomy and sewn down with the longer end of the double ended suture. Great care must be taken to ensure that there is no nipping at the heel of the suture line, as proximal flow is as important as distal flow in these very distal grafts. By positioning the mosquito forceps (which is holding the distal edge of the venous sheet) correctly, it is possible to align the anastomosis without difficulty so that the assistant can concentrate on the anastomosis itself.

An arteriotomy is performed in the crural vessel which should be at least 2 cm in length - the length of this incision may be part of the reason for the success of this procedure. There should be an excess of vein available so that mosquito forceps can be applied to one end in order to anchor and control the vein segment while the anastomosis is being performed. Magnification loupes are essential when constructing an accurate anastomosis. The distal edge of the vein is anastomosed to the apex of the arteriotomy using a 7/0 monofilament suture. The distal edge of the vein is then anastomosed to one side of the arteriotomy using the shorter end of the double ended suture. The venous sheet is then anastomosed along the anterior edge until sutures meet. Redundant vein is resected using a pair of Potts scissors. At this stage it is essential that the two suture ends are tied in order to secure the suture line between vein and artery. The shorter end is then cut and the longer suture used to sew the vein boot to itself.

With magnification and asset routine this anastomosis becomes straightforward. It also has the advantage that the completed anastomosis can be readily inspected to ensure that it is technically satisfactory. Once the boot is complete the anastomosis between PTFE and vein is quite simple.

There is the theoretical risk that a weak vein will blow out, but this is rarely reported despite the large number of arm veins used by surgeons.

The sheet of vein must be kept under slight tension while the anastomosis is being performed - if it is allowed to contract too much then the collar is too baggy under arterial pressure. It is important that the PTFE is cut to the correct length because any tension between vein collar and PTFE (as with any anastomosis) would lead to tearing of the vein at the anastomosis.This technique does, however, have the slight advantage that there is a very small amount of play between PTFE and the venous boot so that any slight movements resulting from changes in the leg position do not affect the artery directly.

MIH eventually starts to develop between PTFE and vein collar but spares the distal artery so that the graft continues to function.

Personal casuistry

Between 1999, Oct.25 and 2002, Sept. 16, in the vascular surgery department of the Cardiovascular diseases Institute, we have performed 29 infrageniculate arterial reconstructions using prosthesis and a vein-cuff of "St. Mary's boot" type. There were 25 men (86.2%) and 4 women (13.8%) with ages ranged between 36 and 86 (median 61.9) years. The basic disease was atherosclerosis in 26 patients (89.6%); the other 3 presented the clinical diagnosis of thromboangiitis obliterans. 21 had ischemic heart disease, 5 valvular heart disease, there were 8 with hypertension and 2 with old strokes; 5 were diabetics and 24 smokers. Other diseases include 8 chronic bronchitis, 6 peptic ulcers, 1 chronic renal failure, 1 contralateral amputation, 6 varices and 2 chronic venous insufficiency.

23 patients (79.3%) presented with critical limb ischemia: 17 in stage IV Fontaine and 6 in stage III. The other 6 patients had intermittent claudication (3) and acute ischemia (3) with a mean delay of 18 hours between onset and admission. 4 operations were performed because of failed.

Infrainguinal grafts with threatened limb (4 femoro-above knee bypasses). In 4 patients the infrainguinal reconstruction with prosthesis and vein-cuff was performed after a previous intervention at the inflow: 1 aortic patch, 1 aorto-bifemoral graft, 1 axillo-femoral graft, 1 ilio-femoral graft and 1 patient with common iliac angioplasty and stent.

All the patients had an aortography which emphasized 3 aortoiliac diseases and 26 infrainguinal occlusive diseases; the patients in acute ischemia also had infrainguinal thrombosis. The run-off was judged depending on the number of calf arteries in continuity with a pedal arch: 0-8 patients, 1-18 patients, 2-2 patients and 3 arteries at 1 patient.

In patients with aortoiliac occlusive disease, we performed combined reconstructions; 2 patients also underwent an arterial reconstruction in the non-threatened limb (1 at the common femoral and 1 at the external iliac); the third patient had a contralateral amputation. In the threatened limb, the distal anastomosis was made at the distal popliteal artery.

In patients with infrainguinal disease, the proximal anastomosis was performed in the common femoral (16), superficial femoral (5), external iliac (2) arteries and in the previous graft (three-1 functionally and 2 with thrombectomy). The distal anastomosis was made at the level of distal popliteal (22), tibioperoneal trunk (1), anterior tibial (1) and posterior tibial (2) arteries.

We used 24 externally reinforced PTFE grafts and 5 Dacron (2 bifurcated) grafts.

We could not use the reversed ipsilateral long saphenous vein because of varices (6 cases), too small diameter (< 3 mm - 6 cases), partial or total fibrosis (12), partially thrombosed (3 cases) and previous use (2 patients). The long saphenous veins with a diameter < 3 mm were not used because the lack of a valvulotome. The vein-cuff (only "St. Mary's boot") was made of remnants of long saphenous vein (26), ipsilateral lesser saphenous vein (2) and arm vein (1).

The arterial reconstructions were accompanied by 2 thrombectomies of the infrarenal aorta, 2 reconstructions of the contralateral limb arteries, 3 common femoral endarterectomies and 2 profundaplasties. In one case of acute ischemia, we associated a venous thrombectomy after arterial clamps release. 10 patients underwent ray-amputations at the end of arterial reconstructios. While in the hospital, the patients received subcutaneous heparin; following this, long-term aspirin (250 mg/ day) was given. The patients in chronic atrial fibrillation received long-term anticoagulation. The postoperative follow-up was between 1-35 months and consisted of clinical examination at 3 months in the first postoperative year and at 6 months later. Graft failure was estimated only on clinical criteria: reappearance of the symptoms, loss of distal pulsations.

In the 30-day postoperative period, one patient with aortoiliac occlusive disease died (mortality rate = 3.4%) because a myocardial infarction; his graft was functional. There were 4 graft thromboses: 3 at 24 hours (1 case with 96 hours of acute ischemia); at 2 patients we performed graft thrombectomy with limb salvage, but the other 2 patients underwent major amputations (amputation rate = 6.8%). One of the major amputations was performed in a patient with 96 hours of acute ischemia (superficial femoral-tibioperoneal trunk PTFE graft and venous thrombectomy). The second patient who underwent a major amputation was at the third infrainguinal reconstruction (extra-anatomically external iliac-anterior tibial bypass) and was our first attempt with "St. Mary's boot" technique. Excepting these three major events (1 death and 2 major amputations), all the other 26 grafts were functionally at 30 days (14 patients with distal pulse).

In the first 30 postoperative days, we also recorded other complications: one ventricular fibrillation, one digestive bleeding because of a peptic ulcer, one popliteal hematoma, 3 inguinal lymphoreeas and 5 minor wound problems.

The mean hospitalization stay was 24 days (ranges: 12-37 days).

The postoperative follow-up emphasized the following results: 5 failed grafts (at 2, 4, 9, 11 and 28 postoperative months, respectively) which required major amputations and one death (myocardial infarction) at 30 months.

The cumulative graft patency was: 93% at 1 month, 85% at 6 months, 76% at 12, 18 and 24 months, and 70% at 30 months respectively.

The limb salvage rate was: 92.8% at 1 month, 89.2% at 6 months, 85% at 12, 18, 24 months and 81% at 30 months respectively.

Discussions

In the absence of a suitable venous conduit, infra-geniculate bypasses can be performed with prostheses or arterial and venous allografts. PTFE grafts are extensively used in lower limb revascularizations. Parsons et al performed 63 femorocrural PTFE grafts without any adjunctive procedure and described a primary patency rate of 39% and 28% at 3 and 5 years, respectively. Secondary patency rate at 3 and 5 years was 55% and 43%, respectively, and limb salvage was 71% and 66%, respectively. They discussed that these results justify this strategy, in fact being a better option than amputation in patients without autologous vein. They, also, emphasized postoperative anticoagulant therapy and duplex surveillance to improve patency by early correction of restenosis (12). In other series, the patients received long-term antiplatelet drugs.

During recent years, arterial allografts have regained interest for the treatment of critical ischemia and limb salvage. Magne et al. have performed 74 grafts, 50 of which at the level of crural arteries. Their primary patency rate at 1 year and 30 months was 72% and 30% respectively, and secondary patency was 79% and 50% at the same intervals, respectively. These encouraging early results are important, despite the difficulties with harvesting and preservation, the issue of immunology, and late graft degradation. Cryo-preserved venous allografts have also been applied; however, clinical results are disappointing. Martin et al published a series of 115 cases with cryopreserved saphenous veins and reported a secondary patency rate at 2 years of 25% (13).

Important technical components of a femoroinfrageniculate bypass comprise the level of the proximal anastomosis, the route of the graft and the different fashions of the distal anastomosis, with or without adjunctive procedures. The proximal anastomosis should be performed at a normal caliber and more or less undiseased artery, being the common femoral artery in the majority of cases.In patients who already underwent several groin dissections, the profunda might serve as an inflow source.A venous or prosthetic supragenicular graft can also be used for the proximal anastomosis. The routing of the prosthesis can either be anatomic or extra-anatomic, however, anatomic tunneling is often hazardous in patients who were operated before. Kinking at the level of the knee and compression in superficial routes can be avoided by reinforced prosthetic grafts. Several adjunctive procedures at the level of the distal anastomosis have been performed to alleviate the discrepancy of graft - (5-6 mm) and artery (2 mm) diameters. Various studies have tried to ameliorate the results of prosthetic grafts using additional procedures. Composite grafts offer an interesting solution if a venous segment with sufficient length can be harvested: the prosthesis-vein anastomosis is located above the knee and the venous segment crosses the joint and is sutured to the recipient artery. Recently, Favre et al reported on 77 femorocrural PTFE-vein composite grafts and described a primary patency rate of 53% and 32% at 6 months and 3 years, respectively. Secondary patency rates at the same time intervals were 60% and 39% respectively. These results are comparable to those obtained with PTFE only. Among the adjunctive procedures, the Taylor patch showed a patency for prosthetic grafts to the tibioperoneal trunk of 58% and 54% at 3 5 years, respectively.

Stonebridge et al performed a randomized multi-center study comparing prosthetic grafts with and without a Miller cuff (14). One and two year patency rates for grafts with a venous cuff were 78% and 49%, respectively as compared to 62% and 19%, respectively for grafts without a cuff. The St. Mary's boot has been performed with PTFE femorocrural grafts showing long-term patency rates of 20% to 25% inferior to those obtained with in-situ venous grafts (15). In the hands of the authors, additional venous cuffs seem to offer excellent results. However, other studies illustrate no beneficial effects. Nevelsteen et al reported the results of a randomized multicenter study; femorocrural grafts with a venous cuff carried a patency rate at 2 years of 37% as compared to 53% for grafts without a cuff. Creation of an adjunctive arteriovenous fistula aims for improved hemodynamic profiles at the distal anastomosis and reduced MIH with cosequent improved patency. Harris et al published a study on infrapopliteal venous grafts, PTFE conduits with arteriovenous fistula and PTFE grafts with combined fistula and venous cuff (7). Cumulative patency rate at 2 years was 68% for venous grafts, 61% for PTFE grafts associated with combined fistula and cuff and 28% for PTFE conduits with fistula only.

The European Consensus on critical limb ischemia describes in recommendation 25 that a reconstructive procedure should be attempt if there is a 25% chance of saving a useful limb for the patient for at least one year. Comparison of cost-benefit analyses of femoroinfrapopliteal bypasses and major amputations in patients with critical ischemia are in favor of distal revascularization. The cost for a patient with a major amputation continues during time whereas the cost after an ideal revascularization is limited to the procedure and hospital stay (16).

Our experience with infrageniculate prosthetic grafts and adjunctive procedures is limited to only 29 cases and only to "St. Mary's boot" vein cuff. Despite this, we can confirm the value of the procedure; moreover, the unexpected long-time good results made it our second choice in infrainguinal arterial revascularizations after reversed ipsilateral long saphenous vein. In our opinion, to prevent aneurismal development of the vein cuff, the venous segment has not to be too large and the arteriotomy not too long.

Conclusions

The results of prosthetic femoroinfrageniculate bypasses in the treatment of critical ischemia justify their use in the absence of autogenous vein and must be preferred over primary major amputation. Besides the arterial anatomy, the indication for this surgical strategy should depend on patient's life expectancy and degree of autonomy.

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Silver-coated polyester grafts in prevention of prosthetic graft infection*)

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Abstract

Background: *Prevention of graft infection by use of in situ implanted silver-coated prosthetic grafts is new and promising method.*

Aim: *The aim of this study was to compare the postoperative outcome in patients with the increased risk for postoperative graft infection (inflammatory aneurysm, arterial occlusive disease with gangrene, re-do revascularization, concomitant systemic infection) in whom silver-coated polyester prosthesis was used, with postoperative outcome in Inflammatory (mycotic) aneurysm was recognized as symptomatic in the absence of rupture, with elevated sedimentation rate, occasional fever and positive blood culture, leukocytosis, and intraoperative signs of inflammation of the aneurysmatic wall (dense, shiny, hyper-vascularization of the retroperituneum, centered over the aortic aneurysm. Other reasons for preventive implantation of Silver graft in patients with imminent infection was arterial occlusive disease with gangrene (18%), re-do revascularization (11%), and concomitant systemic infection (0.4%).*

Methods: *From November 2001 to January 2006, 105 patients with the increased risk for postoperative infection of the arterial by pass graft were entered in this prospective non-randomized study. Accordingly to attending surgeon's preference, 57 patients (45 men, 12 women; mean age 68 years) were operated using silver-coated polyester prosthesis, and the control group consisted of 48 patients (33 men, 15 women; mean age 67.9 years) with collagen-coated Dacron graft placement. During the follow-up period of 24.8±11.9 months (minimum 1 month, maximum 59 months), patients were followed for combined end-point that included all-cause mortality, leg amputation and graft infection.*

Results: *There were no differences between the groups with respect to demographics, vascular status and surgery. Approximately two thirds of patients in each group underwent aorto-biliacal reconstruction, whereas urgent operation was performed in 19/57 (33.3%) patients with silver and 21/48 (43.8%) patients with Dacron graft. During the follow-up, 4/57 (7%) patients in group with silver-coated graft, and 10/48 (20.8%) in group with Dacron graft had combined end-point. Only 1/57 (1.8%) patient died perioperatively in group with silver graft, and 2/48 (4.2%) in group with Dacron graft. Kaplan-Meier analysis showed that patients with silver graft less frequently met combined end-point than patients with Dacron graft (log rank = 4.41, p = 0.03). In multivariate analysis, the only variable independently predictive of combined end-point was urgent operation (OR 3.48; 95% CI, 1.07-11.29).*

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Conclusion: *Our data demonstrate favorable outcome with silver-coated polyester graft, as compared to collagen-coated Dacron graft, in prevention of postoperative complications in patients with high-risk for infection of arterial graft.*

Key words: *silver-coated graft, Dacron-coated graft, infection, prevention.*

Introduction

Prevention and management of arterial prosthetic graft infection is one of the most difficult challenges to the vascular surgeon today. Development of graft infection depends on the implantation site, the urgency of the operation, the underlying diseases and the immunological status of the patient. Graft infections are most frequent after emergency operations, in anastomosis with femoral artery or after subcutaneous prosthesis position (1-7).

The prevention and treatment of arterial prosthetic graft infection requires meticulous attention and dedication. Mortality rates reported in earlier series ranged from 25% to 88% (1) with amputation rates from 5% to 25% (1-7).

Over the last 3 decades, the incidence of prosthetic aortic graft infection for aortic tube grafts, aorto-bi-iliac and aorto-bifemoral grafts has consistently been in the range of 0.5% to 5% (3-10). A lower incidence of graft infection can be obtained by avoiding groin incisions, along with the administration of appropriate perioperative prophylactic antibiotics (11-15). Graft infection is frequently associated with direct contamination at the time of implantation or local contamination afterwards, the type of the graft, secondary infection from hematogenous seeding, and low immunological resistance of the patient (4, 10-15).

New strategies for prevention of graft infection are currently the subject of research. The use of in situ implanted silver-coated prosthetic grafts is new and promising method, since bacterial resistance develops more rapidly and more easily with antibiotic agents than with antiseptic agents, such as silver acetate (2, 4).

As clinical data on this important topic are limited, we designed the present study to compare postoperative outcome in patients with the increased risk for postoperative graft infection (inflammatory aneurysm, arterial occlusive disease with gangrene, re-do revascularization, concomitant systemic infection) in whom silver-collagen coated polyester Silver prosthesis was used, with postoperative outcome in control group of patients with collagen-coated Dacron graft placement.

Methods

Patients

From November 2001 to January 2006, 105 consecutive patients with the imminent infection of arterial by-pass graft (inflammatory aneurysm, arterial occlusive disease with gangrene, re-do revascularization, concomitant systemic infection) were enrolled in this prospective study at *Dedinje Cardiovascular Institute*. Inflammatory (mycotic) aneurysm was recognized as symptomatic in the absence of rupture, with elevated sedimentation rate, occasional fever and positive blood culture, leukocytosis, and intraoperative signs of inflammation of the aneurysmatic wall (dense, shiny, hypervascularization of the retroperituneum, centered over the aortic aneurysm. Other reasons for preventive implantation of Silver graft in patients with imminent infection was arterial occlusive disease with gangrene (18%), re-do revascularization (11%), and concomitant systemic infection (0.4%). Accordingly to attending surgeon's preference, 57 patients (45 men, 12 women; mean age 68 years) were operated using silver-coated polyester prosthesis (InterGard Silver prosthesis, InterVascular, La Ciotat, France). The control group consisted of 48 patients (33 men, 15 women; mean age 67.9 years) with collagen-coated Dacron graft placement.

Operative technique

In all cases in-situ prosthetic replacement was done because renal or visceral perfusion would be compromised by aortic excision. During surgery, specimens were taken for bacteriological analysis. In all patients, povidone-iodine standard solution was used for irrigation of the possibly infected field, after removal of the necrotic thrombus and the surrounding tissue. The prosthetic graft was covered with peritoneum or pedicled anterior omentoplasty was performed.

Postoperative treatment

Postoperative antibiotic therapy was routinely administered (ceftriaxone, amicacin, metronidazole), and was adjusted after antibiogram. Serial ultrasound of the prosthesis, and CT-scan when necessary, were obtained 6 months after surgery, and every 6 months afterwards.

Follow-up

Patients were followed for combined end-point that included all-cause moratlity, leg amputation and graft infection. If one patient had more than event, only the most serious event was considered for final analysis (that is, in ascending order, graft infection, leg amputation, and death). Patients were followed for 24.8 ± 11.9 months (minimum 1 month, maximum 59 months).

Statistical analysis

All data are expressed as mean ± standard deviation. *T-test* and *chi-square tests* were used for comparisons between the subgroups for continuous and categorical variables, respectively (a probability value of $p < 0.05$ was considered significant). Kaplan-Meier curves were constructed to assess event-free survival for combined end-point, all-cause mortality and occurrence of amputation and infection during follow-up and log-rank statistics was used to assess differences between silver and Dacron grafts. Univariate and multivariate regression analysis were performed to assess predictors of combined end-point during follow-up.

Results

Study patients

A total of 57 patients were operated using silver graft, whereas 48 patients were operated using collagen-coated Dacron graft. Baseline demographic and clinical characteristics of enrolled patients are shown in Table 1. Briefly, patients were predominantly older males with a number of risk-factors for atherosclerosis and adverse outcome following surgery. There were no differences between two groups of patients with respect to any of these variables.

Vascular status and surgery

Data regarding patient's vascular status and surgery are detailed in Table 2. The majority of patients in both groups were operated due to aneurysm of the abdominal aorta, and the most frequent risk-factors for subsequent infection were inflamed infrarenal aneurysm and grade IV ischemia of the lower limbs. Approximately two thirds of patients in each group underwent aorto-biliacal reconstruction, whereas urgent operation was performed in 19/57 (33.3%) patients with silver and 21/48 (43.8%) patients with Dacron graft. Only 1/57 (1.8%) patient died perioperatively in group with silver graft (due to acute myocardial infarction), and 2/48 (4.2%) in group with Dacron graft (due to acute myocardial infarction and multi-organ failure, respectively). Additionally, two more patients in the Dacron graft group died postoperatively (due to stroke and kidney failure). Again, variables regarding patient's vascular status and surgery were similar between the groups.

Follow-up

Patients were followed for 24.8±11.9 months (minimum 1 month, maximum 59 months). During the follow-up, 4/57 (7%) patients in group with silver graft, and 10/48 (20.8%) in group with Dacron graft had combined end-point. On the other hand, all-cause (including perioperative) mortality, infection, and amputation were found in 1/57 (1.8%), 4/57 (7%), and 3/57 (5.3%) patients with silver graft, and 4/48 (8.3%), 6/48 (12.5%), and 7/48 (14.6%) patients with Dacron graft, respectively.

When looking at Kaplan-Meier curves, it can be appreciated that patients with silver graft had less complications that is less frequently met combined end-point than patients with Dacron graft (Figure 1A). Additionally, these patients also demonstrated significant trend toward lower mortality (Figure 1B) and less amputation (Figure 1C). There was no difference with respect to incidence of infection (Figure 1D) between the groups.

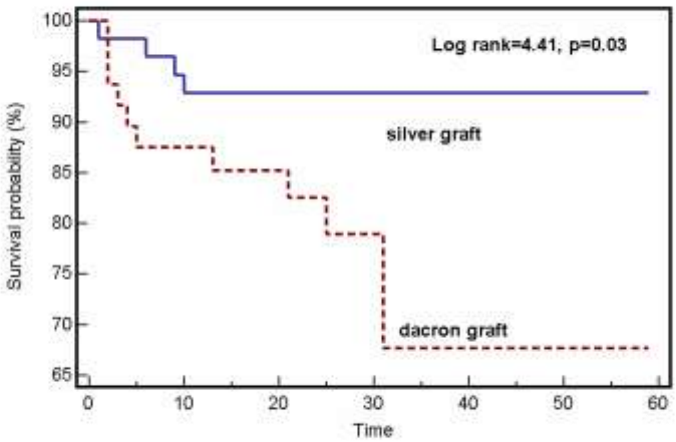

Figure 1A: Kaplan-Meier curves for event-free survival for patients with silver and Dacron graft for combined-end point

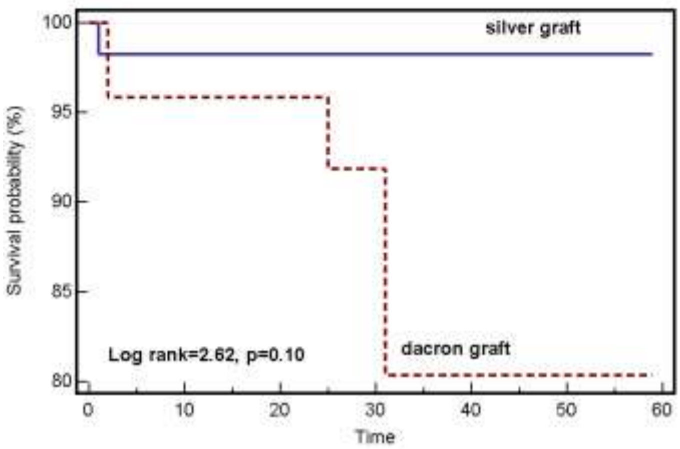

Figure 1B: Kaplan-Meier curves for event-free survival for patients with silver and Dacron graft for mortality

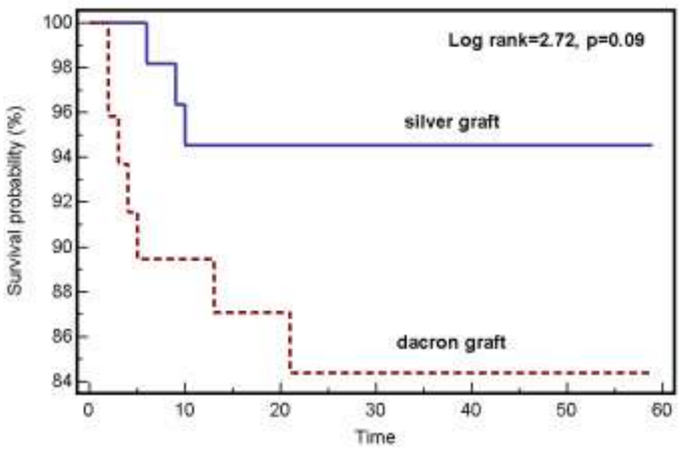

Figure 1C: Kaplan-Meier curves for event-free survival for patients with silver and Dacron graft for amputation

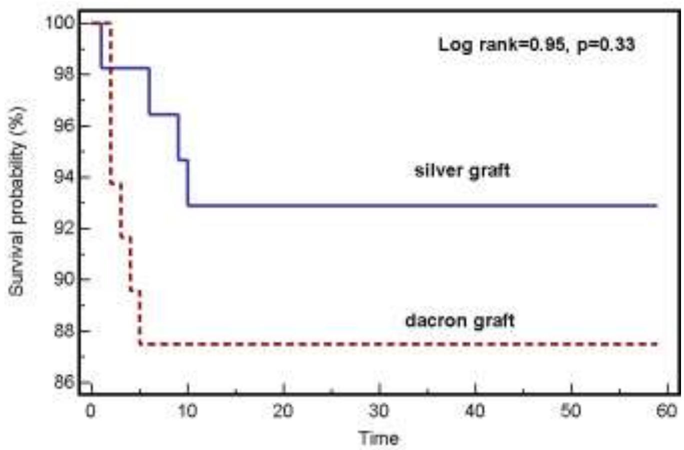

Figure 1D: Kaplan-Meier curves for event-free survival for patients with silver and Dacron graft for infection

All variables in Tables 1 and 2 were entered in univariate analysis, but the only variables associated with combined end-point during follow-up were type of graft (silver or Dacron), urgent operation and history of coronary artery disease (Table 3). When entered in multivariate regression model, the only variable independently predictive of combined end-point was urgent operation (OR 3.48; 95% CI, 1.07-11.29). The same variable was also only variable independently predictive of infection (OR 4.38; 95% CI, 1.06-18.85). No variables were independently predictive of mortality or amputation.

Table 1: Baseline demographic and clinical data

	Silver graft (n=57)	*Dacron graft (n=48)*	*P*-value
Sex (male)	45/57	33/48	0.27
Age (years)	68 ± 4.5	67.9 ± 4.5	0.96
Smoking	42/57	34/48	0.82
Hypertension	15/57	16/48	0.52
HLP	22/57	17/48	0.84
DM	30/57	24/48	0.85
COPD	8/57	5/48	0.77
CKF	18/57	12/48	0.52
CAD	13/57	10/48	0.99

Abbreviations:
CAD - *coronary artery disease*; CKF - *chronic kidney failure*;
COPD - *chronic obstructive pulmonary disease;*
DM - *diabetes mellitus*; HLP - *hyperlipoproteinemia*

Table 2: Vascular status and surgery

	Silver graft (n=57)	*Dacron graft (n=48)*	*P*-value
Reason for operation			
- aneurysm	42/57	33/48	0.66
- stenosis	15/57	15/48	
Risk-factors for infection			
- inflammatory aneurysm	38/57	29/48	0.93
- PSA in the groin	4/57	4/48	
- grade III ischemia	2/57	3/48	
- grade III ischemia and SI	3/57	2/48	
- grade IV ischemia	10/57	10/48	
Graft location			
- aorto-biliacal	38/57	29/48	0.80
- femoropopliteal	10/57	10/48	
- interposition in the groin	9/57	9/48	
Urgent operation	19/57	21/48	0.32
Perioperative mortality	1/57	2/48	0.59

Abbreviations: PSA - *pseudoaneurysm;* SI - *systemic infection;*

Table 3: Variables associated with combined end-point in univariate regression analysis

	F	*P*-value
Urgent opération	**4.82**	**0.030**
Graft type	**4.40**	**0.038**
CAD	**4.23**	**0.042**

Abbreviations: CAD - *coronary artery disease;*

Discussion

The main finding of our study is that implantation of silver-coated polyester Silver prosthesis provides additional benefit over collagen-coated Dacron graft in patients with the increased risk for postoperative graft infection (inflammatory aneurysm, arterial occlusive disease with gangrene, re-do revascularisation, concomitant systemic infection). Occurrence, as well as prevention and treatment of arterial prosthetic graft infection, is complex and needs additional elaboration.

Arterial prosthetic graft infection

The leading cause of graft infection is contamination during initial surgical procedure. Emergency surgery, poor sterile technique, bowel injury during the operation, extensive lymphatic manipulation or injury during the dissection, prolonged preoperative hospital stay exposing the patient to virulent pathogens, repeated operations, and prolonged operating time are predisposing factors for graft infection (1-20). This is line with our findings since urgent operation was the only variable in our series that was independently associated with combined end-point, as well as the only variable independently predictive of infection of prosthetic graft.

Early (up to four months after arterial graft implantation) and late infections are distinguished. More than half of all graft infection occurs early. Infection of aortic prosthesis occurs after an average of 40 months after implantation and infection of peripheral prostheses on average of seven months after implantation (4, 7-9, 37). In our series there was only one early infection in the Silver graft group, but statistically this was not significant compared to Dacron graft group.

The most common bacteria cultured from infected grafts include *Staphylococcus aureus, Staphylococcus epidermidis,* diphtheroids, and gram-negative enteric organisms (11). S. *aureus* was the cause of infection in 43%, *Escherichia coli* in 17%, *Staphylococcus epidermidis* in 14%, *Pseudomonas* species in 10%, *Proteus* in 8%, and *Klebsiella* in 4% of the cases reported by Calligaro et al (5). *S. epidermidis* has been reported to be an increasingly common primary pathogen of infected aortic grafts (15, 21, 22).

Between 6% and 27% of aortic aneurysm walls that otherwise appear completely normal will have positive intraoperative culture results (23-30, 43, 44). However, these findings do not appear to correlate always with subsequent development of graft infection. Is it unclear, if positive aortic aneurysmal wall culture mandates treatment with prolonged intravenous antibiotics, especially when there are no other clinical or intraoperative findings suggesting a primary infected aortic aneurysm. These cultures during open operative repair have demonstrated higher rates of *S. epidermidis* versus S.

aureus and gram-negative bacteria (23-27, 31). In addition, methicillin-resistant S. aureus has been reported to cause as many as 20% to 25% of vascular infection, raising the concern that a more virulent bacteria might colonize a newly inserted graft (32, 33).

Transient colonic ischemia has been shown to lead to early and late graft infections in animal models (34). Bacteria migrate through the wall of the bowel as a result of the alteration in biochemical gradients normally maintained by continuous blood flow during normal physiology. The longer the ischemia lasts, the more risk for bacterial translocation, colonization, and potential infection. Other causes of hematogenous spread of bacterium include dental manipulations, urologic procedures, and endoscopic procedures. Prophylactic antibiotics are commonly used to prevent potential seeding of synthetic material when procedures such as these are performed (34).

Prevention of arterial prosthetic graft infection

One of the most important strategies to prevent graft infection is administration of preoperative prophylactic antibiotics. Randomized, double blind clinical trials have proven the efficacy of prophylactic antibiotics in both intravenous and topical forms (35-39). It is critical that intravenous antibiotics be administered within 1 hour of the skin incision. Administration of antibiotics before this time is of no benefit and may actually be harmful by predisposing antibiotics resistance. The duration of intravenous antibiotics after surgery is controversial. There are no sound data to prove that even 24 hours of antibiotics postoperatively is worthwhile compared to simply maintaining peak serum levels during the operation, but certainly they should not be continued more than 24 hours for routine cases.

The use of in situ implanted silver-coated prosthetic grafts is new and promising method. The disinfectant action of silver compounds was already documented in antiquity and middle ages. The long recognized efficacy of silver on microbial agents and the efficacy of silver used as an antimicrobial agent on medical devices (40-43) led us to use the InterGard Silver prosthesis (InterVascular, La Ciotat, France) for prevention of infection of the prostheses. Manufactured of knit or woven polyester, the Silver prosthetic graft is coated with type I bovine collagen and silver acetate. Silver acetate inhibits colonization of the prosthesis and contiguous tissues by micro-organisms during the postoperative period. The results of in vitro and in vivo animal studies have demonstrated the absence of local or systemic toxicity of the Silver prosthesis and its antimicrobial efficacy; 25% of the silver salts remained on the prosthesis 20 days after implantation (44). The silver impregnated prosthesis fulfils the licensing criteria for implants and is CE-certified. Our patients with silver graft had less complications than patients with Dacron graft. Additionally, these patients also demonstrated significant trend toward lower mortality and less amputation.

Experimental studies have shown that gelatin-coated polyester prostheses impregnated with rifampicin exhibit satisfactory resistance to *S epidermis* but are insufficient against MRSA and *Escherichia coli* (45, 46). These experimental findings emphasized the limitations of rifampicin-bonded polyester grafts for management of major aortic graft infection with MSRA. This problem warrants particular attention because of the appearance of rifampicin-resistant strains of *S epidermis* (47).

The evolution of nosocomial infections highlights the changing epidemiology of infection, because bacteria such as *S aureus* and *S epidermis* are increasingly resistant to antibiotic therapy (48). Because of risk for bacterial resistance to rifampicin, alternatives to the antibiotic agents bonded to these prostheses must be envisaged for in situ replacement of infected aortic prosthetic grafts. Experimentally, bacterial resistance develops more rapidly and more easily with antibiotic agents than with antiseptic agents (49). Silver compounds are acting as an anti-septic with many advantages: lack of resistance, wide range of activity profile including MRSA, sustained availability at an effective dose during 2-4 weeks on the prosthesis (4, 49).

Since the protective action of silver is greatly reduced after approximately four weeks, the graft must be evaluated by ultrasound, and CT scan if necessary. The justification for a protracted antibiotic therapy might be inferred from this, especially when possible foci of infection are present or when there is prolonged lymph secretion. This also explains why it may make sense to replace once more the silver-coated prosthesis that was prophylactically implanted and then become infected. If possible, veins should be used as in-situ by pass graft for peripheral vessels because of the better patency rate.

Clinical implications

Our data suggest that silver-coated polyester grafts should be preferred over collagen-coated Dacron graft in patients with the increased risk for postoperative graft infection. It appears that silver-coated polyester grafts may be of particular value in high-risk patients referred for urgent operation.

Study limitations

The major limitation of our study is that the patients were not randomized to receive silver-coated polyester or collagen-coated Dacron grafts. However, the groups were similar with respect to all major demographic, clinical and operative characteristics, so we believe that the comparison between two treatment options is valid. Additionally, the number of patients in our study is relatively small and larger series and longer follow-up will be required for definitive assessment of the role of silver-coated polyester prosthesis in prevention of high risk infection of arterial graft.

Conclusion

Our data demonstrate favorable outcome with silver-coated polyester graft, as compared to collagen-coated Dacron graft, in prevention of postoperative complications in patients with high-risk for infection of arterial graft.

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Revascularization with silver-coated polyester grafts in management of prosthetic graft infection: Long term follow-up[*)]

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Abstract

Background: *High mortality and morbidity rates with traditional treatment of infected prosthetic arterial grafts have led many surgeons to consider novel strategies. The use of in situ or extra-anatomically implanted antimicrobial silver- collagen coated prosthetic grafts is new and a promising method.*

Aim: *In this article the authors present single center long-term results of total, or partial, graft excision, and redo revascularization with silver-coated polyester Silver prosthesis in patients with arterial graft infections*

Methods: *From November 2001 to January 2006, 47 consecutive patients (35 men, 12 women; mean age 68 years) with the infection of arterial by-pass graft were enrolled in this prospective study at the Dedinje Cardiovascular Institute. Infection was managed with either total or partial excision of the infected graft and re-do revascularization with in situ or extra-anatomically implanted silver-coated polyester graft. Assessment of outcome was based on survival, limb salvage, persistent or recurrent infection, and prosthetic graft patency.*

Results: *Graft infection was managed with either total (n = 38) or partial (n = 9) excision of the infected graft, and re-do revascularization was done in situ (n = 28) or extra-anatomically (n = 19) using silver-coated polyester graft. Emergency surgery was done in 39% patients. Mean follow up was 25.5±14.9 months (range 1-59). Perioperative mortality was 10.6%, and all patients died of prosthetic graft infection. Actuarial survival at during follow-up was 78.7%. Major amputations were noted in 3.6% of patients, and recurrent infection developed in 19.1% of patients. There was no prosthetic graft thrombosis during the follow-up. Reinfection was identified as the only variable independently predictive of mortality (OR 40.83; 95% CI, 5.72-294.42).*

Conclusion: *Our results demonstrate favorable long-term outcome with silver-coated polyester prosthesis used to treat arterial graft infection, although significant mortality and morbidity remain major clinical problem in this subset of patients.*

Introduction

The infection of prosthetic graft is one of the most difficult challenges to the vascular surgeon today. Although estimated at 0.5% to 5%, (1-5) the true incidence is certainly higher (2-4) because patients are lost to follow-up or the follow-up is of insufficient duration, so information about late infections are lacking. Arterial graft infection depends

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on the site of implantation, the urgency of the operation, the underlying diseases and the immunological status. The graft infections are more frequent after emergency operations, in anastomosis with femoral artery or in subcutaneous prosthesis position (1-7).

Surgical therapy is always necessary since antibiotic therapy alone will rarely cure clinically significant infection. The management of prosthetic graft infections consists of excision of the infected graft, and extra-anatomic bypass grafting. (2, 4-6). High mortality and morbidity rates with traditional treatment of infected prosthetic arterial grafts have led many surgeons to consider novel strategies. Alternative treatment approach include in situ replacement of the infected prosthesis with an arterial allograft (5) or autogenous vein graft, (6) and reconstruction with an antibiotic 7 or silver impregnated prosthetic graft (7, 42, 43).

The long recognized efficacy of silver on microbial flora and the efficacy of silver used as an antimicrobial agent on medical devices (2, 8-11) led us to use the antimicrobial silver-collagen coated prosthetic grafts, InterGard Silver (InterVascular, La Ciotat, France) for management of infected aortic prostheses. Manufactured of knit or woven polyester, the Silver prosthetic graft is coated with type I bovine collagen and silver acetate. Silver acetate inhibits colonization of the prosthesis and contiguous tissues by microorganisms during the postoperative period. The results of in vitro and in vivo animal studies have demonstrated the absence of local or systemic toxicity of the Silver prosthesis and its antimicrobial efficacy; 25% of the silver salts remained on the prosthesis 20 days after implantation. (12, 13) The use of in situ or extra-anatomically implanted antimicrobial silver-collagen coated prosthetic grafts is new and promising method (2). In this article we present single center long-term results of total, or partial, graft excision, and redo revascularization with silver-coated polyester Silver prosthesis in patients with arterial graft infections.

Material and methods

Patients

From November 2001 to January 2006, this non- randomized prospective study included 47 consecutive patients (35 men, 12 women; mean age 68 years) with the infection of arterial by-pass graft treated with silver prosthesis. Diagnosis was based on clinical and ultrasound examination, preoperative arteriography and *computed tomography* (CT). When possible, cultures were obtained before surgery, and appropriate antibiotic therapy was administered.

Surgery

Due to complexity of the problem no uniform surgical treatment protocol was used, and this matter was left entirely to the discretion of an attending surgeon. The graft infection was managed with either total (n = 38) or partial (n = 9) excision of the infected graft and re-do revascularization with in situ or extra-anatomically implanted silver-coated polyester graft.

As a general rule, total graft excision was performed when the infection involved the entire prosthesis; partial excision was performed when infection was limited to the body or a single limb of the prosthesis and when the remainder of the prosthesis was well-encapsulated.

During surgery, specimens were taken for bacteriologic analysis, and the excised prosthetic graft was placed in culture medium. Povidone-iodine standard solution was used for irrigation of the infected fields after debridement of surrounding tissues. Intraoperative lavage with disinfectant solutions was performed, but only before implantation of silver-coated prosthesis, since the silver may otherwise be washed out. The prosthetic graft was covered with a pedicled anterior omentoplasty when possible.

Postoperative treatment

Postoperative antibiotic therapy averaged 35 days (range 17-66) and consisted of ceftriaxone, amicacin and metronidazole. Serial CT scans of the silver prosthesis were obtained before discharge from the hospital, 6 months after surgery, and then every 6 months.

Follow-up

Patients were followed for combined end-point that included all-cause moratlity, leg amputation and graft infection. If one patient had more than event, only the most serious event was considered for final analysis (that is, in ascending order, graft infection, leg amputation, and death). Mean follow up was 25.5 months (range 1-59 months). The primary end points of the study were patency of the Silver prosthetic graft, limb salvage, and patient survival.

Statistical analysis

All data are expressed as mean + standard deviation. Kaplan-Meier curves were constructed to demonstrate event-free survival for combined end-point, all-cause mortality and occurrence of reinfection and amputation during follow-up. Univariate and multivariate regression analysis were performed to assess predictors of cardiovascular events during follow-up.

Results

Study patients

Study group consisted of 47 patients. Baseline demographic and clinical characteristics of enrolled patients are shown in Table 1. Briefly, patients were predominantly older males with a number of risk-factors for atherosclerosis and adverse outcome following surgery.

Table 1: Baseline demographic and clinical data

	Patients	Percent	Abbreviations:
Sex (male)	**35/47**	**74.4%**	
Age (years)	**68.1 ± 4.7**	**NA**	
Smoking	**35/47**	**74.4%**	CAD - *coronary artery disease;*
Hypertension	**35/47**	**74.4%**	CKF - *chronic kidney failure;*
HLP	**20/47**	**42.5%**	COPD - *chronic obstructive pulmonary disease;*
DM	**12/47**	**25.5%**	DM - *diabetes mellitus;*
COPD	**7/47**	**14.8%**	HLP - *hyper-lipoproteinemia*
CKF	**0/47**	**0%**	
CAD	**23/47**	**48.9%**	

Vascular status and surgery

Data regarding patient's vascular status and surgery are detailed in Table 2.

Table 2: Vascular status and surgery

	Patients	Percent
Reason for previous operation		
- aneurysm	42/47	89.4%
- stenosis	5/47	10.6%
Graft location		
- aorto-bifemoral	20/47	42.6%
- femoropopliteal	20/47	42.6%
- iliacofemoral	7/47	14.9%
Clinical presentation		
- purulent secretion	28/47	59.6%
- apscess	8/47	17.0%
- sepsis	4/47	8.5%
- ischemia	4/47	8.5%
Isolated bacteria		
- Staphylococcus sp.	28/47	59.6%
- Enterococcus sp.	8/47	17.0%
- Klebisella sp.	4/47	8.5%
- Pseudomonas sp.	4/47	8.5%
- Candida	3/47	6.4%
Urgent operation	**18/47**	**38.3%**
Perioperative mortality	**5/47**	**10.6%**

The vast majority of patients were previously operated due to significant atheroscleorotic stenosis of the arteries supplying lower limbs, with aorto-biliacal and femoropoliteal reconstruction performed in over 40% of patients each. Clinical presenting before current operation with silver graft most frequently included purulent secretion, abscess and sepsis. Infection was found at the following locations: whole Y graft in 15/47 (31.9%); body and limb of Y graft in 2/47 (4.3%); limb of Y graft in 3/47 (6.4%); whole femoropoliteal graft in 16/47 (34%); part of femoropopliteal graft in 4/47 (8.5%); and, whole ileofemoral graft in 7/47 (14.9%) of patients. The most frequently isolated bacterias were staphylococcus and enterobacter species. Urgent operation was performed in 18/47 (38.3%) patients, and 5/47 (10.6%) patient died perioperatively.

Follow-up

Patients were followed for 25.5±14.9 months (minimum 1 month, maximum 59 months). During the follow-up, 13/47 (27.7%) patients had combined end-point. On the other hand, all-cause (including perioperative) mortality, reinfection, and amputation were found in 10/47 (21.3%), 9/47 (19.1%), and 3/47 (6.4%) patients.

Kaplan-Meier curves are showing temporal incidence of combined end-point (Figure 1A), all-cause mortality mortality (Figure 1B), infection (Figure 1C), and amputation (Figure 1D).

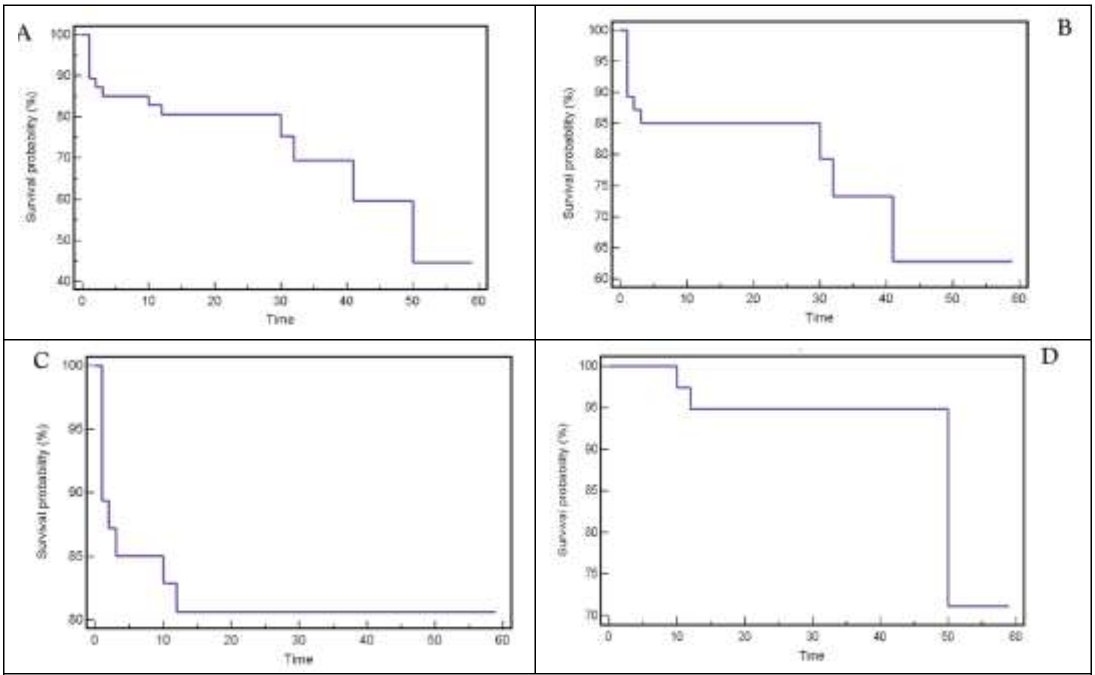

Figure 1: Kaplan-Meier curves for event-free survival for A) combined-end point, B) mortality, C) infection, and D) amputation

All variables in Tables 1 and 2 were entered in univariate analysis, but the only variables associated with combined end-point during follow-up was urgent operation (F = 8.24, p value = 0.006), which was also independently predictive of comined end-point in multivariate regression analysis (OR 6.25; 95% CI, 1.53-25.41). On the other hand, urgent operation and reinfection were identified to be associated with mortality during follow-up (F = 5.84, p value = 0.02, and F = 37.03, p value < 0.001, respectively), but only reinfection was identified as variable independently predictive of mortality (OR 40.83; 95% CI, 5.72-294.42). No variables were independently predictive of reinfection and amputation.

Discussion

The results of our series are comparable to previous reports (Table 3). Perioperative mortality was 10.6%, and all patients died due to complications of prosthetic graft infection. Secondary infections have been noted in as many as 27% of recent series.

Table 3: Previous studies of tretment of vascular graft infection

Author	Year	No. of patients	Mean follow-up (months)	Operative Mortality (%)	Amputation (%)	Secondary infection (%)
Conventional, extra-anatomic grafting						
O'Hara et al[19]	1986	54	13	28.0	27	27
Bacourt et al[14]	1992	98	34.6	24.0	16	7
Sharp et al[20]	1994	20	–	3.7	5	5
Yeager et al[4]	1999	60	41	13.0	10	10
Bandyk et al[18]	2001	31	26	21.0	9	3
In situ graft replacement						
Allograft						
Kieffer et al[5]	1993	43	13.8	12.0	0	7
Verhelst et al[23]	2000	90	36.0	17.0	1	1
Leseche et al[21]	2001	28	35.4	17.8	0	0
Vogt et al[22]	2002	49	27.0	6.0	0	2
Noel et al[16]	2002	56	5.3	13.0	5	4
Autogenous vein						
Nevelsteen et al[25]	1995	15	17	7.0	7	0
Clagett et al[24]	1997	41	32	7.3	5	0
Bandyk et al[18]	2001	10	26	10.0	10	3
Antibiotic bonded prosthesis						
Hayes et al[26]	1999	11	–	18.0	0	9
Young et al[27]	1999	9	36	8.0	0	11
Bandyk et al[18]	2001	16	18	0.0	0	10
Silver coated prosthesis						
Zegelman & Günther[15]	2002	44	11	6.5	–	6.5
Batt et al[42]	2003	27	17	16.6	0	3.7
Zegelman & Günther[43]	2003	126	10	7.6	–	8.0

Recurrent infection developed in 19.1% in our series, with mean follow-up of 25.5 months (range 1-59 months), which can be explained by high-risk profile of these patients for infection (retroperitoneal and/or inguinal abscesses, graft-duodenal fistulas, colonic fistula), and frequent urgent surgery because of a life-threatening complications of arterial graft infection.

Our patients had extensive clinical signs of infection (Table 2), with Staphylococcus and *Enterococcus species* being the most frequent isolates. The same distribution was reported by Zegelman and Günther, (15) who found *S epidermis* in 6 patients, *Pseudomonas* in 11 patients, and *S. aureus* in 47 patients in their series. In our series, the infected prosthesis was surrounded by purulent material in 37 patients; even in these conditions, the Silver prosthesis resisted infection, and no anastomotic rupture occurred. Thorough debridement of all infected surrounding tissues is essential and must be completed with irrigation with povidone-iodine solution; the prosthetic graft should also be covered with a pedicled omentoplasty when possible (2, 16, 42).

The treatment of prosthetic graft infection must be established individually in each patient. In our series, total (n = 38) or partial (n = 9) excision of the infected graft and redo revascularization was done with in situ (n = 28) or extra-anatomically (n = 19) implanted Silver graft. Partial excision was used for patients in poor general condition in whom the remainder of the prosthesis was macroscopically free of infection.

Extra-anatomic bypass grafting has several disadvantages compared to in situ replacement: the procedure is time consuming and patency at long-term is not so good. Theoretical advantage of extra-anatomic bypass grafting is lower risk for graft infection, because revascularization is performed at a distance from the infection site. However, blood supply to the pelvis and the left colon is usually compromised with extra-anatomic bypass grafting, because it is impossible to revascularize the internal iliac arteries or the inferior mesenteric artery (colonic and pelvic ishaemia) (2, 14, 42).

Conventional surgical management of partially infected prosthetic grafts consists of complete excision. However, it is demonstrated that when the remainder of the prosthesis is well-encapsulated, it can be safely left in place (2, 17, 42). For patients with poor general condition this reduces operative morbidity and mortality; the new prosthesis is placed in situ in an adjacent position. The apparently better outcome with partial graft removal may not result from the technique but because the infection was limited.

In situ replacement with cryo-preserved arterial allograft is another option for treatment of these infected grafts. In experimental studies, allografts were more resistant to infection than conventional prostheses were, (30-32) although a report from the Mayo Clinic16 found that 23% of complications were attributable to the allograft, including hemorrhage, persistent infection, occlusion, and pseudoaneurysm.

Autogenous reconstruction with the superficial femoral veins is effective means to prevent secondary infection, but the additional operative time required is not always compatible with life-threatening situations or fragile patients. (18) Previous deep venous thrombosis is a contraindication to this operative approach. A history of femoropopliteal reconstruction complicates excision of a segment of the superficial femoral vein. (25) Postoperative compartment syndrome has also been described in 12% of patients. (24) Recent publications (5-16, 18-29, 42) have reported the safety of in situ replacement of infected prosthetic grafts or mycotic aneurysms of the infrarenal aorta using various graft materials (Table 3).

The efficacy of rifampicin-impregnated polyester prostheses for in situ replacement of infected aortic prosthetic grafts has been demonstrated both experimentally (33, 34) and in clinical trials. (18, 26, 27) However, their efficacy depends on the bacterium responsible for the infection. Experimental studies have shown that gelatin-coated polyester prostheses impregnated with rifampicin exhibit satisfactory resistance to *S. epidermis* but are insufficient against MRSA and *Escherichia coli.* (35, 36) Hayes et al, (26) demonstrated the limitations of rifampicin-bonded polyester grafts for management of major aortic graft infection with MSRA. This problem warrants particular attention because of the appearance of rifampicin-resistant strains of *S. epidermis* (37).

The evolution of nosocomial infections in Europe highlights the changing epidemiology of infections. Bacteria such as *S. aureus* and *S. epidermis* are increasingly resistant to antibiotic therapy. (38) Because of risk for bacterial resistance to rifampicin, alternatives to the antibiotic agents bonded to these prostheses must be envisaged for in situ replacement of infected aortic prosthetic grafts. Experimentally, bacterial resistance develops more rapidly and more easily with antibiotic agents than with antiseptic agents. (39) Silver compounds are acting as an antiseptic with many advantages: lack of resistance, wide range of activity profile including MRSA, sustained availability at an effective dose during 2-4 weeks on the prosthesis (43).

The antiseptic properties of silver salts have long been recognized. Because of their biocompatibility, and experimental and clinical efficacy when used as antimicrobial agents on implantable medical devices, (8-11) we selected the Silver prosthesis for management of infected prosthetic grafts. The silver impregnated prosthesis fulfils the licencing criteria for implants and is CE-certified.

Our study showed that in situ Silver prostheses replacement is a safe and effective option for management of infected arterial prosthetic grafts. A recent experimental study (40) reported that rifampicin -impregnated prostheses are more resistant to infection than Silver prostheses are. But this study is suffering from important drawbacks; an unrealistic model of infection, different body weights of the infected dogs, use of an highly rifampicine-susceptable strain of bacteria and many more. Besides, clinical trials do not confirm these experimental findings. In deed, it appears that secondary infections are more frequent with rifampicin-impregnated prostheses than with Silver prostheses (Table 3). This discrepancy between experimental findings and clinical trials is probably attributable to the fact that *S. aureus* and *S. epidermis* develop resistance to rifampicin more rapidly than to silver acetate impregnation (26, 36, 38, 42).

The importance of avoiding reinfection can not be overemphasized in these patients, as our data show that reinfection is associated with 40 times greater likelihood of death. Therefore, every attempt must be taken to avoid reinfection and Silver prostheses may play significant role in that sense.

The major limitation of the study is that this is a single centre study with a limited number of patients. As this was non-randomized study, there was a substantial case-to-case heterogeneity, but it has to be acknowledged that prospective randomized study of patients with graft infection is very difficult, if not impossible, to perform. However, larger series with longer follow-up will be required to compare the role of effectively evaluate silver-coated polyester Silver prosthesis in the management of patients with infected arterial graft.

Conclusion

Our results demonstrate favorable long-term outcome with silver-coated polyester prosthesis used to treat arterial graft infection, although significant mortality and morbidity remain major clinical problem in this subset of patients. It appears that Silver graft may be an appropriate option for treatment of infected aortic grafts, particularly when autogenous deep vein reconstruction is not possible. However, larger series will be required to fully evaluate the role of silver-coated polyester Silver prosthesis in the management of patients with infected arterial graft.

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Special vascular access for hemodialysis in patients with exhaustion of the upper limb veins using the axillary artery*)

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Abstract

This study describes our experience with axillary artery to axillary vein or axillary artery to jugular vein politetrafluoroethylene bridge fistulas for hemodialysis access. The purpose of the study was to determine the incidence of complications and the durability of the access to better determine the role of this procedure in the dialysis access algorhythm.

Materials and methods: *A single team experience over a period of 10 years was retrospectively reviewed.*

Results: *17 axillary grafts were placed in 16 patients. All were used for dialysis. At the time of access creation the patients had been undergoing dialysis for a mean of 68 months (4 to 216 months), had a mean of 8.5 previous access procedures and had exhausted all arm sites. The patency rate was 64.7% at 3 years. The incidence of infection and thrombosis were comparable with conventional arm bridge fistulas. Neither vascular steal phenomenon nor neurologic injury occurred in this series.*

Conclusions: *Axillary artery to axillary vein or axillary artery to jugular vein politetrafluoroethylene bridge fistula is an excellent and durable secondary access strategy. We recommend that it be used after exhaustion of conventional arm sites.*

Keywords: *vascular access, ePTFE, axiloaxillary graft, axillo-jugular graft.*

The incidence of end-stage renal disease (ESRD) and the number of patients who are treated with maintenance hemodialysis continue to increase. Vascular access dysfunction remains the leading indication for hospitalization in the population of patients who undergo dialysis. In the present period in Western Europe and the USA this hospitalization accounts for 15-20% of hospital stays.

Since its introduction in 1965 the wrist radial-cephalic (*Brescia Cimino*) autogenous arteriovenous fistula has been the access site of first choice. That fistula has achieved this ranking because of its simplicity, durability and relative freedom of complications (particularly infection and thrombosis) that limit the durability of bridge fistulas that use

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synthetic vascular grafts. Fistulas made from autogenous vessels have a high primary failure rate, especially if marginal veins are used. Though, once they are established they have the best cumulative patency curve of all access strategies. Wrist vessels are the first choice vessels where fistula creation is attempted. When wrist vessels are inadequate, antecubital vessels or even neck vessels may be used.

When one of these fistulas can not be created, a bridge fistula is required. After experience with numerous materials including autogenous saphenous vein, autogenous collagen tubes created by the mandril technique and various vascular graft materials, the *politetra-fluoro-ethylene* (PTFE) bridge fistula has become the most popular procedure. These accesses have a limited life expectancy that depends on the site chosen for arterial inflow and the quality of the venous outflow. The arm is the preferred location because of the ease of needle puncture, as well as the abundant collateral flow that can provide adequate circulation in the event of vascular complication associated with this access. The use of leg vessels entails a greater risk of infection and ischemia, and it requires minimally diseased vessels, which may not be available in patients in this population. In addition to being less convenient to cannulate, there is considerable belief that the risk of late graft infection is higher with leg vein grafts.

When arm sites have exhausted, options include the use of the leg sites or, alternatively, the use of other rather unusual sites. One of these sites is the anterior chest wall, with grafts based on the axillary or subclavian vessels and outflow through either the axillary or jugular routes. We have favored this approach when arm sites have become exhausted as a result of thrombosis, when vascular steal occurs or if the arm vessels are too small to support modern high-flux dialysis. This report describes our experience during a 10-year period. No large series of axillary artery-anterior chest wall grafts has been previously described in the literature. The largest study includes a number of 26 procedures. Thus, the incidence of vascular steal, infection, thrombosis and other complications has not been established for purposes of comparison with other alternatives for secondary access for hemodialysis.

Patients and methods

From 1991 to 2001, 702 operative procedures were performed for dialysis access by our team. 158 procedures (22.5%) were primary wrist or elbow autogenous arteriovenous fistulas. 142 new vascular grafts were placed, of which 17 (11.97%) were based on the axillary artery and terminated in the ipsilateral, contralateral axillary or jugular vein.

The 16 patients were 12 women and 2 men. In one case a second graft was inserted due to late failure of the first graft by thrombosis. The demographics of the patient group are listed in table 1.

Table 1: Patient information

Number	**16**	**Cause of renal failure:**	
• Male	4	• Diabetes	7
• Female	12	• Hypertension	4
Age	51 years (25 - 72 years)	• Other	5
Duration of dialysis	68 months (4-217 months)		

There was a wide range of age, from 25 to 72 years. These patients had been undergoing dialysis for an average of 68 months. One patient has been dialysis dependent for 18 years.

The mean number of previous operative procedures performed for dialysis was 8.5 per patient. The absolute number ranged from 2 to 28 (table 2).

Table 2: Number of previous access procedures

No. of previous procedures	**<5**	**5-10**	**10-20**	**>20**
No. of patients	**3**	**9**	**3**	**1**

All patients had exhausted sites from at least one arm, and as many as four extremities had been used (table 3).

Table 3: Number of extremities exhausted

No. of extremities	**1**	**2**	**3**	**4**
No. of patients	**2**	**11**	**2**	**1**

In the majority of cases the indication for this form of vascular access was the exhaustion of arm sites (table 4). In two patients, the arm vessels were considered too small to support extremity fistulas. In one case an axilloaxillary graft was placed because a previous arm site had resulted in vascular steal syndrome.

Table 4: Indications for use of axillary artery for access

Exhaustion of conventional sites	**13**
Vessel size	**2**
Vascular steal	**1**

The technique used is that described by Garcia-Grinaldi and Koch. An infraclavicular incision is made and the pectoralis major fibers are separated bluntly. The axillary vessels are exposed medial to the insertion of the pectoralis minos and without dividing that structure. The proximal (arterial) anastomosis is not beveled, but the distal (venous) anastomosis is. We preferred to use for the axillary vein and not some tributary. In case subclavian vein stenosis is not present we preferred the axillary vein to preserve the jugular vein for subsequent venous access should it become required. When the jugular vein was used, it was exposed by dividing a portion of the sternocleidomastoid muscle. In all cases documented in this study the graft used was a 6 mm standard wall ePTFE graft. The grafts are tunneled in the subdermal plane over the sternum and cephalad to any breast tissue. For grafts that terminate in the jugular vein, a counter incision is made and the graft tunneled over the clavicle. In all cases the procedures were performed under general anesthesia. Thrombectomy or revision may be performed under local anesthesia. Thrombectomy usually requires incision over both anastomosis because of the difficulty in negotiating a balloon thrombectomy beyond two right angle turns. If intimal hyperplasia develops at the venous anastomosis the terminus can be changed from the axillary to the jugular vein. The change from the jugular vein to the axillary is also a rare possibility.

Results

All grafts were used for dialysis. The duration of use varied from 2 months to 62 months. 6 grafts have been lost after an average of 8 months of use. The causes of graft loss are listed in table 5. Graft function was prolonged in each case (except for the cases of infection) by thrombectomy or revision before abandonment.

Table 5: Causes of graft loss

Thrombosis	**3**
Infection	**1**
False aneurysm	**2**
Steal	**0**
Ischemia	**0**

Five patients required conversion to a permanent venous access. One patient had a second axillo-jugular graft created. False aneurysms occurred in two grafts. These required abandonment of the access site. One involved the arterial anastomosis and required direct axillary artery repair. One graft was removed after becoming infected atfer multiple surgical thrombectomies. A short stump was left on the axillary artery and the wound healed normally. The remaining 12 grafts have required 7 additional procedures to maintain patency.

Arm ischemia, as a result of vascular steal or from any vascular complication of these procedures, did not develop in any patient. In patients who previously had steal from a brachial artery-based graft, steal did not develop from a graft originating from the axillary artery. Thrombosis was the cause of most graft loss and was treated by simple thrombectomy with or without revision of the venous anastomosis.

Discussion

The arm is clearly the site of first choice for hemodialysis access. Autogenous fistulas in the arms often may be used for years and, when technically feasible to create, may be the only access required. Unfortunately, only a part of patients who have ESRD that requires vascular access have suitable vessels to permit creation of an autogenous fistula. Bridge fistulas with PTFE grafts have become the access of second choice in most centers. Bridge fistulas, however, have a limited life-span, and many patients who undergo dialysis will require replacement of arm grafts even if an aggressive graft-salvage policy is followed. Arm PTFE bridge fistulas have a life-table cumulative patency rate of 50 to 70% at 3 years. The incidence of graft thrombosis in some series is 3.5% per patient-year, requiring graft revision 0.74 times per patient-year. Bridge fistulas most often are lost because of thrombosis, development of false aneurysms or the appearance of vascular steal. Vascular steal occurs most frequently in patients with diabetes. Although steal is sometimes ameliorated with intentional stenosis of the graft near the arterial anastomosis, it frequently requires graft removal. Steal that occurs in one arm is likely to occur in the other arm as well.

When all arm sites have been exhausted or when steal occurs, a secondary site must be chosen. Hertofore, the secondary site most frequently selected is the leg or permanent venous cannulation. The life span of cuffed silicon elastic venous catheters has been clearly shown to be limited by infection. The average life span of venous catheters is less than 12 months, although individual catheters may last as long as 2 years. Leg grafts have the disadvantage that the femoral vessels are more frequently diseased, especially in the aging dialysis population. In this location a vascular complication resulting in diminished nutrient flow more often threatens viability of the affected limb. There is also considerable belief that infection is more common both initially at the time of graft insertion and over time in the grafts originating in the groin.

An alternative approach is to use the axillary artery. This vessel is large but also has excellent collateral flow so that diminished flow through it is less likely to be limb-threatening. The approach to and dissection of the axillary artery is familiar to all vascular surgeons. The skin of the anterior chest wall is thick, resistant to infections and nor oversensitive.

It is thus suitable for tunneling of the PTFE graft, and puncture is convenient. Either the axillary or the jugular vein on the ipsilateral or contralateral side may be used, which provides a number of options for routes of venous outflow. Although this approach was described in 1978, no large series that used the axillary artery has been described, so the incidence of complications and the durability of such grafts have not been established. The experience described here together with some data from the literature demonstrates that this graft has an acceptable thrombosis rate and an acceptably low infection rate, and can easily be revised when necessary. It is suitable for the patient who has had vascular steal from a graft based on the brachial artery. Furthermore, it is well accepted by patients. On the basis of this experience, we believe that it is the access of second choice after arm sites have been exhausted and before resorting to leg grafts or permanent venous catheters.

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Etiological spectrum and therapeutic implications in patients with embolic acute limb ischemia*)

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Abstract

Objectives. *To estimate the etiology of embolic acute limb ischemia and the therapeutic implications.*

Material and methods. *A retrospective study with 106 patients admitted in our clinic between 1.11-20011 and 1.10.2002 with embolic acute limb ischemia. To establish the etiology of embolic events we used clinical exam, electrocardiography, transthoracic echocardiography (82 patients - 77%), transesophageal echocardiography (6 patients – 5.6%) and angiography (26 patients - 24% - intraoperatory control at 18 patients).*

Results. *There were 71 men (67%) with ages between 42 and 93 years and 35 women (33%), with ages between 46 and 88 years, with pelvine limb ischemia - 82 patients (77.3%), upper limb ischemia-22 patients (20.7%) and both pelvine and upper limb ischemia -2 patients (1.8%). Etiological analyze showed the presence of nonvalvular atrial fibrillation at 64 patients (60,4%), with 53 patients over 65 years (82.8%), valvular diseases at 23 patients (21,7%- a case of bacterial endocarditis), coronary- artery disease at 8 patients (7.5%), dilatative cardiomyopathy at 3 patients (2.8%) and at 8 patients the cause remain unclear (7.6%). 36 of our patients (33.9%) were without anticoagulant or antiagregant treatment, 54 patients (50.9%) had only antiagregant treatment, 13 patients (12.3%) were treated with oral anticoagulants, but without biological efficiency and 3 patients (2.8%) had efficient oral anticoagulant treatment.*

Conclusions. *The main cause of limb embolic events in our group was nonvalvular atrial fibrillation (60.4% of cases), especially at aged patients (82.8% were over 65 years). For prevention of arterial limb embolic events it is required an anticoagulant treatment with biological efficiency, even at aged patients with a greater risk of hemorrhagic complications.*

Rewards *- embolic events, acute limb ischemia, treatment*

Introduction

Acute arterial ischemia has a severe prognosis, with high mortality and rise of amputation.

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Incidence of acute limb ischemia is not well known; it was estimated at 14/100000 peoples, representing 14-16% of peripheral arterial disease. The most frequent cause of acute limb ischemia are arterial embolic events (approximately 80% of all events), the other cause is arterial thrombosis (1).

The most important source of embolic events is the heart (above 80% of patients), with high incidence of atrial thrombosis (atrial fibrillation, valvular diseases, valvular prosthesis), ventricular thrombosis (in acute myocardial infarction with or without left ventricle aneurysm, dilatative or restrictive cardiomyopathy) or embolism from vegetations of infectious endocarditis or left heart tumors. The extracardiac sources of arterial embolisms are involved in 5-10% of cases, being represented of: abdominal aorta and ilio-femoral aneurysm with thrombus, instable atherosclerotic plaques and, rarely, paradoxical embolisms in cases of patent foramen ovale or inter-atrial septal defect (2). In 5-10% of cases the source is unknown.

Objective

This study wants to evaluate the etiology and therapeutically implications of embolic acute limb ischemia.

Methods

The study was retrospective, with a group of 106 consecutive patients with surgical interventions for embolic acute limb ischemia in 01.11.2001' 01.10.2002 at *Vascular Surgery Clinic of Institute of Cardiovascular Diseases "Prof. Dr. C.C. Iliescu", Bucharest.*

The evaluation was made by:

- clinical exam;
- electrocardiogram;
- thoracic X-ray;
- 2D and Doppler transthoracic echocardiography;
- transesophageal echocardiography;
- peripheral arteriography (26 patients-24%, at 18 patients - intraoperator control).

Results

There were included 106 patients with embolic acute limb ischemia; their general features and distribution of etiology and treatment are summarized in the next tables and graphics.

Table 1: Characteristics of the patients

Characteristics / Etiology	Nonvalvular atrial fibrillation	Valvular diseases	Coronary arterial disease [CAD]	Dilatative cardio-myopathy [DCM]	Cryptogenetic	Total
Number of patients	64 (60.5%)	23 (21.7%)	8 (7.5%)	3 (2.8%)	8 (7.5%)	106
Age (ans)	59-93 (average - 72,1)	51-88 (average - 67.5)	45-72 (average - 59)	49-63 (average - 57)	50-71 (average 59.6)	45-93 (average- 65.8)
Males	34 (63.0%)	3 (5.5%)	8 (14.8%)	2 (3.7%)	7 (13.0%)	54 (50.9%)
Females	30 (57.7%)	20 (38.5%)	0	1 (1.9%)	1 (1.9%)	52 (49.1%)
Inferior limbs ischemia	51 (79.7%)	15 (65.2%)	7(87.5%)	2 (66.6%)	7 (87.5%)	82 (77.3%)
Upper extremity ischemia	12 (18.7%)	7 (30.4%)	1 (12.5%)	1 (33.4%)	1 (12.5%)	22 (20.8%)
Upper extremity and inferior limbs ischemia	1 (1.5%)	1 (4.3%)	0	0	0	2 (1.9%)
TEE with Fogarty	43 (67.2%)	17 (73.9%)	6 (75%)	2 (66.6%)	8 (1000%)	76 (71.7%)
Endarterectomy	10 (15.6%)	5 (21.7%)	1 (12.5%)	0	0	16(15.1%)
Amputation	11 (17.2%)	1 (4.3%)	1 (12.5%)	1 (33.4%)	0	14(13.2%)
Death	3 (4.7%)	2 (8.7%)	1 (12.5%)	0	1 (12.5%)	7 (6.6%)

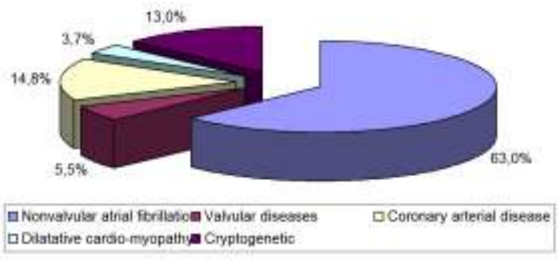

Figure 1: The etiology of embolic events at males

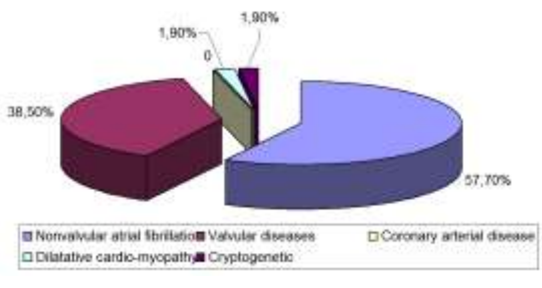

Figure 2: The etiology of embolic events at females

Table 2: Embolic risk factors at patients with non-valvular atrial fibrillation

Risk factors		Males (n = 34)	Females (n = 30)	Total (n = 64)
Low risk		2 (5.8%)	0	2 (3.1%)
High risk	Age > 65 years	32 (94.2%)	30 (100%)	62 (96.9%)
	Hypertension	25 (73.5%)	22 (73.3%)	47 (73.4%)
	Diabetes mellitus	3 (8.8%)	6 (20%)	9 (14.1%)
	Previous embolic events	7 (20.6%)	9 (30%)	16 (25%)
Echo-cardiography	*- Left atrium > 47 mm*	15 (44.1%)	17 (56.7%)	32 (50%)
	- EF < 30%	0	0	0
	- Left atrial thrombus	0	2 (6.7%)	2 (3.1%)
	- Heart failure	4 (11.7%)	4 (13.3%)	8 (12.5%)

Table 3: Embolic risk factors at patients with valvular disease

Risk factors / Valvular disease (n=23)		Mitral stenosis (n=6)	Mitral regurgitation (n=3)	Mitral disease (n=11)	Aortic disease (n=3)
Males	Risk factors (-)	0	1 (33.3%)	0	0
	Atrial fibrillation	0	0	1 (9.1%)	2 (66.7%)
	Previous embolic events	0	0	1	0
	Left atrial thrombus	0	0	0	0
Females	Risk factors (-)	1 (16.7%)	1 (33.3%)	0	0
	Atrial fibrillation	5 (83.3%)	1 (33.3%)	10 (90.9%)	1 (33.3%)
	Previous embolic events	3 (50.0%)	0	3 (27.3%)	1 (33.3%)
	Left atrial thrombus	3 (50.0%)	0	3 (27.3%)	0

Table 4: Embolic risk factors at patients with coronary artery disease and dilatative cardiomyopathy

Risk factors		Myocardial infarction (n=4)	Left ventricular aneurysm (n=4)	Dilatative cardiomyopathy (n=3)
Males	Risk factors (-)	2 (50%)	2 (50%)	0
	Left ventricular systolic dysfunction	0	1 (25%)	2 (66.7%)
	Atrial fibrillation	1 (25%)	1 (25%)	2 (66.7%)
	Left ventricular thrombus	1 (25%)	2 (50%)	0
Females	Risk factors (-)	0	0	0
	Left ventricular systolic dysfunction	0	0	1 (33.4%)
	Atrial fibrillation	0	0	1 (33.4%)
	Left ventricular thrombus	0	0	1 (33.4%)

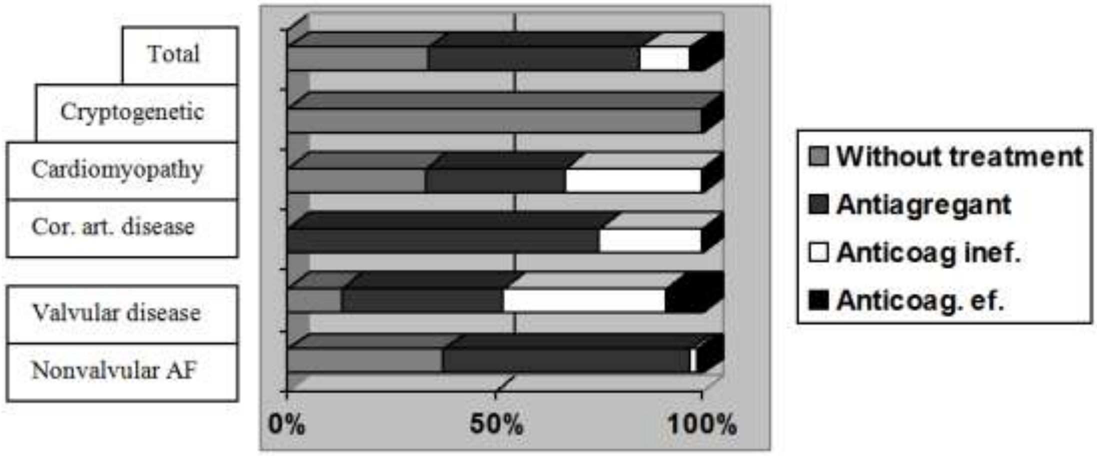

Figure 3: Precedent anticoagulant and antiagregant treatment at patients with acute limb ischemia

Discussion

1. Mainly features

The analyze of features of our group shows that embolic events were produced mainly at elderly (mean age- 65.8 years), especially in subgroups of patients with nonvalvular atrial fibrillation and valvular diseases (mean age 72.1 years and 67.5 years) versus patients with coronary artery disease or dilatative cardiomyopathy (59 years and 57 years); old age ia an important predictive factor of thromboembolic events at first subgroups of patients. The sex distribution shows that females are predominant in the subgroup of patients with valvular diseases (87%) and males in subgroup of patients with coronary artery disease and dilatative cardiomyopathy (100% and 66.6%), and in the subgroup of patients with nonvalvular atrial fibrillations the distribution is approximately equal (53% vs. 47%).

The localization of acute ischemia was in inferior limbs at 77.3% of cases and in upper extremity in 20.8% of cases with two cases of both localization; literature data shows that inferior limb ischemia appears five times more frequent than implication of upper extremity (70-80% of cases with inferior limb ischemia- 35-50% at the crossroad of femoral artery).

2. Etiology

We observed the predominance of nonvalvular atrial fibrillation (60.4% of cases), an important proportion of patients with valvulopathies (21.7%) especially rheumatic mitral disease; at 8 patients (7.6%) the cause was not determined. Comparatively with two decades ago in Romania we observed a change of the etiological spectrum of embolic acute limb ischemia, from the predominance of rheumatic valvulopathies at the predominance of nonvalvular atrial fibrillation. The explication is diminution of cases of rheumatic valvulopathies and augmentation of surgical interventions for valvulopathies at older patients, these patients being more carefully followed after that.

a) In the case of nonvalvular atrial fibrillation the most embolisms are cerebral; the embolic risk is different at patients with valvular and nonvalvular atrial fibrillation (in Framingham study the risk of embolic stroke at patients with nonvalvular atrial fibrillation was 5.6 folds greater than patients with sinusal rhythm and , at patients with valvular atrial fibrillation 17.6 folds greater) (4). Embolic risk is not the same for all patients with atrial fibrillation; there were identified by multivariate analysis five clinical variables at independent predictors for thromboembolic risk- age above 65 years, hypertension, previous embolic strokes, heart failure and diabetes mellitus - for classifying patients with atrial fibrillation with high or low risk. There were identified echocardiografic features of embolic high risk - left atrium above 47 mm, left ventricular systolic dysfunction, thrombus or spontaneous contrast in left atrium (3, 4, 5).

Analyzing the predictors for high embolic risk at our patients we concluded that the most patients are above 65 years (96.9%), with a great proportion of hypertension - 73.4%, previous embolic events (especially stroke - 25%), and, at 50% of patients left atrium was greater than 47 mm.

b) At the patients with valvular diseases the risks of arterial embolic events vary with specific disease. In case of mitral stenosis the literature data shows an incidence of 1.5–4.7% of embolic events, most important risk factors being atrial fibrillation (the risk increase 7-18 folds), previous embolic events and old age. Embolic risk is not proportional with dimensions of left atrium or functional class of heart failure (4, 6). At the patients with mitral regurgitation arterial embolic risk is lower, being estimated at 1-2 events / 100 patients/year in case of moderate mitral regurgitation and 4 events/100 patients/year in case of severe mitral regurgitation and mitral disease (7). At the patients with mitral valve prolapse and aortic valve disease arterial embolisms are rare.

A special category, with high risk of arterial thromboembolic events, are valvular prostheses with an incidence of 1.5 embolic events/100 patients/year at patients with efficient anticoagulant treatment and 4 events/100 patients/year in case of inadequate anticoagulant treatment (3).

In our group there are many cases of arterial embolies in mitral disease (11 cases, vs. 6 cases in mitral disease and 3 cases in mitral regurgitation and aortic disease). Most of the patients have atrial fibrillation (83.3% of the patients with mitral stenosis and 90.9% with mitral disease) and a significant number of previous embolic strokes (50% of patients with mitral stenosis and 27.3% with mitral disease).

There was a single case of infectious endocarditis with vegetation on mitral valve at a patient with rheumatic mitral stenosis with left atrial thrombus and thrombotic aspect of the material extracted with Fogarty catheter. There was not any case of embolic event at patients with valvular prostheses.

c) In acute myocardial infarction the presence of left ventricular thrombus is citated at 30% of patients with anterior localization and below 5% in other localizations. The predictive factors of embolic risk are the size of necrosis, severe systolic dysfunction (ejection fraction below 35%, presence of atrial fibrilation and mobility of the thrombus. The greatest risk is in the first three month after myocardial infarction (4, 8, 9, 10). Of the 4 patients with myocardial infarction in our group nnone has severe systolic dysfunction and only in 1 patient we see left ventricular thrombus. We want to emphasize that only one patient has acute myocardial infarction (at 7th day of evolution) and the rest of 3 patients being at 1-3 month after myocardial infarction.

d) At patients with left ventricular aneurysm the literature data shows the presence of left ventricular thrombi at 46-49% of cases and of arterial embolisms at 10% of cases. After the first 3 month postinfarction the risk is of 0.3%/year- augmented risk persists in case of severe systolic function or protrusive thrombus (11).
In the case of the 4 patients with left ventricular aneurysm in our group, one has severe systolic dysfunction (ejection fraction-30%) and at 2 patients we found intraanevrismal thrombus. All patients are at distance after acute myocardial infarction (above 3 month).

e) At patients with non-ischemic dilatative cardiomyopathy, there is a great variability of the incidence of arterial embolic events (1-12%), the risk being greater in the presence of severe systolic dysfunction (ejection fraction below 35%), atrial fibrillation, previous embolic events and presence of left ventricular thrombi. All patients with dilatative cardiomyopathy (3 cases) have severe left ventricular systolic dysfunction and atrial fibrillation and 1 patient intraventricular thrombus.

f) Mainly, the patients with no cause of arterial embolisms, were younger (mean age-59.6 years), representing 5.6% of all patients (8 cases), with the same proportion as was reported in the literature (5-10% of cases) (2). It is possible that the mechanism of acute ischemia at these patients to be represented of superimposed thrombosis on the atherosclerotic plaque, with fragmentation and distal embolization. We have not any case of aortic aneurysm with distal embolization.

3. Methods of diagnosis

All patients were evaluated by clinical exam, electrocardiography, thoracic X-ray, transthoracic echocardiography. Transesophageal echocardiography was made at 12 patients (11,2%), especially at the patients without an apparent cause of embolic event. This method made possible the diagnosis of infectious endocarditis at one patient with mitral stenosis with negative transthoracic exam. With transesophageal echocardiography we diagnose more frequent left atrial thrombi and spontaneous contrast at the patients with atrial fibrillation and embolic events. However, in clinical studies, it was not validated the value of transesophageal exam for the prediction of a future embolic event (3). Peripheral arteriography was made at 26 patients (24%), at 18 cases as intra-operator control.

4. Treatment

a) Analyzing the presence of previous antithrombotic treatment we observed that a great number of patients has antiagregant treatment (50.9%), and of 16 patients (15.1%) with anticoagulant treatment, at only 3 patients this treatment was correct (INR-2-3). Most patients with nonvalvular atrial fibrillation has no adequate treatment- 38 patients with antiagregant treatment, 24 patients without antithrombotic treatment, only 2 patients with anticoagulant treatment. This situation is explicated by old age of these patients (82.8% of patients above 65 years) and the fear of hemorrhagic adverse events at this group of patients. Now, the guides for treatment of atrial fibrillation (ESC Guide and ACC/AHA Guide in 2001) recommend antithrombotic (antiagregant or anticoagulant) treatment at all patients with atrial fibrilation above 65 years of age, antiagregant treatment at the patients with low risk of embolic events and anticoagulant treatment at the patients with high risk, with a INR of 2-3, in the absence of contraindications (12).

b) Mainly, the treatment of acute limb ischemia was made by thrombembolectomy with Fogarty catheter (71.7% of cases); in 13.2% of cases was necessary the amputation of the limb; in 15.1% of cases was made endarterectomy. After surgical treatment was instituted anticoagulant treatment - initially with continues intravenous administration of unfractionated heparin and after with oral anticoagulants.

5. Evolution and prognosis depend on promptness of the therapy, comorbidities, age

Literature data shows that, after the appearance of embolectomy with Fogarty catheter intrahospital mortality was reduced from 30-50% to 15-30%, and the salvage of ischemic limb is possible in 85-95% of cases (13, 14). In our group are 7 deaths (6.6% of cases), at old patients (above 75 years of age), with old ischemia (after 24 hours from the debut) and with acute renal failure. There is a case of postoperative myocardial infarction with death at the second day at a patient with known coronary artery disease. Post-operative recurrence of arterial embolisms is reported in the literature at 7-12% of cases, being reduced by postoperative anticoagulant treatment (14). In our group of patients there is no recurrence of embolic event in hospital (approximately 7 days) with efficient anticoagulant treatment.

Conclusions

1. The main cause of limb embolic events in our group was nonvalvular atrial fibrillation (60.4% of cases), especially at aged patients (82.8% were over 65 years).

2. For prevention of arterial limb embolic events it is required an anticoagulant treatment with biological efficiency, even at aged patients with a greater risk of hemorrhagic complications.

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Peripheral ischemia caused by paradoxical embolization*)

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Abstract

Background: *Paradoxical embolus is a rarely diagnosed cause of arterial ischaemia, but it would be recognized more often if patients with suspected embolism but without obvious embolic source in the left heart or systemic vessels were investigated more aggressively. This article presents a case of a 54-year-old man who presented to the emergency department with simultaneous deep venous thrombosis, and bilateral acute limb ischemia. Further investigation revealed an atrial septal defect, which led to a final diagnosis of paradoxical embolism (PDE).*

Key words: *paradoxical embolism* (PDE), *deep venous thrombosis* (DVT), *patent foramen ovale* (PFO), *peripheral ischemia, atrial septal defect* (ASD).

Introduction

Paradoxical embolism is a rare disease, difficult to diagnose and underestimated in clinical practice. Paradoxical embolism (PDE) occurring in patients with pulmonary embolism or venous thrombosis when venous embolic material passes through an intracardiac communication with right-to-left shunt, such as the patent foramen ovale or an atrial septal defect, and becoming a systemic arterial embolism. The embolic source in the venous system and the conditions for the development of a right-to-left pressure gradient enabling thrombus material to pass through the septal defect remain unclear.

Estimated to represent 2% of arterial emboli, paradoxical emboli can have catastrophic outcomes, with a reported early mortality rate of 21%; therefore, early diagnosis and treatment are important.

Coexistence of pulmonary embolism and systemic arterial embolism indicates the presence of paradoxical embolism, which suggests a diagnosis of an intra-cardiac defect. The most common intracardiac defect associated with paradoxical embolism is patent foramen ovale (PFO), which has been described in 25-30 percent of individuals. Most patients with a patent foramen ovale (PFO) remain asymptomatic.

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Case Report

A 54-year old man was admitted with 10 hours history sudden onset of severe acute ischemia of the both legs. His past medical history did not reveal embolic cardiac disease or intermittent claudication.

Prior surgical history revealed open appendectomy for the treatment of gangrenous appendicitis and purulent peritonitis 30 days ago.

Physical examination revealed febrile patient, 37.8°C, a blood pressure of 140/99 mm Hg, pulse of 96 beats/min, respiratory rate of 20 breaths/min Oxygen saturation to 98-99% oxygen. The lungs were clear bilaterally, and cardiac examination was normal. There was no jugular venous distension.

Closer examination revealed the left leg to be slightly pale and cool compared to the right. Examination of the leg pulses showed the absence of a left femoral arterial pulse, while in the right leg pulses were palpable as far as the popliteal fossa.

He denied chest pain, palpitations, cough, sputum production, smoking history, trauma or intermittent mild leg pain and swelling in the past.

His anticoagulation work up showed no evidence of factor V Leiden, antiphospholipid antibody screening was negative, and levels of factor VIII and homocysteine were normal. Levels of protein C, S and anti-thrombin III were unreliable in the setting of an acute thromboembolic event or during treatment with heparin.

Chest radiography was normal. Electrocardiogram (ECG) recordings documented constant sinus rhythm.

A transthoracic echocardiogram showed no evidence of intracardiac thrombus. Left ventricular function was normal. No evidence of shunt was seen on this examination.

Duplex ultrasound: Occlusions of the left external iliac and common femoral arteries and right distal popliteal arteries were confirmed by duplex Doppler ultrasonography, which also unexpectedly showed a right popliteal deep vein thrombosis.

Detected occlusion of the left extern iliac artery, superficial femoral artery and fresh emboli in the left profunda femoral artery (Figures 1-2).

Figure 1

Figure 2

Angiography confirmed the ultrasonographic findings and revealed a embolic occlusion of the right popliteal arteries, as well as a partial occlusion of the calf arteries in the absence of atherosclerotic wall lesions (Figures 3-4).

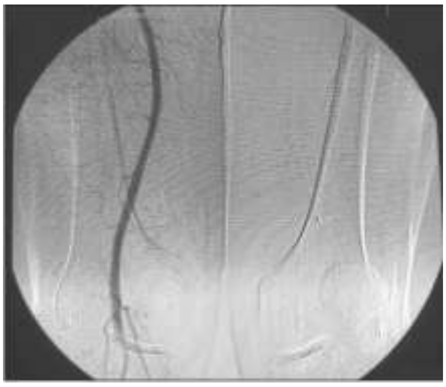

Figura 3 **Figura 4**

Arterial embolism, in particular paradoxical embolus, was suspected.

Transesophageal echocardiography (TEE) did not reveal a cardiac source of embolization but showed tricuspid regurgitation (PAP at least 12 ms); also, TEE identified a 7 mm patent foramen ovale (PFO) (Figure 6) with spontaneous right-to-left shunt (RLS) (Figure 5).

Figura 5: TEE – demonstrating a right-to-left shunt (RLS)

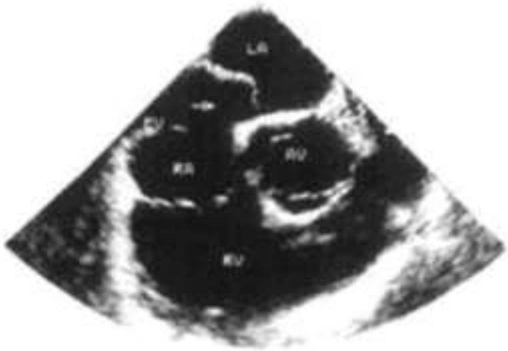

Figura 6: TEE of a patent foramen ovale (PFO)

There was no proof of intracardial thrombus or aneurysm.

The right ventricle was normal, and pulmonary embolism was not confirmed.

The diagnosis at this time was paradoxical embolism, patent foramen ovale, 7mm intraarterial shunt, right leg deep popliteal vein thrombosis and acute bilateral lower limb ischemia by extensive arterial thromboembolism.

So, a diagnosis of paradoxical arterial embolus was made.

Intraoperative findings confirmed the paraclinic diagnosis. This necessitated emergent, surgical bilateral catheter thrombembolectomy of the aortic, iliacal, common, superficial and profunda femoral arteries, popliteal arteries and bilateral tibial-peroneal trunk via bilateral femoral, also left distal popliteal arterio-tomies was performed, successfully.

Doppler ultrasound of the lower extremities done postoperatively revealed no extending of right popliteal vein thrombosis.

The patient's leg perfusion was adequate after thrombectomy.

Postoperatively, to avoid further embolic events the patient received continuous unfractionated heparin followed by long-term oral anticoagulation therapy.

The early postoperative period was very good with no surgical or medical problems. The patient was discharged 2 weeks after surgery, asymptomatic. The patient has had no further embolic episodes, and he has been advised to continue oral anticoagulant treatment.

Discussion

Paradoxical embolism describes the passage of a venous embolus across an intracardiac defect or a right to left shunt across the great vessels to lodge in the systemic arterial circulation. Paradoxical emboli lodge with almost equal frequency in the cerebral or limb circulations, but they may occasionally reach the coronary, renal, or splenic arteries (37% cerebral, 49% peripheral, 9% coronary, 1% renal, and 1% splenic).

When an arterial embolism occurs without the presence of documented risk factors, the probability that the embolism originated in the left side of the heart is small. In this case PDE should be considered, and a search for DVT or PE should be made. The finding of acute PE or DVT, it also demonstrates that embolization has occurred. Pulmonary embolism is present in most reported cases of PDE.

Patients with arterial embolism without evidence of PE intracardiac or proximal arterial source should have an evaluation beginning with TTE.

The most frequently cited criteria for the diagnosis of paradoxical embolism are:

1. Embolism in arterial system that is not originated from left heart or from the arterial system itself;
2. Abnormal communication between the arterial and venous systems as evidenced by imaging tests;
3. Presence of venous thrombosis or embolism in the form of deep vein thrombosis or pulmonary embolism;
4. Increased right sided pressure which contributes right to left shunting be it transient or long-standing.

Because of the importance of DVT as an initial source of PDE, rigorous exclusion of DVT is especially important in patients with unexplained arterial embolic events. It is well established that DVT may be clinically occult even in patients with documented PE (> 50% of cases). This patient most likely has a hyper-coagulable state which predisposed him to DVT-recent abdominal surgery and immobilization.

Treatment consists of anticoagulation to prevent progression of the clot Anticoagulation remains the first line treatment for paradoxical embolus, but when this is contraindicated or compliance with treatment is unlikely to be successful insertion of a vena caval filter will be required. Paradoxical embolus is not an indication for heart surgery unless anticoagulation or a vena caval filter fails to control emboli satisfactorily. Closure of the PFO after the first embolic event is suggested for patients at high risk for a recurrent embolic event (atrial septal aneurysm, high shunting volume, PFO larger than 3.4 mm, high mobility of the PFO valve, a history of recurrent embolic events, and a hypercoagulable state).

In our patient, there are no recurrent embolic events; a follow up TEE is planned to evaluate his right ventricular function and subsequent PFO closure plan will be based on the results of TEE.

Conclusion

No specific preexisting illness was consistently noted, and no comorbid conditions were listed. Risk factors for the development of venous thromboembolism were common and included cancer, recent surgery, immobilization, medical history of DVT and/or PE, obesity, old age, and the presence of anti-cardiolipin antibody.

The treatment includes thrombectomy, thrombolysis, an IVC filter (if indicated) and anticoagulation. If PFO closure is indicated, right ventricular function should be assessed preoperatively to prevent exacerbation of right ventricular dysfunction.

Failure to recognize PDE is potentially disastrous, because leaving patients at risk of limb ischemia, amputation and potentially lethal future embolic events across an unrecognized ASD.

When PDE is suspected, anticoagulation alone is inadequate and emergent surgical consultation is indicated. In this case, immediate diagnosis was crucial to the initiation of therapy to salvage this patient's leg. In addition, investigation of the lower limb symptoms led to the finding of contralateral thrombosis and to the search for the ASD, which connected the systemic arterial emboli to the venous thrombosis.

Abbreviations

DVT = *deep venous thrombosis;* EKG = *electrocardiogram*; PE = *pulmonary embolism;* PFO = *patent foramen ovale*; TEE = *transesophageal echocardiogram;* ASA = *atrial septal aneurysm;* INR = *international normalized ratio*; RLS = *right-to-left shunt.*

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Risk factors for early and late primary patency after aorto-iliac surgery prospective study on 235 consecutive patients*)

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Abstract

Increasing incidence and prevalence of the aorto-iliac pathology, due to the increase of average life expectancy, significant improvement in diagnostic techniques and population's access to top medical services, urged for a continuous evolution of surgical techniques and specific materials, equipments and devices. Recognition, evaluation and analysis of risk factors' influence on the primary patency prove as extremely useful for the improvement of postoperative results.

In the frame of a prospective study which took place between November 2001 and May 2003 in the Department of Vascular Surgery, Timone Hospital, in Marseilles, France, we selected a group of 235 patients diagnosed and operated for aortic and/or iliac pathology. We analyzed the influence on the primary patency of the following risk factors: age, sex, smoking, diabetes mellitus, arterial hypertension, hypercholesterolemia, cardiac, respiratory, neurovascular and renal status.

***Results**: primary patency rates range between 96.8% at 30 days and 84.4% at 5 years. Overall amputation rates range from 1.7% at 30 days to 12.3% at 5 years. Patients were classified in risk groups according to acknowledged recommended standards for reports. Smoking, diabetes, cardiac and renal status are significant risk factors for primary patency.*

Keywords: *primary patency, risk factors, aorto-iliac pathology, age, sex, smoking, diabetes mellitus, hypertension, dyslipidemia, cardiac, respiratory, neurovascular, renal status*

Introduction

Aorto-iliac surgical pathology is represented mainly by primary lesions – aneurysms, occlusions and arterial dissections, and in a much lesser proportion by secondary lesions – anastomotic false aneurysms and aorto-digestive fistulas. Aortic aneurysms affect 2-5 % of men over 60 years old and represent the 13th overall cause of death and the 10th cause of death for men over 55 [1]. Occlusive lesions affect 5-8 % of global over 60 years old population, reaching up to 18 % of men over 65 [2]. The increase

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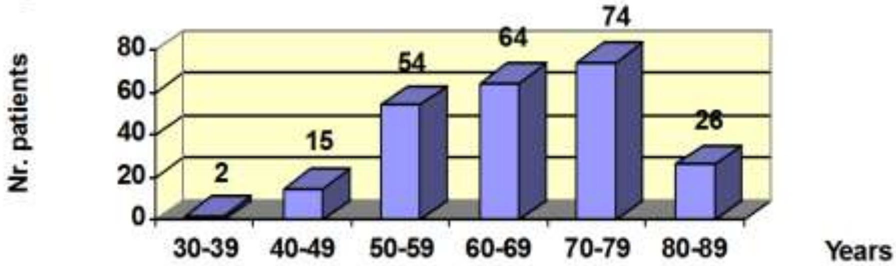
of average life expectancy, significant improvement in diagnostic techniques and population's access to top medical services reflect in continuous increase of incidence and prevalence of this pathology, playing for a major challenge of the contemporary vascular surgery, with important consequences upon the population health status and upon the costs that diagnostic and treatment presume for the medical system. The need to improve postoperative results determined continuous innovations, occurrence of several surgical techniques and specific materials, equipments and devices, beginning with skin incision and ending with continuous graft fabric innovation. Subsequently, classic surgical procedures were associated or replaced by those endovascular and laparoscopic [3, 4]. Technical progress improved results in a considerable measure, but the last years demonstrated a relatively stable evolution. Thus, recent studies focused on the risk factors that, once identified, can lead through exposure decrease to significant improvement of postoperative results. Recognizing as main risk factors age, sex, smoking, diabetes mellitus, dyslipidemia, high blood pressure, cardiac, respiratory, neurovascular and renal status [5, 6], the primary patency is defined by international guides as "*a graft considered to have uninterrupted patency with either no procedure performed on it or a procedure (e.g., transluminal dilation or a proximal or distal extension to the graft) to deal with disease progression in the adjacent native vessel. Thus, the only exceptions that do not disqualify the graft for primary patency are procedures performed for disease beyond the graft and its two anastomoses. Dilations or minor revisions performed for stenoses, dilations, or other structural defects, or closing missed arteriovenous fistulas in an in situ vein bypass graft before occlusion do not constitute exceptions, as they are intended to prevent eventual graft failure*" [7, 8, 9].

Material and methods

In the frame of a prospective study which took place between November 2001 and May 2003 in the Department of Vascular Surgery, Timone Hospital, in Marseilles, France, we selected a group of 235 patients operated through various procedures for aorto-iliac pathology: 110 aneurysms, 110 occlusions, 5 dissections, 4 anastomotic false aneurysms and 6 aorto-digestive fistulas, in a 5-years postoperative follow-up. 208 patients were men (88.5%) and 27 women (11.5%). Mean age for selected patients was 66.1 years, ranging from 30 to 87 years old, standard deviation = 11.2 years. For male patients, mean age was 66.2 years, ranging from 30 to 87 years (SD = 10.98), while for female patients, mean age was 65.5 years, ranging from 31 to 87 years (SD = 13.26). Mann-Whitney test for age variance analysis shows significant differences between selected patients' ages (p = 0.000). Patients' distribution on decades of life is presented in Figure 1.

Fig. 1. Patients' distribution on decades of life.



99 patients (42.1%) presented history of vascular records, 81 (34.5%) cardiac records and 150 (63.8%) other significant medical or surgical records. 142 cases (60.4%) presented specific symptomatology at hospital admission, but 93 were completely asymptomatic.

Clinical examination was relevant in 166 de cases (70.6%), significantly superior for occlusive lesions (100 cases, 90.9%) group compared the aneurysms group (62 cases, 56.4%). 97 patients (41.3%) were assessed with associated peripheral arterial occlusive disease. 40 patients (17%) were operated in emergency, for the rest of them elective surgery was performed.

Average preoperative follow-up between diagnostic and surgery was 379 days, ranging between 1 to 4800 days.

148 patients (63%) were operated by conventional open surgery, in 86 cases (36.6%) endovascular procedures were used and in 1 patient (0.4%) a totally laparoscopic aorto-aortic by-pass was performed.

Secondary patency curves were assessed through Kaplan-Meier method, risk factors were analyzed using ANOVA and Mann-Whitney test and Cox test was used to compare risk factors influence on the secondary patency.

Results

Primary patency rates for the global batch range from 96.8% at 30 days to 84.4% at 5 years.

Global batch, aneurysms and occlusions groups as well as endovascular procedures groups' findings are shown in Table 1 (next page).

Early 30-days primary patency was 96.8% for overall patients, 97.4% for aneurysms and 96.2% for occlusive disease. Depending on the procedure, we found 30-days primary patency of 97.2% for PTA, 95.8% for stent-grafts and 97% for overall endovascular procedures, compared to 96.4% for open surgery.

After 5 years of follow-up, the best primary patency results were found in patients with aortic aneurysms (86.3%), while patients with occlusive lesions presented less favorable results (83.2%). Overall endovascular procedures shown 83.1% patency (82.8% for PTA and 83.8% for stent-grafts), compared to 85.4% for open surgery.

There were noted 4 amputations at 30 days, raising the early amputation rate to 1.7%. Out of them, 2 were major (calf) and 2 minor (1 forefoot, 1 finger). 5-years amputation rate rises to 12.3%, 29 patients required amputations, 15 major (thigh, calf) and 14 minor (forefoot, fingers).

Table 1: Primary patency for global batch and major pathology groups (%).

	Global	AAA	Occlusions	Stent-grafts	PTA
30 days	96.8	97.4	96.2	95.8	97.2
1 yr	92.9	94.1	91.3	90.0	94.5
2 yrs	90.3	91.9	88.1	95.4	92.4
3 yrs	88.0	89.4	86.9	85.0	90.4
4 yrs	86.4	88.6	85.6	94.1	88.0
5 yrs	84.4	86.3	83.2	83.8	82.8

Regarding risk factors, patients were distributed on risk groups as follows:

A) Smoking

- class 0 (never smoked or quit for at least 12 months) = 136 patients (57.9%)
- class 1 (active smokers) = 99 patients (42.1%)

B) HTA

- class 0 (normal tensional values without treatment or requiring maximum 1 drug) = 171 patients (72.8%)
- class 1 (patients requiring 2 or more drugs) = 64 patients (27.2%)

C) Diabetes mellitus

- class 0 (non-diabetic patients) = 200 patients (85.1%)
- class 1 (diabetes mellitus type I or II) = 35 patients (14.9%)

D) Hypercholesterolemia

- class 0 (normal cholesterol values without treatment) = 123 patients (52.4%)
- class 1 (requiring dietary or drug treatment) = 112 patients (47.6%)

E) Cardiac status

- class 0 (asymptomatic, normal ECG) = 151 patients (64.3%)
- class 1 (AMI records, stable/unstable angina, NYHA class III/IV congestive heart failure, LVEF<45%, severe cardiac arrhythmias) = 84 patients (35.7%)

F) Neurovascular status

- class 0 (asymptomatic with carotid stenosis < 70%) = 204 patients (86.8%)
- class 1 (asymptomatic with carotid stenosis > 70%, symptomatic with stenosis < 70%, sequelar or transient stroke records, carotid conventional surgery or endovascular procedures records, carotid occlusion) = 31 patients (13.2%)

G) Respiratory status

- class 0 (no/slight ventilatory dysfunction) = 192 patients (81.7%)
- class 1 (mild/severe ventilatory dysfunction) = 43 patients (18.3%)

H) Renal status

- class 0 (serum creatinin < 1.5mg%) = 199 patients (84.7%)
- class 1 (serum creatinin > 1.5mg%, renal transplantation, nephrectomy) = 36 patients (15.3%)

Discussions

At 30 days, endovascular procedures and aneurysms seem to show the best results, while after 5 years of follow-up, open surgery and aneurysms presented higher patency rates, confirming thus previously published results [10, 11].

A. Age. For the global batch of patients, mean age of the patients who presented primary thrombosis during follow-up was 63.5 years, compared to 66.4 years for those with preserved primary patency. The difference is not statistically significant, p = 0.195 (ANOVA).

B. Sex. 5-years primary patency for the global batch was 89.5% (17 cases out of 19) in women, superior to 83.8% (135 cases out of 161) in men, but without significant difference, p = 0.327 (Cox test).

C. Smoking. 5-years primary patency for non-smokers rose to 93.2%, compared to 80.6% for smokers. The difference is statistically significant, as shown by the Cox test: p = 0,012; Risk Ratio = 2.47 (Figure 2).

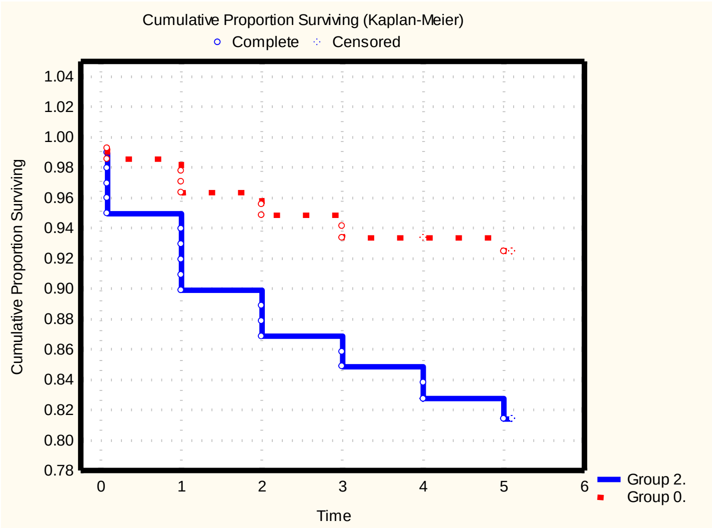


Figure 2: Kaplan-Meier primary patency curves smokers vs. non-smokers.

D. Arterial hypertension. 5-years primary patency for group 0 was 87.8%, compared to 86.9% for group 1. Descriptively, group 0 patients present a slightly superior prognostic, but the difference is not statistically significant (Cox test: p = 0.500) (Figure 3).

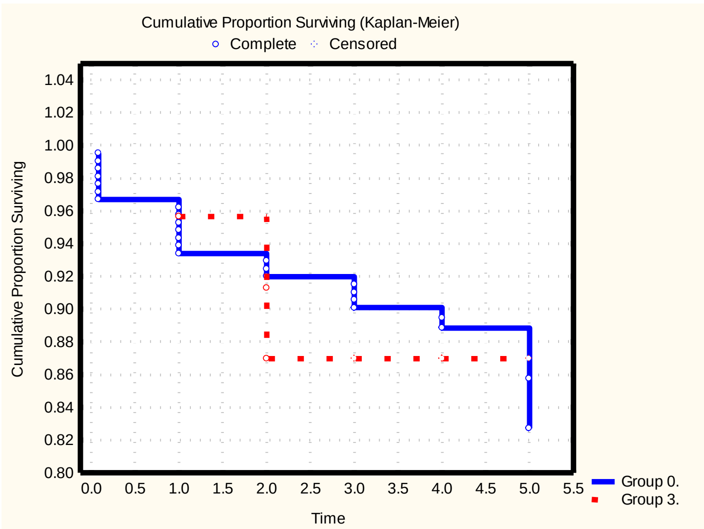


Figure 3: Kaplan-Meier primary patency curves for HTA risk.

E. Diabetes mellitus. 5-years primary patency for group 0 patients was 94.3%, compared to 50.7% for group 1 patients. The difference is statistically significant, demonstrated by the Cox test: p = 0.000 (Figure 4). Diabetic patients present 2-fold higher relative risk of thrombosis (Risk Ratio = 1.95) compared to non-diabetic patients.

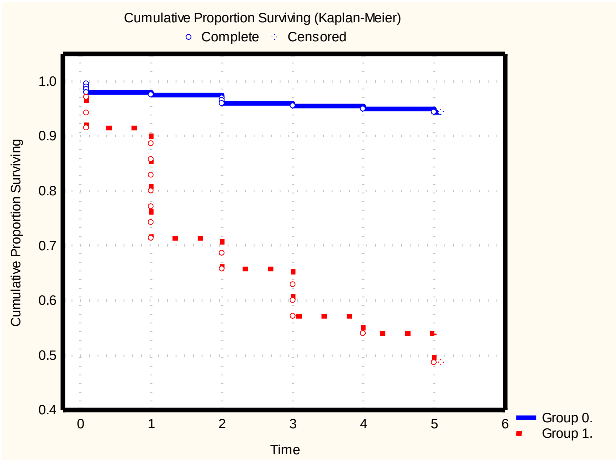


Figure 4: Kaplan-Meier primary patency curves for diabetic risk.

F. Hypercholesterolemia. 5-years primary patency for group 0 was 89.7%, compared to 85.9% for group 1. Descriptively, the patients from group 1 present a more favorable prognostic, but the difference is not statistically significant (Cox test: p = 0.094) (Figure 5).

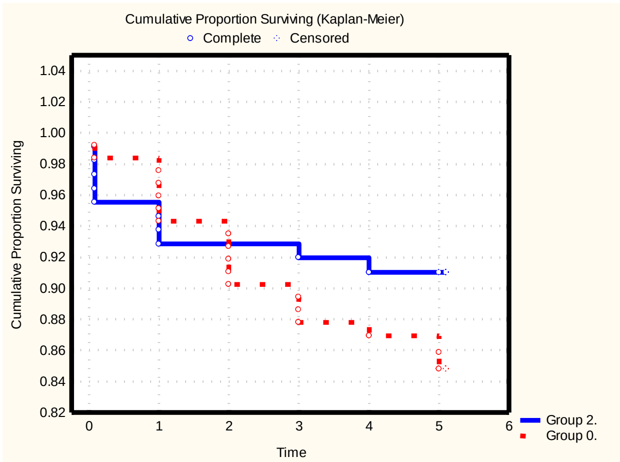


Figure 5: Kaplan-Meier primary patency curves for dyslipidemia risk.

G. Cardiac status. 5-years primary patency for group 0 rises to 93.9%, compared to 76.2% for group 1. The difference is statistically significant, patients with coronary arteries disease having a nearly 3-fold higher relative risk of thrombosis. Cox test: p = 0.004, Risk Ratio = 2.78 (Figure 6).

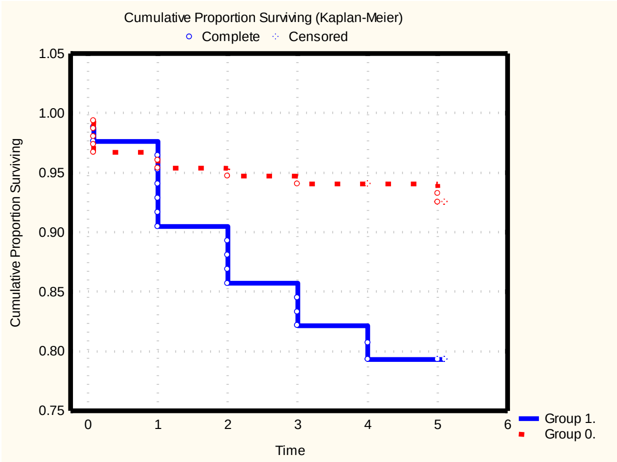


Figure 6: Kaplan-Meier primary patency curves for cardiac risk.

H. Respiratory status. 5-years primary patency for group 0 was 88.2%, compared to 85.4% for group 1. Descriptively, the patients from group 0 present a more favorable prognostic, but the difference is not statistically significant (Cox test: $p = 0.204$) (Figure 7).

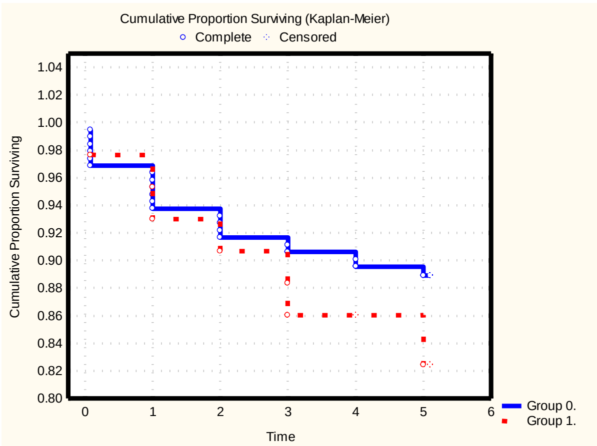


Figure 7: Kaplan-Meier primary patency curves for respiratory risk.

I. Renal status. 5-years primary patency for group 0 was 89.9%, compared to 77.3% for group 1. The difference is statistically significant, Cox test: $p = 0,033$, Risk Ratio = 3.05 (Figure 8).

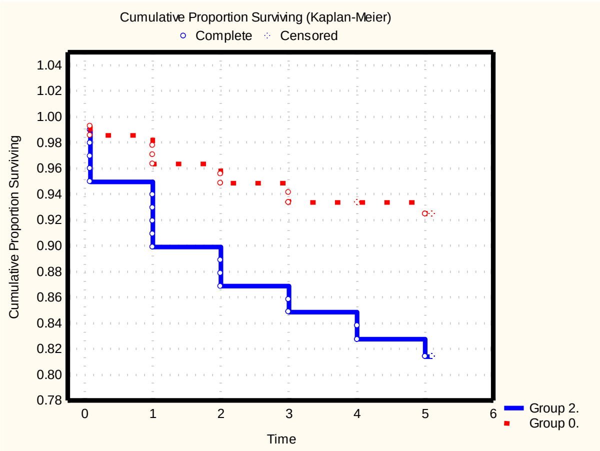


Figure 8: Kaplan-Meier primary patency curves for renal risk.

J. Neurovascular status. 5-years primary patency for group 0 was 88.9%, compared to 78.7% for group 1. Descriptively, the patients from group 0 present a more favorable prognostic, but the difference is not statistically significant (Cox test: $p = 0.183$) (Figure 9).

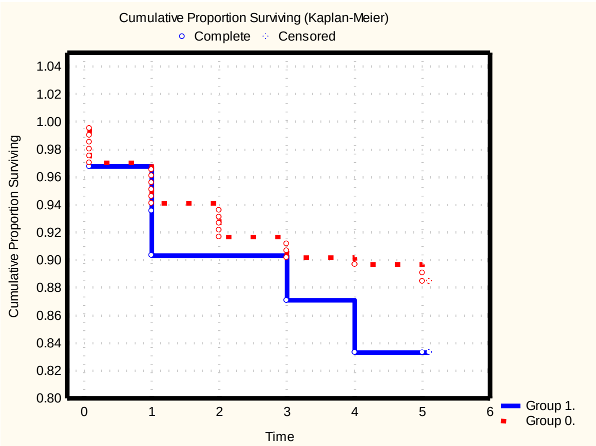


Figure 9: Kaplan-Meier primary patency curves for neurovascular risk.

Conclusions

Primary patency rates significantly improved during the last years, due to improvements in diagnostic and treatment techniques, population's access to top medical services, risk factors identification and decrease of population's exposure to risk factors.

The most favorable results in what concerns the primary patency were noted for patients hospitalized for aorto-iliac aneurysms, while patients with occlusive lesions demonstrate less favorable results. Endovascular procedures and open surgery lead to primary patency rates that are comparable, slightly better for endovascular at 30 days and for open surgery at 5 years, without statistically significant difference. Early 30-days primary patency is not significantly influenced by any of the recognized risk factors.

Late 5-years secondary patency is significantly influenced by the following risk factors: smoking, diabetes mellitus, cardiac and renal preoperative status.

Eviction or at least decrease of exposure to the preoperative risk factors, leading to a redistribution of patients in lower risk classes, could determine a significant improvement of the late primary patency, associated to an improvement of the general status and a decrease in associated pathology, mainly responsible for postoperative complications.

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Obliteration of Saphenous Trunks with Hyperheated Steam*)

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Introduction

Endovenous heating techniques have been in clinical use since 1999. Long-term results are now available for both Radio-frequency and Endovenous laser. These results compare favorably with the reference: high ligation + stripping of the vein.

The cost of the equipment and disposable items necessary to implement these methods is too high for many health systems in the world.

The ideal technique would combine the advantages of both currently used methods, and obviate their drawbacks.

Heating the vein with hyper-heated steam may provide significant medical and economical advantages.

Principle

Water can be found in three physical states: ice, liquid and vapor.

In ice, H_2O molecules stick to one another. If heat is added, they become separated by less than 1 molecular diameter: it is the liquid phase, water as we drink it. If more heat is added, molecular agitation increases and H_2O molecules leave the surface as water vapor.

This process is reversible: when vapor cools down as liquid, it gives back to surrounding molecules the heat which was used to change its state.

A lot of heat is necessary to achieve the transition, thus vapor contains a lot of "latent heat" which can be used for heating tissues. As an example, more than 2000 KJ are needed to vaporize 1 liter of water at atmospheric pressure.

Transition from liquid to vapor occurs at a temperature which is a function of pressure in the liquid: we all know that at atmospheric pressure, this temperature is 100°C.

If the pressure is increased to several hundred times atmospheric pressure, the steam will be emitted at a temperature of several hundred degrees Celsius: it is called "Hyperheated Steam".

Material

Practically, to emit steam at 150°C, we pressurize water at 80 Atm, then push it through a very small diameter tube (100 nm) heated by electrical current. The tube is at the tip of a hand-piece to which a catheter can be connected **(Fig. 2).** The 0.8 mm catheter

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emits vapor near the tip through 2 lateral holes. It can be introduced alone in the vein or in a F5 angiography catheter. A generator controls the process and pressurizes water **(Figure 1).**

Figure 1: The steam generator

Figure 2:
The endovenous catheter

In Vitro Studies

We have conducted studies on freshly stripped segments of Great Saphenous veins. This allowed us to select the best way to deliver steam in order to obtain shrinking of the collagen in the vein wall. We selected 2 pulses of 45 J/cm per centimetre of vein – which is close to what is delivered by endovenous lasers.

Macroscopically, immediate diameter reduction was evidenced **(Figure 3),** with separation of endothelial layer and media. No damage was seen in the adventicia. No perforation was evidenced.

Figure 3: Macroscopic view of heated vein on the left, untreated on the right side.

Microscopically, these findings were confirmed and widening of the media proved the lesion of collagen fibers.

Animal Studies

6 ewes were used for animal studies. The vein treated was the External Saphenous Vein of the posterior limb. 10 limbs were heated by water vapor, 2 by Radio-Frequency: Closure® catheter for comparative purposes. Different heating profiles were tested, with and without tumescence around the vessel.

Temperatures were measured per-operatively at different levels: on the skin, directly around the vein by thermocouple, and in the Inferior Vena Cava. Blood temperature was unchanged. Peri-venous temperature was elevated to 45°C without tumescence, 37°C with tumescence. Skin temperature was not modified.

No hemolysis was observed on blood samples. General parameters were not affected, except in 1 sheep that had tachycardia, but independently of heating. It was rather an anesthetic problem.

The veins were harvested at 1 month (4 limbs) and 3 months (8 limbs). No general complication was observed. No infection.

Veins heated at less than 45 Joules/cm were closed on segments and remained opened in other segments. Veins heated at 90 Joules/cm were closed on their full length.

Microscopic studies showed disappearance of endothelial layer, fibrotic tissue in the lumen extending into the media, no damage to the adventitia.

Clinical Study

A first clinical study was performed on 10 limbs in 8 patients in 2007. All were controlled by Duplex ultrasound 3 months, 1 and 2 years after treatment.

Technique: The procedure is very close to an Endovenous Laser. Vein access is obtained either by phlebotomy or by introduction of a 16G short catheter under Echo-guidance.The heating catheter is directly pushed in the vein, without a guidewire. Due to the shape of the tip, and the relative rigidity, catherization is usually fast and easy. The tip placement is checked by ultrasound: for a GSV, it is kept 3 cm away from the sapheno-femoral junction. Tumescence is then applied.

Vapor is emitted while removing the catheter: 2 consecutive pulses of 45 joules are sent, and then the catheter is removed on 1 cm.

Eccenctric compression is applied under a class 2 stocking. Patient leaves the hospital 2 to 4 hours after the procedure.

Material

Ages were 36 to 65, all were female. 9 veins were GSV and 1 SSV.

Results

No general complication was observed, no DVT. Post-operative pain was minimal: no drugs were given. Return to activity was fast, all patients left the hospital the same day.

1 per-operative complication occurred: a leg skin burn due to insufficient heat insulation of the catheter which came in contact with unprotected skin. This has been corrected on current devices.

All veins were obliterated at 3 months and 1 year, 1 partial reopening was seen at 2 years.

Since this pilot study, more than 1000 patients have been treated in 18 centers with similar long term results.

Discussion

Steam obliteration is safe. The only by-product of this technique is water. As each pulse vaporizes only 0,08 cc of water, a GSV can be obliterated wit 2 to 3 cc of water, a small quantity which will not induce hemolysis.

Its mechanism of action is close to Radio-frequency, with very even heating, as opposed to the more irregular pattern observed after endovenous laser (Proebstle, 1).

The absence of perforation and the fast heat exchange with vein wall lowers the risk of injury to surrounding structures – as a matter of fact, external cooling may be used when the vein is close to the skin, and obviate the necessity of using tumescence: further studies are planned in this direction.

With Laser obliteration, foul-smelling combustion gases are emitted and can be sniffed when removing the catheter: no study have been made of their eventual toxicity.

When compared with Foam obliteration, water vapor has several advantages: no chemical other than water, thus no risk of anaphylactic shock. No risk of deep vein thrombosis. No problem with persistent foramen ovale, or with lung capillary bed late sclerosis.

Conclusions

These results show that hyperheated stem is efficient in obliterating superficial veins at mid-term (2 years). Duplex imaging and measurements are very similar to what is observed after Closure ® RF obliteration.

The reduction in diameter is in line with what we found in a study of 25 limbs treated with Closure® (2).

A randomized multi-center study of Water vapor versus Endovenous laser is being performed at Erasmus Medical Center, Rotterdam (Pr Martino Neumann) to evaluate the advantage expected from this new technique.

Among these, the ability to obliterate perforators and collaterals with the same generator and small catheters or insulated needles is promising.

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La place du LASER endoveineux, dans la chirurgie des varices*)

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Abstract

La technique a été développé par l'équipe du Dr. Carlos Bone en 1997. En utilisant un laser de longueur spécifique se réalise un photocoagulation d'un vaisseau ayant pour cible soit l'oxyhémoglobine seul (810 nm) soit l'oxyhémoglobine et l'eau (940, 980 nm). Les résultats montrent sur les études publiées un taux moyen d'occlusion de 97% à 24 mois. Le LEV doit été curatif et non simplement palliatif, les crosectomies et les phlébectomies restèrent toujours necessaries. Les patients réfutent jusque-là et ceux refusant la chirurgie peuvent constituer une indication et bénéficier au moins d'un LEV du tronc saphène malgré l'indication de la crosectomie, permettait ainsi de supprimer l'essentiel du reflux. Ce traitement concerne aussi bien la chirurgie vasculaire que l'angiologie interventionalle. L'introduction de longueurs d'onde absorbées a la fois par l'eau et l'hémoglobine (980 nm - double pulse) potentialise le résultat.

Introduction

LEV - est une technique récente de scléroser un vaisseau par une méthode de photocoagulation qui produce une rétraction pariétale, en utilisant un laser de longueur spécifique ayant pour cible soit l'oxyhémoglobine seule soit avec l'eau qui lui confère un effet thermique supérieur.

La lumière est véhiculée par une fibre optique introduite par un cathéter de guidage.

Le but est l'oblitération du tronc saphène par sclérose endoveineuse qui est obtenu immédiatement et évolue en quelque mois.

La pratique de LEV nécessite une formation spécifique.

Le principe d'action du LASER

Le laser [*light amplification by stimulated emission et radiation*] est une dispositif optoélectronique, qui émise une lumière: monochromatique (une fréquence unique), cohérente (une phase identique sur le faisceau) et énergétique.

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Elle se comporte dans l'interaction avec le tissues comme une onde électromagnétique: une partie du faisceau est absorbée, une partie réfléchie en dépendant des caractéristiques des tissus rencontres.

La LEV este base sur une action thermique du laser; l'énergie délivrée en bout de fibre optique se transmet a l'hémoglobine qui va transférer sa chaleur a la paroi veineuse.

L'action thermique est composée de 3 étapes:

- Une conversion de lumière en chaleur
- Un transfert de chaleur
- Une dénaturation thermochimique des constituants tissulaires.

Le résultat est un échauffement pariétal suffisant pour léser l'endothélium et rétracter le collagène de la media avec la destruction de l'endothélium et la formation du thrombus qui adhère immédiatement a la paroi veineuse. Comme après une sclérose chimique.

Le chauffage du collagène de la media se traduit par un épaississement pariétal visible en échographie des la fin de la procédure, suivi après d'une rétraction de la paroi qui va permettre l'oblitération définitive de la veine.

Cette action dépend à la fois des paramètres du laser et des coefficients tissulaires (optiques, thermiques, thermochimiques).

Les fréquences de travail des lasers endoveineux ont évolue au cours du temps de la 810 nm initiaux a 840 nm et 980 nm.

Méthodologie

Technique courante

LEV est un acte chirurgical qui se réalise au bloc opératoire, après une consultation préopératoire, bilans cardiologique et biologique.

La durée d'hospitalisation est de 24 heures. L'ambulatoire, est possible sous anesthésie locale quand un seul axe est traite.

On doit faire une cartographie veineuse pour mentionner:

- La profondeur de l'axe a traiter.
- L'épaisseur de la paroi qui peut guider le réglage de la puissance laser
- Le diamètre du vaisseau
- La hauteur précise de la crosse en décubitus
- Le repérage de l'artère fémorale
- Le siège des perforantes avec diamètre, sens circulatoire et profondeur
- Les branches incontinentes
- L'effet de la pose d'un garrot sur le Hunter qui peut diminuer le reflux de la crosse

Aspect chirurgical

La position est le Trendelenburg. Le cathétérisme peut s'effectuer selon 2 modalités:

1. par abord transcutanée-cathétérisme type seldinger (une ponction echo-guide de l'axe saphenien).

2. par abord chirurgicale incision de quelques millimètres puis recherche de la veine au crochet Muller, veinotomie et introduction du cathéter.

On réalise alors l'anesthésie du trajet par tumescence. La solution adoptée est dérivée de celle proposée pour les liposuction-serum physiologique additionne de lidocaine adrénaline 0,03% tamponnée en bicarbonate 1,4%.

Le but est d'infiltrer la gaine peri-sapheniene pour anesthésier le vaisseau, eloigner les structures adjacentes (nerfs, lymphatiques) et comprimer la veine pour diminuer l'afflux sanguin.

L'infiltration est guidée par l'échographie pour s'assurer de la location dans la gaine periveineuse. Les quantités injectées varient selon les auteurs de 60 cc a 300 cc.

Après l'introduction de la sonde jusqu'à la jonction saphéno-fémorale se poursuit la transillumination de la fibre qui permet un repérage de la jonction saphéno-fémorale. La disparition de la lumière à travers la peau signe le passage dans la veine fémorale.

On peut se faire le cathétérisme antérograde avec crosectomie ou sans crossectomie, à partir de la malléole ou de la jarretière et l'endosclerose est rétrograde a partir de 1 à 2 cm en dessous de la jonction saphéno-fémorale. Les impulsions durent une seconde et la puissance est de 12 a 14 W pour 810 nm: En 980 nm. (Laser, Surgyles, Double pulse) à 10 W et 1,5 à 3 secondes.

Le mode de tir peut être pulse ou continu. En mode pulse le laser délivre son énergie pendant une durée réglable, 2 secondes puis un repos d'une seconde et un tir a nouveau.

L'opérateur retire la fibre de quelques millimètres entre deux tirs: par exemple 3 mm si la puissance de tir est de 12 watts, l'énergie délivrée sera de 12 x 2 x 3 = 72 joules/cm.

En mode continu, la fibre est retire lentement mais sans interruption, ce qu'il exposerait moins aux perforations, donc aux hématomes post-opératoires parfois douloureux.

Mais il n'existe pas des études randomisées comparant les deux procédures.

Le laser infrarouge étant par définition invisible a l'oeil, il est associe a un laser Heliumneon de faible puissance. Émettant dans le rouge ou le vert et donc visible a l'extrémité de la fibre. Au moment du tir, particuliermént en mode pulse, cette lumière s'accroît puis diminue progressivement, ce qui traduit le rétrécissement de la veine. Au contraire, un éclair brutal parfois observe témoigne d'une perforation avec combustion partielle de la paroi, source d'hématome et de douleurs post opératoires.

Des problèmes particuliers posent les dilatations ampullaires on sacculaires ou l'échauffement peut être insuffisant, et l'on observera une thrombose avec une réaction inflammatoire sur le trajet, qui pourra se repermeabiliser.

Le tir pulse permet d'insister sur ces zones. On recommande de diminuer l'énergie délivrée au niveau du genou car la grande veine saphène est sous-cutanée et le nerf adjacent colle à la veine peut être lèze par un échauffement trop importante.

Les yeux des personnes pressentes dans la salle sont obligatoirement protéges par de lunettes adaptées.

Après le traitement, se pose un bandage compressif, avec une contention élastique pendant 1 mois - 3 mois.

Il n'y a pas de consensus au sujet de la prophylaxie des thromboses veineuses profondes par héparine de bas poids moléculaire.

On peut instaurer un traitement avec HBPM pour 5 jours a tous patients opères, ou seulement a ceux qu'ont d'antécédents personnels ou familiaux de thrombose veineuse. Les patients peuvent quitter le service deux heures après l'intervention.

La reprise d'activité se fait dans les 72 heurs, 8 jours maximum si plusieurs axes saphènes sont traits en même temps.

La durée globale de la procédure jusqu'au pansement est de 45 minutes a une heure pour un ou deux axes traites.

Résultats

Incidents et complications sont devenus rares et consistent en:

- les brûlures cutanées
- les hématomes douloureux
- les réactions inflammatoires sur le trajet de la veine dues a un chauffage insuffisant
- les thromboses veineuses profondes (1% des cas)
- la repermeabilisation est comparable a celui des autres méthodes endoveineuses: radio-frequence et mousse sclérosante

Avantages

On permet d'éviter les complications liées a l'incision du scarpa (lymphorees et retards de cicatrisation).

On facilite une éventuelle reintervention pour récidive.

On diminue la fréquence et l'importance des hématomes.

On peut reprendre plus rapide l'activité professionnelle.

L'absence de neogenese au niveau de la jonction saphéno-fémorale.

On permette d'intervenir chez des patients anticoagules et porteurs des prothèses cardiaques mécaniques, avec complications thrombotiques minimes Aux Etats Units le LEV est utilise sur des saphènes de gros calibre jusque'a 20 mm.

Conclusion

Le LEV est un traitement prometteur qui nécessite pour utilisation une formation spécifique.

Il constitue une sclérose classique par l'onde laser; mieux absorbé à la fois par l'eau et l'hémoglobine (980 nm) potentialise le résultat.

Les excellents taux d'imperméabilité a deux ans, le fait que l'on puisse traiter des saphènes jusqu-à 28 mm de calibre et la spécificité vasculaire de l'effet thermique laisse présager sa supériorité par rapport aux autres techniques endovasculaires.

Le traitement doit être curatif: les crosectomies et les phlébectomies resteront toujours nécessaires.

L'Incontinence évolue de la crosse impose une crosectomie avec LEV concomitant. Le reflux isole du tronc nécessite seulement un PEV par cathétérisme.

Le LEV permet d'optimiser la coopération angio-chirurgicale dans les choix de stratégie thérapeutique, de traiter uniquement les segments veineux qui sont pathologiques minimisant le traumatisme chirurgical et limitant l'angiogenèse ultérieure.

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The place of endovenous laser in varicose veins surgery*)

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Abstract

The authors are presenting the case of a 56 years old female that presented into the cardiovascular surgery clinic following multiple transient ischemic attacks. The patient proved to have multiple cardiovascular risk factors (hyper-uricaemia, dyslipidaemia, and is a smoker). The imagistic investigations (Doppler evaluation and angiography) showed a stenosis of the internal carotid artery of > 80%. The patient agreed to undergo an endovascular technique-balloon expandable stent Flex force 4/16mm. No filter protection was possible due to the particular anatomy of the patient (kinking of the distal internal carotid artery). Following the procedure, the patient undergone antiplatlet therapy and has been evaluated regularly clinically and imagistic (echo). After 6 months the same evaluation mentioned above proved the existence of a 60% intrastent restenosis. Open surgery was performed: endarterectomy with stent removal and dacron patch of enlargement. Postoperative follow up was without complications. Anticoagulant therapy was started and she had to undergo an echo Doppler evaluation every month. Open surgery for extra cranial carotid stenosis is the gold standard at present. It also is a safe technique for the treatment of intrastent restenosis.

Introduction

Carotid atheromatosis is one of the major causes of stroke. The prevalence of the carotid artery stenosis is 5% in the 6th decade and increase to 10% at ages over 80 years old. Carotid artery stenosis could be symptomatic, discovered during the clinical evaluation or through imaging techniques. The clinic is associated with ischemic transient attacks. The main treatments are: medical therapy, endovascular treatment, carotid endarterectomy (open surgery).

Case report

A 56 years old female, M.A., presented to the cardiovascular surgery clinic following the indication of the family doctor (no emergency) in January 2006 complaining of a progressive "difficulty in speech (debit of speech), balance troubles, right transient partial hemianopsia and tinkling in the left hand".

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The clinical evaluation revealed equilibrium imbalance, dysarthria, amaurosis fugacae, paraesthesia in the left hand, the BP - 140/80mmHg. Personal pathological antecedents were: appendectomy, psoriasis, transient ischemic attacks in the last 3 months that were not medically evaluated, hyperuricaemia, dyslipidaemia, polyarthrosis, and peripheral arteriopathy. The patient was at physiological menopause for 6 years and had not undergone hormone replacement therapy. As behavioral risk factor, the patient was a smoker and had stopped recently. The arteriographic evaluation from 13.01.2006 showed a suboclusive stenosis of the right internal carotid artery located at 2 cm from the bifurcation of the common carotid artery (fig. 1).

Figure 1

The treatment chosen was pharmacologic Sortis 20 mg (atorvastatinum) and Aspenter 75 mg (acetyl salicylic acid) 1/day, dietary indication and stopping smoking. An interim evaluation (01.02.2006) showed: Ap 100%, INR - 1, Fbg 365 mg%, normal blood cell count, normal values of the BUN, GLU, and CRE. The patient was programmed for the endovascular technique and continued the treatment with Sortis 20 mg 1 tablet/day, Aspenter 75 mg 1 tablet/day and dietary restriction.

The patient undergone on 28.03.2006 an implantation of an expandable balloon stent Flex force of 4/16 mm. The use of a protective filter (Filterwire EX) was not possible due to a carotid kinking. The residual stenosis was of 10-15% and the anterograde flow was normal (Figure 2).

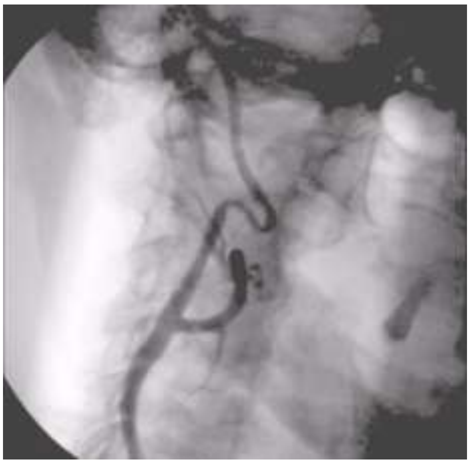

Figure 2: Angiography after stent implantation

There were no neurological complications during the procedure. The patient left the the hospital with the following medication: Aspenter 75 mg 1 tablet/ day, Plavix 75mg (clopidogrelum) 1 tablet/day and Lescol 20 mg/day. The follow-up was using the Echo Doppler evaluation:

On 11.05.2006

- *Right CCA* - IMT 0.7 mm (N), normal flow having Vs max 75 cm/s and VTD 20 cm/s and IR 0.72.
- *ICA* - mixed atheromatosis mostly calcified on a length of 20 mm from the origin of the artery; stent present at the distal part of the atherome zone and more difficult to be identified in the calcified area, flow present on the entire length of the prosthesis having the Vs max of 72 cm/s and VTD 23.5 cm/s and IR 0.67.
- *ECA* - thickened wall, fibrous, with normal flow of Vs max 113 cm/s, VTD 25 cm/s, IR 0.76.
- *Left CCA* diffuses fibrous thickening of the wall, with the 1.3 mm thickness, normal flow, IR 00.71.
- *Bulb* mixed calcified anterior atherome of 1.7 mm thickness.
- *ICA* - small anterior atherome that is calcified and of 1.4 mm thickness, normal flow, IR 0.55.
- *ECA* - normal flow and aspect; IR 0.78.

On 07.08.2006

- *Right CCA* - IMT 0.9 mm (N), normal flow having Vs max 70 cm/s, VTD 20 cm/s, IR - 0.71.
- *ICA* with mixed atheromatosis, mostly calcified on a length of about 2 cm proximally to the bifurcation, with the stent visible at the distal part of the prosthesis; at this point, the ICA has an angle that has normal flow. *The blood flow is present on the entire length of the prosthesis,* proximally with Vs max 58/s, VTD 22.5 cm/s, IR - 0.61 and distally, before the angulation, Vs max 103 cm/s, VTD 26.5 cm/s, IR - 0.74.
- *ECA* - thickened wall, normal flow, IR - 0.8.
- *Left CCA* - IMT of 1.2 mm (mildly higher that normal), normal flow, IR - 0.61.
- *ICA* - few calcified atherome, normal flow, IR of 0.52.
- *ECA* - normal flow and aspect, IR - 0.8.
- The angiographic evaluation on 26.10.2006 showed a 60% stenosis of the distal part of the stent (figure 3).

Figure 3: Angiography showing distal in stent restenosis

On 16.11.2006

The patient presented to the cardiovascular clinic with mild dysarthria. The patient declared to have followed the medication without cessation of smoking. Blood workout -, Fbg - 538 mg%, INR 1.19; Glycaemia 140 mg/dl, normal BUN, CRE, AST, ALT at admittance into the hospital and TQ 11.4sec, Ap 96%, INR 1.03 APTT 26.2 sec, Fbg - 626 mg%, at the time of surgery.

It is decided to undergo open surgery, under general anesthesia - endarterectomy of the CCA and of the ICA with the extraction of the stent that was inclavated in the endartera, and enlargement angioplasty with Dacron patch (Figures 4-5).

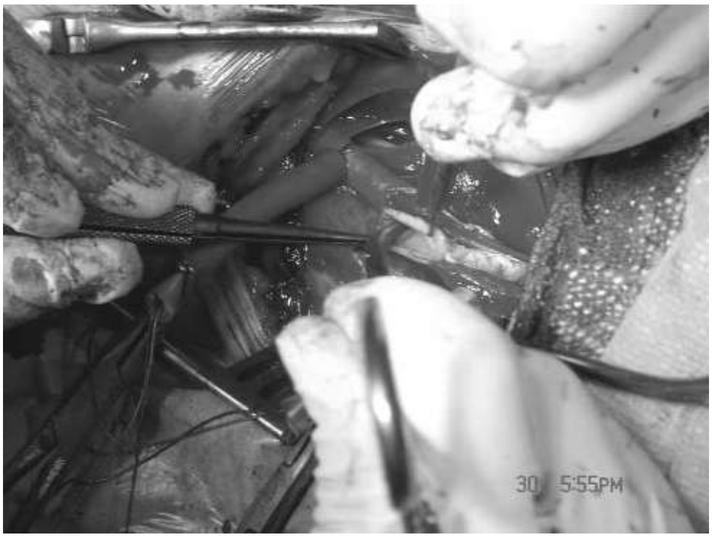

Figure 4:
Dissecting the plaque

Figure 5:
The atherosclerotic plaque with the stent and miointimal hyperplasia

The follow up of the operation was simple. After surgery the patient was under treatment with Trombostop (acenocumarolum) 2 mg 1 tablet/day in order to keep the INR between 2.5 and 3, Aspenter 75 mg 1 tablet/day, Sortis 20 mg 1 tablet/day, and Tanakan 40 mg 3 tablets/day; it was indicated to keep the diet and to stop smoking.

Discussion

The treatment of the extra cranial carotid artery stenosis in our days was subject to many debates, articles and randomized studies comparing the carotid stenting and the open surgery for this pathology (figures 6 a, b). All these studies (except ARCHER) showed that surgery is equal or better than stenting as results to treat carotid artery stenosis.

Randomized trials comparing CAS with CEA

STUDY	SPONSOR	SAMPLE SIZE, n	STUDY DESIGN	RESULTS	STATUS
ARCHeR	Guidant	437	High-risk registry	**30-day results;** *stent patients:* MACE = 7.8%; *Acculink success rate* = 97.8%	FDA approval
ARCHeR RX	Guidant	145	High-risk registry	NA	*Enrollment completed*
BEACH	Boston Scientific	480 (400 evaluable)	High-risk registry	NA	*Enrollment completed*
CABERNET	Endo Tex	380	High-risk registry	NA	*Eurolling*
CREATE	ev3	400	High-risk registry	NA	*Information not provided*

Figure 6a: CAS = *Carotid Artery Stenting;* CEA = *Carotid Endarterectomy*

Summary of evidence comparing CAS and surgery for carotid stenosis [HALLET, 2004]

Authors	N° patients	Grade of evidence	Clinical outcome	Restenosis rate
Naylor	23	Randomized	Surgery > Angioplasty	
Brooks	104	Randomized	Surgery = Angioplasty	
CAVATAS	504	Randomized	Surgery = Angioplasty	Surgery > Angioplasty
Aburahma	83	Non-randomized	Surgery = Angioplasty	Surgery > Angioplasty
Jordan	377	Non-randomized	Surgery > Angioplasty	
Golledge	33 studies	Systematic review	Surgery > Angioplasty	

Figure 6b

The major problem after stenting is the restenosis. The identified factors with the developing of restenosis (myointimal hyperplasia) are: female gender (our case), elevated creatinine level, elevated cholesterol level, plaque type and elevated homocysteine levels.

The classification of restenosis (Bequemin 2006) is: residual (< 2 months), early (< 2 years) and late restenosis (>2 years).

It has to be treated when at duplex scan (echo) the stenosis is more than 60%.

The incidence is 3.9% at 2 years and 8.5% at 5 years (Lamuraglia, 2006).

The treatment of the restenosis is difficult. It may be endovascular (cutting balloon) or surgical (stent extraction with endarterectomy or bypass using saphenous vein or PTFE graft).

In our case, the endarterectomy with stent extraction and Dacron patch enlargement was the solution of choice, because we could also solve the problem of elongated and kinked internal carotid artery. As cerebral protection we have used the Brenner shunt. The intervention was done under general anesthesia with the usual protocol of monitoring (radial artery catether for invasive blood pressure, etc).

The postoperative evolution was simple without any neurological deficits and was discharged at the 3rd day postoperatively with anticoagulant and antiplatelet treatment (Aspirin). This was the first patient with stent early restenosis treated surgically in Romania.

Conclusion

CAS is not opposite to CEA, but a complementary method, witch is indicated to treat high risk patients. The use of cerebral protection devices is strongly recommended. CEA remains the "gold standard" for all the other patients who are candidates for revascularization. The use of a well defined protocol may help to significantly reduce morbidity and mortality rates of open carotid surgery. Surgery is also a safe technique to treat in stent restenosis.

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Actual treatment of varicose disease*)

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The varicose disease is a progressive disease calling for systematic follow up.

The correct management allows for complete diagnosis based on the history, physical examination and laboratory exams.

The history allows making the difference between the varicose disease and secondary, symptomatic varices and those included in the congenital venous malformations.

The physical examination is done in prone position as well as in orthostatism. The following aspects are to be checked:

- cutaneous modifications,
- the presence of edema and its importance (determining the limb circumferences),
- the symmetry of limbs,
- postural modifications and
- any possible associated features of arterial or neurological disease.

As to the varicose disease, the physical examination will ascertain the type, location and distribution of dilated veins. The physical examination represents the C section of CEAP classification (figure 1).

Figure 1: Venous ulcers to the patients with significant incontinence of internal saphenous vein and varicose dilatations (intraoperative view)

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Among other necessary exams, the ultrasonography and Duplex ultrasonography are presently very important for making a correct and complete diagnosis.

The ultrasonography is a non-invasive method, with low price, without any iatrogenic complications, detecting the venous reflow.

The Duplex ultrasonography represents the first choice for varicose disease. It gives information about the venous hemodynamics, the presence or absence of reflow, venous structure and the subfascial course of varicose veins.

The ultrasonography and Duplex permit the definition of E, A and P sections in CEAP classification, a correct classifying and the adequate treatment (figure 2, 3, 4).

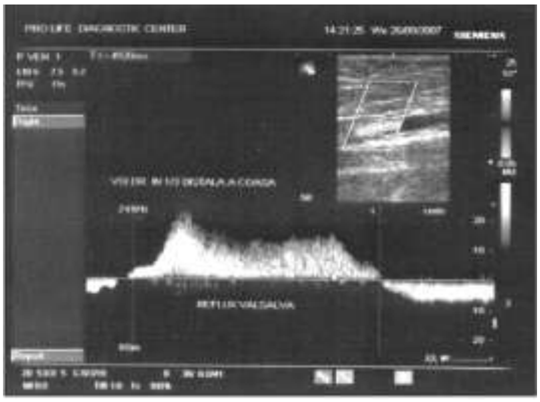

Figure 2a

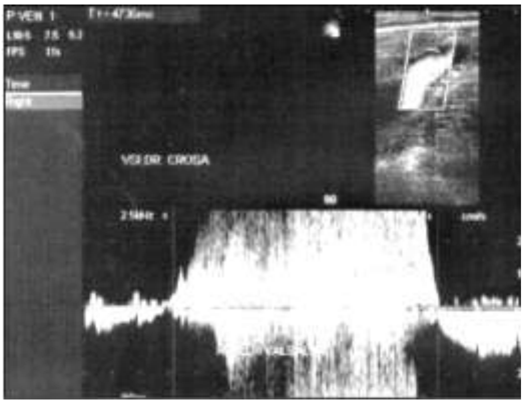

Figure 2b

Figure 2: Presence of reflow

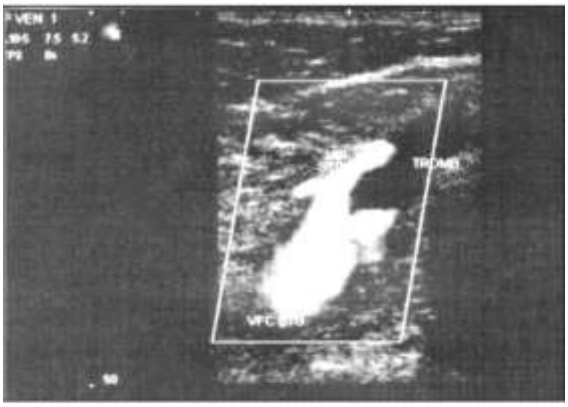

Figure 3: Internal saphenous vein trombosis

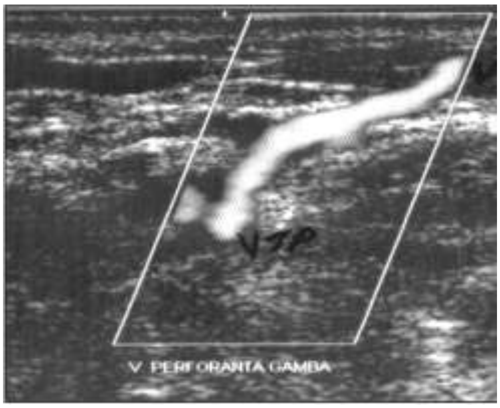

Figure 4: Perforating vein

The patient with venous insufficiency must learn to solve his/her venous dysfunction, to stop the evolution and prevent the possible complications.

The lifestyle must include physical exercises, mobilization (walks, climbing staires), sports (jogging, swimming, cycling, dance), topical cold applications (with vaso-constrictive and anti-inflammatory effects) and postural drainage.

The physical therapy increases venous return and decreases venous pressure. It is directed to the mobilization of the ankle joint and comprises massage, intermittent compression and balneotherapy.

The prevention of varicose disease should impose the modification of personal lifestyle and the use of compressive stockings for persons with prolonged orthostatism (certain type of jobs).

The compressive therapy

The elastic support (passive compression) and the active compression are two different treatment modalities.

The passive compression is not indicated for the varicose disease. It is useful for deep venous thrombosis, lipodermatosclerosis and chronic venous ulcer.

The active compression prevents the development of chronic venous disease, makes its contribution to its treatment, and relieves the pain in patients with varicose disease. It is strongly recommended after surgical, treatment, sclerotherapy and within the management of chronic venous disease.

The active compression is performed with elastic bandage (temporary treatment) or occasionally, mid-term or long-term wearing of elastic stockings.

The elastic stockings are occasionally recommended in patients with a few, light complaints of varicose disease, in patients on long journey and in those with "heavy limbs" sensation.

After surgical treatment, sclerotherapy and during pregnancy, the elastic stockings are to have a mid-term wearing. For a long-term wearing, it is indicated in patients with chronic venous insufficiency, with cutaneous modifications etc.

The active compression is contraindicated in patients with chronic obstructive arterial disease in III or IV stages and in patients with lymphangitis or infective cellulitis.

A difficult to manage heart failure and acute, wet dermatoses are relative contraindications.

The compression is difficult to be obtained in non-coopering patients and in those with severe joint troubles.

The elastic stockings have different lengths and degrees of compression and must be adapted to any particular patient.

Medical therapy

The venoactive drugs have an anti-edematous effect and relieve the symptoms of chronic venous disease ("heavy limbs", pain, "unrested limbs"). They are useful in every stage of chronic venous disease, also as an adjunction to compression, sclerotherapy and surgery. They are recommended to be taken as 3 months' repeated, treatment.

The venoactive drugs belong to several chemical classes and are obtained from plants or by biochemical synthesis.

The mode of action consists in decreasing the edema, improvement in venous tone, improvement of microcirculation through the inhibition of leukocyte migration and adhesion, the inhibition of the aggregation of red blood cells and the decrease in their capacity to be distorted.

The most known and used venoactive drugs are the micronized purified flavonoid fraction, Rutoside-HR, Coumarin and Troxerutin, Escin, Calcium dobesilate, Naftazone.

Sclerotherapy

It consists in injecting an irritating agent into a varicose vein for injuring the endothelium and, as a result, the obliteration of the venous lumen and progressive fibrosis of the venous wall.

It is indicated for the treatment of teleangiectasia, reticular varicose veins and as an alternative to the surgical treatment when there is a postoperative new development of varicose veins and when there is an incompetence of external saphenous vein.

The ideal sclerosing agent must be painless, efficacious and with no secondary effects. A product like this doesn't exist at present. The sclerosing agents act through their osmotic and corrosive effects. The detergent-like products can be emulsified as a foam. The sclerosing agents used in the commercial products are:

Agent's name	Mode of action
Alum chrome with glycerol Iodine	Corrosive
Lauromacrogol Sodium tetradecilsulfate	Corrosive and detergent-like
NaCl 20% Hypertonic Dextrose 66%	Osmotic

There are 3 techniques of sclerotherapy:

1. Classical sclerotherapy

Three schools have evolved: Tournay in France, Sigg in Switzerland and Fagan in Ireland. These schools differ by their method of injection, the patient's position during the injection, the therapeutic approach - from down upwards or the reverse, the duration of applied compression.

2. Echo guided sclerotherapy

This method allows the tracking of the diffusion of the sclerosing agent, the venous spasm after the injection and detects the extravasation. It also permits the control of the result.

3. Foam sclerotherapy with echographic monitoring

It's a modern technique with encouraging results. The compression after the procedure is a component of the treatment. It limits thrombus formation, decreases the perivascular inflammatory reaction, decreases the rate of pigmentation and promotes the formation of a fibrous cord.

The indications are established after 3 consensus conferences, between 1994 and 1995, under the patronage of the International Union of Phlebology. The sclerotherapy is recommended for the treatment of teleangiectasia, reticular varicose veins and the tributaries of saphenous veins. There is no consensus upon the position of sclerotherapy as a first choice treatment for varicose internal saphenous vein. It is an alternative to surgery for the treatment of perforating veins and the external varicose saphenous vein.

The sclerotherapy has the following advantages: can be performed in anticoagulated patients, in the elderly patients unfit for surgery; also useful in cases of recurrences of varicose veins after the stripping procedure and for suppressing the veins that supply the varicose ulcerated zones; it's a method that can be performed even in the medical office.

Its contraindications are rare and relative: allergic reactions, thrombophilia, deep venous thrombosis, pregnancy and lactation, local or systemic infection, uncontrolled systemic arterial hypertension, critical limb ischemia, in patients confined to bed.

Its complications are rare, nearly 1% for experienced doctors. They consist in: pigmentation, newly-formed teleangiectasia, cutaneous necrosis and ulcerations, allergic reactions, amaurosis fugax, superficial thrombophlebitis, deep venous thrombosis.

Laser, electrocoagulation and cosmetical issues

Laser = ***light amplification by stimulated emission of radiation.***

The Laser is a monodirectional, coherent, light ray that may carry a certain quantity of energy.

This method is indicated for the treatment of essential, progressive teleangiectasia, isolated tele-angiectasia, newly-formed teleangiectasia, reticular varicose veins, endovascular photocoagulation of saphenous veins.

The electrocoagulation is an old method, that was renewed and consists in the thermocoagulation of a dilated vein. It's uncommonly used.

The camouflage represents an alternative or an adjunctive for preventing disproportionate or expensive treatments. Artificial creams or cosmetic masks are used.

Surgery

By the surgery of varicose veins one can understand any surgical procedure with the intention of curing the disease. It is necessary to outline several terms:

- "Stripping" is a technique that consists in removal of a vein using a stripper; the involved vein is specified;
- Isolated phlebotomy represents the removal of a vein without using a stripper;
- Sapheno-femoral/popliteal disconnection consists in the resection of terminal saphenous vein, with ligation flush with the deep veins.

The objectives of surgical treatment are:

- Suppression of the venous reflow;
- Removal of varicose veins with their frequently incompetent valves.

The duplex echo showed that varicose veins can exist with no reflow point present. These data modified the etiologic concept of primitive varicose veins according to which the hemodynamic component is probably the first element. The hypothesis that the disease affects firstly the venous wall, is the most probable one. The hemodynamic component is an important one, but commonly only a secondary one because it is generated by the initial disease of the venous wall.

Principles and methods

Removal (exeresis) techniques

The principle consists initially in the suppression of the pathologic reflow from the deep venous system into the superficial one and then in removal of saphenous vein.

The reflow suppression is done through:

a. Crossectomy (sapheno-femoral/popliteal disconnection) with ligation of all collaterals.

b. Ligation of perforating veins under the fascia. Presently this ligation is done endoscopically - subfascial endoscopic perforating vein surgery (SEPS).

The suppression of varicose saphenous vein is performed through endolumenal or exolumenal stripping, cryo-stripping or very uncommonly phlebotomy. These techniques involve the saphenous trunk. Its tributaries (non-saphenous varicose veins) are to be removed by small incisions (phlebectomies) (figure 5).

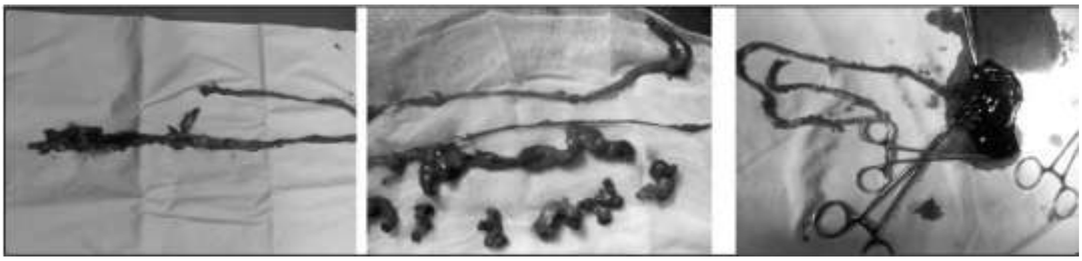

Figure 5: Stripping of varicose saphenous vein with intraluminal trombosis (intraoperative view)

Endovascular techniques

A probe or a catheter are used through endolumenal approach through which, various forms of energy are used with the intention of producing a fibrous reaction of the venous wall with stenosis and consecutive obliteration of the venous lumen. The following techniques are used:

• Radiofrequency ablation (closure) consists in using an electrical current that releases continuous energy which produces intimal lesion, the contraction of collagen in the media, followed by fibrosis and occlusion.

• Laser therapy - the energy is released as a monochromatic light fascicle by a generator; this energy is released discontinuously.

Conservative hemodynamic techniques for the saphenous trunk

This technique has as principle the modification of venous hemodynamics by various single or combined methods. These are:

• The suppression of ostial reflow between the deep venous system and the superficial one through:

- Ligation or section or disconnection of terminal saphenous vein.
- Bandaging, wrapping or valvuloplastia of terminal saphenous vein.

• The suppression of pathologic reflows between the deep venous system and the superficial one through the ligation of perforating veins.

• The re-orientation of reflow from the superficial, pathologic veins, by ligation of the saphenous trunk bellow a possible perforating vein for allowing a re-entrance, with the intention of forcing the reflow through the perforating vein into the deep venous system, as in the CHIVA procedure (ambulatory conservative hemodynamic treatment of venous insufficiency) (figure 6).

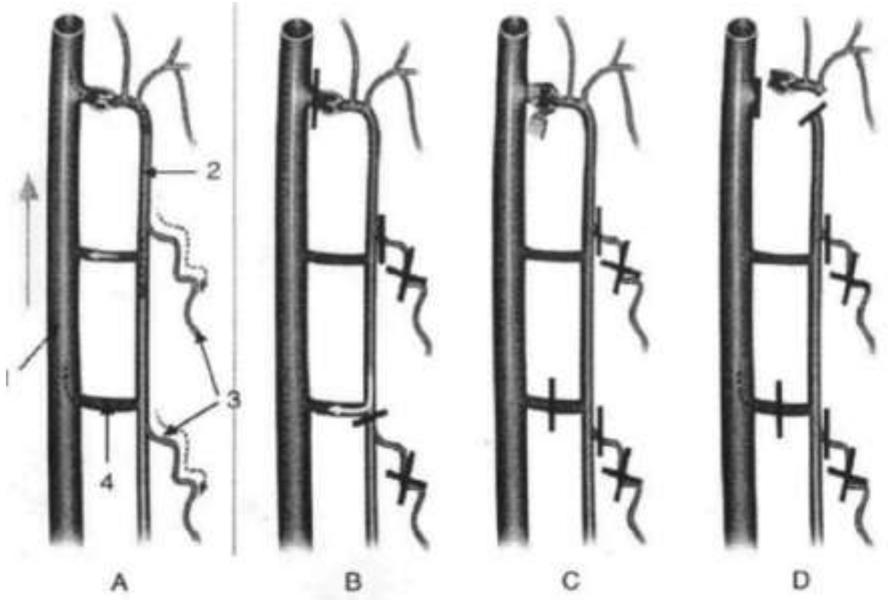

Figure 6: Hemodynamic techniques for the saphenous trunk preservation in varicose vein surgery

• Resection (phlebectomy) of tributaries of saphenous veins.

In all these cases the saphenous vein trunk is left "in situ". Its indications can be regarded as related to:

• Etiology (primitive, secondary varices and congenital malformations).
• Clinical aspect (uncomplicated or complicated varices).
• Special cases (associated with arterial or lymphatic disease).
• Technique used.

The standard exeresis techniques were replaced by "a la carte" procedures: they are limited to the resection of superficial pathologic veins detected by ultrasonography. For the internal saphenous venous trunk one can perform the stripping for the entire trunk (long stripping) or partial stripping (short stripping). The arguments in favor of the stripping would be: the lower postoperative neurological complications and the absence of perforating veins on the distal saphenous trunk.

For the external saphenous vein, the resection of the two superior thirds of the trunk is recommended.

Postoperatively, the active compression for 1 month is recommended.

The postoperative complications are rare - 0.04%. There may be complications like hematomas, local infections, lymphatic complications (especially after re-operation), neurological complications, cutaneous burnings for endovascular procedures, thromboembolic complications, cosmetic complications.

The post-operative follow-up is very important. The varicose disease is a chronic and progressive disorder which a single surgical procedure cannot assure its definitive cure. As complex as it may be a surgical procedure, it cannot treat all the varicose veins. The postoperative Duplex is necessary.

Ambulatory phlebectomy

It is performed through the technique described by Müller. It consists in the extraction of varicose vein under local anesthesia, through minimal incisions, using a hook. It is performed very often within the medical office.

This technique has some advantages: the esthetic aspect and ensures the eradication of the vein without any risk of recanalization; it never induces cutaneous necrosis or hyperpigmentation.

This procedure is indicated in case of varicose tributaries of saphenous vein, reticular varicose veins, perineal varicose veins, the veins on the dorsum of the foot, varicose pearls, some perforating veins.

The contraindications of ambulatory phlebectomy are:

- Absolute: critical ischemia, infection.
- Relative: pregnancy, postpartum, severe coagulation disorders, immuno-suppression.

The potential complications could be:

- Cutaneous: flictenas, hyper/hypopigmentation, local infection, visible scars.
- Vascular: bleedings, hematomas, superficial venous thrombosis, lymphorrhea, lymphatic cysts, newly-formed teleangiectasia.
- Neurological: lesions of sensitive nerves, tarsian syndrome, neuromas.
- Systemic: suffering.

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Place actuelle de la crossectomie dans le traitement de l'insuffisance veineuse de la grande saphène*)

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"Le moyen d'avoir raison dans l'avenir est, à certaines heures, de savoir se résigner à être démodé" Ernest RENAN (1882 - Conférence sur la Nation)

"The way to remain right in the future is, at certain hours, to know how to resign oneself to stay out of date" Ernest RENAN (1882 - Conférence for the Nation).

Abstract

The crossectomy, or resection of the sapheno-femoral junction, formerly systematic, presently knows a reconsideration in its principle, indications and realization. Reasons are not only theoretical on one hand: better knowledge of the hemodynamic and of complexity and diversity of reflux (true ostial reflux - pseudo-reflux or draining flux - non ostial saphenous reflux - non saphenous reflux and also mixted reflux), but practical on the other hand: emergence of numerous alternative methods. Indications are nowadays selective for the only ostial and mixed reflux and remain arguable for the trunk reflux without valvular insufficiency. As for the non-saphenous reflux, frequently encountered (10%), it is very important to identify them and to treat them in a specific way in order to avoid bad results unfairly attributed to the crossectomy technique. This technique here is detailed, encompasses extensive afferentectomy and various treatment processes of the sapheno-femoral junction. Factors of post-crossectomy recurrence are analyzed. The combined crossectomy-venous excision technique, when rigorously performed, remains a reference strategy facing to newly proposed methods, most often competitive between them. The perenity of the crossectomy is therefore demonstrated and validated thanks to its deference of several decades.

Keywords: *Long saphenous vein, crossectomy, afferentectomy, surgery, recurrent varicose*

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Résumé

La crossectomie, autrefois systématique, connaît actuellement une remise en question dans son principe, ses indications et sa réalisation. Les raisons en sont d'une part théoriques: meilleure connaissance de l'hémodynamique, de la complexité et de la diversité des reflux (reflux ostiaux vrais - pseudo reflux ou flux de drainage - reflux saphéniens non ostiaux - reflux non saphéniens et enfin reflux mixtes), mais aussi pratiques: émergence de nombreuses méthodes alternatives. Aujourd'hui les indications sont sélectives pour les seuls reflux ostiaux et mixtes alors qu'elles sont discutables pour les reflux tronculaires sans insuffisance ostiale. Quant aux reflux non saphéniens très fréquents (10%), il importe de les reconnaître et de les traiter de façon spécifique pour ne pas alourdir les mauvais résultats attribués injustement à la crossectomie. Les techniques sont détaillées en insistant sur l'afférentectomie extensive et les diverses procédures de traitement de la jonction saphéno-fémorale. Les facteurs de récidive post-crossectomie sont analysés. La crossectomie-éveinage, sous réserve d'une technique rigoureuse, reste une stratégie de référence face aux nouvelles méthodes proposées, souvent concurrentes entre elles. La pérennité de la crossectomie est éprouvée et validée par un recul de plusieurs décennies.

Mots-Clefs: *Veine grande saphène, Crossectomie, Afférentectomie, Chirurgie, Récidive variqueuse*

"Au commencement … était la crossectomie" que nos Maîtres considéraient comme un geste fondamental et presque toujours systématique dans la chirurgie de l'insuffisance de la grande saphène. Cette attitude dogmatique est remise en question à l'heure actuelle, dans son principe, ses indications et sa réalisation notamment depuis la meilleure connaissance de l'hémodynamique. Pourtant la crossectomie associée à l'éveinage a un recul de plusieurs décennies. Elle a connu des échecs, des récidives, quelques complications, mais aussi d'indiscutables et nombreux succès à court terme (cicatrisation rapide des ulcères), et à long terme. L'éveinage lui-même est devenu de moins en moins iatrogène et peu hémorragique depuis la pratique du stripping par invagination, réactualisé par J. Van Der Stricht. Mais faut-il, pour autant, prôner la crossectomie de principe comme un geste indispensable à tout traitement chirurgical?

Objectifs

I. Analyser les raisons de la remise en cause de ce qui paraissait être un aphorisme, voire un dogme.
II. Poser les indications actuelles de la crossectomie qui ne doit plus être systématique, mais être réalisée de façon SÉLECTIVE, tout comme les éveinages, en fonction de l'exploration pré-opératoire.
III. Préciser la technique de la crossectomie en insistant sur deux points importants: l'afférentectomie extensive, et les différents procédés de traitement de la jonction sapheno-fémorale.
IV. Étudier les facteurs des récidives post-crossectomie.
V. Tenter enfin de conclure sur l'avenir réel du concept de Crossectomie-Éveinage.

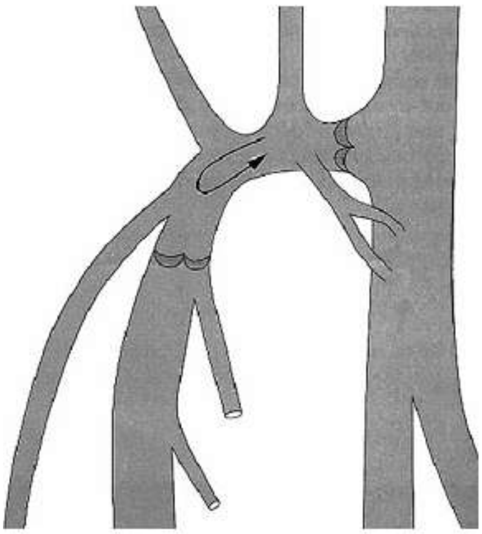
I. Pourquoi Cette remise en question de la crossectomie?

À l'analyse, les raisons apparaissent de deux types, théorique et pratique.

A. ***Les raisons théoriques*** *sont essentiellement:*

1. La mise en évidence et la fréquence, à côté des reflux classiques par incompétence valvulaire des reflux non-ostiaux, des pseudo-reflux qui sont en réalité des flux de vidange ou de drainage, ainsi que des reflux non saphéniens.

2. La meilleure connaissance de sources de reflux pouvant avoir pour origine une insuffisance veineuse sous jacente avec effet "siphon", cause indirecte d'un reflux tronculaire par aspiration. La crosse ne serait, dans un grand nombre de cas, incontinente qu'après une distension tronculaire ou même des réseaux réticulaires. Le phénomène primitif serait alors non pas une valvulopathie mais une pariétopathie des veines des différents réseaux superficiels, la valvule ostiale ne devenant victime de la maladie pariétale qu'ultérieurement et par évolution ascendante. Ainsi se produirait l'ostialisation secondaire d'un reflux non ostial.



a. Aux stades initiaux de la maladie, le jeu valvulaire reste longtemps un élément fondamental de la résistance contre l'insuffisance de la grande saphène. Les études écho-doppler-couleur (1) montrent le rôle joué par les valvules pré-ostiales de la grande saphène et par les valvules pré-terminales de la saphène antérieure et aussi des afférentes (honteuse externe, circonflexe iliaque externe superficielle, épigastrique) elles-mêmes dotées généralement de valvules terminales. La valvule ostiale reste la barrière principale entre les voies superficielle et profonde. Les valvules pré-ostiales de la grande saphène et de la saphène antérieure protégent le tronc saphénien et non la crosse qui, elle, fonctionne plutôt comme un réservoir dont la vidange est contrôlée par la valvule ostiale et les valvules des afférentes. Ainsi s'expliquerait la constatation au doppler-couleur de pseudo-reflux qui sont en réalité des flux de vidange ou de drainage par les afférentes, flux en fait correcteurs par hémodé-tournement de l'insuffisance veineuse sous-jacente. Ces mêmes flux de drainage existent au niveau de la jonction saphéno-poplitée.

b. Si le malade est vu à un stade plus tardif, l'insuffisance devient à la fois ostiale et tronculaire, et chacun des facteurs, qu'il soit pariétal (distension), valvulaire (incompétence), ou hémodynamique (aspiration) va contribuer à l'auto-aggravation de la maladie veineuse.

B. Les raisons pratiques tiennent aux techniques alternatives proposées depuis quelques années:

1. En premier lieu, certaines d'entre elles paraissaient prometteuses:

a. La cryothérapie, qui a connu un indiscutable taux de récidives, qu'il s'agisse de cryo-sclérose ou de cryo-éveinage.

b. La CHIVA, séduisante par son principe, peut être trop complexe, qui est probablement pour cette raison de moins en moins réalisée par la plupart des équipes à l'heure actuelle. Cette stratégie a permis pourtant les premiers vrais raisonnements hémodynamiques dans le traitement des insuffisances veineuses. Elle offre, pour ses défenseurs, des résultats tout à fait satisfaisants, notamment depuis qu'à la fragmentation de la colonne de pression, à la préservation des perforantes de réentrée, on associe des phlébectomies des veines variqueuses non drainables (2).

2. La crossectomie "*sus-fasciale*" qui interrompt en réalité l'éveinage du tronc saphénien à 2, 3, 4 voire à davantage de centimètres de la jonction saphéno-fémorale, ne franchissant en aucun cas le fascia superficialis, ce qui pose le problème sémantique de la dénomination réelle de crossectomie, puisqu'elle laisse en place la crosse et ses afférentes (3). Elle peut néanmoins dans certains cas, et nous verrons pourquoi, donner des résultats satisfaisants.

3. Les nouvelles techniques endoluminales de saphéno-destruction ou de saphéno-réduction par effet thermique: laser endoveineux et radiofréquence, souvent concurrentes entre elles.

4. La saphéno-destruction ou la saphéno-réduction chimique: sclérose échoguidée de la crosse et de la grande saphène, soit par voie percutanée, soit par cathéter endo-luminal, avec différents agents sclérosants, soit liquides, soit sous forme de mousse (4).

5. Le clip endoveineux largué sous contrôle échographique à 5 cm de la jonction saphéno-fémorale utilisé surtout pour des saphènes modérément dilatées entre 4 et 8 mm, et combiné à une sclérose de la crosse.

6. Enfin certaines techniques associent une ligature sous-fasciale du tronc saphénien à une sclérose de la jonction saphéno-fémorale (technique 3 S).

II. Indications actuelles de la crossectomie

La crossectomie isolée n'a que quelques rares indications: intervention sous anesthésie locale chez un patient porteur d'ulcère et dans un état général tel qu'il ne puisse supporter une intervention trop longue, thrombose aiguë de la crosse lors d'une thrombose veineuse superficielle du triangle de Scarpa.

Dans notre pratique, la crossectomie est presque toujours associée à l'éveinage: court jusqu'à la jarretière, moyen jusqu'au tiers inférieur de jambe ou long cruro-malléolaire, et aux phlébectomies des collatérales incompétentes ainsi qu'au traitement des perforantes incontinentes.

Il faut reconnaître que par le passé, faute d'études fines par écho-doppler un trop grand nombre de crossectomie a été réalisé. Certaines d'entre elles auraient pu être évitées surtout dans les stades débutants de la maladie veineuse.

Il est souhaitable désormais de distinguer dans les indications quatre types de reflux: les reflux ostiaux, les reflux saphéniens non ostiaux, les reflux non-saphéniens, les reflux mixtes, et enfin quelques cas particuliers.

1. Les reflux ostiaux

► La logique voudrait la réalisation d'une crossectomie dans toute insuffisance de la grande saphène avec insuffisance de la valvule ostiale. En pratique, les indications sont fonction de différents critères: importance de la symptomatologie, calibre de la crosse, importance du reflux, âge et état général du patient et bien sûr ses desiderata.

► L'un des critères les plus habituels de décision, en dehors du reflux lui-même constaté cliniquement ou à l'échodoppler, est le diamètre de la crosse. La crosse normale mesure entre 3 et 5 mm à l'ostium. À partir de 8 à 10 mm de diamètre, il paraîtrait logique de pratiquer une crossectomie. Il est vrai que l'on peut observer des crosses refluantes de calibre assez bas: 5 à 8 mm, et inversement des crosses mesurant 8 à 10 mm, en orthostatisme, mais non refluantes, ou du moins non encore refluantes. Il s'agit la de là limite inférieure de discussion. Au-delà, les crosses supérieures à 10 mm sont pratiquement toujours refluantes, et ne nous paraissent pas poser de problème d'indication autre que chirurgicale.

► Peut-on, lorsque ce reflux est modéré, c'est-à-dire en pratique lorsque le diamètre de la crosse est inférieur à 10 mm, utiliser d'autres méthodes? Il semblerait que les premiers résultats des méthodes endoluminales (laser-radiofréquence) montrent soit une disparition de la crosse, soit une persistance de celle-ci avec un calibre plus réduit et une régression du reflux ostial, avec une normalisation du calibre des afférentes. Tout ceci a été décrit pour les premières séries et avec un recul de quelques mois. L'explication viendrait de la suppression ou de la réduction du lit du reflux et donc de la suppression de l'effet siphon. Certains opérateurs étendent toute-fois les indications de ces techniques à des crosses de diamètre plus élevé de 25 voire 30 mm et affichent des résultats satisfaisants.

De tels résultats pour l'instant à court terme (2 à 4 ans) semblent cohérents pour des reflux modérés. Ils nous interpellent dans le cas de crosses plus volumineuses car ils paraissent remettre en question le concept de crossectomie dans l'insuffisance ostiale majeure. Or, notre expérience opératoire de ces jonctions saphéno-fémorales dilatées, ampullaires, aux parois amincies et fragiles laisse mal entrevoir une possibilité de réversibilité lésionnelle. Comment de telles crosses pourraient redevenir durablement fonctionnelles, avec un jeu valvulaire normalisé par simple effet chimique ou thermique?

Les effets tissulaires ont été étudiés sur coupes histologiques expérimentales de veines traitées. Ils sont évolutifs pendant plusieurs jours ou semaines après l'intervention. Mais cette évolution reste difficilement prévisible aussi bien dans le temps que dans l'étendue réelle des zones traitées (veines irrégulières, moniliformes) malgré la pratique de l'échoguidage ou de l'angiographie, sous amplificateur de brillance, appareillages et manœuvres qui viennent, par ailleurs, alourdir indiscutablement la procédure et allonger le temps opératoire.

De plus, ces techniques ne sont pas exemptes de complications propres: thromboses superficielles du triangle de Scarpa, brûlures des structures péri-veineuses, et notamment nerveuses, analogues à celles constatées lors de la cryothérapie, perforation du tronc saphénien et fausse route des sondes, reperméabilisation secondaire de la crosse ou du tronc saphénien avec ou sans reflux (5). Des incidents chirurgicaux ou de matériel lors de l'intervention obligent à changer parfois la procédure prévue, éventualité dont le patient doit être informé.

Nous avons nous-mêmes été consultés pour quatre cas de thrombose douloureuse et inflammatoire du triangle de Scarpa (3 cas après radio-fréquence et 1 cas après laser endoveineux).

Il faut tenir compte, cependant, de la courbe d'apprentissage et il n'est pas douteux que ces complications seront de moins en moins fréquentes avec l'expérience des opérateurs et les progrès du matériel. Mais la principale réserve actuelle est l'absence de recul et la persistance d'une crosse qui peut se reperméabiliser comme cela a été constaté dans les premières séries pour quelques cas (4). Il est vrai que la crossectomie de seconde intention pourra toujours pallier aux complications et aux échecs de la méthode.

2. Les reflux saphéniens non-ostiaux

Leur fréquence est évaluée entre 35 et 40% selon de nombreuses études. L'étude récente écho-doppler couleur de Pieri A. et Coll. (1) en retrouve chez 38% des patients. Le mode de recrutement, du moins dans les pays développés, et surtout en milieu urbain, influence les statistiques actuelles. Les patients, notamment les femmes, sont mieux informés et consultent à un stade plus précoce.

Il paraît alors légitime de ne pas proposer de crossectomie en présence d'insuffisance tronculaire avec valvule ostiale continente. Ces reflux non-ostiaux ont pour origine une incontinence de l'un ou plusieurs des systèmes veineux suivants:

- ► Veines périnéales
- ► Veines lympho-ganglionnaires
- ► Veines sous cutanées abdominales
- ► Veines honteuses externes et veines d'origine génitale.
- ► Veines circonflexes iliaques superficielles.
- ► Perforantes ou collatérales de cuisse et de jambe.

De tels reflux peuvent être traités par méthodes endoluminales, mais aussi par éveinage ou par sclérothérapie et contention, méthodes qu'il est judicieux, souvent, d'associer.

3. Les reflux non sapheniens

Ils ont pour origine des veines autres que les systèmes de la grande ou de la petite saphène. Ces veines se connectent directement dans le tronc veineux profond. Leur fréquence est de 10% dans l'étude de Labropoulos et Coll. (6): sur 835 membres inférieurs porteurs d'insuffisance veineuse superficielle, étudiés par écho-doppler-duplex-couleur, 84 membres chez 72 patients présentaient ce type de reflux. La grande majorité (67 patients) était de sexe féminin avec, pour la plupart, un nombre élevé de grossesses.

Certains de ces reflux peuvent coexister entre eux et avec des reflux saphéniens.

10% des patients présentaient une insuffisance veineuse majeure avec ulcère ou troubles trophiques cutanés.

Ces reflux saphéniens ont différentes origines:

- ► Dans 52 cas des veines perforantes de cuisse
- ► 29 cas des veines d'origine haute (18 vulvaires et 11 fessières)
- ► 9 cas des veines du nerf sciatique
- ► 7 cas des veines de la fosse poplitée
- ► 3 cas de veines du genou avec 2 cas de veines latérales du genou et 1 cas de veine du nerf tibial.

Des chiffres analogues (9,9%) de reflux non saphéniens ont été retrouvés dans l'étude de JIANG P. et Coll. (7) sur 1222 patients porteurs de varices 101 présentaient des reflux non saphéniens dont 71 à partir veines épigastriques et 30 ayant pour origine des veines périnéales ou fessières.

De tels reflux, dont la fréquence est considérable, exigent un traitement spécifique, guidé par l'échomarquage précis pré-opératoire. Leur méconnaissance peut alourdir injustement le pourcentage d'insuccès de la crossectomie-éveinage et d'ailleurs de toute autre méthode non suppressive de ce reflux.

4. Les reflux mixtes

Ils restent encore les plus fréquents, du moins parmi les patients adressés aux chirurgiens. L'insuffisance saphénienne est ici ostio-tronculaire et, que la valvule ostiale soit primitivement ou secondairement incompétente, la crosse est souvent dilatée au-dessus de 10 mm de diamètre. D'autres sources de reflux sont associées, d'origines diverses: perforantes, collatérales, veines du système de la petite saphene et reflux non saphéniens, pelviens ou périnéaux notamment.

L'échomarquage pré-opératoire laisse prévoir une intervention parfois longue, bien que restant le plus souvent réalisable en ambulatoire. La crossectomie n'est alors qu'un temps essentiel mais non forcément le plus long. Elle est associée au traitement de toutes les autres sources de reflux par éveinage, phlébectomie ou parfois chirurgie endoscopique sous-fasciale des perforantes. Ces formes relèvent d'une cure chirurgicale la plus complete possible et le suivi phlébologique demeure essentiel.

5. Les cas particuliers

a. La crossectomie reste nécessaire lorsque les méthodes destructives endoluminales sont impossibles ou dangereuses:

- ► Tronc tortueux, dédoublement saphénien en canon de fusil.
- ► Crosse double ou de type insulaire.
- ► Anévrysme de la terminaison de la saphène ou de la jonction saphéno-fémorale elle-même.
- ► Impossibilité de passage des sondes.

b. La saphène antérieure peut être refluante de façon isolée et être responsable d'une varicose de cuisse en écharpe qui peut alimenter un réseau jambier. Si l'examen écho doppler montre l'absence d'atteinte de la valvule ostiale, la conservation de la crosse est possible avec résection par phlébectomies ou par endo-éveinage de la saphène antérieure.

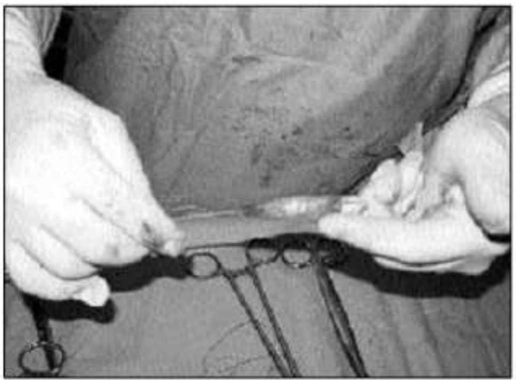
c. Dans les indications, il importe aussi de tenir compte du facteur économique: le prix des sondes endoluminales non encore prises en charge par les organismes sociaux, ainsi que l'investissement en matériel par les établissements ou par les opérateurs eux-mêmes.

III. Les techniques de la crossectomie

Quel que soit le mode anesthésique, la crossectomie est presque toujours associée à un éveinage de la saphène, court, moyen ou long, et à d'autres gestes phlébectomiques.

L'incision cutanée est de 3 à 4 cm, à 1 cm au-dessus du pli inguinal et parallèle à lui, ou dans le pli lui-mème.

Dissection des plans superficiels, individualisation de la jonction saphéno-fémorale et des terminaisons des afférentes à la crosse.



1. L'afférentectomie extensive

Au concept de crossectomie "élargie" souvent retrouvé dans la littérature (8) nous préférons le terme d'afférentectomie extensive plus approprié à notre technique. Chacune des afférentes doit être traitée l'une apres l'autre. L'afférente est saisie sur une pince, dans sa portion proche de la crosse, puis est disséquée de manière à libérer les 3 ou 4 cm distaux. Une autre pince clampe l'afférent le plus loin possible. Cette pince, en traction, permet d'individualiser encore un cordon veineux palpable. La dissection du cordon tendu permet de "déshabiller" la veine, de la libérer des tracti fibreux, de proche en proche et ce parfois jusqu'à une bifurcation ou une trifurcation elle-mème réséquable.

L'interruption de la veine afférente est située le plus loin possible de la crosse, voire en dehors même du triangle de Scarpa, grâce à la traction exercée selon le principe dérivé de la phlébectomie de Muller. Le mode d'interruption de l'afférente est variable selon les opérateurs: ligature, clip, rupture par traction et compression manuelle prolongée ou section après électro-coagulation en deux points si la veine est de petit calibre.

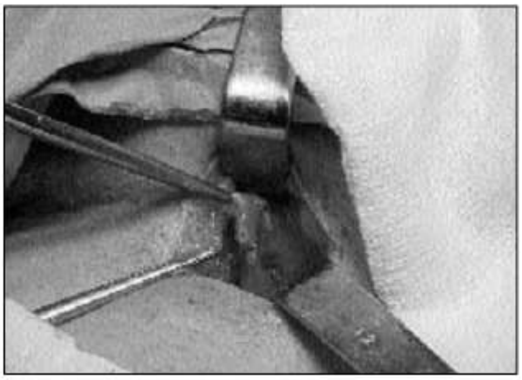
La crosse est ainsi progressivement "squelettisée". Il est souhaitable, pour la clarté de la dissection, d'interrompre les afférentes à leur jonction avec la crosse elle-même, et d'éviter des pinces en grand nombre dans le champ opératoire. Il est tout à fait essentiel de vérifier la totalité de la jonction saphéno-fémorale et d'exposer au mieux les faces de la veine fémorale pour rechercher des perforantes hautes ou des veines isolées s'abouchant directement dans la voie profonde.

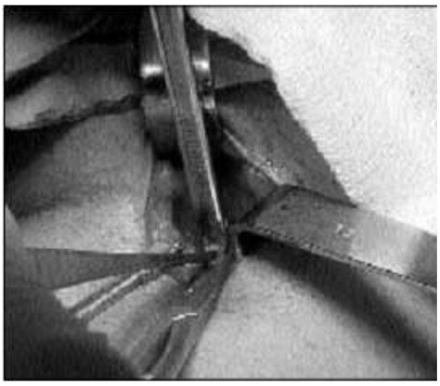
2. Les méthodes de traitement de la jonction saphéno-fémorale

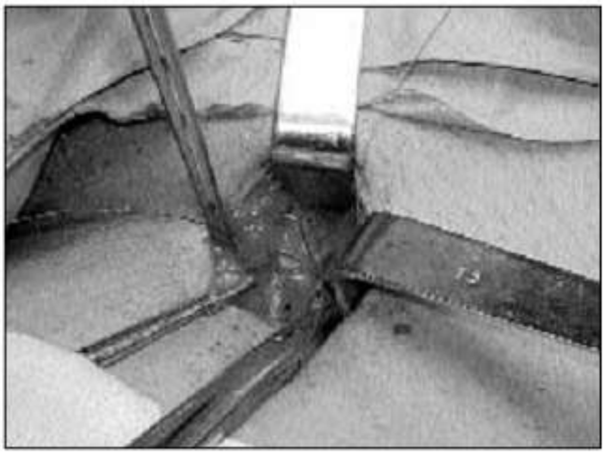
Les opérateurs se sont acharnés à éviter l'angiogénèse à partir du moignon saphénien et émanant de l'endothélium veineux.

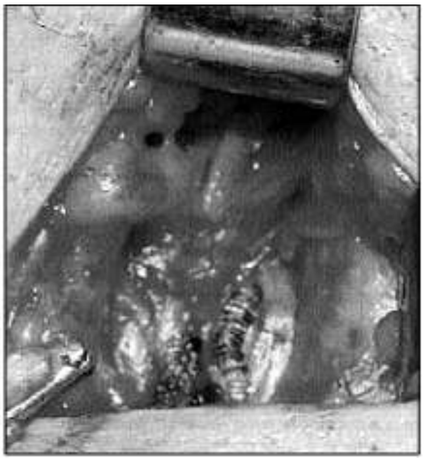
Les méthodes sont nombreuses:

- ► Ligature simple au fil résorbable ou non résorbable en laissant toujours un moignon le plus petit possible que certains coagulent sur leur face endothéliale.
- ► Surjet d'enfouissement du moignon.
- ► Ligature doublée ou appuyée.
- ► Fermeture par un surjet sur la jonction saphéno-fémorale.
- ► Micro-clips posés au ras de la veine fémorale (*vessel closure system*) (9).
- ► Fermeture de la fenêtre ovale.
- ► Mise en place d'un manchon synthétique (PTF) en avant ou autour de la veine fémorale réalisant une valvuloplastie saphéno-fémorale externe.









IV. Facteurs des récidives après crossectomie

On peut les classer en anatomiques, chirurgicaux, hémodynamiques et évolutifs.

A. Facteurs anatomiques

Ils sont liés à une imperfection technique, à une exérèse insuffisante, ou aux variations de la disposition de la crosse:

1. Ligature trop basse de la saphène avec persistance d'un moignon de crosse.
2. Branche antérieure sous faciale, cause la plus fréquente, qui a été prise pour la saphène.
3. Présence d'une saphène accessoire négligée.
4. Collatérale qui s'abouche directement dans la veine fémorale commune.
5. Existence d'une perforante haute.
6. Veine collatérale de la crosse communiquant directement avec le réseau pelvien.
7. On insiste actuellement sur la fréquence des récidives liées aux veines du réseau ganglionnaire et de la lame ganglionnaire inguinale. Elles seraient responsables dans 6% des cas d'une insuffisance primaire, tronculaire de la grande saphène, sans incontinence ostiale.

La mise en évidence par écho-doppler d'un reflux dans ces veines est difficile en pré-opératoire (10) et leur description dans la littérature est généralement faite dans les situations de récidive. Certaines de ces veines ont un trajet trans-ganglionnaire. En présence d'une insuffisance primitive des veines ganglionnaires avec valvule ostiale continente et tronc incontinent, la sagesse est de faire appel aux techniques conservatrices de la crosse. Si une crossectomie est décidée parce qu'il existe une insuffisance ostiale importante, une attention particulière doit être portée à éviter tout traumatisme lymphatique, et de faire, de la même manière que l'on fait une hémostase, une lymphostase avec ligature au fil résorbable et non par électro-coagulation. La même précaution prévaut dans les curages inguinaux, ou pelviens, de même que dans les curages axillaires dans la pathologie cancéreuse du sein.

B. Les facteurs chirurgicaux

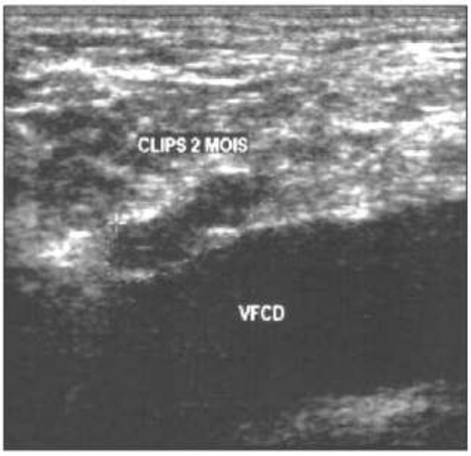
Ils sont liés directement au "geste chirurgical" et sont de trois types:

1. Création d'un hématome important qui va s'organiser et favoriser une néogénèse vasculaire d'où la nécessité de faire une chirurgie la plus exsangue possible, et d'éviter, par une compression suffisante, une hémorragie non contrôlée du triangle de Scarpa.

2. Traumatisme lymphatique qui est source de lymphorrhée mais aussi de récidive à partir des veines de la lame lympho-ganglionnaire. Ceci peut être évité ou minimisé par un repérage précis [utilisation du stripper lumineux ou Visio-stripper (11)], une dissection fine et des gestes atraumatiques, enlevant la crosse, mais seulement la crosse et toutes ses afférentes et ménageant au mieux la lame lympho-ganglionnaire.

3. L'angiogénèse de la zone opératoire: celle-ci peut se développer à partir du moignon saphénien et/ou des extrémités des veines afférentes sectionnées d'où l'intérêt d'effectuer ces interruptions le plus à distance possible de la jonction saphéno-fémorale. Les recherches fondamentales ont mis en évidence différents facteurs de croissance qui sont des agents de réparation et de cicatrisation sécrétés:

- ► Par l'endothélium veineux VEGF (Vascular endothelial growth factor).
- ► Par le tissu conjonctif environnant VGF (Fibroblast growth factor).
- ► Par les cellules endothéliales circulantes (CEC): plaquettes, granulocytes, macrophages. Les CEC voient leur taux augmenter lors de toute intervention chirurgicale, lors des traumatismes fermés, et surtout après sclérothérapie.



Une étude intéressante est celle de J. Strejcek (12) qui effectue des dosages périphériques des CEC, une, deux, et vingt-quatre heures, puis deux jours et dix jours après le traitement de varices. Il constate la présence en plus grand nombre des CEC après scléroses qu'après éveinage, et une normalisation plus rapide des taux de CEC après chirurgie. Cette étude démontre que l'agression endothéliale est moins importante après exérèse qu'avec les méthodes destructives, que cette destruction soit effectuée par effet chimique (sclérose), thermique (laser-radio-fréquence) ou par le froid (cryochirurgie).

C. Les facteurs hémodynamiques

Ils sont liés à une hyperpression dans la voie profonde avec deux mécanismes pouvant s'associer:

a. Insuffisance veineuse profonde ilio-fémorale d'étiologie variable: avalvulation, thrombose et syndrome post-thrombotique, compression pelvienne par tumeur, adénopathies, ou d'origine vasculaire comme dans le syndrome de Cocket, agénésie des veines iliaques beaucoup plus rarement.

b. hyperdistancibilité de la paroi dans certaines conditions (grossesse, orthostatisme prolongé, travail à une température ambiante excessive), sur des terrains prédisposés.

D. Les facteurs évolutifs

Il s'agit là de facteurs liés à la maladie veineuse pariétale, polymorphe, héréditaire, difficile à traiter, souvent générale et de la néoangiogénèse avec des facteurs de croissance dont la connaissance est à ce jour insuffisante pour leur opposer une thérapeutique efficace. La pariétopathie demeure une des principales voies de recherche de l'évolutivité variqueuse.

Malgré ces réserves, la crossectomie, associée à l'éveinage, en respectant une technique rigoureuse, n'est pas une intervention lourde dans la majorité des cas pour un opérateur expérimenté, elle est parfaitement réalisable sous anesthésie locale, et en ambulatoire. Elle est pratiquement dépourvue de morbidité propre si l'on en respecte les indications et les règles techniques opératoires. La cicatrice inguinale est généralement de belle qualité et ne pose pas de problème esthétique.

Les résultats

La littérature fournit des résultats discordants liés à la difficulté de faire des études multicentriques avec des indications et des techniques homogènes et un recul suffisant.

• L'étude qui a le plus de recul est celle de R. Fischer et Coll. (13) qui étudient des récidives à 34 ans de la crossectomie sur 125 patients. Ils constatent 47% de récidives cliniques à la crosse et 60% à l'échodoppler dont 17,6% de pseudo-récidives provenant du voisinage de l'ancienne ligature, 24,8% de varices tronculaires et 17,6% sous forme de corde ou d'écheveau. Cette étude paraît pessimiste. Aucun de ces patients, il est vrai, n'avait pu à l'époque bénéficier de l'indispensable étude échodoppler pré-opératoire.

• En revanche l'étude d'Hammarsten donne 89% d'excellents résultats à 52 mois (14) et celle de Large atteint un chiffre voisin de 89,5% après un suivi de 3 ans (15).

• L'étude de P. Gorny et Coll. sur 321 patients compare CHIVA et crossectomie sur 362 membres dont 194 membres opérés de CHIVA et 168 de crossectomie, la conclusion est sans équivoque favorable à la technique de crossectomie-éveinage (16).

• J.M. Trauchessec sur 1000 afférentectomies élargies réalisées en 12 ans a revu 700 patients: seuls deux d'entre eux ont présenté des récidives par angiogénèse au contact du moignon (17).

Conclusion: modernité du concept de crossectomie-éveinage

1. Aucune méthode ne prétend guérir à coup sûr une "si étrange affection". Aucun traitement ne peut modifier la détérioration pariétale, le terrain variqueux et l'hérédité. Le thérapeute des varices, qu'il soit médecin ou chirurgien, se doit d'être humble et doit savoir se résigner tel un jardinier à rechercher et à traiter périodiquement les "mauvaises herbes " (J. Van der Stricht) en associant toutes les armes à sa disposition.

2. La crossectomie-éveinage reste une méthode de référence mais elle n'est plus systématique mais sélective. Elle doit être réalisée de façon éclectique, en fonction des données de l'exploration pré-opératoire.

3. Quant aux méthodes alternatives qui ont souvent les honneurs des médias, toutes ne nous ont pas convaincus. Certaines nous sont apparues plus hasardeuses, moins efficaces, plus longues, plus coûteuses et plus compliquées que la chirurgie réglée. Les arguments apparents de moindre morbidité, de bénignité, ont, en réalité, peu de poids face à une crossectomie-éveinage dont l'indication est bien pesée avec une technique rigoureuse qui reste une intervention éprouvée et validée, simple, bénigne, économique.

Nous restons cependant ouverts mais vigilants: seules l'épreuve du temps et les études comparatives multicentriques et objectives montreront si quelques unes de ces méthodes (et lesquelles?) pourront bénéficier de la même pérennité que la crossectomie associée à l'éveinage et au traitement de toute source quantifiable de reflux.

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Crossectomie de la jonction sapheno-femorale et veinorraphie fémorale par microclips*)

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Résumé

La chirurgie des varices des membres inférieurs expose chez certains patients, a des récidives variqueuses crurales, dont la cause souvent incriminée est la persistance d'une crosse de saphène interne insuffisamment réséquée, ou d'un moignon de crosse, rendu responsable d'une néo-angiogenese. A partir des données de la littérature, les auteurs pro-posent une technique chirurgicale nouvelle, supprimant le moignon de crosse saphéno-fémorale, ce qui permet de réduire le risque de récidives variqueuses par néogenese. Les premiers résultats, sur un suivi de 6 mois semblent prometteurs, mais demandent une étude prospective, randomisée, à long terme pour juger de l'efficacité durable de cette technique: résection de la jonction saphéno-fémorale avec veinorraphie fémorale par microclips.

Introduction

La chirurgie veineuse superficielle ne se limite plus à la crossectomie et à l'éveinage systématiques des veines saphènes. Des techniques nouvelles ont été présentées récemment, en particulier pour éviter les récidives à partir moignon saphénien. Nous proposons une technique chirurgicale originale supprimant totalement ce moignon résiduel, appliquée chez 41 patients avec un suivi sur 6 mois.

Le syndrome angiogenique du moignon

Le génie évolutif de la maladie variqueuse ou "l'angionéogénese" a suscité ces dernières années une abondante littérature.

Les reprises opératoires pour récidives variqueuses sont estimées de 4 à 25% selon les séries. Glass dans deux études prospectives évalue la survenue des phénomènes angiogéniques à 25 % des cas sur 4 ans, soit un patient sur quatre (5, 6).

Les lésions observées lors de la reintervention ont été:

- plus souvent un cavernome inguinal, fin chevelu veinulaire anarchique, noyé dans le tissu fibreux ou scléreux,
- qu'une véritable néocrosse reconstruisant une saphene néoformée.

Gorny et coll. (7, 8) ont décrit un "syndrome angiogénique du moignon", désignant un processus de néogénese dont le moignon de crossectomie, "véritable plaie vasculaire", se comporte comme le " starter". Tout se passerait comme si l'organisme recherche une cicatrisation et une reconstitution tissulaire à partir du moignon résiduel!

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L'angiogénese est actuellement bien connue de tous les phlébo-angéiologues, la recherche fondamentale ayant mis en valeur l'existence de trois types de facteurs de croissance visant à la cicatrisation après agression chirurgicale:

- facteurs de croissance sécrétés par les agents circulants du sang (plaquettes, macrophages, granulocytes): PDGF, GCSF.
- facteurs sécrétés par l'endothélium veineux: VEGF
- Facteurs sécrétés par le tissu conjonctif environnant: FGF (fibroblast growth factor).

Techniques de prévention des récidives variqueuses crurales

Parmi les causes des récidives, Gorny (7, 8) admet trois facteurs favorisants:

- la faute technique individuelle mettant en cause la compétence et la responsabilité de l'opérateur.
- l'évolutivité naturelle de la maladie, difficile à contenir malgré un bon suivi phlébologique (surveillance échodoppler, sclérothérapie, contention).
- l'évolutivité provoquée: l'angiogénese postchirurgicale.

Nombreux sont les auteurs qui ont recherché une prévention du syndrome angiogénique à partir du moignon. Certains proposent la fermeture de la fosse ovale par des fils résorbables ou non résorbables [Frulini (4), Langé 1998 (9)]. D'autres interposent une plaque de PTFE entre les veines profondes et les tissus superficiels [Creton, 1998 (3)].

Selon Gorny, (7, 8) trois mesures préventives semblent efficaces:

- utilisation de fil non résorbable pour fermer les crosses réséquées.
- l'enfouissement de l'intima exposée au niveau du moignon.
- la réalisation d'un cloisonnement séparant les plans superficiels des plans profonds.

Compte tenu des données de la littérature et en supposant que le moignon saphénien résiduel est le phénomène inducteur des récidives, nous proposons un technique originale simple consistant en la suppression totale de ce moignon. Elle pourrait prévenir ainsi le risque de récidives.

Technique de veinorraphie fémorale par microclips à la pince VCS

A. Description

La jonction saphéno-fémorale abordée par une courte incision dans le pli de l'aine, est isolée après clipage-section le plus loin possible des différentes collatérales.

La dissection découvrira complètement les faces latérales de la jonction et de la veine fémorale, qui sera clampée partiellement.

La jonction est réséquée au ras de la veine fémorale, dont les deux berges sont rapprochées et adossées par une suture mécanique par microclips délivrés par la pince VCS (figure 1).

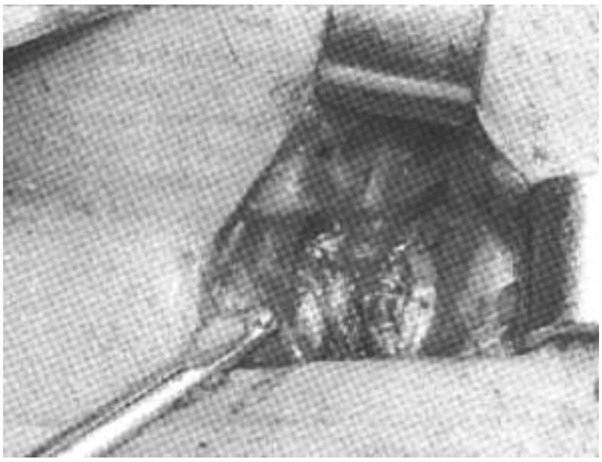
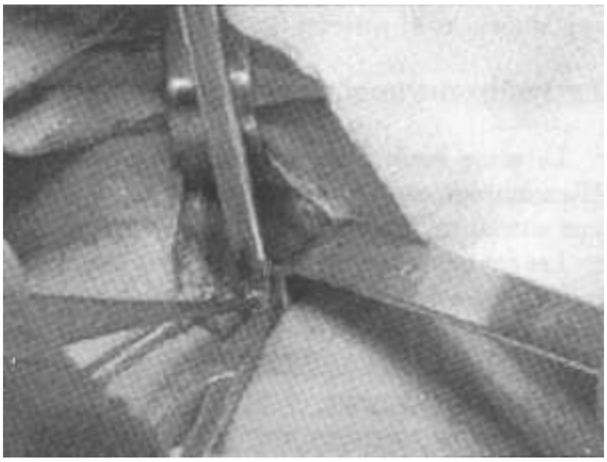


Figure 1



La suture est étanche d'emblée lors du déclampage; les microclips déposés régulièrement un par un fixent l'adventice et la média de la veine fémorale sans perforer l'intima, ne laissant ainsi aucun moignon résiduel (fig. 2) L'intervention se termine de façon classique par la fermeture du foramen ovale, du tissu cellulaire sous-cutané et de la peau.

Figure 2

B. Historique. Avantages et inconvénients

Cormier et coll. dans leur "*Traité de Technique Chirurgicale*" préconisaient déjà en 1977 la section de la crosse sans moignon, ce qui revenait à une veinotomie fémorale classique (2).

J. Baudet en 1994 utilisait des microclips en acier pour des microsutures vasculaires dans les reconstructions plastiques artérielles (1).

Au cours d'un symposium à New York en 1996, Wolff Kirsch introduisait le système de fermeture vasculaire par microclips (Vessel Closure Système ou VCS) et rapportait son expérience in vitro en démontrant qu'au bout de un an, les pontages fémoro-poplités ne subissaient pas au niveau des sites anastomotiques ni hyperplasie intimale, ni chute de pression intraluminale (12).

Frédéric Schild fait les mêmes observations pour les fistules artério-veineuses pour hémodialyse (11).

Richard Perrymann, dans ses travaux sur les porcs, notait sur les anastomoses mécaniques aortiques une intima lisse et l'absence de réaction de l'adventice (10).

Cette technique de suture vasculaire par microclips à la pince VCS n'expose à aucun inconvénient si les microclips sont disposés régulièrement mm par mm, et que les deux berges veineuses sont nettes, peu épaisses et bien adossées.

Les avantages sont réels:

- pas d'hématome pariétal,
- pas de perforation de l'endothélium veineux, donc pas de réaction d'hyperplasie intimale,
- les microclips en titane sont biologiquement inertes.

Résultats et Discussion

Un premier suivi a été réalisé chez 41 patients opérés pour incontinence valvulaire de la jonction sapheno-fémorale, avec un contrôle échographique à un mois, trois mois et six mois.

Une seule récidive a été constatée en dehors de la zone de veinorraphie fémorale. Elle a été traitée avec succès par injections sclérosantes écho-guidées.

Notre série à l'heure actuelle comporte 113 cas de crossectomie complète saphene interne sans moignon résiduel avec veinorraphie fémorale par microclips.

Un suivi actuariel sur cinq ans est en cours.

La technique de veinorraphie fémorale par microclips à la pince VCS est une méthode simple, rapide, praticable de première intention chez la plupart des patients ne présentant pas de surpoids. Il convient d'exclure du bénéfice de cette technique le patient obèse avec une crosse profonde noyée dans le tissu adipeux.

Les indications de cette technique peuvent être étendues à toute chirurgie de crosse saphéno-incontinente associée à des gestes complémentaires sur le tronc saphénien ou sur des collatérales ou perforantes jambières (phlébectomie ambulatoire). Une méthodologie comparative microclips versus ligature classique serait intéressante afin d'évaluer les résultats à long terme et de l'efficacité durable de la méthode.

Conclusion

La suture par microclips VCS de la veine fémorale au niveau de la jonction saphéno-fémorale lors d'une crossectomie est une technique simple et rapide, réduisant l'hématome post-opératoire. La suppression complète du moignon saphénien résiduel associé au cloisonnement des espaces devrait empêcher le développement de l'angiogenese à partir de la zone opératoire.

Pour justifier son intérêt, cette technique de veinorraphie fémorale par microclips nécessite une étude prospective, comparative et randomisée, pour quantifier les résultats à 5 ans.

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Vascular thrombosis in child care practice*)

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Abstract

Although relatively frequent in adult care practice, thrombotic stroke is quite rare in child care practice. The authors analyze the diagnosis and treatment difficulties of vascular thrombosis in children, in terms of their own clinical practice.

Keywords: *Pediatric venous Thrombosis, Nephrotic syndrome, Lupus, Treatment*

Rezumat

Accidentul vascular trombotic, relativ frecvent în patologia adultului, este relativ rar în practica pediatrică. Autorii analizează prin prisma cazuisticii proprii problemele de diagnostic şi tratament în trombozele vasculare la copil.

Cuvinte-cheie: *Tromboza venoasă la copil, Sindrom Nefrotic, Lupus, Tratament*

General considerations

Vascular thromboses represent rare failures in medical practice of the child.

The polymorphism in the etiology, the relative rarity and semiologic complexity make the performance of homogeneous trials difficult, so that the discussion and diagnosis and therapeutic standardization are still in the phase of desideratum. Its high severity, "life threatening", determines the agglomeration of these cases in special intensive care units, so that the approach becomes particular to them.

From point of view of the patient's age, vascular thromboses of the child are divided in two groups:

A. *Neonatal vascular thromboses*
B. *Infant and child vascular thromboses*

We consider that the etiology approach is the main advantage of this classification. Therefore the neonatal vascular thromboses are favored and precipitated by the age particularities (in the "classical" textbooks, the newborn is characterized as suffering from hypothermia, and being at risk for bleeding and hyporeactivity). Circulatory system

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changes at birth, neonatal infections, venous catheterization (especially the umbilical one) required during reanimation and therapy of severe conditions (septicemia, respiratory distress syndrome), as well as the hypercoagulability caused by polyglobulia and fibrinolysis reduction are determinant factors of vascular thromboses. Vascular thromboses are most frequent in neonatology and have various etiology factors; there are two main causes: sepsis and venous catheterization - umbilical ones especially. Renal vein thrombosis, which occurs quite frequent, is generally masked by the main disease, so that the diagnosis is late, after remission, if it was unilateral or with acute renal failure, and the diagnosis is made at ultrasound (enlarged kidneys, with loss of corticomedular differentiation and absence of Doppler signal).

Thrombosis of the trunk of inferior vena cava, an extremely severe complication, usually has a poor prognosis, being incompatible with survival. Portal vein thrombosis – an "extension" of umbilical vein thrombosis, secondary to catheterization and/or administration of hypertonic solutions at this level – is discovered later during history taking when the etiology of prehepatic portal hypertension (Banti syndrome) is investigated.

The arterial thromboses severity index is highest per se and also because of its trigger. The newborn is in severe shock, with extreme palor and visible "gangrene" type thromboses of the extremities (fingers, nose, ear) and echo-Doppler examination reveals the unilateral or bilateral renal artery thrombosis as part of aortic thrombosis (a complication usually incompatible with life). Other localizations are the mesenteric ones, with intestinal necrosis and/or iliac or brachial arterial axes.

The infant vascular thromboses are complications of hypovolemia from dehydration and/or septicemia, the prerenal acute renal failure being the one that provides the clinical spectrum of the case. The hemolytic uremic syndrome is the other etiology that generates vascular thromboses in infant-child age group, with different locations, from the mesenteric and cerebral ones to the coronary location, responsible for the sudden death; other cause of coronary death in children is Kawasaki syndrome.

Vascular thromboses may occur in child during the following illnesses:

- nephrotic syndrome
- disorders of hemostasis
- collagen diseases with positive LA
- primary antiphospholipid syndrome
- factor V Leiden syndrome
- paraneoplastic syndrome
- septicemia
- multiple trauma
- surgery
- central and/or peripheral venous catheters with therapeutic role (thrombosis is secondary to their thrombozation and/or incorrect use).

The main causes of venous thrombosis in children, by M. Robin, C. Bayer 1987, cited by Ellis D. Avner, William E. Harmon, Patrick Niaudet (1)

Local factors	General pathology	Constitutional diseases of hemostasis
Direct venous agression *- venous puncture* *- central catheters* *- ventricular derivation catheters*	Drugs that modify the hemostasis *- oral contraceptives* *- asparaginase*	Constitutional deficit *- ATIII* *- Protein C* *- Protein S*
Venous compression *- plaster* *- fractures*	Nephrotic syndrome Inflamatory diseases *- SLE* *- Ulcerative colitis* *- Crohn disease*	Plasminogen anomalies *- hipoplasminogenemia* *- displasminogenemia,* *- defect of tissue plasminogen activator release*
Perivenous inflamation secondary to infection *- osteomyelitis* *- ENS infection* *- brain venous thrombosis*	Metabolic Diseases *- Homocisteinemia* *- Hyperlipemia* Septicemia *- Staphylococus* *- Candida* *- Streptococus*	
Venous malformations *- agenesia, hipoplasia or ectasia of the profund truncks* *- Membranous obstructionof vena cava*	Other general factors: *- surgery* *- malignant diseases* *- cardiac failure* *- obesity* *- bone marrow involvement* *- physical effort, trauma*	

The diagnosis of vascular thrombosis essentially assumes the recognition of their possible existence and their search; the diagnosis implies the whole medical team involved but also adequate access to medical technology, diagnostic screening.

Diagnosis

Anamnesis should follow two directions: the family history (most hereditary thrombotic diseases have an autosomal dominant transmission with exception: homocisteinemie, plasminogen activator deficiency) and the significant pathology (acquired etiology of thrombosis): antiphospholipid syndrome, nephrotic syndrome, primary autoimmune disease, SLE, Malignancies, Liver Diseases, Renal failure, Sickle cell anemia, DIC, PTT, inflammatory bowel disease. (2)

Establishment of the site and extension of the thrombosis:

☐ Non-invasive: Eco Doppler, CT scan, MRI

Laboratory diagnosis of coagulation: positive inflammatory tests, Functional tests for identification of various anticoagulants factors deficiency (AT III, protein S, protein C), raised PDF, raised D dimmers.

Protein C Deficiency

- Protein C = vitamin K dependent plasma glycoprotein, (synthesis encoded by a gene located on chromosome 2) which was activated functions as an anticoagulant by inactivating FVa and FVIIa (anticoagulant effect)
- It neutralizes the inhibitor 3 of the plasminogen activator
- Plasma levels below 50% (normal range 70-100%) = Thrombosis
- Inherited - autosomal dominant
- The prevalence in the general population: 1:500
- Subdivided into 2 types: Type I Deficiency (low activity and low antigen level) - quantitative, and Type II Deficiency (low activity and normal antigen level) – qualitative
- Patients: homozygous and heterozygous – they have prot C serum levels ~ 50% (they can be asymptomatic or require additional risk factors - pregnancy, estrogen)
- In homozygous newborns may cause a fatal thrombotic disorder, which may present with neonatal *purpura fulminans* or CID
- Diagnosis is made on functional tests (for both types) and immunological tests for type I

(3)

Activated protein C resistance (Factor V Leiden) - identified in 1993

- The most common hereditary predisposition to thrombotic disease
- 20-60% of all patients with recurrent thrombotic complications
- Transmission autosomal dominant
- Breakpoint mutation in the position 1691 of the nucleotide chain that is coding the synthesis of factor V gene (identified in 1994)
- FV Leiden can't be degraded by activated protein C
- Homozygous – by 80 times the risk of thrombosis is higher than the general population
- Heterozygous – by 7-8 times higher risk of thrombosis compared to the population. The risk increases if there are complementary risk factors, genetic or acquired ones: Pregnancy, Contraceptives, Surgery, Trauma
- Clinic - venous thrombosis with different locations

AT III deficiency:

- Transmission: autosomal dominant
- Prevalence in general population: 1:600
- Type I (quantitative deficiency, only heterozygous) - parallel decrease in AT III levels, measured both by functional and immunological tests. It is a gene mutation / deletion, leading to the decreased protein synthesis

- Type II (qualitative deficiency, hetero / homozygous) - breakpoint mutations leading to synthesis of abnormal proteins. Decreasing of AT III activity in functional tests (normal immunological tests) associated with normal amounts of protein
- acquired AT III deficiency: Liver diseases, Nephrotic syndrome, CID, Treatment with oral contraceptives

(4)

Protein S Deficiency - described in 1984

- Protein S - vitamin K dependent plasma protein that mediates the activity of activated protein C, acting as a cofactor in the inactivation reaction of the FVa, FVIIIa and has an inhibitory action on FXA.
- Inherited - autosomal dominant
- Subdived into 2 types:
  - Type I Deficiency (low activity and low antigen level) – quantitative
  - Type II Deficiency (low activity and normal antigen level) – qualitative
- Patients: homozygous (rare) and heterozygous (majority), ~ 50% level

(5)

- In the severe forms - purpura fulminans
- Diagnosis:
  - Screening tests for coagulation are normal
  - The measure is indicated only after exclusion of activated protein C resistance
  - Immunological tests - for quantitative levels of total protein and free fractions

As long as the diagnosis of vascular thrombosis is established, the next step is to determine the location, extension and type of affected vessels: artery (main trunk, side branch), vein (main trunk, side branch), capillary territory, Lymphatic Drainage System.

The level of damage related to the affected organs organ / organs and, consequently, the functional prognosis and / or life depends fundamentally on these data.
(6, 7)

Treatment

The treatment of vascular thrombosis represents a major emergency, the most important factor that influence the early and late prognosis is the period of timebetween the onset and the diagnosis (ischemia, irrigation disturbances). The prevention implies the recognition and the evaluation of the favourable conditions and the establish of the therapeutic measures. Considering all these points we may conclude that it is necessary to treat both the underlying disease and the proper thrombosis.

Thrombectomy – thrombolisis is the mainstain of the therapy. Unfortunately, the late diagnosis or the unfavorable factors like the site and the extension of the thrombosis are the causes of the illusory radical solution.

From a synthetically point of view, the treatment strategy consists of:

- ☐ Heparinotherapy
- ☐ Oral anticoagulants
- ☐ Thrombolitic treatment (fibrinolitic)
- ☐ Surgical treatment
- ☐ The vena cava filter

Thrombolytic agents are difficult to handle, there is no standardization of doses and ways of administration (doses, duration) and, last but not least, they are not always available at the right time. Their strategy and their unique properties related to their use are set as follows:

Throbolithic agents

- ☐ **Streptokinase.** Dose: 4000-6000 UI/BW iv push in 30 minutes, followed by iv infusion 1400-2000 UI/BW/hour for 24 – max 72 hours. It could determine hypersensitivity. It is metabolised by antibodies (patients with a history of streptococal infections or the newborn with maternal antibodies)
- ☐ **Urokinase Dose:** 4400 UI/BW iv push in 20 min, followed by iv infusion 4400 UI/BW/hour – 12 hours. It doesn't cause hypersensitivity. It is not metabolized by antibodies.

Monitoring the Streptokinase and Urokinaze treatment: Thrombin Time (8, 9). Effectiveness – increases aPTT 2-5 times

- ☐ **Tisular activator of fibrinogen.** It is produced in the human body by the vascular endothelium and industrial produced using recombinant technology. Dose – 0,1-0,5 mg/bw/hour

(10)

New thrombolythic agents

- ☐ APSAC – unisolated plasminogen SK activator complex
- ☐ Pro-urokinaze
- ☐ Therapeutical indications in thrombosis: Effective just in case of early administration (first 24-48 hours). Greater risc of hemmorhage than heparine

Under these conditions, anticoagulant therapy is usually a heparin one (intravenous or oral), the main features being the following:

Heparinotherapy: The anticoagulant effect of heparine is not a direct one, but it is done through AT III.

Types of heparin: *Unfractionated* (standard) heparin, *Low molecular wight heparin* (enoxaparine, deltaparine, nordraparine) (LMWH)

- ☐ *Unfractionated (standard) heparin:*
  - endovenous
  - Half-time = 1-2 hours
  - Inactivated in the liver
  - Renal excretion
  - The action is related to the endothelial cells and plasma proteins binding
  - Facility of using

- *LMWH*
  - Half-time: 2 times longer
  - More reduced endothelial and plasma protein binding
  - Subcutaneous byodisponibility is 3-5 times higher
  - Administration does not need laboratory monitoring

Dosing of heparin: Adolescents /elder children – 5000 UI iv push afollowed by 30.000 UI/24h, during the first 24h, then 10.000-20.000 UI every 12 hours, for 5-10 days. Young children – 50 U/Kg iv push, followed by 10-15 UI/bwh/hour infusion, or 75-100 UI/bwh every 4 hours. Enoxparine dosing – 2.5 mg/Kg/day, sc, or 1 mg/kgc x 2/ day, sc

Monitoring TPT at every 6 hours, then daily from initiation. TPTa - 1.5 to 2.5 x N

Complications:
- Major bleeding (5-7%)
- Decreased ATIII
- Thrombocytopenia (6%)
- Thrombocytosis (0.2%)

Overdose heparin - protamine sulphate (PS): 1 mg PS - 1000 IU heparin
(11, 12)

Oral anticoagulants are drugs that inhibit hepatic biosynthesis of Vitamin K - dependent coagulation protein (II, VII, IX, X, C, S)

Features: binds to albumin, metabolizes in the liver, has a half time ~ 36 hours, reach effective serum level after 4-5 days of treatment initiation (13)

Monitoring of prothrombin time / INR, with a goal of INR = 2-3

Dosing of warfarin - 0.1 to 0.15 mg / *Kg* / day (max 10-15 mg / day) - loading dose, then maintenance 2-10 mg / day, depending on INR

Adverse effects: Hemorrhage, Skin necrosis

In case of overdose - Vitamin K, PPC
(14, 15)

Surgery remains elusive in the vast majority of cases because of the exceeding of the optimum duration, but also due to the location and the extent of thrombosis and / or the access to appropriate filter.

Material and method

The Department of Nephrology and Pediatric Dialysis of Fundeni Clinical Institute was established within the Pediatric Clinic Fundeni in December 1992 when the first hemodialysis was performed in a 4 years 10 months old child suffering of hemolytic-uremic syndrome. Today this department is integrated part of *Uronephrology and Renal Transplantation Fundeni.*

Between 1992-2000 we diagnosed and treated in our Department more than 1800 pediatric patients suffering of renal pathology (in 24 beds, 5 posts of hemodialysis and 2 posts of peritoneal dialysis). Out of these 28 children or 1.55% presented various vascular thrombosis. From an ethiologic point of view the statistics are as follows:

1. Systemic lupus erythematosus (S:LE): 7 out of 110 patients (6.36% of the patients with SLE or 0.38% of the total patients in the study)
2. Sepsis: 5 out of 28 patients (17.85 of the patients with sepsis or 0.27% of the total patients in the study)
3. Paradoxal thrombosis (patients with thrombocytopenia <50.000/mmc with malignant desease, who develop vascular thrombosis as part of the paraneoplastic syndrome): 5 out of 537 patients (0.93% of the mentioned subgroup or 0.27% of total)
4. Nephrotic syndrome with clotting disorder (thrombocytosis, hyperfibrinogenic anemia, LA positive): 4 out of 137 patients (2.91% of the patients with nephrotic syndrome or 0.22% of the total)
5. Hemolythic-uremic syndrome: 3 out of 53 patients (5.66% or 0.16% of total)
6. Primary clotting disorders - anti phospholipidic syndrome: 3 out of 15 patients (20% or 0.16% of the total)
7. Major circulatory disorders: 1 patient with bacterian pericarditis (staphylococcus) with inferior vena cava thrombosis (0.05 % of the total patients in the study)

As it may be noticed, SLE has the highest incidence of vascular thrombosis, also due to the high number of patients. The patients diagnosed with SLE underwent a complex and standardized therapy, consisting of an induction phase and maintenance phase, using multidrug therapies: puls-therapy with Cyclophosphamide, cortisone puls-therapy, oral corticotherapy, Azothioprin or Mycophenolate Mofetil, Ciclosporin. 7 patient underwent trough plasmaferesis, 3 of them presenting with severe CNS symtoms (seizures, coma).

Vascular thrombosis in SLE manifested as follows a one patient (R.M., age 16y, female) with capillary thrombosis and secondary necrosis of three phalanxs of the hand and 2 of the legs, also right atrial thrombosis (figure 1-2), a 3 patients with cerebral microthrombosis, a one patient with popliteal thrombophlebitis, one patient with femoral thrombophlebitis and a one patient with axillar thrombophlebitis.

Figure 1: Necrosis of two phalangs of the leg due to Vascular thrombosis in Systemic Lupus erythematosus

Figure 2: Necrosis of right index due to Vascular thrombosis in Systemic Lupus erythematosus

In all these cases treating vascular thrombosis was a major emergency and consisted of iv Heparin or subcutaneous LMWH followed by oral Warfarin. After stabilization it was followed by maintainance treatment with Warfarin/Aspirin and Vessel Due F. For the first of the pre-mentioned cases surgical toilet was performed due to the severity of the necrosis.

Between 1992-2000 we treated 137 patients presenting primary or secondary nephrotic syndrom (the patients were referred to us), in/with a severe condition due to the lack of response to initial therapy and/or important complications. Four of them presented with main blood vessels thrombosis (inferior cava branch). These cases have been diagnosed at the age of primary school/ pre-pubertal. We will present here a patient from Pediatric Clinic, St. Mary, Iasi, Dr. Mihaela Munteanu - for the quality of the prosector images (figure 3-4):

Figure no.3: Thrombosis of inferior vena cava. Aspect of computer tomography, native examination

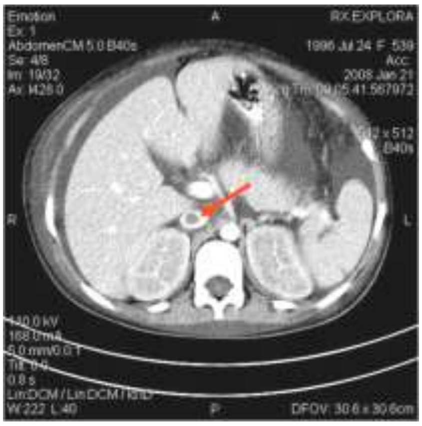

Figure no.4: Thrombosis of inferior vena cava. Aspect of computer tomography with contrast Iv examination.

Figure no.5A: Thrombosis of left renal vein. Aspect of magnetic resonance.

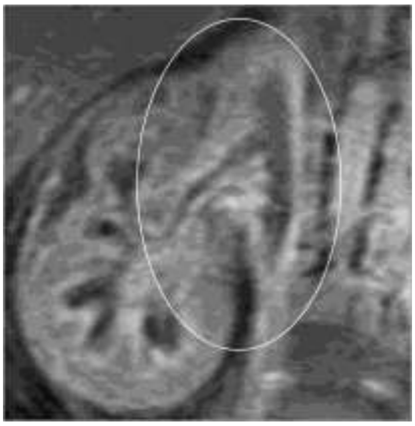

Figure no.5B: Thrombosis of left renal vein - Aspect of magnetic resonance- detail.

In another patient a 8 years age, male *(figure no.5A, 5B),* the nephrotic syndrome had begun atypical with thrombosis of left renal vein (leading to left nephrectomy) followed at 2 weeks by thrombosis of inferior cava branch extended in the right renal vein. Complex tests of the coagulation make the absence of any symtoms until this age and the onset with albuminuria (preceding the thrombosis) lead to labeling as atypical nephrotic syndrom.

In these cases the treatment consisted of:

a) Emergency therapy: iv Heparin, 10 days, followed by LMWH subcutaneous (for 12 days in average) and maintenance therapy with Warfarin and Vessel Due F po.

b) Nephrotic syndrome treatment, emphasizing the hypovolemic therapy - favoring factor of coagulation disorders.

Results and discussions

The course of the disease for four patients was favorable, achieving vascular re-permeability for all patients (medicative thrombolysis). For the patient with left nephrectomy and thrombosis of inferior cava branch, the evolution to renal impairment imposed the inclusion in the extrarenal filtering program, the chosen method being automatic peritoneal dialysis (vascular aproach with catheter or fistula would have been a risk factor!). This patient for whom was also acquired complete vascular re-permeability, the renal scleroatrophic lesions (highlighted by echography and magnetic resonance) have determined, dialysis dependence' even if a reoccurrence of diuresis was achieved but with reduced urinary concentration.

Hemolytic-uremic syndrome (HUS) represents a heterogenic group of disorders of various etiologies but unique pathogeny, which consists of mycroangiophatic hemolytic anemia, thrombocytopenia of consumption and acute renal impairment. Didactic classification in typical SHU (SHU+diarrhea) and atypical SHU (SHU without diarrhea) permits, besides understanding the pathogenic mechanism with CID involvment in the atypical forms also understanding of the therapeutic strategy.

The use of extrarenal filtering and plasmapheresis together with administrating of PPC, transfusion of red blood cells and hydroelectrolytic and acidobasic rebalance have lead to a significant improvement of prognosis. Practically, nowadays – with few exceptions (where the experience and the equipment are vital) – survival is the norm and the renal function restoration with restitutio ad integrum is expected.

From 1992 until now 53 patients with SHU have been treated in our clinic. For 33 of them (62.26%) extrarenal filtering was used with a mortality rate of 8%; n 5 cases due to the young age less then 9 month, youngest being 1 month old only and the small body size (Weight less then 7 kg) peritoneal dialysis was the the treatment choice. For the other patients we used vascular approach for the speed of the action and possibility to alternate the methods: dialysis/ hemodiafiltering/ hemofiltering.

Plasmapheresis was used as well for 2 patients, unfortunately less successful.

For the patients presenting with SHU, vascular thrombosis manifested as follow an one patient, female, a 5 years, with mesenteric infarction with intestinal loop necrosis, necessitated surgical resection. Acute renal impairment benefited of hemodiafiltering. The course of the disease was unfavorable, turning slowly towards CRI and has been included into hemodialysis program after 10 years from the acute episode. An a two patients had stroke, one died during treatment, the other presents with cerebral atrophy with normal intellect and slightly flaccid legs *(figure no.6, 7).*

Figure no.6: Cerebral haemorrhage in the fronto-parietal lobe. Aspect of magnetic resonance

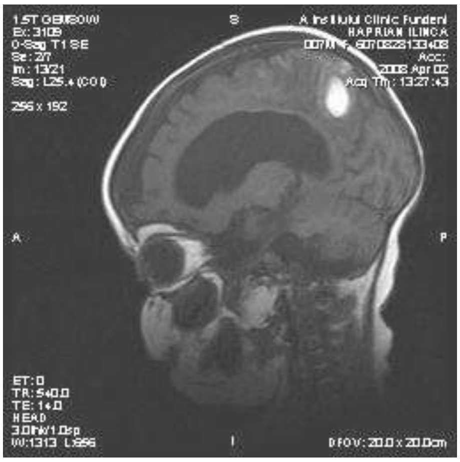

Figure no.7: Cerebral haemorrhage in the occipital lobe. Aspect of magnetic resonance.

Another chapter represents vascular thrombosis in the malignant deseases, where thrombocytopenia as manifestation of the medular impairment syndrome is a protective antithrombotic factor, thus the name of this chapter „Paradoxical thrombosis". During 1992-2010, 12 out of 537 oncopediatric patients necessitated extrarenal filtering therapy: 10 due to the tumoral lyses syndrome and 2 for acute renal failure post-renal-abdominal-pelvic tumor. In all this cases the paratumoral syndrome, the tumoral lyses syndrome and the last but not least the chateter for hemodialysis represented the cause of vascular thrombosis. In other 2 cases thrombosis manifested at cerebral level, with unfavorable course of disease. The other 2 patients had ileo-femoral thrombosis, on the catheterizing axis; in these cases iv Heparin therapy led to medicative thrombosis.

Another cause of vascular thrombosis is septicemia with alterations of vascular flow, disseminate intravascular coagulation with/without associated clotting disorders (lack of AT III or Protein S). This was the case for 9 out of 44 children presenting with toxico-septic status. In 3 cases a lack of AT III (2 patients) and Protein S (1 patient) was found. In one of the cases with shortage of S Protein the sepsis caused thrombosis of left axillar vascular axis and right popliteal artery, the thrombolytic therapy with Streptaze (Intensive Care of „C.C.Iliescu" Institute) failing. For another patient the significant disturbance of venous return secondary to a pericarditis has caused the inferior cav branch thrombosis. In the other 7 cases vascular thrombosis manifested as phlebo-thrombosis, being induced by the septic component, being localized at the lower limb level for 5 patients and upper limb for the other 2.

Conclusions

The use of more and more complex technologies in the severe cases, catheterisation maneuvers for diagnostic and/or therapeutical purpose increase the risk of vascular thrombosis-accidental or expected complication but unavoidable in the assisting conditions within intensive care services.

Recognition of the thrombogenic conditions and early localization (Echo Doppler, MRI) is mandatory for an adequate therapy, decisive factor for a favorable outcome.

Due to the relatively rarity of the cases and etiologic polimorphy it is relatively risky to try a classification and standardization of the diagnosis and treatment.

After reviewing all the available literature it can be stated that vascular thrombosis in children still represents a chapter which is being written from the accumulating clinical experience.

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Part 7.

VENOUS PATHOLOGY

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We hope that this book will serve as a source for fertilizing and evoking new scientific thoughts and experiments in the cardiovascular surgery field.

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Part 8.

CORONARY PATHOLOGY

Coronary Artery Bypass Grafting for In-Stent Restenosis*)

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2. *Hospital Pitié-Salpétrière, American Hospital of Paris, France*
3. *Department of Thoracic and Cardiovascular Surgery, West-German Heart Center Essen, University Hospital Essen, Essen, Germany*

Introduction

In the era of stenting, percutaneous coronary interventions are used as initial revascularization strategy but there is the risk of in-stent restenosis in a significant number of cases (15-45%) [1; 2]. In-stent restenosis is an important clinical problem and those patients are a challenging group for both interventional cardiologists and cardiac surgeons, as generally they are patients with aggressive coronary atherosclerosis to whom the recurrence of stenosis in case of percutaneous approach is probable to happen [3; 4].

In-stent restenosis is mainly caused by intimal hyperplasia and sometimes by stent elastic recoil [1; 5]. There is consistent evidence that the percutaneous re-treatment of these cases leads to suboptimal clinical results and is associated with high risk of additional restenosis or occlusion [3].

We present some cases of coronary in-stent restenosis from the Army's Center for Cardiovascular Diseases in Bucharest. Figure 1 shows right coronary artery stent restenosis with significant hemodynamic impact. Figure 2 represents a LAD stent restenosis and Figure 3 shows a stent occlusion on the segment 2 of LAD (A, B – different incidences). The distal LAD is refilled from the right coronary artery (Figure 3 C).

Figure 4 presents a case of triple coronary vessel disease from West German Heart Center Essen stented on the first diagonal, LAD and Cx.

Evidence from randomized trials and from large registries has proven that concerning three vessel disease CABG is more effective treatment than PCI not only in terms of freedom from recurrent angina and reintervention but also in terms of survival and freedom from major adverse cardiac events (MACE) [6-9].

Still optimal management of in-stent restenosis is controversial, but surgical approach seems to be a good alternative [10].

*) **Romanian Journal of Cardiovascular Surgery ■ 2011, vol. 10, no. 3, pp. 191-198**

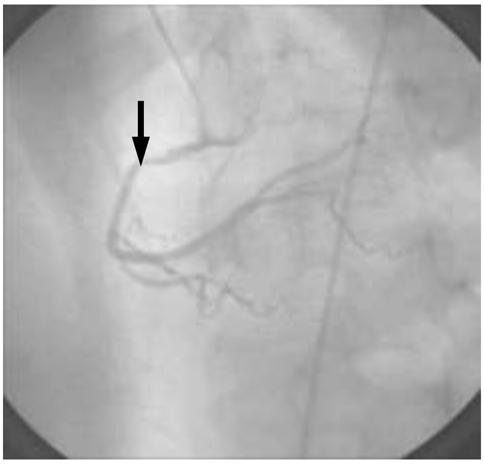


Figure 1: Right coronary artery in-stent restenosis

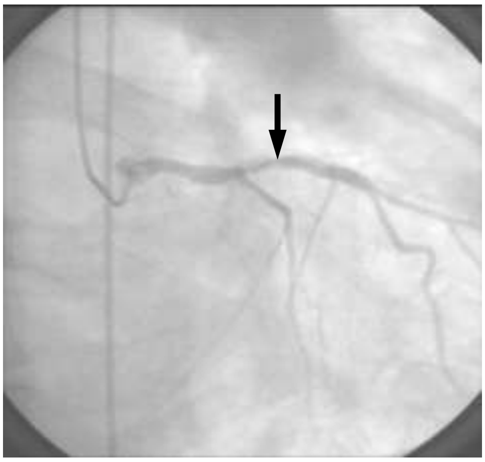
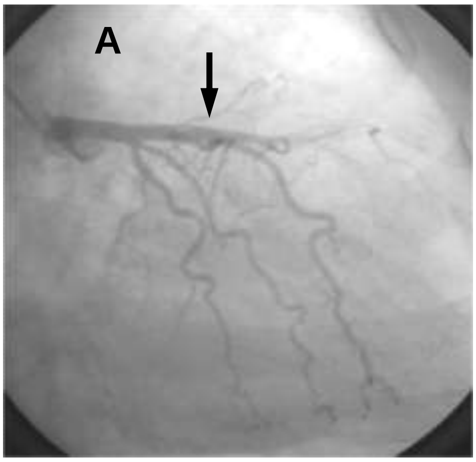
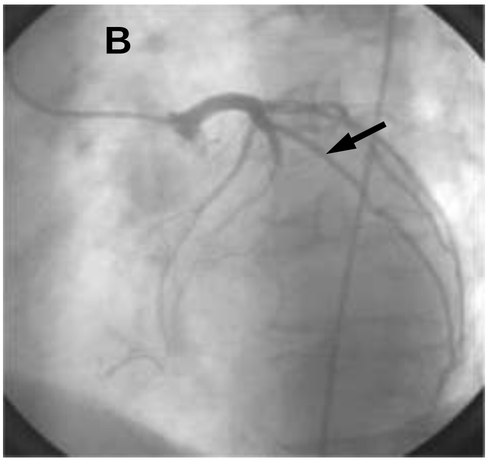


Figure 2: LAD in-stent restenosis





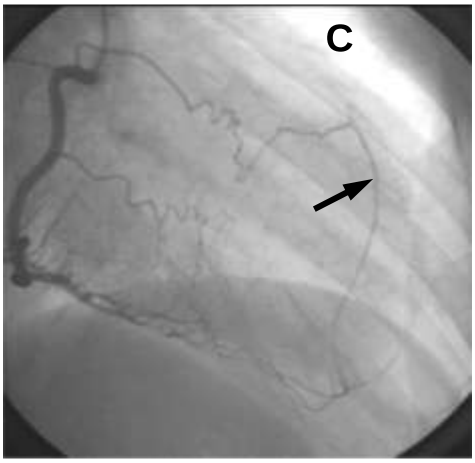


Figure 3 A, B, C:
Occlusion of the stent on LAD

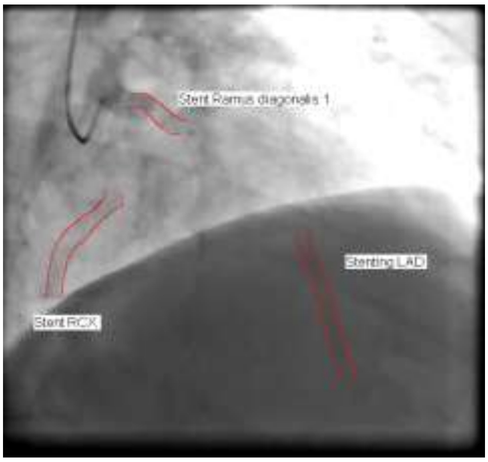


Figure 4. Stenting for Triple Vessel Disease

Coronary endarterectomy and stent removal

Because of the increasing use of multiple stents in diffuse and distal lesions of coronary arteries, the surgeon should use special and difficult techniques in order to perform coronary revascularization. One of them is coronary endarterectomy (CE) and stent removal followed by arterial or venous grafting.

CE was first described by Bailey in 1957 [11]. It is performed in limited cases of diffuse and distal lesions. Livesay and Goldstein [12;13] reported negative evidences in the '90 that CE was associated with a high perioperative risk and poorer log term results but recent reports changes this statement and shows safety and efficacy of CE and bypass grafting [14].

There are just a few studies and case reports regarding the surgical removal of previously implanted stents and subsequent bypass grafting.

Figure 5 illustrates an intraoperative stent removal. This Patient was referred to the Westgerman Heart Center Essen. He had undergone multiple PCIs including multiple stent implantations in all coronary vessels. At time of presentation, he showed in-stent re-stenosis of the left anterior descending artery (LAD), and as one of the main limiting problems, the stent was placed somewhat distal in the LAD. Therefore, the stent had to be removed combined with a CE as shown in figure 5. Figure 6 gives a magnified view of the opened stent showing severe in-stent restenosis.

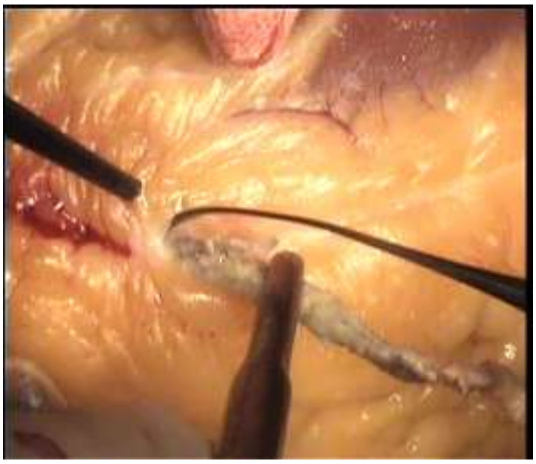


Figure 5: Intraoperative view of stent extraction

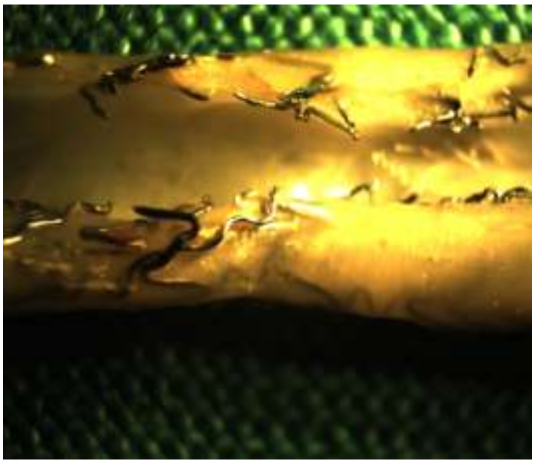


Figure 6: Opened stent, magnification x40 combined with CE

Fukui in Japan [15] reported in his 3 years series 11 consecutive patients with angiographically severe ISR treated with CE and stent removal concomitant with multivessel CABG. Data was analyzed retrospectively: the target vessel was LAD in all patients with a mean interval from the last stent implantation 4.8 +/- 1.9 months. The LIMA was grafted in situ as on-lay patch. They have used the cardio-pulmonary bypass but in some cases they used the off-pump technique. The mean preoperative ejection fraction (EF) was 58.0+/-10.7%. The degree of in-stent narrowing ranged from 75-99%. The mean number of target vessels grafted was 1.6+/-0.7. Before endarterectomy the other coronary vessels were bypassed as usual.

Early postoperative angiography was performed in all patients before discharge in order to explore the patency of the grafts. They didn't register any in-hospital death. There was no significant difference between preoperative and postoperative EF. Hospital stay ranged from 9 to 13 days. The postoperative angiography showed the patency of all grafts. The mean follow up period was 17.3+/- 12.8 months. Endarterectomy of a stented artery is technically demanding and the surgeon must take care in dissecting the atherosclerotic core from the adventitia; it takes longer time in order to finalize the anastomosis. The orifices of side branches should not be occluded during anastomosis of LIMA. In order to avoid early thrombus formation of the endarterectomized vessel they used low dose aspirin (100 mg/day) and warfarin (target INR 2.0) that were started during the hospital stay after initiation of oral ingestion.

In conclusion the presence of one or more stents within the anastomotic coronary segment should not be considered a contraindication for CABG. The extraction of stents and bypass grafting in selected cases is feasible with acceptable mortality and morbidity rates [14-17].

Coronary artery bypass grafting (CABG)

The profile of patients referred for CABG is continuously changing. The patients are older, the coronary lesions are more complex and there are more associated co morbidities such as diabetes mellitus, hypertension, peripheral vascular disease, cerebral vascular disease. The patients are referred for surgery after one or more catheter based revascularization procedures thus with advanced stage and diffuse coronary artery disease [8;18-20].

Endothelial dysfunction induced by stenting is well known and is possible that it could have an adverse effect on adjacent graft patency. Distal microembolization in the downstream vessel from stents is another possible cause of left ventricular dysfunction. The loss of collateral circulation due to occlusion of side branches when long stenting are performed can also alter the left ventricular function. The dual antiplatelet regimens in patients with stents can cause excessive postoperative bleeding if they are not stopped before surgery but we can face stent thrombosis if we stop them before CABG.

A key factor in the PCI first approach must be that the outcome of surgery is not jeopardized by a prior percutaneous procedure [21;22].

The relationship between previous coronary intervention and perioperative outcome after CABG is under study and represents a field of interest of many centers.

A multicenter study investigated that issue. Were involved 8 cardiac surgical centers in Germany and they provided outcome data of 37140 consecutive patients who underwent isolated first time CABG on a five years period. The patients were divided in 3 groups as to their previous status: without any PCI, with one successful PCI, with 2 or more previous percutaneous interventions. The authors looked at the in-hospital mortality and major adverse cardiac events. This study concludes that a history of multiple previous PCI increases in-hospital mortality and the incidence of major adverse cardiac events [6].

Those results were confirmed by Bonaros who investigated 4412 consecutive patients who underwent first time open surgery also on a five year period (2002-2007). He sorted his patients in 2 groups with or without PCI in the last 24 months. Both groups were comparable concerning preoperative linear EuroSCORE. They looked for mortality at 30 days, major cardiac events and perioperative complications. The group with previous PCI had a higher perioperative mortality (4.4% vs 2.4%; $p < 0.001$) and major adverse cardiac events (7.9% vs 4.3%; $p < 0.001$). The incidence of bleeding complications was also higher (5.9% vs 3.8%; $p = 0.017$) as was acute postoperative renal failure (5.9% vs 2.7%; $p = 0.025$). [23] As a conclusion to the results of those studies we can say that a history of elective PCI before CABG should be considered in risk stratification for patients who are scheduled for elective CABG.

Hassan on a Canadian series of patients from 2 surgical centers, on 6032 patients showed that the in-hospital mortality was greater (3.6%) in patients with prior PCI than in those without (2.3%). Using multivariate techniques prior PCI emerged as an independent predictor of postoperative in-hospital mortality [24].

More recently Chocron et al in the IMAGINE trial (2489 patients) states that patients with left ventricular ejection fraction > 40% having a history of PCI have worse outcome post CABG than those with no prior PCI [25].

The SOS (Stent or Surgery) trial [26] published in the Lancet in 2002 is a randomized controlled trial comparing outcomes of percutaneous transluminal coronary angioplasty with CABG. It enrolls 53 centers in Europe and Canada with symptomatic patients with multivessel coronary artery disease randomized to CABG ($n = 500$) or stent assisted PCI ($n = 488$). The primary outcome measure was a comparison of the rates of repeat revascularization. Secondary outcomes included death or Q wave myocardial infarction and all-cause mortality. The median follow up was 2 years and 21% of the patients in the PCI group required additional revascularization compared with 61% in the CABG group. The mortality was lower in the CABG group (2%) than in the PCI group (5%). Among the patients with diabetes mellitus 9% underwent surgery during the first year after PCI.

Barakate [27] investigated 14096 CABG and 4740 PCI on a 17 years experience (1981-1997) in Australia and compared 361 cases of CABG (interval group) who previously had successful PCI with 11909 control patients with primary CABG. This review examines whether prior successful PCI alters outcome following subsequent CABG. The average time interval between PCI and CABG was 13.7 months. The mean number of distal anastomosis for the interval group was 2.9 and in the control group 4.1. The mean number of vessel diseased was 2 in the interval group and 2.6 in the control one. The 30 day mortality was 2% for both patient populations. There were no significant differences in postoperative morbidity and mortality between the two study groups. Johnson et al [28] reported a mean time interval between PCI and CABG of 16.7 months.

We present the French experience of *La Pitie Salpetriere Hospital* (Paris) on one year activity (2000). On 1700 cardiac surgery cases 900 were isolated CABG; from those 122 had previous PCI (13.5%); 100 males and 22 females with a mean age of 61. The majority had one PCI before surgery and 41 had 2 or more PCI before surgery. Those who had required PCI in emergency needed earlier surgery (63+/- 57 days). The risks factors for coronary artery disease in this study are shown in figure 7.

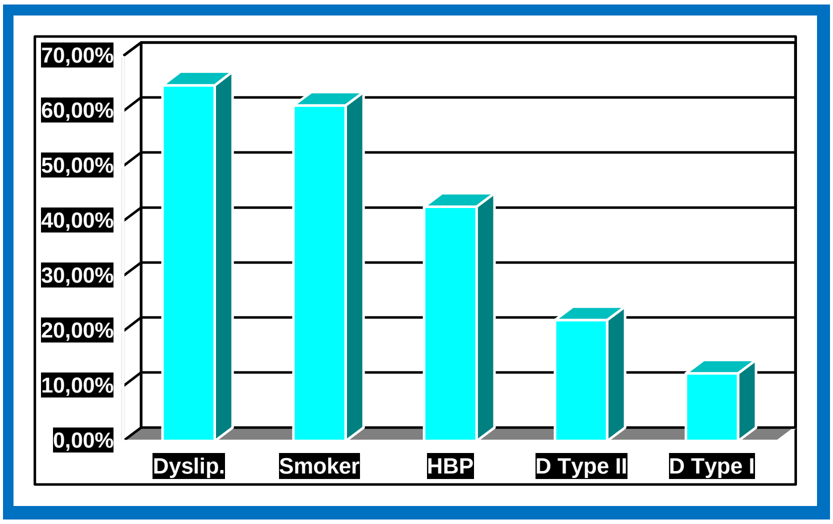


Figure 7: Risk factors for CAD in Pitie-Salpetriere series

The reasons for secondary coronary angiogram for the patients who had just one PCI prior to surgery were: acute myocardial infarction, unstable angina, recurrence of angina, scheduled treadmill or scheduled control angiogram. Of the treated lesions 63.8% were stented. The interval between PCI and CABG was 294+/- 328 days. The number of vessels involved before PCI and before surgery is shown in Figure 8. The number of grafts was 2.6+/-0.9/patient. The distal anastomoses were on LAD in 48% of cases, Cx 31% and RCA 21%. The in hospital mortality was 3.2%

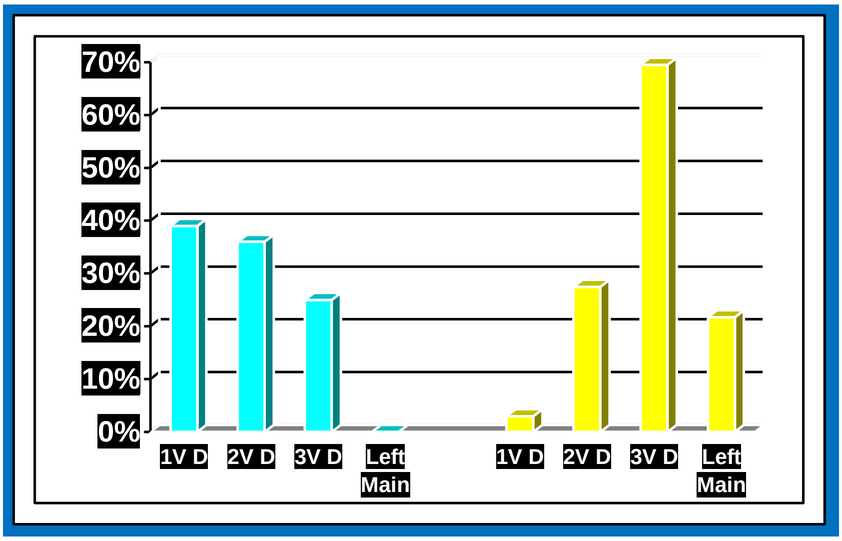


Figure 8: Number of vessels involved in Pitie-Salpetriere series

Recent (2006) single center study in Germany shows that patients with 2 or more prior PCI's have higher in hospital mortality and MACE rates [29]. In the subgroup of patients with multivessel disease and diabetes mellitus the previous PCI before subsequent CABG alters results of surgery [30; 31].

The operative technique is not modified. However the use of arterial grafts is recommended rather than saphenous vein grafts with a better durability [3;32]. Figure 9 shows an intraoperative image of CABG with LIMA on the first marginal and RIMA on LAD. We have used the skeletonized two mammary arteries (left and right).

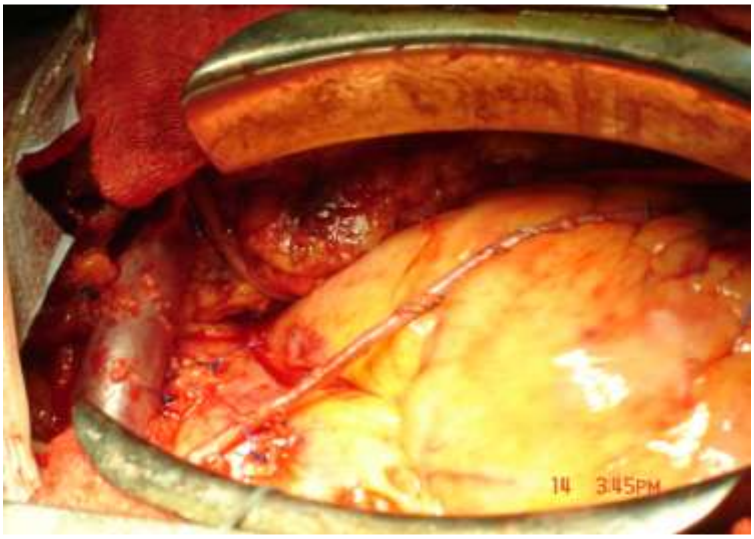


Figure 9: LIMA on Marginal 1 and RIMA on LAD

Sequential grafting of the LIMA to a diagonal branch and the LAD is common practice in many centers [33]. Figure 10 shows the control angiography and multislice CT scan of this technique.

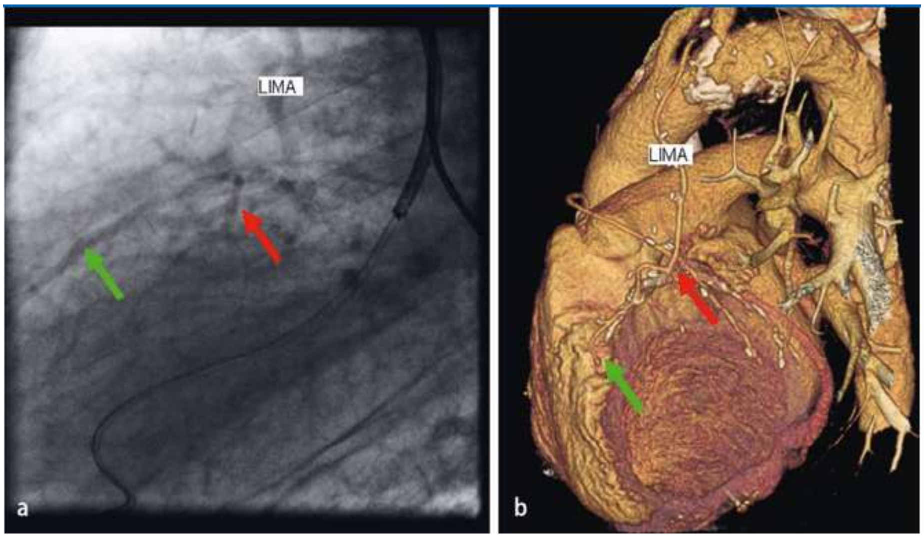


Figure 10: Sequential arterial grafting of a diagonal branch and the LAD artery

a) Angiography: green arrow indicating peripheral LAD anastomosis, red arrow indicating sequential anastomosis to the diagonal branch.

b) Multi-slice CT scan of the sequential LIMA anastomosis: green arrow indicating peripheral LAD anastomosis, red arrow indicating sequential anastomosis to the diagonal branch (from [33] with permission)

In conclusion, with cumulating evidence CABG after prior PCI is associated with poor results (early mortality and MACE) [23;29;30], impaired long-term outcome and quality of life [23; 25; 34]. Even if there are a few studies (from Australia, China and Japan) suggesting that previous PCI is not a predictor for early morbidity and mortality after surgery [22;35].

Discussion

The primary CABG population may have greater pre intervention severity of CAD. But those patients have no increased adverse outcomes when compared to the patients treated by PCI before definitive surgical treatment.

The patient population treated primary by PCI has lower number of vessel involved (one or two coronary vessel stenosis). They have higher reintervention rates than patients treated primary by CABG (30% or more for PCI and 3% for CABG – per 1 year) [27].

The reported literature suggests that CABG is a definitively more cost-effective treatment option for patients with triple vessel disease as well as for diabetic patients, particularly in light of the significant survival advantage conferred by surgery to this later patient cohort [36; 37].

The primary method of myocardial revascularization needs to be carefully selected to obtain durable symptom control for patients with coronary artery disease. PCI procedures often need to be repeated over time and may serve only to delay coronary surgery at substantial financial and personal cost [38].

Conclusions

- CABG has better outcome in patients with ISR rather than the use of interventional methods
- After successful PCI, operative risk for surgery does not increase as long as the coronary bed and the ventricular function are not deteriorated.
- Surgical technique is not modified due to the previous PCI
- Most of the patients who will need surgery after PCI will be operated during the first year
- Rapid evolution of the coronary artery disease seems to be as important as restenosis in determining patients who will require surgery.

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Myocardial Revascularization: Surgery or Stenting?*)

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Introduction

Since the introduction of coronary artery bypass grafting (CABG) in 1967, and percutaneous transluminal coronary angioplasty (PTCA) 10 years later, several major clinical trials have been conducted comparing the two therapeutic strategies, such as the *Bypass Angioplasty Revascularization Investigation* (BARI)[1] and the *Coronary Angioplasty versus Bypass Revascularization Investigation* (CABRI)[2] trials. The seven-year outcome data of the BARI trial (involving 1,829 patients) demonstrated that CABG carried a significant survival benefit over PTCA and this was particularly pronounced in diabetic patients [1]. In addition, nearly 60% of the patients treated with PTCA had to undergo repeat revascularization procedures and half of them relied on CABG as a subsequent therapy [1].

Nevertheless, the past two decades have witnessed a rapid progression of PTCA technology, in particular the development of intra-coronary stents. Drug-eluting stents (DES) especially, appear to have impacted significantly on the current daily practice of treating patients with coronary artery disease [3]. These advances and their immediate influence on clinical practice provide a good example of how technology may shift the paradigm of medicine. Consequently, the mechanism and technique of revascularization needs to be redefined in the present era.

CABG vs Bare Metal Stents (BMS)

The endothelial response to injury during PCI may result in extensive proliferation of smooth muscle cells and extracellular matrix around the angioplasty site, leading to neointimal hyperplasia and restenosis, which in turn may result in recurrent angina and necessitate repeat revascularization [4-6]. Various measures have been proposed to limit this process, such as directional atherectomy, rotablators, or lasers. However, clinical results following these interventions have been largely disappointing as they may cause further damage to the vessel and lead to more severe neointimal hyperplasia [7-10]. The use of stents following PTCA has been suggested as a method of improving the long-term outcome of PCI by reducing the incidence of restenosis and hence the need for repeat revascularization.

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Several randomized controlled trials have been conducted to compare CABG and PCI-with-stent. The *Arterial Revascularization Therapies Study* (ARTS)[11] is one of the largest, and it evaluated the clinical outcomes of 1205 patients over a 5-year period. Although the 5-year mortality rate of the PCI group (8.0%) was comparable with that of the CABG group (7.6%), the need for repeat revascularization was far more frequent in the former group (30.3% versus 8.8%, $p < 0.001$)[11]. In terms of symptomatic relief, angina still presented in 21.2% of the patients after PCI, compared to a significantly lower incidence of 15.5% in the CABG group [11]. Similar findings have been reported by other investigators. The Argentine randomized trial of PCI versus CABG (ERACI-II, n = 450, with a 5-year follow-up)[12] and the Medicine, Angioplasty or Surgery Study (MASS-II, n = 611, with 1-year follow-up)[13] both revealed significantly higher rates of repeat revascularization in patients receiving PCI, despite similar mortality to CABG in these selected patients. Amongst all the major trials comparing stenting and surgery, the *Stent or Surgery* (SoS) trial was the one to report differences in mid-term (as opposed to early) survival. This trial involved 988 patients with multi-vessel disease from 11 European countries and Canada[14]. In contrast to previous studies, a more than twofold increase in death in the PCI group was found at 2-year follow-up (5% in the PCI group versus 2% in the CABG group, p = 0.01)[14].

Although randomized controlled trials represent 'best science' in helping to determine the place of therapeutic interventions, registry data and meta-analyses are also pivotal in reflecting true efficacy of various treatments in the 'real world' which involves a wider spectrum of patients. In a meta-analysis comparing CABG to PTCA with (4 studies), or without (9 studies) stents in 7,964 patients, Hoffman et al [15] found a 1.9% absolute survival advantage favoring CABG over PTCA at 5 years, although this significance may not be maintained at 8 years. In patients with multi-vessel disease, CABG provided significant survival advantages at both 5 and 8 years[15]. Patients randomized to PTCA had more repeat revascularizations at all time points; and with stents, this risk difference was still 15% at 3 years [15]. In addition, patients treated with CABG also had a significantly lower risk of recurrent angina than those receiving PTCA, with a risk difference of 10% at 3 years [15].

A recent propensity analysis involving 6,033 consecutive patients over a 5-year period at the Cleveland Clinic (86% of them received CABG) indicated that in those patients with multi-vessel coronary artery disease and many other high-risk characteristics, CABG was associated with better survival than PCI with stenting after adjustment for risk profiles [16]. In fact, it was found that PCI with stenting was associated with a more than twofold increase in death (hazard ratio, 2.3, $p < 0.0001$), and this difference was observed across all categories of propensity [16]. In diabetic patients (n = 2,319), a higher mortality rate was observed in the PCI group and the most significant difference occurred amongst insulin-treated diabetics in which the adjusted hazard ratio reached 2.6 (95% confidence interval: 1.7-3.9) in the PCI group [16].

Treatment options for diabetic patients with CAD have always been a concern in clinical practice. As many as one third of patients receiving PCI or CABG may suffer from diabetes, as shown in the analysis of various registry data. The BARI trial has shown a sustained survival benefit of more than 20% in patients treated with CABG at 7-years, adding strong evidence that CABG should be the preferable method of revascularization in diabetic patients [1]. The ARTS trial also attempted to address this issue in a subgroup analysis in 211 diabetic patients, and diabetic patients in the PCI group had a higher (though statistically non-significant) 5-year mortality (13.5%) than those treated with CABG (8.3%), and a significantly higher repeat revascularization rate as would be expected considering the results of previous trials[11]. Moreover, comparisons of diabetic and non-diabetic patients in this trial revealed that the diabetic ones were more likely to die when treated with PCI but not with CABG [11]. This finding was echoed by the ERACI-II trial [12]. A meta-analysis by Hoffman et al [15] confirmed a significant survival benefit for CABG over PCI at 4 years but not at 6.5 years, in diabetic patients.

Another meta-analysis by Mercado et al [17] also suggested higher (though statistically non-significant) 1-year mortality in diabetic patients after stenting. More recently, the report of the New York's cardiac registries, which included patients undergoing CABG (n = 37,212) and PCI with stenting (n = 22,102) from 1997 to 2000, confirmed that risk-adjusted survival rates in the PCI group were significantly lower, whereas the repeat revascularization rate was significantly greater, than that in the CABG group at 3 years[18]. In particular, the adjusted hazard ratio for the risk of death after CABG relative to PCI was 0.64 (95% confidence interval: 0.56-0.74) for patients with triple-vessel disease [18]. Although without risk-stratification, Mack et al [19] recorded lower mortality after PCI, the proportion of multivessel disease was greater in the CABG group in their database. It is noteworthy that risk-adjusted survival benefit of CABG over stenting has been repeatedly demonstrated not only in North America [15,16,18] but also in Europe[20].

The *Angina With Extremely Serious Operative Mortality* (AWESOME) trial was conducted to compare PCI and CABG in high-risk patients. A total of 454 patients with refractory myocardial ischemia and one or more risk factors for adverse surgical outcome were included [21]. These risk factors included prior open-heart surgery, age >70 years, LVEF < 35%, MI within 7 days, or use of pre-revascularization intra-aortic balloon pump [21]. Variable proportions of patients received stenting in the PCI group (26% in 1995 to 88% in 1999/2000). Although survival rates in the CABG (79%) and PCI (80%) groups were not significantly different at 36 months, the need for subsequent repeat revascularization was higher in the PCI group [21]. The *Stenting versus Internal Mammary Artery* (SIMA) study [22] compared CABG with stenting in 123 patients with proximal, isolated de novo LAD disease. Although 2-year mortality was not particularly different, a significant and higher incidence of repeat revascularization was documented in the stent group [22]. In contrast, the event-free survival rate in the ARTS trial was significantly higher after CABG than after PCI for patients with triple vessel disease (p = 0.001)[11]. It was acknowledged that in the ARTS trial, patients with left ventricular dysfunction, left main lesion, or concomitant hepatic or renal diseases were excluded[11]. These criteria have provided a frame that may magnify the apparent efficacy of PCI. To put this in context for example, in the New York cardiac surgery registry[18], up to 24% of patients receiving CABG have an ejection fraction less than 40% – these patients are often excluded in the controlled trials yet are the very ones who are known to have a survival advantage with surgical revascularization. Excluding these sorts of patients may well unfairly reduce the potential survival benefits for surgery and introduce a favorable bias towards PCI. Hence, it must be recognized that patients in clinical trials do not necessarily accurately represent those in the "real world".

CABG vs Drug-Eluting Stents (DES)

Although BMS implantation has significantly reduced the incidence of repeat revascularization following PCI, the rate of restenosis remains high. It was not until the emergence of DES that a true reduction in the restenosis rate following percutaneous intervention was reported and this marked a new era in PCI development. We may gain some insight into the effects of this advance in technology and its impact on treatment options by looking at trials comparing DES and BMS.

Sirolimus – Eluting Stents (SES)

The RAVEL Study[23] was the first randomized, double-blind trial that compared the Sirolimus-coated Cypher stent with a BMS in 238 patients with relatively simple, single de novo coronary lesions. Encouraging results were reported with an angiographic restenosis rate of 0% in the SES group and 26% in the standard stent group at 6 months[23]. The 4-year results of the study also revealed sustained and significant reductions in major adverse cardiac event (MACE) and repeat target lesion revascularization (TLR) in the DES group[23]. While the RAVEL trial was criticized for the simple nature of the lesions treated, the larger Sirolimus-coated stent had been developed and a subsequent clinical trial (SIRIUS)[24] involving 1,058 patients with longer coronary lesions was instigated. The 3-year follow-up data showed a significant reduction in TLR and angiographic stenosis in the SES group [24]. The NEW-SIRIUS study, which comprised of Canadian and European data involving 452 patients also showed significant reductions in MACE at 9 months within the SES treated group[25,26]. Other trials on more complicated coronary lesions have also showed positive results. These include the Sirolimus-Eluting versus Uncoated Stents for Prevention of Restenosis in *Small Coronary Arteries* (SES-SMART) trial [27] on small coronary vessels, and the *Stenting of Coronary Arteries in Non-Stress / Benestent Disease* (SCANDSTENT) trial [28] on bifurcation, ostial, angulated and occlusive lesions.

Paclitaxel - Eluting Stents (PES)

Recently, large clinical series such as TAXUS-IV (n = 1,314) [29] and TAXUS-V (n = 1,156) [30] have been published, and these have investigated the TAXUS slow-release stent for "longer" coronary lesions in smaller coronary vessels. Significant reductions in TLR for up to 2 years in the TAXUS-IV trial, and 1 year in the TAXUS-V trial, have been reported [29,30]. The TAXUS-VI (*n* = 446) study [31] also demonstrated a lower repeat revascularization rate following the use of the TAXUS moderate-release stent when compared to BMS.

More recent studies suggest, however, there are concerns aside from restenosis or repeat intervention following DES implantation, which may occur at a higher rate than previously thought. For instance, several groups of investigators have observed the development of subacute or late stent thrombosis [32-35]. Such complications could lead to fatal myocardial infarction even a few years after DES implantation [35].

Other randomized and observational studies have documented a consistent but small increase in the absolute risk for late stent-related thrombotic events with DES.

Comparing DES (47% sirolimus-eluting, 53% paclitaxel-eluting) with BMS using data from 14 randomized trials (involving 6,675 patients), it was found that when stent thromboses occurred more than 30 days after implantation they tended to appear much later with DES than with BMS [36]. In particular, the thrombosis incidence was significantly greater with DES than with BMS more than 6 months and 1 year after implantation. In another single-center observational study, 746 patients who had received 6 months of clopidogrel maintenance therapy during a 6-month randomized DES-versus-BMS trial were followed for an additional 12 months after clopidogrel discontinuation [37]. The incidence of cardiac death or MI after discontinuation of clopidogrel was significantly higher with DES than with BMS (4.9% vs. 1.3%), even after adjustment for potential confounders [37]. Thrombosis-related events occurred at a median of 116 days after discontinuation of clopidigrel, accounting for 25% of late events, and it tended to occur more often with DES than with BMS [37]. Therefore, experts from five major professional societies recently recommend dual antiplatelet therapy for 12 months following DES implantation in patients who are not at high risk for bleeding [38].

This duration exceeds that recommended by the drug manufacturer.

In terms of implications of these factors when considering surgery or percutaneous therapy for patients the 5-year clinical outcomes of the ARTS II *(Arterial Revascularization Therapies Study II)* of the sirolimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions have been recently reported [39].

This showed at 5-year follow-up, the death/stroke/myocardial infarction event-free survival rate was 87.1% in ARTS II SES, versus 86.0% ($p = 0.1$) and 81.9% ($p = 0.007$) in ARTS I CABG and BMS cohorts, respectively. The 5-year major adverse cardiac and cerebrovascular event (MACCE) rate in ARTS II (27.5%) was significantly higher than ARTS I CABG (21.1%, $p = 0.02$), and lower than in ARTS I BMS (41.5%, $p < 0.001$).

The cumulative incidence of definite stent thrombosis was 3.8%. Thirty-two percent (56 of 176) of major adverse cardiac events (MACE) at 5 years were related to possible, probable, or definite stent thrombosis. So it appears from this data, that at 5 years, SES has a safety record comparable to CABG and superior to BMS, but a MACCE rate that higher than in patients treated with CABG, and lower than in those treated with BMS.

Approximately one-third of the events seen with SES may be prevented through the elimination of early, late, and very late stent thrombosis.

Discussion

With the encouraging results from various trials comparing DES and BMS, it is believed that the new technology of DES has the potential to further decrease morbidity and repeat revascularization rate in patients following PCI. However, many of the published trials were done on relatively simple coronary lesions. Even the SES-SMART, SCANDSTENT and TAXUS-V trials could not truly represent the unselected patient population routinely presented for CABG. Moreover, the longest follow-up period in the above studies was only 4 years. There have been concerns over the long-term efficacy of DES, and some authors have postulated that DES might merely be delaying, rather than reducing restenosis, since there may be stent dilapidation following total elution of the drug. It would be unwise therefore to extrapolate data comparing DES and BMS and apply the findings to a comparison of DES with CABG.

On-going clinical trials such as the Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) trial are primary designed to compare the 1 year outcomes of PCI with TAXUS stent and CABG in patients with triple vessel and/or left main coronary artery diseases[40]. This study aims to recruit over 4,250 patients at 90 centers in Europe and the United States. Aiming at reflecting the *"real world"*, the study includes not only the randomized arms but also the 2 ineligible registries and a *"preference registry"* (refusal treatment allocation). It will address some important issues on the relative role of DES and CABG in the treatment of patients with complex coronary artery disease, the short- and long-term cost-effectiveness as well as quality of life and its preliminary report of outcomes is discussed later. Another Future Revascularization Evaluation in patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial was also carried out to compare 5-year mortality in diabetic patients treated with either DES or CABG [37]. Obviously, more large-scale prospective studies will be needed to elucidate and define the accurate role of the currently available treatment strategies in patients with ischemic heart disease.

CABG has stood in test of time for more than 4 decades with excellent success as measured by a variety of clinical outcome markers, and patency rates of the left internal mammary artery grafted to the left anterior descending coronary artery are consistently over 90% at 10 years. The longest trial of BMS has not reached 10-year follow-up.

Moreover, as far as patient survival is concerned, no solid evidence from previous trials comparing BMS and CABG supported superiority of PCI over CABG.. Registry data with much larger patient volumes have also unequivocally indicated survival benefits for patients treated with CABG in comparison to PCI for certain patient groups. It must be acknowledged that while PCI has been changing, advances in many aspects of the CABG techniques have been remarkable. As a result, CABG has been consistently regarded as "gold standard" in treating coronary disease worldwide[38].

It is apparent that CABG provides better protection against repeat revascularizations than PCI with stenting. The high rate of repeat revascularization following PCI should not be overlooked, although the use of stents has substantially reduced this, the figure still remains high (30.3% in the ARTS trial and 28.4% in the ERACI-II trial at five years). Indeed, in these two studies, a significant percentage of patients (34.7% in ARTS and 29.6% in ERACI-II), treated with PCI eventually required subsequent revascularization with CABG, a fact disguising to some extent 'real' differences in reported survival rates since the trial was conducted and analyzed on an intention-to-treat principle. This high rate of repeat revascularization with the need to resort to CABG therefore questions the applicability of the survival data since up to 10.5% and 8.6% of all PCI patients eventually required CABG [11,12].

Perhaps in some ways more important than restenosis is the issue of the completeness of revascularization potentially achieved by the two treatment options? By placing grafts distal to the diseased coronary segment, CABG may deal not only with the immediate culprit lesion but the "future" culprit lesions, whereas PCI only addresses the existing target lesions [39]. For this reason surgery has been considered to carry an intrinsic advantage which makes it superior to PCI irrespective of the type of stent used.

Recently, Hlatky and colleagues [41] reported a pooled analysis of individual data from almost 8000 patients enrolled in ten randomized trials of PCI and CABG over the past two decades. They conclude that, while at a median 6 years' follow-up there was no overall difference in survival, there was a significant survival advantage with CABG in patients with diabetes (hazard ratio 0.70, 95% CI 0.56–0.87) and in those aged 65 years or older (0.82, 0.70-0.97). Furthermore, the combined endpoint of death or repeat revascularization was reduced with CABG (10%) compared with PCI (25%; 0.41, 0.37-0.45). This analysis is probably one of the most definitive and authoritative analyses of the previous randomized trials. There are problems though, however recent this analysis is in that the number of enrolled patients represented only about 5-10% of the eligible population, and the majority had single or double vessel disease with preserved LV function negating the impact of survival as an outcome comparator. A second obvious limitation is that neither the PCI nor the CABG in these trials would be considered 'optimum' by contemporary standards. PCI patients did not receive drug-eluting stents and only 83% of CABG patients received an internal mammary artery, the most important prognostic factor for long-term survival after CABG and a benefit which persists long into the second decade of follow up. Additional recent evidence can also be found in the interim analyses of previously mentioned SYNTAX in 1800 patients with left-main and/or three-vessel coronary artery disease who were randomized to PCI or CABG [40].

The strength of SYNTAX is that it includes "all-comers" and patients with the most complex coronary artery disease. It also maintained a parallel registry of patients excluded from randomization (1077 in the CABG group whose disease was too complex for PCI, and 198 in the PCI group considered to be at excessively high surgical risk). At 1 year (with final analyses at 5 years), 12% of patients who had CABG and 18% of those who had PCI reached the primary composite endpoint of death, myocardial infarction, stroke, or repeat revascularization. Although the difference was largely driven by repeat revascularization with no significant difference in mortality, PCI failed to reach the criteria for non-inferiority, and the authors concluded that "CABG remains the standard of care for patients with three-vessel or left main coronary artery disease".

Conclusions

Over the past decade, the technique and outcome of both CABG and PCI have substantially advanced. Nevertheless, since majority of the clinical trials comparing the two therapeutic strategies have been limited to selected patient populations, optimal treatment modalities for high-risk patients with complex coronary lesions and multiple co-morbidities remain undetermined. Although the rapid growth of PCI industry and the consequent decline in the caseload for CABG has generated much speculation about the future role of each type of intervention, so far no valid data exist to indicate that PCI plus DES could replace CABG entirely. This opinion is largely shared by both surgeons [43,44] and cardiologists [45,46].

A contemporary summary of current opinion is for less severe coronary disease (mainly one-vessel or two-vessel disease and normal left ventricular function), there is little prognostic benefit from any intervention over optimum medical therapy. In symptomatic patients who do require intervention, there is no difference in survival with either PCI or CABG, but there is a significantly higher risk of repeat revascularization with PCI (further emphasized in a recent meta-analysis)[42]. In patients with more severe coronary artery disease, and especially those with diabetes, CABG seems superior in terms of survival and freedom from reintervention. However, the recent SYNTAX data has also pointed out that PCI is a good option for patients who are ineligible for or who refuse CABG.

While applying inferences from published trials and awaiting outcomes of on-going clinical studies, we must bear in mind that patients with complex coronary disease demand safe and cost-effective treatment which provides good long-term quality of life.

Therefore, the choice of myocardial revascularization technique for an individual patient should not simply be based on the anatomical findings. Each patient should be advised by a multidisciplinary team who can present in the most balanced way the advantages and limitations of both PCI and CABG.

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Hybrid Revascularization – A step forward in cardiovascular procedures*)

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Abstract

Objective. *A hybrid therapy combines the treatments traditionally available only in the catheterization laboratory with those traditionally available in the operating room to offer patients the best available therapies for any cardiovascular lesion. We sought to evaluate clinical and angiographic outcomes of hybrid procedures in patients receiving both PCI and other cardiovascular intervention.*

Methods. *We retrospectively analyzed 113 patients with CAD who were referred to our institution for myocardial ischemia and underwent hybrid procedures. Between January 2002 and January 2009, a totally of 113 patients underwent hybrid procedures. In this series, the hybrid sequence, in all cases, included a PCI performed in the cardiac catheterization laboratory, followed by CABG in 23 patients, by valvular replacement in 6 patients (aortic and mitral), by carotid endarterectomy and surgical angioplasty in 12 patients and by peripheral vascular reconstructions in 82 patients.*

PCI was performed using femoral or radial artery access using guided catheter techniques and the surgical CABG, valvular replacement and the peripheral vascular interventions were performed according to our current standard guidelines.

Results. *Clinical follow-up was carried out in 100% of eligible patients. Information about in-hospital outcomes was obtained from an electronic centralized clinical database. After discharge, all clinical follow-up data were prospectively collected by scheduled clinical evaluations or direct telephone interviews. Angiographic follow-up was performed at 6-9 months after the procedure. It was performed at an earlier time if clinically indicated.*

Discussions. *The key requirement in all of these approaches is the need for collaboration between cardiac surgeons, vascular surgeons and interventional cardiologists to obtain optimal patient outcomes.*

Conclusions. *Hybrid revascularization is offered as an alternative strategy for patients with complex cardiovascular diseases. Hybrid CABG/PCI may be reserved for higher risk patients who are not candidates for conventional surgery. In these patients, association of PTA and surgery may help reduce risk.*

Key words: *hybrid therapy, Hybrid revascularization, Hybrid CABG/PCI*

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Objective

A hybrid therapy combines the treatments traditionally available only in the catheterization laboratory with those traditionally available in the operating room to offer patients the best available therapies for any cardiovascular lesion, in order to minimize surgical morbidity has evolved since its implementation in 1990's. Over the past decade, the hybrid strategy has become an attractive alternative to standard surgical or catheter-based techniques.

Combined coronary artery disease with valvular heart disease/ carotid disease/ peripheral vascular disease is a major cause of morbidity and mortality in the adult patient population. The standard treatment for such disease has been open heart surgery in which coronary artery bypass grafting (CABG) is performed concurrently with valve/carotid/ peripheral vascular surgery. With the increasing complexity of patients referred to surgery, some patients may prove to be poor surgical candidates for combined valve/carotid/ peripheral vascular and CABG surgery. For instance, in patients with poor conduit quality, poor coronary target vessel quality, low ejection fraction, or significant comorbidities or in those undergoing reoperative cardiac surgery, the risks of combined procedures may be prohibitively high.

Hybrid CABG/PCI

This term means the combination of traditional surgical methods with PCI. Preoperative or intraoperative treatment of CAD by a percutaneous approach has simplified CABG operations in selected patients:

- PCI of a culprit coronary lesion during an acute coronary syndrome followed by conventional CABG during the same hospitalization
- The lack or poor quality CABG conduits
- A non-graftable but stentable vessel (left circumflex lesions in the atrioventricular groove with small diffuse obtuse marginal)
- Repeat operations in which PCI is preferable to avoid full cardiac dissection
- Or in patients with concomitant pre-existing organs dysfunction, or recent myocardial infarction, or severe atherosclerotic aortic disease (off-pump LIMA-LAD).

There is general agreement that revascularization using the left internal mammary artery (LIMA) to the left anterior descending artery (LAD) provides a long-term prognostic benefit in patients with multivessel CAD, primarily related to its resistance to thrombosis and atherosclerosis, and may be responsible for the majority of the survival benefit associated with CABG [14]. Five-year patency rates of the LIMA-LAD are between 92% and 99% [15, 16] and 10-year patency rates are between 95% and 98% [17, 18]. Moreover, based on its anastomotic location in the mid LAD and its long-term patency, patients treated with a LIMA-LAD are protected against MI from disease progression in the more proximal vessel [19].

Accordingly, there has been interest in the use of "hybrid" myocardial revascularization (HMR) in selected patients with multivessel CAD. The term HMR can be broadly encompassing, and may include PCI of the "culprit" vessel in patients with ST elevation MI followed by conventional CABG later in the same hospital admission.

The purpose of this review is to outline the indications and contraindications of this novel method of revascularization in patients with complex CAD.

Hybrid valve/PCI

The rationale for this combined procedure is to convert a high-risk valve/CABG into a lower risk isolated valve procedure, or in CABG patients with poor CABG conduit, in which PCI with DES may be a better option.

Hybrid valve surgery is especially suitable for patients with acute coronary syndrome (unstable angina, acute myocardial infarction, or cardiogenic shock) and known valve disease. In this approach, usually PCI is performed first to the culprit lesion, stabilizing the coronary lesion, and then, during the same hospital stay, the valve lesion is addressed 5 to 7 days later. This approach converts an emergent/urgent concomitant coronary and valve surgery into a more elective isolated valve surgery.

Traditionally valve/CABG surgery has twice the mortality of isolated valve surgery. In high-risk patients with multiple comorbidities, such as increased age, low ejection fraction, morbid obesity, and pulmonary or renal dysfunction, it may even be higher. Thus, combining two low-risk strategies, PCI (1%) mortality in elective settings, with isolated valve surgery is very appealing to reduce the overall operative risk.

Hybrid carotid/PCI

It is well-known that patients with significant carotid disease have an increased risk of stroke during CABG. A new report, published in the September 2009 issue of "Archives of Neurology" showed that stroke rates were significantly higher among patients who received combined endarterectomy and cardiac surgery.

The indication for carotid revascularization should be individualized after discussion by a multidisciplinary team including a neurologist. The timing of the hybrid procedures should be dictated by local expertise and clinical presentation targeting the most symptomatic territory first. Indication for carotid revascularization in patients scheduled for CABG depends on the symptomatic status, gender and stenosis severity. In our series, all patients had undergone previous PCI of coronary lesions before carotid surgical endarterectomy due to acute coronary syndrome. The most important aspect of reducing mortality is the speed of reperfusion. The shorter is the time between the onset of symptoms and the intervention, the greater the benefit.

Hybrid peripheral vascular disease (PVD)/PCI

CAD and PVD remain highly prevalent in the population due to population ageing, smoking, diabetes, unhealthy lifestyles, and the epidemic obesity, and frequently coexist. The management of combined CAD and PVD is a common challenge and brings with it numerous clinical dilemmas.

In patients with unstable CAD, vascular surgery is postponed and CAD treated first, except when vascular surgery cannot be delayed due to a life threatening condition.

Prophylactic myocardial revascularization with PCI prior to high-risk vascular surgery was considered in stable patients who had persistent signs of extensive ischemia or a high cardiac risk.

In high-risk patients, performing PCI before vascular surgery, converts a high-risk cardiac and vascular procedure into a lower-risk vascular procedure.

Methods

Since January 2002, our institution has used HR in selected patients as an alternative to conventional CABG with multivessel coronary artery disease (CAD) involving the LAD. We investigated whether HR was a valid alternative to conventional CABG in patients with multivessel CAD. We present in this paper our experiences with HR using a combined approach of advanced PCI and conventional CABG, valvular, carotid endarterectomy and peripheral vascular surgical interventions.

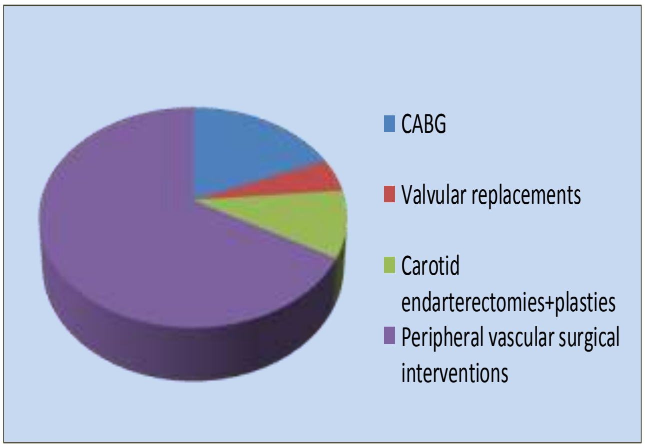


Figure 1: The types of operations performed in IBCV Iasi, between 2002-2009

Patient selection. From January 2002 to January 2009, a total of 113 patients, with a mean age of 65 years, underwent HR. Most of the patients were males 85.84% and only 14.15% were females. Associated comorbidities consisted of 6.19% diabetes mellitus, 32.74% hypertension, and 9.73% prior myocardial infarction. 91 patients had one coronary artery lesions, 19 had two coronary artery lesions, six of them had associated valvular disease, and 82 had concomitent peripheral vascular disease. So, in these series, the hybrid sequence, in all cases, included a PCI performed in the cardiac catheterization laboratory, followed by CABG in 23 patients, by valvular replacement in 6 patients (aortic and mitral), by carotid endarterectomy and surgical angioplasty in 12 patients and by peripheral vascular reconstructions in 82 patients. In these series, the HR sequence, in all cases, included a PCI performed in the cardiac catheterization laboratory followed by a surgical intervention with an average time of 2.0±0.9 days later. All patients subsequently underwent repeated coronary angiography.

Hybrid CABG/PCI

There are three general approaches to the timing of the revascularization procedure. The first approach is to perform PCI well in advance of surgical revascularization. These may include patients in whom the non-LAD "culprit" vessel requires urgent PCI, and the surgical revascularization to the LAD is delayed for days to weeks. The advantage of this approach is that any lesions not successfully treated with PCI would be amenable to surgical revascularization. The disadvantage of this approach is that the surgical revascularization is performed while on the combination of aspirin and clopidogrel, which may increase the surgical bleeding [20, 23]. Stopping the clopidogrel within 6 months of DES placement may increase the risk of stent thrombosis [24].

A second approach is one in which PCI is performed within hours of surgical revascularization, either in the same "hybrid" operating room or with PCI performed in the catheterization laboratory with immediate transportation to the operating suite. The advantage of working within a single room are the improved logistics and coordination of care, although this procedure still requires the professional support of both the interventional cardiologist and the cardiac surgeon. In this circumstance, clopidogrel, 300 mg, is given just before the procedure [21]. Because the efficacy of clopidogrel is time dependent, the LIMA-LAD grafting can be completed before the maximum effect of the clopidogrel loading dose [25, 26]. The effect of the reversal of heparin at the end of the bypass procedure on stent patency is not known.

The final option is to stage the PCI 3–5 days after surgical revascularization, at which time the patient can receive dual antiplatetet therapy and be discharged on the following day [22]. The disadvantage of this approach is that any lesions not successfully treated with PCI would require repeat surgical revascularization. Case selection is paramount to less complex lesions or lesions in which revascularization is not critically important to the patient's long-term survival.

We retrospectively analyzed 23 patients with refractory unstable coronary syndromes, who underwent PCI first, with balloon angioplasty or BMS/DES, followed by CABG, a few hours or days after. Of the 23 patients, the number of patients with single, double, triple-vessel disease, and LM disease were 2, 3, 5, and 13, respectively. Conduits used for CABG were LIMA, RIMA and radial artery or the saphenous vein.

Hybrid valve/PCI

The rationale behind hybrid valve surgery is to substitute PCI for CABG to convert a valve-CABG procedure, with higher risk, into an isolated valve procedure, with lower risk and shorter time of extracorporeal circulation and aortic clamping. Of our 6 patient, 2 underwent replacement of mitral valve, and 4, replacement of the aortic valve. 2 patients had ballon angioplasty, and 4 patients had BMS.

Hybrid carotid/ PCI

We decided to pursue a strategy of staged PCI followed by carotid endarterectomy and surgical plasty in 12 patients with acute coronary syndromes and 70-99% carotid stenosis. In order to stabilize the acute coronary syndrome and reduce the risk of myocardial infarction and recurrent ischemia, we decided to treat the most severe lesion, with balloon angioplasty in 8 patients, and with stents in 4 patients.

Hybrid peripheral vascular/PCI

We retrospectively analyzed 82 patients with coronary artery disease, who underwent elective peripheral vascular surgery (aortoiliac and femuropopliteal bypasses).

Patients were eligible for PCI when at least one of the following conditions was met: the patient suffered from acute coronary syndrome, or the patient had multiple vessel disease with impaired left ventricle systolic function (LVEF < 40%).

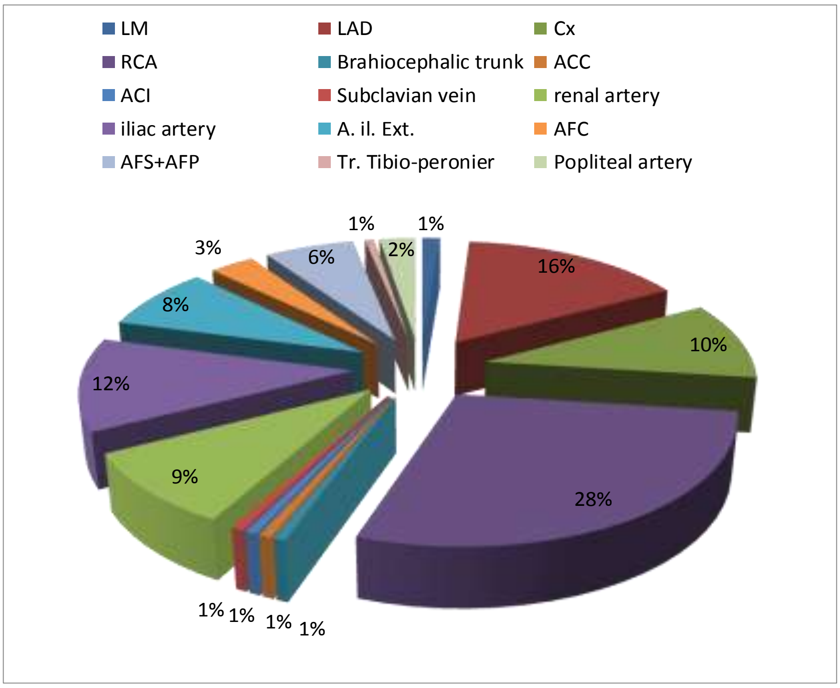


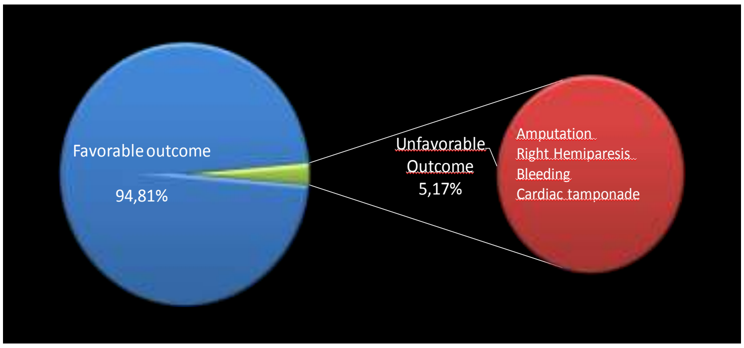
Figure 2: Types of interventional procedures

Percutaneous coronary intervention.

PCI was performed using femoral or radial artery, after obtaining written informed consent. The right coronary artery (RCA) and left circumflex artery (LCX) underwent PCI when appropriate.

After PCI, all patients underwent elective surgery.

Results



HR aims to achieve full revascularization without compromising the survival advantage of the LITA-to-LAD graft.

End points. The rate of procedural success was 94.81%, and the 12-months incidence of complications 5.17%.

In particular, 3 patients had post-operative bleeding requiring reintervention, and one patient had pericardial tamponade requiring pericardial drainage 4 days after CABG. No patient died after the procedures.

In the carotid group, the post-operative course was uneventful, without any stroke or myocardial infarction.

The median duration of post-operative hospital stay was 9 days (range 7 to 14 days). The median duration of intensive care unit stay was 3 days (range 2 to 5 days), and the median ventilation time was 12 hours. The median duration of extracorporeal circulation was 78 minutes, and the median duration of clamping time was 47 minutes.

Clinical follow-up was carried out in 100% of eligible patients. Information about in-hospital outcomes was obtained from an electronic centralized clinical database. After discharge, all clinical follow-up data were prospectively collected by scheduled clinical evaluations or direct telephone interviews. A favorable overall complication profile was encouraging, with a 14% need for redo PCI and a 99% survival at one year. Angiographic follow-up was performed at 6-9 months after the procedure. It was performed at an earlier time if clinically indicated.

Although intraoperative costs were increased, postoperative costs were reduced for the HMR compared with classical CABG, resulting in similar overall total costs. Assignment to the HMR was an independent predictor of shortened time to return to work. Patient satisfaction after the hybrid procedure, as judged on a six-point scale, was greater with HMR compared with classical CABG.

Discussion

Coronary artery bypass grafting of the left anterior descending coronary artery (LAD) using internal mammary artery (LIMA) has been shown to be more effective than interventional treatment with respect to event-free survival and relief of ischemic symptoms (1, 2). Internal mammary graft to LAD has a patency rate of more than 95% at 5 years.

Percutaneous interventional treatment of coronary lesions of the circumflex system or the right coronary artery is less frequently associated with subsequent restenosis than treatment of LAD lesions (3–7). The early restenosis rate of “non-LAD” vessels after percutaneous coronary intervention (PCI) is no longer very different from the early occlusion rate of venous bypasses, but after the initial critical restenosis period of six months, the results of PCI are more stable (8–10). Hybrid revascularization (HR) as reported in this article provides complete revascularization in selected patients.

In discussing the applicability of the hybrid concept, the sequence of the procedure is also important. As presented in this article and other similar studies, some authors perform PCI first, with the option that in case of any interventional complication, surgery will effectively treat the underlying coronary disease as well as the interventional complication in one procedure (11, 12).

The timing of the two procedures evokes considerable debate with no definite consensus at the current time and perhaps a case-by-case basis would be most appropriate.

The hybrid revascularization procedure may be especially useful in complex LAD lesions, restenotic lesions in LAD, acute myocardial infarction in “non-LAD” territory, high-risk elderly patients with multiple comorbidities and patients with severe left ventricular systolic dysfunction who are not ideal candidates for conventional bypass surgery.

Conclusions

Hybrid CABG/PCI may be reserved for higher-risk patients that are not candidate for conventional CABG. In these patients, performing PCI first, may help reduce the risk. Patients may thus recover faster with shorter lengths of stay in the hospital and return to work more quickly than with conventional CABG (7). PCI of multivessel CAD is limited due to incompleteness of revascularization and the need for repeat procedures due to restenosis with resultant loss of initial cost savings (13).

Hybrid valve/PCI represents an excllent alternative to conventional valve/CABG in some high-risk patients, particularly in those who presents after acute coronary syndromes, and in some patients who require reoperative valve surgery.

Even if a randomized clinical study is needed to verify our clinical approach, our findings indicate that, in high-risk patients with CAD suitable for CABG and carotid artery disease, valvular disease or peripheral arterial disease, hybrid revascularization by PCI, immediately or at distance, followed by CABG is a feasible and promising therapeutic strategy.

As new options for and approaches to PCI and surgery continue to evolve, both the interventional cardiologist and the cardiac surgeon should participate in the formulation of a patient's treatment plan. In doing so, the clinicians involved should consider not only issues related to risks, but also those related to long-term patency and survival of the patient. This approach does promise to be another advancement in our ability to successfully and safely perform coronary revascularization. As further improvements in technology continue, we should expect to see a greater number of patients with multivessel coronary artery disease undergo complete revascularization using either the percutaneous route alone or using the hybrid approach.

This approach also creates a tighter focus for the modern surgeon who functions as part of the team, which is crafting a strategy in which the surgical component confers a life-extending advantage with a lower attendant morbidity and mortality consistent with the goals of PCI.

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Routine early coronary angioplasty after thrombolysis versus ischemia guided angioplasty after thrombolysis in acute ST-elevation myocardial infarction - efficiency and advisability in the Romanian health system*)

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Abstract

Since current guidelines emphasize that primary coronary intervention (PCI) is currently the preferred reperfusion therapy in patients with acute ST-elevation myocardial infarction but many hospitals lack PCI facilities and thrombolysis is often the eligible approach, the purpose of the present study was to evaluate the management of acute ST-elevation myocardial infarction patients in our clinic.

Methods: *625 patients with acute ST – elevation myocardial infarction admitted in our clinic from January 2010 until May 2011 where analyzed on discharge from hospitalization following acute ST-myocardial when treatment management was taken into account as well as left ventricle ejection fraction (EF%). The average duration of hospital stay in intensive care coronary unit was determined. Approximately 30 days after the acute coronary event death, reinfarction, recurrent ischemia and severe heart failure were analyzed.*

Results: *2.88% patients only received thrombolytic therapy (group A), 57.12 % were referred to primary PCI < 6 hours (group B), 14.56% initially received thrombolytic therapy and then referred to PCI < 24 hours from onset of symptoms (group C) and 25.44 % were invasively evaluated but no revascularization therapy was performed (group D). The average duration of hospital stay in intensive care coronary unit for the whole group was 3.3±1.18 days. Average value for the left ventricle ejection fraction was 40±8.17 in group A, 46±9.12 in group B, 45±8.2 in group C and 39±7.76 in group D. 30 days after the acute the prevalence of death, reinfarction, recurrent ischemia and severe heart failure encountered 8.17% in group A, 2.8% in group B, 3.29% in group C and 11.11% in group D and average values for the left ventricle ejection fraction were: 42±8.13 (group A), 48±9.72 (group B), 48±9.13 (group C) and 40±7.8 (group D).*

Conclusions: *Our study demonstrated a superior efficacy of primary PCI as well as of the thrombolytic therapy followed by PCI in less than 24 hours on 30 days primary end-point (death, reinfarction, recurrent ischemia and severe heart failure) then thrombolytic therapy alone in patients with acute ST-elevation myocardial infarction.*

Key-words: *Coronary angioplasty, ST – elevation myocardial infarction, thrombolytic therapy*

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Introduction

Current guidelines emphasize that primary coronary intervention (PCI) is currently the preferred reperfusion therapy in patients with acute ST-elevation myocardial infarction [1]. Nevertheless, many hospitals lack PCI facilities and therefore, thrombolysis is still considered the eligible approach if the time delay from the onset of pain and the balloon inflation is over 2 hours [1].

Initial results of studies regarding early PCI post thrombolysis were disappointed but also conducted in an era were stents, thienopyridines and glycoprotein IIb/IIIa inhibitors were not in current use [2]. Since the addition of a thienopyridine to aspirin and fibrinolytic drugs improves infarct artery patency [3] and mortality [4], adding these evolving pharmacotherapies as an adjunctive to fibrinolysis throws a new light on the subsequent role of a routine early PCI in the first 24 hours after acute ST-elevation myocardial infarction versus ischemia-guided PCI.

This strategy has been the object of study of a recent meta-analysis by Souza et al. [5], who, after analyzing eight trials (PRAGUE [6], SIAM III [7, 8], GRACIA-1 [9], CAPITAL-AMI [10], CARESS-in-AMI [11, 12], WEST [13], TRANSFER-AMI [14] and NORDISTEMI [15]) and a total of 3195 patients concluded that, where primary PCI is not a feasible option for acute ST-elevation myocardial infarction, early routine PCI within 24 hours of thrombolysis should be performed. When using routine early PCI, Souza et al. also noticed that the major benefit at 30 days was the reduction of the composite of mortality, ischemia and re-infarction driven by the reduction in ischemia and re-infarction events [5].

Similar results were obtained by *Borgia et al.* in another meta-analysis, which demonstrated that routine early referral for PCI after fibrinolysis in patients for whom primary PCI is not readily available leads to a significant reduction in reinfarction, recurrent ischaemia and the combined endpoint of death/reinfarction, during the first month after STEMI [16].

Despite these consistent results, European Society of Cardiology Guidelines for the management of acute ST-elevation myocardial infarction stipulates that, once thrombolysis successfully performed, coronary angiography may be performed within 3-24 hours after start of fibrinolytic therapy, in order to avoid an early PCI during the prothrombotic period following fibrinolysis, on the one hand, and to minimize the risk of re-occlusion, on the other hand (IIa class of recommendation, level of evidence A) [1].

On the basis of these data, the management of acute ST-elevation myocardial infarction in the Romanian health system remains debatable.

The purpose of the present study was to evaluate the management of acute ST-elevation myocardial infarction patients in our clinic.

Methods

625 patients with acute ST – elevation myocardial infarction admitted in our clinic from January 2010 until May 2011 where analyzed. Inclusion criteria were represented by acute ST- elevation myocardial infarction within 12 hours from onset of symptoms on admission. Patients were analyzed on discharge from hospitalization following acute ST-myocardial when treatment management was taken into account as well as left ventricle ejection fraction (EF%). The average duration of hospital stay in intensive care coronary

unit was determined. Approximately 30 days after the acute coronary event death, reinfarction, recurrent ischemia and severe heart failure were analyzed.

Results

Out of the 625 patients, a small number (2.88% - group A) only received thrombolytic therapy. Most of the patients (57.12% - group B) were referred to primary PCI < 6 hours (figure **1**), 14.56% - group C, initially received thrombolytic therapy and then referred to PCI < 24 hours from onset of symptoms (figure 2, next page) and 25.44% - group D were invasively evaluated but no revascularization therapy was performed and patients in group D were either referred to surgical therapy or continued with conservatory medical approach (figure 3, next page).

The average duration of hospital stay in intensive care coronary unit for the whole group was 3.3±1.18 days. Average value for the left ventricle ejection fraction was 40±8.17 in group A, 46±9.12 in group B, 45±8.2 in group C and 39±7.76 in group D. 30 days after the acute the prevalence of death, reinfarction, recurrent ischemia and severe heart failure encountered 8,17% in group A, 2.8% in group B, 3.29% in group C and 11.11% in group D and average values for the left ventricle ejection fraction were: 42±8.13 (group A), 48±9.72 (group B), 48±9.13 (group C) and 40±7.8 (group D) (figure 3).

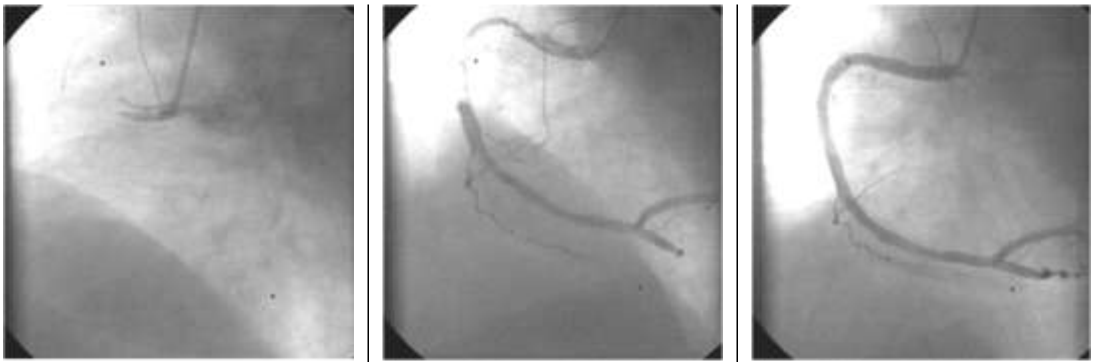

Figure 1a: Right coronary artery (RCA), TIMI 0 flow before angioplasty was performed

Figure 1b

Figure 1c: Right coronary artery after PTCA (primary PCI), TIMI flow III

Figure 1: Acute inferior ST-elevation myocardial infarction at 3 hours from onset of symptoms

Discussions

Preliminary data from the RO-STEMI registry, the first Romanian registry for acute ST-elevation myocardial infarction have recently been published [17]. RO-STEMI analyzed 19510 patients with acute ST-elevation myocardial infarction from 43 Romanian centers during 1997-2009, patients that were referred to conventional treatment, thrombolysis or primary PCI. First introduced in the Romanian registry in 2002, primary PCI is was only performed in 18.08% RO-STEMI patients during 2006-2009, thus leading to an inferior mortality rate in compare to the 2002-2005 period (10.83% vs. 13.73%, $p <$ 0.0001) [18].

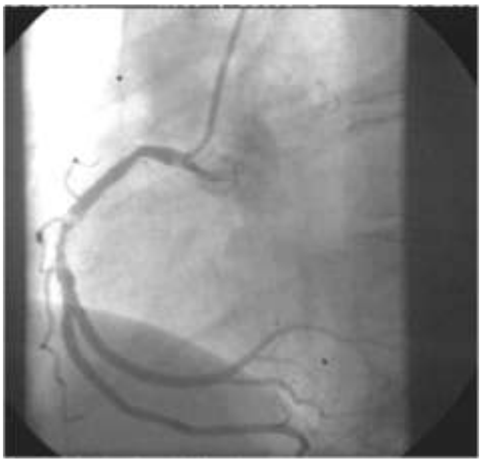

Figure 2a: RCA, distal TIMI flow III before angioplasty

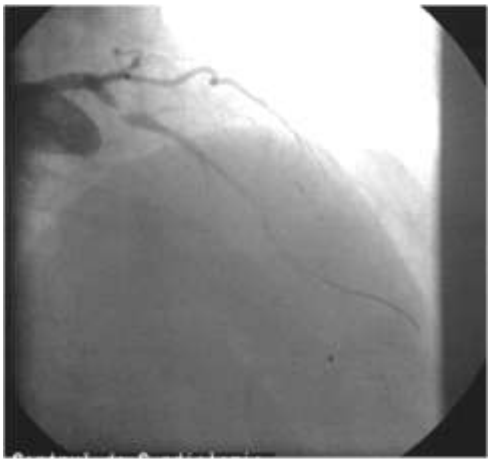

Figure 2b: TIMI flow II in the left anterior descendent artery (LAD) before angioplasty

Figure 2c: RCA after PTCA, TIMI flow III

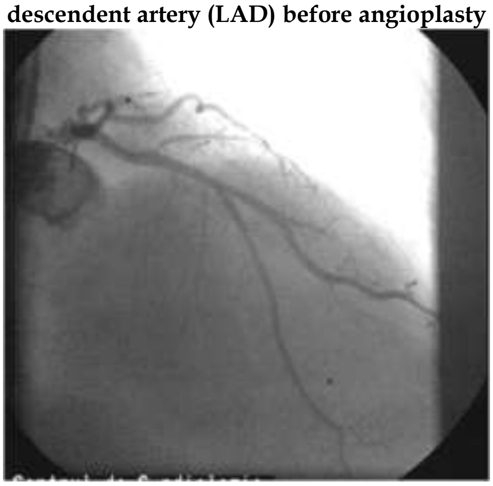

Figure 2d. LAD after PTCA, TIMI Flow III

Figure 2: Acute inferior and anterior ST-elevation myocardial infarction, in which case thrombolysis was performed at 2 hours from onset of symptoms, followed by PCI at 6 hours from onset symptoms (PTCA on RCA and LAD)

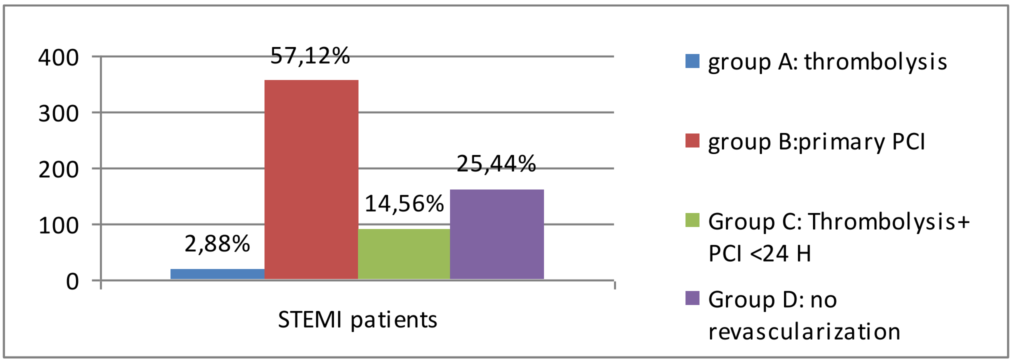

Figure 3: Treatment management in the analyzed group

In our study, the highest proportion of patients was referred to primary PCI (57.12%).

Moreover, our results demonstrated that approximately 30 days after the acute coronary event, groups B (primary PCI group) and C (PCI< 24 hours group) encountered an inferior rate of either death, reinfarction, recurrent ischemia or severe heart failure, respectively 2.8% and 3.29% in compare to thrombolysis alone group (11.11%) or the group of patients without an immediate revascularization approach (8.17%). That is the main argument that supports the pathway for the care of patients with acute ST-elevation myocardial infarction in our clinic, pathway that stipulates that, if primary PCI cannot be performed in less than 2 hours from onset of symptoms, patients should receive thrombolytic therapy and then should be referred to PCI in under 24 hours from onset of symptoms.

On the basis of the data already discussed [5] the same strategy was adopted by *Sanchez et al.*, in the *Hospital General Universitario Gregorio Maranon* and its area of care [19]. Also, in a meta-analysis conducted by Collet et al., and based on 1508 patients, results have demonstrated that systematic angioplasty immediately following thrombolysis deceased the risk of death or reinfarction by 48% compared to a conservative strategy (angioplasty reserved for recurrent ischemia) [20]. Results of the CARESS study which included 600 patients treated in a noninterventional center by half dose reteplase and abciximab also demonstrated that, angioplasty immediately after transfer compared to rescue angioplasty (in case of persistent ST-segment elevation or clinical deterioration) decreased the 30-day combined incidence of death, recurrent infarction or refractory ischemia by 60% (4.4% vs 10.7%; p = 0.0004), without increasing the risk of major bleeding or stroke [21].

On the other hand, benefits of early routine post-thrombolysis PCI vs. primary PCI are yet to be determined, the ongoing GRACIA-4 trial being the one that will compare the clinical efficacy of primary PCI vs. thrombolytic treatment followed by PCI in patients with STEMI.

Conclusions

Taking this data into account, our study demonstrated a superior efficacy of primary PCI as well as of the thrombolytic therapy followed by PCI in less than 24 hours on 30 days primary end-point (death, reinfarction, recurrent ischemia and severe heart failure) then thrombolytic therapy alone in patients with acute ST-elevation myocardial infarction. Also, in the hope of improving mortality rates after acute ST-elevation myocardial infarction, we support the constant use of thrombolytic therapy when estimated time delay from the onset of pain until balloon inflation is over 2 hours, procedure followed, if possible by routine early primary coronary intervention in less than 24 hours from onset of symptoms.

Study Limitations: Our study analyzed a small number of patients. Also, on long term, ventricular remodeling and benefits on left ventricle function were not being analyzed, since our study only took into account major cardiovascular events (death, reinfarction, recurrent ischemia and severe heart failure) after acute ST-elevation myocardial infarction on short term (30 days).

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Revascularisation myocardique par pontages artériels*)

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Résumé

Depuis les grandes études (CASS, Européenne, Vétérans), le pontage mammaire interne s'est imposé comme la technique de référence en chirurgie coronaire. Le pontage mammaire bilatéral a été très controversé; actuellement il est admis qu'il a un effet additionnel sur le pronostic vital et fonctionnel des patients lorsqu'il revascularise le réseau coronaire gauche. L'artère radiale et l'artère gastro-épiploïque droite sont souvent utilisées en complément pour une revascularisation artérielle exclusive, sans que leur impact positif sur les résultats de la chirurgie coronaire n'ait été montré. Une stratégie chirurgicale qui intègre le matériel disponible, la spécificité des patients et les perspectives de résultats à moyen et long terme, est proposée.

Mots-clés: *pontage coronaire, artère mammaire interne, artère radiale, artère gastro-épiploïque*

Le principe de l'utilisation de greffons artériels en chirurgie coronaire repose avant tout sur la dégradation inéluctable et continue des pontages veineux avec un taux de perméabilité à 10 ans inférieur à 60% [1]; les greffons perméables présentant le plus souvent des anomalies intra-luminales susceptibles de progresser. Cette altération des pontages veineux s'accélère après la 5^{e} année post-opératoire et est significativement corrélée au recul post-opératoire, à l'existence de maladies métaboliques: diabète ou dyslipidémie, et à la survenue d'événements cardiaques post-opératoires: récidive angineuse ou infarctus du myocarde [2]. En revanche, le bénéfice pour les patients de la revascularisation de l'interventriculaire antérieure par un pontage artériel mammaire interne gauche a été clairement montré: comparé à l'utilisation d'un pontage veineux, à 10 ans le risque de décès est diminué 1,6 fois, le risque d'infarctus 1,4 fois, le risque de réintervention deux fois et le risque de tout événement cardiaque post-opératoire de 1,3 fois [3]; du fait de l'excellente longévité des pontages mammaires internes avec un taux de perméabilité à 10 ans de 90% [4]. Ces résultats ont imposé le pontage mammaire interne comme la technique de référence pour revasculariser l'interventriculaire antérieure, devant être réalisé chaque fois qu'il est possible d'autant que son utilisation n'augmente pas le risque opératoire.

Le bénéfice démontré du pontage mammaire interne-IVA a incité de nombreuses équipes à utiliser le deuxième pédicule mammaire interne pour revasculariser le réseau

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circonflexe ou coronaire droit, en association au pontage mammaire interne-IVA. Le concept du double pontage mammaire interne repose donc sur l'hypothèse d'un effet additionnel d'un deuxième pédicule artériel sur les résultats de la chirurgie de revascularisation myocardique, avec un bénéfice cumulé des pontages mammaires internes. L'intérêt des deux pédicules mammaires internes en chirurgie coronaire a été controversé du fait de l'absence d'étude randomisée ou multicentrique. Néanmoins, se dégage un consensus pour admettre que le risque opératoire des doubles pontages est peu différent de celui observé pour les procédures utilisant un seul pédicule mammaire interne [5-7]. En cas de pontage mammaire interne bilatéral, les facteurs pronostiques habituels de la chirurgie coronaire sont trouvés; l'utilisation des deux pédicules mammaires internes n'augmente pas la morbidité périopératoire des patients à l'exception du risque de médiastinite qui semble accrue en cas d'obésité ou de diabète [8]. De même, cette technique n'augmente pas le risque opératoire chez les patients de plus de 65 ans ou en cas de réopération [6]. L'excellence des pédicules mammaires internes droit ou gauche en termes de perméabilité et de débit est la même [9, 10].

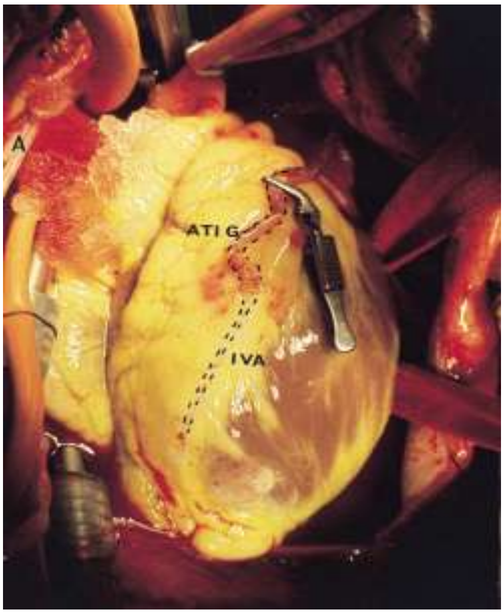

Figure 1 A: Implantation de l'artère thoracique interne gauche (ATIG), pédiculée squelettisée, sur une interventriculaire antérieure (IVA)

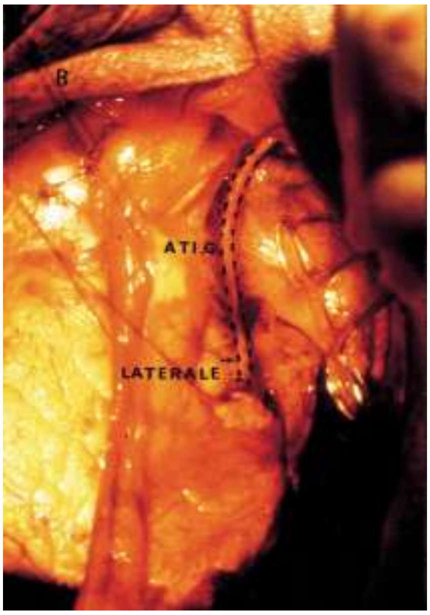

Figure 1 B: Implantation de l'artère thoracique interne gauche, pédiculée squelettisée, sur une branche latéro-circonflexe.

Le pontage mammaire interne bilatéral assure une suppléance coronaire satisfaisante à l'effort et représente une réserve coronaire suffisante pour le réseau coronaire gauche même en cas de greffon séquentiel avec deux ou trois anastomoses par pédicule [11]. L'utilisation des greffons mammaires internes séquentiels permet d'augmenter le nombre d'anastomoses artérielles par patient sans compromettre leur excellente perméabilité [12].

Bien qu'il existe un certain consensus pour préconiser l'utilisation des artères mammaires internes en greffons pédiculés, certains auteurs ont développé l'utilisation de l'artère mammaire interne droite en greffon libre aorto-coronaire associé au pontage classique mammaire interne gauche-IVA afin d'augmenter la longueur du greffon mammaire disponible et donc d'optimiser les possibilités de revascularisation myocardique artérielle complète [13]. Cette technique est controversée car elle s'accompagne d'une altération de la perméabilité à long terme du greffon mammaire libre [4, 12]. Un compromis technique a été proposé par Tector [14] avec un greffon mammaire interne droit libre mammaire-coronaire, c'est-à-dire réimplanter latéralement sur le pédicule mammaire interne gauche réalisant ainsi un greffon en T. Bien que cette technique semble préserver la perméabilité mammaire à long terme, elle est controversée du fait de sa difficulté technique et de la dépendance de la totalité de la revascularisation coronaire à partir du seul pédicule mammaire interne gauche avec un risque d'hypoperfusion coronaire [4].

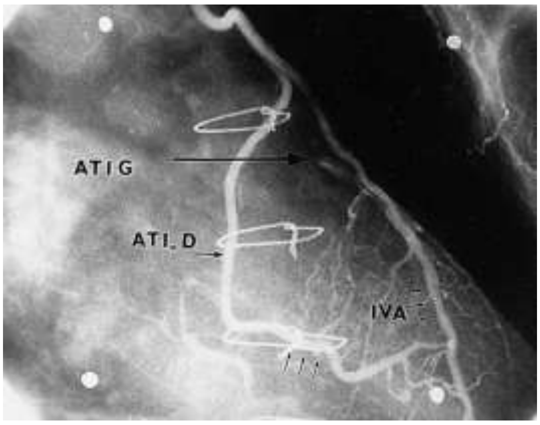

Figure 2: Contrôle d'une implantation en Y de l'artère thoracique interne droite à destinée latéro-circonflexe, sur l'artère thoracique interne gauche à destinée interventriculaire antérieure.

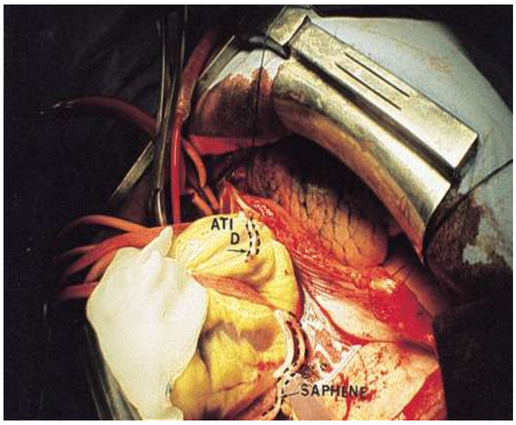

Figure 3: À la partie supérieure: implantation d'une artère thoracique interne droite en greffon libre et en séquentiel sur deux branches du réseau circonflexe. À la partie inférieure: implantation séquentielle en saphène sur l'interventriculaire postérieure et la rétroventriculaire gauche

La réalité d'un effet additionnel du deuxième pédicule mammaire interne sur les résultats à moyen terme de la chirurgie coronaire a été difficile à mettre en évidence; le bénéfice du pontage mammaire interne bilatéral semblait tardif [6], vraisemblablement parce que l'impact de la revascularisation du réseau circonflexe ou coronaire droit est moindre que celui de la revascularisation de l'IVA; sans doute également du fait des grandes variations d'utilisation du deuxième pédicule mammaire interne: revascularisation du réseau circonflexe ou coronaire droit, greffon séquentiel ou non, greffon libre ou pédiculé, pontage veineux associé ou non. Cependant, Pick [15] a montré dans une étude comparative non randomisée que par rapport au pontage mammaire interne unique associé à des pontages veineux, le pontage mammaire interne bilatéral revascularisant de façon préférentielle le réseau coronaire gauche, améliorait de façon significative à 10 ans le pronostic vital et fonctionnel des patients.

De même Schmitt [16] dans une étude comparative non randomisée a montré que l'utilisation préférentielle des deux artères mammaires internes pour revasculariser le réseau coronaire gauche permettait d'améliorer de façon significative le pronostic vital des patients à partir de la cinquième année post-opératoire par rapport à une revascularisation mammaire bilatérale intéressant l'IVA et le réseau coronaire droit. Cet impact positif du pontage mammaire interne bilatéral sur le pronostic fonctionnel et vital à long terme des patients a été confirmé de façon indiscutable par deux études comparatives importantes portant sur plusieurs milliers de patients: selon Buxton [17] le pontage interne bilatéral est un facteur prédictif indépendant des taux de mortalité tardive, d'infarctus myocardique secondaire et de réopération; selon Lytle [18] le pontage mammaire interne bilatéral diminue de façon significative le risque à long terme de décès, de réopération et d'angioplastie coronaire; dans ces deux études, le pontage mammaire interne bilatéral a été réalisé de façon préférentielle pour revasculariser le réseau coronaire gauche.

Ces résultats ont incité de nombreuses équipes à considérer le pontage mammaire interne bilatéral comme la technique de référence optimale en chirurgie coronaire et à rechercher un troisième pédicule ou greffon artériel susceptible d'être associé aux pédicules mammaires internes afin de réaliser des revascularisations myocardiques artérielles exclusives. L'artère épigastrique a été peu utilisée; sa structure histologique favorise le spasme et le développement de lésions athéromateuses [19]. L'artère radiale connaît un regain d'intérêt important bien que son prélèvement nécessite un deuxième site opératoire. Sa longueur et sa structure sont adaptées à des pontages coronaires multiples et elle est utilisée en greffon libre soit aorto-coronaire, soit mammaire-coronaire [20]. L'utilisation technique est peu différente de celle d'un pontage veineux classique et sa perméabilité à 5 ans est satisfaisante, en moyenne 85% [21]; ces deux critères ont beaucoup contribué au développement de son utilisation parfois bilatérale [22]. Le prélèvement de l'artère radiale n'a pas de conséquence fonctionnelle sur le membre supérieur après vérification préopératoire de la perméabilité des anastomoses palmaires par test d'Allen. L'utilisation de l'artère radiale comme alternative à une deuxième mammaire semble diminuer l'incidence des infections sternales post-opératoires [23], mais risque de compromettre les résultats à moyen et à long terme compte tenu de la différence de perméabilité de ces deux greffons artériels.

L'artère gastro-épiploïque droite est également très utilisée [24]; son prélèvement ne nécessite pas un autre site opératoire, sa structure histologique est peu différente de celle de l'artère mammaire interne [19], sa perméabilité à 5 ans est satisfaisante, en moyenne 92% [25, 26] et elle assure une suppléance coronaire satisfaisante à l'effort [24]. Son utilisation n'augmente pas le risque opératoire et n'induit pas de morbidité spécifique. Elle est utilisée pédiculée, le plus souvent pour revasculariser le réseau coronaire droit en alternative à un pontage veineux ou à un pontage artériel libre.

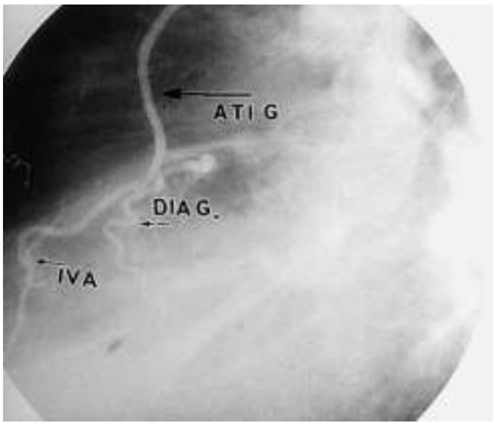

Figure 4: Contrôle d'un pontage séquentiel artère thoracique interne gauche, diagonale interventriculaire antérieure

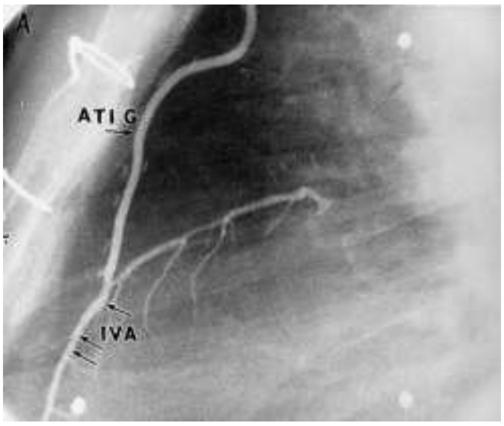

Figure 5 A: Contrôle d'un pontage artère thoracique interne gauche interventriculaire antérieure

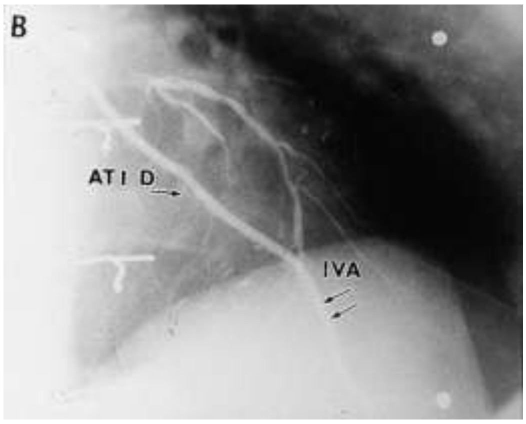

Figure 5 B: Contrôle d'un pontage artère thoracique interne droite pédiculée interventriculaire antérieure (passage antérieur)

La combinaison de ces différents greffons artériels permet de réaliser des revascularisations myocardiques artérielles exclusives, techniques qui s'imposent progressivement comme le *gold standard* en chirurgie coronaire [27, 28]. Sa réalisation n'augmente pas le risque périopératoire et les résultats à moyen terme sont actuellement très encourageants avec une survie à 5 ans supérieure à 90% pour des taux de récidive angineuse faibles, inférieurs à 15% à 7 ans [29].

On peut ainsi définir une stratégie chirurgicale en chirurgie coronaire qui intègre le matériel disponible, la spécificité des patients et les perspectives de résultats à moyen et à long terme. Le pédicule mammaire interne reste de façon indiscutable le matériel de choix et de référence et il ne semble pas licite d'utiliser un autre greffon artériel en alternative à un pédicule mammaire interne. L'absence de pontage mammaire interne-IVA doit être exceptionnel et fortement justifié. Les deux pédicules mammaires internes sont utilisés de façon préférentielle pour revasculariser le réseau coronaire gauche avec une large utilisation des pontages mammaires internes séquentiels pour des revascularisations myocardiques les plus complètes possibles. La limite du pontage mammaire interne bilatéral est la dilatation des cavités ventriculaires lorsque la longueur des pédicules mammaires internes est insuffisante; le deuxième greffon artériel est alors utilisé en greffon libre: mammaire interne en première intention, artère radiale en deuxième intention et pontage veineux en troisième intention. Pour des raisons anatomiques, la revascularisation du réseau coronaire droit est l'apanage de l'artère gastro-épiploïque droite lorsqu'on en a l'expérience. Ses limites d'utilisation sont des antécédents de chirurgie abdominale, une pathologie digestive ou un diamètre insuffisant de l'artère; les alternatives sont un greffon radial libre ou un pontage veineux.

La revascularisation myocardique artérielle est techniquement plus exigeante et nécessite une protection myocardique optimale. En fin de procédure, le débit dans les greffons artériels doit être maximal et la prévention des bas débits post-opératoires est essentielle afin d'éviter le cercle vicieux: bas débit cardiaque, bas débit dans les greffons artériels, ischémie myocardique, bas débit cardiaque.

Le bénéfice de la revascularisation myocardique artérielle n'étant pas encore validé par des études comparatives randomisées, le contrôle du risque opératoire est capital. L'indication de revascularisation myocardique artérielle doit être adaptée. Elle est fortement recommandée en cas de réopération, chez les patients jeunes de moins de 65 ans, lorsque l'espérance de vie du patient est supérieure à l'espérance de vie des greffons veineux, et lorsqu'il existe une probabilité importante de dégradation rapide des pontages veineux: dans les maladies métaboliques (diabète, dyslipidémie, insuffisance rénale chronique) et lorsque le réseau coronaire est grêle ou de mauvaise qualité. L'indication peut être discutée lorsque l'espérance de vie des patients à moyen terme est faible: chez les patients de plus de 75 ans, en cas de pathologie associée évolutive. L'indication doit être enfin prudente lorsque le risque opératoire est susceptible d'être augmenté par une procédure artérielle en cas d'insuffisance respiratoire sévère ou en cas de dysfonction ventriculaire gauche sévère où il existe un risque élevé de bas débit cardiaque post-opératoire.

Conclusions

La revascularisation myocardique artérielle est certainement à ce jour une technique de référence en pathologie coronaire, dont les résultats à long terme dépendront davantage de la dégradation du réseau coronaire que de l'altération des pontages artériels multiples. Il faut cependant garder à l'esprit qu'il n'existe pas une technique et des patients, mais des techniques et un patient.

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Morbidity and mortality associated with harvesting of the left internal mammary artery*)

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Abstract

The left internal mammary artery is the gold standard among the grafts used for coronary artery bypass grafting. Even though the left internal mammary artery was used before the saphenous vein as a graft, it was initially not very popular because of the difficulty of its mobilization and the perceived associated morbidity.

Aim: *To present the difficulties encountered with harvesting of the left internal mammary artery. To assess whether the use of the left internal mammary artery is associated with an increased morbidity or not.*

Materials and methods: *A descriptive observational study on 500 patients operated between January 1997 and August 2002. A control group of 100 patients in whom no left internal mammary was harvested was used for comparison. The patients of the control group were operated between January 1995 and August 2002. The difficulties encountered during harvesting, the postoperative morbidity, perioperative mortality and the rate of early reoperation were studied.*

Results: *In the majority of cases (84%) the harvesting of the left internal mammary artery was uneventful. The harvesting was considered difficult but could be used in 50 cases (10%). In 6% the left internal mammary artery could not be used as a graft. The reasons for not using the left internal artery as a graft were insufficient flow despite no signs of surgical damage, surgical damage to the artery, hemodynamic collapse of the patient requiring emergency CPB and abnormal adherence of the artery to the thoracic wall. Postoperative complications needing reoperation were encountered in 7.8% of patients. The early mortality was 3.6%. There was no significant difference between the study group and the control group regarding post-operative morbidity and mortality. The only significant difference noted was the thoracic drainage fluid (980 ml vs. 670 ml in the control group).*

Conclusions: *The left internal mammary artery can be used as a graft for CABG in the majority of cases, even in instances when harvesting is difficult. Harvesting of the left internal mammary artery does not appear to influence postoperative morbidity. Harvesting of the left internal mammary artery may encounter serious difficulties related to anatomy, morphology and surgical technique.*

Key-words: *Left internal mammary artery, harvesting, morbidity.*

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Background

The left internal mammary artery is the graft of choice for coronary artery bypass grafting. Its long term patency is the best among all grafts used for myocardial revascularization with a patency rate exceeding 90% at ten years in many studies (1, 2). Not only the early and long term patency makes the left internal mammary artery the graft of choice but also other data indicating that the use of this graft appears to confer a survival benefit when compared to those patients who have had saphenous vein grafting to the anterior descending coronary artery (3). Even though the left internal mammary artery was used before the saphenous vein as a graft, it was initially not very popular because of the difficulty of its mobilization and the perceived associated morbidity.

Aim

We try to present the problems encountered with harvesting of the left internal mammary artery. We also try to assess whether the use of the left internal mammary artery is associated with an increased morbidity or not.

Materials and Methods

We retrospectively analyzed the files of 500 patients suffering coronary artery bypass grafting with the use of the left internal mammary artery between January 1997 and August 2002.

We studied especially the problems related to the surgical harvesting of the left internal mammary artery and to its use as a bypass graft.

We analyzed the postoperative complications and concentrated our attention on those complications most likely to be influenced by the harvesting and use of the left internal mammary artery as compared to patients where only saphenous vein grafts are used.

We excluded from our study complications that are non-specific to coronary artery surgery such as neurological, renal, intestinal or hepatic complications. We also excluded from our study the cardiac complications as we focused our interest on the surgical aspects of the harvesting of the internal mammary artery.

We recorded the perioperative mortality and the rate of reintervention. In this latter instance we recorded in how far the left internal mammary artery was involved in producing the event that led to the need for reintervention (especially as a source of bleeding).

After this descriptive study we also performed a comparative study using as control group a series of 100 patients in whom only saphenous vein grafts were used for CABG and the left internal mammary artery was not harvested intentionally. These 100 patients were operated between January 1995 and August 2002.

Surgical technique

The same technique was used in all studied patients. The left pleural cavity is opened intentionally in all cases. The left internal mammary artery was harvested pediculated, non-skeletonized. The endothoracic fascia was cut using the electrical cautery. Most of the rami of the left internal thoracic artery were also transected using the electrical cautery. Metal clips were used occasionally for larger rami or for bleeding rami. Careful hemostasis in the mammary artery bed is achieved before systemic heparin administration and division of the distal end of the artery.

The left internal mammary artery was in all cases anastomosed terminally to the left anterior descending artery.

Results

The mean age of our patients was 56 years (56 ± 7 years, 32 - 82 years). The male to female ratio was 412/88 (82.4% male, 17.6% female). The mean age of the male patients was inferior to the mean age of the female patients (54 ± 8 vs. 61 ± 9 years).

36 patients (7.2%) were operated on in an emergency status. 180 patients had a prior myocardial infarction (36%). 289 patients (57.8%) were in NYHA III or IV functional class.

Most patients received 3 grafts (171 patients - 34.2%). In table 1 we depicted the number of grafts received by the patients in our study group.

Table 1: Number of grafts used in the patients studied

No. of grafts	1 graft	2 grafts	3 grafts	4 grafts	5 grafts
No. of pts.	54	97	171	101	76
%	10.8	19.4	34.2	20.2	16.2

In 420 of the 500 cases (84%) the harvesting of the left internal mammary artery was uneventful.

In 50 patients (10% of the patients of the study group) the harvesting was considered difficult but successful. Hemorrhage or very abundant adipose tissue obliterating a clear view of the left internal mammary artery during harvesting was encountered in 8 cases (1.6% of all harvested left internal mammary arteries).

In 17 cases (3.4% of all harvested left internal mammary arteries) an important spasm was noted. The spasm eventually remitted. Papaverine flushing of the artery and clip ligation of the distal end leaving arterial pulsations dilate the artery before its use as a graft were routinely used in our patients.

The left internal mammary artery was considered tiny, fragile and/or having thin walls in 14 cases (2.8% of all harvested left internal mammary arteries). The flow was however considered satisfactory and the arteries were used as grafts.

In 11 cases (2.2% of all harvested left internal mammary arteries) the artery was considered a little short due to either high bifurcation or a distal lesion produced during harvesting.

In 30 cases (6% of all harvested left internal mammary arteries) the left internal mammary artery could not be used as a graft.

In 12 cases (2.4%) the left internal mammary artery had an unsatisfactory flow despite no signs of surgical damage to the artery. The decision for using or not using the artery as a graft was subjective.

Surgical damage to the left internal mammary artery during harvesting (wound, dissection) occurred in 9 cases (1.8%).

Hemodynamic collapse of the patient with the need for emergency cardiopulmonary bypass made the harvesting of the left internal mammary impossible despite the surgeon starting the harvest in 6 cases (1.2%).

Abnormal adherence of the left internal mammary artery to the thoracic wall was considered the reason for failure of harvesting of the graft in 3 cases (0.6%).

The left internal mammary artery was used as a graft in 476 of the 500 cases (95.2%). The artery was used as a pedicled graft in all but 6 cases, when it was used as a free graft. No sequential anastomoses (kissing anastomoses) were performed in our study group.

Postoperative complications

A total of 39 patients needed early reoperation (7.8% of all patients of the study). The main causes of reintervention were sternal wound infection (15 cases – 3% of all patients) and bleeding (14 cases – 2.8% of all patients). The reason for early reintervention is presented in **table 2.**

Table 2: Causes of early reintervention

	n	%	% of reintervention
Hemorrhage	14	2.8	35.90
Tamponnade or suspicion of tamponnade	4	0.8	10.26
Sternal deep wound infection	15	3.0	38.46
Sternal mechanical dehiscence	4	0.8	10.26
Other	2	0.4	5.13
TOTAL	**39**	**7.8**	**100**

Only in 2 of the 14 cases of early reintervention for hemostasis was a source of bleeding related to the left internal mammary artery. In other 5 cases was another surgical bleeding source identified, while in 7 cases the bleeding was diffuse and no surgical source could be identified.

In the following tables we present the rates of infectious and non-infectious complications.

Table 3: Postoperative infectious complications

Complication	n	%
Postoperative mediastinitis	15	3
Bronchopulmonary infections	41	8.2
Superficial sternal wound infection	11	2.2
Systemic sepsis	10	2

Table 4: Postoperative non-infectious complications

Complication	n	%
Left phrenic nerve paralysis	11	2.2
Left pleural effusion needing needle aspiration	22	2.4
Left pleural effusion needing tube drainage	21	4.2
Atelectasia	10	2.0
Pneumothorax	7	1.4
Other	6	1.2

The early mortality in our 500 studied patients was 3.6% at 14 days from the operation (18 deaths). The causes of death are presented in **table 5**.

Table 5: The causes of early postoperative death

Cause of death	n	%
Low cardiac output syndrome	5	27.77
Multiple system and organ failure	4	22.22
Uncontrollable infection	4	22.22
Other (including unexplained)	5	27.77
TOTAL	**18**	**100.00**

The comparative study compared a set of parameters in patients in whom the left internal artery was used as a graft with the same parameters in the patients of the control group. The only significant difference noted was related to the total thoracic drainage fluid that was 980 ml/patient on average in the study group as compared to only 670 ml in the control group.

Table 6: Parameters assessed in the comparative study

Parameter	Study group (LIMA)	Control group (no LIMA)	Significance
Infectious complications	15.4%	14%	No
Mediastinitis	3.0%	2%	No
Reintervention for bleeding	2.8%	3%	No
Early postoperative mortality	3.6%	4%	No
Volume of drainage fluid	980 ml	670 ml	

Discussions

The left internal mammary artery can be used as a graft for coronary artery bypass grafting in the vast majority of cases (95.2% in our study). Our results confirm the literature data. We do not routinely assess the patency of the left internal mammary artery preoperatively. The decision whether to use or not the left internal mammary artery for myocardial revascularization is taken by the surgeon intraoperatively and relies mainly on subjective appreciation in our department.

In as much as 10% in our study the harvesting was considered difficult. In only about 2% of the cases was harvesting technically difficult. This represents certainly an underestimation.

We have found that postoperative bleeding is more important in case of use of the left internal mammary artery as compared with the non-use of this graft and the exclusive use of saphenous vein grafts. Except for that, however, no other statistically different increase in postoperative morbidity could be found related to the harvesting and use of the left internal mammary artery. This findings support the clinical data reported by Avila et al (1), Cosgrove et al. (4) or Cron et al. (5).

A special mention is related to the rate of phrenic nerve paralysis. The rate of only about 2% is clearly an underestimation. Studies where routine fluoroscopic examinations were performed in patients in whom the left internal mammary artery was harvested have shown an incidence of left phrenic nerve paralysis of around 10%.

The early mortality rate does not significantly differ among the two study groups in our work. However, our study is rather small, while consistent data in the literature indicates that the use of the left internal mammary artery is associated with a decrease in early mortality. The difference is the more obvious the greater the number of patients compared.

Conclusions

There are no significant differences in postoperative morbidity related to the harvesting and use of the left internal mammary artery. The only significant difference we found regards the volume of the post-operative thoracic drainage fluid.

These findings even more support the use of the left internal mammary artery in all cases where the anterior wall of the left ventricle needs to be revascularized.

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Robotically-assisted closed chest Coronary Artery Bypass Grafting surgery on beating heart. Technique Description*)

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This work describes the totally endoscopic, closed chest robotically-assisted technique for coronary artery bypass surgery on beating heart using the da Vinci™ Surgical System. Included are technical components, pre-operative considerations, intraoperative technique tips and post-operative recommendations, as well as troubleshooting suggestions. The cooperation and support from the entire operating room team enhances the success of any new technique. Training considerations for all members of the team needs to be discussed prior to start the robotically program.

Experiences to date have suggested that most technically challenging portions to the robotically assisted closed chest Beating Heart LIMA-LAD bypass may be the mobilization of the arterial conduct, the stabilizer placement as well as the anastomosis. The reason for this is quite straightforward: most cardiac surgeons are not familiar with videoscopic internal thoracic artery mobilization combined with off pump anastomosis. Additionally, the surgeon must understand the anatomy as viewed from the endoscope and incorporate this into selecting proper port placement. Using endoscopic technique, the artery as seen from the lateral side must be appreciated. Most cardiac surgeons are more comfortable viewing the internal thoracic artery from the medial side through a median sternotomy. The Endowrist™ articulated robotic instruments facilitate totally endoscopic surgery, where the 3D stereoscopic vision plays major role. The endoscopic stabilizer introduced through a subxyphoidian approach facilitates safe Closed Chest CABG Surgery on Beating Heart.

About Da Vinci™ Surgical System

The basis of the dexterity experienced in open surgery relies on the almost unlimited wrist, elbow and shoulder's degree of freedom.

The degree of freedom in endoscopic surgery is limited because instruments need to be long and are manipulated through fixed ports. The surgeon has to move around these fixed ports.

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In order to solve these limitations tools have been developed that have an articulation at the tip, which increases the degrees of freedom. Addition of the wrist at the tip of the instrument gives tool manipulation much more complex. Computer assistance is warranted, as the human brain cannot efficiently manipulate articulated instruments by mechanical means. A robotic wrist provides articulated motions with a full 7 degrees of freedom inside the abdominal or thoracic cavities (EndoWrist™ technology (Figure 1 & 2).

Figure 1: Endowrist ™ technology at instrument tips

Figure 2: Motion scaling

Computer interfacing and robotics allow for remote control surgery (telesurgery), for more precise manipulations by downscaling the surgeon's motions and by allowing surgeon's good ergonomic position.

Human robotic surgery was introduced by Cadiere's team (St Pierre Hospital, Brussels, Belgium) in March 1997 when the first telesurgical laparoscopic cholecystectomy was performed together with Dr Himpens at Dendermonde, Belgium. The first telesurgical laparoscopic Nissen fundoplication was performed by the same team in May 1998.

In early may of 1998 Carpentier and Loulmet perform the first robotic cardiac surgical operations, which included an atrial septal defect closure and several mitral valve repairs. Later that month Mohr and Falk performed additional mitral operations and the first robotic coronary anastomosis.

Broussais group describes the world's first totally endoscopic coronary bypass (June 1998). All groups used the same surgical device (da Vinci™; Intuitive Surgical, Inc, Mountain View, Calif).

The surgeon's console

The da Vinci™system consists of a master console that that connects to a surgical '*manipulator*' with two instrument arms and a central arm to guide the endoscope. Two 'master' handles at the surgeon's console are manipulated by the user. The position and orientation of the hands on the handles trigger highly-sensitive motion sensors and translate to the end of the instrument at a remote location (Figure 3).

The surgeon sits comfortably at a master console located at a distance from the patient with eyes focused down toward the operative site mirroring an open surgical technique and the slave unit provides "tele-presence" within the chest for micro instruments manipulation.

Figure 3: Hands position corresponds to instrument tip orientation

Superior ergonomic design allows surgeon to become immersed in the operative field (Figure 4). A 10 mm high-resolution 3D 30° endoscope (with two three- chip charge coupled device – CCD cameras) is used for better perception of depth and optical resolution. The endoscope is held by the central four DOF manipulator of a remote centre design, similar to the slave tool manipulator. The camera manipulator is capable of positioning the tip of the endoscope in 3D by working through the fulcrum made by the port incision at the body wall. This Navigator™ Camera Control system gives the surgeon a 3rd arm to hold and move the camera without the need for an assistant.

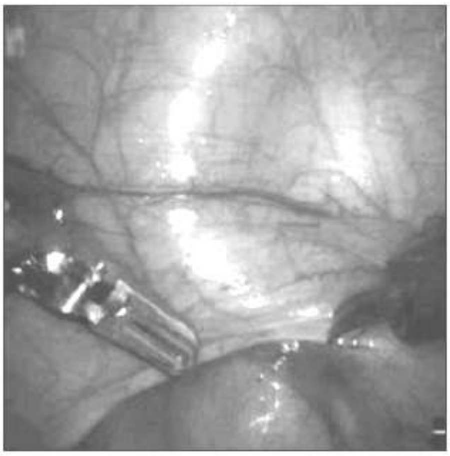

Figure 4: Intraoperative image

The surgical arm cart

Handles motions are sensed by high-resolution motion sensors, processed and transferred to the two surgical manipulators. These slave manipulators (surgical arms) provide three degrees of freedom (pitch, yaw, insertion). The surgical instrument is attached to the surgical arm. The instrument tip is provided with a mechanical cable-driven wrist (Endo-wrist Technology), which will add four more degrees of freedom (internal pitch, internal yaw, rotation and grip). The grip is programmed to 1.0 Newton.

In order to enhance precision, the system allows for scaling of the handles-surgical arms motion relationship. A motion scale of 3:1 will move the instrument 1 mm inside the abdomen for every 3 mm motion at the master console.

In addition, unintended movements caused by human tremor are filtered by a 6 Hz motion filter.

The robotic arms together with robotic instruments attached on it can be disconnected from the master-handles by the clutch foot pedal, in order to obtain a more comfortable and ergonomic position of the surgeon hands at the console.

The 3D imaging system

The high resolution 3D endoscope consists of two three chip charge-coupled (CCD) device cameras (InSite) with two high-intensity light sources to ensure a bright image of the operative field. Lenses of 30° can be used. The 30° scope can be fixed either down or upside looking. The video image enables up to 15 fold magnification according to the working distance compared to the operative field. The endoscope is attached to the robotic camera arm and once inserted it can be moved from the console by the surgeon by pressing the camera food switch. This will lock the instrument arms and gives the operator control of the camera through the master manipulators.

Communication between operating and assistant surgeon

Adequate coordination between the surgeon at the console and his assistant at the operating table is guaranteed by a permanent communication. In some operating rooms the surgeon's console is installed in a separate room connected with a microphone to the operating room. In other hospitals the console may be in the same room.

Patient Selection for Robotically-Assisted BHTECAB Surgery

The standard contraindication for cardiac surgery, both conventional and minimally invasive, should be practiced when selecting patients for BHTECAB procedures including renal insufficiency, severe peripheral vascular disease, occlusion of left subclavian artery, heavily calcified aorta, severe pulmonary disease and diffusely calcified coronary disease.

Patient Positioning and port placement

The patient is positioned at the left edge of the table in order to facilitate access to the internal anatomy with minimal collisions both internally and externally. External collisions typically occur between the patient's anatomy, either shoulder or hip, and the arms of the surgical cart when mobilizing the distal and proximal part of the LIMA, respectively.

Figure 5: Port placement and patient positioning

When preparing the patient and placing leads/defibrillator pads on the chest, care needs to be taken in account that port will be placed on the left lateral and mid-clavicular areas of the thorax. The external defibrillators pads are so, placed quite posterior with patient rotated a 20° on right side. A roll is placed under the mid-thorax (from scapula to lower ribs). The patient's arms are by patient's side taped around.

Port site location is an important aspect to the success of the procedure. Port sites are determined primarily on successfully mobilizing the LIMA from its origin at the subclavian artery to the 6th intercostals space.

All ports are placed on the left hemithorax as follows: camera port is usually placed first in the 5th left intercostal space on the anterior axillary line. Insuflation with CO2 through the Camera Port maintains a pressure between 6-10 mmHg (high flow) prior to introduce the endoscope. This lowers the left ventricle creating more space between the left ventricle and the sternum. Right and left instrument ports are usually located in the 3rd intercostal space and 7th intercostal space respectively, on the left mid-clavicular line.

Once the ports are in place the sterile draped robotic arms are docked and fixed to the trocars on specific angles while calibration is performed.

The phrenic nerve is followed as it traverse the pericardium up to the internal mammary artery origin. The mammary artery is located where it is most visible (usually the 2nd intercostals space). Its path is followed superiorly up to the apex of the left chest near the origin at the subclavian artery. The LIMA is than dissected distally to the 6th intercostals space – usually the mid 1/3 is covered by adipose tissue and the lower 1/3 is obscured by the muscle. Arterial pulsations observed through the soft tissue can be used as a guide. Low monopolar cautery settings are recommended starting at 25 watts.

The dissection is started by incising the parietal pleura with cautery where it is most visible, usually at the 2nd rib, 1 cm medial to the artery. A micro-bipolar forceps is used on the left robotic arm while on the right robotic arm a monopolar cautery blade can perform the dissection. As there is low tactile feed-back at the surgeon's console, care must be taken not to place undue tension on the pedicle.

Exposing the LAD

This step is performed very often prior to the LIMA dissection as it provides an opportunity to evaluate the length of the Mammary Artery. The length of the LIMA should neither be too short, self explanatory, neither too long which could result in the LIMA twisting or kinking. There is a tendency to misinterpret the coronary anatomy when working endoscopically. The endoscopic view is much more limited than what has been typically seen in either conventional or minimally invasive cases. Also, the image is magnified. Incising the pericardium with a large window is vital to successfully locating the LAD as well as taking sufficient time to locate all known anatomical markers and then proceeding to the anticipated location of the LAD. The phrenic nerve is located at the lateral aspect of the pericardium. The pericardial fat is excised medially allowing lateral draping. A longitudinal incision over the medial aspect of the pericardium is performed. This incision is enlarged medially and longitudinally towards the apex, creating a window. The proximal LAD is than located as it exits the AV groove left of the pulmonary artery. Once the Left Ventricle and the Right Ventricle is identified, the septum (area of depression) is noted.

Preparing the LIMA

It is currently recommended that the distal end of the LIMA be prepared internally while in situ using an articulated Endwrist™ potts scissors. A 1 cm area of the mammary pedicle is skeletonized at 7 cm proximal from the distal end of the artery – for bulldog placement (Scanlan™). Heparin is administrated after skeletonization and prior to attaching the bulldog to the LIMA. A stay suture is placed in the pedicle of the LIMA onto the pericardium near the anastomosis site. The LIMA is distally clipped while the transsection and the spatulation is performed.

The stabilizer introduction

The endoscopic stabilizer is introduced via a 12 mm diameter incision located at the subxyfoidian area, 1 cm left from the median line. Under direct control of vision (both externally and internally), the stabilizer is positioned above the area where the anastomosis will be performed. By manipulating it internally with two articulated robotic needle drivers while the assistant orient from the patient side its position, the stabilizer is placed and stay rigid by attaching it on the Endoboy arm on the operating table. Both endosuction lines are activated which maintains the stabilizer in a fixed position, while the EndoIrrigator line is on in order to clear the anatomy where the anastomosis is to be performed.

By the aid of two sylastic loops, the LAD is occluded distally and proximally.

Figura 6: Intracorporeal closed chest anastomosis

Arteriotomy

The arteriotomy is performed as in standard practice. The endoscope is switched now in a 30° position looking down. Since the image is 15 times magnified, it is advised that the spatulated portion of the pedicle be in view when extending the arteriotomy to ensure matching. Using the scalpel blade 15° the midline artery is incised. The arteriotomy is extended longitudinally using the articulated potts scissors. The length of the jaws of the potts scissors are is used as a guide when extending the arteriotomy.

Coronary anastomosis

The coronary anastomosis is performed using a 7.5 cm length double armed running suture. As with the open technique we begin by parachuting the graft down to the vessel. The anastomosis is performed as a mirror image of the current technique performed in open case. First stitch is placed in the pedicle outside to inside. After three stitches the pedicle is parachuted down. The needle is than placed in the pericardium maintaining some tension on the suture. The back wall is attached next by either continuing around the anastomosis or using the other needle and proceeding in a counterclock-wise direction till complete. The intracorporeal knot is easily performed at the end of the procedure with the help of two articulated MicroForceps.

Conclusion

The Beating Heart Closed Chest Coronary Artery Bypass Surgery is today reality. The procedure is feasible and gains more and more adoption with the introduction of the robotic surgery. The major advantage is for the patient: minimally invasive surgery as it avoids any sternotomy or thoracotomy. Three ports are necessary for the robotic arms: two ports of 8 mm diameter for the articulated robotic instruments and one port of 12 mm diameter for the Camera holding the endoscope. A fourth 12 mm diameter port is necessary for the stabilizer. The procedure is obviously less invasive because of the closed chest procedure as well as because of the off pump issues. Patient recovery is faster as leaving the hospital after one week while the post-operative pain is lower. There is less risk for infection while return to normal activity can be done after two weeks. This abstract wants to be a summary description of the technique of Robotically Assisted Closed Chest Coronary Artery Bypass Grafting on Beating Heart. More studies are necessary in order to prove the efficacy with more clinical outcomes.

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Laser transmyocardial revascularization - Reality and expectation*)

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Cardiovascular medicine is nowadays confronted with an increasing number of patients with coronary artery disease that have had a long course of the disease, have suffered a number of interventions, either surgical or percutaneous, for myocardial revascularization, are older, have severe lesional morphology and are generally sicker. This shift in coronary artery disease patients can be considered as the price paid for the increase in the performance of therapeutic means and, generally speaking, for the increase in life expectancy and aging of the population.

In this subgroup of patients revascularization procedures carry both high mortality and morbidity (1). Moreover, in many cases no such technique can be expected to carry success due to particular lesional morphology.

Any new therapeutical approach or technique that can be applied in such cases raises many hopes. It does so both in the medical world as well as among patients. For a technique using Lasers this is particularly true, given the special resonance of the term. Not very infrequently patients who can be managed properly and successfully by a classical means of revascularization ask for being revascularized "with the Laser". It is not only happening in patients with coronary artery disease but also in patients with varicose veins or with abdominal pathology who ask for a "Laser therapy", even though the term is used inappropriately in these latter cases.

The idea of revascularizating the ischemic myocardium using channels that link the myocardium to the left ventricular cavity appears promising. However, there have been many attempts to perform such channels in the past but success has been marginal, mainly because the patency of these channels could not be maintained. As early as 1965 Sen et al. proposed the generation of transmural channels in the left ventricular wall (2). Only in 1982 did Mirhoseini propose the use of Laser energy for this kind of channels hoping that by this technique a better patency could be granted (3).

These many transmyocardial channels would ideally allow arterial blood from the left ventricular cavity to directly perfuse the ischemic myocardium. Experience has shown this to be only a marginal event at best. The channels generated using the Laser transducer actually thrombosis very early.

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There is, though, some efficiency of the use of the Lasers on the heart. The so-called Laser "*transmyocardial revascularization*" (TMR) brings improvement in angina symptoms and exercise capacity (4). The mechanism of this improvement is still under debate. While placebo is unlikely to act exclusively, neovascularization induced by the local inflammatory response to the action of the Laser, damage to the nerve endings and the pericardial incision may all play a role (5). Promotion of neoangiogenesis appears to be the central mechanism of action, local growth factors that induce the development of new small vessels being released. However, improvement in myocardial perfusion could only be proven on radionuclide scan (positron emission tomography but not Thallium scans) and this improvement is marginal (6).

That improvement in myocardial perfusion after Laser TMR is not dramatic is also reflected in results such as long or even mid-term survival. There has not been any significant improvement in one-year survival with the use of the technique (7). The only significant improvement observed was the one concerning improvement of angina and of the quality of life of the patients. Some studies show a benefit in terms of survival at one year in patients that have received both CABG and Laser TMR (in territories where bypass grafting was considered impossible). This better outcome resides mainly on the lower periprocedural mortality rate that was, though, very high in both study groups compared (8).

Improvement on angina is important. It appears in 70 to 80% of the treated patients. It has to be said that patients receiving Laser TMR therapy are usually patients in who maximal pharmacological therapy proves unsatisfactory. It is this benefit of Laser therapy that is for what Laser is used today (9).

Although the number of patients with end stage coronary artery disease is increasing, still the ones in who no revascularization procedure can be performed and symptoms cannot be controlled by even maximal pharmacological therapy is a minority. It is this minority that represents the main target for Laser TMR and it is only symptomatic relief that is the best of the result that can be hoped. Laser TMR can also be used as an adjunct to CABG for territories where grafting or PTCA is impossible. It must be again underlined that Laser TMR is not an alternative to CABG or PTCA and stenting but a procedure for symptomatic palliation for cases where the two techniques can not be applied.

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Myocardial revascularization using arterial T Graft - which conduit should be chosen for free graft?*)

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Abstract

Background: *The T graft is achieved by the end-to-side implantation of a free arterial graft into the left internal thoracic artery (LITA), which remains in situ. It is still being discussed which conduit is suited best as a free graft.*

Methods: *Two groups of patients are compared. Right internal thoracic artery (RITA) was used as a free graft within group I (n = 129) and radial artery (RA) within group II (n = 84).*

Results: *RITA was used more often with male patients (p < 0.02) and with patients presenting a reduced left ventricular ejection fraction (p < 0.03). The coronary anastomosis per patient averaged higher in group II versus group I (p < 0.002). There was no significant difference between the groups concerning early mortality (0.8% in group I and 1.2% in group II) and morbidity. Postoperative chest tube output was significantly higher in group I than in group II (p < 0.05). Mean follow-up time was 35.2 ± 28.3 months. There was no significant difference regarding late mortality (6.9% in group I and 5.3% in group II) and the recurrence of angina (Group I: 6 cases respectively 5.5%; Group II: 3 case respectively 4.2%). Because recurrence of angina or questionable chest pain angiography was performed with 22 patients showing a patency rate of 90.9% in group I and of 93.1% in group II.*

Conclusions: *Based on our experience we advise using RITA as a free graft with tall men also in cases of reduced left ventricular ejection fraction, diabetes and obesity. RA should be used with small women if there is a high risk of bleeding and if it is necessary to have several coronary anastomosis.*

Keywords: *myocardial revascularization, left internal thoracic artery, T graft*

Introduction

The clinical results of surgical myocardial revascularization mainly depend on the patency rate of bypass material used. According to numerous studies the use of left internal thoracic artery (LITA) in situ for the revascularization of left anterior descending

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artery (LAD) shows excellent results. In comparison, the patients' survival rate was lower when venous bypasses were used in this position and recurrent angina, myocardial infarction and reoperations occurred earlier and more frequently [Acinapura 1989, Loop 1986]. Similarly, the use of venous bypasses for revascularization of circumflex artery and right coronary artery did not show any better results [FitzGibbon 1991].

Based on these findings LITA was established as the conduit of choice for the revascularization of LAD twenty years ago. At the same time the question arose whether right internal thoracic artery (RITA) would show better results than venous bypasses in ensuring the supply for another stenosed coronary vessel. The bilateral use of internal thoracic artery turned out to be the best solution for the problem as shown in the majority of studies in this field [Galbut 1990, Lytle 1999].

The clinical trend of replacing venous bypasses by arterial ones was also supported by a number of biochemical studies proving that arterial bypasses show better antithrombotic, antispastic and antiatherosclerotic qualities. Arterial endothelium produces more prostacyclin than venous endothelium, so there is less risk of a thrombosis with an arterial bypass than with a venous one [Chaikhouni 1986]. Also, more vaso-dilatative mediators like nitrogen monoxide are released from arterial bypasses as compared to venous ones [Rosenfeldt 1999].

In consequence, there is less danger of a spasm when arterial bypasses are used. Antiatherosclerotic qualities like fast lipolysis, slow fat absorption and well-preserved lymphatic drainage are higher in arterial grafts than in venous ones [He 1999]. Based on these results the demand for more arterial bypass material rose. Radial artery (RA) was used increasingly with good results [Acar 1998, Royse1999] once the original techniques of removal and implantation had been revised. There were also good results using gastroepiploic artery [Grandjean 1996. Sato 2000].

However, the excellent results of revascularization of LAD with the aid of LITA could neither be reached using RITA nor RA or gastroepiploic artery. Therefore the question arose whether these results were influenced by the quality of the bypass material or by the techniques of implantation. In order to achieve better hemodynamic conditions for bypass flow Mills [Mills 1982], Sauvage [Sauvage 1986] and Tector [Tector 1994] used the so-called T graft. For this, LITA was anastomized in situ with LAD and RITA was used as a free graft for the supply of further stenosed coronary vessels.

The T graft is formed by the implantation of the proximal end of RITA into LITA. Myocardial revascularization using T graft has since then been adopted by several research teams and has been used with very good results [El Nakadi 2000, Pevni 2001, Tatoulis 1999, Wendler 2001]. A slight variation of the method just described is using RA instead of RITA, which has also been used with very good results [Calafiore 1995, Iaco 2001, Sundt 1999, Tatoulis 1999, Wendler 2001]. However, it is still being discussed, which of the two conduits described above can provide better results as a free graft. Our study is aimed at a comparison of RITA and RA as parts of a T graft and tries to clarify the advantages and disadvantages of the said conduits on the basis of short and midterm results.

Materials and methods

Patient population

From June 1997 to June 2001 213 patients suffering from a coronary artery disease underwent total arterial myocardial revascularization using a T graft at our clinic. In 129 cases (group I) the T graft consisted of LITA in situ and of RITA as a free graft. With 84 patients (group II) the T graft was fashioned from LITA and RA as a free graft. The clinical dates of these two groups are shown in Table 1.

Table 1

	LITA+RITA T Graft (n = 129)	LITA+RA T Graft (n = 84)	*p* value
Sex (female)	14 (10.8%)	20 (23.8%)	< 0.02
Mean age (years)	59.2 ± 8.9	61.7 ± 9.2	ns
Coronary artery disease			
• one vessel	2	1	ns
• two vessel	36	14	ns
• three vessel	91	69	ns
Previous myocardial infarction	68 (52.7%)	35 (41.6%)	ns
NYHA class			
• I	2 (1.5%)	2 (2.4%)	ns
• II	25 (19.4%)	14 (16.7%)	ns
• III	75 (58.1%)	61 (72.6%)	ns
• IV	27 (21%)	7 (8.3%)	ns
Diabetes mellitus	25 (19.4%)	23 (27.4%)	ns
Hyperlipidemia	107 (82.9%)	71 (84.5%)	ns
Obesity	66 (51.2%)	51 (60.7%)	ns
Hypertension	89 (69.0%)	65 (77.4%)	ns
Smoking	82 (63.6%)	44 (52.4)	ns
Mean LVEF	58.1 ± 14.1%	62 ± 14.2	< 0.03
Operative priority			
• elective	43 (33.3%)	35 (41.7%)	ns
• urgent	74 (57.4%)	46 (54.7%)	ns
• emergent	12 (9.3%)	3 (3.6%)	ns

Originally we saw an indication for revascularization using an arterial T graft with patients under the age of 60 or when venous bypass material was amiss or insufficient. On growing more experienced we also used this method on patients up to 70 years of age. The necessity for having several coronary anastomoses in patients with a short sternum was found to be a contraindication against using the LITA+RITA T graft. Neither diabetes, nor obesity or a combination of both risk factors were seen as contraindication in group I. For establishing the blood flow figures within the hand when we planned to remove RA a preoperative Allen-test was used as described by Royse [Royse 1999]. RA was not used after a positive Allen-test, renal failure, a stenosis of subclavian artery, Raynaud's or Dupuytren's diseases. It was only removed from the non-dominant forearm. With all patients we aimed for complete myocardial revascularization. All coronary vessels showing a high grade of stenosis (>80%) according to the angiography were taken into consideration for revascularization. In case of one such vessel being too small in diameter (< 1.5 mm) or of a seriously affected structure of the coronary wall bypassing was omitted and the myocardial revascularization was considered incomplete.

Surgical protocol

With the patients of group I, the first step was to prepare LITA with pedicle using a "no-touch" technique. For this electrical coagulation (Force 2, Valleylab Inc, Pfizer Hospital Products Group, Boulder, Colorado, USA) was used at low power (40 Watt). Big side branches of the LITA were supplied with titanium clips (Ligaclip® MCA, Ethicon Endo-Surgery Inc, Cincinatti, OH, USA). Proximally, LITA was prepared up to its origin from subclavian artery and distally down to the fork into epigastric artery and musculophrenic artery. After the distal removal of LITA approximately 2 ml of a solution consisting of 50mg papaverine (Paveron®, Linden Arzneimittel Vertrieb GmbH, Heuchelheim, BRD) and 5000 IU heparine (Liquemin®N, Hoffmann-La Roche AG, Grenzach-Wyhlen, BRD) ad 100 ml sodium chloride solution 0.9% were given intra-arterially, and the distal end of LITA was occluded. Next, RITA was prepared free in an analogous manner from its origin to the bifurcation, then removed and carefully examined as to its tightness by an intravasal application of the heparinized papaverine solution described above. RITA was then stored in heparinized papaverine solution up to its implantation. With the patients of group II, RA was removed parallel to the preparation of LITA. Again this was achieved using a "no-touch" technique. The examination of tightness and the storage up to the implantation was conducted with the help of the heparinized papaverine solution. The incision on the forearm was closed after blood stilling and before extracorporal circulation. All operations were conducted by the same surgeon using extracorporal circulation at moderate hypothermic conditions (32°C) and cardioplegic solution (Custodiol®, Dr. Franz Kohler Chemie GmbH, Alsbach-Hahnlein, BRD) under cardiac arrest. First the coronary vessels of the posterior and/or lateral walls were anastomozed to the free graft (RITA for group I and RA for group II), then the distal end of LITA was anastomozed with the LAD and finally the proximal end of the free graft was implanted into LITA using an end-to-side technique. All anastomoses were completed using continuous sawing techniques and an 8-0 polypropylene thread (Prolene®, Ethicon GmhH, Norderstedt, BRD). The central implantation of the free graft took place while the aorta was still cross-clamped in order to avoid a mismatch at this location.

Spasmolythic therapy

In order to reduce the risk of an RA-spasm the patients of group II were given intravenous diltiazem hydrochloride (Dilzem®, Godecke AG, Berlin, BRD) in a dosis of 0.5 µg/kg/min immediately after the end of cross clamping the aorta. This spasmolythic therapy was continued for three months after the operation using oral in-take of diltiazem hydrochloride in the dosis of 180 mg/day.

Statistics

All data were analyzed using the Sigma Stat (SPSS Science, Chicago, IL, USA) software package. All continuous values are expressed as mean values ± standard deviation. The data of the two groups were compared using the *Student's t-test.* Regarding categorial data, the comparison between the two groups was performed with *chi-squared test* or *Fisher's exact test*. The data are expressed in absolute and relative figures. A p-value < 0.05 was considered to indicate statistical significant differences.

Results

The average number of coronary anastomoses per patient was 3.3 ± 0.8 in group I and 3.7 ± 0.8 in group II and was therefore significantly higher in group II ($p < 0.002$). With 72.1% of the patients of group I ($n = 93$) and with 86.9% of the patients in group II ($n = 73$) a complete myocardial revascularization could be achieved where there was no statistically significant difference between the groups. The time during which the aorta was cross-clamped averaged at 73.2 ± 18.9 min with the patients of group I and 73.5 ± 17.5 min with those of group II, thereby displaying no difference between the two groups. Early lethality, defined as death within the first 30 days after the operation, ranged at 0.8% ($n = 1$) for group I and 1.2% ($n = 1$) for group II. Postoperative chest tube output reached an average of 858.4 ± 500.4ml in group I and 731 ± 380.4ml in group II and therefore was significantly higher in group I ($p < 0.05$). Blood substitution, however, showed no statistically significant difference between the two groups. It averaged at 704.9 ± 436.6 ml in group I and 625 ± 307.6 ml in group II. The analysis of postoperative complications showed no significant differences between the two groups (Table 2).

Table 2.

	LITA+RITA T Graft (*n* = 129)	**LITA+RA T Graft (*n* = 84)**	***p* value**
Early mortality	1 (0.8%)	1 (1.2%)	ns
Myocardial infarction	4 (3.1%)	0	ns
Low output syndrome	3 (2.3%)	1 (1.2%)	ns
Postoperative blood loss	858.4 ± 500.4 ml	731 ± 380.4 ml	0.05
Re-operation for bleeding	4 (3.1%)	1 (1.2%)	ns
Respiratory failure	12 (9.3%)	12 (14.3%)	ns
Renal failure	2 (1.5%)	0	ns
Sepsis	3 (2.3%)	0	ns
Mediastinitis	1 (0.8%)	1 (1.2%)	ns

Mean follow-up time was 35.2 ± 28.3 months and involved 192 (91%) of the patients. 19 patients (group I:12 and group II:7) were lost for follow-up. Late mortality lay at 6.9% ($n = 8$) for group I and 5.3% ($n = 4$) for group II. This difference did not amount towards statistical significance, though. 102 patients (94.4%) of group I and 69 patients (95.8%) of group II were asymptomatic. Because recurrence of angina or questionable chest pain coronary angiography was performed with 22 patients. 40 (90.9%) of the 44 examined coronary anastomoses of group I were patent, compared to 27 (93.1%) of the 29 anastomoses examined in group II. So the patency rate of bypass materials used was 96.4% for LITA, 89.3% for RITA and 88.2% for RA. A reintervention was necessary in 3 patients. One patient of group I with initially left main coronary artery stenosis had to be operated because closure of all peripheral T graft anastomoses and instable angina. In 2 other patients with stenosis of RA free graft, PTCA of native coronary arteries could be performed with relief of angina. Four patients within group II showed in angiographies progression of atherosclerosis in other (not operated) coronary arteries. In 3 cases, a successful angioplasty was performed.

Discussion

There still are many open questions concerning the concept of total arterial myocardial revascularization, such as the sequence when choosing the conduit and the technique used for the implantation of the conduit. The supply of LAD with the aid of LITA in situ remains standard procedure. It is being debated, however, which conduit should be chosen in the second instance. Most teams discuss whether RITA or RA offers a better solution. With the use of bilateral ITA there are the disadvantages of having long operation times, complex anastomoses and the conduit length being reduced. The use of RITA in situ drastically limits the possibility of conducting several coronary anastomosis. The removal of RA on the other hand causes an additional scar and is unpopular with the patients for aesthetic reasons. The central implantation of RITA or RA as a free graft in the area of the front wall of ascending aorta leads to a mismatch concerning the thickness of the wall and the diameter of the anastomozed vessels. The transplant is exposed to disadvantageous pressure and flow parameters in the area of implantation. These conditions lead to a hyperplasia of the intima [Calafiore 1994]. The introduction of the T graft provided an elegant solution for this problem by avoiding an aortic bypass anastomosis.

Our study examines short and midterm results after the use of either RITA or RA as a free graft within a total arterial myocardial revascularization using a T graft. Among our patients we used RITA as a free graft with a significantly lower percentage of women. Women are mostly smaller than men and they have a shorter sternum and therefore it is to be expected that RITA is not long enough for the sequential supply of several posterior-wall vessels. Other teams are also prone to use RA more often than RITA with women [Lemma 2001, Wendler 2001]. Based on our experience it is a fact that the implantation of RITA as a sequential graft is more demanding than that of RA, especially with women, because of its morphological characteristics such as short diameter, lesser length and reduced thickness of wall.

Some authors consider diabetes and obesity - especially when occurring simultaneously - as risk factors for mediastinitis [El Nakadi 2000, Kouchoukos 1990, Tatoulis 1999], when referring to the use of both ITA. We distanced ourselves from this hypothesis and were nevertheless able to keep the rate of mediastinitis in our patients low (0.8%). There was no difference between the rates of mediastinitis of the two groups examined. From this perspective RA does not appear to be more advantageous than RITA with diabetics and obese patients.

With the patients of group I there were significantly less coronary anastomoses than with those of group II while the aortic cross clamping time was the same for both groups.

This result can - in our opinion - be viewed as a hint towards the fact that the use of RITA as a free graft is more demanding than the implantation of RA.

When both ITA are used the postoperative chest tube output ranges between 775 ± 580 ml [Uva 1998] and 1042 ± 708 ml [Lemma 2001] per patient. With our patients chest tube output averaged at 858.4 ± 500.4 ml within group I and so was significantly higher than in group II. Nevertheless, there was no higher need for blood substitution with the patients of group I. Besides, the rate of reoperations for bleeding was not significantly higher with group I than with group II. It is a fact that the use of both ITA causes a bigger intra-thoracial bleeding area and that therefore more blood loss is to be expected. It is advisable to still the blood carefully using electric coagulation on the smaller side branches of ITA and to use titanium clips on the bigger ones.

Although the patients of group I showed a comparatively worse status at the beginning (lower left ventricular ejection fraction and more frequent incompleteness of revascularization because of a poor coronary status), early mortality and morbidity showed no statistically significant difference between the two groups. Therefore such high-risk patients are apt to being treated with a myocardial revascularization using a T graft consisting of LITA and RITA.

Late mortality proved to be higher in group I: 6.9% (n = 8) than in group II 5.3 (n = 4). This difference was not statistically significant, however. It can be surmised that certain characteristics of the patients in group I (e.g. the poor coronary status and the reduced left ventricular ejection fraction) led to a faster progress of the coronary heart disease and to cardial complications and therefore raised the mortality. Other teams report about late mortality rates of 7.5% after 3 years [Pevni 2001] and 13.2% after 4.2 years [Tector 2001] after a myocardial revascularization with the help of the LITA + RITA T graft and about 1.2% after 9.5 ± 6.1 months [Weinschelbaum1997] and 12.2% after 35 ± 25 months [Iaco] when making use of the LITA+RA T graft.

The longer term clinical results of the two groups examined proved to be equally good. 102 patients (94.4%) of group I and 69 (95.8%) of group II showed no angina. This result can be considered very good with an averaged follow-up of 35.2 ± 28.3 months. According to literature, 93.4% of the patients operated on using a LITA+RITA T graft showed no signs of angina after 35 months [El Nakadi 2000], 94.1% after 4.2 years [Tector 2001] and 97.6% after 14-36 months [Pevni 2001]. The freedom of angina after the use of the LITA + RA T graft is 95.1% after 9.5 ± 6.1 months [Weinschelbaum 1997] and 97.2% after 41 ± 30 months [Iaco 2001].

When doing coronary angiographies we observed 6 cases of occluded anastomoses during the follow-up period: one of LITA, three of RITA and two of RA. Three of these occlusions (one LITA and two RITA) occurred with the same patient. This patient had been revascularized in the left coronary system using the LITA+RITA T graft because of a solitary stenosis of the left main coronary artery. Postoperative coronary angiography showed a string phenomenon of the entire T graft. Since this incident there have been no more arterial T graft revascularizations with patients suffering from solitary stenoses of left main coronary artery. The reasons for the two closures of RA anastomoses could not be found. Our rate of open anastomoses for the RA shafts of the T graft even in symptomatic patients is higher (88.2% after 35.2 ± 28.3 months) than the one by Sundt [Sundt 1999]: 82% after 9.5 ± 8.3 months. Iaco [Iaco 2001] reports better results after 48 ±

27 months, measuring a patency rate for the RA conduit of the T graft amounting to 93.8%.

On the basis of our study neither one of the two free grafts examined (RITA or RA) can generally be recommended as the "conduit of second choice". In our opinion the choice should be made for each case individually. We prefer using RITA with tall men when there is no necessity for a large number of anastomoses for complete revascularization; also with patients with a reduced left ventricular ejection fraction, with coronary arteries of a small diameter and in cases where a scar on the forearm is not acceptable. Diabetes and obesity - in our view - are no contraindications to the bilateral use of ITA. RA should rather be chosen with small women when there is a high risk of postoperative bleeding and if there is the necessity of having more than three coronary anastomoses for the myocardial revascularization.

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Right Coronary Artery Revascularization – Controversy and Facts*)

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Abstract

Objective: *The current study is oriented towards the statistical processing and interpretation of the coronary artery by-pass grafting procedures in which the radial artery was used as a graft on the right coronary artery.*

Materials and method: *We studied retrospectively all the patients undergoing a CABG procedure at IBCV "Prof. Dr. George I. M. Georgescu" Iasi during 2000-august 2010. Out of a total of 963 patients, we selected a group of 181 patients in which the radial artery was used as a graft for the right coronary artery.*

Results: *In 163 (90.05%) patients there was only one graft on the right coronary artery, and in 18 (9.94%) patients there were two grafts on the right coronary artery (in 16 patients the radial artery was mounted sequentially and in 2 patients the radial artery was used alongside the right internal mammary artery). In our study group 12.70% of patients underwent complex surgical procedures (CABG concurrent with other intra- and extracardiac procedures). The overall mortality was 1.65%.*

Conclusions: *This study reveals an ascending trend in the incidence of the CABG procedures that incorporate the radial artery as a graft for the right coronary artery in the period 2000-august 2010 in our clinic. The overall mortality was 1.65%, results that are superior to those quoted in the reference literature. Our experience proves that the radial artery is indeed a graft that can be mounted successfully on the right coronary artery and therefore disputes the studies that disregard this arterial graft's patency.*

Objective

The current study is oriented towards the statistical processing and interpretation of the coronary artery by-pass grafting procedures, performed at the Cardiovascular Institute Iasi, in which the radial artery was used as a graft on the right coronary artery.

Improved long-term outcome with internal mammary artery grafts combined with progressive disease of saphenous vein grafts has prompted increasing efforts at coronary revascularization using arterial conduits. Recently there has been a revival of interest in

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the use of the radial artery (RA) for coronary artery bypass grafting (1) with encouraging short-term results (2).

Carpentier and colleagues first proposed the use of the radial artery for CABG in 1973 (7), but within a few years reports of spasm and occlusion led to its abandonment. In 1989, and inspired by several angiographically patent radial artery grafts up to 18 years after the original operation, Acar and colleagues again proposed the use of this artery for CABG (8). Improved surgical harvesting techniques and the administration of antispasmodic drugs have resulted in several groups reporting angiographic patency rates in excess of 90% at one year (9-13) and up to 90% at five years (2, 3).

The radial artery is a muscular artery with a prominent adventitia (14). The more muscular media of the radial artery explains in vitro and clinical observations of an increased tendency to spasm compared with the IMA (15). We reported that an increased tendency to spasm in the proximal radial artery, because of more smooth muscle, is minimised by its greater functional diameter (15). Because the vasa-vasorum of the radial artery does not penetrate into the media (14), oxygen and nutrients are provided by luminal diffusion, which suggests that transposition of the radial artery as a free graft should not have adverse ischaemic implications for the vessel wall over the long term.

Radial artery provides additional arterial conduit with very low harvest related morbidity. This conduit provides superior patency to saphenous vein graft (SVG) in the setting of high-grade stenosis regardless of the target territory and with minimal harvest site complications. The radial artery is a versatile conduit that provides clinical benefit in a large variety of patients undergoing CABG.

This study aims to report the results of coronary artery bypass surgery during a period of change from traditional aorta-coronary surgery with few arterial conduits to total arterial revascularization in the majority. The effect of this change on in-hospital mortality has been examined.

Patients and methods

We studied retrospectively all the patients undergoing a CABG procedure at IBCV "Prof. Dr. George I. M. Georgescu" Iasi during 2000 - August 2010. Out of a total of 963 patients, we selected a group of 181 patients in which the radial artery was used as a graft for the right coronary artery (Figure 1, next page).

The radial artery (RA) is easily harvested, versatile, has excellent handling characteristics, and has become the arterial conduit of third choice (2). Issues remain concerning its optimal use, however, particularly with reference to preoperative assessment, harvesting techniques, vasospasm prophylaxis, grafting strategy, and long-term patency.

Preoperative assessment of the RA and collateral hand circulation is mandatory to avoid hand ischemia in patients with an inadequate collateral circulation. The most widely used clinical test for assessment of adequate collateral circulation to the hand is the modified Allen test. In our own practice, patients have the RA safely harvested after clinical assessment only (3). In patients with equivocal or positive Allen tests, further imaging is performed with duplex ultrasonography. Use of bilateral forearm duplex scanning when clinical assessment is equivocal has enabled the use of RA conduits in 99% of patients scheduled for total arterial coronary artery bypass grafting (CABG) (3).

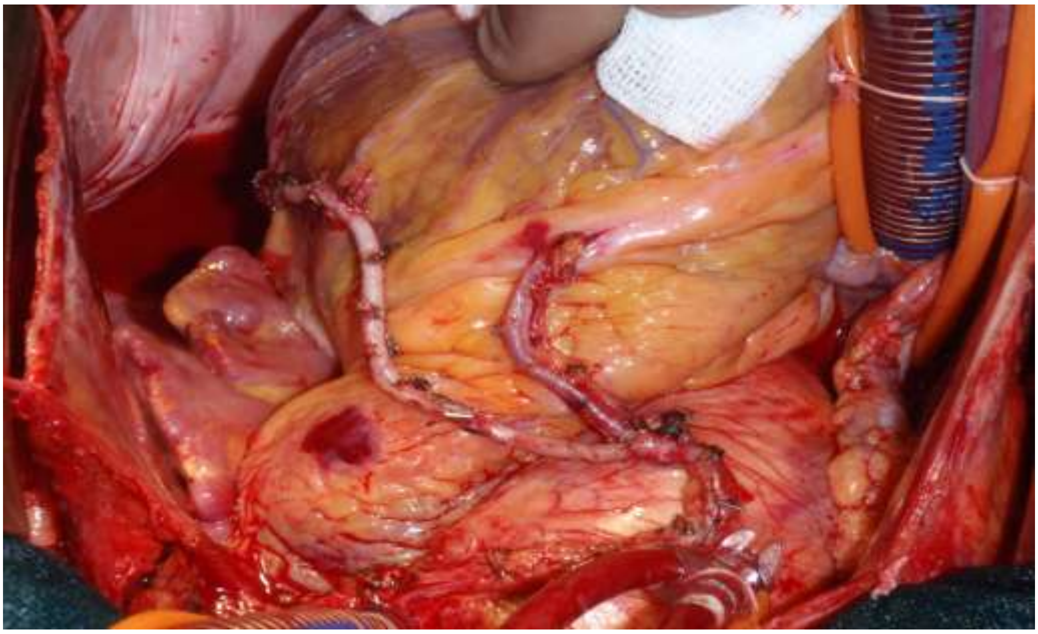


Figure 1: Intra-operative image of total arterial revascularization with radial artery on RCA coronary grafting

We also use other assessment techniques, such as digital pulse oximetry, and Doppler ultrasonographic methods.

Improved harvesting techniques are fundamental to the current success of radial grafts in CABG. Further refinements may result in improvements to graft function, reduced complications, and greater patient satisfaction.

Vasospasm has been reported in 4% to 10% of all RA grafts. This may have potentially significant adverse consequences in terms of perioperative myocardial infarction and low cardiac output syndrome and its sequelae, including extended intensive care stays and increased mortality. Pharmacologic prevention of RA spasm has been fundamental to its revival as a conduit for CABG. Clinically useful agents should ideally be effective against a wide variety of endogenous vasoconstrictor substances liberated because of surgical stress or the inflammatory response to cardiopulmonary bypass, as well as exogenously administered inotropes or vasoconstrictors. Finally, the agent should neither cause local injury to the conduit nor have harmful systemic effects. Currently no agents, alone or in combination, can be defined as an ideal antispasmodic, warranting continued development of vasodilator strategies for RA grafts.

Papaverine, a short-acting phosphor-diesterase inhibitor, is a widely used topical vasodilator for arterial conduits. However, in vitro studies demonstrate that the efficacy of papaverine diminishes after 30 minutes (4). Thus papaverine may ameliorate spasm during RA harvest but not throughout the intraoperative and immediate postoperative period. Additionally, the preparation is acidic and may damage the endothelium.

The ultimate patency of radial-artery grafts depends on the severity of the bypassed native-vessel stenosis, due to the competitive flow phenomenon - the greater the native-vessel flow, the more likely the graft will occlude.

Radial artery grafts bypassing less-severe target lesions have an increased risk of developing the "string sign" or diffuse luminal narrowing at angiography. This graft complication, which is less likely with high-grade target lesions, is likely caused by spasm of the smooth muscle in the arterial media; the SVG contains little of this smooth muscle.

Compared with the saphenous vein grafts (SVG), radial-artery grafts were significantly less likely to occlude and as likely to be fully patent at one-year angiography.

Of considerable interest is the comparative performance of RA versus long saphenous vein conduits. Occlusive disease of vein grafts remains a major limitation of CABG, with as many as 75% of vein grafts severely stenosed or occluded at 10 years, although refinements in harvesting techniques and the use of aspirin and statins may contribute to improved vein graft performance in contemporary CABG.

To address some of these issues, three prospective, randomized, controlled trials comparing RA with other conduits with the intention of complete angiographic follow-up are in progress. The results of the *Radial Artery Patency Study* (RAPS) and the Radial artery Versus *Saphenous Vein Patency study* (RSVP), are awaited. Recently, the interim (5 year) results of the *Radial Artery Patency and Clinical Outcome* (RAPCO) study, a prospective, randomized trial comparing RA with saphenous vein grafts and free right ITA grafts (8), have been reported. Five-year patency rates between RA and right ITA are 95% versus 100%, respectively, and those between RA and saphenous vein are 87% versus 94%, at least according to the small number of patients who have undergone early repeated angiography. No statistically significant differences in graft patency have been demonstrated between RA and other conduits.

Optimal placement of radial artery grafts to achieve satisfactory long-term patency remains controversial. The concept of competitive flow suggests that graft flow is influenced by native coronary flow. Grafted conduits may therefore fare better in conditions of poor native coronary flow, typified by high-grade coronary stenoses. There is accumulating evidence that grafting the RA to coronary targets with moderate stenoses (<70%) results in reduced anastomotic patency (6).

Nevertheless, recognizing the fact that failure of the RA graft is more prone to occur when there is less than 75% stenosis in the native coronary artery, we have reserved this technique for those with stenosis exceeding 75%. Certainly in clinical terms, no patient has presented with recurrent angina.

Data were obtained through the revision of the clinical charts and hospital database.

All patients had at least 75% stenosis in the proximal PDA or RCA. CABG was performed via a median sternotomy in all cases. Both ITA were harvested as pedicled (LIMA) and skeletonized (RIMA) conduits and bathed in a swab containing papaverine. The RA was harvested and stored in heparinized blood containing papaverine prior to performing the anastomosis. Using standard CABG techniques, the heart was positioned and grafting was performed. There was predominantly one graft configuration based on the ITA: the left ITA was anastomosed to the LAD, with the right ITA anastomosed to the obtuse marginal coronary artery as a composite Y graft from the left ITA, but in 2 patients, the right ITA was used as a composite graft with the radial artery to the right coronary artery. In some situations, the right ITA was used as a sequential graft to the diagonal and to the obtuse marginal system, with the left ITA placed on the LAD. The heart was then repositioned, the distal end of the RA was anastomosed to the PDA, cardioplegia was given trough the graft, and then anastomosed proximally to a disease-free area of the aorta.

Composite grafts have the major advantage of facilitating a less touch of the aorta, thereby reducing the risk of embolic debris from the ascending aorta. Potential disadvantages of composite grafts compared with conventional aorta-coronary RA grafts are the relative technical difficulty and the reliance on single inflow (proximal left ITA) to supply all grafted territories.

Results

In 163 (90.05%) patients there was only one graft on the right coronary artery, and in 18 (9.94%) patients there were two grafts on the right coronary artery (in 16 patients the radial artery was mounted sequentially and in 2 patients the radial artery was used alongside the right internal mammary artery). In our study group 12.70% of patients underwent complex surgical procedures (CABG concurrent with other intra- and extracardiac procedures). The overall mortality was 1.65%. All radial artery grafts were patent and there were no operative complications in any patient, and they were discharged uneventfully. **84.53%** were male, with a median age of 57.83 years, and **15.46%** were female, with a median age of 60.39 years.

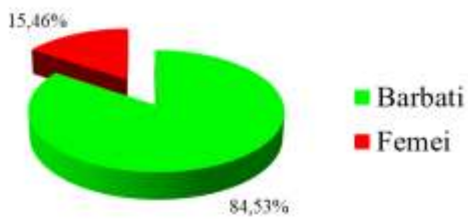


Figure 2: Gender distribution of patients submitted to radial artery-right coronary artery grafting

The distribution of the number of grafts was as follows: 32.04% had 3 grafts, 29.85% had 4 grafts, 23.20% had 2 grafts, 12.15% had 5 grafts, 1.65% had only one graft, and 1.30% had 6 grafts (Figure 4).

Among several other factors in coronary surgery, the results depend on the quality and durability of the grafts. Revascularization employing arterial conduits, namely radial artery, has been playing a growing role, with the aim of replacing the autologuos saphenous vein. The benefits and risks of this strategy is still a matter of controversy.

From 163 (90.05%) patients, there was only one graft on the right coronary artery, and from 18 (9.94%) patients, there were two grafts on the right coronary artery (in 16 patients the radial artery was mounted sequentially and in 2 patients the radial artery was used alongside the right internal mammary artery). In our study group, 12.70% of patients underwent complex surgical procedures (CABG concurrent with other intra- and extracardiac procedures). The overall mortality was 1.65%.

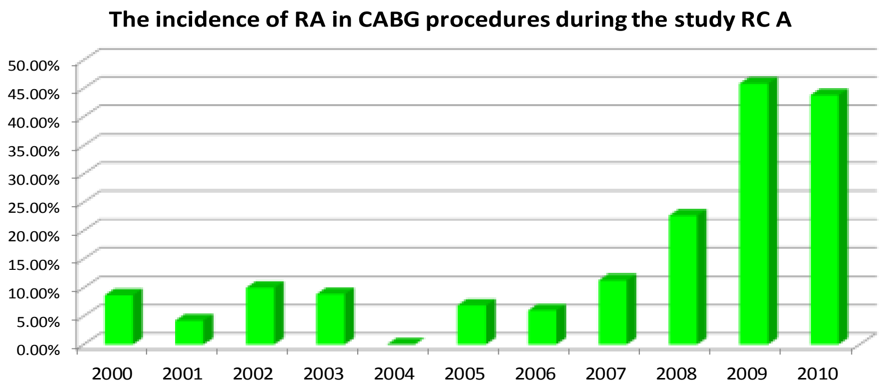


Figure 3: The incidence of RA in CABG procedures in IBCV Iasi

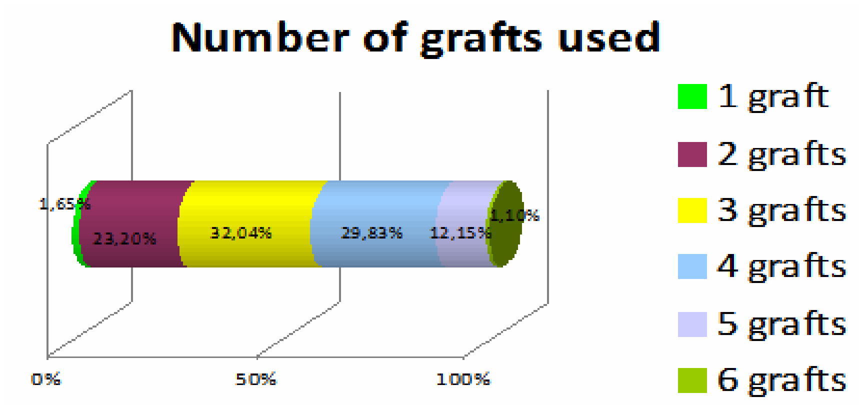


Figure 4: Distribution using the number of grafts used

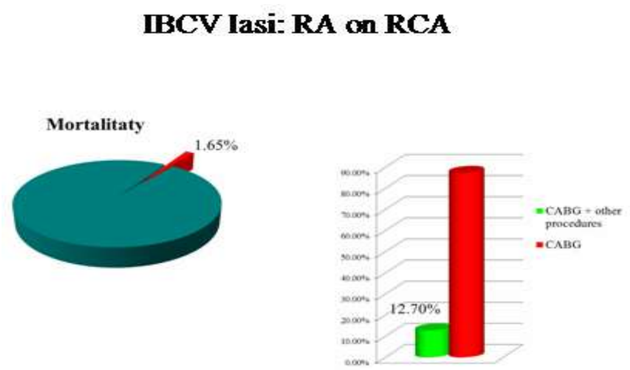


Figure 5: Distribution of procedures and the overall mortality

The average time spent in the ICU was 6 days.

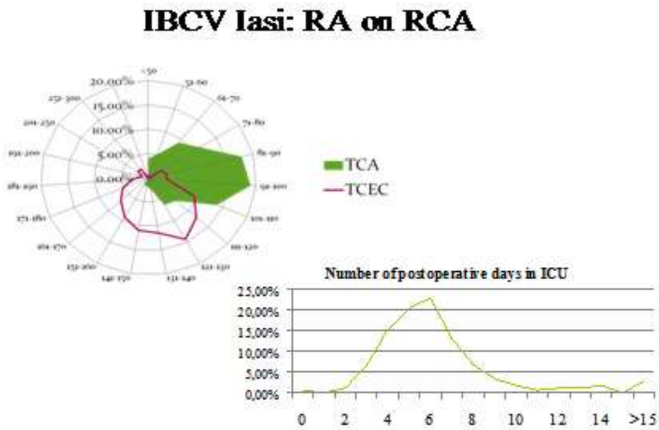
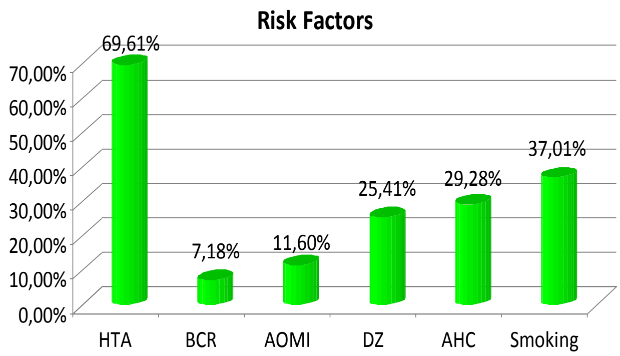
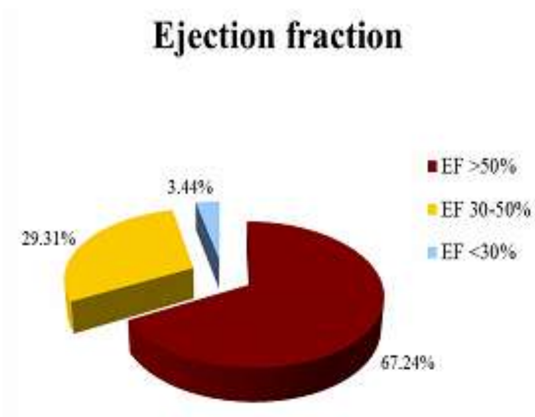


Figure 6: Intra-operative data and the number of postoperative days in ICU



Among risk factors, the most important were arterial hypertension, smoking, and diabetes mellitus.

Figure 7: Trends in the distribution of the most important risk factors



From 181 patients, 67.24% had a LVEF >50%, 29.31% had a LVEF of 30-50%, and 3.44% had a LVEF less than 30%.

Figure 8: Ejection fraction distribution

Independent preoperative predictors of increased in-hospital mortality included renal failure, redo-coronary artery surgery and IABP use.

Discussion

The attractions of the radial artery to the surgeon are immediate and obvious: it is a versatile conduit that can be harvested easily and safely, it has handling characteristics superior to those of other arterial grafts, and it reaches comfortably any coronary target (1). For the patient it offers the long term prospect of superior patency compared to vein grafts (2, 3) and the immediate benefit of avoiding the frequently underestimated morbidity of leg wounds (4).

Several groups have reported radial artery patency rates to non-left anterior descending coronary vessels in excess of 90% at one year (8-13) compared with vein graft patency rates of around 80% at one year (12). This may reflect the superior haemodynamics of radial artery grafts, which have no valves and are more uniform in calibre than vein grafts. Furthermore, whereas the diameter of the radial artery exceeds the coronary artery by only 20%, that of vein grafts is often in excess of 50% (15), promoting relative stasis in the vein graft.

Two groups have reported five year radial artery patency rates of between 83% (16) and 92% (17). Posatti and colleagues obtained consent for repeat angiography at five years in 62 of their first 68 consecutive patients. The patency rate for the radial artery was 92% compared with 100% for the IMA and 74% for vein grafts (17). In 50 of Acar et al's first 102 consecutive patients who consented to repeat angiography at five years the patency of the radial artery was 83% versus 91% for the IMA (16). While the superior patency of the IMA is due at least in part to its invariable placement to the left anterior descending coronary artery, the superior patency of the radial artery over vein grafts, when both are placed to secondary targets, is probably because of development of atherosclerosis in the latter. Both groups made two important additional observations:

- most of the radial artery grafts that failed had been placed to native coronary arteries without "significant" stenosis (<70%)
- radial artery grafts that had either "occluded" or shown evidence of spasm at early angiography frequently appeared patent and disease free at five years, implying that vasoreactivity of this artery is maximal in the early postoperative period.

The most important potential advantage for the patient is improved long term graft patency compared to venous conduits. The use of one or both radial arteries is an attractive option in patients suitable for total arterial revascularisation but in whom there are possible contraindications to the use of both mammary arteries (such as diabetic or obese patients). Another advantage is that forearm wounds heal very well in comparison to leg wounds, promoting earlier post-operative mobilization (18). The avoidance of leg wounds is of even greater importance in obese patients.

Conclusions

This study reveals an ascending trend in performing CABG procedures that incorporate the radial artery as a graft for the right coronary artery between 2000-august 2010, in our clinic. The overall mortality was 1.65%, results that are superior to those quoted in the reference literature. Our experience proves that the radial artery is indeed a graft that can be mounted successfully on the right coronary artery and therefore disputes the studies that disregard this arterial graft's patency.

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Off-pump coronary artery by-pass grafting in elderly patients*)

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Abstract

Aim: *The assessment for specific features in postoperative evolution of the elderly patients with off-pump myocardial revascularization.*

Materials and methods: *21 elderly patients with off-pump myocardial revascularization are studied comparative with other 21 patients over 75 years with conventional myocardial revascularization (mortality and cardiac/extracardiac morbidity are studied).*

Results: *The perioperative mortality was significantly higher for the patients with conventional revascularization, and the incidence for perioperative myocardial infarction (9.52%), atrial fibrilation (33.33%) and neurological complication with coma were lower in "off pump" revascularization. The duration of hospitalization and intensive care stay were lower for the "off pump" group.*

Conclusion: *1. "Off pump" myocardial revascularization is a safe and good method for the elderly patients with lower mortality and lower rate of cardiac and extracardiac (especially neurological and renal complication). 2. For this category of patients the hybrid procedure and incomplete but efficient revascularization are good solutions.*

Keywords: *off-pump, elderly patients, postoperative evolution, neurologic disfunction*

Background

Today, cardiac surgeons are confronted with an increasingly higher number of elderly patients with important associated morbidity, high risk, but with surgically correctable coronary artery disease. In attempt to reduce complications and improve surgical outcomes of coronary revascularizations – performing myocardial revascularization without cardio-pulmonary by-pass avoids the systemic deleterious effects of extra-corporeal circulation. Because severe calcifications of ascending aorta are usually present at this age – "no touch" technique gives many advantages for this category of patients.

Aim

The purpose of this study is to analyze the impact of "off pump" myocardial revascularization for elderly patients comparative with conventional revascularization during the 30 postoperative days.

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Materials and Methods

We studied 21 patients over 75 years old, operated in our hospital between 2000-2004 with "*off pump*" *procedure* - and another 21 patients over 75 years old with conventional revascularization during the same years. The clinico-demographic characteristics of these patients are described in table 1.1.

Table 1.1: Clinico-demographic characteristics

Features	Off-pump	CABG	*p*
Cases	21	21	-
Age	75 – 82 (79)	75 – 81 (76)	-
Sex	2 F – 19B	1 F – 20 B	-
Instable angina	19 (90.484%)	21 (100%)	> 0.05
Recent myocardial infarction	2 (9.52%)	–	0.368717
Left main stenosis	14 (66.67%)	6 (28.57%)	0.432657
Delayed urgencies	21 (100%)	21 (100%)	
Previous PTCA	7 (33.33%)	–	0.012983 S
Previous CABG	3 (14.29%)	2 (9.52%)	> 0.05
Diabetes mellitus	7 (33.33%)	11 (52.38%)	0.552098
Arterial hypertension	21 (100%)	21 (100%)	-
Hyperlipoproteinemia	21 (100%)	21 (100%)	-
Obesity	8 (38.1%)	4 (19.05%)	0.171857
Chronic kidney failure	4 (19.05%)	2 (9.52%)	0.659243
Previous stroke	8 (38.1%)	2 (9.52%)	0.029727 S
Chronic Obstructive Pulmonary Disease	4 (19.05%)	1 (4.76%)	0.340617

The patients were predominantly males with very severe angina – with strong motivation for revascularization. Two patients of lot A have recently myocardial infero-lateral infarction with active ischemia and needed urgently revascularization. 10 patients of both groups have left main stenosis with tritroncular coronary artery disease. 7 patients of group A have prior endoluminal myocardial revascularization with restenosis. The preoperative morphological characteristics of both groups of patients are presented in table 1.2 (next page)

All the patients cumulate many associated renal, respiratory, neurological diseases and peripheral obstructive disease. The intraoperative characteristics of two groups are described in table 1.3 (next page).

We performed a complete revascularization for 19 patients in group B and 13 patients in group A. For two patients of group A with "left main stenosis" and severe calcifications of ascending aorta we are realized a "no touch" revascularization. 4 patients of group A had a hybrid poor general condition with MIDCAB-LAD revascularization and endoluminal revascularization of a big marginal artery. In group B for two patients with severe calcifications of ascending aorta the proximal implants were on the brachio-cephalic trunk and for patients we are converted the on pump technique in off pump technique (no touch). Usually we harvested the left internal mammary artery, except two patients with severe proximal subclavian artery stenosis.

Table 1.2: Preoperative morphological characteristics

Angiographic aspect of the coronary artery	Off-pump	CABG	*p*
Good quality vessels	13 (61.90%)	6 (28.57%)	0.029998 S
Satisfactory vessels	4 (19.05%)	5 (23.81%)	> 0.05
Small vessels with calcification	4 (19.05%)	10 (47.62%)	0.049535
Occlusive Peripheral Arterial Disease			
• aorto-iliac	2 (9.52%)	1 (4.76%)	> 0.05
• femuro-popliteal	5 (23.81%)	4 (19.05%)	> 0.05
Good quality LAD	13 (61.90%)	6 (28.57%)	0.029998 S
Monovascular disease	7 (33.33%)	2 (9.52%)	0.132529
Bivascular disease	2 (9.52%)	7 (33.33%)	0.132529
Trivascular disease	16 (76.19%)	12 (57.14%)	0.599126
Complete revascularization	15 (71.43%)	19 (90.48%)	0.238455
Efficient revascularization	2 (9.52%)	2 (9.52%)	0.599126
Hybrid revascularization	4 (19.05%)	-	0.114802
Calcified aorta	6 (28.57%)	2 (9.52%)	0.238455
EF < 30%	2 (9.52%)	8 (38.1%)	0.039727 S
LVDD > 6.5	2 (9.52%)	4 (19.05%)	0.93243
IABP	-	-	-

Table 1.3: The intraoperative characteristics of two groups

Features	Off-pump	CABG	*p*
Medial sternotomy	21 (100%)	21 (100%)	-
Operation duration	2.5 - 5.5 (2.9 h)	4.5 - 7.5 (4.5 h)	-
Miocardial ischemia	-	45 - 70 (62 min)	-
CPB duration	-	80 - 160 (115 min)	-
Normotermia	-	4 (19.05%)	-
LIMA	21 (100%)	19 (90.48%)	0.4687
BIMA	4 (19.05%)	0	0.1148
Lateral clamping	15 (71.43%)	19 (90.48%)	0.2384
"No touch"	6 (28.57%)	2 (9.525)	0.2384
Another sites of implant	2 (9.52%)	2 (9.52%)	0.5991
Conversion	2 (9.525)	4 (19.05%)	0.6592

Only for the group A and for "no touch" technique we've used both internal mamary artery but without sequential or y "montage" without radial or gastro-epiploic artery. The saphenous grafts puts many problems at this age – because they are sometimes fibrotic or with varicosities or with excessive fragility.

Ascending aorta manipulation is very important at this age – "no touch" technique, "single cross clamp technique", other sites for proximal implants and single lateral clamping during "off pump" revascularizations are some rules for preventing ascending aorta lesions, dissections or neurological complications.

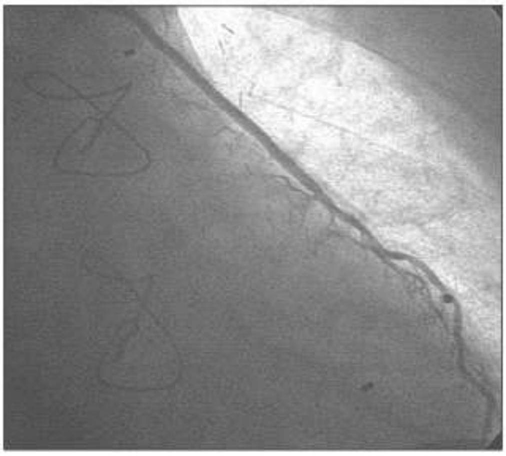

Figure 1: Revascularization of LAD with right internal mammary artery

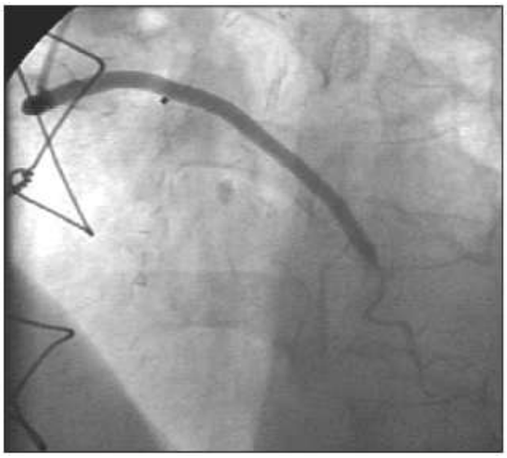

Figure 2: Saphenous vein graft implanted on diagonal coronary artery (notice the great diameter of the vein compared with coronary artery)

Results

In the table 1.4 (next page) are the results obtained from the measuring of each parameter studied in relation with the postoperative moment. After the statistical analysis of the variation of the parameters from the table it can be seen that:

1. There was no early death in off pump group and 2 deaths in conventional group.
2. Higher incidence of hemodynamic complication: low cardiac output, perioperative infarction and atrial fibrillation for conventional revascularization.
3. Mechanical ventilation hours, ICU stay, hospitalization were lower in "off pump" revascularization group.
4. Increase level of creatinine serum to the patients with chronic renal failure in conventional group
5. Neurological complication and neuro-cognitive dysfunction were significaly lower in "off-pump" revascularization group.

Conclusions

1. "Off pump" myocardial revascularization is a safe and good method for the elderly patients with lower mortality.

2. "Off pump" myocardial revascularization has a lower cardiac morbidity (myocardial infarct, low cardiac output and atrial fibrillation) than conventional revascularization.

3. There are significant differences in extracardiac morbidity (neurological and renal dysfunction) who sustained off pump procedure.

4. "No touch" technique and "*single cross clamp*" technique are some rules for preventing ascending aorta lesions, dissections or neurological complications.

5. For this category of patients the hybrid procedure and incomplete but efficient revascularization are good solutions.

Table 1.4: The first 30-day postoperative period

Features	Off-pump	CABG	*p*
Low cardiac output	2 (9.52%)	5 (23.81%)	0.4076
IABP	0	0	-
Acute myocardial infarction	1 (4.76%)	2 (9.52%)	> 0.05
Atrial fibrillation	2 (9.52%)	7 (33.33%)	0.1325
Mechanical ventilation (h)	6 - 10 (7)	12 - 21 (14)	-
ICU stay	24 - 72 (52)	24 - 144 (72)	-
Spitalization - days	5 - 11 (8)	8 - 16 (10)	-
Bleeding > 500 ml	4 (19.05%)	5 (23.81%)	> 0.05
Redo for hemostasis	1 (4.76%)	2 (9.52%)	> 0.05
Mediastinitis	1 (4.76%)	1 (4.76%)	-
Plague complication:			
- seroma	1 (4.76%)	0	-
- mobile sternum	2 (9.52%)	1 (4.76%)	> 0.05
Acute renal failure	0	0	–
Chronic renal failure	2 (9.52%)	4 (19.05%)	0.6592
Neurological complication:			
- transient ischemic attacks	1 (4.76%)	1 (4.76%)	-
- stroke	1 (4.76%)	2 (9.52%)	-
- stoke + coma	0	2 (9.52%)	0.4687
Neuro-cognitive dysfunction	2 (9.52%)	8 (38.1%)	0.02972
Death	0	2 (9.52%)	0.46871

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Prognostic significance of restrictive left ventricular diastolic filling pattern in patients with left ventricular systolic dysfunction undergoing coronary artery bypass grafting*)

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Abstract

Purpose: *The assessment of the influence of restrictive left ventricular diastolic filling pattern on postoperative course in patients with left ventricular systolic dysfunction undergoing CABG. The assessment of the postoperative evolution of the LV diastolic filling pattern in patients with LV systolic dysfunction who underwent CABG and their prognosis at I year postoperatively.*

Materials and methods: *A prospective study on 156 patients with LV systolic dysfunction (LVEF < 40%) who underwent CABG. Ultrasonographic assessment was performed at 10 days, 1, 3, 6 and 12 months postoperatively. Patients were grouped according to the presence or absence of the LV restrictive filling pattern (groups A and B, respectively). The statistical analysis used SYS7AT and SPSS programs for simple linear and multivariate regression analysis, calculation of the correlation coefficient and calculation of the relative risk. Results; Postoperative cardiovascular morbidity and early mortality were higher in group A (61 vs. 23.75%, 34.2 vs.11.25%). The NYHA functional class improvement was more important in group B but there was no significant difference concerning the LV wall motion score. The mean LVEF increase at 1 year from the operation was more important in group B compared to group A. The LV end-diastolic volume was a prognostic factor for the postoperative evolution of the LVEF. The LV restrictive fitting pattern was also associated with a negative influence on postoperative LVEF increase. An early diastolic filling deceleration time <150 ms, a LVEF<20% and an LVEDV index > 100 ml/m^3 were.*

Conclusions*: 1. The LV restrictive diastolic filling pattern in patients with LV systolic dysfunction who undergo CABG is correlated* with a higher morbidity and early post-operative *mortality as well as with a lack in improvement in LV systolic function. 2. The restrictive LV filling pattern, decreased LVEF (< 20%) and LV end diastolic volume index >100 ml/m^2 were independent predictors for increased perioperative and early postoperative mortality. 3. The pattern of preoperative LV diastolic filling is predictive of the postoperative evolution of the LVEE at 1 year.*

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Background

Ischemic heart disease is a cause not only of anginal pain but also of progressive deterioration of left ventricular pump function. Ischemic heart disease affects both systolic and diastolic ventricular function. Revascularization, surgical or by percutaneous techniques, is very effective in treating anginal pain. Its effect on left ventricular dysfunction is not as predictable as it is on angina. The pattern of left ventricular filling is one of the possible predictors of postoperative evolution of left ventricular function. It is supposed that a restrictive filling pattern implies a poorer prognosis in comparison with other filling patterns.

Purpose

1. The assessment of the influence of the restrictive left ventricular diastolic filling pattern on the postoperative course in patients with coronary heart disease and left ventricular systolic dysfunction undergoing coronary artery bypass surgery.
2. The evaluation of the postoperative evolution of the left ventricular diastolic filling pattern in patients with left ventricular systolic dysfunction who undergo coronary artery bypass grafting and their prognosis at 1 year postoperatively.

Materials and methods

We performed a prospective study on 156 patients with LV systolic dysfunction defined as a left ventricular ejection fraction of less than 40% on whom coronary artery bypass grafting was performed. The patients with restrictive left ventricular filling pattern were consecutive while the others were chosen to mach the former.

Exclusion criteria were the presence of acute myocardial infarction, the presence of a left ventricular aneurysm, the presence of significant comorbidities (diabetes mellitus, renal failure) and the presence of associated valvular lesions.

All patients were assessed by means of cardiac ultrasound at 10 days, 30 days, 3 months, 6 months and 12 months postoperatively.

The 156 patients, 120 male (76.92%), with a mean age of 62.2 ± 9.3 years, were grouped in two groups according to the left ventricular diastolic filling pattern. **Group A** (76 patients) comprised the patients with a left ventricular restrictive filling pattern while **group B** (80 patients) comprised the patients with a non-restrictive left ventricular filling pattern. The two groups were matched with regard to age, gender and the presence of other risk factors.

The statistical analysis used the SYSTAT and SPSS programs for simple linear and multivariate regression analysis, calculation of the correlation coefficient and calculation of the relative risk.

Results

The postoperative cardiovascular complications and early mortality rate were significantly higher in group A (61% and 34.2%, respectively) compared with group B (23.75% and 11.25%, respectively) (figure 1).

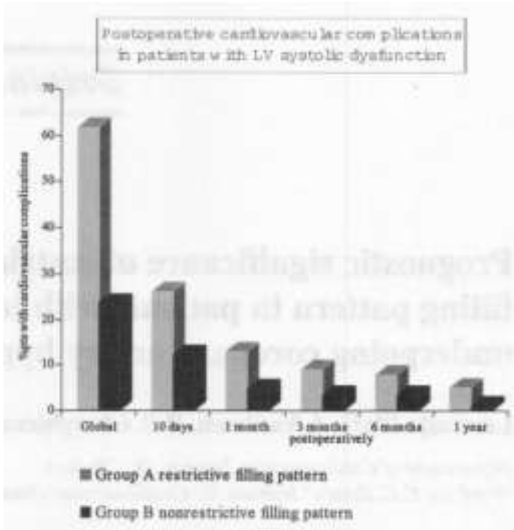
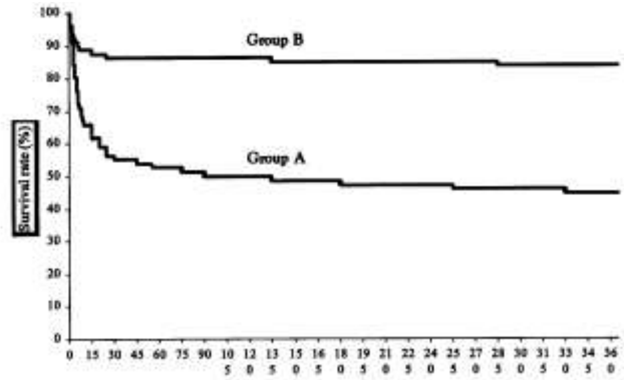
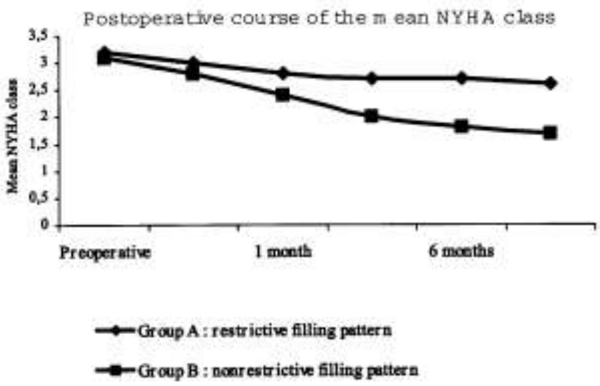


Figure 1: Rate of cardiovascular complications in group A and group B



The one-year survival was also significantly better in group B than in group A, as shown in figure 2.

Figure 2: Survival rates in group A and group B



Functional improvement as reflected by the functional NYHA class was better in group B than in group A. In group A the mean functional NYHA class decreased at 1 year from the operation from 3.2 to 2.6 as compared with a decrease from 3.1 to 1.7 in group B patients. There was no significant difference with regard to the left ventricular wall motion score between the two groups (figure 3).

Figure 3: Postoperative improvement in NYHA class in group A and B

There was a significant difference regarding the mean increase in left ventricular ejection fraction at 1 year postoperatively between the two groups. The mean increase was 12.3% for group A as compared with 21.7% for group B (figure 4).

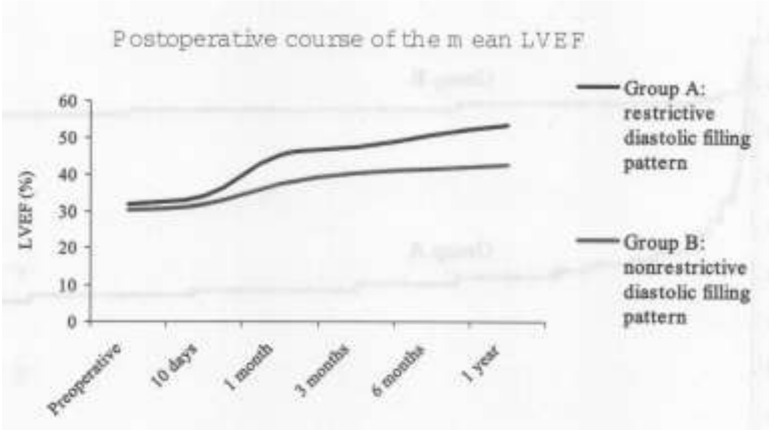


Figure 4: The evolution of IV ejection fraction at 1 year from the operation

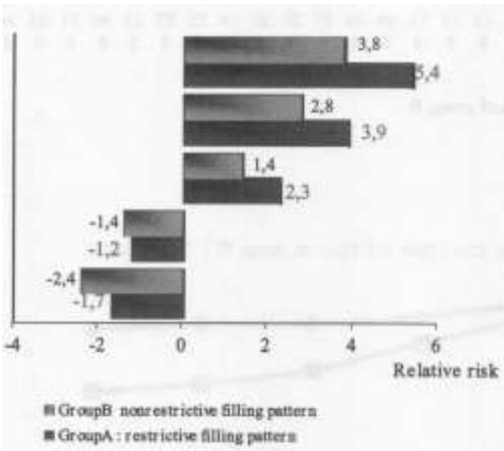


Figure 5

The preoperative left ventricular end diastolic volume index was predictive for the postoperative evolution of the left ventricular ejection fraction. The cutoff between protective and risk value for postoperative increase in left ventricular ejection fraction was a *left ventricular end diastolic volume index* [LVEDVI] of 86 ml/m^2. There was an almost linear relationship between preoperative LVEDVI and postoperative evolution of LVEF. The relation was closer for group A, especially for high LVEDVI values (figure 5).

The multivariate regression analysis found some independent predictors of incresed perioperative and early postoperative mortality. These predictors were: an early diastolic filling deceleration time less than 150 ms, a left ventricular ejection fraction less than 20% and a left ventricular end diastolic volume index greater than 100 ml/m^2 (see next table).

	Value [ml/m^2]
LVEDVI	**> 112**
	100-112
	86-100
	70-86
	< 70

At one year postoperatively the diastolic filling pattern remained restrictive in 76.53% of patients in whom it was restrictive preoperatively and became restrictive in 17.91% of patients with a non-restrictive preoperative filling pattern.

Conclusions

1. The LV restrictive diastolic filling pattern in patients with LV systolic dysfunction who undergo CABG is correlated with a higher morbidity and early postoperative mortality as well as with a lack in improvement in LV systolic function.

2. The restrictive LV filling pattern, decreased LVEF (<20%) and LV end diastolic volume index > 100 ml/m² were independent predictors for increased perioperative and early postoperative mortality.

3. The pattern of preoperative LV diastolic filling is predictive of the postoperative evolution of the LVEF at 1 year.

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Intraoperative angiography - a valuable method for quality control in off pump coronary artery surgery[*)]

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Abstract

Purpose. *The information obtained by intraoperative graft angiography in off pump coronary artery bypass grafting remains a matter of debate despite the fact that anastomotic revision rates in the range of 10% after intraoperative grafting. Intraoperative angiography is reported in the literature. We present our initial experience, with intraoperative angiographic evaluation of grafts performed on the beating heart.*

Methods. *29 coronary artery bypass grafts were investigated in 23 patients (20 male, 3 female), age 61 (44-74). Transfemoral angiography was performed before (n = 8) or after sternotomy closure (n = 15) using a DEC 9800 mobile C-arm. Examination times were 25 (8-80) min and fluoroscopy times were 469 (6-1337) sec. 150 (50-470) ml of contrast agent were needed to visualize the grafts.*

Results. *No technical complications specific for angiography occurred. Except for 3 aorto-coronary vein grafts all bypass vessels could he visualized. Spasm of the graft and/or target vessel was present in 11/29 grafts, which responded well to intraluminal nitroglycerine in 9 of these. 2 grafts were severely stenosed requiring surgical revision. In addition 2 proximal target vessel occlusions were noted, which were left because of lacking intraoperative ischemic.*

Signs. *There was no hospital mortality and no perioperative myocardial ischemic event.*

Conclusion. *This experience suggests that despite being a time consuming examination technique intraoperative angiography can reveal valuable information that may demand surgical consequences.*

Keywords: *beating heart; intraoperative control angiography*

Introduction

The first *coronary artery by-pass* (CABG) using *left internal mammary artery* (LIMA), performed in early 1967 by V. I. Kolesov, was a *minimal invasive coronary artery bypass* (MIDCAB) without *extracorporeal circulation* (CPB), on the beating heart, even without

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cineangiography. In the last years myocardial revascularization *off-pump* (OPCAB), was resurfaced and rafinated by a large number of surgeons. However, the major concern and criticism of beating heart bypass is accuracy of distal anastomosis and complete revascularization concept.

The long-term outcome of CABG is influenced by a lot of factors; coronary anatomy, run-off, the conduit choosed (arterial or venous), the evolution of coronary disease (influenced by drugs and patient's style of life) and not in the last time by the surgical technique the distal and proximal anastomoses. For a better results we should influence favorable how many factors are possible. In our institution at University of Innsbruck, we are performing the majority procedures for myocardial revascularitation, approximately 400 CABG per year. From this 20%, are performing Off-pump, OPCAB, MIDCAB and *Total Endoscopical Robotically* (TECAB) with DaVinci System. To assess the accu racy of our performing, we checked by intraoperative angiography the anastomoses in 23 patients and a follow-up control at 3 months later on.

Material and Method

We investigated a number of 29 anastomoses in 23 patients (20 male, 3 female), age 61 (44-74 years) performed by MIDCAB in 9 and OPCAB 14 (with Robotic LIMA take-down in 7 patients). The target vessels and conduits used are listed in Table 1.

Table 1: Lot of Patients with Off-Pump Bypass and Intraoperative Angiography. The target vessels and conduits used.

Patients nr.	23
• Male	20
• Female	3
Age (years)	61 (44-74)
MIDCAB	9
OPCAB	14
Robotic LIMA take-down	7
LIMA-LAD	20
LIMA-Diag	1
SVG-Diag	1
Radial artery - Diag	1
Radial artery - RCA	3
SVG-RCA	3
SVG-Cx (Y-Graft)	2
SVG-Obtuse marg (Y-Graft)	1

Surgical Technique of Bypass

MIDCAB patients, were operated by a left anterior thoracotomy (right side for RCA bypass, in 1 patient), 6-8 cm incision, in 4TH intercostal space using a special CTS retractor for easier direct LIMA preparation. External defibrillator was placed for an eventually ventricular fibrillation and a double-lumen endotracheal tube for single lung ventilation.

After completion of LIMA pedicle dissection between 5TH intercostal space and proximal as far is possible, the heparin 1.5 mg/kg intravenously is injected and pedicle divided. A papaverine solution 40mg/10ml saline is injected in pedicle belong LIMA to prevent the spasm. The pericardium is opened in front of frenic nerve and the prepericardial fate is dissected and used at the end to cover the anastomosis for a better protection. Stability of the coronary artery is assured by compression with CTS device and local occlusion was achieved with special silastic loops around LAD distal and proximal. Sometime when the ECG show early modification, intracoronary shunt has been used or a preconditioning of myocardium by 5 minute occlusion followed by reperfusion, was achieved. Distal anastomosis between LIMA-LAD, were performed in running suture technique using Prolene 7/0 or 8/0, Ethicon. Excessive bleeding from the septal in some cases was controlled with a sterile, humidified carbon dioxide blower (Medtronic). After declamping of LIMA pedicle, the flow was observed filling the distal coronary and perfect hemostasis was achieved sometime with Bioglue. Transit time flow is recorded with CardioMed Flowmeter. Pericardial flap is resumed in some points and anastomosis is covered with the prepericardial fate flap. Intraoperative angiography is then performed by surgeon and cardiologist through the femoral artery access.

OPCAB is another favorite technique in our Department in special for the patients with severe aortic atherosclerosis, where is a high risk for cerebral stroke or in patients with comorbidities (renal failure, cerebral stroke, diabetic) when CPB should be avoided. A median sternotomy is performed and LIMA is prepared under direct vision (or Robotically Assisted with DaVinci, before sternotomy, in 7 patients).

In the same time, saphenous vene and/or radial artery are prepared, depending by the number of diseased coronary arteries. For aortic atherosclerosis screening is used TEE by an expertised anesthesiologist (descending, aortic arch) and by epiaortic ultrasound. In situation of severe aortic atherosclerosis we perform OPCAB and extraanatomical construction for proximal anastomosis, Y-graft, avoiding side aortic clamp. General heparinization 1.5mg/kg is administered and LIMA distal divided. Our off-pump lot from 2000 up to now resume more than 150 patients, MIDCAB, OPCAB and *Total Endoscopical* Robotically Assisted (TECAB) but the aim of our study is resumed only for the angiographical control. All the coronary arteries were approached using almost all the commercially coronary immobilizer available (Octopus 2, CoroNeo, Medtronic, Genzyme). Central anastomoses were performed by side lateral clamp with running suture of Prolene 6/0 or Y-graft (vein or radial artery anastomosed to LIMA). At the end of anastomosis, flow in the LIMA, *saphenous venae graft* (SVG) or *radial artery graft* (RA) is measured and recorded by Transit-Time and Doppler Flowmeter (Cardio Med Flowmeter model, CM-2800).

The angiographies were performed with open chest in 8 patients (theoretical risk for infection) and after closure in 15 patients. A Heart-Lung Machine (Stockert-SIII, Munich, Germany) is keaping dry in a room neighbor (in this fashion, the oxygenator and tubes can be used in the next three days) and can be set up in case of necessity. Special continuous monitoring of cardiac function is performed by transesophagial ecocardiography (TEE) using a Vingmed-Sonos 5500 Hewlett-Packard, by an anesthesiologist with very good expertise in ecographical examination. Also, for aortic atherosclerosis screening, an epi-aortic ultrasound examination is used in patients operated by median sternotomy.

Intraoperative Angiography Examination

For intraoperative angiography we used a portable special System-Digital Mobile C-Arm Series 9800; OEC Medical System-specifically designed and modified for coronary imaging (Figure 1).

Figure 1: Portable special System-Digital Mobile C-Arm Series 9800.OEC Medical System. Intraoperative angiography performance (University Hospital of Innsbruck)

The images are digital processed to be visualized in real time or as still image, permitting a frame with frame study. Femoral arterial access was chosen for all patients and angiography was carried out after completion of anastomosis in 8 patients (chest, still open) and after sternal closure in 15 patients. A 6 F IMA catheter were used for injection of the left internal mammary artery, 6 F right coronary artery catheter were used for injection of coronary grafts. This examination is performing in a complex team, with a cardiologist cooperation and involving the cardiotechnician in technology manipulation. The examination time was mean 25 min (8-80 min), fluoroscopy time 469 sec. (6-1337), radiation dose 39291 mGy (11967-174398) using Visipaque TM contrast agent, 150 ml (50-470). In patients with graft or native coronary spasm, a 250 µg of nitroglycerine (NTG) were injected into the graft.

The lesions were classified after FitzGibbon scale as: grade A, excellent graft unimpaired run-off, grade B, stenosis reducing caliber of proximal, distal anastomoses or trunk to < 50% of the grafted coronary artery, grade C, occlusion (7.20). In the patients with spasm or surgical revision, anastomoses were controlled after intraluminal Nitroglycerin administration or after surgical solved problem.

Results

There was no hospital mortality and no perioperative myocardial ischemic event or complication related with angiography. No patients in this group had to be converted to CBP during the procedure. No arterial access problems, arrithmias, perioperative myocardial ischemia and recurrence of angina. In one patient hemodynamic instability was medical managed and in one patient CKMB > 50 U/I.

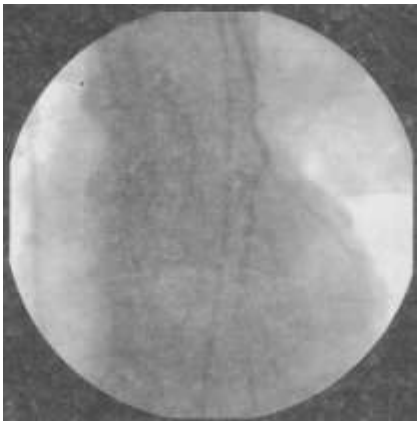
Angiographic Findings

Grafts visualised in 29/33, graft patency 29/29, significant anastomotic stenosis

4/29, surgical graft revision 2/29, spasm graft and/or target vessels, 11/29, relief of graft and/or target vessel spasm after intraluminal nitro 9/11 (Table 2).

Table 2: Findings of intraoperative angiography.

Graft visualised	29/33
Graft patency	29/29
Significant anastomotic stenosis	4/29 (13.7%)
Surgical graft revison	2/29 (6.8%)
Additional vein graft to stenosed PLA	1/29
Spasm graft and/or target vessel	11/29 (51.2%)
Relief of graft and/or target vessel spasm after intraluminal Nitro	9/11



One patient presented a snare lesion, distal from anastomosis place, partial solved after intracoronary NTG administration (Figure 2).

Figure 2: Intraoperative angiography showing, a snare lesion (arrow) on LAD, distal to anastomosis Intraluminal NTG administration, partial release the spasm. However, at 3 months follow-up was normal.

Intraoperative Graft Failure Management

Out of 29 visualised anastomosis, 11 showed spasm, NTG 25Cμg was administered with relief or reduction in 9 patients (Figure 3).

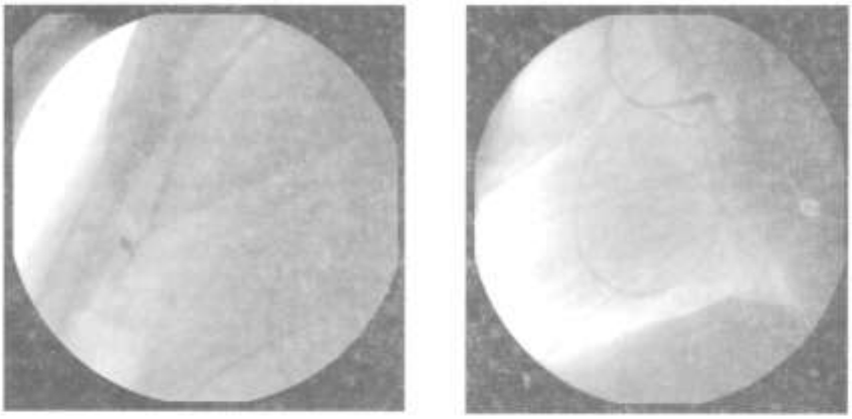


Figure 3: Intraoperative angiography showing spasm of LAD, solved after intraluminal NTG

At 3 months angiographic control, all the grafts - even this with spasm persistency - were normal. Surgical immediate revision was performed in 2 patients, for severe stenosis (grade B) on anastomosis site and another 2 patients, the anastomosis was reajusted by supplimental sutures and Bioglue removal.

Follow-up at 3 Months

Three months later 13 patients (6 with normal anastomoses, 7 with spasm or revision) were controlled angiographicaly (Table 3).

Table 3: Angiographic findings at 3 months follow-up

Patients	Intra-Op finding	Therapy Intra-Op	Result Intra-Op	Follow-up, 3 months
1	ok	no	ok	ok
2	spasm	NTG	Spasm reduced	ok
3	spasm	NTG	Spasm reduced	ok
4	spasm	NTG	Spasm reduced	ok
5	spasm	NTG	Spasm reduced	ok
6	ok	no	ok	ok
7	spasm	NTG	Spasm reduced	ok
8	Anast. stenosis	Revision	ok	ok
9	ok	no	ok	ok
10	Anast. stenosis	Revision	ok	ok
11	ok	no	ok	ok
12	ok	no	ok	ok
13	ok	no	ok	ok

All the graft checked were patent, even those with intraoperative spasm reduced but persistently. One patient with LIMA-LAD bypass received stenting of distal RCA and PTCA of postero-lateral RCA-system during control-angiography. Another patient after LIMA to LAD graft showed LAD stenosis which received PTCA and stent.

Discussion

The evolution of surgical procedures from the first direct approach of coronary arteries up to robotic assistance revascularization is spectacular and had a stroking impact, benefiting thousands of people during the last half of the 20™ century. Surgeons may approach minimally invasive CABG in any of several ways; MIDCAB, OPCAB, Heart Port and MIDCAB, TECAB (17, 22). However, the major concern of these new advances is proving their advantages over the conventional methods. Quality of anastomosis (18) and complete revascularization are the Achilian sensitive point. The patient should leave the operative theatre with the best anastomosis (19, 20).

Introduced by Sones and Shirey, at the Cleveland Clinic in 1962, "Cine-Coronary Angiography", represented the cornerstone in coronary artery management, visualization of diseased coronary arteries. Over years remained the most confident examination of the coronary arteries pre-, intra- and postoperatively.

Postoperative angiographic examination show graft failure in 5% to 20%, in some cases necessitating remake of the anastomosis (1, 3, 5, 6, 9, 11, 12).

Early postoperative graft failure has to be attributed to technical problems; stricture of anastomosis, improperly place chosen, small vessel, bad run-off, lesion of conduit or target vessel during manipulation (LIMA dissection, snare lesion of LAD). Performed intraoperative angiography has the advantage over postoperative, the possibility for immediate revision of a graft failure (25). The most common finding in our study and from publication (1, 2, 5), spasm was present in 11 from 29 anastomosis (51,2%). No differention was observed between MIDCAB and OPCAB relating, normal intraoperative findings, grafts with spasm or anastomosis failure.

In 11/29 anastomoses was present and managed by intraluminal Nitroglicerin 250μg administration. Didn't totally disappear in all the patients. However, at the follow-up 3 months this anastomosis was normal, making angiogram difficult to interpret because not all findings are of importance for later patency (1, 14). Snaring suture for coronary artery bleeding control can produce lesion (8), which we identified in another histological study (16).

Perioperative myocardial infarction occurs with a incidence 3-10% and is a significant factor of morbidity and mortality. In a study from Leipzig group, incidence was 6.4% and angiography (performed out of operative theater, because of myocardial infarction) findings resulted in 34/131 patients with acute myocardial postoperative infarction, reoperation, with 9.3% mortality for revision and 39% for immediate reoperation due to homodynamic instability (3).

Surgical revision due to severe stenosis in this study 2/29 anastomoses (6.8%), were the failure was prompt revised, avoiding possible postoperative myocardial infarction. For all the patients under beating heart transit-time flow is assess, but the sensitivity of this direct, simple investigation doesn't correlate well with anastomoses quality (21, 23, 24). In one patient with severe anastomotic stenosis, revised, the correlation between transit time flow before and after correction, was very sensitive, 24 ml/min and 103 ml/min (Figure 4).

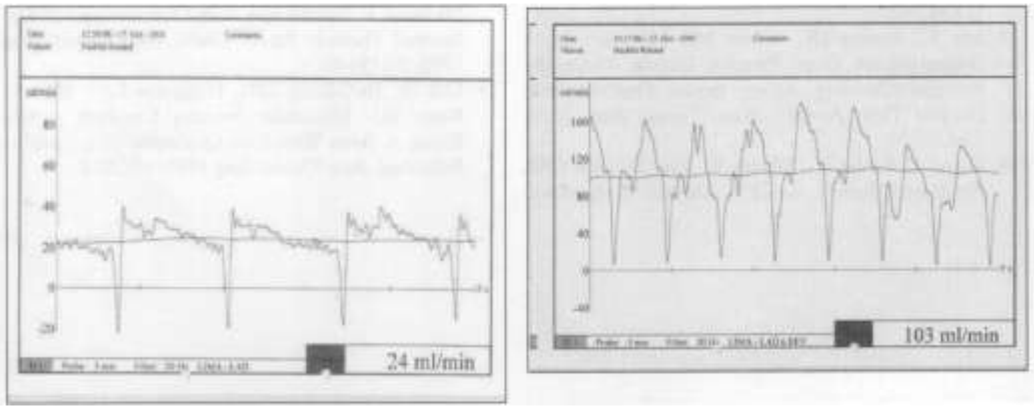


Figure 4: Transit time flowmetry in one patient with severe stenosis (grade B), before and after surgical revision

Some authors (6) are using planed intraoperative angiography for MIDCAB, combined with PTCA for other coronary vessels. Recent technological advance have provided many sophisticated stabilizing devices, instruments for better approach of coronary arteries and also quality control instruments of our work.

Conclusion

Intraoperative angiography is a time consuming and additional expensive examination, in special when taking in consideration such expensive procedures, TECAB, Heart Port Access, but give valuable information during off pump CABG and not only. When looking over findings, spasm and surgical revision, the concern and skepticism of some colleagues seem to be justified. However, permitting the surgeons to immediately appraise the anastomoses and to revise, can reduce postoperative complications, reducing the final cost to justify this examination. Our lot of study is too small and we just started with TECAB, extensive examination will be necessary to implement this examination in our routine. The present controversies will continue until sufficient arguments sustain this method.

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Perioperative Echocardiography Indications in Mitral Valve Surgery Depending on the Cost-Benefit Report

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Abstract

Aim: *1. To establish the implications that using perioperative transoesophageal echocardiography(TEE) has on prognostic in patients with different types of mitral valve diseases; 2. To estimate the correlation between the diagnostic done by intraoperative TEE and the surgical diagnostic; 3. Cost-benefit analysis of performing perioperative TEE in valve surgery and establish its perioperative indications.*

Material and method: *Prospective study on 499 patients with mitral valve diseases undergoing cardiac surgery in the Institute of Cardiovascular Diseases "C.C.Iliescu", Bucharest, in 3 years. 2 groups were defined: group A – 125 patients who underwent intraoperative TEE before or after the cardiopulmonary bypass (CPB) and group B – 374 patients who did not underwent intraoperative TEE.The data base was built using Visual Fox Pro and the statistical analysis used the SYSTAT si SPSS programs to measure the power association between the prediction variables and outcomes. Calculation of the cost-benefit report for each type of echocardiography indication was done using a special programme which took into account different data from data base and economic data from the specialised Institute departments. A score was calculated as follows: a cost-benefit report >1 considered* unfavourable*; a cost-benefit report =1 classified as relative indication; a cost-benefit report <1 was considered* favourable.

Results: *From 499 patients diagnosed with mitral valve lesion undergone the surgical intervention: 5 with mitral valvuloplasty (1.002%), 392 (73.56%) - mitral valve replacement with metallic prosthesis and 102 (20.44%) - mitral valve replacement associated with another valve replacement. Depending on the cost-benefit report, the indications of performing perioperative TEE revealed by our study on patients with mitral valve lesions undergoing cardiac surgery, can be synthesised as follows: standard indications: Intraoperatively for: guiding the mitral valve valvuloplasty; diagnosis of associated valve lesions by appreciating the severity and the opportunity of surgical correction; establishing the causes of intraoperative acute haemodynamic dysfunction, life threatening; routine evaluation in three valve replacement. Early postoperatively, in intensive care unit for: suspicion of pericardia or pleural collections; establishing the aetiology of an acute haemodynamic dysfunction; evaluating the severity of a restant mitral insufficiency after mitral valvuloplasty. Relative indications: Intraoperatively for: preoperative diagnosis in patients with left ventricle systolic dysfunction and associated valvular lesions; Early postoperatively, in intensive care unit for appreciating the right ventricle systolic performance in patients undergone triple valve replacement. Uncertain indication: Intraoperatively for: preoperative diagnosis of mitral valve lesion or associated valve lesions in patients with poor acoustic window; routine assessment of the prosthesis after the cardiopulmonary bypass. Early postoperatively, in intensive care unit for: suspicion of pulmonary emboli; suspicion of*

thrombosis of mitral or aortic prosthesis; diagnosis of the associated valve lesions severity.

Conclusions: *1. The particularities of performing the intraoperative transoesophageal echocardiography are related, firstly, to the poor haemodynamic status of patient undergoing the surgical intervention. 2. Before the cardiopulmonary bypass, the intraoperative transoesophageal echocardiography is useful for the new information that it provides. It indirectly determine the decreasing of the postoperative complications, the decreasing of early postoperative mortality rate and amelioration of the immediate and the long term prognosis and improvement of the quality of life. In certain situations, the information provided by the intraoperative transoesophageal echocardiography before the cardiopulmonary bypass can modify the surgical strategy. 3. Intraoperative transoesophageal echocardiography performed after the cardiopulmonary bypass turned out to be useful for both surgeon for a immediat outcome regarding the surgical intervention and for the anaesthesiologist. 4. Taking into consideration the cost-benefit report, the indications of performing perioperative transoesophageal echocardiography (adapted to specific conditions in our country), we identified 3 categories: 1 - standard indications 2 - relative indications; and 3 - uncertain indication, with low usefulness.*

Background

Intraoperative and early postoperative transesophageal echocardiography (TEE) has became a standard procedure in various cardiovascular surgical interventions and also for selected cases in non-cardiac surgery. Due to extension of the indication for intraoperative TEE and increasing experience in performing this procedure, its impact on surgical interventions and therapeutical decision become more and more important [1-7].

The particularities of performing the intraoperative TEE are related, firstly, to the poor haemodinamic status of patient undergoing the surgical intervention. Many specific intraoperative parameters could have a significant impact on evaluation by TEE of an important number of cardiac lesions, especially regarding the assessment of the valvular regurgitation degree. These parameters, which can be differently controlled are: preload variability (with the intravascular volume status, vasodilator treatment and parameters related to general anaesthesia), afterload variability (vasopresor treatment, inotrop positive treatment or vasodilator treatment, presence of an intraaortic contrapulsation balloon, obstruction of the ejection tract of left ventricle and other parameters related to the general anaesthesia), presence of the arrhythmias and myocardial function (which can be variably recuperated after hypothermia or after the administration of the cardioplegic solutions) [8-14].

Thus, the echocardiografist in the operative room has the task to interpret these parameters, to integrate them taking into account the particularities of each case and give the surgeon more accurate data.

Aim of the study

1. Establishing the implications that perioperative TEE performed in patients with different types of mitral valvular diseases has on their prognostic.

2. Estimating the correlation between the diagnostic done by intraoperative TEE and the surgical diagnosis.

3. Cost-benefit analysis of performing perioperative TEE in valve surgery and establish its perioperative indications.

Material and method

We performed a *prospective* study on 499 patients with mitral valve diseases undergoing cardiac surgery in *"C.C. Iliescu" Institute for Cardiovascular Diseases, Bucharest,* between January 1st, 2000 and January 1st, 2003. Patients were divided in 2 groups taking into consideration intraoperative TEE performed as imagistic procedure:

- **Group A** – 125 patients who underwent intraoperative TEE before or/and the CPB
- **Group B** – 374 patients who did not underwent intraoperative

The study *protocol* was completed with demographic data, details related to the valvular lesions, specific indication for performing perioperative TEE, its impact on the decision making during the surgery and in early postoperatively and the patients evolution immediate postoperative and at 1 month after.

The data base was done using Visual Fox Pro programme. The main variables used were: *Prediction variables*: patient ID Data, preoperative diagnosis, surgical risk (calculated using a scale from 1 to 10 taking into account different preoperative parameters: age, co-morbidities, gravity of the cardiac lesions (NYHA class), type and duration of surgical intervention, associated risk factors), type of surgical intervention, if the intraoperative TEE modified the surgical strategy and how, specific variables related to the surgical performance: duration of surgical intervention, intraoperative complications,if the intraoperative TEE performed in intensive care unit immediate postoperatively modified the specific treatment and how. *Outcomes variables:* presence and type of postoperative complications, death and its causes. The statistical analysis was performed using the SYSTAT and SPSS programs for:

Measurement of the power association between the prediction variables and outcomes using the tests:

a) for qualitative variables: *CHI square test or Fischer exact test*.

b) for quantitative variables: T test (*Student test*), ANOVA test or *U test* depending of the samples volumes and *Kruskal Wallis nonparametric tests*..

There were used, also, the following methods of statistical correlation:

- ✓ *Analysis of simple linear and multivariate regression* for quantitative variables;
- ✓ *Relative Risk* calculation and the *confidence interval* 95%;
- ✓ *Positive and negative predictive value* calculation
- ✓ *Cost-benefit report* calculation for performing the perioperative echocardiography of cardiac diseases underwent surgical correction. It was determined using a special programme, which using the data from the data base and different economic data from the specialized departments from our Institute, has performed the assessment of the efficiency of using perioperative echocardiography in cardiac surgery.

Calculation of the cost-benefit report for each type of echocardiography indication was done taking into account the parameters related to procedure (cost of each echocardiography per patient, number of echocardiographies/patient and per surgical cardiac diseases, information provided by the perioperative echocardiography). Parameters dependent of surgical intervention taken into consideration were postoperative mortality rates for surgical intervention on subgroups of patients taking into account the individual risk, early postoperative specific mortality rates depending on the performing or not the perioperative echocardiography, immediate and long term postoperative complications rates depending on the performing or not the perioperative echocardiography, quality of life at 1 month postoperatively on risk subgroups and on surgical interventions depending on the performing or not the perioperative echocardiography. Parameters dependent on patient taken into account in this analysis were age, gender, co-morbidities, associated risk factors.

On these parameters there were calculated a risk score which was used then for estimation of cost-benefit report associated to using the perioperative echocardiography on types of surgical interventions. Parameters dependent on the hospital taken into account were: complication rates for which the perioperative echocardiography does not bring an additional benefit for diagnosis, accessibility to the echocardiograph use, personnel training, training curve.

Data were grouped on surgical lesions types and the surgical interventions according to the exposure level to the risk factors. For each exposure level there were introduced the number of patients performed the perioperative echocardiography (cases) and the number of patients who have not performed perioperative echocardiography (controls). The confounders were controlled by stratification. Data interpretation was performed taking into account the following hypothesis:

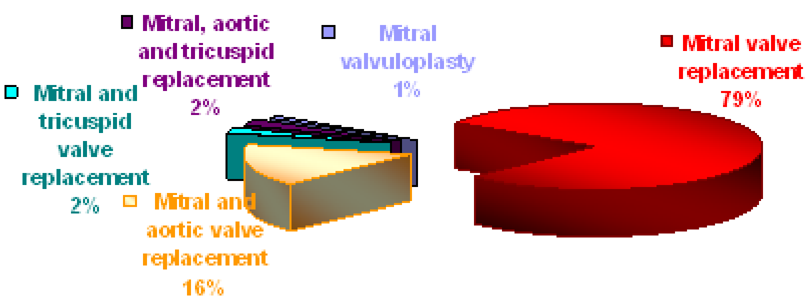
- a cost-benefit report **> 1** was considered *unfavourable* from economical point of view; for these patients the perioperative echocardiography was considered as having *uncertain indication*;
- a cost-benefit report **= 1** included the patients subgroups classified as with *relative indication* for performing perioperative echocardiography, risks and benefits of performing it being appreciated on case to case basis;
- a cost-benefit report **< 1** was considered *favourable* from economical point of view; for these patients the perioperative echocardiography was considered as a *standard indication,* being recommended in every case.

Results

499 patients were diagnosed with mitral valve lesion (isolated or associated to another valvular lesions) and undergone the surgical intervention in our clinic in the study period. In 5 patients were performed mitral valvuloplasty (1.002%), 392 patients (73.56%) underwent mitral valve replacement with metallic prosthesis (345 patients with bi-leaflet prosthesis and 47 patients with mono-leaflet prosthesis) and 102 patients (20.44%) underwent mitral valve replacement associated with another valve replacements (mitral and aortic valve replacements in 75 patients – 15.63%, mitral and tricuspid valve replacements in 12 patients –2,4% and mitral, aortic and tricuspid valve replacements in 12 patients –2.4%) (Figure 1).

The dynamics of the indications for TEE in the three years of the study were different depending on the surgical intervention. Thus, the TEE were performed in all the patients with the mitral valvuloplasty both before and after the CPB. Regarding the isolated mitral valve replacement, the frequency of TEE solicitation by surgeon or anaesthesiologist in operative room were increased 4 times in 2002. Analysing this subgroup by the valvular lesion for which there were performed the mitral valve replacement, intraoperative TEE was solicited more frequent in 2003, especially for the patients with ischemic mitral insufficiency by prolaps or infective endocarditis (Figure 2).

Figure 1. Study group structure depending on the type of the surgery performed



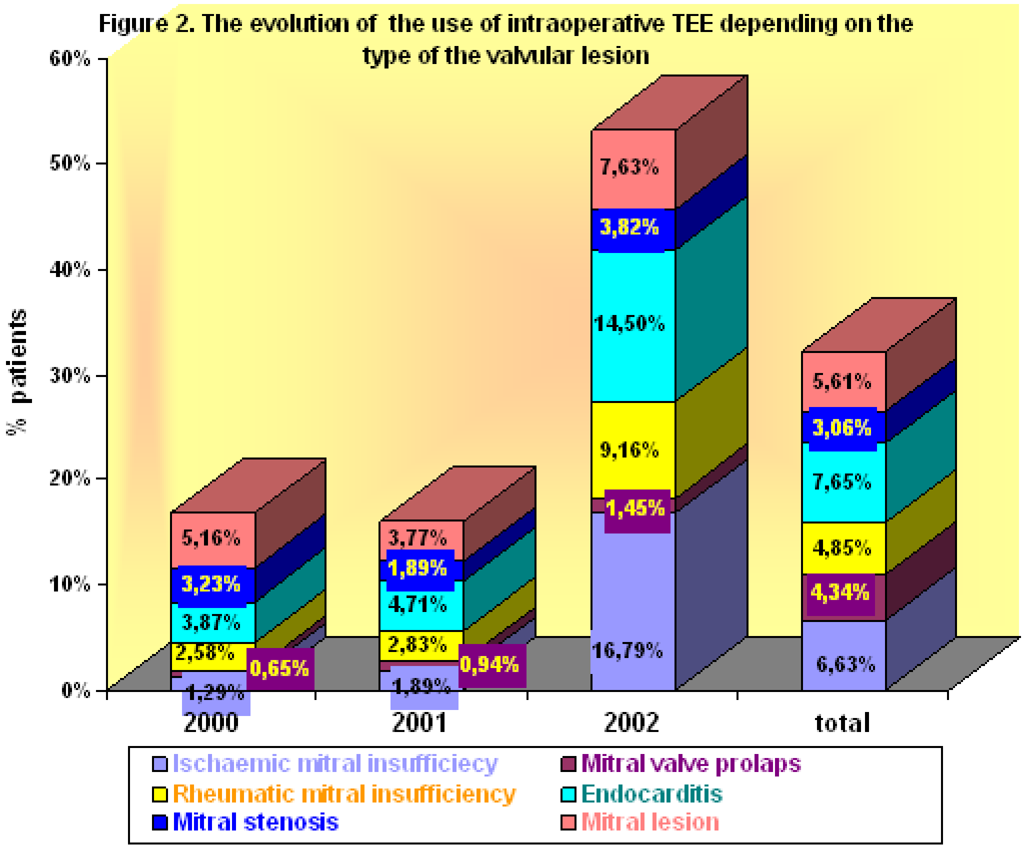


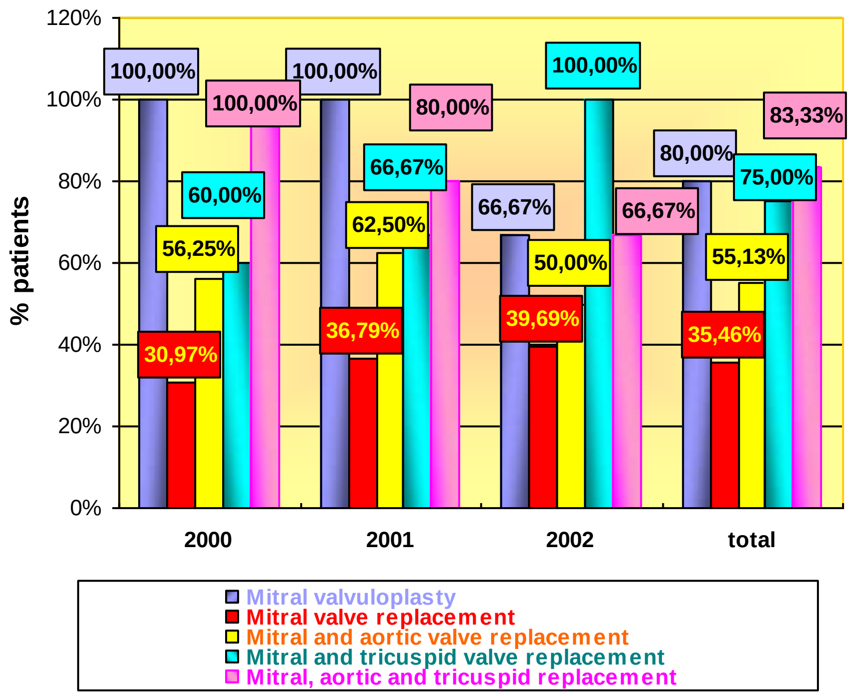
Figure 2. The evolution of the use of intraoperative TEE depending on the type of the valvular lesion

Regarding the frequency of intraoperative TEE performed in patients undergone associated mitral valve replacement with aortic or tricuspidian ones, it was increased in 2001 and decreased in 2002 regardless the type of valvular lesion.

For patients undergone triple valve replacement, TEE were indicated in about 2/3 patients, in 2002.

Early postoperatively, in the intensive care unit, the indication for performing TEE in patients with mitral valve lesions were variable in time but its frequency were increased (Figure 3).

Figure 3. Dinamics of early postoperative TEE indication in intensive care unit in mitral valve surgery



The exception were triple valve replacement, for which the TEE indication in intensive care unit in the three year study has significantly decreased, probably because the increased frequency of the TEE solicitations in operative room in these patients. Because the low number of patients the decreasing number of TEE solicitations in patients undergone mitral valvuloplasty cannot be interpreted.

The detailed cost-benefit analysis in patients with mitral valve lesions performed perioperative TEE has shown a low efficiency of this investigation in patients undergone isolated mitral valve replacement. The benefit of this diagnostic method was superior for the patients undergone mitral valvuloplasty and for associated valve replacements (Figure 4):

- In all patients undergone mitral valvuloplasty, TEE were performed intraoperatively both before CPB and after cardiac time of the intervention for evaluating the restant mitral insufficiency and for appreciating the opportunity of re-intervention for mitral repairing or valve replacement. The cost-benefit report for this investigation were >1, but without statistic significance because the low number of patients;

▪ Among the 390 patients undergone isolated mitral valve replacement, there were been performed TEE in 120 patients (32.14%) as follows: in 49 patients (12.5%) TEE were solicited only before CPB, in 30 patients (7.65%) it was performed both before and after CPB and in 47 patients(11.99%) TEE was only performed after CPB.

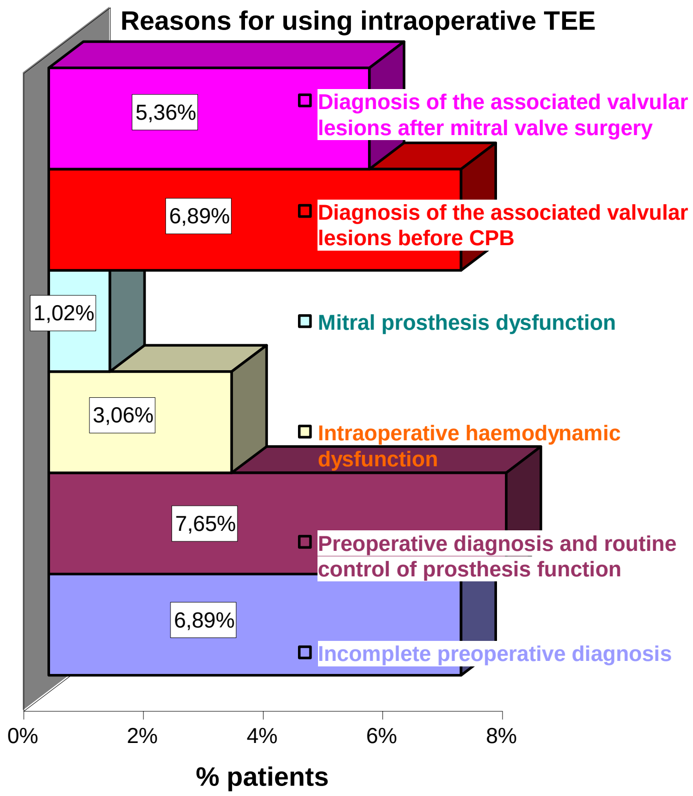


Figure 4: Cost-benefit report for the use of intraoperative TEE in patients with isolated mitral valve replacement

The reasons of performing TEE were:

♦ In 27 patients (6.89%) TEE was only performed before CPB for a correct and complete preoperative diagnostic concerning the mitral lesion mechanism and severity with regards to the opportunity of mitral valvuloplasty (8 patients) or of mitral valve replacement. The indication for TEE had an overall cost-benefit report>1, unfavourable for these patients. However, in subgroup of the patients with ischemic mitral insufficiency undergone also coronary artery bypass grafting, this investigation turned out to be very useful with a sub-unitary cost-benefit report (0.97). In the same time, in patients with mitral insufficiency and severe left ventricular systolic dysfunction, intraoperative TEE had a cost-benefit report=1.

♦ In 30 patients (7.65%), TEE was performed both before CPB for a more accurate diagnosis and after CPB for routine control of prosthesis function, with a supraunitary cost-benefit report. The cost-benefit report were superior (=1) in patients with a dilated left ventricle cavity.

♦ In 22 patients (3.06%), TEE was performed intraoperatively after the surgical correction for assessment of acute haemodinaminc dysfunctions, life threatening. In 20 patients TEE has revealed the cause of haemodinamic dysfunction and helped in the optimal choise of treatment strategy, with a favourable cost-benefit report. Thus, in 12 patients, intraoperative TEE has revealed a filling deficit, in 7 patients has revealed global left ventricle systolic dysfunction with a severe contractility disturbance (being necessary the aortic contapulsation in 5 patients); in one patient has shown a right ventricle systolic dysfunction and in 2 patients it could not reveal the cause of the haemodinamic dysfunction. In 4 patients (1.02%), intraoperative TEE was used for suspicion of the prosthesis dysfunction, but it was confirmed in none of the patients, so, the cost-benefit was unfavourable. However, in 21 patients (5.35%), intraoperative TEE was performed after the mitral valve replacement for the assessment of associated valve lesions which could have been under-evaluated preoperatively due to the mitral valve lesion. Thus, in 16 patients, intraoperative TEE has infirmed the presence of a haemodinamic significant associated aortic insufficiency and in 3 patients has revealed the presence of a haemodinamic significant associated aortic insufficiency (which was surgical corrected in the same operative time in 2 patients). In 2 patients, intraoperative TEE has infirmed the presence of the tricuspid lesion. In these situations the cost-benefit associated to this imagistic method was subunitary and intraoperative TEE could be included among the standard indications for these patients.

♦ In 27 patients (6.89%), TEE was only solicited before the CPB for confirming or infirming the presence of associated valvular lesions. In this subgroup, in 7 patients, TEE has indicated the corrective surgical intervention at other valves but mitral valve (undiagnosed preoperatively), which lead to a change in the surgical strategy (4 patients with associated aortic valve replacement, 1 patient with associated tricuspid valve replacement and 2 patients with associated tricuspid valvuloplasty). In this subgroup of patients the cost-benefit associated to this imagistic method was =1.

Regarding the benefit of the early postoperatively TEE in intensive care unit, the cost-benefit report has not shown a good efficiency of performing this investigation, in patients taken into study. In our three year study, the early postoperative TEE was performed in 41,08% among the patients with valvular lesions undergone surgical correction. The indication for performing this investigation were not different from the other categories of patients. As exceptions we have noticed 5 patients undergone mitral valvuloplasty, in 3 among them the early postoperative TEE was performed for appreciating the severity and the mechanism of a probable restant mitral insufficiency, with a subunitary cost-benefit report. Thus, the indication for the early postoperatively TEE in intensive care unit were the following (Figure 5):

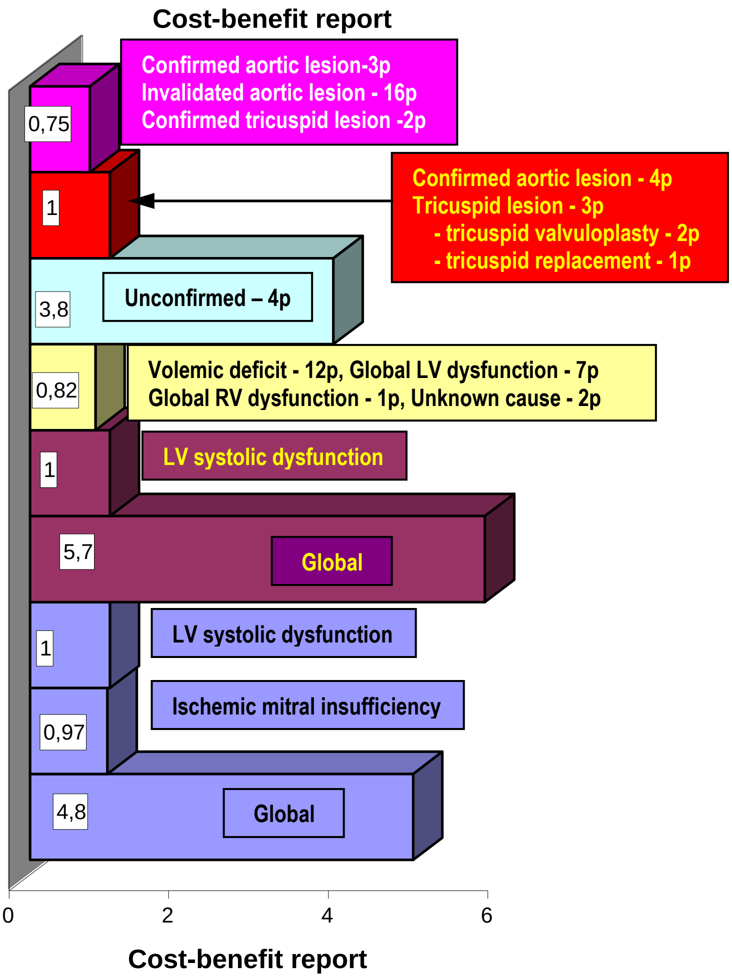


Figure 5: Cost/benefit report for using the ecocardiography postoperatively immediate in intensive care unit in patients with surgical mitral valve lesion

♦ In 95 patients (19.04%), early postoperatively TEE was performed for acute haemodinamic dysfunctions, suddenly developed or for haemodinamic instability, with a subunitary cost-benefit report. Thus, in 47 patients, TEE has revealed a filling deficit, in 7 patients – left ventricular global systolic dysfunction, in 2 patients – segmentary kinetic modifications, in 5 patients – significant pulmonary hypertension, in 2 patients – pulmonary thrombembolism and in 30 patients - pericardia or pleural effusion which have been evacuated.

♦ In 23 patients (4.61%), TEE were performed for the suspicion of pericardia or pleural effusions, confirmed in 18 patients, with a subunitary cost-benefit report.

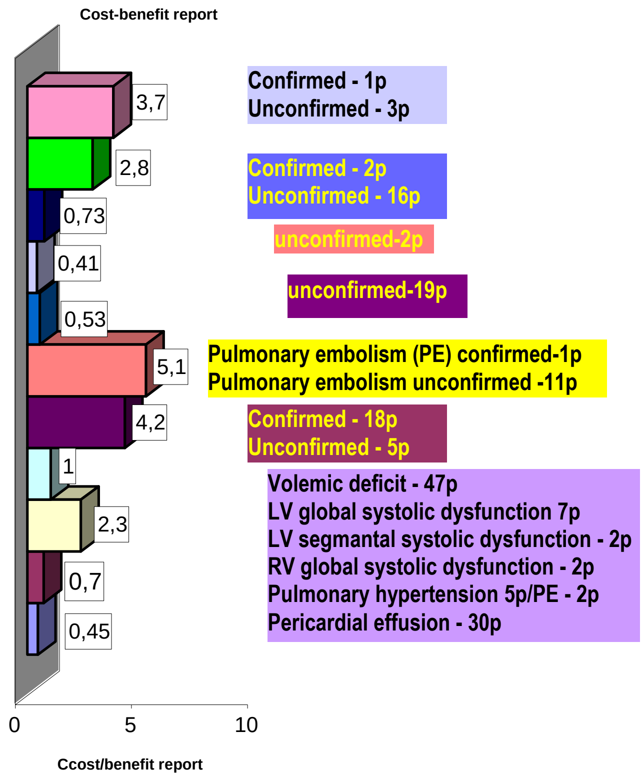
♦ In 12 patients (2.40%), TEE was performed for a suspicion of pulmonary embolia, confirmed in 1 patient with a supraunitary cost-benefit report, having a less relevance for diagnosis than other more invasive investigations.

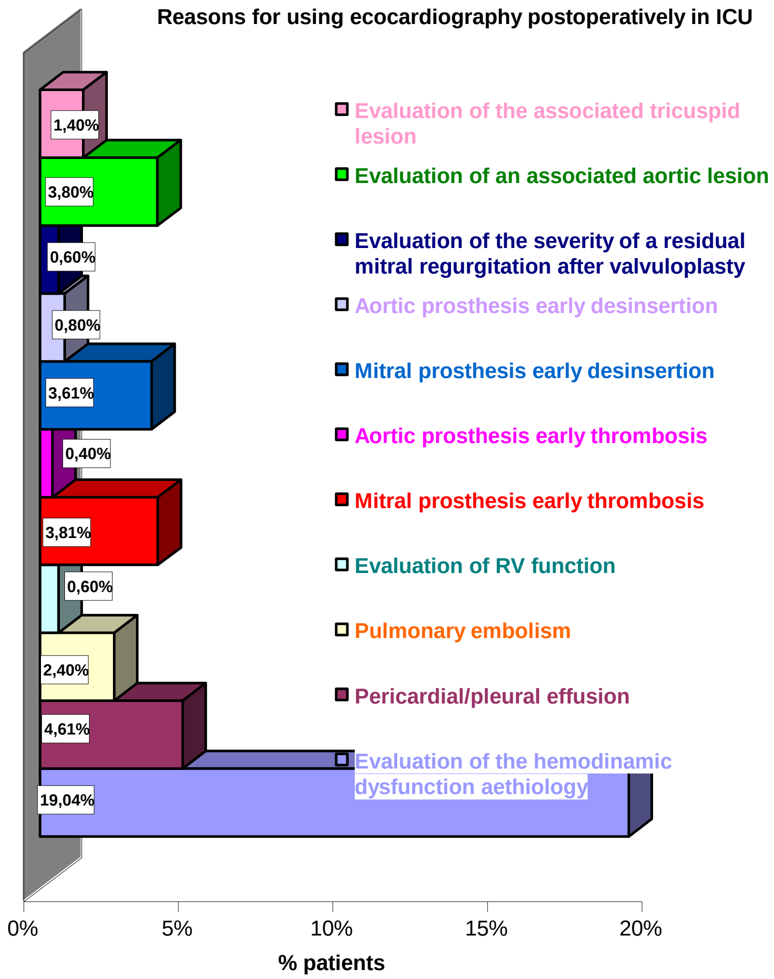
♦ In 43 patients (8.62%), the early postoperatively TEE was performed for the suspicion of early mitral prosthesis dysfunction (37 patients) or aortic prosthesis dysfunction (in 6 patients from the subgroup of patients undergone two or three valves replacement). Thus, in 19 patients, this investigation was performed for early incomplete prosthesis thrombosis, this hypothesis being infirmed in all patients with a supraunitary cost-benefit report. The same pattern was noted for patients with suspicion of early aortic prosthesis thrombosis (2 patients). For para-prosthesis leaks by early desinsertion of prosthesis annulus, performing the early postoperatively TEE had subunitary cost-benefit report, being a standard indication. In 18 patients with suspicion of paravalvular leak, it was confirmed in 2 patients by the early postoperative TEE, imposing re-intervention and in 4 patients with early prosthesis des-insertion suspicion, one was confirmed imposing re-intervention.

♦ In 3 patients (0.6%), the early postoperatively TEE was performed for appreciating the severity of a restant mitral regurgitation after mitral valvuloplasty with a subunitary cost-benefit report, as it was mentioned above.

♦ In 26 patients (5.21%), the early postoperatively TEE was performed after the isolated or associated mitral valve replacement for appreciating the severity of the associated valvular lesion known preoperatively, with a supraunitary cost-benefit report.

♦ In 3 patients (0.6%), the early postoperatively TEE, was performed for appreciating the right ventricle systolic performance, with a unitary cost-benefit report.





Discussions

Surgical interventions for mitral valvuloplasty or for valve replacement need the intraoperative TEE both before and after CPB for many reasons. The dynamic of its use is variable depending on the type of surgical intervention, data revealed by our study being similar with those published in the literature. Thus, TEE were performed in all patients undergone mitral valvuloplasty both before and after CBP. In the literature, this imagistic investigation is used mainly for monitoring the surgical intervention of mitral valvuloplsty than for other surgical interventions, its dynamic being with a positive trend between 1991-1998 [29-32].

Regarding the isolated mitral valve replacement, the frequency of TEE solicitation in operative room, in our clinic, has increased 4 times in 2002. This can be explained by the accessibility to this investigation, on one hand, and by the surgeon and anaesthesiologist excessive prudence asking for this investigation as a routine one for prosthesis control after the cardiac time of the intervention, on the other hand. However, these arguments cannot entirely explain this spectacular increase in its indication. Analyzing this patient subgroup depending on the type of valvular lesion for which there were undergone isolated mitral valve replacement, intraoperative TEE was performed more frequently for ischemic mitral insufficiency because the number of these patients was increased in 2003 than the previous years. The references regarding this imagistic method for isolated mitral valve replacement have shown that there were noticed a increased trend of its solicitation between 1991-1995, with a flat trend after that.

Immediate postoperatively, in intensive care unit, the indication for TEE was variable in time, but with an overall positive trend. As exception it was noticed the triple valve replacement with a negative trend, explained by the increased solicitation of this investigation intraoperatively and by surpassing the training curve, with decreasing of the mortality and morbidity rates. Decreasing the indication for immediate postoperatively TEE in intensive care unit, for patients undergone mitral valvuloplasty cannot be interpreted because the low number of patients.

The benefit of intraoperative TEE in our clinic was inferior those from literature. Thus, the cost-benefit report for performing this imagistic method was favourable from economic point of view for TEE performed before CPB for diagnosis of ischemic mitral regurgitation severity and mechanism and for evaluating the opportunity of a conservative mitral surgical intervention. After CPB, TEE was performed for appreciating the degree of restant mitral regurgitation after mitral valvuloplasty or after coronary artery bypass grafting for ischemic mitral insufficiency. This method was also used for establish the severity of mitral lesions appreciated preoperatively "at the border of haemodinamic significance", associated to an aortic lesion after the aortic valve replacement. In patients with associated infective endocarditis to the mitral lesion, the cost benefit report was also efficient.

Early postoperative TEE, in intensive care unit in patients with mitral valve lesions undergone surgical treatment, was performed for suspicions of pericardia or pleural collections, determining the aetiology of an acute haemodinamic dysfunction, suddenly developed immediate postoperatively, unexplained by other investigation methods and when it is no time for performing other invasive investigations. It was also useful for establishing the severity of a restant mitral insufficiency after mitral valvuloplasty. In all these situation the cost-benefit report was favourable.

There were noticed some differences regarding the indications of TEE between the results of our study and the literature. Thus, in guidelines published, the standard indications for performing TEE do not take into consideration some patients subgroup for which in our study we have found a favourable cost-benefit report, such as for diagnosis of associated valve lesions (aortic or tricuspidian) by appreciating the severity and the opportunity of surgical correction, after the mitral valve surgical treatment and for triple valve replacement. This can be interpreted, on one hand, because the low number of patients with this pathology in country where there were a successful programme for cardiac arthritis prevention, and, on the other hand, because of an accurate preoperative diagnosis due to the high technologies used.

Regarding the use of TEE immediate postoperatively in the intensive care unit for suspicions of pericardia or pleural collections or for establishing the severity of a restant mitral insufficiency after mitral valvuloplasty, this indications were not found in the published guidelines. As it was mentioned before, the frequency of pericardia or pleural collections in other clinics is very low and for its diagnosis there are used other investigations. In other clinics, the experience in mitral valvuloplasty is higher, the surgical intervention being practically monitored by TEE, which leads to a decreasing the number of solicitation of this intervention postoperatively.

Regarding the routine evaluation of the prosthesis after CPB, it is presented as relative indication in literature, but in our study it turned out to be with low benefit, being included in the third category with uncertain indication. A possible explanation for this difference is the high experience of valve replacement in our clinic, TEE being solicited only for special situations or for high suspicion of prosthesis dysfunction.

Conclusions

1. Intraoperative TEE has practically replaced epicardial echocardiography as imagistic alternative procedure being considered as golden standard in some cardiac surgical interventions assurring the safety of the surgical performance.

2. The particularities of performing the intraoperative TEE are related, firstly, to the poor haemodinamic status of patient undergoing the surgical intervention.

3. Before CPB, the intraoperative TEE is useful for the new information that it provides, helping in diagnostic and in surgical strategy optimal choise. Frequently the intraoperative TEE infirms the presence of valvular lesions significant haemodinamic, discovers morphological valvular destructions, the presence of intracavitar thrombi or can diagnosis a foramen ovale patent which cannot be seen before, can detect segmental kinetic modifications de novo and can provide important details for establishing the aetiology of the lesion and for choosing an optimal therapeutic decision. It can indirectly determine the decreasing in frequency of postoperative complications, the decreasing of early postoperative mortality rate and amelioration of immediate and long term prognosis and improvement of the quality of life. In certain situations, the information provided by the intraoperative TEE before CPB can modify the surgical strategy.

4. The concordance between the diagnosis provided by TEE before CPB and surgical diagnosis is good, in general, many of the discordances being related to the description of the valvular morphology. The diagnostic discordances could lead to wrong surgical strategy choise. These cases are very rare and depends not only on the echograph performance and echographist experience but also on the surgeon and anaesthesiologist concerning the interpretation of the information provided.

5. Intraoperative TEE performed after CPB has numerous advantages being useful for both surgeon for an immediate outcome regarding the surgical intervention and for the anaesthesiologist, the information presented by this investigation guiding the therapeuthic decision. Frequently, this imagistic method was solicited after CPB for verifying the valvular repairment, for appreciating the severity of an aortic insufficiency after the surgical correction of an aortic dissection and for establishing the aetiology of intraoperative haemodinamic dysfunctions in patients with difficult evolution.

6. Due to increased use of intraoperative TEE, there is a need of well trained specialists to perform this investigation.

7. The cost-benefit analysis has shown that the indications of performing perioperative TEE (adapted to specific conditions in our country) in patients with mitral valve lesions undergoing cardiac surgery, can be synthesised as follows:

Category I (standard indications):

A. Intraoperative TEE for:
- Determining the mitral valve regurgitation mechanism and severity, guiding the mitral valve valvuloplasty;
- Diagnosis of associated valve lesions (aortic or tricuspidian) by appreciating the severity and the opportunity of surgical correction, after the mitral valve surgical treatment;
- Establishing the causes of intraoperative acute haemodinamic dysfunction, life threatening;
- Routine evaluation in three valve replacement (mitral, aortic and tricuspidian).

B. Early postoperative TEE, in intensive care unit for:
- Suspicion of pericardia or pleural colections;
- Establishing the aetiology of an acute haemodinamic dysfunction, suddenly developed immediate postoperatively, unexplained by other investigation methods and when it is no time for performing other invasive investigations;
- Evaluating the severity of a restant mitral insufficiency after mitral valvuloplasty

Category II (relative indications):

A. Intraoperative TEE for:
- Preoperative diagnosis in patients with left ventricle systolic dysfunction and associated valvular lesions to the mitral one;

B. **Early postoperative TEE,** in intensive care unit for appreciating the right ventricle systolic performance in patients undergone triple valve replacement (mitral, aortic and tricuspidian).

*Category III (uncertain indication, with low usefulness)***:**

A. Intraoperative TEE for:
- Preoperative diagnosis of mitral valve lesion or associated valve lesions in patients with poor acoustic window, whom were not adequately explored preoperatively;
- Routine assessment of the prosthesis after the CPB;

B. **Early postoperative TEE,** in intensive care unit for:
- Suspicion of pulmonary embolia;
- Suspicion of thrombosis of mitral or aortic prosthesis;
- Diagnosis of the associated valve lesions severity.

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Revascularization score and myocardial protection in CABG*)

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Abstract

Background: *The SYNTAX Score (SYNergy between PCI with TAXus and Cardiac Surgery) is an important analyzer for studies of anatomical lesions (ALS). We propose to study the revascularization score (RVS) witch is the indirect relation with ALS.*

Purpose: *We had studied the relations between ALS and RVS in the strategies of myocardial protection by the cardioplegia in CABG. The efficiencies of cardioprotection strategy were analyzed by the myocardial viability, by the inotrop positive agents used and echocardiographycal perioperator parameters: systolic and diastolic myocardial function (Tei index and ISMVS).*

Methods: *We had analyzed the ALS by coronarography in 186 patients, used the SYNTAX score and from these results we had determined the indirect relation with the RVS (RVI). From the ALS and RVS we hade studied the strategy of myocardial protection by cardioplegy and the effect on the myocardial function evolution from the inotrop effect and the echocardiographical parameters (Tei index and LVMSI).*

Results: *The ALS in all patients (186) was between 30-70 patients so: 30/10p, 40/20p, 50/32p, 60/43p, 70/80p and the RVS was: < 1 (25p – 13.4%); < 3 (111p – 59.6%); < 5 (42p – 22.5%); < 6 (8p – 14.5%). In the CABG we used: internal mammary artery (146p – 25.5%), the venous graft (426p – 74.5%) and the total number of the grafts was 572. Revascularization index (RVI) (RVS/ALS) was < 0.1 (108p); < 0.2 (44p); 0.3 (22p); < 0.4 (12p). The priority administration of cardioplegia solution after RVI: < 0.01-0.1 (anterograd); 0.1-0.2 (retrograde) and 0.2-0.4 (alternative). The inotrop effort after CABG was class: A (96p), B (59p), C (23p), D (8p). The Tei index and LVMSI are arise in the first 8 days after surgery and remain in the high values in special in the 1-3 days after CABG.*

Conclusions: *ALS, RVS, RVI are the important parameters for the evaluation of the cardioplegia strategy from the priority way of administration and this have an important influence upon the myocardial viability. IRV is the rapport RVS/ALS and is important marker for the strategy of revascularization and cardio-protection.*

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Introduction

The selection of the patients suitable for surgical revascularization is difficult due to the anatomical complexity of the lesions and because of this when quantifying the lesions we must take into consideration three important criteria: the inclusion of all patients in the study, agreement concerning the treatment and the complex coronary lesions. For these considerations the **SYNTAX** score (*SYNergy between PCI with TAXus and Cardiac Surgery*) was developed; it includes the coronarographic analysis of the most important factor witch is the anatomical lesions, simultaneously evaluating the revascularization opportunities.

The surgical revascularization strategies are evaluated according to the coronary anatomy, the coronarographic evaluation, the lesions complexity and the ss myocardial performance index. The definitory elements of the SYNTAX score are: the coronary dominance, the classification and the quantification of the coronary lesions based on the most important parameters: luminal diameter narrowing, total occlusion, bifurcation and trifurcation lesions, ostial stenosis, tortuosity, length, calcification, thrombus, diffuse lesions and vessel length.

Each lesion may contain one or more segments, so, each segment is analyzed and it contributes individually to the outcome of the global score. The individual characteristics of the lesion are quantified by the criteria that we reminded above and the principal that dominates this evaluation is: proximal lesions (stenosis or occlusion) are introduced in SYNTAX score with high grades. The quantification according to this global score system is important, not only to determinate the revascularization procedure (PCI or CABG), but it may also be used by new criteria (the revascularization score, the index of revascularization – parameters that haven't been analyzed untill now in other studies), as well as for the selection of the surgical revascularization strategy, from choosing the right type of graft to the myocardial protection tactics and the extracorporeal circulation.

Methods

A number of 186 patients were revascularized by CABG and the *anatomical lesion score* was analyzed (**ALS**) for each patient, than the theoretical *revascularization score* was calculated (**RVS**) and the myocardial protection strategy was selected according to these parameters.

We did the coronarographical assessment according to the SYNTAX score and we covered the analysis steps of coronarography according to the algorithm of this quantification: dominance, number of lesions, segments involved per lesion and lesion characteristics (total occlusion, bifurcation, trifurcation, ostial lesion, tortuosity, length > 20mm, calcification, difuse stenosis, small vessels).

ALS was calculated after coronarographical analysis and included all the algorithm elements.

Using these criteria we established the "***R****evascularization Score*" (RVS) that represents the theoretical possibility of quantified surgical revascularization, that is opposite proportioned to ALS, taking into account that the possibility of proximal grafting ensures a larger area of revascularization. We kept the segments numbering that are suited to revascularization and the defining elements of the SYNTAX score and we deduced RVS (figure 1, next page).

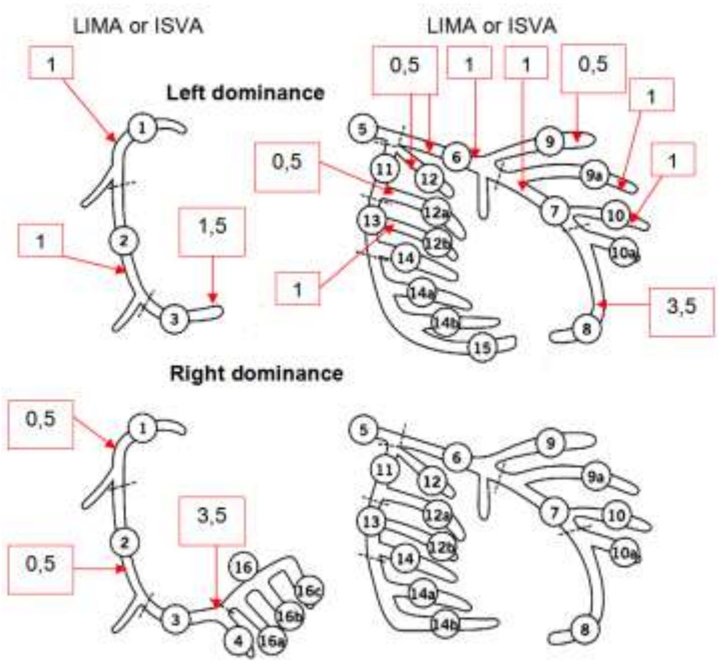

Figure 1: Revascularization score (RVS), the definition of coronary dominance segments and the importance of the revascularization (deduced from SYNTAX score)

The segments that are suited for grafting, calculated score and the graft structure (arterial or venous) and RVS for each segment are detailed in Table 1.

Table 1: ***Revascularization score*** **(RVS), the deduced from SYNTAX score inverted as value and adapted to the segments suited for grafting. (LIMA** – *left interna mammary artery;* **ISVA** - *inverted saphenous vein autograft*; **EL** – *end-lateral anastomosis*; **LL** – *lateral lateral anastomosis*)

Coronary artery	Segment suited for graft	Score (points)
LAD (Left Anterior Descending)	6	1
	7	1
	8	3.5
Diagonal 1. 2 (Dg1,2)	9,9a 10,10a	0.5 1
Circumflex artery (branches)		
Obtuse marginal 1 Obtuse marginal 2	12a 12b	0.5 1
Intermediate artery	12	0.5
Right coronary artery	1	0.5
	2	0.5
	3	1
	4	3.5
	16	3.5
Graft type and distal anastomosis	AMI	0.5
	AVSI	1
	EL	0.5
	LL	1

The revascularization index represents the proportion RVS/ALS.

The cardioplegic strategy was established according to anatomical and structural coronary lesions this way: antegrade (the aortic root), retrograde (in the venous sinus) and after distal anastomosis (figure 2, next page).

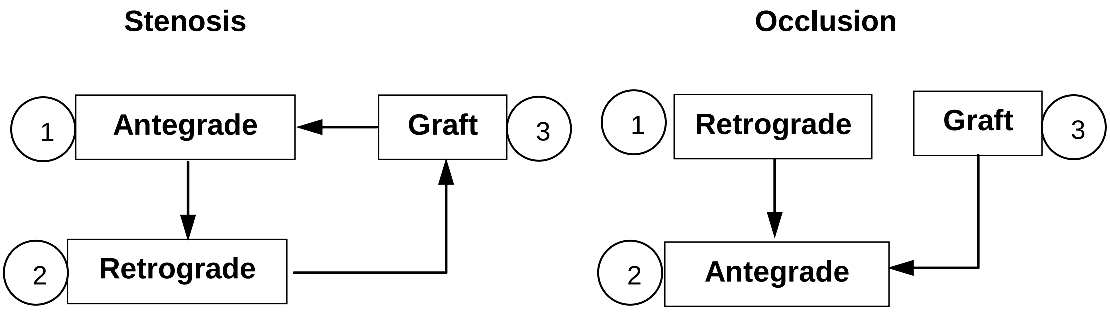

Figure 2: The cardioplegic administer strategy according to the lesions (stenosis/occlusion); 1, 2, 3 – the priority of the administer way.

For occlusive lesions the retrograde administer strategy of cardioplegic solution was initially retrograde.

We used St. Thomas cardioplegic solution which has the following composition: Na — 120 mmol/l, Cl – 160 mmol/l, K — 16 mmol/l, Ca — 1.2 mmol/l, Mg – 16 mmol/l, $NaCO_3$ — 10 mmol/l (27).

The quantification of the inotrop positive effort has been done on the scale A, B, C, D according to the number of inotrop positive agents, their concentration and circulatory assisting methods (figure 3).

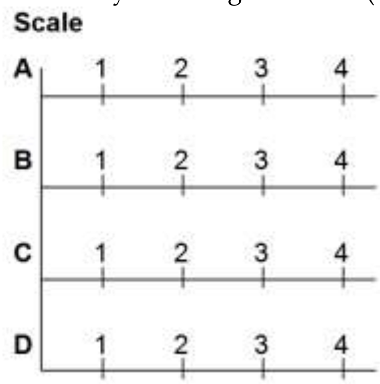

Figure 3: Inotrop positive effort scale: A – using a positive inotrop agent from minimum (1) to maximum (4); (2=50% from the highest dose, 3=75% from the highest dose); B and C - for double and triple medication; D – we used D when the C(4) necessary is not sufficient and the assisting methods are required: CEC D(4); IABP :1/1 (D3, 1/2 (D2); 1/3 (D3)

The myocardial performance was evaluated by the perioperatory echocadiography taking into account the systolic function (score index of the motion LVMSI and the systolic and diastolic performance – *Tei index*).

Results

By studying ALS for each patient, we observed the right dominance (RD) at 108 patients (56.9%) and left dominance (LD) at 80 patients (41.3%). The total score of all the patients is drawn in figure 4. The number and type of the executed graft are shown in figure 5. Their distribution per number of patients is shown in table 2.

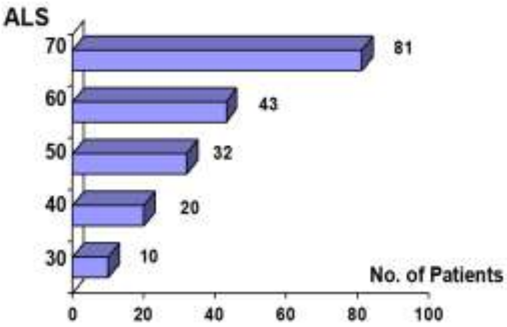

Figure 4. The anatomical lesion score [ALS] distribution for significant stenosis and total occlusion per number of patients

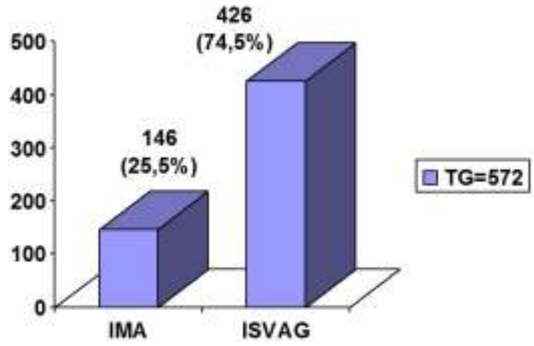

Figure 5: *Internal mammary artery* (IMA) using of the *total* number of *graft* (TG) and *inverted saphenous vein graft* (ISVAG) using

Tabel 2: The distribution of graft number per total number of patients (%)

Graft number	Patients number	Percent (%) of total number of patients	Total graft	No. graft / patient
1	4	2.15	4	1
2	46	24.73	92	2
3	76	40.86	228	3
4	52	27.95	208	4
5	8	4.31	40	5
Total	186	100	572	3.07

The revascularization index (IRV) values RVS/ALS - figure 6.

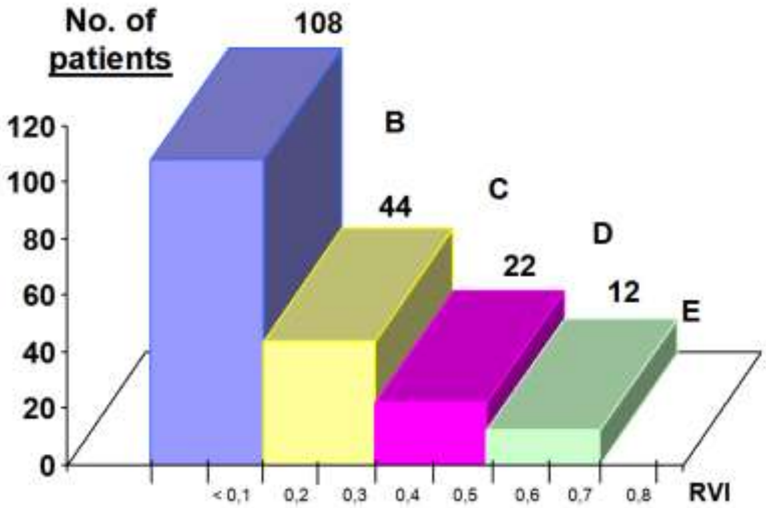

Figure 6:
The myocardial *revascularization index* (RVI) value of the number of patients and the surgical risk (A=*low*, B=*medium*, C=*medium-high*, D=*high*, E=*no option*)

The optimal administer way depends on the cardioprotection strategy. The interaction with RVI is shown in figure 7.

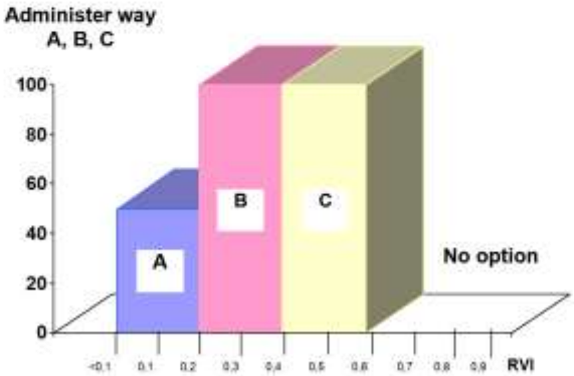

Figure 7: The antegrade (A), retrograde (B) and alternative (C) administer priority according to revascularization index

The connection between the number of grafts and cardioplegic necessary is shown in figure 8 and figure 9 (including the K overdose at bloody cardioplegy).

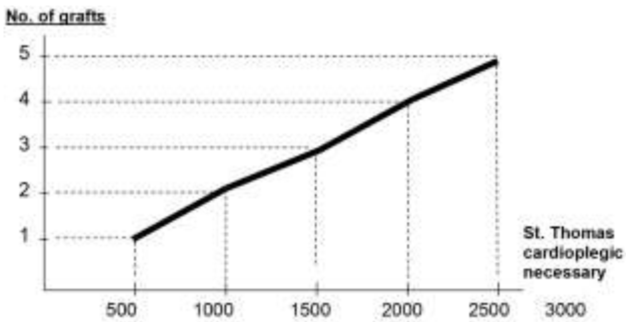

Figure 8: The connection between number of grafts and cardioplegic necessary

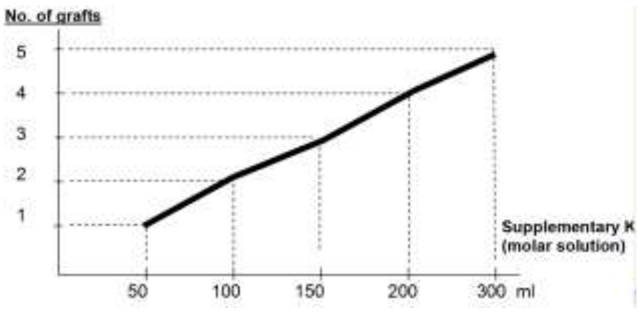

Figure 9: The connection between number of grafts and K necessary in cardioplegic solution

We took as myocardial viability marker the inotrop positive necessary effort. The way of using this parameter per number of patients is shown in figure 10.

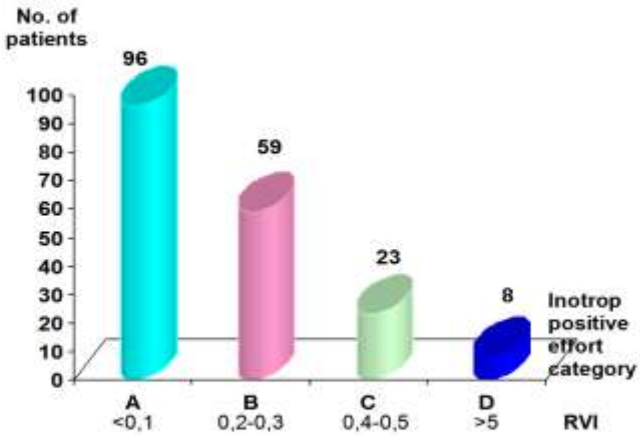

Figure 10: The number of patients distribution according to the inotrop positive necessary valued in scale A, B, C,D and myocardial revascularization index

We also used an echocardiographic parameter; the myocardial function was valued by the perioperatory and postoperatory echocardiography by Tei index and LVMSI index. The results are shown in figure 11 and figure 12.

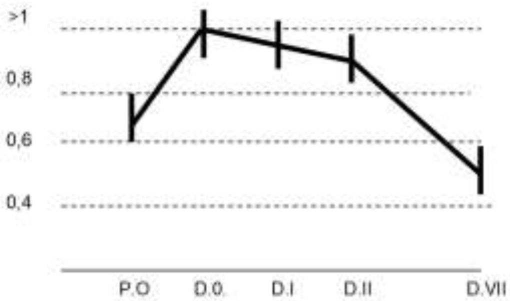

Figure 11: The relation between Tei index preoperatory (P.O.) and postoperatory

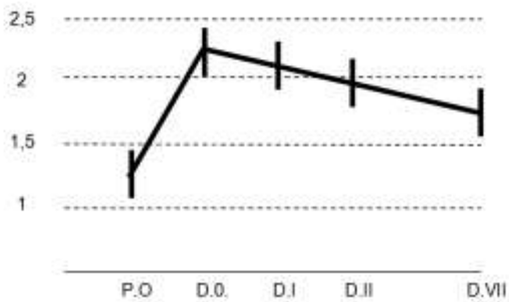

Figure 12: LVMSI: preoperatory and postoperatory assessment (D.O. = operatory day, D.I – D.VII = postoperatory days)

Discussions

In this study we did the lesion analysis in SYNTAX score, we also studied its relation with myocardial protection strategy according to RVI, as it represents a synthesis of those done before and above all it gives high value to the anatomical lesion structure and opens certain revascularization criteria.

The RVS is the most relevant element of CABG revascularization ways, mostly because it is easy to read. Thus a high ALS, the surgical revascularization provides a proximal anastomosis of venous or arterial graft which supposes a low RVS, according to opposite proportioned connection.

Using RVI in therapeutic decision and myocardial protection strategy we tried to establish its importance in revascularization decision starting with cardioplegy necessary assessment and ending with inotrop positive effort necessary assessment, in order to maintain the hemodynamic stability.

There is no equation to determinate ALS-number of grafts; still RVS and RVI depend both of anastomosis sequence and the necessary of grafts. More than that, this necessary is required by the cardioplegic solution sequence of administration.

The main idea in cardioplegic strategy is to make it intrude into all myocardial area, both into that with stages of stenosis or occlusion and into that which presents no intruding difficulties.

The strategy of cardioprotection was differently done by ALS, RVS, RVI parameters, both as sequence point of view and cardioplegic solution necessary. The optimal administration way was analyzed according to the same parameters so that the myocardial viability could be maintained while heart stop by intruding the cardioprotector into coronary artery, whatever the intruding way.

The cardioplegic necessary was different for the number of grafts: 3-4 grafts (2000-2500ml); 2-3 grafts (1000-1500ml); 1-2 grafts (500-1000ml).

The supplementary K dose was also accordingly with the number of grafts: 1-2 grafts (50-100ml); 2-3 grafts (100-150ml); 3-4 grafts (150-200ml), 4-5 grafts (200-300ml).

Taking into account the importance of ALS, RVS, RVI, we may say that there is a straight connection between RVI and inotrop positive effort. This is very important both as surgical strategy and cardioprotection and evolutive process.

The assessment of inotrop positive effort on A, B, C, D categories was very useful and the assessment of RVI at myocardial viability parameters, as well as choosing the proper medicine combination was required by the hemodynamic answer according to the criteria of maintaining the myocardial performance stability as an answer to the medication.

We studied the most representative echocardiographic parameters for segmentary kinetics, both for the systolic and diastolic component. The postoperatory heart performance gets to normal within 7 days, which shows that some other elements may be involved: inflammation, leucocitary activity, the spread of ischemical lesions.

Conclusions

There is a direct connection between lesion coronary anatomy and cardioprotection methods to preserve myocardial viability. This is very important in myocardial protection strategy from the point of view of administration way, grafts necessary, inotrop positive agent, as well as sequential surgical technical or "end-lateral".

RVI translates, if the revascularization is completed, the important element of CABG option, the cardioplegy necessary and postoperatory evolution.

The late heart performance revival asses by *Tei index* and LVSVM can be explained by complex phenomena which can be explained by studying myocardial ultrastructure.

Limitations

The anatomic-lesion assessment by SYNTAX score is to be clinically applied and its implementing as a alternative to the quantification of RVS and RVI hasn't been analyzed until now in other studies.

This phenomena can be explained by the fact that after revascularization of the LV segments which are in a state of pre-operatory hibernation or stunning maintain this state or are increased after revascularization.

The relationship between RVI and LVMSI wasn't conclusive because all the patients we studied had a slowly positively favorable hemodynamic evolution; this may be explained by the fact that after revascularization some LV segments have improved cardiac performance and others were decisive.

We may also explain this discordance by the fact that *Tei index* is synthesis of the systolic and diastolic LV function and the quick comeback post-CABG is probably caused by the systolic function, while slowly reversible LVMSI can be explained by the persistence of the diastolic dysfunction.

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Assessment of myocardial revascularization effects at patients with ventricular arrhythmias and coronary artery disease*)

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Abstract

Introduction: *Coronary artery disease (CAD) is one of the most commune causes of ventricular arrhythmias. Frequent association between ventricular arrhythmias and arrhythmogenic sudden death in CAD create therapeutically aspects not elucidated yet.*

Objectives: *The aim of study was to determine the relations between myocardial revascularization therapy - coronary artery bypass graft (CABG) and coronary angioplasty (PTCA) - and ventricular potential malign arrhythmia (VPMA) (cuplated VPC, VPC > 10/hour, NSVT - Morganroth classification), in patients (pts) with stabile CAD.*

Methods: *765 patients with stabile angina and ventricular potential malign arrhythmia were evaluated angiocoronarographic, echographic, programmed electrical stimulation (PES), standard ECG, Holter ECG, radiologic, and stress test. From 765 patients with CAD and VPMA 169 pts. (22.9% from cases) were revascularizated, 77 pts. (10.06% from cases) CABG surgery and 82 pts. (10.71% from cases) PTCA with or without stenting.*

Results: *Pts. with inducible sustained ventricular tachycardia by programmed electrical stimulation PES + (129 pts., 16.86% from cases) 19 pts.(2.5% from cases) CABG vs 9 pts. (1.17% from cases) with PTCA (p > 0.05). In 333 pts., with arrhythmogenic myocardic ischemia detected by Holter ECG/24 hours (Holter +) the distribution of myocardial revascularization was similar (40 pts., 5.22% from cases with CABG vs 46 pts., 6.01% from cases with PTCA) (p > 0.05). The study included 225 pts. with positive stress test, 45 pts. was revascularizated , 18 pts. (2.35% from cases) with CABG and 27 pts. (3.52% from cases) with PTCA (p > 0.05). Revascularizated pts. represent an increased percent with prior myocardial infarction in subgroup with CABG vs. PTCA (39% from cases, p < 0.05 vs. 25% from cases, p<0.05). Revascularizated pts. presented similar distributions of VPMA in subgroups with CABG and PTCA.*

Conclusions: *VPMA was not influenced by myocardial revascularization, CABG or PTCA, the incidence being similar (50.94% vs 47.2%; p < 0.05) with pts. medicaments treated.*

Keywords: *Coronary artery disease, ventricular potential malign arrhythmia, myocardial revascularization therapy*

*) **Romanian Journal of Cardiovascular Surgery ■ 2008, vol. 7, no. 3, pp. 173-174**

Introduction

Coronary artery disease (CAD) is one of the best known causes of ventricular arrhythmias. In Romania was found an increase of CAD in period 1976-1996 with a plateau evolution in the last 7 years.

It is considering that the prevention effort and therapeutically methods development determinates this evolution (1).

Numerous effectuated studies demonstrate the frequent association between ventricular arrhythmias and arrhythmogen sudden death in patients with CAD, remaining a lot of evolutive and therapeutically unknown aspects.

Objectives

The aim of study was to determine the role of myocardial revascularization therapy - coronary artery bypass graft (CABG) and coronary angioplasty (PTCA) - and ventricular potential malign arrhythmia (VPMA) (couplated VPC, VPC > 10/hour, NSVT - Morganroth classification (1), in patients (pts) with stabile CAD.

Methods

765 patients with stabile CAD and VPMA were evaluated angiocoronarographic, echographic, programmed electrical stimulation (PES), standard ECG, Holter ECG, radiologic, and stress test. From 765 patients with CAD and VPMA 169 pts. (22.9% from cases) were revascularizated, 77 pts. (10.06% from cases) CABG surgery and 82 pts. (10.71% from cases) PTCA with or without stenting (Table 1).

The inclusions criteria in study lot was: presence of myocardial ischemia clinical and paraclinical diagnosticated (stress test, Holter ECG, echocardiography), coronary atherosclerotic lesions evidentiated by angio-coronarography, presence of VMPA, NYHA I-II cardiac insufficiency.

The exclusions criteria for study lot were: acute coronary syndrome, maligned ventricular arrhythmias, atrial fibrillation, valvulopaties, pericardities, cardiac congenital disease, myocardities, documented dilative cardiomyopaties, and patient's noncompliance.

Statistic analysis was made registering all the data in a base *EPI INFO* format.

Was calculated: medium values, standard deviations, proportions or percents for qualitative characteristics and the correlations from this indicators.

According with p-values we considered: 0.01 < *p-value* < 0.05 – statistically significant, 0.001 < *p-value* < 0.01 –very statistically significant and *p-value* < 0.001 – high statistical significance.

Results

Basal clinical and paraclinical characteristics of revascularisated pts. is presented in Table 1.

The medium age was 56, limits between 41 and 72.77% males.

Table 1: Revascularisated pts. characteristics

	CABG (N=77)	PTCA (N=82)	*p*
Sex (males)	56 (73%)	62 (76%)	> 0.05
Age (years)	55 ± 8.3	53 ± 7.9	> 0.05
Diabetus (%)	15 (19%)	14 (17%)	> 0.05
Arterial hypertension	34 (44%)	34 (41%)	< 0.05
Prior myocardial infarction	30 (39%)	20 (25%)	< 0.05
Smokers	32 (41%)	32 (39%)	< 0.05
Dislipidemy (nr./% pts.)	37 (48.5%)	41 (49.9%)	> 0.05
Total Cholesterol	223.9 ± 38.6	221.4 ± 38.6	> 0.05
LDL – cholesterol	132.7 ± 31.6	130.5 ± 33.4	> 0,05
HDL – cholesterol	40.7 ± 8.7	40.7 ± 9.8	> 0.05
Triglycerides	199.7± 78.3	197.9± 83.6	> 0.05
ECG characteristics			
QT > 440 ms	18 (23%)	16 (20%)	> 0.05
QTc > 440 ms	20 (26%)	20 (25%)	> 0.05
Unda Q	28 (37%)	18 (22%)	< 0.05
FEVS (%) medium	43 ± 4.8	49 ± 5,6	< 0.05
Akinesy	29 (37%)	27 (33%)	< 0.05
Hipokynesy	38 (49%)	39 (51%)	> 0.05
Nitrates	52 (68%)	54 (66%)	> 0.05
Beta-blockers	29 (38%)	30 (37%)	> 0.05
Calcium channel blockers	10 (13%)	13 (16%)	> 0.05
ACE inhibitor	38 (49%)	34 (41%)	< 0.05
Diuretics	29 (38%)	33 (40%)	> 0.05
Aspirin	47 (61%)	70 (85%)	< 0.05

The results shows that pts. with inducible sustained ventricular tachycardia by programmed electrical stimulation PES + (129 pts., 16.86% from cases) 19 pts. (2.5% from cases) CABG vs 9 pts. (1.17% from cases) with PTCA ($p > 0.05$).

In 333 pts., with arrhythmogenic myocardic ischemia detected by Holter ECG/24 hours (Holter +) the distribution of myocardial revascularization was similar (40 pts., 5.22% from cases with CABG vs 46 pts., 6.01% from cases with PTCA) ($p > 0.05$).

The study included 225 pts. with positive stress test, 45 pts. was revascularizated, 18 pts. (2.35% from cases) with CABG and 27 pts. (3.52% from cases) with PTCA ($p > 0.05$).

An important subgroup study lot is represented by pts. with prior myocardial infarction CABG vs. PTCA (39% from cases, $p < 0.05$ vs. 25% from cases, $p < 0.05$).

Revascularizated pts. presented equivalent distributions of medicament therapies in subgroups with CABG vs. PTCA with exceptions of Aspirin (85% from cases of PTCA vs. 61% from cases of CABG; $p < 0.05$) and ACE inhibitors (49% from cases with CABG vs. 41% from case of PTCA; $p < 0.05$).

Table 2: Configuration of myocardial revascularization pts. from study group

Study group (N = 765 b)	CABG (N = 77)	PTCA (N = 82)	Without revascularization (N = 527)	*p*
PES + (129 b)	19 (24.6%)	9 (10.9%)	100 (18.9%)	< 0.05
Holter + (333 b)	40 (51.9%)	46 (6.01%)	247 (46.8%)	< 0.05
VPMA + (75 b)	9 (11.6%)	14 (17.0%)	52 (9.8%)	< 0.05
VPMA - (258b)	31 (40.2%)	32 (39.0%)	195 (37.0%)	< 0.05
Stress test + (225b)	18 (23.3%)	27 (31.9%)	180 (34.1%)	< 0.05
VPMA + (75 b)	6 (7.8%)	11 (13.4%)	58 (11.0%)	< 0.05
VPMA - (150b)	12(15.6%)	16 (19.5%)	122 (23.1%)	< 0.05

Revascularizated pts. presented similar distributions of VPMA in subgroups with CABG and PTCA (CPV > 30 hour; 15 pts.-19.5% from cases vs. 21 pts. 25.6% from cases; CPV cuplated 11 pts., 14.3% from cases vs. 18 pts., 21.9% from cases and NSVT in 5 pts., 6.5% from cases vs. 11 pts., 13.4% from cases), see Table 3.

Table 3: VPMA distribution in revascularizated pts.

Study group (N = 765 b)	Revacularizated (N = 159)		Nonvascularizated (N = 527)	*p*
	CABG (N = 77)	PTCA (N = 82)		
CPV > 30 hour	15pts. (19.5%)	21pts. (25.6%)	105pts. (19.9%)	< 0.05
CPV cuplated	11pts. (14.3%)	18pts. (21.9%)	85pts. (16.1%)	< 0.05
NS-VT	5pts. (6.5%)	11pts. (13.4%)	59pts. (11.2%)	< 0.05

Results evidentiated that VPMA wasn't influenced by myocardial revascularization therapy CABG or PTCA the incidence of VPMA being close with that of pts. that received medicament treatment (50.94% vs 47.2%; $p < 0.05$).

Conclusions

Evaluating surgical myocardial revascularization or interventional coronarian procedures in 159 pts. with stabile CAD, we show that VPMA was not influenced by myocardial revascularization therapy - CABG or PTCA, the incidence being similar (50.94% vs 47.2%; $p < 0.05$) with 527pts. medicamentos treated.

This study illustrated in accordance with several studies that an important arrhythmogenic factor is postmyocardial infarction scars associating with acute myocardial ischemia.

Discussions

CASS study investigated the myocardial revascularisation impact by aortocoronarian bypass and described that pts. with trivascular coronary disease has survive at 5 years was 98% for CABG and 94% for pts. with medical treatment [2].

CASS study conclusions was in concordance with those communicated by *Wyse D* in which myocardial revascularization represents a treatment generally accepted for acute ischemia but the role in the secondary prevention of complex ventricular arrhythmias is in controversy [3]. In accordance with observations of *Kron, I.L. and colab* in the presence of acute ischemia as the isolate cause of the apparition of ventricular arrhythmias, myocardial revascularization was proofed benefic in the case of unicoronarian severe lesions [4].

In the presence of other arhythmogenic factors, like postmyocardial infarction scare it isn't probable to realize complete protection [5].

Pts. with post-myocardial infarction scars, acute ischemia and frequent spontan or inducible NS-VT, myocardial revascularization therapy must be combined with AICD implantation. *CABG patch study* observed that pts. with post-myocardial infarction scars, acute ischemia must be an important arrhythmogenic factor, this aspect explaining the missing of the benefit of AICD implantation at pts. with surgical myocardial revascularization. Preventive effects of CABG are important in pts. with trivascular, proximal severe, left main coronary lesions associating with important myocardial dysfunction [7, 8].

Observational studies suggest that pts. with complex ventricular arrhythmias after recent myocardial infarction are not influenced by myocardial revascularization therapy. Myocardial revascularization therapy is not preventing cardiac arrest in pts. with left ventricular dysfunction even ventricular arrhythmias appeared with transitor myocardial ischemia [6].

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Evaluation of perioperative stroke in patients undergoing coronary artery bypass graft (CABG) surgery*)

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Abstract

Introduction: *Severe atherosclerosis of the ascending aorta or aortic arch is associated with increased risk of perioperative stroke for patients undergoing coronary artery bypass graft (CABG) surgery.*

Objectives: *The aim of study was to determine the relations between the severity of the aortic atheroma and perioperative risk of neurological complications after CABG.*

Methods: *378 patients undergoing CABG was investigated by trans-esophageal ehocardiography (TEE) with 17.4% patients found to have severe atheroumatos aortic disease in the aortic arch or ascending, tranverse, and descending aorta. The degree of atherosclerotic disease was graded according to the system developed by Katz grade 1 = absence of significant disease, grade 2 = extensive intimal thickening, grade 3 = sessile atheroma < 4 mm thick, grade 4 = protruding atheroma > 4 mm, and grade 5 = mobile atheroma.*

Results: *Analysis revealed that increased mortality was associated with acute MI (P = 0.04), number of grafts (P = 0.02), age (P = 0.02), history of stroke or cerebrovascular disease (P = 0.03), Cronic Heart Failure (P = 0.02), and peripheral vascular disease (P = 0.02). These findings stratify patients for neurologic risk and guide operative management. Off-pump coronary artery bypass technique was associated with decreased stroke (P = 0.05), with lower rates of post-operative atrial fibrillation, and a shorter duration of hospitalization.*

Conclusions: *CABG surgery in patients with severe atheroumatos aortic disease is associated with risk for neurological complications. The TEE has been shown to be a precise way of estimating the degree of atherosclerotic disease of the aortic arch and directs alternative of suitable surgical technique that keeps away from any manipulation of the ascending aorta - off-pump coronary artery bypass.*

Keywords: *coronary artery bypass graft surgery, transesophageal echocardiography, atheroumatos aortic disease, stroke, off-pump coronary artery bypass*

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Introduction

Severe atherosclerosis of the ascending aorta or aortic arch is related with augmented risk of perioperative stroke for patients going through coronary artery by-pass graft (CABG) surgery. The severity of the aortic atheroma was estimated by transesophageal echocardiography (TEE) and was related to the perioperative risk of neurological complications after CABG. Each patient is evaluated and graded for the presence of atheroma in the ascending, transverse, and descending aorta.

Objectives

The aim of study was to determine the relations between the severity of the aortic atheroma and perioperative risk of neurological complications after CABG. This study was deliberated to stratify patients for neurological risk and direct operative management.

Methods

378 patients undergoing CABG was investigated by transesophageal ehocardiography (TEE) with 17.4% patients found to have severe atheroumatos aortic disease in the aortic arch or ascending, transverse, and descending aorta. The degree of atherosclerotic disease was graded according to the system developed by Katz grade 1 = absence of significant disease, grade 2 = extensive intimal thickening, grade 3 = sessile atheroma < 4 mm thick, grade 4 = protruding atheroma > 4 mm, and grade 5 = mobile atheroma.

Results

Patients who underwent CABG were matched by age, ejection fraction, history of stroke, cerebrovascular disease, diabetes, renal disease, nonelective operation, and previous cardiac surgery (table 1).

Table 1: Patient characteristics in the study group

	All Patients N (%)
Number of patients	378
Mean Age (yrs) ± SD	54 ± 8.67
Urgent or emergent operation	243 (64.3%)
Renal disease	41 (10.9%)
Stroke or cerebrovascular disease	72 (19.2%)
Age ≥ 80 y	16 (4.4%)
EF ≤ 30%	55 (14.5%)
Previous M.I.	272 (72.2%)
Male gender	234 (62.7%)
PVD	138 (35.9%)
Previous cardiac operation	35 (9.3%)
Diabetes	79 (20.8%)
COPD	60 (16.1%)
Preoperative IABP	14 (3.4%)
CHF	106 (28.2%)

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; IABP, intra aortic balloon pump; MI, myocardial infarction; OPCABG, off pump coronary artery bypass; PVD, peripheral vascular disease.

From intra-operative and postoperative data between the conventional CABG and OPCAB patient groups we find appreciably lower incidences of stroke was noted in the OPCAB group. Stroke takes place in 4.9% of the conventional CABG patients and in 1.4% of the off-pump coronary artery bypass patients (P = 0.08). Off-pump coronary artery bypass technique was associated with decreased stroke (P = 0.05), with lower rates of postoperative atrial fibrillation, and a shorter duration of hospitalization.

Risk factor analysis for all patients in both groups demonstrated that age ≥ 70, renal disease, CHF, history of stroke or cerebrovascular disease, peripheral vascular disease, and ejection fraction < 30% were associated an increased risk of hospital mortality. Analysis revealed that increased mortality was associated with acute MI (P = 0.04), number of grafts (P = 0.02), age (P = 0.02), history of stroke or cerebrovascular disease (P = 0.03), Chronic Heart Failure (P = 0.02), and peripheral vascular disease (P = 0.02). These findings stratify patients for neurological risk and guide operative management.

Table 2: Comparison of intraoperative and postoperative data between CPB-CABG and OPCAB groups

	CPB-CABG (n = 65)	OPCAB (n = 65)	*P* value
Bypass time (min) ± SD	107.6	NA	
Cross clamp time (min) ± SD	57.6	NA	
Hospital mortality (%)	11.4%	3.8%	0.003
Number of grafts	2.84 ± 0.82	1.4 ± 0.83	< 0.001
Re-operation for postoperative bleeding (%)	5.7%	0.6%	0.01
New renal failure (%)	3.5%	3.1%	0.79
Mechanical ventilation >24 hour (%)	8.6%	4.1%	0.03
GI bleeding	1.9%	1.9%	1.00
Stroke	4.9%	1.4%	0.08
Complication free (%)	78.7%	194 (91.9%)	<0.001

Discussions

Atheromatous disease of the aorta has been recognized as an autonomous risk factor for stroke and mortality associated with traditional cardio-pulmonary bypass CABG. (1) Important decreases for off-pump coronary artery bypass in post-operative morbidity, in the elderly were reported by a group from Harefield, England. (2) Additional studies that did not center on high risk factions (elderly, previous neurological event, re-operation or impaired LV function) did not show a decrease in stroke rate with off-pump coronary artery bypass. (3) Limitations of the study were the fear that disease in the distal ascending aorta was not completely estimated by TEE, nonrandomized approach by diverse surgeons of the appliance of the off-pump coronary artery bypass technique over the time period of this study and differential number of distal bypass grafts in the patient groups.

Conclusions

CABG surgery in patients with severe atheroumatos aortic disease is associated with risk for neurological complications. The TEE has been shown to be a precise way of estimating the degree of atherosclerotic disease of the aortic arch and directs alternative of suitable surgical technique that keeps away from any manipulation of the ascending aorta – off-pump coronary artery bypass. The current study demonstrates that off-pump operations in patients with severe atheromatous aortic disease were linked with a lower risk of stroke, when balanced with risk patients undergoing traditional cardio-pulmonary bypass.

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Early extubation in the O.R. after coronary artery bypass graft surgery: indications, rezults and costs/benefits ratio*)

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Abstract

The goal of our study was to evaluate whether the early extubation in the operating room (E.E.O.R.) after coronary surgery (CABG) would provide cardiorespiratory and metabolic stability, without significant complications in the postoperative period. In this study were included twenty patients; all the patients were extubated in the operating room at end of the surgical procedure and MAP, HR, SaO_2, PaO_2, $PaC0_2$, pH and SvO_2 were measured at different moments: before extubation, soon after extubation, in the ICU, 1 hour and 6 hours after extubation. Data were computed using the t-test and the sign test ($p < 0.05$). SaO_2, PaO_2 and SvO_2 significantly decreased immediately after extubation, remaining within physiological limits and the significantly improved in the next 6 hours. $PaC0_2$, MAP and HR had no significant variations. No patient was reintubated for cardiac, respiratory or bleeding reasons. Our study suggests that E.E.O.R. is safe in correctly selected CABG patients without any serious complication related to it.

Introduction

Early extubation (< 8 hours after cardiac surgery) or "fast-track" technique is a method already well known as being safe from the medical point of view, and efficient from the economically point view (costs/benefits ratio) (1, 2) if it is used on patients selected after clearly defined criteria (3).

However, there is a lack of studies dedicated to the early extubation in the operating room technique in the literature, this being a reason for which the technique is not widely spread in the clinical practice, despite the fact the technique has an increasingly number of advocates.

Materials and Methods

In our study were included twenty patients who were proposed for open heart surgery for CABG, patients from the 1st and the 2nd Cardiovascular Surgery Clinics of the *Institute of Cardiovascular Diseases "Prof. C. C. Iliescu" from Bucharest.*

In the day prior to operation, at the pre-anesthesia exam, the patients fulfilling the including criteria of our study (criteria which will be summarized in the next section) were informed about our intention to include them in the study group, about the potential benefits of the technique, and about the fact that the technique is not universally accepted.

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In the study were included only the patients who gave their consent.

Including criteria

In our study were included only the patients who underwent CABG surgery and fulfilled the following criteria:

a) *Left ventricular ejection fraction (LVEF) > 50%.*
b) *Higgins score < 4.*

a. We included from the patients with coronary artery disease only those with a LVEF higher or at least equal to 50%, therefore with a good left ventricle function prior to CABG, assuming that awakening from anesthesia and the spontaneous breathing recovery requires an additional sparing of energy. All that additional energy spared, characteristically required for the awakening period, requires the augmentation of the oxygen delivery (DO2). The DO2 augmentation is made by cathecolaminergic stimulation, which increases the heart rate (HR) and the level of the inotropic state. On the other side, HR and the inotropic state are major determinants of the myocardial oxygen consumption (MVO2), therefore the prerequisite for the myocardial energy balance to remain in a steady state is that the coronary circulation has not significant disturbances. Therefore the awakening period major requires are a good coronary bed function and a myocardium able to adequately react to the sympathetic stimulation.

We assumed that all major problems of the myocardial vascularization will be resolved by the surgical procedure, and if we include patients with a good contractile function prior to surgery there will be provided all the cardiac requirements to adapt at the awakening period and spontaneous breathing recovery.

Left ventricular ejection fraction was assessed by angiography and/or echocardiography. We considered that LVEF it is for sure above 50% when at least one of the assessment methods mentioned above found values of 50% or higher and when the difference between LVEF values obtained with both methods was not higher then 5%.

There were excluded from the study all the patients with a left ventricular aneurysm.

b. Higgins score < 4.

The second including criterion was a general score of preoperative gravity. We chose the score proposed by T.L. Higgins in 1996 for selecting the patients for the "fast-track" technique programs, and consisting from the following criteria (3):

Emergency surgery	6
Blood creatinine > 1.9 mg%	4
Blood creatinine between 1.6 and 1.9 mg%	1
Severely impaired left ventricular function	3
Cardiac surgery procedures before	3
Mitral regurgitation	3
Age above 75 years	2
Age between 65 and 75 years	1
Compensated COPD	2
Hematocrit < 34%	2

Aortic stenosis	1
Weight < 65 kg	1
Compensated diabetes mellitus	1
Neurological disorders	1

Up to this score can be included in an early extubation program only the patients with a score bellow or at most equal to 4.

Therefore we included in our study 20 patients with coronary artery disease who were informed about the study and consented to be included, patients with a LVEF > 50% and with a preoperative gravity Higgins score < 4.

Anesthesia protocol

All the patients were pre-medicated with morphine sulfate 0.1 meg / 10 Kg BW via intramuscular route.

In the OR just after the arrival is administered oxygen trough a face mask and it is started the monitoring of the patient, ECG with a five leads cable, being displayed D II and V5 derivations, NIBP, pulse oximetry, catheterization of a peripheral vein and of the left radial artery, and, after the induction of anesthesia, the placement of a pulmonary artery catheter Swan-Ganz type for measuring: pulmonary capillary wedge pressure (PCWP), pulmonary artery pressure (PAP), central venous pressure (CVP), cardiac output (CO), and SvO_2 values by sampling some blood from the pulmonary artery and analyzing with the blood gases measurement device.

Induction of anesthesia was made the following trough a peripheral vein: Fentanyl 7 mg / Kg BW + Midazolam 0.1 mg / kg BW + Atracurium 0.6 mg / kgBW.

Maintenance of the general anesthesia was made with:

- Propofol 4 - 8 mg/Kg BW/h before cardiopulmonary bypass and 3 mg/Kg BW/h during and after cardiopulmonary bypass.
- Atracurium 0.4 mg / Kg BW / h before and after cardiopulmonary bypass, and 0.8 mg / Kg BW / h during cardiopulmonary bypass.
- Isoflurane.

Within 20-30 min before the sternum closure it is stopped the administration of Propofol and Atracurium and the Isoflurane administration is stopped when it is started the skin suture.

After the cessation of propofol infusion it was given 3 mg / kg BW of Tramadol in 20 minutes for providing postoperative analgesia.

It was also given ranitidine 100 mg i.v. for preventing the occurrence of stress ulceration of the stomach and duodenum.

Meanwhile, in the time ranged between sternum closure and skin dressing is made a complete assessment of the patient state in order to identify the potential pathological circumstances that prevent early extubation in the OR.

For that reason are made the following assessments:

a. hemodynamic assessment:

- all the ECG are displayed for identifying myocardial ischemia;
- evaluation of the following hemodynamic parameters:
  - systolic arterial pressure (SAP);

- diastolic arterial pressure (DAP);
- mean arterial pressure (MAP);
- right atrium pressure (RAP);
- pulmonary capillary wedge pressure (PCWP);
- pulmonary artery pressures;
- cardiac output (CO);
- cardiac index (CI);
- systemic vascular resistance (SVR);
- pulmonary vascular resistance (PVR);

- hourly urinary output.

b. ***Metabolic, water and electrolytes assessment:***

- Arterial blood gases analysis: PaO_2, $PaCO_2$, pH, HCO^{3-}, BE;
- Mixed venous blood analysis: SvO_2;
- Serum lactate level;
- Blood glucose level;
- Blood Na^+, K^+, CI, and ionized calcium.

c. ***Hematological assessment: Hb, Ht, ACT (activated clotting time);***

d. ***Bleeding trough drainage tubes evaluation.***

e. ***Measurement of the esophageal and rectal temperature.***

For continuing the protocol of early extubation we assumed that are required the following:

- Absence of any signs of ischemia on ECG;
- Absence of tachycardia (HR > 100 b/min);
- Absence of bradicardia (HR < 60 b/min);
- Absence of any rhythm and conduction abnormalities;
- SAP > 100 mm Hg and 60 mm Hg < MAP < 105 mm Hg;
- PCWP < 18 mm Hg and/or RAP < 9 mm Hg.
- CO > 4 1/min and/or CI > 2.4 1/min/m^2;
- SvO_2 > 70%;
- Absence of the metabolic acidosis;
- Serum lactate level < 20 mg%;
- Ht > 30% and/or Hb > 10 g%;
- ACT < 130 seconds;
- Serum electrolytes and glucose within normal limits;
- Absence of a major bleeding trough the drainage tubes;
- Rectal temperature > 36,5°C;
- No other inotropes than dobutamine 10 meg/Kg BW /min.

If the criteria from above are fulfilled the protocol is continued. At the end of the surgical procedure the patient is awakening in a mean period between 2 and 12 minutes after the skin dressing, and begins the respiratory function recovery.

We assumed that the spontaneous breathing is efficient if are found the following values:

- PaO_2/FiO_2 ratio > 100 and/or PaO_2 > 80 mm Hg;
- SaO_2 > 95%;
- pH > 7.3;
- $PaCO_2$ < 50 mm Hg;
- Tidal volume > 5 ml / kg BW;
- 10/min < respiratory frequency < 25/min;
- hemodynamic stability;

Method used for collecting and processing the data

If the criteria mentioned above are fulfilled, hemodynamic parameters (HR, MAP), metabolic (SvO_2), blood gases (pH, PaO_2, SaO_2, $PaCO_2$), absence or presence of the pain are written in the patient chart for the moment T_0 (prior to extubation).

Then the patient is extubated and is receiving O_2 trough a face mask. After that is transported to the ICU.

At the moment of arrival in the ICU the patients are reassessed and the same parameters are recorded for the moment T_1 (soon after extubation).

The same parameters are recorded and written in the chart at one hour after extubation (T_2) and six hours after extubation *(T_i)* (see the chart below).

For all the twenty patients was followed this protocol.

The goal of the study was to evaluate the safety of the early extubation in the OR technique applied to the patients who underwent myocardial revascularization under cardiopulmonary bypass.

Patient…. …….. study chart / EEOR

	pH	**PaO_2 $PaCO_2$**	**HR MAP**	**SaO_2**	**SvO_2**
T_0 (prior to extubation)					
T_1 (soon after extubation, in the ICU)					
T_2 (1 hour after extubation)					
T_3 (6 hours after extubation)					

- data obtained were collected in charts made for every parameter: MAP, HR, PaO_2, $PaCO_2$, SaO_2, pH, SvO_2, for each moment being calculated the average value and the standard deviation. Statistical analysis was made with t-test and sign test ($p < 0.05$).
- there was considered "events" and selected and analyzed in consequence the following circumstances:
    - HYPOXEMIA (SaO_2 < 90%);
    - HYPERCAPNIA ($PaCO_2$ > 46 mm Hg);
    - ACIDOSIS (pH < 7.35);
    - SvO_2 < 65%.
- The length of ICU stay was analyzed alone and the data obtained are: 31.2 ± 1.05 hours or 1.6 ± 0.02 days.

Results

In the following table 1 are the results obtained from the measuring of each parameter studied in relation with the postoperative moment.

Table 1

	T_0 (prior to extubation)	T_1 (prior to extubation)	T_2 (1 hour after extubation)	T_3 (6 hours after extubation)
MAP (mm Hg)	87.4 ± 10.8	90.4 ± 9.9	88.4 ± 13.3	79.1 ± 20.2
HR	101.2 ± 8.9	101.4 ± 9.2	96.6 ± 12.5	95.1 ± 13.1
SaO_2 (%)	98.7 ± 1 (*)	97.1 ± 2.7 (**)	97.1 ± 2.4 (**)	98.7 ± 1
PaO_2 (mm Hg)	255.9 ± 126 (*)	154 ± 93.5 (**)	149.1 ± 83 (**)	183.8 ± 65.4
$PaCO_2$(mm Hg)	43.3 ± 4.9	45.5 ± 4	44.6 ± 4.9	44.9 ± 4
SvO_2 (%)	72.5 ± 4.2 (*)	67.2 ± 4.9 (**)	69.6 ± 6.1	75.6 ± 3
pH	7.35 ± 0.05	7.33 ± 0.05 (**)	7.35 ± 0.04	7.37 ± 0.04

Values are expressed as mean value ± standard deviation;
(*) $p < 0.05$ T_1vs. T_0;
(**) $p < 0.05$ T_3 vs. T_l and T_3 vs. T_2

After the statistical analysis of the variation of the parameters from the table it can be seen that: Immediately after the extubation (Tl) there is a statistical significant decrease of the values of the PaO_2, SaO_2 and SvO_2 beside the values measured prior to extubation (To). However, this decrease of the values of the parameters that express blood oxygenation and of the values of SvO_2 has no clinical relevance, this values remaining between normal limits.

The subsequent evolution of these parameters (PaO_2, SaO_2, SvO_2) and, in addition, of the pH shows a significant improvement in the next six hours after the extubation (T_3 vs. T_i and T_3 vs. T_2). So, the mild acidosis that appears soon after extubation (T_l) it correct itself fast (in one hour after extubation - T_2 -) and progressively (normal values at six hours after extubation - T_3 -). There were no statistical significant variations of the heart rate (HR), mean arterial pressure (MAP) and $PaCO_2$ in our study. From the point of view of the clinical circumstances named by us "events", their occurrence was:

- HYPOXEMIA ($SaO_2 < 90\%$): 2 episodes at the same patient;
- HYPERCAPNIA ($PaCO_2 > 46$ mm Hg): 22 episodes at 11 patients;
- ACIDOSIS (pH < 7.35): 26 episodes at 12 patients;
- $SvO_2 < 65\%$: 3 episodes at 3 patients.

Those events identified in our study had a clinical relevance only in the case of one patient who developed an episode of atrial fibrillation in the circumstances that he associated simultaneously 3 "events": hypoxemia + acidosis + diminished SvO_2.

Considering the clinical course of the patients from the group of this study, none of them was reintubated for any cardiac or respiratory causes or for major postoperative bleeding. The patients with coronary artery disease who underwent "fast track" technique had a length of stay in the ICU significantly shorter (31.2 hours or, in days -

1.6) than the other patients from the same period who received a "conventional" anesthesia (48,3 hours respectively 2.8 days), therefore diminishing the costs of staying in the ICU.

Conclusions

1. Early extubation in the OR after general anesthesia with propofol is an anesthesia technique which can be also used in the coronary artery surgery, considering the following requirements:
   - An anesthesia and intensive care team (doctors, nurses, etc.) skilful and trained, and able to provide professional support for a "fast track" program.
   - A surgical team able to support by the means of a quick and accurate procedure a "fast track" program.
   - A perfect collaboration between those two teams, concerning the protocol and the patients selection criteria.
2. Our study suggests that EEOR in coronary artery surgery applied on the patients accurate selected is a safe technique, without any specific complications, and does not generate any additional risk factors of perioperative morbidity or mortality.
3. EEOR in coronary artery surgery, at least in our study, it proved to be a significant way for shortening the length of stay in the ICU and, consequently, for diminishing the costs per acta.
4. Both the EEOR and the conventional early extubation (< 8 hours postoperative) are two important ways to fulfill the desideratum of improving the costs/benefits ratio of the medical act: "TO DO MORE WITH LESS".

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Myocardial bridge: clinical review and anatomical study*)

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Abstract

Myocardial bridging still represents a debated entity. The possibility of coronary artery compression has brought into attention this otherwise old anatomical finding. The claimed consequences of arterial compression range from benign to sudden cardiac death or otherwise, from no symptoms, to angina and even myocardial infarction. A clear delineation between myocardial bridge as an anatomical variation and respectively adjuvant or determinant in the disease process is difficult to be done and should be performed nowadays with the aid of new diagnostic tools and the therapeutical decision must be taken in each given case. A clinical review is presented, in order to show that myocardial bridging does not equal coronary arterial compression, that in most symptomatic or complicated cases, myocardial bridging is not the sole modification found and that a more complex interpretation must be sought by the physician either as a clinician or explorationist. In order to complete this image, a presentation of an anatomical study follows, demonstrating some unusual forms of myocardial bridges.

Introduction

The course of the coronary arteries has been divided from didactic and nonetheless practical points of view, into an epicardial and respectively an intramural one. In spite of that in several cases, exceptions to this "rule" are encountered. "Recurrent" epicardial branches sometimes may be seen emerging from deeper intramural rami; on the other hand, segments of the epicardial coronaries are at times covered by muscle. In this latter case, the term "myocardial bridge" is applied.

Coronary myocardial bridging has been recognized by earlier anatomists (1) and still represents a highly-debated topic among these (2, 3, 4).

Greater attention has been drawn after the first angiographic documentation of systolic compression and narrowing of the LAD in a young patient (5). Since then, after four decades, numerous studies have been performed and various theories regarding the role of the myocardial bridging in cardiac pathology have also emerged. At one end of this wide spectrum, myocardial bridges are regarded as normal anatomical variations; at the other, these could be responsible of causing acute coronary syndromes and sudden cardiac death.

Challenge is high because no uniform experience exists and because the incidence of this condition largely varies, probably due to the differences in the methods of observation. Autoptic studies reveal prevalences between 5.4 - 85.7%! (3, 6). Angiographic studies report figures between 0.5-1.6% or 7% (7, 8, 9, 10), with a higher incidence associated with the male sex and systolic overload of the left ventricle.

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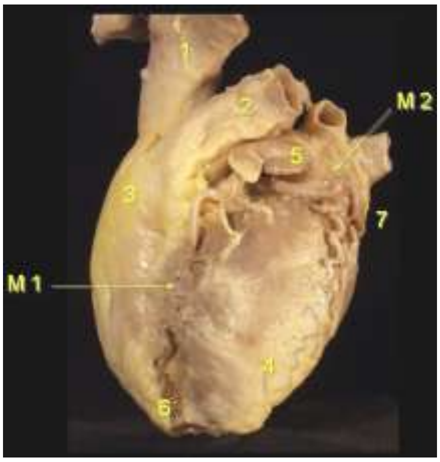


Figure 1

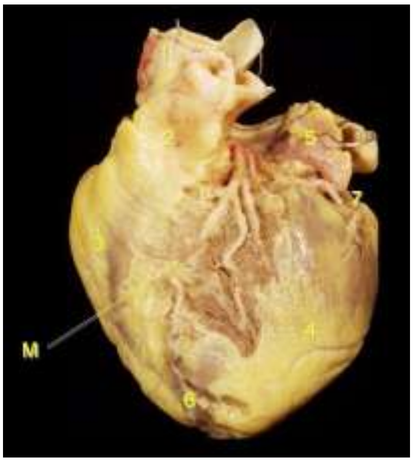


Figure 2

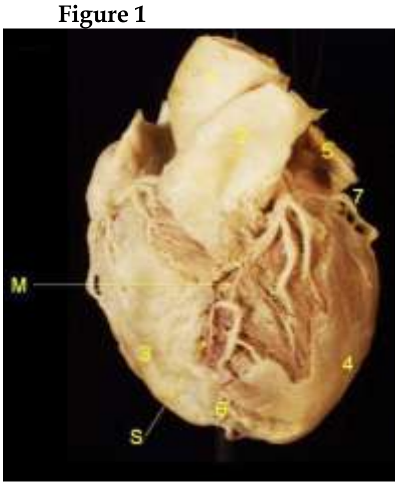
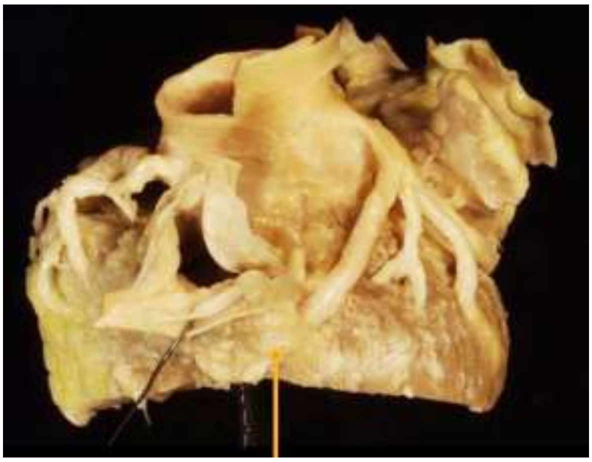


Figure 3



MYOCARDIAL BRIDGE OVER THE LAD

Figure 4a

ATRIAL MYOCARDIAL BRIDGE
OVER THE CIRCUMFLEX BRANCH

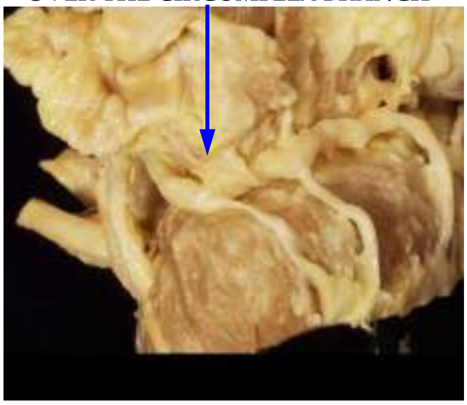


Figure 4b

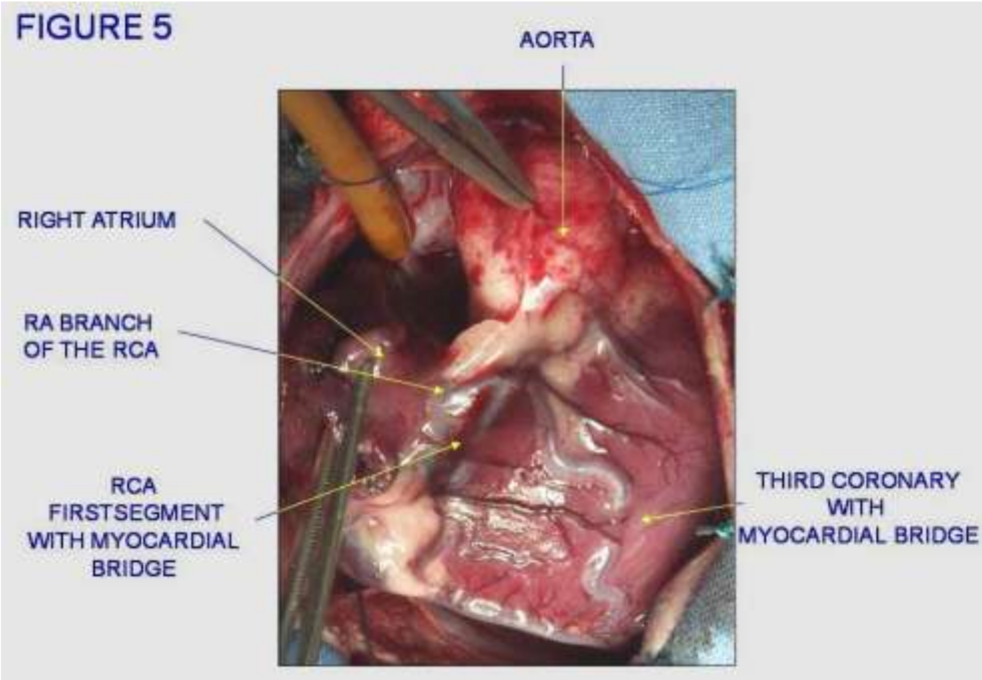


Figure 5

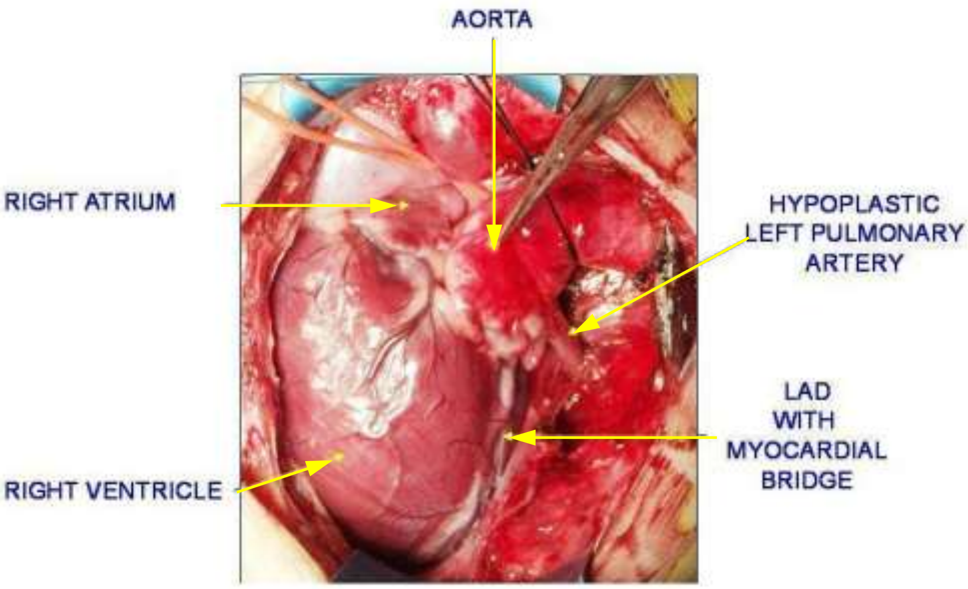


Figure 6

Some important questions arise and these have obvious consequences for both the clinician as well as for the explorationist:

- are myocardial bridges normal anatomical variations, related to the individual and/or species?
- in what measure these anatomical variations can influence on the pathological process; and do they have a predominant or auxiliary role in the disease process?
- does myocardial bridging evolve over time in the same person? Is there any indication for a preventive therapy?
- are the intramyocardial segments of the coronaries more protected or more prone o develop atherosclerosis?
- are there many more forms (types) of myocardial bridges and which would be the most unfavorable?
- is there a characteristic form of extrinsic compression of the coronary arterial segment at level of the bridge?
- is it there a relation of causality between a rare event as sudden death and an uncommon condition as myocardial bridge and can this be demonstrated?
- can we develop any parallel between myocardial bridge and other pathologic conditions that include coronary artery compression as the case of hypertrophic cardiomyopathy?

Embriology

The early tubular heart is a bilaminar structure initially, consisting of an internal layer (the endocardium) and an external one (the myocardium). As development proceeds, a third layer is added (external to the myocardium); this is the epicardium. It derives from small aggregates of cells on the coelomic wall between the sinus venosus and the liver (which in avian species form the proepicardial organ). This is a transient structure. Epicardial cells spread over the surface of the myocardium in a rostral-dorsal direction to eventually form a continuous layer. There follows a process of epithelial-mesenchymal transformation (EMT), that generates migratory cells from the epicardium which penetrate heart tissues providing a progenitor population that eventually seeds the entire coronary vascular bed (11, 12, 13). Another second extracardiac cell population has an important role in patterning the coronary vasculature: the cardiac neural crest cells (CNC). The CNC per se does not contribute to the cellular elements of the developing coronary arteries, however parapsymathetitic ganglia of CNC origin are found in close association with them. The CNC cells reach the base of the cardiac outflow tract and it is likely that they have a role in the remodeling process which occurs during coronary development.

The *Epicardial-Derived Cells* (EPDC) invade the muscular wall of the heart and the endocardial cushions and differentiate into several cell types: interstitial fibroblasts, coronary smooth muscle cells and adventitial fibroblasts.

The atrioventricular and the interventricular groove are the first to be covered by the EPDC.

Some endothelial cells migrate across the complete thickness of the myocardium and might touch the endocardial lining (12) however, without establishing anastomoses between the cardiac chamber lumen and the growing coronary system.

The origin of the coronary endothelium is still controversial. It might at least partially originate as EPDCs.

A plexus of small vessels is formed. The primitive coronary lattice is initially connected only to the sinus venosus. The connection with the aorta is a later event. It is still unclear what signals guide the endothelial cells to come into contact with the aorta (the normal point of ingression) rather than with the pulmonary trunk. After flow is established in the coronary plexus, the differentiation in arteries and veins takes place; flow and pressure gradient have an important role besides the paracrine stimuli.

Thus, the formation of the coronary system represents a paradigm of vasculogenesis (primary formation of vessels by self-assembling on mesenchimal precursors) in its early phase (14) while angiogenesis (vascular growth by outgrowth of preexisting vessels) will occur in a second phase (15).

The vicinity with the developing ventricular myocardium and the fact that the first to appear are the primordiums of the coronary arterial branches at the level of the atrioventricular and respectively interventricular sulci (of which, at times either more superficial or deeper branches will be selected), could explain the partial intramural course of the afore mentioned rami. Some species differences might also exist (vide infra).

Anatomy

Different types of myocardial bridges can be encountered, depending on:

A. The location of the bridge:

- over the LAD (the most frequent) especially its midportion;
- over the circumflex;
- over one of their branches (rare);
- over the right coronary (rare) (16);
- unusual locations: right marginal branch (17), variant circumflex artery (18)

B. The number of bridges:

- singl site;
- multiple bridges;
- over the same or more arteries.

C. The width of the bridge:

- narrow bridge (usually slender and weak, although sometimes highly-compressive Cf. references 29 and 33);
- wide bridge.

D. The origin, disposition and course of the muscular fibres (19):

- superficial bridges, crossing the artery (LAD) towards the apex of the heart either perpendicularly or at an acute angle. This type, apparently doesn't seem to constrict the artery in systole;
- more conspicuous bridges taking the form of a muscle bundle arising at the level of the right ventricular infundibulum or apical trabeculae, crossing the artery transversely, obliquely or helically before terminating in the interventricular septum. These seem to twist the vessel and thus compromise its diastolic flow.

E. The type of myocardium in the bridge:

- atrial;
- ventricular.

F. The general context of the given person:

- bridges in individuals with no apparent cardiovascular disease;
- bridges in individuals with cardiovascular pathology, as hypertrophic cardiomyopathy, coronary atherosclerosis. Some particular forms should be presented at this point: atherosclerotic lesion on the right coronary + muscular bridge over the LAD (20), in which the compression produced by the bridge can precipitate ischemia. Another example is that of hypertrophic cardiomyopathy, in which compression is produced at level of both the LAD and its septal branches (21).

G. The artery beneath the bridge (pathological and angiographic aspect):

- rectilinear profile;
- looping of the artery (i.e. accentuated "descent" of the artery from its normal epicardial course into the myocardium: the "U-sign").

From all the above, it is clear that many variations and associations are possible, making thus various statistics difficult to compare. From the practical point of view, it is obvious that the finding of a myocardial bridge represents only one preliminary element of a more complex and individualized clinical-diagnostic framework.

Comparative anatomy

The presence of two main coronary trunks represents a later and more evolved acquisition on the animal scale (e.g. not all avian species have two coronaries). Even when talking about two coronaries, we usually assume the fact that the LAD, circumflex and right coronary artery - must be considered as the essential, elementary units of coronary anatomy (22).

With respect to the course of the coronary arteries, the mammalian hearts can be classified as follows:

- ***type A:*** rat, guinea pig, hamster - with intramyocardial course;
- ***type B:*** human, sheep, dog, cat - with predominantly epicardial course and frequent intramural course;
- ***type C:*** horse, cow, pig - with entirely epicardial arteries (6, 23, 24).

A direct correlation with cardiac pathology in the afore mentioned species is difficult to be done at the present moment.

The claimed consequences of myocardial bridging

Myocardial bridging represents usually a benign condition with an excellent long-term survival (25). On the other hand, its presence has been linked to myocardial ischemia, infarction (26 - 35), exercise-induced tachycardia (36), conduction disturbances (37, 38) and sudden death (39, 40, 41, 42).

The relationship between atherosclerosis and myocardial bridges is still controversial:

while some authors indicate the fact that atherosclerosis is uncommon within a bridge (2, 4, 6, 23, 42, 43), others report the opposite (44). Taking into account the multitude of anatomical forms, one can not accept only "the protective effect" of the intramural portion of a given coronary artery; atherosclerosis can probably develop as easy (or even easier) in the case of some particular forms of myocardial bridging.

Experimentally created myocardial bridges (45) confirm the ischemic distress induced by the compression of the coronary artery.

Some particular aspects warrant further analysis and discussion (see below).

Pathophysiology

In normal hearts, left coronary arterial flow is predominanlty a diastolic event, whereas right coronary flow is both systolic and diastolic due to the lower transmural pressure (46). Under normal conditions coronary flow occurs during diastole with only 15-20% of flow during systole. As a myocardial bridge causes only systolic compression of the coronary artery the exact cause for ischemia and other associated complications is not fully known. Subendocardial regions have higher intramural pressure compared to intracoronary pressure during diastole (24). The role of systolic compression of coronary arteries in altering this already high-pressure gradient, is unclear. The following mechanisms have been proposed:

- systolic recoil: with increased heart rate, the time required for recoil of systolic compression encroaches upon diastole compromising the filling of coronary arteries, leading to ischemia (47);
- spasm: exercise may induce spasm of the coronary arteries especially in the regions of systolic compression leading to subsequent events and studies have demonstrated artificially reproduced spasm in the area of myocardial bridging in association with chest pain, increased lactate production and deterioration of global and regional ventricular function;
- elevated thromboxane B 2 levels in setting on myocardial bridge;
- persistent distal closure after systole;
- local thrombus formation: increased local shear forces may induce platelet activation;
- coronary endothelial dysfunction at the sites of myocardial bridging (48).

Another important detail is represented by the concomitant compression of the septal branches (of the LAD): it seems that the septal compression is determinant in inducing myocardial ischemia, at least in some studies (49). In cases of hypertrophic cardiomyopathy, as well as in other hypertrophic conditions, angiographic obliteration of the septal branches (originating from both the LAD and respectively from the posterior interventricular branch) that occurs during systole is present in about 70% of the cases: the septal blanching phenomenon. It has been associated with the degree of left ventricular hypertrophy and with thallium perfusion abnormalities (50, 51, 52). In such cases, for example, the surgical release of the bridged artery will not improve myocardial perfusion.

Compression may result in elliptical narrowing of the coronary artery and not the concentric narrowing typical of coronary disease. As a consequence, the relations between the maximum diameter and luminal diameter in an ellipse, are different from those of a circle: a 50% concentric decrease in arterial diameter decreases luminal area by 75%; the area will be reduced by about 30% if the artery is distorted into an ellipse (23). In order to reduce flow substantially, diastolic coronary artery compression must remain at maximum severity. Therefore, anatomical muscular bridges do not always lead to coronary compression.

The coronary flow reserve represents another important detail. It is reduced in conditions as hypertrophic cardiomyopathy, elevated left ventricular diastolic pressure, abbreviated diastolic intervals and systolic arterial compression (53). Thus, a distinction should be made between the bridging and respectively, the coronary compression. The apparent discrepancy between the prevalence of myocardial bridges as found on autoptic statistics and on angiographic series respectively, can be explained by this difference.

In some studies, the distribution of thallium abnormalities was often unrelated to the coronary artery compressed (49). Individual anatomical variations and coronary typology could offer an explanation of this phenomenon (54).

The length of the compressed segment is also important besides the systolic narrowing. A scoring system has thus been proposed, taking into account both parameters (Table 1). A usual score varies from 2 to 5. Values greater than 5 indicate most severe compression.

Table 1: Scoring system to quantify degree of systolic narrowing (from reference 24 - see also text for details)

	Score
Systolic narrowing	
< 50%	1
50 - 75%	2
> 75%	3
Length of compressed segment	
< 1 cm	1
> 1 cm	2

Diagnostic tools

Most bridges are asymptomatic. Individuals may present with dyspnea, dysrhythmia, chest pain or even sudden death. As stated before, symptoms could be related to the compression, to the degree of compression and to the associated pathologies.

Some diagnostic tools are helpful in both indicating the presence of myocardial bridging and the coronary artery compression.

A. Angiography

Besides offering informations on the coronary tree, ventricular anatomy and function, three signs are considered characteristic and of much help in the differential diagnosis:

- systolic compression/narrowing of the arterial lumen: "the milking effect". With vasodilator administration, the systolic narrowing is accentuated facilitating angiographic diagnosis;
- an accentuated "descent" of the artery from its epicardial course into the myocardium: "the U-sign", provides an indirect evidence of myocardial bridge;
- the systolic compression/occlusion of the septal arteries: "the septal blanching" phenomenon (vide supra).

B. Intravascular ultrasound

- the echolucent "halfmoon phenomenon" (55);
- intravascular Doppler velocity profile shows characteristic changes of rapid early diastolic filling ("finger tip" phenomenon) and mid diastolic deceleration and plateau in the late diastole ("spike and dome" pattern). In systole, paradoxycal flow can also be detected in the proximal coronary segment (which is characteristic of a myocardial bridge) (42,56).

C. Thallium-201 scintigraphy

Exercise-induced defects have been reported in some studies (57), while in another study no significant perfusion abnormalities were noted (9).

Therapy

A. Asymptomatic patients

No therapy is warranted although a clear distinction should be made between bridging and the presence of compression. Another point is to take into account the conditions under which the patient has been investigated: angiography, intravascular ultrasound and scintigraphy are not screening tests and probably in these cases, the presence of myocardial bridges should be considered either as a concomitant pathologic lesion or as concomitant benign finding.

Asymptomatic patients can also present with signs of coronary compression both transitory as well as more constant. Management is still controversial and a therapeutical decision should be taken following an algorhythm adapted to the general conditions of the individual patient.

B. Symptomatic patients, lacking other potential causes

- pharmacological therapy, aiming towards reducing preload and vasospasm (nitrates) (47, 58), obtaining negative chronotropic and negative inotropic effects (beta-blockers, calcium channel blockers) (35, 59);
- percutaneous revascularization: coronary stent implantations prevent external compression. Successful resolution as detected by scintigraphy has been described (60). Complications have been reported to occur with stent implantation and rotational atherectomy in myocardial bridge (61). Use of baloon-expandable stent and high-pressure deployment (preferably with intravascular ultrasound guidance) is required for optimal stent placement and may reduce the occurrence of instent restenosis (62).
- surgery. Surgical decompression or coronary bypass can be performed.

Interventions for lesions proximal to the myocardial bridge deserve special attention, as distal bridging may become more apparent and reduce the run-off facilitating the thrombosis (recipient artery or graft).

In all cases, a thorough and careful patient selection, a proper timing and association of therapeutical principles should be done.

Conclusions

More attention has been drawn by the possible compression due to myocardial bridges.

Myocardial bridging could represent an anatomical variation but in some cases it can produce or precipitate various coronary syndromes, of which, the most debated is sudden cardiac death.

A review of the literature shows that bridging does not equal compression and that compression is a demonstrable consequence in some groups of patients or under particular conditions. Coronary artery compression could not be important "per se" if not associated with septal branch compression, left ventricular hypertrophy, shortened diastolic intervals and not the least, atherosclerosis. In other cases, myocardial bridging is the only pathological modification proved either by "in vivo" diagnostic tests or by "post mortem" examination.

However, a direct correlation between bridging and disease should be done very cautiously, as many more questions arise. Probably, myocardial bridging must be considered today, not as the sole explanation for a multitude of pathological processes but as an important element in the diagnosis of the otherwise complex group of coronary syndromes.

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Appendix: Anatomical study

Some particular forms of myocardial bridging are subsequently presented, in order to complete the physician's image.

A number of 48 human hearts from both male and female adult patients, deceased of non-cardiac causes - have been dissected by the author. Hearts were studied in the Institute for Pathology at "Niguarda" Hospital, Milan and in the "HM Dissection Center" at San Donate Hearts were fixed by injection of formalin into the coronaries and respectively, retrogradely in the coronary sinus and subsequent immersion in the same. Hearts were dissected after a fixation period of at least one week and after temporary immersion in absolute alcohol. Microdissection technique was associated to the gross anatomical procedure. Photographical recording of the specimens was performed by the author in the above mentioned centers.

Photographical recording of two pediatric patients was also performed, in the Cardiac Surgery Department, at San Donato Hospital, Milan. The first was a patient with double outlet right ventricle; the second, a patient with tetralogy of Fallot.

In the pathology series a number of 3 hearts with myocardial bridging were observed (i.e. 6.25%). Two of these had double bridging: over the LAD and respectively, over the circumflex. The third, presented a quite "usual" bridge over the middle tract of the LAD, but the artery underneath presented an altered caliber. There were no signs of myocardial infarction (both macroscopically and microscopically).

The first surgical case had also a double bridge: over the first part of the right coronary artery and over a large "third coronary" - both apparently asymptomatic.

The second surgical case presented a normal course of the coronaries and a bridge over the middle portion of the LAD. No surgical decompression was intended, as the bridge was totally asymptomatic and the artery showed no "U-sign" or alteration in its caliber.

Explanatory notes accompany each figure (see legends for details).

Abnormal aortic origin of the left coronary artery from the right sinus of valsalva (sinus 1), successfully treated by modified reimplantation technique*)

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Abstract

Abnormal connection between the coronary arteries and the aortic sinuses has protean manifestations and might be the cause of sudden death especially in young athletes. Diagnosis and therapeutic approach are not always straightforward, as a direct cause-effect relationship is not easily demonstrable in every patient. The case of a young boy who developed chest pain and syncope under physical stress as the first manifestation of an abnormal aortic origin of the left coronary artery is described. Coronary artery narrowing was due to the stretching of the intramural segment of the left main trunk. The diagnostic steps and the particular surgical solution are subsequently presented.

Note*: in this article, the nomenclature of the aortic sinuses also known as "The Leiden Convention" is being used: sinus 1 = the right facing sinus; sinus 2 = the left facing sinus; sinus 3 = the non-facing (or non-coronary) sinus. The inter-coronary commissure means the commissure between the left and respectively right aortic cusps.*

Key words: *Coronary anomaly, Sudden death, Coronary angiogram, Intermittent myocardial ischemia, Surgical technique*

Introduction

The definition of a ***coronary anomaly*** represents a complex issue and any thorough approach should take into account anatomical and pathophysiological criteria as well as the envisaged clinical consequences and patient's prognosis. Based on their clinical relevance, anomalies have been classified as involving obligatory ischemia, involving absent ischemia or respectively, involving exceptional ischemia (1).

Coronary anomalies occur in 0.2-1.2% of the general population (2) and most are unrelated to any symptomatology. In some cases however, angina or less specific signs may draw attention toward the anomaly. Sudden cardiac death in otherwise asymptomatic individuals represents the most fearful complication; however a clear-cut relationship between the anomaly and the acute event is difficult to ascertain although some authorities stress this relationship (3, 4).

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The abnormal aortic origin of a coronary artery is usually associated with an intramural course, and with traveling the space between the aorta and pulmonary trunk. The alleged pathophysiologic mechanisms involved are multiple: a) deformation of the ostium, especially when located close to a commissure or when slit-like, b) alteration of the angle of origin of the abnormal vessel, c) acute systolic stretching and narrowing of the intramural segment d) scissors-like compression by the pulmonary trunk e) diastolic compression by the intercoronary commissure (5).

Many of these mechanisms may coexist in the same patient, thus requiring a well individualized surgical planning and approach.

Surgical technique must take into account the location of the ostium, the position and length of the intramural segment and the quality of the coronary wall. The usual procedure used in these cases consists in "unroofing" the intramural segment and relocating the coronary to its normal sinus by performing a more distal anastomosis and reattaching the aortic commissure when needed (5, 6). The proximity of the aortic cusps or of the commissure may add difficulties, hazards or complications to these techniques.

We hereby present our experience with a patient successfully treated with a modified reimplantation technique.

Case report

A 14-year-old apparently healthy and previously asymptomatic boy had an episode of chest pain followed by syncope while playing soccer, 9 months prior to the admission in our hospital. Cardiac arrest was certified and resuscitated by a veterinary physician. Patient regained conscience "*after a few minutes*". Recovery of the patient was complete. The patient remained asymptomatic following this acute event and underwent various diagnostic interrogations. All tests were within normal limits. QT interval showed values in their higher range (QTc 400-460 ms) but otherwise the ECG showed no particular alterations either at rest or under stress. Neurological examinations were negative. Echocardiographic examination revealed an abnormal origin of the left main coronary artery from the aortic sinus 1 ("right facing sinus") with a proximal intramural course.

The patient was subsequently referred to the pediatric cardiology and cardiac surgery department for a more detailed diagnostic study.

On examination he was looking healthy, with no particular abnormal physical findings. Pulse rate was 78/min blood pressure was 115/65 mm Hg.

Laboratory tests showed only mild eosinophylia (patient previously diagnosed with atopy). ECG at rest and under exercise, chest X-ray showed no pathologic modifications.

Angiography: demonstrated a normal aorta and left ventricle with a normal contraction pattern. Coronary artery distribution was within normal limits with all three main coronary trunks showing a normal course and ramifications. The left system was dominant. The only alteration found was an abnormal origin of the left main coronary trunk from the aortic sinus 1 ("right facing aortic sinus") with an intramural proximal part. Branching pattern and rami were normal. Simultaneous injection of contrast media in the pulmonary trunk and the left main, failed to demonstrate vascular compression by the pulmonary root. Instead, stretching of the intramural segment was apparent with intermittent narrowing of the left main coronary trunk.

MRI and CT scan certified the abnormal origin of the coronary artery, its intramural course and the lack of extrinsic compression (Figures 1, 2 and 3).

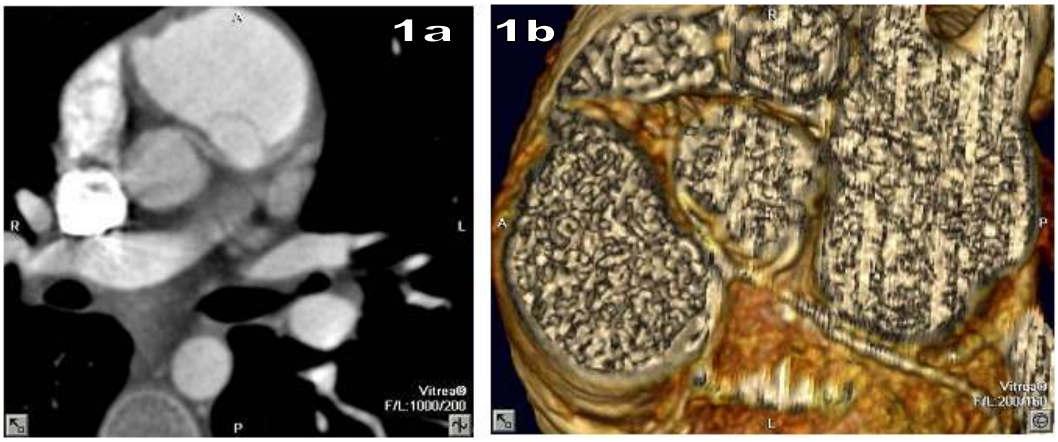

Figure 1: CT scan (a) and MRI (b) images revealing the abnormal origin of the left coronary artery and its proximal course. Note the intramural segment and its course between the aorta and the pulmonary trunk

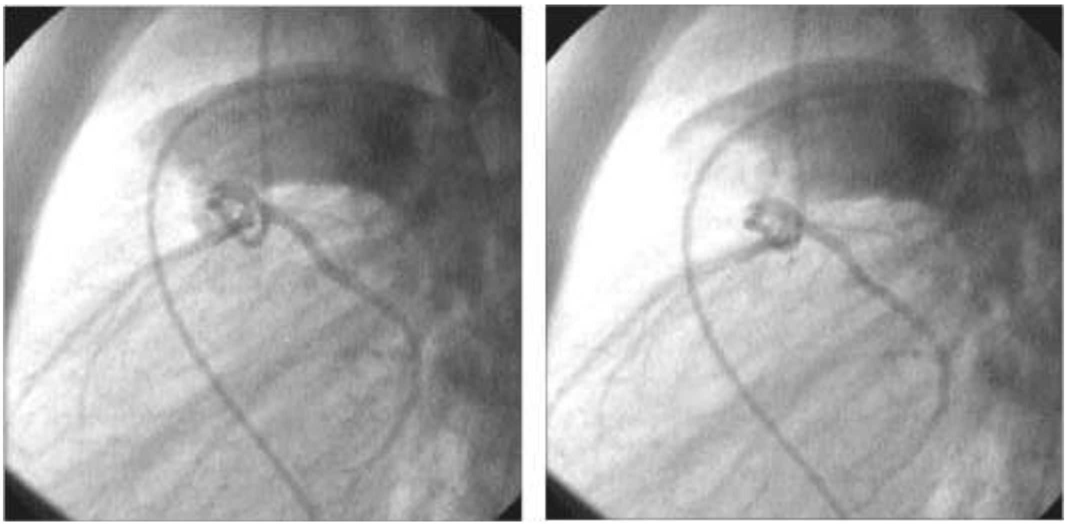

Figure 2: Angiographic aspect of the origin of the left coronary artery

Simultaneous injection of contrast media in the pulmonary trunk and into the left coronary artery fails to demonstrate any extrinsic compression by the former

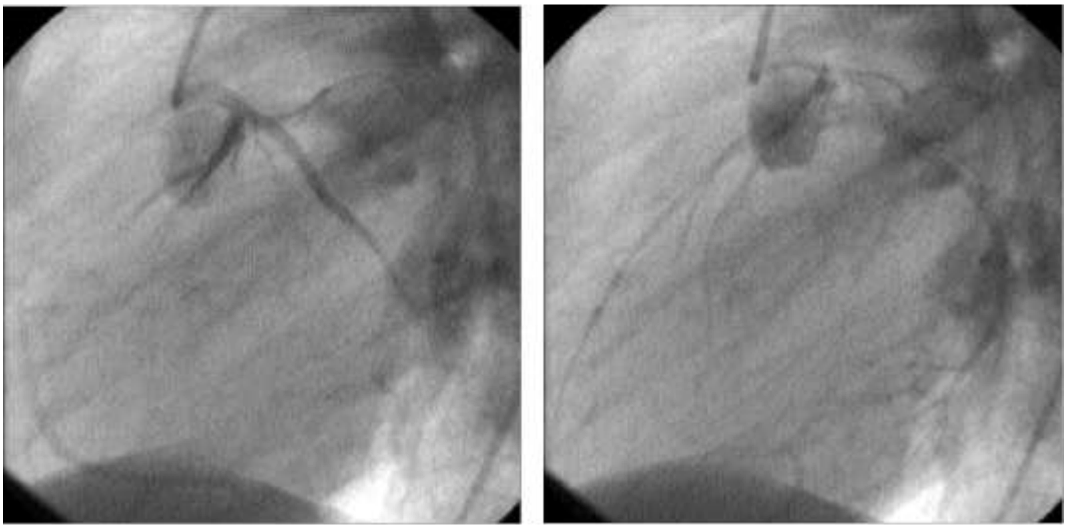

Figure 3: Angiographic demonstration of the stretching of the left coronary intramural segment

Systolic distension of the aortic root induces stretching and subsequent narrowing of the intramural segment of the left coronary artery

Due to the potential high risk complications of the otherwise intermittent stretching and narrowing of the dominant left coronary artery, and because of the length of the narrowed segment (more than 15 mm), surgical correction instead of stenting was planned (7).

The patient underwent operation in median sternotomy under CPB at 28°C. The left coronary artery was found to originate from a separate ostium in the aortic sinus 1 ("anterior" or "right facing sinus of Valsalva"). It coursed over the aortic root (showing an intramural segment of about 2 cm); at the level of the aortic sinus 2 ("left facing sinus"); subsequently it diverged from the aortic wall and presented normal relationships, dimensions, course and ramifications. No compression by the pulmonary trunk was evident at this point. Instead, systolic distension of the aortic root was evident with stretching of the intramural segment of the left coronary artery (Figure 4).

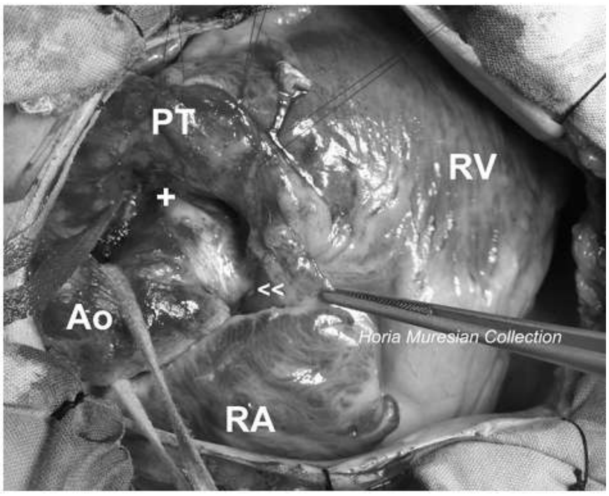

Figure 4: Intraoperative aspect (I). *The pulmonary trunk (PT) was retracted from the aorta (Ao). Both the anomalous origin of the left coronary artery from the sinus 1 (<<) and its course between the aorta and the pulmonary trunk (+), are evident. RA = right atrium and appendage. RV = right ventricle*

After aortic cross clamping the aorta was transversally opened. The aortic root and valve were found to be normal in shape and configuration. The right coronary artery presented a normally located ostium, normal dimensions, course and ramifications. The left coronary had a separate ostium in the aortic sinus 1, however closer to the intercoronary commissure. Ostium was circular, of normal dimensions and located proximal ("upstream") to the sinotubular junction. (Figure 5)

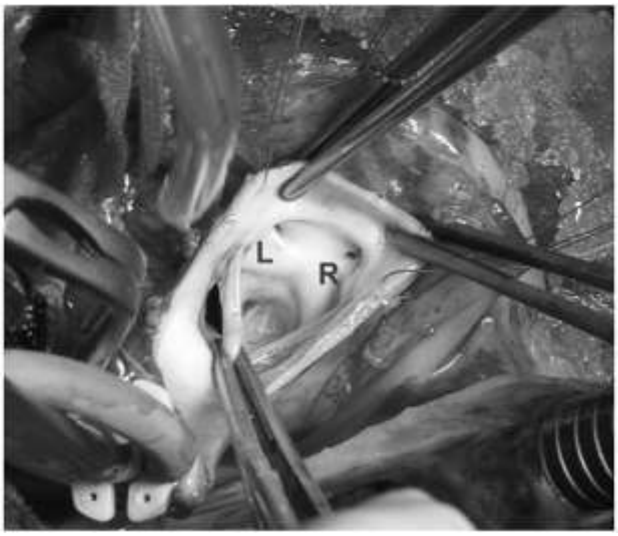

Figure 5: Intraoperative aspect (II)
Both coronary ostia (L and R) are located at the level of the sinus 1 (right-facing sinus). The right aortic cusp is retracted

The length of the intramural segment and the thinness of the coronary wall precluded the detachment of a coronary button for subsequent reimplantation. "Unroofing" of the intramural segment from the inside, would have imposed the detachment of the intercoronary commissure together with an important part of the adjacent right and left aortic cusps. Thus, an alternative approach was chosen. At the very point of divergence of the left coronary from the aortic wall (i.e. in correspondence with the left aortic sinus), a 2.8 mm punch hole was made in the aortic wall. A longitudinal arteriotomy was also made at the level of the opposite coronary wall (at the point where the left coronary was already extramural and with a thicker wall). Anastomosis between the two was performed using continuous 8-0 Prolene suture. The original ostium was not closed (Figure 6).

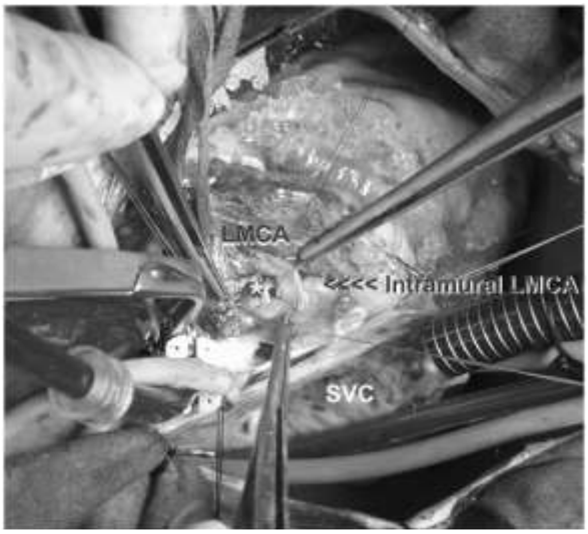

Figure 6. Intraoperative aspect (III)
A new ostium for the left coronary artery was created (*). The "free" part of the left coronary (LMCA) beyond the intramural segment, was subsequently anastomosed at this very level. The intramural LMCA is also evident (<<<<). SVC = venous cannula in the SVC (through the right atrium).

The remainder of the operation proceeded in the regular way. Patient was weaned off bypass uneventfully. ECG showed no alterations. Postoperative course was uneventful. The patient was extubated 8 hours postoperatively. Cardiac enzymes, ECG in the postoperative period showed no ischemic alterations.

Comment

A definitive and clear cut relationship between a coronary anomaly and a clinical event is difficult to prove especially in the living patient (8). Surgical indication, timing of surgery and the choice of the planned technique are even more important in young patients in whom bypass procedures pose some particular problems among which, the choice of conduit and the need for future reoperations.

This case illustrates and stresses some interesting aspects:

• stretching of the abnormal coronary was intermittent and thus difficult to reproduce and ascertain in the cath lab or under treadmill test; repeat catheterization was necessary and peer review was requested;

• ultrasound examination proved to be an important screening and diagnostic test (9, 10).

• the patient had a left dominant system - a condition which could explain the dramatic effects of an even intermittent compression;

• stretching represented the main mechanism of coronary narrowing. The ostium of the abnormal coronary was circular, of normal dimensions and was not compressed by the intercoronary commissure. The pulmonary trunk did not contribute to the extrinsic compression of the artery (11);

• the intramural segment had a thinner wall, difficult to handle had a reimplantation or button transfer technique been planned;

• "unroofing" of the intramural segment from the inside would have imposed the detachment of the intercoronary commissure and of a large part of the right and left aortic cusps: a delicate and hazardous procedure and with dubious indications in this particular case;

• the resultant "new ostium" is a latero-lateral anastomosis between the left coronary trunk and the aortic sinus 2 ("left facing sinus"). Mobilization of the left coronary facilitated the placement of the neo-ostium and avoided distortions or tensions at this level. However, we preferred to leave the original ostium patent as it might also function as "a security valve" should the anastomosis fail in a way or in another. Secondly, this might also offer a model of the possible evolution of the abnormal origin and intramural segment as the child will grow.

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Morbi-mortalité de la chirurgie coronaire chez le patient age en Algerie*)

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Résumé

Près de 10% de la population algérienne (estimée à 38 millions d'habitants) est âgée de plus de 70 ans, et ils sont nombreux à présenter une coronaropathie. Par ailleurs, l'espérance de vie à 70 ans semble encore importante.

***Objectif:** Évaluer les résultats d'une chirurgie coronaire chez ces patients.*

***Méthodologie:** Nous avons comparé 88 patients septuagénaires consécutifs ayant subi un pontage aorto-coronarien isolé entre 2006 et 2009 à 165 patients de 50 à 60 ans. Les deux groupes ont été appariés selon les principaux facteurs de risque. Nous avons pris contact avec les patients par téléphone et leur avons fait parvenir un questionnaire sur la qualité de vie.*

***Résultats:** La mortalité opératoire s'élevait à 2,3% chez les septuagénaires, par rapport à 1,2% chez les 50 à 60 ans (P non significatif). Il y avait plus de bas débit, d'insuffisance rénale aiguë postopératoire et de transfusion chez les septuagénaires. La survie à long terme (durée moyenne du suivi de 2,8 ans) était plus élevée chez les 50 à 60 ans: 89,7% par rapport à 77,9% (P=0,025). Nous avons constaté quatre facteurs de risque indépendants d'augmentation de la mortalité à long terme; âge, diabète, antécédents d'accident vasculaire cérébral et de transfusion sanguine postopératoire.*

***Conclusion:** Pour des septuagénaires sélectionnés, on peut proposer une chirurgie coronaire isolée, et les résultats à court et à moyen terme seront comparables à ceux d'une population plus jeune.*

***Mots-clés:** morbidité, septuagénaire, pontage aorto coronarien, mortalité*

Abstract

***Background:** Almost 10% of Algerian population (estimated to 38 millions of people) is more than 70 years old, many of whom present with a coronaropathy. Moreover, it appears that life expectancy at 70 years of age is still important.*

***Objective:** To evaluate the results of coronary surgery among these patients.*

***Methods:** Eighty-eight consecutive septuagenarians who had an isolated coronary artery bypass surgery between 2006 and 2009 were compared with 165 patients 50 to 60 years of age; the two groups had been paired according to the main risk factors. Patients were contacted by telephone and then received a quality-of-life-related questionnaire.*

*) **Romanian Journal of Cardiovascular Surgery ■ 2009, vol. 8 no. 3-4, pp. 142-150**

Results: *Operative mortality was 2.3% in the septuagenarian versus 1.2% in the 50- to 60-year-old group (P not significant). There was more low cardiac output syndrome, postoperative acute renal failure and transfusion in septuagenarians. Long-term survival (average duration of follow-up was 2.8 years) was higher in the 50- to 60-year-old group: 89.7% versus 77.9% (P=0.025). Four independent risk factors of long-term increased mortality were found: age, diabetes, history of stroke and postoperative blood transfusion.*

Conclusion: *For selected septuagenarians, an isolated coronary surgery can be proposed, with short- and medium-term results comparable with those of a younger population.*

Keywords*: Coronary artery bypass graft surgery, Morbidity, Septuagenarian, mortality*

Introduction

Le nombre de septuagénaires augmente en Algérie avec, au 1er janvier 2006, presque quatre millions d'Algériens âgés de 70 ans ou plus. La chirurgie coronaire, dans cette tranche d'âge, est justifiée, d'une part en raison de l'espérance de vie relativement longue des patients de 70 ans (6,65 ans chez l'homme, 8,66 ans chez la femme) et d'autre part en raison d'une atteinte cardiovasculaire symptomatique chez 40% d'entre eux. Les gros progrès réalisés en matière de technique chirurgicale et de prise en charge péri-opératoire permettent de proposer à un nombre croissant de ces patients une chirurgie coronaire. Cependant, ces patients ont un athérome aortique fréquent (1), une tolérance à l'ischémie diminuée (2) et des comorbidités souvent associées, ce qui entraîne classiquement une plus grande morbidité par rapport à des patients plus jeunes, la mortalité opératoire allant jusqu'à 11,5% selon les études (3). La qualité de vie à distance de l'intervention doit également être prise en compte chez ces patients: une récupération plus longue après l'opération et un changement fréquent du cadre de vie en cas de séjour prolongé en milieu hospitalier peuvent modifier radicalement leur mode de vie.

Cette étude vise à analyser les résultats à court et à moyen terme de la chirurgie coronaire isolée chez le septuagénaire et à comparer ces résultats avec ceux d'une population de 50 à 60 ans ayant subi la même intervention.

Matériel et méthodes

Population

Nous avons inclus rétrospectivement 88 patients consécutifs de 70 ans et plus (groupe 1) et 165 patients de 50 à 60 ans (groupe 2; témoins) opérés de pontages coronaires isolés entre mai 2006 et décembre 2009. Un ratio de deux témoins pour un patient de plus de 70 ans a été choisi afin d'augmenter la puissance de l'étude. Pour chaque septuagénaire, nous avons donc sélectionné deux patients de 50 à 60 ans selon 7 facteurs d'appariement: le sexe, les antécédents d'artériopathie des membres inférieurs, d'accident vasculaire cérébral (AVC), de broncho pneumopathie chronique obstructive, la technique chirurgicale (circulation extracorporelle [CEC] ou cœur battant), le degré d'urgence, et la fraction d'éjection du ventricule gauche (FEVG). Onze cas n'avaient qu'un seul témoin correspondant.

Collecte des données

Nous avons utilisé les dossiers papier du service pour connaître les données préopératoires, péri opératoires et postopératoires précoces des patients. On a téléphoné à tous les patients (n = 253) afin de connaître les évènements cardiaques survenus depuis l'intervention et les traitements suivis.

Définitions

Chirurgie en urgence: réalisée dans les 24 heures suivant le cathétérisme cardiaque. Chirurgie en semi-urgence: réalisée au cours des cinq jours suivant le cathétérisme cardiaque. Infarctus postopératoire enzymatique: un taux de MB-CPK supérieur à 100 µg/L. Infarctus électrique: apparition sur l'ECG postopératoire d'une onde Q de nécrose. Bas débit: index cardiaque inférieur à 2,5 L/min/m^2 après obtention d'une normo thermie. Déficit neurologique: AVC transitoire (<24 heures) ou définitif. Insuffisance rénale: taux de créatinine supérieur à 200 µmol/L. La FEVG était le plus souvent évaluée en échographie-doppler cardiaque trans-thoracique. Insuffisance cardiaque dans le suivi: œdème des membres inférieurs, dyspnée ou antécédent d'œdème pulmonaire.

Sélection des patients

Une intervention chirurgicale n'était décidée qu'après discussion médicochirurgicale, en privilégiant chez le sujet âgé la cardiologie interventionnelle. L'existence de tares associées invalidantes, en particulier neurologiques, était considérée comme une contre-indication à la chirurgie.

Technique opératoire

Tous les patients ont été opérés par sternotomie médiane. Après le temps de prélèvement des greffons (artère mammaire interne gauche plus ou moins droite selon la technique de squelettisation, veine saphène interne), les patients ont été opérés sous CEC ou à cœur battant. La chirurgie sous CEC se fait en hypothermie modérée (33 degrés environ), la protection myocardique étant assurée par une solution de cardioplégie sanguine froide. En cas de chirurgie à cœur battant, la stabilisation myocardique est réalisée à l'aide d'un stabilisateur Octopus^{MD}. Les indications respectives entre cœur battant et CEC sont définies ailleurs (4), mais brièvement, la chirurgie à cœur battant est réservée aux patients les plus atteints (FEVG basse, aorte calcifiée), en cas de disposition anatomique favorable, en favorisant une revascularisation toute artérielle, afin d'éviter toute manipulation aortique.

Analyse statistique

La comparaison des variables fait appel à un test t de Student non apparié pour les données quantitatives et à un test de χ^2 pour les données qualitatives. Les courbes de survie ont été établies selon la méthode de Kaplan-Meier. La comparaison des courbes de survie a fait appel au test du Log-rank pour la survie observée dans les deux groupes ou pour la comparaison avec les données générales de la population française. Le seuil de significativité retenu pour l'ensemble des tests est $p < 0,05$.

3. Résultats

Les caractéristiques préopératoires, opératoires et les complications postopératoires sont résumées dans les tableaux respectifs 1, 2 et 3. Aucun des pontages réalisés à cœur battant n'a nécessité de CEC d'assistance ni de conversion.

Tableau 1: Données pré-opératoires

Caractéristiques pré-opératoires	> 70 ans (n=88)	50-60 ans (n=165)	*p*
Age (ans)	73,1+/-2,4	56,1+/-2,8	< 0.0001
Sexe féminin [n%]	29,6%	29,1%	ns
Artériopathie [n%]	22,7%	21,8%	ns
BPCO [n%]	7,9%	3,6%	ns
ATCD d'AVC [n%]	5,7%	4,2%	ns
FEVG moyenne%	60,2+/-15	63,4+/-14,4	0,90
Tabac [n%]	35,2%	54,5%	0.02
HTA [n%]	59,1%	64,2%	ns
Diabète [n%]	14,8%	29,7%	0.01
Créatininémie (µmol/L)	124,6+/-43,5	102,2+/-29,4	< 0.0001
IDM récent (<48h) [n%]	5,7%	6,1%	ns
IDM ancien [n%]	31,8%	29,1%	ns
SCA [n%]	30,7%	21,8%	ns
FA [n%]	11,4%	7,3%	ns
ATCD d'angioplastie [n%]	9,2%	13,5%	ns
NYHA moyenne	1,40	1,31	ns
Euroscore moyen	7,3+/-2,1	3,4+/-1,9	< 0.0001
Liste des abréviations:			
BPCO	*bronchopneumopathie chronique obstructive*		
AVC	*accident vasculaire cérébral*		
FEVG	*fraction d'éjection ventriculaire gauche*		
HTA	*hypertension artérielle*		
IDM	*infarctus du myocarde*		
SCA	*syndrome coronarien aigu*		
FA	*fibrillation auriculaire*		

Tableau 2: Données opératoires

Données opératoires	> 70 ans (n=88)	50-60 ans (n=165)	p
Degré d'urgence [n%]			
Réglé	82,9%	89,1%	ns
Semi-urgence	9,1%	4,2%	ns
Urgence	7,9%	6,7%	ns
Cœur battant [n%]	1,8%	2,4%	ns
Nombre moyen de pontages	3,1+/-1,1	3,1+/-1,1	ns
AMIG [n%]	97,7%	98,8%	ns
Saphènes [n%]	81,8%	55,2%	< 0.0001
Durée CEC (min)	85,6+/-20,8	83,6+/-29,4	ns
Durée clampage aortique (min)	44,6+/-17,2	47,2+/-17,7	ns

Liste des abréviations:	
AMIG	*artère mammaire interne gauche*
CEC	*circulation extra-corporelle*

Tableau 3: Complications postopératoires

Suites opératoires	> 70 ans (*n* = 88)	50-60 ans (*n* = 165)	*p*
Durée d'intubation (h)	6,8+/-1,5	10,3+/-5,4	ns
Durée réa (j)	6,4+/-2,6	4,1+/-1,8	ns
Durée d'hospitalisation (j)	12,1	12,2	ns
IDM enzymatique [n%]	4,2%	5,3%	ns
Nécrose sur ECG [n%]	2,2%	2,4%	ns
Saignement (ml)	725+/-420	700+/-350	ns
Transfusion [n%]	50%	25,6%	< 0.0001
Reprise pour saignement [n%]	4,6%	2,4%	ns
Bas débit [n%]	19,3%	9,7%	0.0300
Passage en FA [n%]	29,4%	29,9%	ns
Sortie du service en FA [n%]	6,8%	1,8%	0.0300
Troubles neurologiques [n%]	1,4%	0,6%	ns
Insuffisance rénale [n%]	7,9%	1,2%	0.0050
Dialyse [n%]	1,1%	0,6%	ns
Créatininémie de sortie (µmol/L)	107,6+/-35,7	94,3+/-24	0.0050

Mortalité postopératoire

Deux patients sont décédés dans chaque groupe, tous durant la même hospitalisation que leur intervention et avant le trentième jour postopératoire. Le taux de mortalité chez les plus de 70 ans est de 2,3% par rapport à 1,2% chez les 50 à 60 ans (n.s.).

Survie à long terme

Il existe 5,1% de perte au suivi dans notre étude. La durée moyenne de suivi est de 35,7 mois, soit environ trois ans, avec des extrêmes variant de 0,5 an à 3,2 ans. Nous observons que les 50 à 60 ans ont une survie significativement plus élevée à moyen terme (à trois ans) que les septuagénaires (89,7% par rapport à 77,3% respectivement [P = 0,025] (voir figure 1). La survie à long terme des septuagénaires opérés est supérieure à celle des septuagénaires de la population générale Algérienne, de façon significative (figure 2) alors que celle de la cohorte des 50 à 60 ans n'est pas différente (figure 3). Les causes de décès tardifs étaient souvent inconnues. La plupart étaient des morts subites dont l'origine cardiaque n'avait pas été démontrée. Par ailleurs, il y a eu deux décès par bas débit postopératoire, un décès par cancer du colon en phase terminale, une nécrose mésentérique et un œdème aigu du poumon. Nous ne connaissons pas l'étiologie exacte des autres décès tardifs. En étude multivariée par régression logistique, nous avons retrouvé quatre facteurs indépendants associés à un risque de surmortalité tardive: l'âge supérieur à 70 ans (RRR = 7,4; P = 0,006) les antécédents d'AVC (RRR = 7,9; P = 0,003), le diabète (RRR = 7,1; P = 0,007) et la nécessité d'une transfusion postopératoire (RRR = 1,3; P = 0,05).

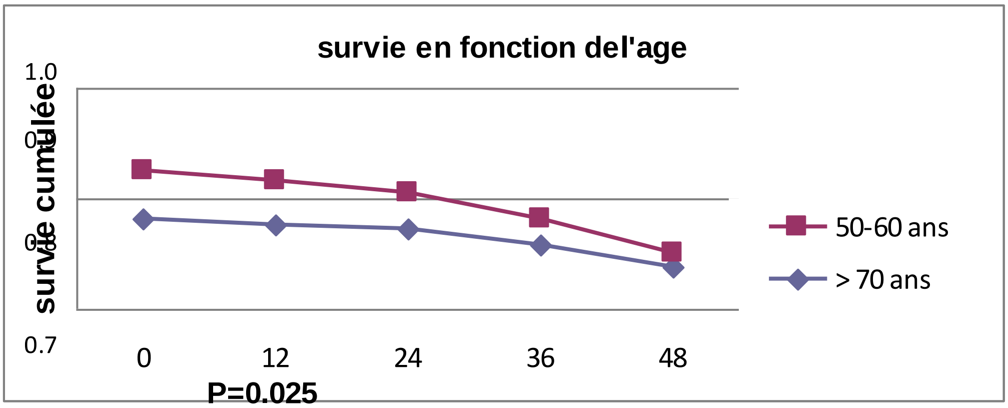

Figure 1: Survie en fonction de l'âge.
Survie cumulée (nombre de patients survivants par classe d'âge)

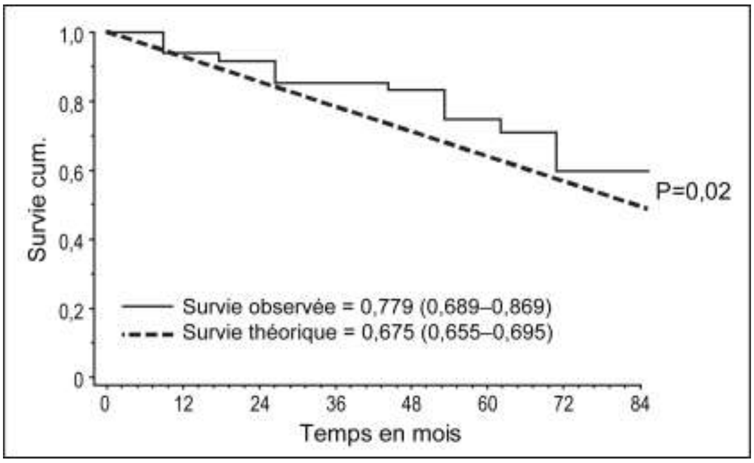

Figure 2: Comparaison entre la survie théorique et observée chez les patients de plus de 70 ans.
Survie observée: survie dans notre étude.
Survie théorique: survie de la population générale

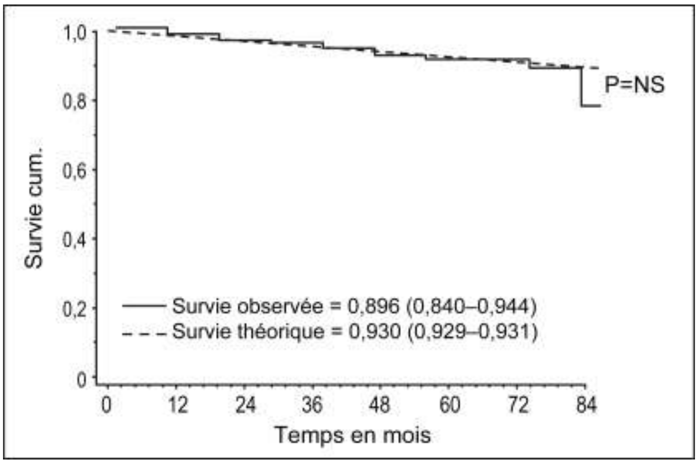

Figure 3: Comparaison entre la survie théorique et observée chez les 50–60 ans.
Survie observée: survie dans notre étude.
Survie théorique: survie de la population générale

Qualité de vie à long terme:

Le taux de réponse au questionnaire de qualité de vie était de 71%. Les septuagénaires ont une capacité physique à l'effort plus faible que les patients plus jeunes. Cependant le score d'état de santé global est identique dans les deux classes d'âge. Sur le plan thérapeutique, les traitements pris par les patients au long cours sont résumés à la figure 4. Les évènements cardiovasculaires à long terme (angor, récidive d'infarctus, coronarographie de contrôle, angioplastie) sont représentés à la figure 5, 79,4% des septuagénaires étant exempts d'évènements coronariens à long terme.

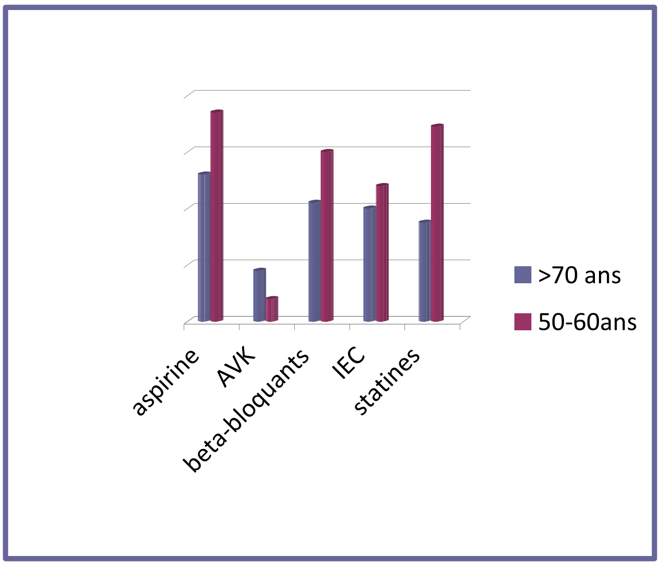

Figure 4:
Traitement pris au long cours. Toutes les différences sont significatives.

AVK: anti-vitamines K;
IEC: inhibiteurs de l'enzyme de conversion

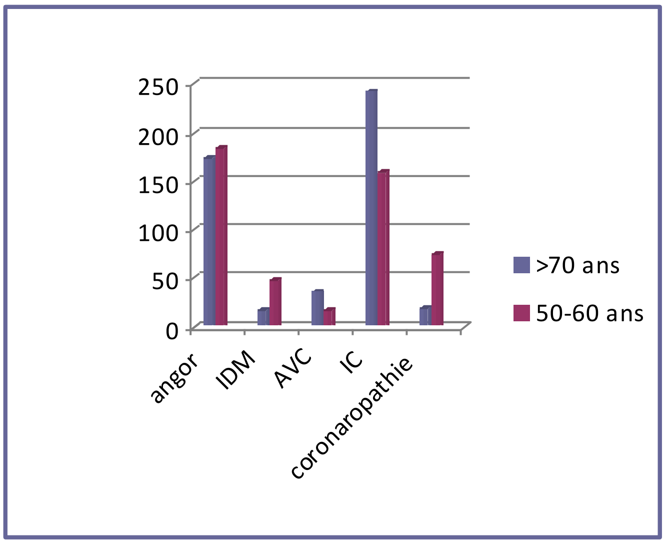

Figure 5:
Évènements cardio-vasculaires à long terme. P non significatif pour toutes les variables.

IDM: ***infarctus du myocarde;***
AVC: ***accident vasculaire cérébral;***
IC: ***insuffisance cardiaque***

Discussion

Les résultats de cette étude montrent que pour des septuagénaires sélectionnés, la chirurgie coronaire isolée peut être proposée et s'associe à une mortalité opératoire comparable à celle d'une population plus jeune. Par ailleurs, de façon intéressante, ces septuagénaires opérés présentent une survie significativement supérieure à celle des septuagénaires de la population générale algérienne et une qualité de vie satisfaisante. L'analyse de la morbidité postopératoire établit un taux significativement plus élevé d'insuffisance rénale postopératoire, de bas débit et de recours aux amines en postopératoire ainsi qu'un taux de transfusion supérieur chez le septuagénaire, ce qui est en accord avec les publications (5–8). Par contre, il y a eu très peu de complications neurologiques (un seul AVC dans chaque groupe: un réel AVC prouvé par TDM chez une patiente de 63 ans, et un AIT avec TDM normale chez un septuagénaire, les deux ayant été opérés sous CEC). Dans ce cas, il existe probablement un biais, car les patients ayant une aorte calcifiée, habituellement considérés à risque d'AVC, ont été opérés à cœur battant, ce qui explique probablement le faible taux d'AVC postopératoire (9-10).

Le taux de mortalité opératoire est variable dans les publications, allant jusqu'à 11,5% (3). Si le taux de mortalité précoce est relativement bas chez les septuagénaires (2,3%) et non significativement différent des patients plus jeunes contrairement à d'autres séries (3,5–7), cela est probablement dû à la sélection rigoureuse des patients septuagénaires qui sont plus souvent en classe I ou II de la *New York Heart Association*, contrairement aux autres séries (jusqu'à 98% des patients en classe III ou IV [20]), avec un Euroscore moyen plus bas que dans d'autres études. Nous n'avons pas réalisé d'études statistiques visant à trouver des facteurs prédictifs de mortalité précoce, en raison du faible nombre de décès.

Sur le plan de la technique opératoire, le type de greffon, artériel ou veineux, ainsi que le mode de revascularisation, à cœur battant ou non, sont également des éléments importants. Pour ce qui est du greffon, les bienfaits sur la survie d'une artère mammaire interne ont été clairement démontrés, y compris chez le sujet âgé (13), et notre attitude est conforme aux recommandations puisque dans notre série, la plupart des patients (autour de 98%, quelle que soit la classe d'âge) ont été revascularisés à l'aide de l'artère mammaire interne gauche. Par ailleurs, les veines saphènes sont plus souvent utilisées en complément chez les patients de plus de 70 ans, tandis que les 50 à 60 ans profitent plus fréquemment d'une revascularisation complètement artérielle (44,8% dans le groupe 2 par rapport à 18,2% dans le groupe 1). Pourtant, malgré un geste plus lourd et plus long sur le plan technique et un risque plus élevé (en particulier chez les patients obèses et diabétiques) de complications infectieuses locales, la revascularisation tout artérielle devrait, en théorie, être proposée davantage aux patients âgés puisqu'elle permet de limiter les manipulations de l'aorte. En effet, il a été nettement démontré que les emboles cérébraux mesurés en doppler trans-crânien (HITS) sont directement proportionnels au nombre de manipulations aortiques (14), l'idéal étant de réaliser une revascularisation artérielle à cœur battant selon la technique sans manipulation de l'aorte (15). En réalité, les veines saphènes sont encore souvent utilisées en complément chez le sujet âgé en raison de la plus grande rapidité et simplicité du geste, (l'IVA étant revascularisée avec une artère mammaire [13]), et on recommande alors la réimplantation sous clampage total du pontage saphène afin d'éviter le clampage latéral de l'aorte, source d'embols en cas d'athérome. Pour ce qui est du mode de revascularisation, la chirurgie à cœur battant semble l'emporter par rapport à la chirurgie sous CEC chez le sujet âgé(9), même si d'autres remettent cette constatation en question (16). Dans notre étude, nous n'avons pas évalué ce paramètre, étant donné la sélection des patients et le faible nombre de décès.

Toutefois, l'analyse des résultats ne doit pas comporter uniquement l'analyse de la morbidité et de la mortalité opératoire compte tenu de la lourdeur de cette chirurgie et de la lenteur de la réadaptation postopératoire, particulièrement à cet âge. L'analyse de la survie à long terme et de la qualité de vie doit être intégrée à toute démarche d'analyse de la qualité des soins chez le sujet âgé. La survie à long terme, de 85% au bout de trois ans dans notre série, est conforme aux résultats contenus dans les publications: de 71,2% (3) à 87% (17) au bout de trois ans. De plus, la comparaison de la survie des patients septuagénaires avec des patients du même âge dans la population générale en Algérie (survie théorique) montre que les opérés ont une survie à trois ans significativement supérieure à celle des septuagénaires de la population générale, alors que pour les 50 à 60 ans, la survie est identique entre les opérés et la population générale (figure 3) (2). Ce résultat est très encourageant, même s'il existe évidemment un biais de sélection, les septuagénaires opérés étant probablement en meilleur état général que les septuagénaires de la population générale. En ce qui concerne la qualité de vie à long terme, « l'état de santé » des septuagénaires est identique à celui des 50 à 60 ans. Par ailleurs, 95,6% des opérés septuagénaires de notre étude vivent à domicile (taux supérieur à celui de la population générale des septuagénaires [29]), ce taux étant identique chez les 50 à 60 ans.

Sur le plan thérapeutique à long terme, nous observons que les sujets plus jeunes sont traités de façon optimale, alors que les plus de 70 ans ont plus tendance à avoir le « traitement minimal efficace » et sont plus souvent sous anticoagulants, probablement en raison d'une plus grande prévalence de fibrillation auriculaire chronique dans cette classe d'âge (20). À l'égard des évènements cardiovasculaires à trois ans, près de 80% des octogénaires sont exempts d'évènements coronariens à long terme, sans différence significative avec les patients plus jeunes.

Les limites de cette étude sont celles inhérentes à une étude uni-centrique et rétrospective. Cependant, les données ont été recueillies de façon prospective. L'autre limite est le taux de retour incomplet des questionnaires. Enfin, l'évaluation par le patient de son état de santé et la définition d'insuffisance cardiaque sont des données en partie subjectives.

Conclusions

Malgré un taux plus important d'insuffisance rénale, de bas débit et de transfusions postopératoires par rapport aux sexagénaires, les septuagénaires qui peuvent profiter d'une chirurgie coronaire s'associent à un faible taux de mortalité précoce, à une bonne qualité de vie et à une meilleure survie à long terme que les sujets du même âge dans la population générale. Il serait intéressant de procéder à une étude comparative auprès d'un groupe supplémentaire de patients septuagénaires traités par angioplastie coronaire.

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Part 9.

NON-CORONARY CARDIAC PATHOLOGY

Surgical management and outcome in primary cardiac tumors*)

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Abstract

Introduction. *Primary cardiac tumors represent a very rare entity within an incidence between 0.0017-0.19%. The majority of the tumors are benign and within this group myxomas constitute the most frequently found tumor.*

Material and Method. *Between 1998-2004, we performed 3325 open heart procedures at the Institute of Cardiovascular Medicine from Timisoara. Primary cardiac tumors represented only 0.63% (21 patients). The majority of these, 71.5% (15 cases) were benign, while 28.5% (6 patients) represented malign tumors. Age ranged between 3 months and 75 years old and the male/female ratio was 1/4. The treatment of choice was surgical removal, regardless with etiology under cardiopulmonary bypass and reconstruction of the structures involved (walls, valves).*

Results. *The early and late postoperative results of the patients with benign tumors (atrial myxomas) were very good, with no mortality. In contrast, the postoperative results for the excision of malign tumors are much worse, in-hospital mortality was 33.3% and all the other patients died within the first postoperative year due to local relapse and metastases.*

Conclusion. *Surgical intervention is the choice management regardless with the origin of all primary cardiac tumors. If left untreated, benign tumors expose the patients to very severe complication, especially cerebral embolism or mechanical obstruction, while their excision resulted in very good survival rate and quality of life. For malign tumors even cardiac transplantation can't improve the long term evolution. However, effective palliation with resection and adjuvant therapy may prolong life.*

Key words: *Cardiac tumors, surgical treatment, outcome*

Rezumat

Introducere. *Tumorile cardiace primitive sunt entități foarte rare cu o incidență între 0,0017-0,19% pe serii largi autopsice. Majoritatea sunt tumori benigne, iar dintre acestea mixoamele reprezintă grupul cel mai frecvent.*

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Material şi Metodă. *În perioada 1998-2004, au fost efectuate 3325 operații pe cord deschis în Institutul de Boli Cardiovasculare Timişoara. Dintre acestea au fost operate 21 (0,63%), tumori cardiace primare, 6 pacienți (28,5%) cu tumori maligne, 15 (71,5%) cu tumori benigne. Vârsta pacienților operați a fost între 3 luni şi 75 de ani, majoritatea de sex feminin (76,1%). Tratamentul a fost chirurgical indiferent de etiologie constând în rezecția tumorii cu ajutorul CEC şi refacerea structurilor afectate (pereți, valve).*

Rezultate. *În cazul celor 15 tumori benigne operate, rezultatele au fost excelente, fără mortalitate precoce şi pe termen lung, fără recidiva locală. Dar extrem de sever în cazul tumorilor maligne, cu mortalitate perioperatorie de 33,3%, iar postoperator toți pacienții au decedat într-un interval de 6-12 luni, prin recurența locală sau metastaze.*

Concluzii. *Tratamentul chirurgical este metoda de ales indiferent de etiologia tumorii. Rezultatele sunt foarte bune în cazul tumorilor benigne, neoperate expunând pacienții la complicații şi deces prin embolii sau obstrucții mecanice. În cazul tumorilor maligne rezultatele sunt sumbre, chiar şi transplantul cardiac nu poate prelungi pe termen lung viața. Cu toate acestea, efectul paliativ, de rezecție asociat cu terapie adjuvantă poate prelungi viața.*

Introduction

Primary cardiac tumors are fortunately a very rare entity with an incidence between 0.0017-0.19%, in general unselected necropsy series (3). From all the cardiac tumors, the primary cardiac tumors constitute just a small minority, 5-10%.

The majority of the tumors are benign and myxomas represent the largest group of the benign tumors. Other benign tumors found are lipomas, rhabdomyomas and papillary fibroelastomas. The malignant tumors represent less than a quarter of the total of primary cardiac tumors. The types of cardiac malignancies include: angiosarcoma, rhabdomyosarcoma and fibrosarcoma.

Patients and Methods

We performed 3325 open heart procedures between 1998-2004 at the *Institute of Cardiovascular Medicine from Timisoara.* Only 21 patients (0.63%) were operated for primary cardiac tumors.

Age ranged between 3 months and 75 years, with an average of 51 years. Gender distribution showed female preponderance (76.1%).

Symptoms are often unspecific and this makes the diagnosis more difficult. While dyspnea (present in 61.9% of the patients), angina (14.2%) and atrial fibrillation (57.1%) were the usual clinical aspects at patient's admission, two patients presented signs of right cardiac failure (jugular pressure raise, hepathomegaly and edema) and 3 patients were asymptomatic (had been detected echographically, following routine medical examination).

All patients were investigated by transthoracic or transesophageal echocardiography. The sensitivity of the method was 90.4% and the specificity was 95%. Echocardiography could reveal not only the location of the tumor, but also its size, shape, plan of insertion, extension within the walls and could estimate the functional impairment it produces. In our group of study, echocardiography detected location of the tumor in left atrium (66.6%), right atrium (9.5%), right ventricle (19%) and left ventricle (4.8%).

Whenever there is the suspicion of a cardiac malignancy, the investigation should be extended by the use of computer tomography (CT-scan) and magnetic resonance imaging (MRI) T-scan. In this way we can diagnose a primary extracardiac tumor with secondary cardiac involvement and we accurately estimate the extension of a cardiac tumor, especially by metastases at the level of mediastinum, lung, liver or other organs. As for the angiocoronarography, although procedural risks are described, our policy was to perform it for all the patients older than 45, irrespective to the absence of angina or risk factors for coronary artery disease.

Although the sensitivity of imaging methods in detecting cardiac tumors was high, neither echocardiography, nor CT-scan or MRI could accurately predict pathological type of a tumor. Some morphological details (location, shape, plan of insertion, extension) could be important for estimation of a malignant nature of a tumor or for suspicion of a specific benign cardiac tumor, but only the histo-pathological examination of the tumoral piece will confirm the diagnosis.

Once diagnosed, a cardiac tumor represents absolute indication for surgery. The patients should be operated as soon as possible since there is an important risk for complications, mainly embolization with a tumoral fragment and mechanical obstruction of one of the cardiac valves.

Medical treatment was sometimes necessary to support patient's cardiac status, but the only option available for all the patients with cardiac tumors was surgical removal. The approach was by median sternotomy, cardiopulmonary bypass using bicaval cannulation, normothermia, antegrade (and retrograde, when right atrium was not involved) blood cardioplegia. The appropriate access opening was used, according to the involved location of the tumor. Once identified, the tumor was excised as possible following the principles of an oncological exclusion. The tumoral pieces were all submitted to histopathology examination. The results for the pathological typing of the tumors are presented in table 1.

Table 1: Tumors characteristics and location in heart

Tumor type		Location	Extension	Valvular involvement
Benign tumors				
myxomas	**12**	Left atrium		Mitral valve (1)
lipoma	**1**	Left atrium		
fibroelastoma	**1**	Left ventricle		
rhabdomyoma	**1**	Right atrium		
Malignant tumors				
Angiosarcoma	**12**	Right atrium	RV	Tricuspid valve
Rhabdomyosarcoma	**1**	Right ventricle	LV, RA	Tricuspid valve
Lymphosarcoma	**1**	Right ventricle	Great vessels	
Mezotelioma	**1**	Pericardium	LV,RV	
Fibrosarcoma	**12**	Left atrium	RV, LV	Mitral valve

For the left atrium tumors, supposed to be myxomas, the approach was through the left atrium after the groove dissection, but with minimal manipulation before aortic cross-clamping to avoid tumor fragments embolism. In one case we used a special aortic cannula with Embolex filter for fragments capture. Types of procedures performed for benign tumors are illustrated in table 2.

Table 2: Operations performed for benign tumors

Type of operation
11 simple resections of the tumor
1 resection + closure of foramen ovale by suture
1 resection + CABG (saphenous vein graft on RCA)
1 resection + patch closure of ASD+ tricuspid de Vega annuloplasty
1 resection of AV junction + aortic and mitral valve replacement (mechanical prostheses

As for the malignant tumors, the approach aimed as much complete tumoral resection as possible, even if that meant replacing valve or wall structures by reconstructive procedures. Of course, this was not possible in all the above mentioned patients (table 3).

Table 3: Operations performed for malignant tumors

Type of operation	
2	resection + partial RV, RA resection + patch reconstruction + TV replacement
1	resection + LA resection + MV reconstruction
1	resection + partial RA resection+ bovine pericardium reconstruction
1	CABG (LIMA on LAD) - no resection
1	patient died of cardiac arrest during angiography

Results

Since the results are completely different, benign and malignant tumors are to be considered separately.

There was no mortality for the group of patients with benign tumors, nor any recurrence within 1 year postoperative period occurred. The early postoperative morbidity was 26,6% (4 patients) and consisted in: 1 patient with bleeding that required reintervention for hemostasis, 1 patient with sick sinus syndrome that required a pacemaker and 2 patients with postoperative atrial fibrillation, converted into sinus rhythm with Amiodarone.

The results in case of malignant tumors were, as expected, much worse. Although no intraoperative death occurred, the mortality after 1 year from the moment of operation was 100%. Here are some particular cases.

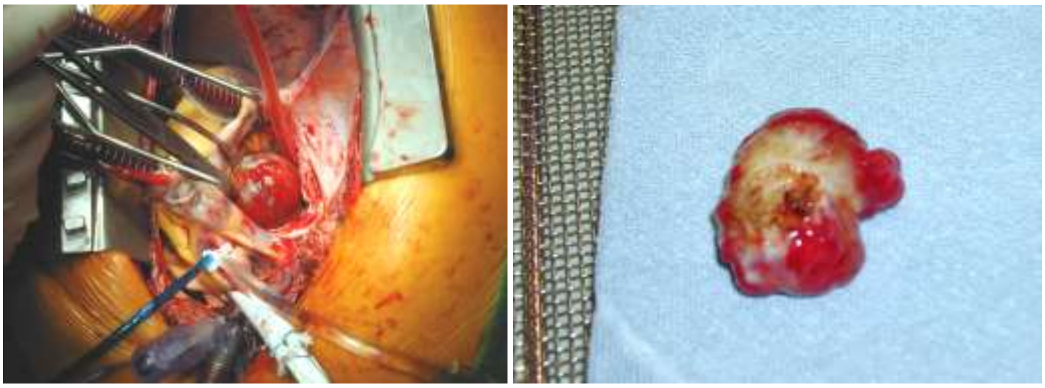

Figure 1: A young female (PH, 47 years old, female) with myxoma of LA diagnosed very late, after two years of diffuse complains

Figure 2: Sever ostial stenosis of RCA on LAO incidence and normal left coronary artery.

Case report 1

A 42 years old female presented for months with diffuse chest pain, fatigue, night sweats, pericardial effusion and treated for the lung tuberculosis until she underwent operation in another cardiac surgery department where only a biopsy was performed: the result was angiosarcoma of right atrium. Finally she was operated and the RA resected and reconstructed with a bovine pericardium. Unfortunately she died six months later with lung metastases (figure 3).

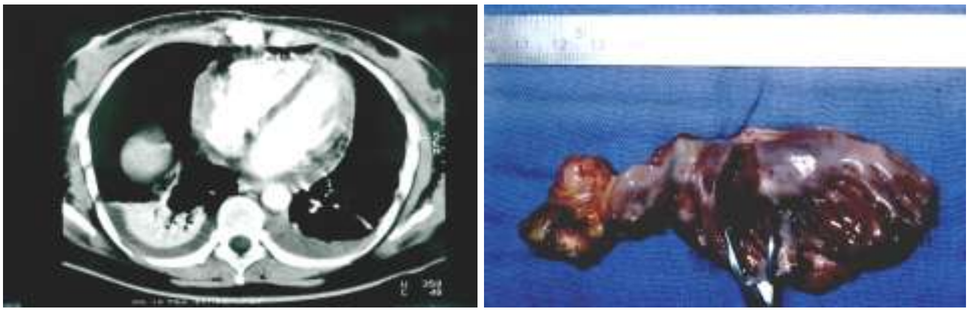

Figure 3: RA angiosarcoma operated by resection and bovine pericardium reconstruction, died six months after operation by lung metastasis

Case report 2

Right ventricular tumors often present with right heart failure as a result of obstruction to right ventricular filling or outflow and the diagnosis can be mistake as massive pulmonary embolism. This was the situation of one of our patient B. M, 52 years old, female with right atrium, tricuspid valve and right ventricle invasion of a rhabdomyosacroma (Figure 4). The tumor was removed using bipolar access to RA and RV outflow tract with tricuspid total invasion and resection, replacement with a mechanical valve prosthesis Omnicarbon 27 mm. The early evolution was favorable with rapid recovery, but unfortunately due to local relapse the patient died after six months.

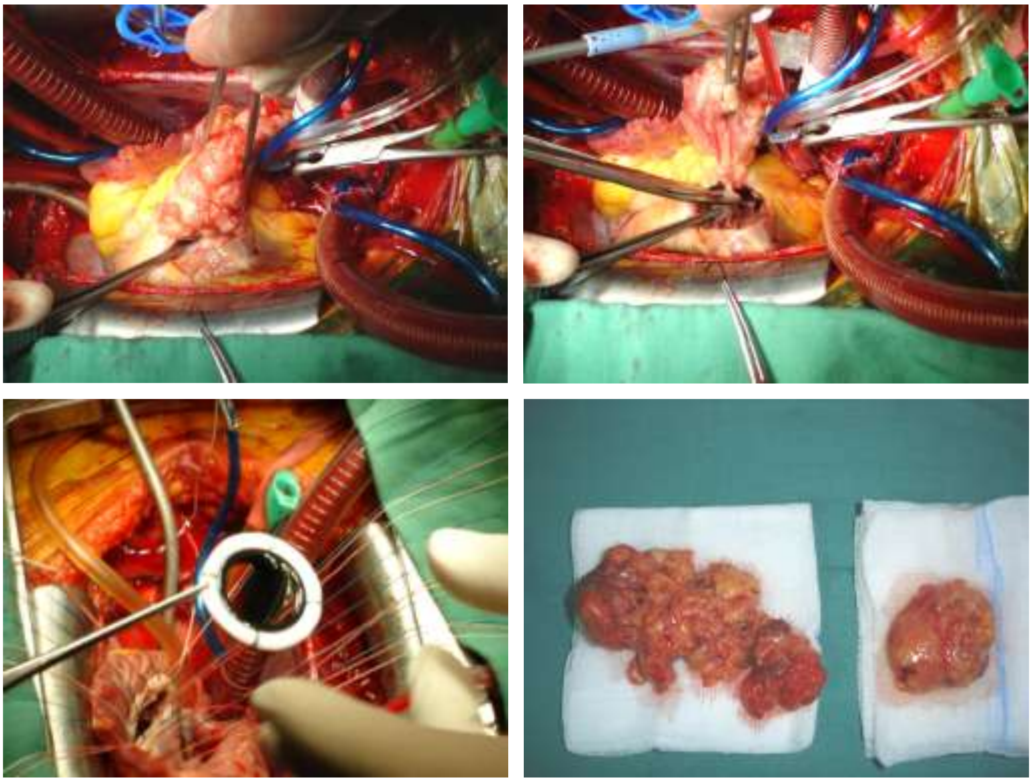

Figure 4: Right atrium, tricuspid valve and right ventricle obstruction by a massive rhabdomyosarcoma. Tricuspid valve replacement with a mechanical Omnicarbon 27 mm

Case report 3

A young patient 30 years old was referred for chest pain and underwent a coronaroangiography to establish the diagnosis. During the procedure he got a cardiac arrest and all the resuscitation maneuver remained without success. At the necropsy the diagnosis was clarify, a large invasive lymphosarcoma involving and obstructing the RV outflow tract and the great vessels, aorta and pulmonary truck (figure 5).

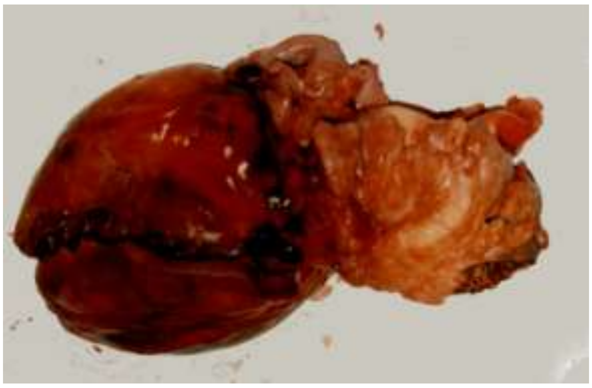

Figure 5: Great vessels invasion by a lymphosarcoma in a young 30 years old, male

Case report 4

A female, PC, 60 years old with coronary artery disease and a stent implantation two years ago in Germany was referred for the chest pain reappearance, angiography was performed and the patient was scheduled for a coronary artery bypass. Intraoperatively a tumor involving the right ventricle and pulmonary artery (mesothelioma) was diagnosed and the revascularization limited to a LIMA-LAD, by-pass on the beating heart under cardiopulmonary support. She died some hours later with low cardiac output syndrome in spite of IABP insertion and maximal dosage of inotropes (figure 6)

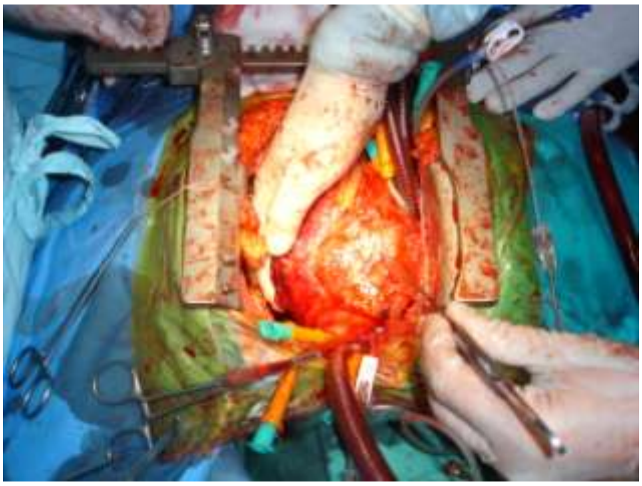

Figure 6: The right ventricle tumor in 60 years old, female scheduled for a CABG

Discussion

Primary cardiac tumors are uncommon and represent only 5-10% of all the tumors, in our group 0.63% from all the open heart procedures, 3325 during six years. With the advanced diagnosis technology, TE echocardiography, spiral CT, contrast MRI, the screening method, primary cardiac tumors became more frequently. The pathological nature of primary valve tumors is difficult to determine on the basis of preoperative clinical presentation and echocardiography.

However, the exact incidence of each specific tumor type cannot be stated. From the literature, about 70-80% of all cardiac tumors are benign histologically and of these more than 80% are myxomas and the remainder 15-20%, are malignant.

Cardiac myxomas are very rare diagnosed on the basis of history, clinical examination and in the majority of patients are notorious for mimicking a great variety of cardiovascular disease, infectious or collagen diseases (2).

Therefore a high index of clinical suspicion by the physician is essential for it early and correct diagnosis, otherwise very simple performed by echocardiography (2) and also a complete examination (coronarography) should be done in some patient (7).

Surgical treatment is easy with excision of tumor, the prognosis of this category of patients is excellent, when the operation is performed in time, before some fatale cerebral embolic complication or sudden death.

Also, during intervention (Jones), a surgical approach to atrial myxomas should allow minimal manipulation of the tumor, provide adequate exposure for complete resection of tumor, allow inspection of all four heart chambers, minimize recurrence, and be safe and efficacious. They use a biatrial approach to myxoma (6). Others consider the exposure of the left atriotomy approach to be adequate and have demonstrated the low recurrence rates and safety of this technique. We used the left atrium approach for the tumors located in LA, but whit bicaval cannulation and total CPB, which give the possibility to open RA whenever is necessary (2, 7). When the valve is involved, the procedure includes either a valve repair (one patient with DeVega tricuspid repair) or valve replacement (double valve replacement with mechanical prosthesis) whenever the damage and safety reason imposed to do.

Regarding the extension of excision, controversy still persists. Some authors recommended a large excision and septum patch repair. However, we and majority of others authors used the simple resection without any higher recurrence. Early result for benign tumors resection, in young patients without any severe associated disease should be with zero mortality and long term survival, alike to general population.

From the malign cardiac tumors, sarcomas are the most common and of these the angiosarcoma and rhabdomyosarcoma are the most common forms, also in our surgical series.

Clinical manifestations include peripheral shortens of breath, edema, hepatomegaly, ascites, syncope, cardiac failure symptoms from obstruction of flow or interference with valvular function, cardiac dysrhythmias are also a common and sudden death.

Operation is not an effective treatment for the great majority of primary malignant tumors of the heart because of the large mass of cardiac tissue involved or the presence of metastases.

It is generally agreed that all valve tumors must be resected. If the valve tumor is malignant, complete resection of the tumor and replacement of the involved valve is the best choice (4, 5).

In this series, 2 patients had a malignant tricuspid valve tumor, extended from RA trough the tricuspid valve, fulfilling the RV up to the pulmonary valve. After tumor resection, the valve was replaced with a biologic Pericarbon in one case respectively Omnicarbon mechanical valve in the second.

The major role for surgery in such cases is to establish a diagnosis in order to exclude the possibility of a curable benign tumor.

Nevertheless, in some cases palliation of hemodynamics and/or constitutional symptoms and extension of life may be achieved by aggressive therapy.

Survivals of 1 to 3 years have been reported following: partial resection, chemotherapy, radiation therapy, orthotopic cardiac transplantation or various combinations of these modalities.

Some success in palliation of symptoms has been reported following the combination of chemotherapy, but not in our two cases. Lymphosarcoma of the heart frequently responds to chemotherapy, radiation therapy, or both. Unfortunately, many other reports indicate a failure to alter the course of cardiac sarcomas despite various combinations of surgery, chemotherapy and radiation therapy.

Conclusions

Surgical intervention is the choice management regardless with the origin of all primary cardiac tumors.

The result for benign tumors are excellent, otherwise the patient is exposed to a very severe complication like cerebral embolism or mechanical obstruction.

For malign tumors, even cardiac transplantation can't improve the long term evolution.

In the absence of randomized clinical trials it is not clear whether adjuvant chemotherapy may be beneficial in patients in whom "curative" surgery has been performed. The role of radiation therapy is less well known. However, effective palliation with resection and adjuvant therapy may prolong life.

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Bridge to transplantation with the MicroMed DeBakey VAD axial pump: a single center report*)

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Abstract

Background. *Pulsatile left ventricular assist devices are an accepted therapy for bridging patients with end-stage heart failure to heart transplantation. Implantable pulsatile devices are very large and major complications as bleeding, thromboembolism and infection are reported. The DeBakey VAD, a continuous axial flow pump that weighs 93 g, has been introduced into clinical practice as bridge to transplant.*

Methods. *From April 2000 till March 2003 14 patients (10 male, 4±14 years; 8 dilated idiopathic cardiomyopathy, 5 ischemic cardiomyopathy, 1 pulsatile device failure) with end-stage heart failure were implanted with a DeBakey VAD for bridge to transplantation at our Institution. Before the implant all the patients suffered of severe heart failure despite maximal pharmacologic support and were put on the waiting list.*

Results. *Ten patients were successfully transplanted after 51±49 days of assistance (range 11-141 days). Two patients died during assistance of multiorgan failure. No patients needed additional right ventricular mechanical assistance. Left ventricle/LVAD thrombosis occurred in one patient and was successfully conservatively treated. No clinically elevation of plasma-free hemoglobin was detected. No device, drive line or abdominal pocket infection occurred. No device failure occurred.*

Conclusions. *In our experience the axial continuous flow DeBakey VAD obtained an elevated rate of success associated with low risk for complications. Patients tolerated continuous blood flow pattern for extended periods which makes this device a valuable alternative to pulsatile ventricular assist devices for bridge to transplant.*

Introduction

The growing number of patients waiting for heart transplantation has more than tripled from 1989 to 1998 and the number of registrants increased by 21% between 1995 and 1998 (1); since the low number of suitable organs available has led to an increase in

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transplant waiting time, up to 30 percent of patients die before cardiac transplantation (2), and many require continuous intravenous inotropic support. In recent years mechanical ventricular assist devices as a bridge to heart transplantation (HTx) has become a standard in clinical practice.

Pulsatile left ventricular assist devices (IAAD) are currently use to bridge these patients to HTx, even if, technical improvements as well as development of small, wearable and mechanically reliable circulatory assist pumps, have encouraged their clinical application and has demonstrated their effectiveness (3,4), however, their clinical use has been complicated by bleeding, infection, and thromboembolism (5).

Recently a new generation of LVAD, the non-pulsatile axial-flow pump, have been introduced and tested; the DeBakey VAD is an implantable left ventricular assist device axial pump with electromagnetic control. Its development was initiated in 1988 (6, 7). In the scope of a left ventricular implantable assist device (8), the challenges taken up by the DeBakey *VAD* were: the choice for a non-pulsatile flow and miniaturization (diameter 30.5 mm, length 76 mm and weight 95 g).

Material and Methods

Between November 1985 to March 2003, 667 patients underwent HTx at "A. De Gasperis" Cardiac Surgery Department in Milan. Among these patients, since March 1988, 121 were supported with a mechanical circulatory assist device in the form of left, right or bi-ventricular assist pumps. Mechanical circulatory assistance as a bridge to HTx was used in 81 of the patients. From April 2000 to March 2003, 14 patients (10 males, mean age 43 ± 13 years) were assisted with the continuous axial flow MicroMed DeBakey VAD™ pump and are the subject of this review. All patients had experienced a sudden or gradual deterioration of their heart function requiring a change in their waiting list priority to Status I for HTx.

The causes of heart failure were: idiopathic dilated cardiomyopathy in 8 patients pts (80%), ischemic heart disease in 5 (36%), in one patient the DeBakey VAD was used after a failure of a pulsatile device implanted in an other Institution. Clinical characteristics of the patients are reported in Table 1.

Table I: Patients clinical characteristics pre-implant

	Mean ± SD
Age (years)	42±12
BSA (mz)	1.7+1.15
AP (mmHg)	73±6.2
PAP (mmHg)	32.4+10.5
RAP (mmHG)	17.5±2.9
PCWP (mmHg)	24.9+10.1
CI (l/min/mz)	1.56±0.55
PVR (WU)	5.412.3
Serum Creatinine (mg/dl)	1.1810.24
Total Bilirubin (mg/dl)	1.8911.3
AST(U/L)	75.3171.2
ALT(U/L)	26.8155.9

Abbreviations:
BSA*: Body Surface Area.* AP*: Aortic Pressure.* PAP*: Pulmonary Artery Pressure.*
RAP*: Right Atrial pressure.* PCWP*: Pulmonary Capillary Wedge Pressure.*
CI*: Cardiac Index.* PVR*: Pulmonary Vascular Resistance.*
AST*: Aspartate aminotransferase* ALT*: Alanine transaminase.*

The inclusion criteria for enrollment and use of an assist device were: left atrial pressure or wedge pressure > 18 mmHg and cardiac index < 2 1/min/m^2 or systolic pressure < 90 mmHg while on therapy with intra-aortic balloon pump and vasopressor agent (dopamine > 10 mg/kg/min, dobutamine > 7.5 mg/kg/min, epinephrine > 0.02 mg/kg/min, isoproterenol > 0.5 mg/kg/min or milrinone > 0,5 mg/ kg/ min). All patients provided their written informed consent for device implantation.

MicroMed DeBakey VAD™

This device consists of three subsystems: a miniaturized axial flow pump actuated electromagnetically, an external controller and a clinical data acquisition system (CDAS). A titanium inflow cannula connects the pump to the apex of the left ventricle and a Vascutek Gelweave* vascular graft connects the pump to the ascending aorta. An ultrasonic flow probe is placed around the outflow conduit. The pump motor cable and the flow probe's wiring are exteriorized above the right iliac crest and attached to the VAD controller system (Figure 1).

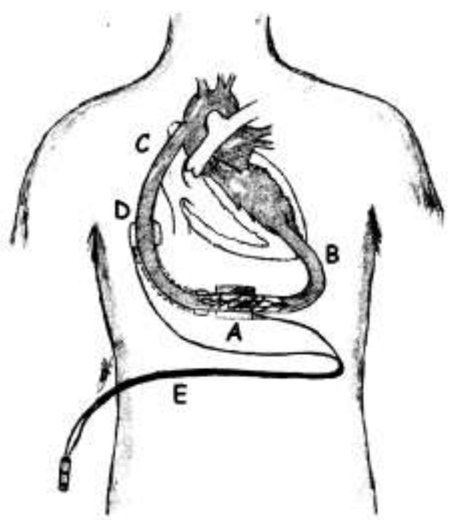

Figure 1: The MicroMed De Bakey VADTM human configuration: die titanium axial flow pump (A) connects the apex of the left ventricle (B) to the ascending aorta (C). The outflow graft to the ascending aorta gets through an intra-thoracic Doppler flow probe (D). The pump motor cable and the flow probe's wiring are exteriorized above the right iliac crest (E) and attached to the VAD controller system.

The pump is 30.5 mm in diameter, 76.2 mm in length and weights 93 gm. It is designed to achieve a blood flow of 5 L/min, against 100 mmHg pressure, with a motor speed of 10,000 rpm and a power input of 10 Watts. The controller is designed to operate the pump, the controller's primary power is provided by two external 12-volt DC batteries. The controller displays pump operating parameters and provides audible as well as visual alarms. The CDAS records and displays pump data (pump speed, pump flow, current and power, and signals) and can be used to modify the pump speed, its primary purpose is to supply power and communicate with the controller; CDAS regulated pump functions. The entire system weighs 2.5 Kg. (9).

Implant procedure

Patient's preparation and monitoring did not differ from other assist devices. A preoperative transesophageal echocardiography (TEE) performed in all patients allowed to detect patent foramen ovale or intracavitary thrombi and to evaluate bi-ventricular function. After cardiopulmonary bypass (CPB) weaning, a TEE was performed to verify the correct inflow cannula position, the loading optimal level and the right ventricular function.

In all cases, the operation was performed through a median sternotomy, no abdominal wall pocket was created. All implantations were performed under CPB with cardioplegic arrest in following order: implantation of the apical inflow cannula and sewn to the apical fixation ring, tunneling of the percutaneous cable at the exit side above the right iliac crest, anastomosis of the outflow graft on the ascending aorta, air deairing, and starting of the DeBakey *VAT)* during gradual CPB weaning-off.

To avoid adhesions and to facilitate surgical reentry at the time of the transplantation, the pericardial closure and wrapping of the VAD and the outflow cannula is done with a Gorelex® membrane (W.L. Gore & Assoc, Flagstaff, AZ) as we previously described (10).

Over the first 48 h the pump speed was progressively increased without exceeding 10,000 rpm, to maintain a minimal speed rotation with a satisfactory cardiac index.

Anticoagulation

Anticoagulation management is based on the protocol proposed by the group of the "*La Pitie-Salpetriere*" *hospital in Paris* (11, 12) and is the same protocol that we use for all patients receiving an LVAD. During the first 24 hours postoperatively, the patients receive no anticoagulation. Thereafter, intravenous heparin therapy is started according to *thromboelastography* (TEG) modified with heparinase and APTT (1.5 to 2 times normal value).

Long-term anticoagulation consists of sodium warfarin (dosage according to international normalized ratio of prothrombin time - INR/PT. 2.5-3.5 x normal value) and enoxaparine (2,000-4,000 Ul/die). This protocol is very careful in regards to platelet activity by including dypiridamol (800 mg/die I.V. intraoperatively and thereafter 800 mg/die orally) and aspirin (100 mg daily). When thrombocytosis or platelet-related hypercoagulability is discovered, ticlopidine (250mg/die) is added to the regimen. Pentoxifylline (400 mg/die I.V. initially and thereafter 800 mg/die orally) is used to further improve hemoreology.

The efficacy of this anticoagulation treatment is monitored by TEG (daily in the acute phase, then weekly when the patients are moved to regular ward and later on whenever it is necessary).

Results

All patients survived the implantation procedure. Weaning from extracorporeal circulation was facilitated, in all patients, with the use of inotropic drugs (dopamine, epinephrine, phosphodiesterase-III inhibitors) and nitric oxide.

The mean duration of MicroMed DeBakey VAD™ support was 59±48 days (range 11-161 days), the cumulative time of support was 27.8 months. Two patients (14.2 %) died while on LVAD due to multi-organ system failure (MOSF) after 13 and 44 days of circulatory assistance. All other patients, recovered rapidly from the operation and were discharged from the ICU to the ward care where they performed regular physical training. As each patient gained confidence with the MicroMed Debakey VAD™ they were taught to manage the device themselves. In our initial experience, the patients assisted with the DeBakey VAD™ were not discharged from hospital, all last three patients have been discharged home.

Ten patients (71.4 %) underwent HTx from 11 to 141 days after LVAD implant. Nine of the ten transplanted patients were discharged home. One patient died of graft failure due to acute rejection 29 days after HTx.

Complications

Two reoperations for bleeding complications were necessary. One patient had one minor neurologic event (slight aphasia lasting less than 30 min), 101 days after LVAD insertion. Contrast CT scan showed a small area of hypodensity compatible with ischemic damage in the left frontal region. One patient experience a major neurologic event after 97 days of support, he had a sub-aracnoideal haematoma, surgically removed. None of the LVAD patients experienced any septic episodes. None of the patients showed signs of inflammation or infection at the exit site of the transcutaneous cables.

Renal failure occurred in one pt with MOSF. Liver failure occurred in 2 patients.

None of the patients had severe right ventricular failure (defined as cardiac index less than 2 L/min /m^2 despite a central venous pressure of 18-22 mmHg and maximal pharmacologic support with inotropic drugs and vasodilators) requiring right ventricular assistance.

On the 112* day of support, one patient experienced possible thrombosis of the DeBakey VAD™ pump despite a normal anticoagulation profile. This complication was suspected because of an increase in Current and Power registered by the controller with a decrease in pump flow rate. Before proceeding to pump replacement, upon recommendation of the manufacturer's technical support staff, we performed endoventricular thrombolysis, by direct delivery of rTPA (*recombinant Tissue Plasminogen Activator*) into the IV as we have previously reported (13). After 20 minutes, power and current values began to diminish, flow rate increased and the clinical status began to improve. After three hours, Current and Power values reached normal ranges, with flow rate normalization (4.5 l/min) and complete hemodynamic recovery. Neither major nor minor neurological events were observed. In the following days, the pump function was appropriate and on POD 142, the patient had a successful cardiac transplantation.

Indices of hemolysis indicated by *plasma-free hemoglobin* (fHb) and *lactate dehydrogenase* (LDH) showed episodes of slight hemolysis. Isolated transient peaks of fHb were detected in a few patients similar to reports by other Authors (14); the plasma fHb peaks were not related to clinical or mechanical events. The level was persistently elevated in one patient during CVVH and normalized after cessation of this treatment. LDH levels also increased in a few patients over the period of cardiac assist similar to other reports (14). The increase in LDH levels was not related to the plasma fHb rise.

Discussion

Despite experimental works reporting pulsatile flow superiority compare to continuous flow (15), the DeBakey VAD has provided satisfactory results support in patients with end-stage heart failure (7,9). Clinical experience has shown compatibility of non-pulsatile blood flow with adequate end-organ perfusion for periods of up to several months (9). Our study is confirmatory to other reports and shows safety and efficacy on this device (16, 17, 18).

In selecting patients we considered factors related to the device characteristics and to the patients probability to get a suitable donor heart in an adequate time frame after the device implantation. Consequently we did not implant this device in patients with a large body surface area, (e.g. > than 2 m^2). Other indications for device implantation such as the preoperative end-organ function (especially liver and kidneys) followed the criteria used for all patients that needed an LMYD.

In our experience the MicroMed DeBakey \AD™ is an effective device as a bridge to HTx with a high success rate. These results are due to improvement in end-organ function achieved by multiple factors including the function of the DeBakey VAD™, and strict adherence to our anticoagulation protocol. Therefore, a low rate of adverse events such as bleeding, thromboembolism and infection was encountered in this study and by others (14, 17, 18). We attribute the low incidence of bleeding complications in this study mainly to the careful application and monitoring of "La Pitie" anticoagulation protocol (11, 12), which has a multi-systematic approach to all the determinants of the coagulation cascade.

The DeBakey *VAD* miniaturization permits small surgical incision together with a strictly intrathoracic implantation of the pump. By avoiding the making of an abdominal nesting site, this device provides a better comfort to the patient and reduces device infectious complications.

Inflammation or infection at the motor cable exit site was not observed in our patients. This was probably related to both the small diameter and flexibility of the percutaneous cable and to the lack of pump motion due to non-pulsatile flow.

Conclusion

In conclusion, the continuous axial flow MicroMed DeBakey VAD™ as bridge to heart transplantation demonstrated a good hemodynamic performance and low incidence of major complications and achieved a high rate of conversion to HTx.

The advantages of miniaturization and ease of implantation provided by this new device support are encouraging so far.

We thank Cristina De Santis for the cooperation and drawing.

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Acute fulminant myocarditis-mechanical circulatory support a chance to recovery*)

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Abstract

Acute-fulminant myocarditis is a disease with unclear pathophysilogy and etiology, difficult diagnosis and very large spectrum of clinical presentation. Very rare is presentation with hemodynamic instability or franc acute cardiogenic shock. Such patients if the diagnosis isn't giant cell myocarditis, have an excellent prognosis for complete long term recovery if they are supported aggressively. An aggressive approach to the use of mechanical support is strongly recommended. Survival, either by bridge to transplantation or recovery, should approach 70%.Transplantation should and can often be avoided. We present a young, 24 years female, with acute-fulminant myocarditis with chlamidia pneumonia and Parvovirus B19, acute cardiogenic shock, which was first supported by ECMO for 48 hours and then Thoratec bi-ventricular assist device, to support her hemodynamic. After two weeks, she recovered with normal cardiac function and was weaned from mechanical circulatory support. This case report, show that full cardiac recovery is possible and even likely despite fulminant and catastrophic presentation, avoiding a cardiac transplantation with his implication.

Background Case Report

Acute fulminant myocarditis is a disease with unclear pathophysiology and etiology, difficult diagnosis and very large palette of clinical presentation. Very rare is presentation with hemodynamic instability or acute cardiogenic shock (1). Moreover, *chlamidia pneumoniae myocarditis* is an uncommonly described disease. We present this case report, with such pathology, first time diagnosed a live, which has been successfully treated by BVAD-Thoratec.

A 24-year old female (Sweedish snowboard teacher) had: fever, fatigue, dyspnea and broncho-pulmonary complains, in December 2000 - March 2001 treated empirically

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with antibiotics; admitted in our Department of Cardiac Surgery Innsbruck (March 14, 2001) with critical status. On arrival she was with respiratory failure, hypotensive, tachycardic, high fever (39.5°C), elevated CRP of 5 mg% (normal value: < 0.7 mg%), increased Troponin I level, 160 g/l (normal value: 0.0-0.5 /g/l). She was emergently intubated due to this situation.

Transesophagial Echo (TEE) showed an evident impairment of both left and right ventricles contractility, but with normal diameters and normal valvular function, without pericardial effusion. Computer Tomography (CT), found pleural effusions and infiltrations of both lungs, hepatomegalia and intraperitoneal fluid. First samples of blood and sputum from aspiration were sending to microbiology laboratory and intravenous antibiotic management started with an association between ceftriaxon and erytromycin. But subsequently the next hours she developed a frank acute cardiogenic shock requiring high doses of inotropic support

Repeated TEE examination yielded rapid deterioration of LV function with EF to a minimum of 10%. After an episode of ventricular fibrillation and cardiopulmonary resuscitation an extracorporeal membrane oxygenation (ECMO) via percutaneous femoral vessels access was implanted to stabilize the situation. After 48 hours under ECMO hemodynamic didn't improved and decision for long-term mechanical circulatory support Thoratec (Thorated Laboratories Corporation, Pleasanton, CA) was made. The CPB was established and the inflow cannula was placed into the apex of LV and the outflow cannula was sutured to the ascending aorta (LVAD). Intra-operative TEE study decided the necessity for bi-ventricular support because of RV distension and consequently BVAD was implanted and ECMO was in this time explanted (figure 1).

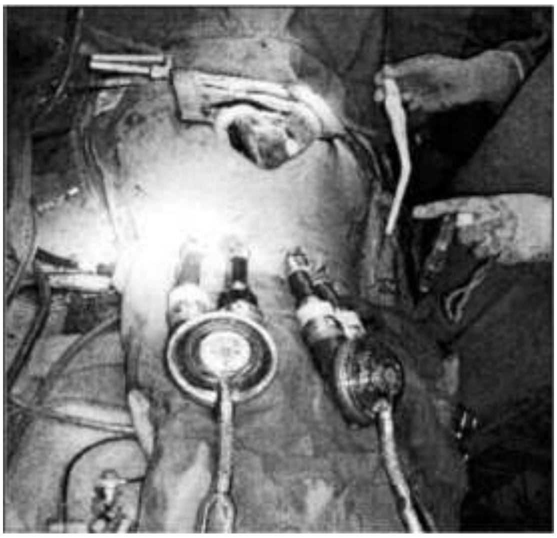
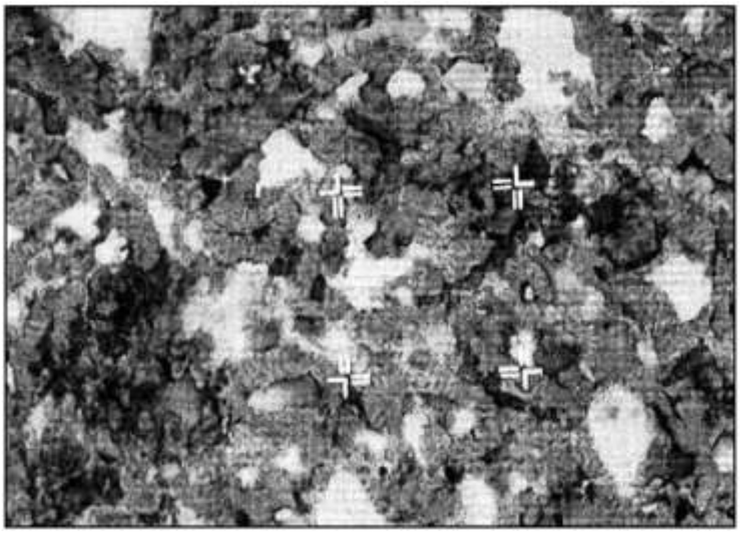


Figure 1: Intraoperative view of Thoratec BVAD implantation, already working ECMO with arterial and venous cannula in the right femoral region (before expantation)

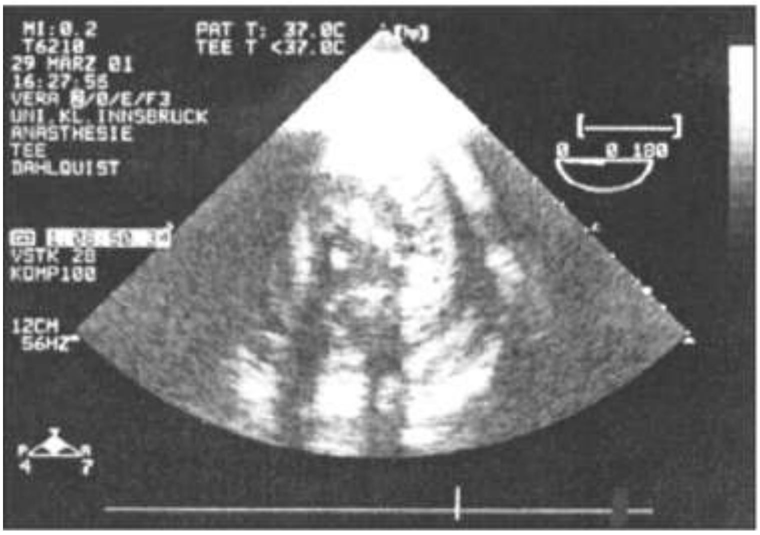
In this time several endomiocardial biopsy specimens (EMB) were collected for histopathology and sent to different laboratory (Austria, Germany) for study.

The final diagnosis of acute myocarditis was made certainly some day later after histopathology which proved massive, diffuse lymphocytic infiltration with myocite necrosis consistent with fulminant myocarditis (after Dallas criteria). Biopsy tissue specimen contained also DNA of Chlamidia pneumoniae and, surprisingly Parvovirus B19 by PCR and Southern-blot (figure 2).



Under BVAD implantation several episodes of ventricular fibrillation occurred and requiring transthoracic defibrillation. The patient homodynamic however remained completely stable unde BVAD augmentation (LV: 5.2 l/min, RV: 4 l/min) with renal function recovery.

Figure 2: Histopatological confirmation of acute fulminant myocarditis, massive lymphocytic infiltration with myocyte necrosis



She was specific treated with erythromycin and unburden the diseased heart by assist device patient slowly recovered and after 12 days successfully weaned from BVAD, showing good cardiac recovery. TEE at that time of explanation revealed nearly complete restitution of ventricular function **(figure 3).**

Figure 3: TEE after BVAD explantation showing recovery of LV contractility with EF-45%, without pericardial effusion

The blood checking showed with blood count, CRP and Troponin I reached almost normal values. Another 14 days later the patients being now mobilized was referred to her home hospital to continue the rehabilitation program. At discharged she had sinus rhythm, chest X-ray without signs of pleural effusions or congestion, laboratory findings were inconspicuous. Medication at discharged consisted of oral /3-blocker and diuretic and a course of oral erytromycin was given to prevent a relapse. One year later she is fully recovered.

Discussion

Acute myocarditis, inflammation of the heart muscle, is a very severe disease, with a large spectrum of symptoms and difficult to manage. Diagnosis is based on the cardiac clinical symptoms after exclusion of, ischemic, valvular, collagen vascular endocrinopathies and autoimmune etiologies (1). But the final diagnosis depends by EMB on the presence of an inflammatory infiltrate (lymphocytic) associated with myonecrosis according with Dallas criteria. In our patient we had previously some months, floulike symptoms and on admission very severe founding of inflammation, with increased PCR, leucocytes, Troponin I and EMB showed massive, diffuse lymphocytic infiltration with myocyte necrosis.

Regarding the etiology of acute myocarditis, a large variety of infections, systemic diseases, drugs, and toxins have been associated with the development of this disease. However, *Chlamidia pneumonie* is often found in patients with bronchopulmonary disorders but chlamidia pneumonie myocarditis is an uncommonly described disease, mostly first diagnosed at necropsy (13). To our knowledge it hasn't been published this situation while the patient was still alive. Such patient with acute myocarditis, if the diagnosis is not giant cell myocarditis, have excellent prognosis for complete long term recovery if they are supported aggressively (6, 7, 8). The histological predictors of recovery are not very clear (4, 9).

No specific therapy is currently available in acute myocarditis, treatment remains primarily supportive. Standard immunosuppressive therapy has not proved his effective in adults (3, 6). Very rarely the patient's clinical evolution is more fulminant leading to acute cardiogenic shock, severe hemodynamic decompensation requiring mechanical circulatory support (7). That there is a little medical report of using mechanical support for acute myocarditis (Westaby, described from literature 11 other cases) (6). Long-term recovery after mechanical support for acute myocarditis remains unclear (9). Even, in case of chronic dilatative cardiomyopathy some authors reported a recovery, but this report is considered more anecdotal (4).

Several assist devices are now currently available for postcardiotomy shock (first used by DeBakey 1963) (12) "bridge to recovery" or to "including ECMO, ABIOMED (Danvers), Thoratec (Thoratec Lab. Plesanton, CA), Berlin Heart and centrifugal pumps. However, ECMO is a poor method of supporting such patients because it doe not decompress the LV and may produce increased LV wall stress or promote thrombus formation in spite of anticoagulation (2). Our experience laso, suggested the need of ECMO replacement with assist device. Like assist device we have available in our Department, ECMO (Medtronic), Thoratec, Berlin Heart for adults and children and IABP (Datascope.System 97, Bard).

Thoratec Reports a total of 40 patients with acute myocarditis supported by Thoratec VADs, 28 (70%) BVAD, and 16 (40%) LVAD. From these 16 patients (40%) recovered and 14 (35%) patients were discharged from hospital. Another 18 patients (45%) were transplanted and 17 discharged. Overall survival was 78% (12). Survival, under mechanical circulatory support for acute fulminant myocarditis, bridge to recovery or to transplantation should approach 70% and an aggressive approach to use early at the beginning of cardiogenic shock of assist device is advised (1). Better is to avoid cardiac transplantation in this young patient.

Conclusion

This case report show that full cardiac recovery is possible despite fulminant and catastrophic presentation, with acute cardiogenic shock, avoiding a cardiac transplantation by intensive mechanical circulatory support and specific therapy.

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The importance of surgery in controlling the electrical storm in a patient with an implantable cardioverter and left ventricular anevrysm*)

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Abstract

Introduction*: An electrical storm is defined as multiple occurrences (at least 3) of ventricular tachycardia/fibrillation within a 24-hours period. It has an Incidence of 10-20% of implanted ICD patients.*

Material and Methods: *We report here on a successful treatment of electrical storm that was refractory to amiodarone and β-blockers in a 60-years-old ICD recipient who underwent surgery for ischemic cardiomyopathy and huge LV aneurysm. LV aneurysm resection, Cooley left ventricular remodelling and surgical revascularization of the myocardium with the left IMA on LAD anastomosed in Y fashion with the left radial artery sequentially on the obtuse marginal artery and on the posterolateral artery of ACX were performed under extracorporeal circulation.*

Results*: At 15 months we noticed a marked improval of the systolic function; the ICD did not record any therapeutic episodes.*

Conclusions*: Surgical management could be an effective treatment for patients with ischemic heart diseases, ventricular aneurysms and refractory electrical storms to antiarrhytmic drugs.*

Key words: *electrical storm, implantable cardioverter deffibrilator, surgical revascularization*

The electrical storm is defined as the appearance of 3 or more than 3 episodes of sustained of ventricular tachyarrythmias in 24 hours (1). The majority of ventricular tachycardias (VTs) occur in patients with structural heart disease, predominantly coronary heart disease. The non-ischemic conditions are represented by Brugada syndrome and long QT syndrome (2). Its incidence is situated between 10 and 20 percents in patients with implantable cardioverter defibrillators (1). The electrical storm represents a major medical emergency.

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Implantable cardioverter defibrillators (ICDs) are first-line therapy in patients with VT and structural heart disease. The implantable devices are associated with antiarrythmic therapy (Amiodarone, beta blockers, Procainamide).

Catheter ablation is often very efficient in eliminating ventricular tachycardia. However, several factors make catheter ablation of VT more difficult than ablation of supraventricular tachyarrhythmias:

- The infarct region is often large.
- The induced VT can be unstable or hemodynamically only poorly tolerated and therefore "unmappable".
- Though most commonly located in the subendocardium, the critical VT zone can occasionally be epicardial or intramural in location. For these cases, an epicardial ablation technique was described by Sossa in 1998 (3).

In many cases, several reentrant circuits may coexist (4).

It has been demonstrated that electrical storm was associated with worse HF morbidity and mortality and has a very negative psychological impact, profoundly affecting the quality of life of these patients (5).

An effective alternative to these techniques is the surgical treatment of patients with an ischemic substrate.

We present the case of a 60- years-old patient who underwent successful surgery for ischemic cardiomyopathy and huge LV aneurysm. From 2007 he was known with insulin dependent diabetes mellitus. In August 2007 he suffered an inferior myocardial infarction and in July 2008 an extensive anterior infarction. In 2008 he received an implantable cardioverter defibrillator. He presented in our hospital with frequent episodes of ventricular tachycardia, which were refractory to beta blockers and Amiodarone. More than that, the treatment with Amiodarone has to be stopped in December 2008 due to QTc prolongation more than 30%. On the 23rd of July 2008 the patient presented 15 episodes of ventricular fibrillation, which necessitated 21 electrical shocks (Figure 1).

The echocardiographic exam showed a severe depressed systolic function (left ventricle ejection fraction of 16%, with a huge apical aneurysm) (Figure 2, 3, 4). TAPSE was 11 mm, indicating also right ventricle dysfunction.

The coronary angiography showed severe tri-vessel disease (Figure 5, 6, 7, 8) and the ventriculography confirmed the poor ejection fraction and the presence of the aneurysm (Figure 9).

LV aneurysm resection, Cooley left ventricular remodelling and surgical revascularization of the myocardium with the left IMA on LAD anastomosed in Y fashion with the left radial artery sequentially on the obtuse marginal artery and on the posterolateral artery of ACX was performed under extracorporeal circulation.

The postoperative evolution was excellent. We noticed a marked improval of the functional class. At 15 months the graft patency was verified by arteriography, left ventricular function by ultrasound and ventriculography, and also was recorded the ICD history. The postoperative ejection fraction increased to 45-50% (Figure 10, 11, 12). The ICD did not record any therapeutic episodes (Figure 1). All the grafts were patent (Figure 13, 14). The ventriculography showed no apical aneurysm (Figure 15).

BIOTRONIK ICS 3000 SW 702.A

Florea, Vasile

Lumax 340 VR-T S/N 0060430990

PID 31 RAM ID 5.2.1

Holter - Episodes 09/24/2010 13:22

No.	Time	Zone	RR [ms]	Description	RR [ms]
45	07/23/09 10:01	VF	230	2 Shocks	1055
44	07/23/09 10:00	VF	177	2 Shocks	895
43	07/23/09 10:00	VF	175	2 Shocks	1021
42	07/23/09 09:59	VF	247	1 Shock	1001
41	07/23/09 09:57	VF	178	2 Shocks	1114
40	07/23/09 09:56	VF	203	1 Shock	999
39	07/23/09 09:56	VF	122	1 Shock	1009
38	07/23/09 09:55	VF	260	1 Shock	999
37	07/23/09 09:54	VF	339	1 Shock	999
36	07/23/09 09:53	VF	181	2 Shocks	360
35	07/23/09 09:53	VF	352	1 Shock	1000
34	07/23/09 09:52	VF	165	1 Shock	971
33	07/23/09 09:51	VF	262	1 Shock	702
32	07/23/09 09:50	VF	185	1 Shock	551
31	07/23/09 09:50	VF	180	2 Shocks	708
30	07/19/09 20:54	VT2	285	3 ATP's	465
29	07/19/09 20:54	SVT	297		***
28	07/19/09 20:50	VT2	296	2 ATP's	587
27	03/23/09 13:30	VF	249	1 Shock	683
26	03/23/09 10:32	VF	235	1 Shock	643
25	03/23/09 10:20	VF	235	1 Shock	676
24	03/23/09 09:58	VF	278	1 Shock	674
23	03/23/09 06:52	VF	258	1 Shock	710
22	03/23/09 05:03	VF	243	1 Shock	706
21	03/23/09 03:22	VF	244	1 Shock	724
20	03/22/09 20:29	VF	248	1 Shock	663
19	03/22/09 18:18	VF	248	1 Shock	598
18	03/21/09 22:13	VF	259	1 Shock	644
17	03/21/09 04:28	VF	247	1 Shock	661
16	03/21/09 01:29	VF	241	1 Shock	725
15	03/20/09 20:58	VF	243	1 Shock	646
14	03/20/09 13:31	VF	264	1 Shock	598
13	03/19/09 13:22	VF	252	1 Shock	622
12	03/18/09 15:11	VF	249	1 Shock	638
11	03/18/09 15:09	VF	264	1 Shock	669
10	02/14/09 17:35	VF	295	1 Shock	699
9	12/07/08 17:48	VF	227	1 Shock	658
8	12/07/08 17:47	SVT	321		***
7	12/07/08 17:47	VT2	317	1 ATP	393
6	12/07/08 17:46	VF	273	1 Shock	548
5	12/07/08 17:45	VF	199	1 Shock	515
4	12/07/08 17:44	SVT	380		***
3	10/27/08 11:12	VF	271	2 Shocks, induced	957
2	10/27/08 11:07	VF	283	1 Shock, induced	***
1	10/27/08 11:05	VF	263	1 Shock, induced	799

Display episodes [x] AT/AF [x] VT/VF [x] SVT [ ] Since last follow-up

Figure 1: History of preoperative arrhythmic events

Figure 2: Preoperative long axis parasternal view

Figure 3:
Preoperative 4 chambers apical view

Figure 4:
Preoperative 2 chambers apical view

Figure 5:
Preoperative coronarography

Figure 6: Preoperative coronarography

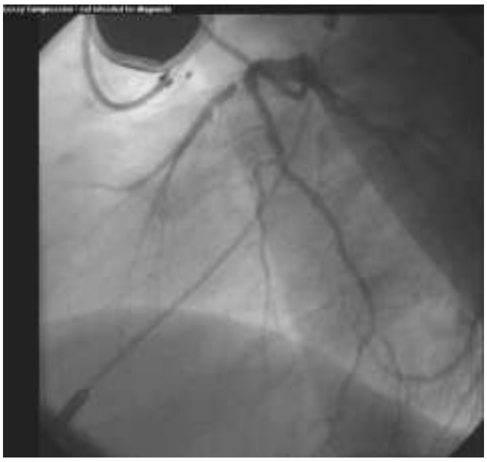

Figure 7: Preoperative coronarography

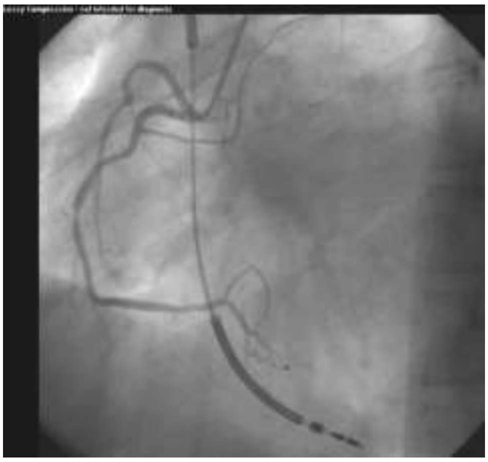

Figure 8: Preoperative coronarography

Figure 9: Preoperative ventriculography

Figure 10: Postoperative long axis apical view

Figure 11: Postoperative 4 chambers apical view

Figure 12: Postoperative 2 chambers apical view

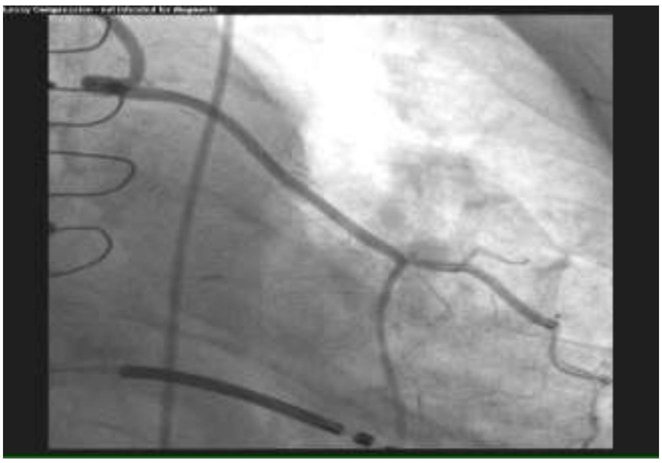

Figure 13: Postoperative coronarography – Patent graft

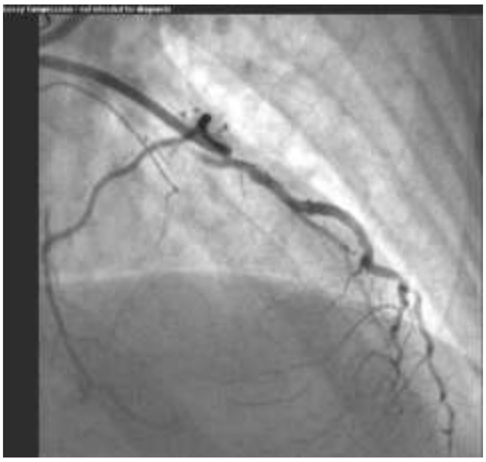

Figure 14: Postoperative coronarography

Figure 15: Postoperative ventriculography

Conclusions

Electrical storms are frequent in patients with ischemic heart diseases and ICD. The management requires use of both simple and sophisticated methods, but often these expensive methods remain ineffective. In coronary artery disease patients, surgical revascularization can relieve the ischemic substrate of electric storm, hence prevents sudden death effectively. Also there are still very few data in literature, our data is consistent with the international experience (6, 7, 8), showing that surgical management (myocardial revascularization and excision of the scar tissue) could be an effective treatment for patients with huge aneurysm and refractory electrical storms to antiarrhytmic drugs.

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The treatment of chronic atrial fibrillation by radiofrequency ablation in open heart surgery*)

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Introduction

Atrial fibrillation (AF) is associated with 30% to 50% of mitral valve diseases with surgical indication; even if a lot of patients are in sinus rhythm after the operation, only 10% of them presents sinus rhythm 1 year after the operation.

Atrial fibrillation is a well-known risk factor for thromboembolism (1), it decreases cardiac output and, in many patients, is badly tolerated being responsible for severe complains, in spite of medical treatment (2, 3). It multiplies the risk of death by two and the risk oh stroke by five. Consequently, attempts have been made to treat this condition, particularly in mitral patients. Surgical correction of atrial fibrillation in patients with other cardiac pathology that requires surgical intervention such as mitral valve disease was never considered as a standard approach. Several methods for the surgical treatment of AF have been described (4, 5), the most common approach, in mitral patients, being the "Maze" operation. Excellent results with this and other alternative techniques have been reported (6, 7). However, the results were poor with regard to restoration of bilateral atria contraction (8). It was demonstrated that AF treatment could be achieved by functionally excluding selected areas of the atria with the percutaneous endocavitary radiofrequency ablation (9), but this method exposed to serious thromboembolic complications. The intraoperative use of this method could overcame this problem, since the clots can be easily removed under direct vision in the operating room. The effect of the radiofrequency currents consists in fat lysis, myocyte degeneration and protein coagulation which lead to endocardial transmural lesions (10).

Material and Methods

Patients

Between 01.07.2000 and 30.06.2002, 26 patients (13 males and 13 females) with chronic AF were operated. There mean age was 69.5 years, and the AF was present for a period ranging from 6 months to 8 years.

All the patients presented mitral stenosis. Associated pathologies were present in one patient (aortic valve disease). The patients had a good ejection fraction (EF), the mean EF was 60 ± 4%.

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The association of amiodarone with betablokers represented the preoperative treatment; the postoperative guidelines consisted in anticoagulation for six months, amiodarone for three months and cardioversion in case of recurrence.

Surgery

Surgery was performed under extracorporeal circulation, using the standard method (bicaval canulation) in all patients. After cardiopulmonary bypass was established, patients were cooled to 32°C. Myocardial protection was achieved with cold blood cardioplegia infused ante- and retrogradly. The left atrium was opened with an incision parallel to the interatrial groove in front of the right pulmonary veins.

Before starting the procedure, cold saline was infused inside and outside the atrium and a compress was placed behind the atrium to prevent esophagus damages. After the inspection of the atrial cavity and the mitral valve, the radiofrequency catheter was placed inside the right atrium in such a way that a continuous line around the right pulmonary vein was obtained, extending the incision in front of the pulmonary veins around its superior, posterior and inferior limits. Ablation was performed by firing sequentially each one of the seven electrodes of the radiofrequency catheter (Thermaline Probe) during 120 sec, to achieve a temperature of 60 to 70°C. A second circular ablation, around the left pulmonary veins was performed using the same technique. All patients had isolation of the pulmonary veins performed like in the figure 1.

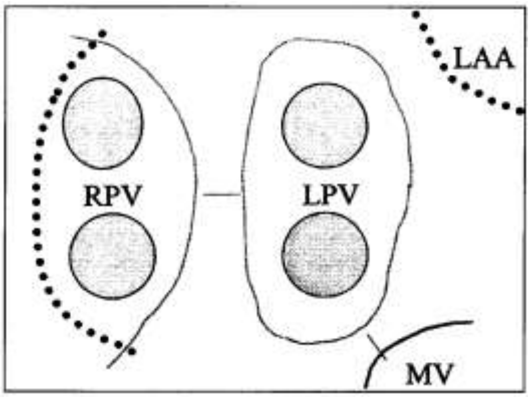

Figure 1: Bilateral pulmonary veins' isolation viewed from the left atrium.

After this procedure, the left atrial appendage was surgical excluded in all cases. The mitral and additional associated surgical procedures were then performed in a conventional way. Mitral valve operations were replacement in 12 cases, repair in 13 cases, in one case the mitral valve replacement was associated with aortic valve replacement.

Follow up

The patients were evaluated on discharge from the hospital, 3 and every 6 months thereafter. The mean follow-up was 18 ± 6 months.

Results

As a consequence of the ablation there were no local or general complications, no atrial wounds, there was no reintervention for bleeding attributable to the radiofrequency procedure.

In the first post-operative week, only one death was observed, not related to the radiofrequency ablation, 8 patients presented sinus rhythm and one pace-maker implant was necessary.

The follow-up was 100%complete. The length of it is up to 24 month, all the patients had a follow up more than 6 months.

Late 2 deaths were occurred, not related to the surgical procedure. Thirteen patients (50%) regained normal sinus rhythm and another 8 (42.4%) patients remained in FA. The remaining two patients (7.6%) required permanent pacing.

The post-operative treatment was represented by warfarine in 16 patients, and antiarrythmic drugs in 15 patients. There was no cardioversion reported (follow-up error?).

Discussion

In recent years, the popularity of simplified intra-operative ablation approaches to treat atrial fibrillation has been progressively increasing. Comparison between published results of AF surgery, from distinct groups, is difficult. Differences in criteria for patient selection and for assessment of surgical results can contribute to the discrepancies between our results and those reported by others.

The Santa Cruz score (11) considers rhythm and contraction of each atria, for the assessment of the end result of these operations. Because of each multivarious based ranking, it becomes a more accurate way of evaluating results, thus substituting the comparison between different methods. Unfortunately, we didn't have all this criteria because of the difficulties during the entire period of the follow-up.

Our technique, reported also by Melo et al. (9), consists in replacement of surgical incisions by radiofrequency ablation, a technique used also by the electrophysiologists for percutaneous treatment of atrial arrhythmias. In these cases, it was associated with a variable degree of thromboembolic events. With endocardial ablation late thromboembolic events never occurred, neither in our experience nor in the literature (9).

In our experience, sinus rhythm was restored in practically all the patients immediately after surgery (like in the literature), but only 8 of 26 patients treated preserved the sinus rhythm in the first postoperative week. After minimum 6 months, 13 patients presented sinus rhythm, which is a very good result, even better than the series published in the literature. The postoperative medical treatment explains maybe the better percentage of patients in sinus rhythm after 6 to 24 months postoperatively.

It is clear that radiofrequency ablation is a very fast procedure and the risk for complications is minimal, if carefully used. At the moment, this is the most effective and safe method to induce scars in the atria (12). Development of catheters specifically designed for this purpose will further hasten and improve the efficacy of this procedure.

Conclusions

We conclude that atrial fibrillation surgery can be safely performed with intraoperative radio-frequency ablation, the final results being as good as surgical incisions, even better. This method has also the advantage of being faster and safer, so it represents a very good indication for atrial fibrillation surgery. The successful rate at 18 moths was 50% in 26 patients treated with this technique.

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Recent data regarding the cardiopulmonary bypass induced inflammatory response*)

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Inflammation that is encountered in patients suffering open heart surgery is due to a series of cellular and humoral complex interactions that enclose pathways of activation that more or less overleaf. A series of compounds results from this activation. Among these, there are: thrombin, activated factors of complement, cytokines, activated leukocytes, adhesion molecules, activated mast cells. The activation process is redundant and often much exaggerated. As a consequence, the inflammatory response overshoots its target of protection of the own organism coming into contact with a huge foreign surface and becomes harmful to its own systems. The resulting dysfunction of various organs may manifest as coagulation disorders, respiratory failure, myocardial dysfunction, renal failure or neurocognitive defects.

The inflammatory response associated with cardiopulmonary bypass (also known as post-CPB inflammatory response) often presents as a systemic inflammatory response (SIRS - systemic inflammatory response syndrome) that is similar to that encountered in sepsis. This inflammatory response is one of the main arguments in favor of off-pump cardiac surgery. It needs to be stressed, though, that even in off-pump cardiac surgery a relatively intense inflammatory response may appear, inflammatory response that is very similar to that encountered in on-pump cardiac surgery.

As shown above, many systems are activated by cardiopulmonary bypass. Many of these systems are activated in cascade and have links between them or even share common pathways. For example, the coagulation system and inflammation are closely interrelated. The close relationship between inflammation and coagulation is encountered at the level of humoral and cellular components but foremost at the level of coagulation and fibrinolysis proteases.

A central role in the development of post-CPB inflammatory response is played by thrombin. Despite high-dose heparinization with long ACT's, on cardiopulmonary bypass certain levels of circulating thrombin are encountered.

Thrombin plays a pivotal role in coordinating, integrating and regulating hemostasis. Depending on the circumstances, it can either promote or prevent blood clotting. This effect of thrombin is known as the "thrombin paradox". The balance of prothrombotic and antithrombotic activities of thrombin is determined by at least two variables: the concentration of free thrombin in blood and the presence or absence of intact endothelial cells at thrombin's site of action. When free thrombin is available in blood in high concentrations and especially where intact endothelium is not present,

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thrombin is a potent inductor of clotting by activation of several coagulation factors leading ultimately to fibrin formation, factor XIII activation and promoting of fibrin cross-linking and activation and aggregation of platelets. In these procoagulant conditions reciprocal, interdependent and mutually self-amplifying interaction occurs between thrombin generation and platelet activation. Membranes of activated platelets facilitate thrombin generation and platelet activation. Conversely, thrombin is a potent activator of platelets, stimulating the availability of additional activated platelet surface for further thrombin generation.

At lower concentrations of thrombin and in the presence of intact endothelium, the antithrombotic effects of thrombin predominate. Low levels of thrombin stimulate increased levels of the endogenous anticoagulant, activated protein C. Furthermore, intact endothelium, by means of endothelial thrombomodulin, removes free thrombin from the circulation. Low concentrations of thrombin also stimulate t-PA release and the release of antiplatelet PGI2 and NO from endothelial cells. Thus, thrombin plays a central role in modulating the state of blood coagulability, depending on its free concentration in blood and the presence or absence of intact endothelial cells at its site of action.

Thrombin is produced mainly as a result of the contact of blood with the wide surface of the extracorporal circuit. Thrombin is also produced as a result of the activation of the components of the system of inflammation. Tissue factor is expressed in high concentrations on monocytes activated by cytokines, monocytes that play a major role in the defense process. Both the humoral and cellular components of inflammation (local and systemic) induce endothelial cell activation. This activation is associated with the expression of various adhesion molecules on the cell membrane and with the production and release of different proinflammatory cytokines. Adherence of inflammatory cells is by these means facilitated. The adhesion and activation of proinflamatory cells is associated with release of cytotoxines that promote endothelial damage. Endothelial cell damage produces areas of denuded subendothelial tissue that is rich in tissue factor. The extrinsic activation pathway of coagulation is promoted and the end result is also thrombin formation.

Thrombin can induce a wide variety of celular responses. Thrombin is a strong activator of endothelial cells. Its action increases the expression of cell adhesion molecules and especially of P-selectin. Consequently, adhesion, activation and diapedesis of neutrophyl granulocytes are promoted. This process is also associated with a degree of endothelial damage produced by the activating granulocytes. Leukocytes are also directly activated by thrombin by means of specific membrane receptors for thrombin. The release of chemotactic and proinflammatory cytokines is stimulated. Aside from the specific receptors for thrombin, thrombin also activates a group of leukocyte membrane receptors known as PAR's (protease activated receptors). These are transmembranary receptors that induce G-protein mediated cell activation.

Circulating monocytes and leukocyte fragments that are encountered in the blood flow as a result of CPB associated cellular damage express tissue factor, too. This tissue factor acts as a receptor for platelets and activated endothelium. Concentration of monocytes and leukocyte fragments in centers of inflammation takes place. Focal cell accumulation pushes the balance between procoagulant and anticoagulant factors toward procoagulation. As a result new quantities of thrombin are generated.

A particular form of proinflammatory stimulus is the ischemia-reperfusion phenomenon. Cell damage produced especially by oxygen free radicals induces an inflammatory response that is mediated by cytokines and adhesion molecules. Recruitment and activation of monocytes, neutrophyles and other cells takes place. Cell activation favorizes the generation of thrombin that on its turn supports the inflammatory process. The activation of PAR'S induces the expression and release of soluble proinflammatory factors as IL1 and IL.6, chemotactic factors as IL8 or monocyte chemotactic factor 1 (MCF 1), and adhesion molecules as P-selectin, E-selectin or ICAM 1 (inter-cellular adhesion molecule).

Neutrophyle granulocytes are the main cells involved in the post-CPB inflammatory response. Loss well-known is the role of mast cells and bazophyles. Recent data indicate the fact that the activation of mast cells and bazophyles play a key role in coupling of inflammation with coagulation. Mast cells have an ubiquitary tissue distribution but are particularly concentrated in the perivascular space of certain organs as is the heart, skin, lung or intestine. The usual pathway of mast cell and bazophyle activation implies IgE, but these cells can be activated also in the absence of this antibody. Their activation is associated with the release of a great variety of mediators that influence the activity of virtually all cells involved in inflammation: endothelial cells, leukocytes, platelets, myofibroblasts. Meanwhile the proteases that are released contribute in the remodeling of extracellular matrix.

Complement activation may consecutively activate neutrophyle granulocytes. Complement activation may be due to the presence of an immune stimulus (the presence of imune complexes) or directly as a consequence of the action of heparin, protamine, endotoxins e.a. The C5a component of complement acts on high affinity ligands on the membrane of neutrophyles and platelets initiating the activation of these cells. The activation of neutrophyles is considered to be one of the causes of the post-transfusion syndrome (including the transfusion related lung injury - TRALI) and also of the pulmonary vasoconstriction that appears after protamine administration. The use of an antagonist of complement activation - Pexelizumab, a monoclonal antibody against C5a - may represent a future effective method for avoiding the inflammatory response appearing under these circumstances.

Post CPB inflammatory response may induce coagulation system disturbances that resemble the syndrome of disseminated intravascular coagulation - DIC. This is characterized by a fall in platelet count, fall of the level of fibrinogen, increase of the D-dimer levels and increase of coagulation times (PT, APTT). These changes can also be encountered in the usual, non-complicated patient suffering on-pump cardiac surgery. A central role in the pathophysiology of DIC is played by antithrombin III (AT III). Often patients with open-heart operations (especially those receiving preoperatively heparin) have an AT III deficiency. CPB produces also a fall in AT III levels. AT III seems to play a central role in the prevention of end organ damage consecutive to inflammation being in itself antiinflammatory. The therapeutic administration of AT III (isolated or in various associations) is now being evaluated as a measure to treat post CPB inflammatory response.

An important component of the anti-inflamatory therapeutic approach is the administration of aprotinin. Aprotinin is a well known protease inhibitor of animal origin (extracted from bovine lung). The effect of aprotinin in reducing postoperative blood loss and need for transfusion is now established. Aprotinin is routinely used in patients receiving pre-operatively aspirin and in patients suffering cardiac reoperations. The use of aprotinin is not associated with an increased risk of vein graft thrombosis, peri-operative myocardiac infarct or perioperative renal failure. It also appears that the incidence of perioperative stroke is influenced favorably by the use of aprotinin. The antiinflammatory effect of aprotinin is dose-dependent. Its mechanism of action in this regard is complex and is due mainly to the inhibition of activation and adhesion of neutro-phyles.

Aprotinin selectively blocks a receptor PAR that is present on the platelet surface (PAR 1). This receptor is activated by thrombin. Aprotinin does not alter other mechanisms of platelet activation.

It has been proven that aprotinin decreases the rate of neutrophyle migration through the endothelial barrier. Aprotinin inhibits the expression of various adhesion molecules o the endothelial cell surface. The expression of these molecules (as are ICAM 1, VCAM 1) is stimulated by the action of TNFa. This is probably the main mechanism of neutrophyle tissue migration inhibition. It is suggested that aprotinin is rather antithrombotic and antiinflammatory than prothrombotic. The beneficial role of aprotinin administration is once more underscored.

It may be concluded that to the present day our knowledge regarding the pathophysiology of end-organ damage secondary to CPB is relatively scarce, as are the approaches to influence and limit those. There is enough space in the future to add to the few therapeutic options available today others to counterbalance the exaggerated, redundant activation of inflammation and its negative effects on various organs and systems. We know and are able to detect a large number of mediators with more or less important actions. We do not know what the consequences of selective blockade of one or more of these could be. Pharmacological or biological agents or combinations of these to decrease the deleterious effects of the systemic response to CPB remain to be identified and the results of their use assessed.

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Chronic constrictive pericarditis associated with Dubin-Johnson Congenital Jaundice*)

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Abstract

Constrictive pericarditis is characterized by the encasement of the heart by a rigid, thickened, non-pliable pericardium and by the diastolic impairment of the heart due to dense fibrosis and adhesions of the pericardial layers. We present the case of a patient known with Dubin-Johnson jaundice who presented with exertional dyspnea and fatigue. Noninvasive and invasive investigations confirmed the clinical supposition of constrictive pericarditis. The surgical treatment consisted in complete lysis of the intrapericardial adhesions, with removal of the thickened and calcified areas of the visceral pericardium and antero-lateral interphrenic pericardectomy. The association between Dubin-Johnson and constrictive pericarditis is purely incidental and does not influence neither the therapeutic approach for constrictive pericarditis nor the surgical outcome.

Keywords: *constrictive pericarditis, jaundice, pericardectomy*

Rezumat

Pericardita constrictivă este caracterizată de îngroşarea şi uneori calcificarea celor două foiţe ale pericardului, cu formarea unor aderenţe între ele şi de disfuncţia diastolică pe care aceste modificări ale pericardului o determină. Prezentăm cazul unui pacient cunoscut cu icter congenital Dubin-Johnson care s-a prezentat cu dispnee la efort şi fatigabilitate. Investigaţiile noninvazive şi invazive au confirmat suspiciunea clinică de pericardită constrictivă. Tratamentul chirurgical a constat în liza completă a aderenţelor intrapericardice, cu eliminarea zonelor fibrozate şi calcificate ale pericardului visceral şi pericardectomie antero-laterala interfrenică. Asocierea icterului Dubin-Johnson cu pericardită constrictivă este pur întâmplătoare şi nu afectează abordul therapeutic sau evoluţia postoperatorie.

Cuvinte cheie: *pericardită constrictivă, icter, pericardectomie*

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Introduction

Constrictive pericarditis (CP) is characterized by the encasement of the heart by a rigid, thickened, non-pliable pericardium and by the diastolic impairment of the heart due to dense fibrosis and adhesions of the pericardial layers.

Although the etiology spectrum has changed dramatically over the past decades, almost 42% of the cases with CP have no identifiable cause. While not easily recognizable, CP is a severe disease with rapid progression of symptoms leading to early death if left untreated. Pericardectomy is the procedure of choice and the results improved significantly in the last decades, despite the enlargement of the co-morbid spectrum of surgically approached CP.

Dubin-Johnson jaundice is an autosomal recessive congenital disease characterized by a genetic defect of the protein responsible with the excretion of the conjugated bilirubin through the canalicular membrane of the hepatocyte into the bile, thus resulting in permanent increase of the plasmatic level of conjugated bilirubin.

Case report

Patient B.T. is a 62 year old male, known with a Dubin-Johnson jaundice syndrome. The patient has been in atrial fibrillation for more than 6 months.

During the previous three months before admission he accused worsening exertional dyspnea, fatigue, edema and dyspepsia. The patient has not undergone any cardiac or thoracic surgery before and had no history of chest trauma, tuberculosis or irradiation therapy. General presentation at admission revealed an intense generalized jaundice, but with only a moderate hepatomegaly and no splenomegaly. Several clinical signs, although nonspecific for CP, constituted important markers of the diastolic impairment: ankle edema, distended jugular veins and the above mentioned hepatomegaly.

Auscultation offered an important sign, the so called "pericardial knock", a diastolic sound that marks the abrupt cessation of the rapid filling. Both the Kussmaul sign (an increased venous pressure during inspiration due to the inability of the constricted right heart to accommodate the normally increased venous flow) and the paradoxal pulsus (due to the prominent right ventricular filling at the expense of the left ventricular filling, with subsequent decrease of left ventricular stroke volume and pulse amplitude during inspiration) were absent.

Electrocardiogram showed atrial fibrillation with diffuse low-voltage aspect and T wave flattening. Chest X-ray (Figure 1) *revealed a slightly enlarged cardiac silhouette, a moderately enlarged upper right mediastinum (due to dilatation of the superior vena cava), a moderate right pleura effusion and relatively homogenous diffuse calcification of the pericardium, better seen on an image at the angiogram* (Figure 2).

Figure 1: Chest X-ray of the patient with enlarged rightupper mediastinum and right lower pleural effusion.

Cardiac echography was an important diagnostic tool. The M-mode demonstrates diffuse thickening of the pericardium with calcification. Two dimensional echography shows moderately enlarged atria, apparently normal end-diastolic volumes of both ventricles, normal ejection fraction of the left ventricle and especially leftward displacement of the interventricular septum.

Cardiac catheterization and angiography were performed. Hemodynamic data were valuable adding to the echographic findings: the "dip plateau" aspect of the ventricular pressures and the prominent X and Y waves of the jugular venous pressure. Calcifications along the pericardium were clearly visible (Figure 2) *and the coronary arteries were normal. Laboratory data indicated a markedly increased bilirubinemia* (291µmol/l), *mostly based on the conjugated fraction* (273 µmol/ℓ). *Once the diagnosis of CP was reached, the surgical indication was clear. Median sternotomy has been used to access the pericardium and a careful dissection starting with the anterior pericardium freed all the adhesions between the parietal and visceral layers.*

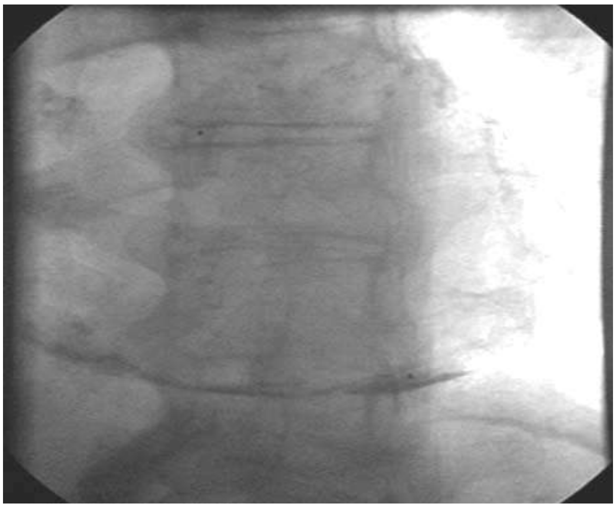

Figure 2: Pericardial calcifications.

Furthermore, the visceral pericardium was subsequently cleaned up by all fibrosed and calcified segments. Anterior interphrenic pericardectomy has been performed (Figure 3). *Postoperative evolution of the patient was very good, with relief of dyspnea and other symptoms connected to CP. No complication (low cardiac output or any other) occurred.*

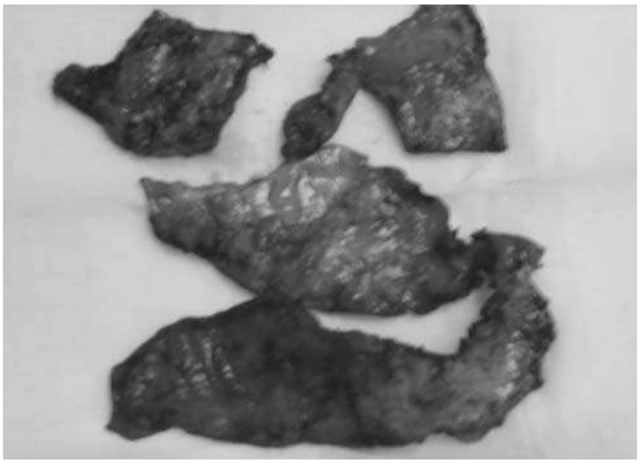

Figure 3: Excised fragments of pericardium

Discussion

CP is usually the late consequence of an initial episode of acute pericarditis, which may not be detectable clinically, characterized by fibrin deposition, often with a pericardial effusion. There may be one or several recurrent episodes, followed by organization and resorbtion of the effusion that will eventually lead to chronic fibrous scarring, thickening and calcification of the pericardium with obliteration of the pericardial space. Sometimes it requires months or even years after the initial episode for CP to become manifest.

In the past, the mean identified cause for CP was tuberculosis. This declined dramatically in the western developed country, but it still accounts for an important proportion in the rest of the world, including our country. Postsurgical CP increased largely during the last two decades, mostly because of the highly increased number of cardiac operation. Practically all the cardiac operations lead to the formation of adhesions between the two layers of the pericardium, but usually these adhesions are not thickened. Literature data indicate only 0.3% the incidence of CP after cardiac surgery. Irradiation therapy also became widenly used and subsequently one of the important causes of CP. Still, in nearly 42% of the patients with CP, no cause can be clearly identified (in some of these cases, viral etiology is suspected for the initial episodes of acute pericarditis, but this is often very hard to prove), forming the so called idiopathic CP group.

Clinical manifestations of CP are mostly nonspecific and often relate to the right cardiac failure symptoms and signs: edema, jugular venous distension, hepatomegaly, ascite, anorexia, fatigue. Dyspnea is often present, attributable to left heart diastolic dysfunction. Kussmaul sign is present in over 60% of the patients with CP, denoting an increased rigidity of the pericardium. Paradoxal pulsus may appear in 30% of the patients with CP, its low frequency compaired with cardiac tamponade being explained by the fact that pericardium became completely noncompliant and does not permit the even transmission of intrapleural pressure, which augments RV filling, combined with the primary inspiratory decrement in LV filling.

Chest X-ray is offering nonspecific data. The cardiac silhouette may be small, normal, or enlarged. Cardiac enlargement may be apparent because of coexisting pericardial effusion, the contribution of an enormously thickened pericardium, or preexisting cardiac chamber enlargement or hypertrophy. The right superior mediastinum may be prominent as a result of dilatation of the superior vena cava, and left atrial enlargement is common.

Extensive calcification of the pericardium is present in approximately half the patients and raises the possibility of a tubercular etiology.

ECG is nonspecific but often reveals diffuse low voltage with nonspecific ST-T changes. Atrial arrhythmias including atrial fibrillation may be present, related to underlying myocardial abnormalities, epicardial inflammation and calcification, as well as atrial dilatation.

Echography is the easily available tool for diagnosing CP, although its sensitivity and specificity are not as high as for other parietal disorders. *M*-mode echocardiography shows pericardial thickening in constrictive pericarditis, either two parallel lines representing the visceral and parietal pericardia separated by a clear space of at least 1 mm, or multiple dense echoes. Other *M*-mode echocardiographic abnormalities include abrupt posterior motion of the interventricular septum in early diastole, coinciding with the pericardial knock, abrupt posterior motion during atrial systole, reduced amplitude of left ventricular posterior wall motion, and premature pulmonary valve opening secondary to a high right ventricular early diastolic pressure. Two-dimensional echocardiography in constrictive pericarditis shows an immobile and dense appearance of the pericardium, abrupt displacement of the interventricular septum during early diastolic filling ("*septal bounce*"), prominent early diastolic filling, and an abnormal contour of the junction of the left ventricle and left atrial posterior wall. Dilatation of the hepatic veins and inferior vena cava, intense and spontaneous contrast in the inferior vena cava, and distention of the inferior vena cava with blunted respiratory fluctuations in diameter ("*plethora*") are also observed in patients with constrictive pericarditis. Other important echographical aspects are characteristic respiratory variations in Doppler flow velocities. Although two-dimensional imaging may confirm thickening of the pericardial layers, limitations of near field imaging limits accurate imaging of the pericardium by ultrasound. Recent studies suggest transesophageal echo may be more promising.

Both CT and MRI scanning techniques provide superior images for assessing pericardial thickness and delineating its conformation (eccentric and concentric) around the heart. Both techniques show excellent correlation in measurement of pericardial thickness confirmed at surgical exploration or by autopsy.

Cardiac catheterization is useful in the assessment of patients suspected of having constrictive pericarditis to assess the increased filling pressures, to evaluate myocardial systolic function, to obtain complementary data necessary for differentiation between constrictive pericarditis and restrictive cardiomyopathy, and to exclude compression of the coronary arteries or regional outflow tract compression by the fibrotic pericardium. Catheterization of both the right and left ventricles should be performed to permit simultaneous recording of right and left heart filling pressures. Typical findings include the elevation and virtual identity (within 5 mm Hg) of right atrial, right ventricular diastolic, left atrial (pulmonary capillary wedge), and left ventricular diastolic pressures. Right atrial pressure is characterized by a preserved systolic x descent, a prominent early diastolic y descent, and a and v waves that are small and equal in height and result in the typical M or W configurations.

Natural history of CP was never fully assessed since prospective studies comparing outcome for patients treated medically with patients undergoing pericardectomy have never been performed. However, observational studies and case reports suggest that in most instances CP without surgical intervention causes a progression of symptoms and, frequently, early death.

Chronic constrictive pericarditis is a progressive disease without spontaneous reversal of either pericardial thickening or abnormal symptoms and hemodynamics. The majority of patients who are symptomatic and come to medical attention, become progressively more disabled by weakness, ascite, and peripheral edema and subsequently suffer the complications of severe cardiac cachexia.

Surgical treatment is practically the only option in severe CP. Once the diagnosis has been established, any important delay should be avoided for the above mentioned reasons and not only for those (see the postoperative results).

The operation consists of a complete lysis of the intrapericardial adhesions, with removal of the thickened and calcified areas of the visceral pericardium and antero-lateral interphrenic pericardectomy. The approach may be by median sternotomy or by anterolateral thoracotomy. Sometimes, cardiopulmonary by-pass may be necessary. If extensive calcifications due to tuberculosis are present, the extent of pericardial removal should be increased to a subtotal pericardectomy.

The outcome of surgery for chronic constriction has been influenced over time by changes in the underlying disease states and by evolution of surgical technique and management, with current operative mortality approaches 7-10%. Operative mortality significantly lower (vs. historical standards of nearly 25% perioperative mortality) was attributed to improved anesthesia, medical management, surgical techniques, and perioperative care, but late survival results were somewhat disappointing. Many patients suffer postoperative low-output syndrome. Although the large majority exhibit improved functional class, hemodynamic abnormalities, particularly diastolic filling impairment, may remain abnormal initially. Persistent diastolic abnormalities after pericardectomy correlate well with patients who have had symptoms longer preoperatively. This finding supports the recommendation that pericardectomy be performed promptly in symptomatic patients with constrictive pericarditis.

Among patients who survive the operation, symptomatic improvement can be expected in about 90 per cent and complete relief of symptoms in about 50 per cent of patients. Dubin-Johnson jaundice syndrome is quite rare. Jaundice is generalized, due to moderately or highly increased levels of conjugated bilirubin. The transport of the conjugated bilirubin over the canalicular membrane of the hepatocyte is impaired, while in the Rotor syndrome, very similar as for the clinical features, the intracell storage of conjugated bilirubin is altered. Both are asymptomatic, although the Dubin-Johnson may rarely lead to moderate hepatomegaly and mild gastro-intestinal symptoms (dyspepsia, anorexia). The specific diagnosis is the determination of urinary coproporphirine, whose isomer I is predominant in Dubin-Johnson syndrome. No association was reported in the literature between CP and Dubin-Johnson jaundice.

Conclusions

The association between Dubin-Johnson and constrictive pericarditis is purely incidental and does not influence neither the therapeutic approach for constrictive pericarditis nor the surgical outcome.

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Advantages and disadvantages of different pericardial closure techniques and materials after cardiac operations using the heart-lung machine*)

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Abstract

Objective: *Retrosternal and intrapericardial adhesions develop when the pericardium is left open after cardiac operations under extracorporeal circulation, leading to an increase in mortality and morbidity in the event of reoperation. Numerous methods of pericardial closure have been developed but the ideal way has not been found. The aim of our investigation was to study the most employed methods of pericardial closure and to compare them with a new one using a parieto-mediastinal pleural flap developed by us.*

Methods: *Four methods were studied in 24 Goettingen miniature pigs divided into four equal groups: group A (reference group): direct pericardial closure, group B: pericardial closure by means of a parieto-mediastinal pleural flap, group C: pericardial closure by means of a Biocor bovine pericardial patch and group D: pericardial closure by means of an expanded polytetrafluorethylene patch. After a period of 8.4 months, the animals were reoperated and intrapericardial macroscopic and microscopic findings were recorded.*

Results: *All of the methods of pericardial closure employed ensured protection of the heart and great vessels during resternotomy. Autologous tissues (group A and B) provided better protection against adhesions and epicardial reactions than foreign materials (group C and D). Using the point scores after analysis of the macro and microscopic findings, group B proved superior followed by group A. Group C was in last place with the worst results. Some better results were found in group D.*

The results of our investigation allow the following conclusions to be drawn: direct pericardial closure after cardiac operations should principally be carried out. Pericardial closure by means of a parieto-mediastinal pleural flap is a promising method, particularly if direct closure is not possible. The use of biological materials, e.g. Biocor bovine pericardial patch, is not to be recommended. The use of the expanded polytetrafluorethylene patch should be limited to pericardial closure after correction of congenital cardiac anomalies.

Keywords: *Pericardial substitute, adhesion, cardiac surgery, reoperation*

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Introduction

After cardiac operations, the pericardium can often no longer be closed directly because enlargement of the heart or is deliberately left open. Direct closure is also no longer possible if the pericardium has been used to correct a cardiac defect or following a reoperation. Epicardio-sternal and intrapericardial adhesions that develop postoperatively increase the mortality and morbidity of reoperation [1-5]. The goal of pericardial closure is restoration of the continuity of the pericardial space with or without the aid of pericardial substitutes, thus protecting the intrapericardial structures in the event of resternotomy and avoiding the formation of adhesions and an epicardial reaction. A large number of autologous, xenologous and synthetic materials that make closure of the pericardium possible if direct suture is impracticable have been investigated. As an autologous graft, Kohanna used fascia lata [6] and Pacholowicz and Shawarby used peritoneum [7, 8]. Pericardial closure by means of a parieto-mediastinal pleural flap is a new method developed by us, which uses an autologous (pericardium-like) patch on a pedicle as a pericardial substitute. A large number of xenografts have been tested in animal experiments and clinical studies. Glutaraldehyde-fixed bovine pericardium has been used most often [9-13]. The variety of synthetic materials used for pericardial replacement is also very large. From the range of these materials, expanded polytetrafluorethylene (ePTFE) (Gore-Tex® Surgical Membrane, W.L.Gore & Assoc. Inc., Flagstaff, USA) has proved to be the best [14-19].

The aim of our investigation was to determine the extent to which the closed pericardium ensures that the intrapericardial structures are protected during resternotomy; if the amount of intrapericardial adhesions and the epicardial reaction is dependent on the pericardial substitute employed and the feasibility and value of a new pericardial closure method by means of a parieto-mediastinal pleural flap compared with the other materials used in the study.

Materials and methods

In order to cover all the possible methods of pericardial closure in a representative fashion, an autologous patch, a xenologous and a synthetic pericardial substitute were chosen. The standard direct pericardial closure was used as reference. The parieto-mediastinal pleural flap was used as autologous patch. From the range of biological materials, the Biocor bovine pericardial patch (Biocor® No-ReactTM Bovine Pericardial Patch, Biocor Industria e Pesquisas LTDA, Belo Horizonte, Brazil) and the ePTFE from the range of the synthetic materials was selected. The Goettingen miniature pig was chosen as the experimental animal. The study was conducted in 24 female animals with the authorisation of the Animal Protection Committee of Braunschweig Regional Government, in compliance with the European Convention on Animal care and under the supervision of the Animal Protection Representative of the Medical Faculty of the Georg August University Goettingen. The weight of the animals at the time of the operation was 37.92 +/- 2.17 kg (26.3-70 kg). They were aged 10-12 months.

After attachment of the heart-lung machine, extracorporeal circulation (ECC) was carried out for 30.04 +/- 0.72 min (25-38 min). A membrane oxygenator (Oxy51®, Sorin Biomedica S.p.A., Saluggia, Italy or Sarns 6443®, 3M Medica GmbH, Borken, FRG) was used. During ECC, the core temperature of the animals was initially cooled down to 32°C, and after 15 minutes, the core temperature was warmed up again to 36°C. After the period of ECC, the 24 animals were allocated to four groups of six animals each for the further procedure. In each group one of the pericardial closure procedures or materials was employed, which was determined randomly on the day of operation. In group A the pericardium was closed directly after apposition of the edges, using interrupted sutures at approx. 1.5 cm intervals. The length of the closed pericardial incision was 12.33 +/- 0.30 cm (11-13 cm). In group B the pericardium was closed using a parieto-mediastinal pleural flap on a pedicle. After a vertical incision of the left pleural space, the parietal pleural flap was separated from the anterior inner side of the chest wall by blunt and sharp dissection. In order to preserve the blood supply an approx. 2 cm wide pedicle was created from the mediastinum outwards. The thickness of the flap was 1 to 5 mm. The area of the pleural flap was 57.00 +/- 2.72 cm^2 (48-65 cm^2). The flap was then transposed with the mesothelial surface on the anterior wall of the heart and its margins were fixed to the edges of the pericardium with interrupted sutures at 1.5 cm intervals. A Biocor bovine pericardial patch was used for pericardial closure in group C. The size of the patch, which was cut to an oval shape in relation to the extent of the pericardial incision, was 119.16 +/- 12.03 cm^2 (96-180 cm^2). During implantation, one half of the circumference of the patch was fixed to the right margin of the pericardium with interrupted sutures at approx. 1.5 cm intervals and the remaining half of the circumference of the patch was sewn onto the inner surface of the pericardium on the left side. In group D, the pericardium was closed with the aid of an ePTFE patch. The size of the patch was 72.00 +/ 0.00 cm^2. The implantation method corresponded to that used in group C. The operating time was 104.33 +/- 2.91 min (87-135 min). All animals survived without operative complications.

Postoperative recovery was protracted in two animals. Mobilisation took place on the first postoperative day, and the animals were also allowed their first feed on the morning after the operation. Gastrointestinal haemorrhage occurred as a late complication in one animal 182 days after operation.

All animals were reoperated after a period of 250.83 +/- 3.99 days (195-274 days) in the same order as the primary operations. After resternotomy retrosternal and intrapericardial adhesions were divided. The time necessary for this procedure was noted. Six parameters were studied to document and evaluate the macroscopic intraoperative findings (Table 1). An assessment scale was developed.

Normal findings were given 0 points, slight changes 1 point, significant changes 2 points and severe alterations 3 points. Afterwards biopsies were taken from 2 different regions of the heart for histological examination: epicardial surface of the left ventricle in contact with the pericardial substitute and epicardial surface of the right ventricle away from the surface of the pericardial substitute. The pericardial substitute material was removed in toto. Graduated sections were prepared and stained with haematoxylin-eosin and Masson-Goldner trichrome. The preparations were examined by light microscopy. Two “blind” histological assessments were made. Nine parameters were examined to document and assess the histological findings (Table 2). The same assessment scale as for macroscopic findings was used.

Statistics

The data obtained in this investigation are shown as the mean. The standard deviation is used as a measure of scatter. Statistical analysis was performed using a commercial statistics programme (Statistica for Windows Release 5.0, © 1995 by Statsoft Inc., Tulsa, USA). An exact Kruskal-Wallis text was performed first in order to determine whether the treatment or method of pericardial closure employed had any effect at all. If the effect of treatment was significant, group B was then tested against groups A, C and D. The exact Wilcoxon-Mann-Whitney test was used for this. The questions were aimed at detecting any kind of difference and therefore a two-sided test was used. 5% was set as the global probability of error (level). For the subsequent group comparison, the level was adjusted according to the Bonferroni-Holm procedure.

Results

Repeat sternotomy without any complications proved possible in all animals. Slight injuries to the cardiac surface were caused in two animals from each group during cardiac exposure. No injuries to the great vessels or coronary arteries occurred in the course of any reoperation. Cardiac exposure during the operation was fastest in group B. Dissection of the heart took longest in group C.

After adding all the points concerning the macroscopic parameters, group B was in first position with 33 points, followed by Group A with 36 points. Group D was in third place with 70 points and group C, in last place, had the worst results with 76 points (Table 1). Regarding the amount of intrapericardial adhesions in and outside the pericardial closure area showed group A and B the best results.

	Group			
Parameter	**A**	**B**	**C**	**D**
1. Intrapericardial adhesions in the pericardial closure area	9	5	15	14
2. Intrapericardial adhesions outside the pericardial closure area	4	4	10	9
3. Adhesion-free areas	8	9	18	17
4. Epicardial reaction in the pericardial closure area	7	6	12	12
5. Epicardial reaction outside the pericardial closure area	4	3	9	8
6. Pericardial substitute	4	6	12	10
Total	**36**	**33**	**76**	**70**

The most animals in group C and D had severe adhesions especially in the region of the pericardial substitute (Fig. 1a-d). Markedly more work was required to expose the heart in these groups. Adhesion-free regions of the heart were found mainly in groups A and B. Epicardial reaction in and outside the pericardial closure area was benign in groups A and B. The animals in group C achieved consistently poor results: a significant epicardial reaction of the entire heart was found in 50% of the cases. Regarding the pericardial substitute material yielded group C and D rather poor results. Severe alterations in the implanted pericardial substitute material were found especially in group C.

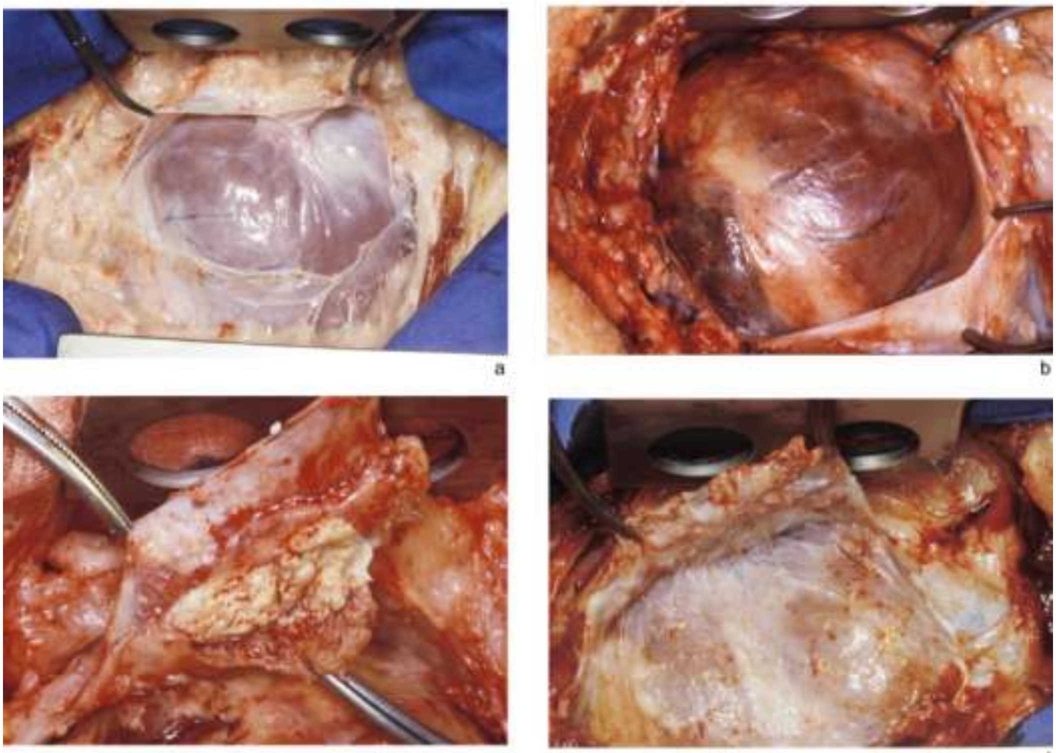

Figure 1: Macroscopic findings 8.4 months postoperatively.
a. **group A** (direct pericardial closure): solitary adhesion in the region of pericardial closure. There is only a slight epicardial reaction around the adhesion. The anatomy of the coronary vessels is easy to identify.
b. **group B** (pericardial closure by means of a parieto-mediastinal pleural flap): adhesion-free intrapericardial cavity.
c. **group C** (pericardial closure by means of a Biocor bovine pericardial patch): severe alteration in the pericardial substitute material with calcifications and extensive intrapericardial adhesions.
d. **group D** (pericardial closure by means of an expanded polytetrafluorethylene patch): mild changes in the pericardial substitute. Because of the severe epicardial reaction the coronary anatomy is unrecognisable.

After adding all the points concerning the histological parameters achieved group B the first place or the best results in the assessment, with 12 points. Group A was in second place with 27 points. Group D was in third place with 58 points and the last place or the worst results belonged to group C with 67 points (Table 2). Concerning the integrity of the mesothelial cell layer in and outside the pericardial closure area group B and C represented the extremes. The uniformity of the findings in groups B and C is worthy of mention. The mesothelial cell layer was intact in most of the cases in group B and showed extensive destruction in most of the cases in group C. Regarding the inflammatory reaction of the subepicardial tissue in and outside the pericardial closure area group B achieved the best score. Group A achieved equally good results. In contrast, group C was in last place. Moderate inflammation was found in group D. Epicardial adhesions were somewhat similar for all four groups. Group A was in first place and group D was last. The status of the explanted pericardial substitute material hardly changed in comparison with the native material in groups A, and B. Marked changes were found in group C. Calcification of the pericardial substitute material was found in all groups, but most frequently in group C.

		Group			
Tissue section	**Parameter**	**A**	**B**	**C**	**D**
Epicardium left	1. Integrity of the mesothelial cell layer	3	1	12	7
	2. Inflammatory reaction	3	0	8	11
	3. Adhesions	4	5	5	7
Epicardium right	4. Integrity of the mesothelial cell layer	4	0	7	7
	5. Inflammatory reaction	4	0	6	7
	6. Adhesions	3	0	4	7
Pericardial substitute	7. Integrity of the material structure and form	1	3	9	2
	8. Inflammatory reaction	3	2	8	6
	9. Calcium deposits	2	1	8	4
	Total	**27**	**12**	**67**	**58**

Statistical analysis yielded significant differences in the macroscopic (p = 0.0009) and microscopic findings (p = 0.0007) for the four methods of pericardial closure that were investigated. With regard to the macroscopic findings, there was:

- a significant difference between group B and group C: $p = 0.0043 < 0.05/3 = 0.0167$
- a significant difference between group B and group D: $p = 0.0065 < 0.05/2 = 0.025$
- no significant difference between group B and group A: $p = 0.8463 > 0.05$

Based on the microscopic findings it was shown that there was:

- a significant difference between group B and group C: $p = 0.0022 < 0.05/3 = 0.0167$

and also

- a significant difference between group B and group D: $p = 0.0065 < 0.05/2 = 0.025$ but
- no significant difference between group B and group A: $p = 0.0866 > 0.05$.

In conclusion, the results of pericardial replacement by means of a parieto-mediastinal pleural flap are significantly better than those of replacement using Biocor bovine pericardial patch and ePTFE patch.

Discussion

Retrosternal and intrapericardial adhesions are an important variable for the higher mortality and morbidity after repeat cardiac surgery.

All living tissues react to a local stimulus by inflammation [20]. The local inflammatory reaction induced by ECC and surgery represents the first stage in the formation of intrapericardial adhesions. The precursor of the adhesions is the blood that collects immediately after operation in the pericardial space. The blood coagulates as a result of the coagulation cascade, and these results in the formation of a coagulum. Operative trauma, and ECC in particular, lead to impairment of the fibrinolytic activity of the mesothelial cell layer [9, 10, 21], and so the intrapericardial thrombus is only partially lysed and forms fibrinous deposits in the pericardial space. Between the third and the fifth postoperative days, the first collagen fibres appear as a result of the activity of the fibroblasts that have migrated into the intrapericardial thrombus and the more time elapses the more connective tissue is formed. Collagen formation and fibroblast proliferation continue in the course of the second and third postoperative weeks. Further deposition of collagen is a long drawn-out process, which is probably only complete several months postoperatively. At this time, extensive adhesions bring about obliteration of the pericardial space by a connective tissue mass [22]. In summary, the existence of mesothelial cell trauma and the presence of extravasated blood are necessary for the formation of adhesions. Both requirements are met and intensified after cardiac surgery using ECC. The experimental investigation of the effect of pericardial substitutes on the prevention of adhesions is therefore appropriate only if it takes place after the use of the heart-lung machine.

Pericardial closure with or without the aid of a substitute, ensured protection of the retrosternal and intrapericardial structures in all animals when performing resternotomy, so that there was no case of injury to the heart or great vessels. The soft retrosternal adhesions were divided in all the animals in groups A and B without any problem. A different situation was observed in groups C and D. Here, dissection of the retrosternal space was made difficult by dense adhesions in two cases in each group. Such findings can be interpreted as the sign of a reaction of the surrounding tissues to the implanted foreign material. The intrapericardial adhesions appeared moderate to severe in the animals in group A. They were usually located more in the pericardial closure area and were more marked here than in the remainder of the pericardial space. Pericardial closure per se, with or without the aid of a substitute, cannot completely prevent the formation of adhesions. These occur in sites where the pericardial trauma has most damaged the mesothelial cell layer or has reduced the fibrinolytic activity. In the direct pericardial closure group, the intrapericardial adhesions in the region of the direct closure were more marked than the adhesions beneath the parieto-mediastinal pleural flap. These findings support the hypothesis that the pleural flap can exert a greater inhibitory effect on the process of the formation of adhesions because of its greater fibrinolytic activity (less exposure to intraoperative trauma) compared to the pericardium.

Intrapericardial adhesions were present in all the animals in groups C and D. They were dense and could only be divided by blunt and sharp dissection. These findings again confirm the theory that fibrinolysis by the mesothelial cell layer of the pericardium dissolves the original fibrinous adhesions and thus retards the formation of adhesions. As a result of the technique used to insert the pericardial material, part of the pericardial surface was, in practice, covered over and its fibrinolytic activity was neutralised. The epicardial reaction that was observed usually corresponded to the severity of the adhesions. In the majority of cases in groups A and B, it was assessed as mild. The good results can be explained mainly by the postoperative absence of a foreign material in contact with the epicardium. The epicardial reaction was usually significant in the animals in groups C and D, which led to marked difficulties in identifying the coronary anatomy. In the animals in groups A and B, the heart could be exposed quickly and without problems.

In contrast, dissection of the heart took longest in the animals in group C, which was to be expected in view of the extent of the adhesions. The pleural flap integrates well in the region of the implant site so that only minimal changes take place in its form and structure. The time required for flap preparation has practically no effect upon the total duration of the operation. Respiratory complications as a result of dissection of the flap did not occur. These results support the conclusion that dissection of the pleural flap represents a harmless procedure. The Biocor bovine pericardial patch appeared macroscopically altered in all cases. In two cases, it was significantly changed and in one case severely changed as a result of the formation of a cyst. The ePTFE patch also showed macroscopic changes in all cases. In the majority of cases, these consisted of fine creases that promoted the attachment of adhesions. In one case, the ePTFE patch led to the formation of a cyst, which could be explained either by a severe postoperative inflammation or by poor implantation technique. The structure of the patch remained unchanged in all cases. With regard to the integrity of the mesothelial cell layer, microscopic examination in all cases, both in the region of the direct pericardial closure and in all the other areas, showed minimal damage to the mesothelial cell layer or only small gaps between the mesothelial cells. The well-preserved (regenerated?) mesothelial cell layer explains the formation of only a few soft adhesions. The adhesions found in a few cases with an intact mesothelial cell layer can probably be attributed to regeneration of the mesothelial cells being completed too late or fibrinolysis commencing too late. The integrity of the mesothelial cell layer was usually preserved, both in the parieto-mediastinal pleural flap and in the epicardial preparations from the animals in group B, and active fibrinolysis thus explains the low-grade adhesions that were found in this group. Microscopic examination in the region of the Biocor bovine pericardial patch and the ePTFE patch showed in all cases an intrapericardial mesothelial cell layer that had many gaps or was completely destroyed.

The major lesions, which were probably even more marked in the immediate post-operative period and were compensated only minimally by mesothelial cell regeneration, led to inhibition of fibrinolysis and gave free rein to the process of adhesion formation. In the absence of foreign materials, there was a minimal subepicardial inflammatory response in the animals of groups A and B. The subepicardial inflammatory response found in the animals in groups C and D, although present, was only mild considered overall. Presumably, the original inflammation had subsided after an implantation period of over eight months and only its consequences or a global thickening of the epicardium was visible. The intrapericardial adhesions in the region of the pericardial direct closure and those in the region of the parieto-mediastinal pleural flap were usually mild and of the loose fibrinous type and thus agreed with the macroscopic appearance. The intrapericardial adhesions in the animals in groups C and D were usually of the fibrous type. This is regarded as evidence of a completed reaction caused by the foreign material, bovine pericardium or ePTFE. The theoretical advantages of the No-ReactTM procedure with regard to calcification were not observed. Half of the Biocor bovine pericardial patches showed calcium conglomerations microscopically, which in one case were extensive. Both with regard to the macroscopic appearance and the microscopic results, the parieto-mediastinal pleural flap group B achieved first place in the course of this investigation. The worst score or the last place was occupied by the Biocor bovine pericardial patch group C. This confirms the hypothesis that the pleural flap, being an autologous material with fibrinolytic activity, can best replace the pericardium and its functions and those foreign materials, especially xenografts such as the Biocor bovine pericardial patch in this case, cannot prevent the process of adhesion formation and the epicardial reaction.

After cardiac operations involving ECC, the pericardium should be closed in patients in whom there are foreseeable reasons for anticipating a further cardiac operation. The method of choice is direct pericardial closure, which should be performed in patients with good haemodynamics immediately after the ECC.

Direct pericardial closure should not be performed in patients with impaired cardiac function, especially if the circulatory instability has emerged perioperatively. In such cases, as well as in patients after myocardial revascularisation, when the internal mammary artery has been implanted in situ unilaterally or bilaterally, and after reoperations, a parieto-mediastinal pleural flap should be used to close the pericardium. The advantages of using the parieto-mediastinal pleural flap are those of direct pericardial closure, in that fewer adhesions are to be expected because of the increased fibrinolytic activity, and also the absence of any constrictive effect of the pericardial closure on a dilated failing heart. If the method is used after myocardial revascularisation using the left or both internal mammary arteries in situ, kin king of this bypass graft by direct pericardial closure is avoided. The method is almost essential in reoperations, as the native pericardium has impaired fibrinolytic activity. In cases, where the two methods mentioned above cannot be used, for example after correction of congenital cardiac anomalies in childhood, pericardial closure by means of an ePTFE patch should be considered as an alternative. On the basis of the investigation presented here, use of biological grafts is not advisable.

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Part 10.

CAROTID ARTERY PATHOLOGY

Lesional levels determining cerebrovascular insufficiency*)

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Abstract

Stroke, as an extreme manifestation of cerebrovascular insufficiency, is the third cause of mortality in developed countries. The residual disability, after a recovered stroke, is substantial: 40% need special care, and 10% need permanent care. Topographically, cerebrovascular insufficiency may be determined by lesions situated at different levels of the arterial tree: carotid level, supra-aortic level, aortic level and cardiac level.

The paper presents the modalities of surgical treatment in cerebrovascular insufficiency, depending on the extracerebral arterial lesional level, on a group of 218 patients treated in the Cardiovascular Surgery Clinic of Timisoara. Between 1998-March 2006, 218 patients with cerebrovascular insufficiency were operated on in the Institute of Cardiovascular Diseases of Timisoara, the Cardiovascular Surgery Clinic: carotid stenosis (151); brahiocephalic arterial trunk occlusion (7); subclavian artery occlusion (17); aortic arch syndrome (3); thoracic outlet syndrome (36); Takayasu disease (4). Age limits were 13-83. There were 68.68% men and 31.32% women. The surgical approach was the following: carotidian endarterectomy and patch plasty (68 cases, of which 43 had also aorto-coronary bypass, 5 had peripheric revascularization too, and 1 patient needed also aortic valvular replacement); carotidian endarterectomy (44 cases); carotidian plasty (37 cases); internal carotidian artery reimplantation (2 cases); aorto-brachio-cephalic arterial trunk bypass (7 cases); subclavian artery endarterectomy (10 cases); aorto-subclavian bypass (10 cases); cervical rib resection (14 cases); anterior scalenotomy (15 cases); first rib resection (4 cases); middle scalenotomy (3 cases); aorto-bicarotidian bypass (4 cases). Postoperative mortality in carotidian diseases was 2.64%; in supra-aortic artery lesions 0% and the general mortality was 1.83%. At crossroads between several domains (neurology, neurosurgery, radiology, interventional cardiology, cardiovascular surgery), this pathology may be controlled by diagnostic and therapeutic optimization. The surgical treatment is considered the "golden standard" in the treatment of extracerebral arterial lesions. In order to prevent cerebrovascular strokes and to lower the socio-economic impact determined by this pathology, the practical implementation of guidelines and internationally accepted recommendations regarding the surgical treatment is called for.

Key words: *cerebrovascular insufficiency, carotid, surgery*

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Rezumat

Accidentul vascular cerebral, ca manifestare extremă a insuficienței circulatorii cerebrale, reprezintă a treia cauză de mortalitate in țările dezvoltate. Disabilitatea reziduală, după un AVC recuperat este substanțială: 40% necesită îngrijiri speciale, iar 10% necesită îngrijire permanentă, totală. Topografic, insuficiența circulatorie cerebrală, poate fi determinată de leziuni situate la etaje diferite ale arborelui arterial: etaj carotidian, etaj supra-aortic, etaj aortic şi etaj cardiac.

Lucrarea prezintă modalitățile de tratament chirurgical în insuficiența circulatorie cerebrală, în funcție de etajul lezional arterial extracerebral, pe un lot de 218 pacienți tratați în Clinica de Chirurgie Cardiovasculară Timişoara. În perioada 1998 - martie 2007, în Institutul de Boli Cardiovasculare Timişoara, Clinica de Chirurgie Cardiovasculară, au fost operați 218 pacienți cu insuficiență circulatorie cerebrală: stenoză carotidiană (151); ocluzie trunchi arterial brahiocefalic (7); ocluzie arteră subclavie (17); sindrom de arc aortic (3); sindrom de apertură toracică superioară (36); boala Takayasu (4) Limitele de vârsta au fost 13-83 ani. Ponderea pe sexe a fost: bărbați = 68,68%, femei = 31,32%. Abordarea chirurgicală a fost: endarterectomie carotidiană şi plastie (68 cazuri, din care 43 au beneficiat şi de bypass aorto-coronarian, 5 şi de revascularizare periferică, iar 1 caz şi de înlocuire valvulară aortică); endarterectomie carotidiană (44 cazuri); plastie carotidiană (37 cazuri); reimplantare de arteră carotidă internă (2 cazuri); bypass aorto-trunchi arterial brahiocefalic (7 cazuri); endarterectomie arteră subclavie (10 cazuri); bypass aorto-subclavicular (10 cazuri); rezecție coastă cervicală (14 cazuri); scalenotomie anterioară (15 cazuri); rezecție prima coastă (4 cazuri); scalenotomie medie (3 cazuri); bypass aorto-bicarotidian (4 cazuri). Mortalitatea postoperatorie în cazul afecțiunilor carotidiene a fost 2,64%; a leziunilor arterelor supra-aortice 0%; iar mortalitatea generală a fost de 1,83%. Aflată la confluența mai multor specialități (neurologie, neurochirurgie, radiologie, cardiologie intervențională, chirurgie cardiovasculară), această patologie poate fi ținută sub control prin optimizarea diagnostică şi terapeutică. Tratamentul chirurgical este considerat "standardul de aur" în tratarea leziunilor arteriale extracerebrale, iar pentru prevenția accidentelor vasculare cerebrale precum şi pentru scăderea impactului socio-economic determinat de această patologie este necesară implementarea practică a ghidurilor şi recomandărilor internaționale acceptate cu privire la tratamentul chirurgical.

Cuvinte cheie: *insuficiență circulatorie cerebrală, carotidă, chirurgie*

Background

Most cerebrovascular diseases manifest themselves by a sudden onset of a focal neurological deficit, which may remain unchanged or may progress rapidly. This sudden onset of a non-convulsive focal deficit defines the term of stroke.

A thrombus, an atheroma or an embolus may determine a critical stenosis or may block the blood vessel, producing a spasm and ischemia with cerebral infarction; or a vessel may break causing intracerebral haemorrhage or subarachnoid.

Stroke, as an extreme manifestation of cerebrovascular insufficiency, is the third cause of mortality in developed countries (USA, EU), after cardiovascular diseases and cancer (1). 35% of the patients who have survived a stroke are estimated to have another one in the following 5 years, with a mortality of 65%. The residual disability, after a recovered stroke, is substantial: 40% need special care, and 10% need permanent care. Therefore, the economic impact of a stroke is not to be taken lightly, as it is considered responsible for 0.19-0.47 of the gross internal product (GIP) of a country (2, 3).

We notice the great number of strokes, practically equal to that of ischemic cardiopathy (33.2% by strokes, respectively 33% by ischemic cardiopathy in Romania, as compared to 30% mortality by cerebrovascular diseases in the world and 27.2% in Europe, and the mortality by ischemic cardiopathy, with a percentage of 44% in the world and 50.8% in Europe) (4).

The forementioned data show the importance of a primary and secondary prophilaxy, as well as the need for an adequate treatment of risk factors of stroke. Stroke incidence increases with age; thus, the disabilities stroke provokes affect many persons who are in their "golden years" (5).

About 85% of strokes are ischemic, resulting from thromboses or embolisms of cerebral arteries (6). If embolisms are likely to appear on vessels without lesions, thromboses appear on pathologically modified areas.

This pathology is situated at crossroads between several domains: neurology, neurosurgery, radiology, interventional cardiology, cardiovascular surgery. We think that these lesions, which are responsible for the acute or cronical reduction of cerebral flow, may be described under the unique name of cerebro-vascular insuffiency.

Material and methods

The paper analyses the way in which the postoperative results appear, depending on the lesional level, responsible for cerebrovascular insuffiency. To that effect, a study has been undertaken on a group of 218 patients with cerebrovascular insuffiency of extracerebral origin, operated on in the *Institute of Cardiovascular Diseases of Timisoara, The Cardiovascular Surgery Clinic,* during 1998 - March 2007.

Lesional topography, of therapeutic importance, distinguishes between intracerebral lesions and extracerebral lesions; the latter may appear at different levels of the arterial tree (Figure 1): carotid lesions, supra-aortic lesions, aortic lesions and cardiac lesions.

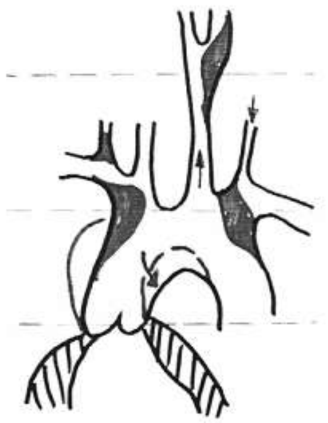

Figure 1: The topography of extracerebral lesions, which may determine cerebrovascular insufficiency (7)

CAROTID LESIONS	Isolated Bilateral	Symptomatic Asymptomatic
	+ coronary lesions	
	+ peripheric lesions	
SUPRA-AORTIC LESIONS	BCAT, SA, C occlusion	
	Aortic Arch Syndrome	
	Takayasu Disease	
	Furt arterial - TOS	
AORTIC LESIONS	Thoracic aortic dissection	
	Thoracic aortic aneurysm	
CARDIAC LESIONS	Valvular	
	Atrial thrombosis	
	Ventricular thrombosis	
	Cardiac tumors	
	Atrial fibrillation	
	ASD	

Abbreviations	• BCAT = *brahiocephalic arterial trunk* • SA = *subclavian artery* • C = *carotid artery* • TOS = *thoracic outlet syndrome* • ASD = *atrial septal defect*

The demographic features of the group pointed out the prevalence of cerebrovascular insufficiency in male, the distribution by gender being as follows: male = 68.68%, female = 31.32%, as well as in the seventh decade of life, the age limits being between 3-83 years (Figure 2, 3).

All the 218 patients were also investigated by angiography, and the results showed lesions, which determined cerebrovascular insufficiency: carotid stenosis (151); brahiocephalic arterial trunk occlusion (7); subclavian artery occlusion (17); aortic arch syndrome (3); thoracic outlet syndrome (36); Takayasu disease (4).

The operative indications were taken in conformity with AHA (*American Heart Association*) (8) international guidelines, uninanimously accepted and briefly presented below.

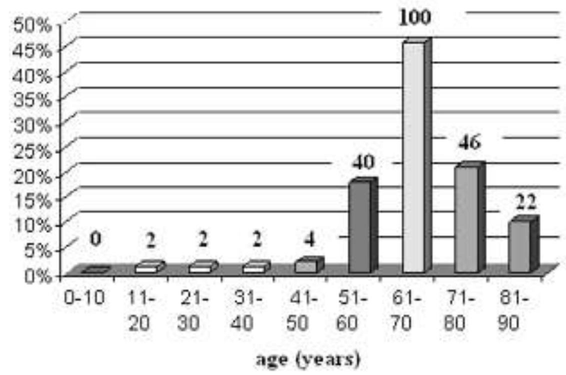

Figure 2: The distribution by age

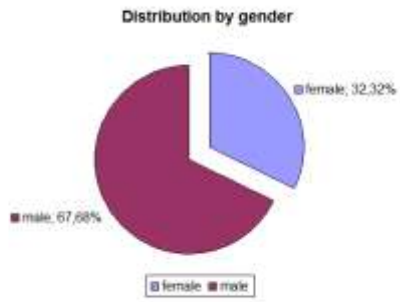

Figure 3: The distribution by gender

Symptomatic patients

• patients who have suffered from recent cerebral ischemic strokes (but > 1 month), recovered or partially recovered, with stenosis between 70-80% (ECST = *European Carotid Surgery Trial*) or between 50-70% (NASCET = *North American Symptomatic Carotid Endarterectomy Trial*). These differences are the result of the two trials, ECST and NASCET, different methods of calculating the stenosis;

• the surgery for stenosis between 0 and 29% is not advisable;

• the indication for stenosis between 30 and 69% is debatable; the surgery for stenosis below 50% is not recommended.

Asymptomatic patients

There is an actual preoccupation for diagnosis of asymptomatic patients with carotid lesions and for their surgical approach, before a major cerebral event. The surgical indications are taken in conformity with the trials, in accordance with the level of experience of the clinic (the surgeon) that performs the endarterectomy (the operative risk).

Patients with asymptomatic carotid artery disease

For patients with a surgical risk <3 % and life expectancy of at least 5 years:

1. Proven indications: Ipsilateral carotid endarterectomy is acceptable for stenotic lesions (≥ 60% diameter reduction of distal outflow tract with or without ulceration and with or without antiplatelet therapy, irrespective of contralateral artery status, ranging from no disease to occlusion [Grade A recommendation]).

2. Acceptable indications: Unilateral carotid endarterectomy simultaneous with coronary artery bypass graft for stenotic lesions (60% with or without ulcerations with or without anti-platelet therapy irrespective of contralateral artery status [Grade C recommendation]).

3. Uncertain indications: Unilateral carotid endarterectomy for stenosis > 50% with B or C ulcer irrespective of contralateral internal carotid artery status (Grade C recommendation).

For patients with a surgical risk of 3% to 5% and for patients with a surgical risk of 5% to 10%, indications are unchanged from the original guidelines:

For patients with a surgical risk of 3% to 5%

1. Proven indications: None
2. Acceptable but not proven indications: ipsilateral carotid endarterectomy for stenosis 75% with or without ulceration but in the presence of contralateral internal carotid artery stenosis ranging from 75% to total occlusion
3. Uncertain indications:
    - Ipsilateral carotid endarterectomy for stenosis 75% with or without ulceration irrespective of contralateral artery status, ranging from no stenosis to occlusion;
    - Coronary bypass graft required, with bilateral asymptomatic stenosis > 70%, unilateral carotid endarterectomy with coronary artery bypass graft (CABG);
    - Unilateral carotid stenosis > 70%, CABG required, ipsilateral carotid endarterectomy with CABG.
4. Proven inappropriate indications: None defined.

For patients with a surgical risk of 5% to 10%

1. Proven indications: None
2. Acceptable but not proven indications: None
3. Uncertain indications:
    - Coronary bypass graft required with bilateral asymptomatic stenosis >70%, unilateral carotid endarterectomy with CABG;

- • Unilateral carotid stenosis > 70%, CABG required, ipsilateral carotid endarterectomy with CABG;

4. Proven inappropriate indications:
   - • Ipsilateral carotid endarterectomy for stenosis 75% with or without ulceration irrespective of contralateral internal carotid artery status;
   - • Stenosis ≤ 50% with or without ulceration irrespective of contralateral carotid artery status.

Results

Of the total of 218 patients with cerebrovascular insufficiency, 151 had lesions at the carotid level. 69.06% of those were symptomatic (with antecedents of stroke in 21.58% of the cases), and 30.93% were asymptomatic.

From the patients with lesions at the carotid level, 102 had isolated carotid lesions, 43 had associated coronary lesions, 5 had also peripheric lesions, and 1 had an associated aortic valvular lesion.

The surgical approach for this group of patients was the following: simple endarterectomy (44 cases); endarterectomy and patch widening plasty with synthetic or venous patch (68 cases); widening plasty with synthetic or venous patch (37 cases); endarterectomy with internal carotid artery reimplantation into the common carotid artery (2 cases). The results of the surgery in the case of the patients with cerebrovascular insufficiency, operated on for lesions at the carotid level, are summarized in table 1.

Table 1: Lesions at the carotid level

Lesion	No. of patients	Complications (stroke)	Mortality
Isolated	**102**	**2.94%**	**1.96%**
+ coronary	**43**	**9.3%**	**6.9%**
+ peripheric arteries	**5**	**0**	**0**
+ aortic valve replacement	**1**	**0**	**0**

67 patients had lesions at the supra-aortic level, which led to cerebrovascular insufficiency. From those, 7 patients had brahiocephalic arterial trunk occlusion, operated on by an aorto-brahiocephalic arterial trunk bypass; 17 patients had subclavian artery occlusion, operated on by thromb-endarterectomy (10 cases) or aorto-subclavian bypass (7 cases); 3 patients had aortic arch syndrome, which called for an aorto-subclavian bypass; 36 patients had thoracic outlet syndrome, operated on by the following surgical approaches: cervical rib resection (14 cases), first rib resection (4 cases); anterior scalenotomy (15 cases), middle scalenotomy (3 cases); 4 patients suffered from Takayasu disease, operated on by an aorto-bicarotidian bypass. Both postoperative mortality and morbidity for this subgroup of patients equaled 0.

The cerebrovascular insufficiency determined by lesions at the aortic level, through aortic dissection, is well known. Due to the overemphasizing the statistic results, this subgroup hasn't been analyzed in the study.

At the cardiac level, the cerebrovascular insufficiency, present under the form of a post cardiac surgery stroke, was encountered in 1.23% after coronary surgery (1.14% under extracorporeal circulation and 0.09% in beating-heart surgery) and in 0.26% after valvular surgery.

The synthetic results, regarding the patients operated on for cerebrovascular insufficiency in our clinic, are illustrated in table 2.

Table 2: Synthetic results depending on the lesional level

Lesion	No. of patients	Complications (stroke)	Mortality
Carotidian	**151**	**5.29%**	**2.64%**
Supra-aortic	**67**	**0%**	**0%**
Overall	**218**	**3.66%**	**1.83%**

Conclusions

At crossroads between several domains (neurology, neurosurgery, radiology, interventional cardiology, cardiovascular surgery), this pathology may be controlled by diagnostic and therapeutic optimization.

It is important to diagnose at a wide level asymptomatic lesions, in order to decide on the most adequate operative moment. There are two studies which provided information on the efficiency of carotid endarterectomy in asymptomatic patients. The overall risk of stroke in patients randomized for non-surgery was so low (11.0% at 5 years) that even the relative reduction of stroke in patients randomized for surgery, preceded by angiography (up to 5.1% at 5 years) conferred a real benefit of 5.9%. In other words, about 85 patients must be operated on, in order to prevent a stroke in the following year (9).

The practical implementation of guidelines and internationally accepted recommendations regarding the surgical treatment is necessary.

The carotid surgery should be performed or directly supervised by surgeons who have specialized in carotid endarterectomy.

The carotid surgery should be only performed in or in collaboration with the centers with the necessary competence in neurology and neuroradiology.

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Conventional surgical treatment of carotid endarterectomy "the gold standard"*)

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Introduction

Stroke ranks as the third cause of death and the first cause of permanent disability in the most industrialized countries. Ischemia attack prevails up to 85% (1, 2). Patients having carotid stenosis above 80% show a stroke per year ratio 10 times greater than patients having carotid stenosis below 40% (3). 75% of strokes concerns elderly persons beyond 65, whereas 24%/year of strokes affects octogenarian (4).

In 2040, in Italy, 41% of the population will be older than 60.

50% of carotid disease concerns persons beyond 65 years old. Therefore, considering that both mean age and life expectancy are constantly increasing, the number of persons concerned by cerebrovascular diseases is growing up too. Carotid disease forms the first cause of death within cardiovascular diseases.

Surgery is considered the most effective way to prevent cerebrovascular diseases on patients with high grade carotid stenosis as proved by the most known prospective multicenter randomized international trials (NASCET, ESCT, ACAS) (5 - 6).

Carotid surgery is about 50 years old. In the last 20 years well-proved results were achieved due to surgical and anaesthesiological techniques improvement as well as better inputs definition. It represents the most frequent arterial surgical intervention within vascular surgery. High accurate pre and per operative diagnostic as well as development of noninvasive techniques too, led to fast growth of carotid surgery.

Surgical indications

CEA indications are consistently proved both on symptomatic and asymptomatic patients. Following NASCET and ESCT (1, 4) studies surgical interventions on symptomatic patients with carotid stenosis > 70% is highly recommended.

In 1998 the AHA confirms, provided life expectancy >5 years, that the complication rate after carotid endarterectomy should be maintained at an extremely low rate < 3% by surgeons to keep the beneficial effects of carotid endarterectomy over medical therapy, in particular on asymptomatic patients.

Plaque surface morphology, considering his embolic potential, is an additional important parameter to take into account in establishing surgical indications (7).

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Carotid surgery, like all surgeries, involves some degrees of risk, even though quite low. Risks have to be reduced to the bare minimum, by vascular surgeons, using the actual techniques in the most appropriate way. CEA is a quite serious technique and has to be performed by well-specialized trained surgeons.

Surgery technique

The CEA technique is conventionally undertaken by a longitudinal arteriotomy and primary closure (standard CEA). This technique is easy and needed short clamping time. Eversion carotid endarterectomy employs a transverse arteriotomy and reimplantation of the carotid artery. Advantages eversion CEA:

1. avoids problems related to the standard CEA (particularly on small size ICA);
2. avoids patches employment (infections associated to synthetic patches and dilatation or degeneration/rupture of venous patches);
3. allows to adjust overall length (kinking, coiling);
4. reduced re-stenosis incidence Complications associated with a distal intimal flap (end point endarterectomy).

Carotid endarterectomy with patch closure avoids problems related primary closure particularly on small size artery and reduce re-stenosis incidence.

Immediate and remote re-stenosis results may depend on the used surgery technique. Following the EVEREST multicenter randomized trial, we have attended at (8), it has been estimated the impact between surgery technique used for CEA and restenosis incidence, two techniques of interventions have been compared: standard with direct suture and eversion.

The EVEREST trial has involved a quite important number of patients (1353 in 30 months), and provided good statistics and significant results. Follow up was very accurate.

The eversion technique has shown a lower number of re-stenosis compared to the standard technique with direct suture.

In study of Katras T (9) (prospective, non-randomized), the restenosis rate was 1.7% after eversion CEA, 9.3% after CEA-primary closure, and 6.5% after CEA-patch angioplasty (P < 0.05). Clamping time was significantly shorter for eversion CEA compared with patch standard procedures.

The Cochrane review (2001) randomized trials comparing eversion to conventional techniques carotid endarterectomy. There were no significant differences in the rate of perioperative stroke and/or death and stroke during follow-up between eversion and conventional CEA techniques. Eversion CEA was associated with a significantly lower rate of restenosis > 50% during follow-up. However, there was no evidence that the eversion technique for CEA was associated with a lower rate of neurological events when compared to conventional CEA.

Clamping tolerance (intraoperative monitoring)

To determine clamping tolerance the most sensitive and reliable method is direct clinic evaluation of awake undergoing carotid CEA using local anesthesia. This kind of anesthesia allows evaluating the shunt use to insure cerebral perfusion. Shunt introduction is quite delicate therefore it has to be used suitably.

Clamping tolerance determination is more complex when using general anesthesia. Cerebral ischemia detection is required. Several techniques have been proposed: stump pressure measurement, *Trans-Cranial Duplex* scan (TCD), *Electro-Encephalon-Graphic* (EEG), *Somatic-Sensorial Potentials* (SEPs) and cerebral flux measurement with Xenon 133 (rCBF).

At present no one cerebral monitoring is unfailing and it cannot always be applied.

Compared to local anesthesia each monitoring technique has shown false-negative and false-positives results. Furthermore each monitoring technique has its own drawbacks, like high cost, specialized and trained personnel request (rCBF, EEG, SEPs), limited applicability (TCD).

According to our recent study, presented at SCV (*Société de Chirurgie Vasculaire*) yearly conference, intervention under general anesthesia using sophisticated methods shows no significant statistical reduction complications compared to intervention carried out using stump pressure monitoring only.

The intraoperative control (quality control in carotid surgery)

Technical mistakes are one of the most important reasons of per-operative stroke in carotid surgery and a possible cause of re-stenosis too. However there is no common agreement about the best method to locate their imperfections: intimate flap, angularities, residual plaques, etc.). Prevention is best. Immediate correction of technical mistakes cannot guarantee neither neurological nor re-stenosis complications. The most suitable method is chosen upon: sensibility and specificity to find out technical defaults and daily use feasibility.

Many suggest using angiography to find out technical defaults: completion angiography use is anyhow restricted since it is quite difficult to get suitable intraoperative images (only mono-planer projections). Furthermore this technique is relatively risky. Therefore complementary intraoperative investigations, less invasive, like Color Duplex scan have been suggested.

Intraoperative Color Duplex Scan allows to identify intimate flap thrombus, stenosis or residual plaque, kinking. The Duplex scan method allows measuring the hematic flux speed. Decision about immediate correction of technical mistake is associated to both the importance (e.g. severe stenosis) and the default type (e.g. thrombus) found out (10).

Intraoperative Duplex is both no invasive and low cost. These are its main advantages, however intra-cranial circle visualization is not allowed. Furthermore this technique requires well-experienced operators to explain the intraoperative images, thus avoiding false-positive risks (carotid re-investigations or minor defaults) or, less frequently, false-negative (no diagnosis of present default).

In our study, Eco-color-doppler has shown higher sensitivity diagnosis accuracy compared to DSA (87% vs 59%) to detect minor technical problems (ESVS Annual meeting - Copenhagen 1999 - Cardiovasc Surg in press).

Endovaecular treatment

PTA associated to stent use is now generally accepted for symptomatic treatment of patients with carotid re-stenosis > 80%.

PTA with stent on primary carotid stenosis is largely debated.

Preliminary studies (CAST I) did not provide exciting results. Several studies have shown that embolism ratio is consistently higher during endovascular procedure compared to conventional surgery. Therefore new filter systems to each emboli have been developed. During last year new trials both in Europe and USA (SAPHIRE trial, CHRS, EVA 3S, CREST, CAVATAS 2, SPACE) have been launched in order to better define the endovascular treatment for primary carotid stenosis pathology.

According to some authors carotid stenosis endovascular treatment can be applied particularly on patients with high surgical risk (11).

The patients with increased risk (NASCET and ACAS trials exclusion to surgical treatment) were: age > 79 years old (12), contralateral carotid occlusion, high carotid bifurcation, carotid restenosis, severe cardiopathy (atrial fibrillation, valvular heart disease, unstable angina), lung failure, liver failure, kidney failure (creatinine > 3 mg/dl). Patients affected by one or more of these diseases were considered high-risk for cardio-vascular and neurological per-operative morbi-mortality (13).

According to retrospective study on 366 carotid endarterectomies carried out by the New Orleans group (14), no significant statistic differences of morbid-mortality among high-risk surgical patients (following NASCET and ACAS standards) versus other patients were found. Therefore it would be useful to precisely define true high-risk surgical patients for endovascular treatment benefit (15, 16).

CEA is experienced hands appears to have a very low risk of perioperative stroke or death. Patients who are trial ineligible do show a trend toward higher neurologic morbidity, but these rates are still within the suggested standards set by the AHA. As importantly, this group of "HIGH RISK" patients has outcomes from CEA that compare favorably with those of carotid stenting. Treatment decisions should be individualized, but on the basis of the study, trial ineligibility per se should not be considered a reason to eschew CEA in favor of carotid stenting.

Beyond initial enthusiasm (17), indication of carotid stenosis endovascular treatment has to be verified versus immediate and remote expected results. These results have to be compared to good results of conventional surgery treatment, actually still the gold standard (18).

Table 1. Our experience - Jan 1997 -Dec 2002

1362 CEA		
CEA (standard)	656	48.2%
CEA (eversion)	567	41.6%
Patch	122	8.9%
Bypass	17	1.3%

Table 2: Our experience - Jan 1997 - Dec 2002

Mean Age: 63.5 year (38 - 89 years)

1362 CEA	patients	Percents [%]
Male	915	**74%**
Female	321	**26%**
Total	**1,236**	**100%**

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Particular methods of carotid revascularization*)

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Abstract

Introduction. *Carotid revascularization is standardly represented by the endarterectomy of the internal and/or common carotid arteries associated or not with several other vascular surgical techniques (resections, angioplasties). This situation is obviously possible in case of localized lesion at the level of the carotid bifurcation, which by the way represents the most frequent localization.*

Objective. *We would like to present the existent surgical treatment options for stenotic carotid affections localized downstream from the carotid bifurcation (aortic arch, brahiocephalic trunk, common carotid arteries). The atherosclerotic stenosis from this territory are frequently represented by stenosis or occlusion of the common carotid artery, respective stenosis of the brahiocephalic trunk. The pathology affecting the aortic arch and which can determine alterations of the brain circulation is represented by dissection of the aortic arch. Seldom situations are represented by aortic arch aneurysms (saccular) and intraluminal thrombosis of the aortic arch. A relatively frequent situation is represented by common carotid lesions which appear in open or closed cervical trauma.*

Material and method. *The study material was represented casuistry of Cardiovascular Surgical Hospital Targu Mures, all chosen cases being treated at this facility.*

Results. *We present cases of common carotid arterial reconstruction, aortocarotidian bypass, aortic-subclavian-carotid bypass, subclavian-carotid bypass and indirect reconstruction of brahiocephalic trunk dissection.*

Conclusions. *The pathology of supraaortic arterial systems is clearly dominated by internal carotid stenosis. Although referred rarely, cases about lesions of brahiocephalic trunk or common carotid arteries are severe and their treatment is sometimes about difficult and complex abordations, marked by features depending on the patient*

Rezumat - Tehnici particulare de revascularizare carotidiană

Introducere. *Revascularizarea carotidiană este reprezentată în mod standard de endarterectomia arterei carotidei interne şi/sau comune asociată sau nu cu diverse alte tehnici de chirurgie vasculară (rezecţii, angioplastii, etc). Această situaţie este evident posibilă în cazul localizării leziunii la nivelul bifurcaţiei carotidiene, care reprezintă de altfel cea mai frecventă localizare.*

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Obiective. *În lucrarea de față dorim să prezentăm opțiunile chirurgicale existente pentru tratamentul afecțiunilor stenotice carotidiene situate în amonte de bifurcația carotidiană (arc aortic, trunchi brahiocefalic, artera carotidă comună). Stenozele aterosclerotice din acest teritoriu sunt reprezentate frecvent de stenozele sau ocluziile de artere carotide comune, respectiv stenoze de trunchi brahiocefalic. Patologia care afectează arcul aortic şi care poate determina afectări ale circulației cerebrale este reprezentată de disecția de crosă aortică. Situații mai rar întâlnite sunt reprezentate de anevrismele de crosă aortică (saculare) şi tromboza intraluminală de crosă aortică. O situație relativ frecventă o reprezintă leziunile arterei carotide comune care apar în cazul traumatismelor cervicale deschise sau închise.*

Material şi metodă. *Materialul de studiu a fost reprezentat de cazuistica Clinicii Chirurgie Cardiovasculară Târgu Mureş, toate cazurile alese pentru exemplificare fiind tratate chirurgical în acest serviciu.*

Rezultate. *În lucrarea de față prezentăm cazuri de reconstucția arterială carotidiană comună, by-pass aorto-carotidian, by-pass aorto-subclavio-carotidian, by-pass subclavio-carotidian respectiv reconstrucție indirectă a unei disecții de trunchi brahiocefalic.*

Concluzii. *Patologia sistemelor arteriale supraaortice este dominată net de stenozele de arteră carotidă internă. Deşi referite rar, cazurile care prezintă leziuni ale arcului aortic trunchiului brahiocefalic sau arterelor carotide comune sunt grave iar tratamentul lor necesită de multe ori abordări dificile sau complexe, grevate de particularități in funcție de pacient.*

Introduction

Carotid revascularization is standardly represented by the endarterectomy of the internal and/or common carotid arteries associated or not with several other vascular surgical techniques (resections, angioplasties). This situation is obviously possible in case of localized lesion at the level of the carotid bifurcation, which by the way represents the most frequent localization.

Objective

We would like to present the existent surgical treatment options for stenotic carotid affections localized downstream from the carotid bifurcation (aortic arch, brahiocephalic trunk, common carotid arteries). The atherosclerotic stenosis from this teritorry are frequently represented by stenosis or occlusion of the common carotid artery, respective stenosis of the brahiocephalic trunk. The pathology affecting the aortic arch and which can determine alterations of the brain circulation is represented by dissection of the aortic arch, frequently cointeressed in type A aortic dissections. Seldom situations are represented by aortic arch aneurysms (saccular) and intraluminal thrombosis of the aortic arch. A relatively frequent situation is represented by common carotid lesions which appear in open or closed cervical trauma.

Material and method

The study material was represented casuistry of Cardiovascular Surgical Hospital Targu Mures, all chosen cases being treated at this facility.

Results and discussion

Surgical techniques are standardly divided in reconstructive and arterial bypass interventions. Exceptionally indirect methods may also be used. Arterial bypass techniques can be anatomical or extra-anatomical. For the described region, anatomic techniques assumpt aortocarotid bypass, whilst the extra-anatomical ones surmise subclavian-carotid bypass.

The etiology of the described lesions is in the great majority represented by atherosclerosis, but we may notice other rare causes like aortic dissection, open or closed cervical trauma, localized intravascular thrombosis at the level of the aortic arch.

1. *Common carotid arterial reconstruction*

The present etiology in our casuistry was represented by closed cervical trauma. As local favorizing factor we highlight the atheromatous plaque.

The benefits of this procedure are represented by the simple latero-cervical abordation, a relatively simple surgical method, the facile use of intravascular shunt.

Indications of the procedure are represented by focal lesions of the common carotid, medium and distal portion (aneurysm, pseudoaneurysm, stenosis).

2. *Aortocarotidian bypass*

It is a complex surgical method. Its benefits are represented by: anatomic by-pass, possible for both common carotid, with possible association or not - carotid endarterectomy. The disadvantages of the procedure are the need of a complex abordation, cervical and thoracic (median or partial sternotomy superior till the IV intercostal space), reason why it is indicated in situations when the procedure is contemporaneous with cardiac surgical interventions. Its indications: common carotid stenosis, common carotid occlusions with permeable intern carotid in context with associated cardiac interventions (ex. aortocoronary bypass) or in case of indisponibility of other supraaortic branches for extraanatomic bypasses.

Figure 1: Post-traumatic pseudo-aneurysm, right common carotid.

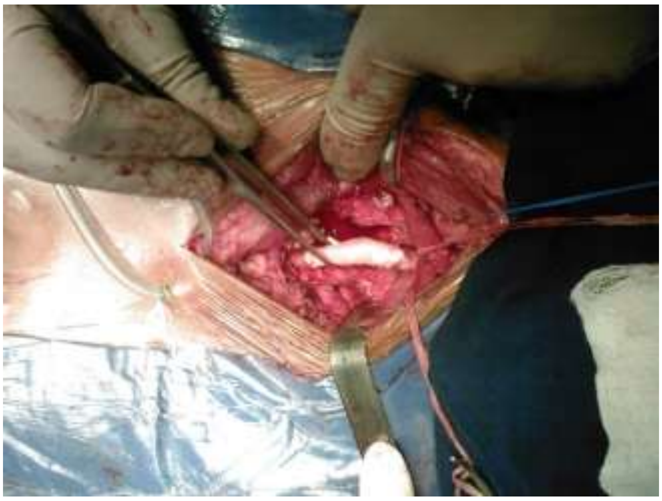

Figure 2: Reconstruction of the right common carotid with Gore-Tex patch associated with local endarterectomy (at local endovascular inspection a localized atheromatous plaque is shown perilesional – favorizing factor for posttraumatic formation of pseudoaneurysm).

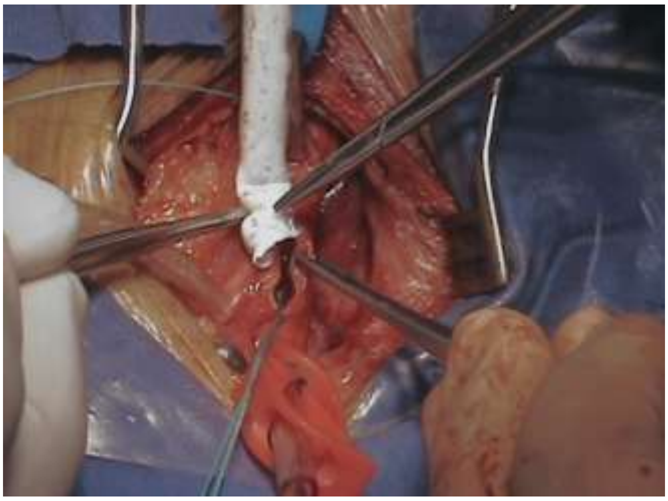

Figure 3: Distal anastomosis of an aortocarotid bypass with Gore-Tex prothesis of 6 mm in diamether.

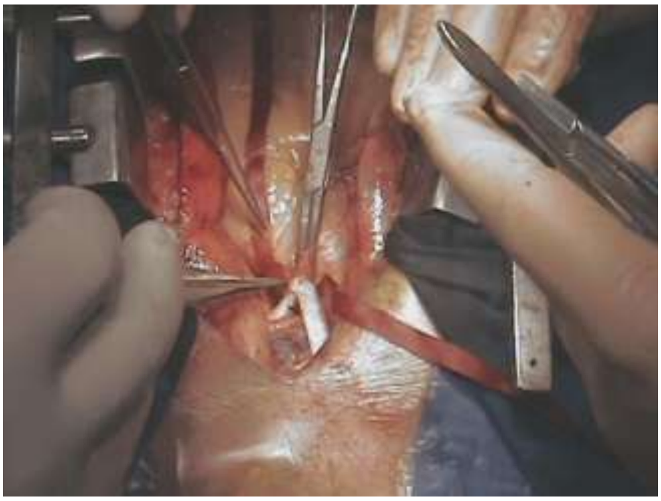

Figure 4: Proximal anastomosis of aortocarotid bypass on the ascendent aorta.

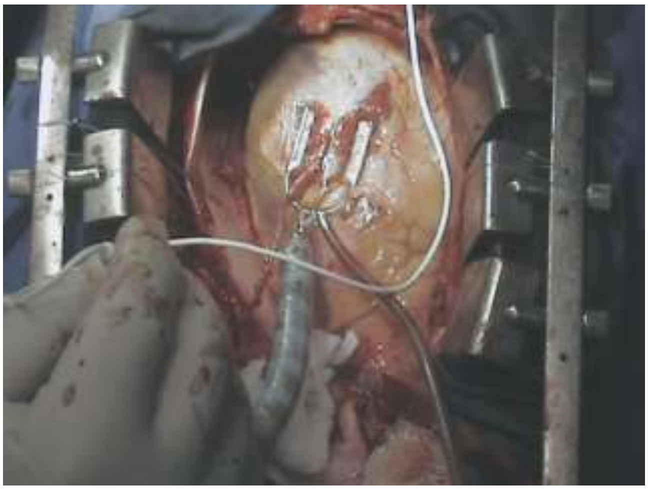

Figure 5: Associated intervention (OPCAB – anastomosis of the left internal mammary with the descendent anterior on beating heart).

Figure 6: Aortocarotid bypass and anastomosis of the internal mammary with the anterior descendent – final intrapericardic aspect.

3. Aortic-subclavian-carotid bypass

Represents a precise surgical intervention, using bifurcated “Y” prothesis anatomically disposed, representing as an advantage of the method. It is useful in brahiocephalic trunk stenosis (on the right) or in combined lesions of common left carotid with left subclavia (on the left). It may be associated with adjuvant interventions, like carotid endarterectomy, vertebral artery enlargement plasty, segment V1.

Figure 7: Aorto-subclavian-carotid by pass – tunelizing the bifurcated prothesis.

Figure 8: Aorto-subclavian-carotid bypass–proximal anastomosis

4. Subclavian-carotid bypass

It is a surgical intervention indicated in common carotid stenosis. The distal carotid bypass may be done on several segments of the common carotid artery, meaning right after the emergence, on the proximal segment (short subclavian-carotid bypass). Another possible solution is the common carotid bypass on the medium segment, situation when the bypass is intermediary. The feature is used in cases when the lesion extends more then the initial portion. The last variant is represented by the distal subclavian-carotid bypass, on the bifurcation of the common carotid artery. It is a long bypass, useful when the lesions include the whole common carotid artery.

The proximal subclavian-carotid bypass assumes a unique supraclavicular abordation.

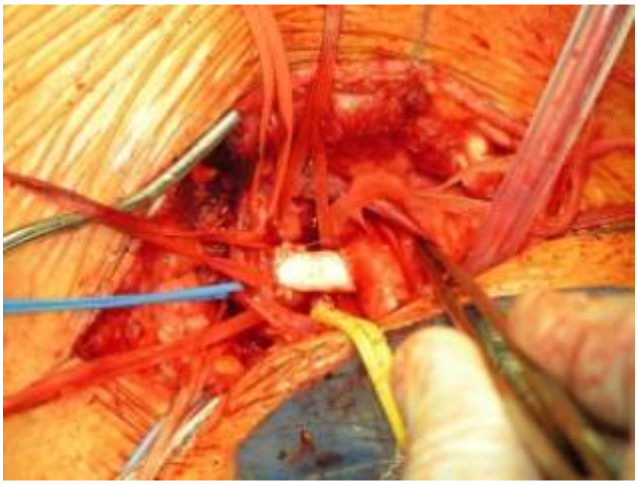

Figure 9: Short subclavian-carotid bypass (proximal common carotid artery) – final aspect

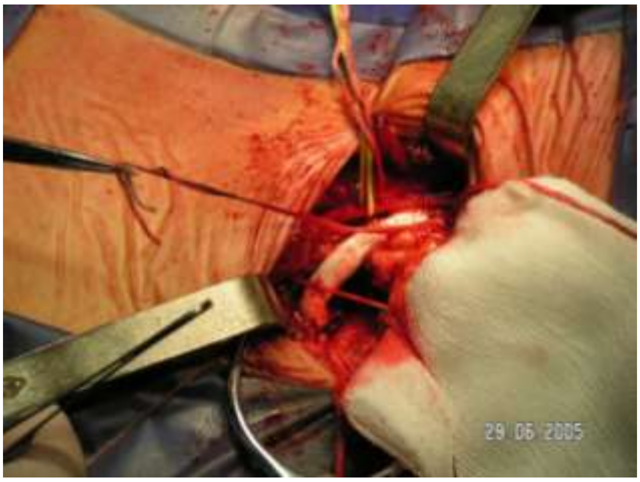

Figure 10: Intermediar subclavian-carotid bypass (medial segment, common carotid artery) – final aspect.

Figure 11: Subclavian-carotid byapss (intermediar segment of the common carotid artery). With Gore-Tex prothesis of 6 mm diamether.

The distal subclavian-carotid bypass assumes mixt abordation, supraclavicular fossa and carotic trigonum. The proximal anastomosis is on the subclavian artery, the distal one being on the bifurcation of the ipsilateral common carotid. It might be associated with carotid endarterectomy.

5. Solving a brahiocephalic trunk dissection

Ascendent aortic and arch dissections might involve or interest the emergence of the great supraaortic vessels. Reconstruction techniques are represented by the above represented bypasses or in select cases, indirect methods, which do not adress the brahiocephalic trunk or the left common carotid, but the acctual dissection, eliminating the false lumen. Biological adhesives and reinforcement procedures might be used in order to eliminate the false lumen from the circulation.

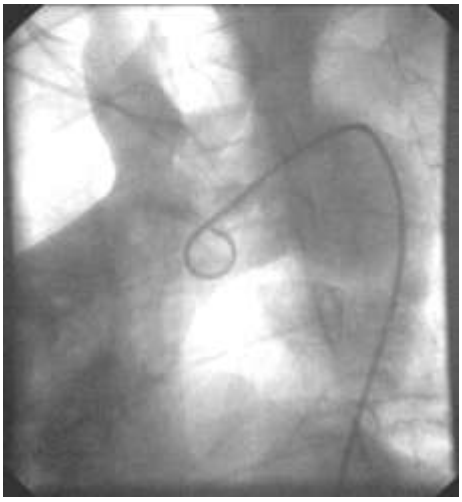

Figure 12: Brahiocephalic artery dissection (in context of a dissection of the ascendent aorta Stanford A Debakey II).

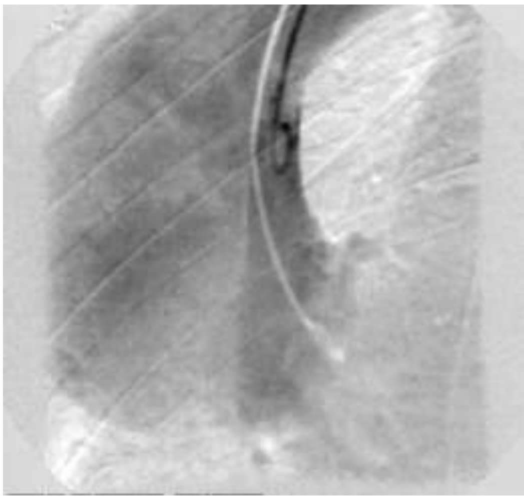

Figure 13: Ascendent aortic dissection Stanford A Debakey II – dissection fold continuing on the brahiocephalic artery.

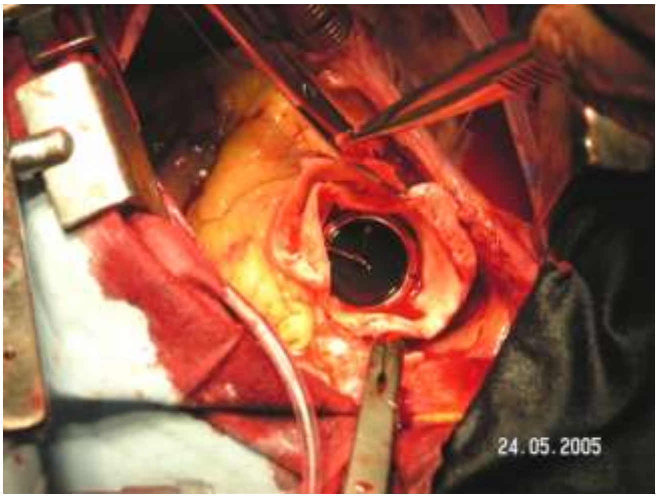

Figure 14: Dissection of ascendent aorta (after replacing the aortic valve).

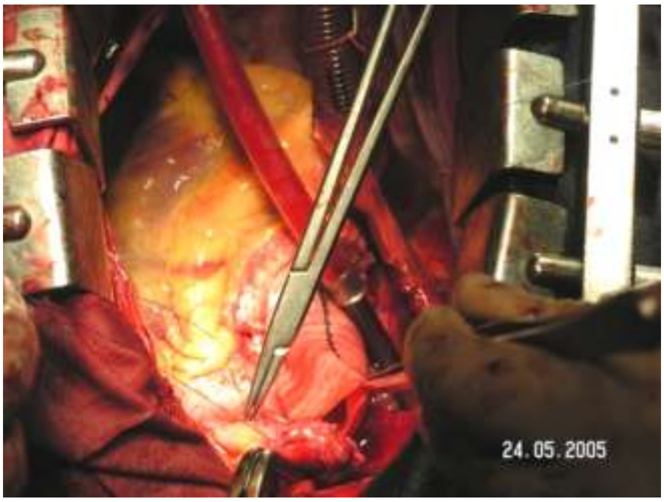

Figure 15: Indirect reconstruction of the brahiocephalic trunk through elimination of the false lumen (unifying by using biologic adhesive, respective the reinforcement of the aortic cross blunt with internal and external bandelets).

Conclusions

The pathology of supraaortic arterial systems is clearly dominated by internal carotid stenosis. Although referred rarely, cases about lesions of brahiocephalic trunk or common carotid arteries are severe and their treatment is sometimes about difficult and complex abordations, marked by features depending on the patient.

The Surgery for Vertebro-Basilar Insufficiency*)

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Abstract

Background. *With cerebrovascular disease, medical attention and interest are focused mainly on the carotid system of arteries and especially on the area of the carotid bifurcation. Due to their complexity, arterial diseases in the vertebro-basilar system are more difficult to both diagnose and treat. Moreover, as compared with the carotid system, there is no unanimous opinion between centers and specialists, regarding the timing of surgical treatment in the vertebro-basilar system and the necessary procedures to be applied. Concomitant lesions in the carotid arteries and their branches render the clinical picture even more protean and more difficult to interpret.*

Material and methods. *A number of 36 consecutive patients with lesions affecting either solely the vertebro-basilar system or with associated lesions in the carotid system were operated over a three-year period. The surgical techniques were multiple and generally complex – as required by the severity of the arterial lesions or by the clinical manifestations. The main diagnostic elements and the resultant surgical procedures are extensively presented.*

Results. *Revascularization of the vertebro-basilar system was highly-successful in the series studied with no mortality and with only a minor postoperative stroke in the carotid territory. Surgical manoeuvres in spite of their complexity did not complicate the intra- and the postoperative course of the patients. Intraoperative monitorization was facilitated by the use of loco-regional anesthesia.*

Conclusions. *The detailed diagnostic workup and the emergent surgical techniques envisaging the vertebro-basilar system represent necessary conditions for a proper and efficient approach to the patient with cerebrovascular disease. The author's experience with a number of 36 cases draws attention toward this particular anatomic district, clinically manifesting in numerous non-characteristic ways, a system with a particular physiology, requiring individualized surgical indications and techniques.*

Introduction

Compared with the carotid system of arteries, the clinical picture of vertebro-basilar arterial insufficiency is protean, the signs and symptoms being easily overlooked[1] or confounded with more benign conditions. The emerging consequences are however more

*) **Romanian Journal of Cardiovascular Surgery ■ 2009, vol. 8, no. 1-2, pp. 49-72**

severe and more disabling as compared with the carotid territory. The clinical presentation and the diagnostic interrogation are rendered more complex by the presence of concomitant arterial lesions in the carotid system, aortic arch (and subclavian arteries) or of the intracranial arterial segments and usually requires a multispecialist approach.

Moreover, there is no unanimous agreement regarding the necessity of treating the lesions in the vertebro-basilar system: a wide opinion is that the lesions in the vertebro-basilar system will compensate or even reverse after treating the carotid lesions[2]. Beside the stenotic/occlusive mechanism, **the atheroembolic mechanism of stroke** in the vertebro-basilar system is also less contemplated. In this latter respect, moderate or even severe vertebral artery stenoses but with unstable or ulcerated plaques, are often overlooked on the assumption that the contralateral vertebral artery will offer a compensatory flow.

The aim of this article is to present the specific characteristics of the vertebro-basilar arterial system together with the author's experience in treating the vascular lesions by using various surgical methods, and to draw attention on the particularities of the diagnostic workup and therapeutic approaches.

Special features of the vertebro-basilar system

The two vertebral arteries frequently depict an asymmetric outline, with one being "dominant". The first part of the subclavian arteries giving origin to the vertebral arteries must also be included in the general picture of the vertebro-basilar system both in normal and in disease. Not infrequently, the left vertebral artery may originate directly from the aortic arch, between the left carotid and the left subclavian artery respectively[3]. Hence an angiographically "absent" left vertebral artery must be sought either by direct catheterization or by performing an arch aortography.

A practical classification of the segments of the vertebral arteries is reported here[4, 5] (figure 1, next page).

- **V0 = origin**. The very origin of the vertebral artery is called the V0 segment. The purpose of assigning a separate name to this portion of the vertebral artery assists in drawing the attention toward the adjacent parts of the subclavian artery (or of the aortic arch); lesions of these closely-related arterial segments may limit, modify or even contraindicate surgical (or percutaneous) approaches.
- **V1 = pre-transversal extraosseous**. This is the portion of the vertebral artery most accessed in surgery. With older age or atherosclerotic disease, the V1 portion can show significant kinking. This is the portion of the vertebral artery that can be mobilized most, allowing for example, its re-implantation in the common carotid artery. This portion of the vertebral artery can be easily confused with the inferior thyroid artery. This latter structure lies however in a more superficial plane (anterior to the vertebral artery) and characteristically, gives off numerous cervical branches. Another important detail is that the vertebral artery represents the first (the most proximal) branch of the subclavian artery.

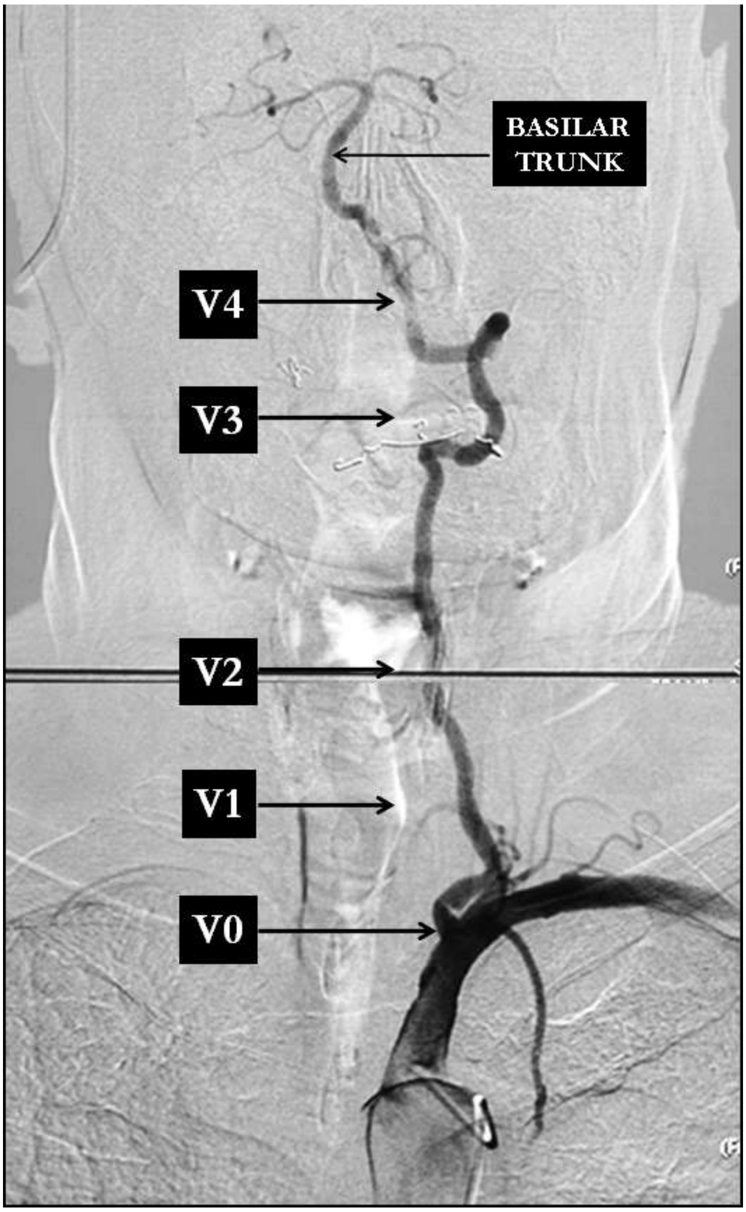


Figure 1

- **V2 = interosseous**. Surgical access to this part is more striving for the surgeon due to the need for partial bone resection. Lesions of this portion of the vertebral artery can be however treated more conveniently and more rapidly, by using the percutaneous techniques. The vertebral artery is accompanied by a plexus of veins and by sympathetic nerves derived from the cervical ganglia, forming the vertebral nerve. This segment of the vertebral artery gives off branches to the cervical nerves, vertebrae, intervertebral joints, neck muscles and for the cervical spinal cord. A prominent branch at C5 level anastomoses with the anterior spinal artery. The anastomoses with the deep cervical and with the ascending cervical artery can become conspicuous and offer parallel arterial pathways toward the distal vertebral artery (V3 segment). Inversely, such well-developed anastomoses may promote the steal syndrome even in case of occlusion of the vertebral artery at its origin (V0 and V1 segments).
- **V3 = distal extracranial** or **the atlas loop**. The artery runs laterally and then vertically toward the transverse foramen of the atlas; after passing thorough the foramen, the artery winds medially along the lateral mass of the atlas, pierces the posterior atlanto-

occipital membrane, entering the dura mater and the arachnoid at the level of the foramen magnum. The suboccipital portion of the vertebral artery from the transverse foramen of the axis (C2), to the posterior atlanto-occipital membrane, is a relatively long segment, allowing a proper surgical exposure for a bypass at this level. Numerous muscular and articular branches must be identified and interrupted, at this level.

- **V4 = intracranial**. This segment of the vertebral artery lies entirely in the subarachnoid space. Before the confluence of the two vertebral arteries, each gives off some important branches in the intracranial portion: the posterior spinal artery, the posterior inferior cerebellar artery (PICA) and the anterior spinal artery. A lower (i.e. more proximal) origin of the PICA may impede surgical manoeuvres at the level of the intracranial vertebral artery.

Numerous ANASTOMOSES exist between the carotid and the vertebro-basilar system of arteries:

- **Cervical level**. There are no direct communications between the common or internal carotid arteries with the vertebral arteries. The only notable anastomoses are established between branches of the external carotid artery and subclavian arteries: superior thyroid (external carotid) with inferior thyroid (subclavian) or the deep and the superficial branch of the occipital artery (external carotid) with the deep or ascending cervical arteries (subclavian) and with the muscular branches of the vertebral artery
- **Intracranial level**. The arterial circle (Willis) represents the most important communication between the basilar artery and the emerging posterior cerebral arteries, and the terminal portion of the carotid arteries – by way of the posterior communicating artery.

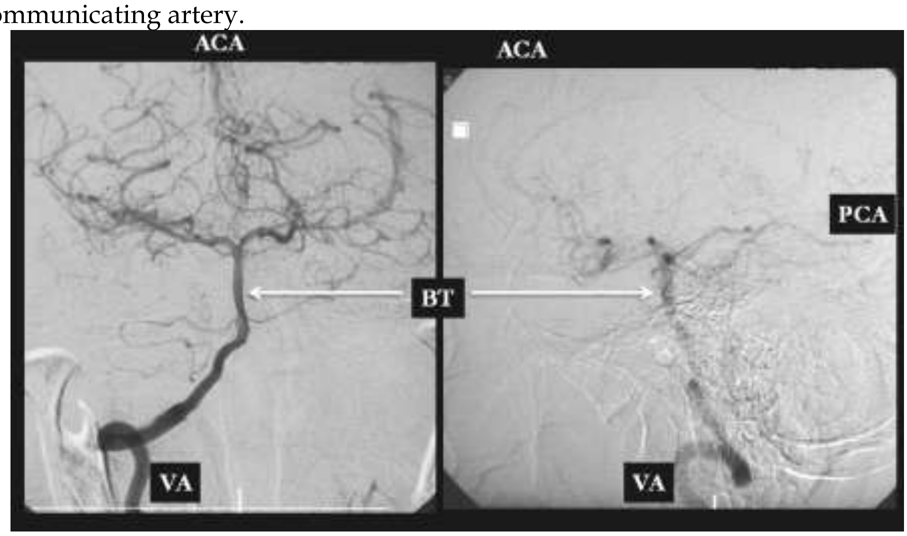


Figure 2: Anastomoses between the anterior and posterior circulation of the brain

The deep arterial branches from the arterial circle are terminal branches, but the cortical branches of the anterior, middle (carotid) and posterior (vertebro-basilar) cerebral arteries are connected through the leptomeningeal anastomoses. Such anastomoses may become conspicuous with occlusion of one of the main trunks. Variations in the makeup of the arterial circle explain the different clinical manifestations or the individual variations during carotid or vertebral artery clamping[6].

- **Vestigial anastomoses** between the two systems are represented by the proatlantal, hypoglossal, otic, trigeminal or stapedial arteries. The persistence of such arteries may explain atypical clinical manifestations or different tolerance to carotid clamping, in individual patients[7-15].

THE TERRITORY OF VASCULARIZATION OF THE VERTEBRO-BASILAR SYSTEM is both wide and important. It comprises the brainstem, the cerebellum, a great portion of the cerebral cortex while the deep central branches are distributed to the basal nuclei and thalamus[16]. The various syndromes described so far, reflect the severity of the vascular lesions, the clinical significance and the dismal prognosis: medial medullary syndrome (vertebral or proximal basilar artery occlusion), lateral medullary syndrome (vertebral, PICA or medullary arteries occlusion), complete unilateral medullary syndrome (vertebral artery occlusion), medial inferior pontine syndrome (occlusion of paramedian branches of the basilar artery), lateral inferior pontine syndrome (anterior inferior cerebellar artery occlusion), lateral ponto-medullary syndrome (vertebral artery occlusion), medial middle pontine syndrome (occlusion of paramedian middle branches of the basilar artery), lateral middle pontine syndrome (occlusion of short circumferential branches), medial superior pontine syndrome (occlusion of distal paramedian branches of the basilar artery), lateral superior pontine syndrome (superior cerebellar artery occlusion), basilar artery syndrome (occlusion of basilar or of singular vertebral artery), temporal and occipital cortical syndromes (occlusion of the cortical branches of the posterior cerebral artery: anterior temporal, posterior temporal, calcarine and parieto-occipital arteries), midbrain, subthalamic and thalamic syndromes (occlusion of the deep branches of the posterior cerebral artery: peduncular, mesencephalic postero-medial choroidal, hippocampal and splenial arteries).

THE DIAGNOSTIC WORKUP comprises the following steps:

- **History and physical examination.** The clinical presentation in the individual patient is usually highly variable. The transient ischemic attack in the vertebro-basilar system includes vertigo, dizziness, ipsilateral facial numbness, contralateral limb numbness, diplopia, hoarseness, dysarthria, dysphagia, and rarely hemiparesis, while cerebral infarction may manifest with any of the numerous syndromes presented above. A particular mention must be made at this point regarding the lesions in the vertebro-basilar system, diagnosed during routine diagnostic interrogation for suspected lesions in the carotid system of arteries.
- **Cardiologic clearance**. Diseases representing a risk for the development of a stroke must be identified if present. Higher-risk conditions include atrial fibrillation, mitral stenosis, mechanical valvar prosthesis, left ventricular dysfunction and intracavitary thrombi, recent myocardial infarction, infective endocarditis. Lower-risk conditions include: calcifications of the mitral annulus, mitral valve prolapse, patent foramen ovale, aneurysm of the atrial septum, aortic stenosis with valvar calcification. Pre-operatively, the patient must be ideally in a stable condition especially regarding the

hemodynamic status, blood pressure levels, the presence of dysrhtythmia or heart failure.

- **Doppler examination**. A complete ultrasound workup must be performed including the carotid system of arteries, the subclavian arteries, the vertebro-basilar system, and not least, the intracranial circulation. Data regarding the diameter of the vertebral arteries and the direction of flow are very important. A thorough staging of the arterial lesions is highly significant in view of the therapeutic planning and for the choice of the proper surgical indication. There is no unanimous agreement and no comparative statistics regarding the data on the severity of stenotic lesions in the vertebro-basilar insufficiency as compared with the carotid system of arteries. There is no accepted "stenotic threshold" above which surgery or angioplasty should be employed, in the vertebro-basilar system. Severe kinking of the vertebral arteries may add further deleterious hemodynamic effects, which can be revealed by means of the Doppler interrogation and not least, and specially while allowing various postures of the head and neck. Again, there is no unanimous agreement on the IMT index values (intima/media thickness) in the case of the vertebro-basilar system.
- **Angiographic interrogation**. A 4-vessel angiogram (including extra- and intracranial exam) completed by aortic arch angiogram offers additional valuable data and is especially indicated with suspected "lower" lesions on the arch or on the origin of the cervical vessels. The intracranial distribution of the main trunks allows a better planning of the surgical act and the order of vessel clamping. Angiogram adds more important details as compared with the carotid system, where lesions are mostly located at the level of the bifurcations. The Doppler examination cannot offer but indirect data on the origin of the subclavian arteries or of the aortic arch, while a low-grade stenosis plus kinking of the vertebral artery appears as a severe stenosis on the echogram. Moreover, if a revascularization of the vertebral artery at suboccipital level is contemplated, the angiogram will offer important additional details on the adjacent arteries that can be used as donor arteries (external carotid and its main branches for example). Angiography also offers data on the anatomic variations of the basilar trunk, or of the origin of the PICA (posterior inferior cerebellar artery).
- **CT scan or MRI interrogation**. These diagnostic tests offer details on the presence of infarctions or lacunae. An arterial stenosis or plaque can be defined as "symptomatic" in the presence of previously unknown lacunae or cerebral infarctions in the very same vascular territory. Identification of vulnerable, unstable, complicated plaques and details on the intimate composition of the plaque, are all best accomplished by the MRI interrogation, although rarely performed due to the costs and longer examination times.
- **MRA** (magnetic resonance angiography) may substitute the classical angiogram, although it represents only a diagnostic tool with no therapeutic (e.g. percutaneous) possibilities. It may represent a sound screening procedure and a useful test during follow up.
- **Spirometry** with both static and dynamic lung volumes is mandatory in the planning of the surgical act, and not least regarding the type of anesthesia envisaged.
- **Endocrine evaluation** especially for diabetes or even borderline glucose intolerance

The risk stratification in the case of carotid lesions is usually well correlated with the initial symptom or sign, being higher with stroke, less with hemispheric TIAs and least with amaurosis[17]. However, this cannot be accomplished in the vertebro-basilar system where such a staging of signs and symptoms is not evident and where any delay can have dismal consequences.

Although the diagnostic elements are all well known and established, **THE SURGICAL THERAPY** is less contemplated (as compared with the medical treatment and the percutaneous manoeuvres). However, surgery may offer a better alternative both on short and on long term and this aspect will be illustrated in this article. A number or 36 consecutive patients with lesions in the vertebro-basilar arterial system were surgically treated over a 4-year period.

Patient Data

TABLE 1: PATIENT DEMOGRAPHICS

AGE (years)	MALE (No)	FEMALE (No)
46-50	3	0
51-55	9	1
56-60	5	3
61-65	4	1
66-70	2	4
71-75	1	1
75-80	2	0
Total / sex	26	10
TOTAL	36	

Patient demographics

As illustrated in **TABLE 1** male patients were younger. Additionally, more of the male patients presented with more severe neurologic symptoms and more had a previous stroke.

Clinical presentation

Patients displayed the following signs and symptoms, upon admission in the hospital (**TABLE 2).**

TABLE 2: CLINICAL PRESENTATION

CLINICAL SIGN / SYMPTOM	No of patients
Stroke in the territory of the PCA*	1
Vertigo, dizziness, unstable gait	4
Previous stroke in the territory of the PCA + vertigo	2
Neurologically instable: loss of consciousness when sitting up	3
Stroke in the carotid territory + vertigo and dizziness	7
TIA in the carotid territory + vertigo and dizziness	9
Dizziness + upper limb ischemia	8
Asymptomatic / minor unspecific symptoms	2
TOTAL	36
*** PCA** = *Posterior Cerebral Artery*	

Noticeably, a large number of the patients presented with concomitant lesions in the carotid territory and with a polymorphous symptomatology. Three of the patients were neurologically instable, with loss of consciousness when sitting up or while performing Valsalva manoeuvres (sneezing or coughing). Upper limb ischemia represented one of the major complaints in less than a quarter of the patients. Two of the patients who had occlusion of the subclavian artery plus occlusion of the first and second portion of the ipsilateral vertebral artery (V1 and V2) presented with signs of upper limb ischemia and vertebral steal syndrome, through enlarged cervical anastomoses, although clinically the distal pulse was palpable.

Comorbidities

The patients presented numerous associated diseases. A significant number had 2 or more comorbidities (**Table 3**)

Table 3: COMORBIDITIES

DISEASE	MALE (No)	FEMALE (No)
AHT[1]	**4**	**1**
COLD[2]	**2**	**0**
CRF[3] in haemodialysis	**1**	**0**
Ischemic heart disease + AHT	**2**	**1**
Diabetes + AHT	**3**	**6**
AHT + COLD	**7**	**0**
Diabetes +AHT + COLD	**7**	**2**
Total / sex	**26**	**10**
TOTAL	**36**	

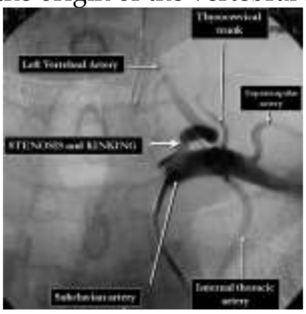
[1] **AHT =** *Arterial Hypertension*
[2] **COLD =** *Chronic Obstructive Lung Disease*
[3] **CRF =** *Chronic Renal Failure*

Male patients presented with more numerous associated diseases and with more severe forms of chronic obstructive lung disease. Ischemic heart disease included previous myocardial infarction and/or angina. Peripheral vascular disease was present in 8 male patients and in 3 female patients (not illustrated in the table). One male patient required simultaneous lower limb revascularization for severe ischemia.

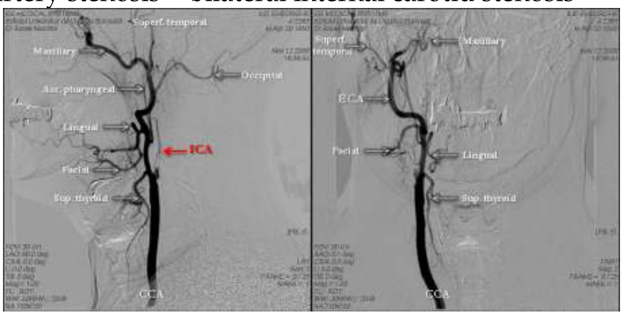
Arterial lesions

The following types of arterial lesions were observed in this series of patients (Table 4):

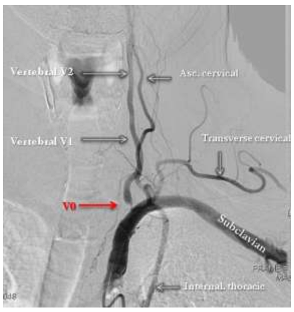
TABLE 4: ARTERIAL LESIONS IN THE CASE SERIES

ARTERIAL LESIONS	No
Stenosis ± kinking of the origin of the vertebral artery  Figure 3	3
Vertebral steal syndrome: occlusion of the brachiocephalic trunk  Figure 4	2
Vertebral steal syndrome: occlusion/severe stenosis of the subclavian artery  Figure 5	3
Vertebral steal syndrome: occlusion of the subclavian artery + bilateral carotid stenosis	3
Vertebral steal syndrome: occlusion of the subclavian artery + vertebral artery (V1-V2) – steal through collaterals (see Figure 6, next page)	2

<table>
<tr><td>

Figure 6</td><td></td></tr>
<tr><td>Vertebral steal syndrome: occlusion of the subclavian artery + stenosis of ipsilateral carotid bifurcation</td><td>8</td></tr>
<tr><td>Vertebral steal syndrome: occlusion of the subclavian artery + stenosis of contralateral carotid bifurcation</td><td>2</td></tr>
<tr><td>Vertebral artery stenosis + bilateral internal carotid occlusion</td><td>2</td></tr>
<tr><td>Vertebral artery stenosis + bilateral internal carotid stenosis


7A


7B


7C</td><td>5</td></tr>
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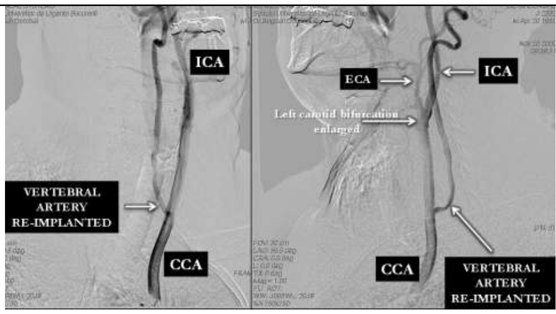
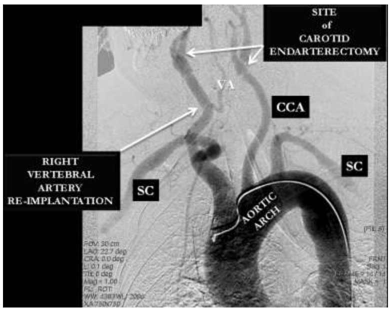
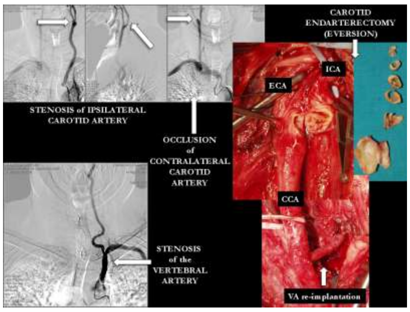
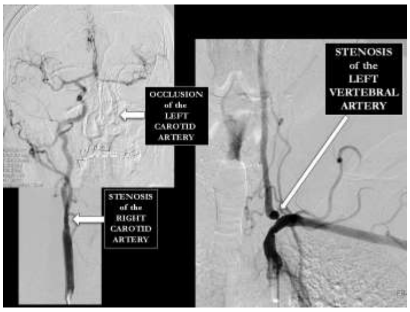
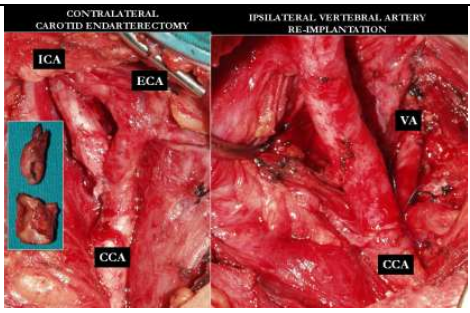
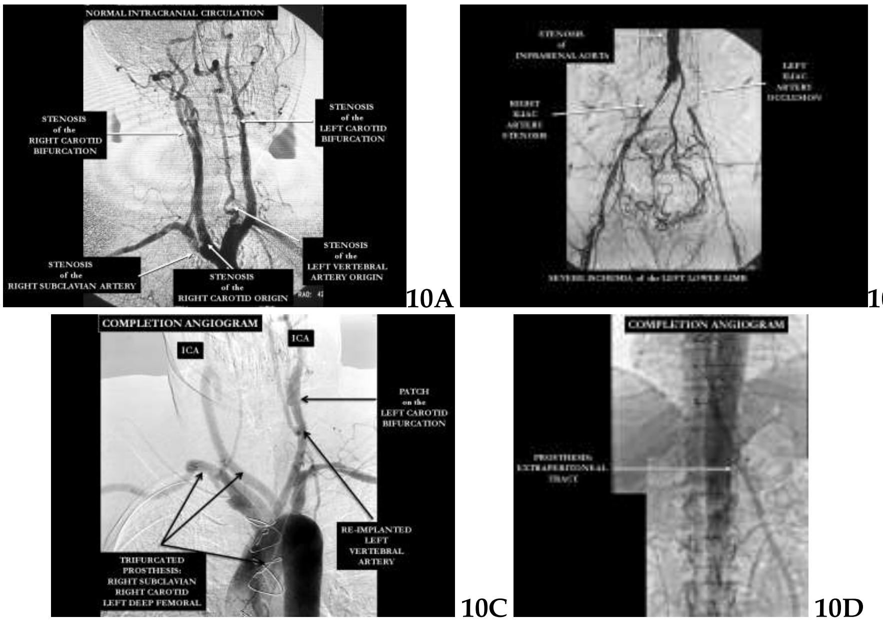
 7D  7E **Figure 7**	
Vertebral artery stenosis + ipsiteral internal carotid stenosis  **Figure 8**	**2**
Vertebral artery stenosis + contralateral internal carotid stenosis  9A	**1**

 9B **Figure 9**	
Vertebral artery stenosis + internal carotid stenosis + subclavian artery occlusion	**1**
Multiple neck vessel arterial disease: subclavian, carotid, vertebral + lower limbs  10A 10B 10C 10D **Figure 10**	**1**
Vertebral artery occlusion (V1-V2) + internal carotid occlusion + subclavian artery occlusion	**1**
TOTAL	**36**

As illustrated in **Table 4,** only a small percentage of the patients presented with "pure" lesions of the vertebral artery (or of the first portion of the subclavian artery): most patients had diffuse arterial disease either involving the supra-aortic trunks and branches, or the lower limbs. The diagnostic approach and the surgical indication and technique – were hence more elaborated and more challenging. A complete revascularization was envisaged every time while weighing the benefits of the operation and the risks of a longer and a more complicated procedure on one hand and on the other hand, the risks of non-treating all vascular lesions in a single operative moment (further details are offered below).

In this series, the diagnostic workup consisted in: Doppler examination (including the transcranial Doppler), 4-vessel angiogram, cardiologic and neurologic clearance, spirometry, cerebral CT of MRI.

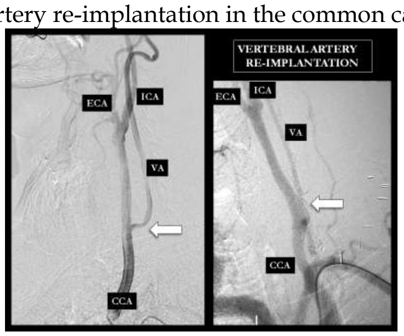
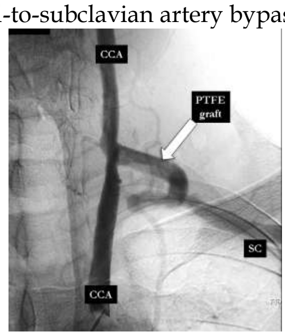
Surgical Procedures

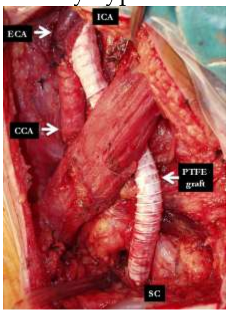
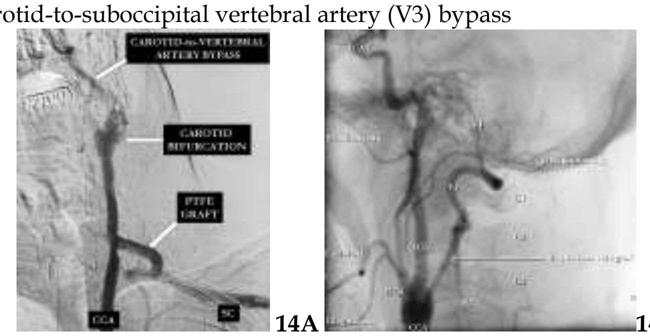
The patients underwent various surgical procedures. All operations requiring median sternotomy were performed under general anesthesia. Operations involving only the cervical approach were performed either under general anesthesia, or under loco-regional anesthesia (cervical block): **tables 5 and 6.**

Table 5: TYPES OF ANESTHESIA USED

General anesthesia (with naso- or orotracheal intubation)	**25**
Loco-regional (cervical plexus block ± interscalenic block)	**11**
TOTAL	**36**

Table 6: SURGICAL PROCEDURES

Type of procedure	No. of patients	Notes
Vertebral artery re-implantation in the common carotid artery  **Figure 11**	**3**	**L-L or L-T**
Common carotid-to-vertebral artery bypass	**2**	**PTFE graft**
Common carotid-to-subclavian artery bypass  **Figure 12**	**5**	**PTFE graft**
Re-implantation of the subclavian artery into the common carotid artery	**2**	

Carotid bifurcation endarterectomy + carotid-to-subclavian artery bypass  Figure 13	6	PTFE graft
Carotid bifurcation endarterectomy + re-implantation of the subclavian artery into the carotid artery	1	
Carotid bifurcation endarterectomy + re-implantation of the vertebral artery into the common carotid	2	
Carotid bifurcation endarterectomy + carotid-to-subclavian artery bypass + carotid-to-suboccipital vertebral artery (V3) bypass  14A 14B Figure 14	2	Saphenous vein graft on the vertebral artery
Simultaneous bilateral carotid endarterectomy + carotid-to-subclavian artery bypass	1	PTFE graft
Simultaneous bilateral carotid endarterectomy + vertebral artery re-implantation into the common carotid	5	
Subclavian-to-contralateral subclavian and carotid artery bypass	1	Dacron graft
Ascending aorta-to-right subclavian and right carotid bypass	3	Median sternotomy + cervical approach
Ascending aorta-to-carotid and bilateral subclavian artery bypass	1	
Brachiocephalic trunk-to-left subclavian, left carotid and left vertebral artery bypass	1	
Ascending aorta-to-right subclavian, right carotid and left femoral artery bypass + left carotid endarterectomy + left vertebral artery re-implantation	1	
TOTAL	**36**	

The re-implantation of the vertebral artery in the common carotid artery[18] is performed either through a supraclavicular approach or through a single longitudinal cervical incision[19]. A combined incision (longitudinal plus supraclavicular) for carotid and vertebral artery exposure was used in 4 of the patients depicting shorter neck. In one of the 4 afore mentioned patients, the transversal canal at C6 level was open, in order to obtain a longer segment of the vertebral artery.

The common carotid-to-vertebral artery bypass represented an alternative of the former technique, used in 2 patients who depicted very frail vertebral arteries. A 6 mm. PTTFE graft was used for the bypass.

Common carotid-to-subclavian artery bypass was deployed in 5 patients with vertebral steal syndrome due to severe stenosis or occlusion of the origin of the subclavian artery. The same 6 mm. PTFE reinforced graft was used. The prosthesis was tunnelled underneath the sternocleidomastoid muscle.

An alternative of the technique mentioned above, is the (latero-terminal) re-implantation of the subclavian artery in the common carotid artery (with the creation of "a neo-brachiocephalic trunk"). The procedure requires a more extensive mobilization of the origin of the subclavian artery, including the origin of the vertebral artery. However, in none of the patients was necessary the ligature of the internal thoracic artery.

With concomitant disease at the level of the ipsilateral carotid bifurcation, an additional endarterectomy was initially performed, followed by the re-implantation of the subclavian artery in the common carotid artery (1 patient). However, the mostly used technique was endarterectomy and carotid bifurcation-to-subclavian artery bypass with a 6 mm. PTFE graft. As previously mentioned, the prosthesis was tunnelled underneath the sternocleidomastoid muscle.

When no significant lesions of the subclavian artery were present, the technique of carotid endarterectomy plus vertebral artery re-implantation in the common carotid artery was used.

In 2 patients, multiple arterial lesions were present: stenosis at the level of the carotid bifurcation, stenosis or occlusion of the first portion of the subclavian artery and occlusion of the first and second part of the vertebral artery (V1-V2). In spite of the vertebral artery occlusion at origin and intertransversal portion, the vertebral steal syndrome was present, through enlarged cervical collaterals, which connected the suboccipital vertebral artery (V3) to the second and third part of the subclavian artery. These patients had also palpable distal pulse in the upper limb. Such complex lesions required a complete revascularization consisting of carotid-to-subclavian bypass, followed by carotid endarterectomy and eventually by carotid bifurcation-to-suboccipital vertebral artery venous bypass[20] (with the creation of a carotid "trifurcation".

As bilateral carotid disease is frequently associated with subclavian or vertebral artery disease, in the series of patients presented, 1 patient underwent simultaneous bilateral carotid endarterectomy plus carotid-to-subclavian artery bypass, while the reminder 6 patients underwent simultaneous bilateral carotid endarterectomy plus vertebral artery re-implantation in the common carotid artery. A special note is that all these patients were operated under loco-regional anesthesia.

With extensive disease in the upper aortic system, involving almost if not all the cervical vessels, a broad and complex revascularization was achieved through a combined approach: median sternotomy plus bilateral cervical incision. The donor vessel was the ascending (intra-pericardial) aorta and in only 1 case, the brachiocephalic trunk (this patient had a previously undiagnosed dilation of the ascending aorta). The distal target vessels were the carotid bifurcations, the subclavian and the vertebral arteries.

THE SHUNT was used only in 2 patients, of which one had occlusion of the brachiocephalic trunk (ascending aorta-to-common carotid shunt) and the other had a single vertebral artery patent but severely stenosed at origin (both internal carotid arteries and the contralateral vertebral artery were occluded). In this latter case, a temporary shunt was used between the ipsilateral subclavian artery and the vertebral artery.

Results

Patient follow-up ranged from 3 years to 1 month.

All patients had an early Doppler interrogation at 2-3 weeks postoperatively, repeated at 6 months interval. All patients who underwent complex surgical procedures had an additional early postoperative angiogram. All bypasses, conduits, etc. remained patent during follow-up.

One patient with carotid endarterectomy plus common carotid-to-vertebral artery bypass had a minor (non-disabling) stroke in the carotid territory during his in-hospital stay. There were no deaths in this series. One female patient had a retractile cervical scar, after a combined longitudinal and supraclavicular approach. Three of the patients had transitory Horner syndrome. The patients with revascularization of the suboccipital part of the vertebral artery (V3) fared well with no neurological complications; one of these patients experienced left-sided headaches for about 3 weeks postoperatively.

Discussion

In medical practice, when confronted with the patient with cerebrovascular disease, the physician's attention is mainly focused on the carotid system of arteries, less on the aortic arch and branches, and in a much lesser degree on the vertebro-basilar system. Endarterectomy of the carotid bifurcation appears at first glance to be a relatively easy procedure, especially when performed under loco-regional anesthesia or when deploying time-saving procedures such as the eversion technique or the direct closure of the arteriotomy. The area of the carotid bifurcation is consequently the preferred area for many categories of specialists in spite of the fact that the phenomenon of cerebral arterial insufficiency represents the consequence of numerous factors acting at various levels, either in sequence or concomitantly. The long vascular pathway between the heart and the brain is monitored and approached by various specialists, having different conceptions, skills and preferences. It is in this very context that the vertebro-basilar system is generally less investigated and even less approached therapeutically. As compared with the carotid system of arteries, in the case of the vertebro-basilar system, larger studies and statistics on the degree of stenosis and on the patient outcome and risks are lacking.

Moreover, as previously stated, **the atheroembolic mechanism of stroke in the vertebro-basilar system** is less contemplated, while it is well known, both in the case of the carotid arteries, as well as in the case of the coronary arteries, that moderate stenoses and instable plaques constitute the main cause of cerebral or coronary infarction 21.

The aim of this article and the purpose of presenting this series of patients is to draw attention on this particular vascular territory that can be pathologically involved either singularly, or in concomitance with the carotid arterial system. Out of the numerous and sometimes ambiguous diagnostic data and particulars, the emerging therapeutic indication and associated procedure, rarely represent a straightforward process.

The series of patients presented, form a heterogeneous group. The arterial lesions ranged widely, from no vertebral lesion at all (occlusion of the subclavian artery with vertebral steal syndrome) to complex multi-vessel disease including the carotid, subclavian, vertebral, and iliac arteries. It is thus difficult to compare different therapeutic approaches, indications and not least, results – in such a protean group.

In spite of this detail, it is noteworthy mentioning the following aspects:

- Cerebrovascular arterial disease includes lesions at various levels, depicting different degrees of severity existing either as separate entities, or adding up their potential deleterious effects. A thorough stratification of severity of the disease and of the potential consequences is not straightforward and usually requires a multispecialist approach (surgeon, neurologist, and cardiologist).
- Attention is mainly focused on the carotid system of arteries, the vertebro-basilar system being often overlooked, especially because the symptomatology is less characteristic. Due to the important territory of vascularization, the vertebro-basilar system must be carefully and fully explored and the lesions must be efficiently treated
- Decision on which lesions and when to treat such lesions in the vertebro-basilar system is not as clearly settled as compared with the carotid arteries. Moreover, **ASYMPTOMATIC** vertebro-basilar lesions pose both technical and ethic problems
- The surgery for vertebro-basilar insufficiency is much more technically demanding (including both anesthesia and surgery)
- Individual anatomic variations must be thoroughly sought as the therapeutic planning and methods vary accordingly, especially in case of highly asymmetric vertebral arteries or with incomplete arterial circle (of Willis)
- In patients with extensive and severe carotid disease, the vertebral arteries might represent the only remaining direct source of vascularization of the brain and both the diagnostician and the surgeon must be familiarized with treating stenotic lesions in the vertebro-basilar system
- The long cervical tract of the vertebral arteries is amenable to various surgical and percutaneous procedures reducing thus the need for transcranial revascularization procedures
- Performing operations under loco-regional anesthesia, offers a better comfort to the surgeon and allows the use of selective shunting only – a procedure more difficult to apply in the case of the vertebral artery.

Final Remarks

The vertebro-basilar system has an important territory of vascularization, asking for a thorough diagnostic workup and for a more complex and for more elaborate surgical techniques. Such techniques, gain wider acceptance among surgeons, although a unanimous opinion regarding when and how to treat such arterial lesions, is still lacking. The case series presented, in spite of its heterogeneity, draws the attention toward less expected but otherwise highly-present diseases, affecting either the vertebro-basilar system, or both the vertebro-basilar system and the carotid system of arteries.

Figure Legends

Figure 1: THE SEGMENTS OF THE VERTEBRAL ARTERY

Angiogrphic aspect of the left vertebral artery in an antero-posterior view. The vertebral artery originates from the first part of the subclavian artery. The very origin in sometimes called the V0 segment. The extraosseous pre-transversal segment V1 comprises the portion between the origin and the transversal foramen of the C6 vertebra (although variations are described, with the vertebral artery travelling as far as C2 in an extraosseous tract. This portion of the artery is most accessible surgically. The interosseous segment V2 defines the part of the vertebral artery running through the transverse foramina of the cervical vertebrae from C6 through C2. The cervical cranial nerves lie on a more posterior plane with respect to the artery. The atlas loop forms the V3 segment of the artery, readily reachable through a suboccipital approach. The intracranial V4 segment is sometimes subdivided into two parts, extra- and intradural. A particular detail regards the origin of the posterior inferior cerebellar artery (PICA), as early origin of the PICA might impede surgical manoeuvres on the intracranial portion of the vertebral artery.

Figure 2: ANASTOMOSES BETWEEN THE ANTERIOR AND POSTERIOR CIRCULATION OF THE BRAIN

Image illustrating the angiographic aspect in the case of a patient with bilateral internal carotid artery occlusion, occlusion of the contralateral vertebral artery and stenosis of the single patent vertebral artery (VA) - antero-posterior in the left panel, and lateral view, in the right panel. The basilar trunk (BT) is hence fed by the single vertebral artery. Efficient anastomoses between the posterior and respectively, the anterior circulation, allow the filling of the anterior portion of the arterial circle (Willis), of which the anterior cerebral artery (ACA) and the middle cerebral artery are well visible. Note also that all the important branches of the arterial circle – anterior, posterior as well as contralateral – are all fed by the single vertebral artery. Such cases however reflect both a good compensatory circulation and a slower evolution of the occlusive lesions. Another compensatory mechanism is provided by the anastomoses between the external and internal carotid artery (not shown in this figure).

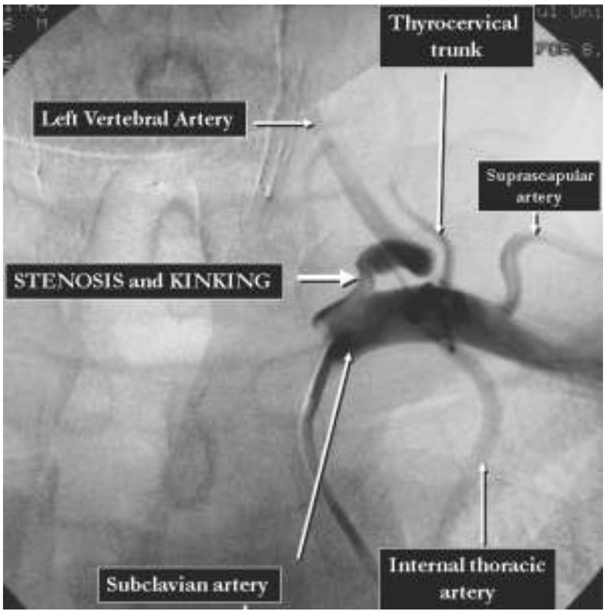


FIGURE 3: STENOSIS ± KINKING OF THE ORIGIN OF THE VERTEBRAL ARTERY

Angiographic aspect of the origin of the left vertebral artery depicting both stenosis and kinking. In this patient, the subclavian artery has no apparent stenotic lesions; consequently, the vertebral artery can be re-implanted either into the subclavian artery or into the carotid artery (the latter technique was eventually chosen). The deployment of a stent is limited or impossible, due to the kinking of the V1 segment of the vertebral artery. The kinking itself, with a relative excess in length of the vertebral artery, facilitates the re-implantation into the carotid artery and allowing a more gentle curve of the re-implanted vertebral artery.

Figure 4: VERTEBRAL STEAL SYNDROME: OCCLUSION OF THE BRACHIOCEPHALIC TRUNK

Two angiographic images (belonging to the same patient), depicting occlusion of the brachiocephalic trunk and steal syndrome through the right vertebral artery. The latter, shows a completely inverted direction of blood flow, eventually filling the right subclavian artery and the right common carotid artery. The left panel demonstrates an antero-posterior view, while the right panel, an oblique view of the same case. Note that the two vertebral arteries have the same diameter, thus facilitating the vertebral steal.

Figure 5: VERTEBRAL STEAL SYNDROME: OCCLUSION/SEVERE STENOSIS OF THE SUBCLAVIAN ARTERY

The angiographic image demonstrates a typical case of a patient with pre-occlusive stenosis of the left subclavian artery. In such cases with a high-degree stenosis, the ipsilateral vertebral artery is seldom visible, being filled mostly in a retrograde manner, from the contralateral vertebral artery, through the posterior cerebral circulatory system. Note also the extensive lesions on the subclavian artery (comprising its first, second and even third part: stenting of the origin of the subclavian artery will treat only partially the atherosclerotic lesions, while the stent itself might also cover the origin of the left vertebral artery.

Figure 6: VERTEBRAL STEAL SYNDROME: OCCLUSION OF THE SUBCLAVIAN ARTERY + VERTEBRAL ARTERY (V1-V2): STEAL THROUGH COLLATERALS

Two of the patients in this series, had this very angiographic aspect, of vertebral steal syndrome, but with occluded origin and first tract of the vertebral artery (V1 and partially, V2). In spite of the occluded large portions of vertebral artery, the steal occurred through enlarged collaterals and anastomotic pathways between the suboccipital and upper intraosseous vertebral artery and the subclavian artery. The subclavian artery was filled, as demonstrated in the angiographic image; the patients had palpable distal pulse in the left upper limb, although experiencing limb ischemia with exercise. The intraosseous portion of the vertebral artery (V2) remained only partially patent, the patients requiring a suboccipital approach of the vertebral artery and revascularization at this very level (V3). The enlarged collateral vessels are the deep cervical artery and the ascending cervical artery.

Figure 7: VERTEBRAL ARTERY STENOSIS +BILATERAL INTERNAL CAROTID STENOSIS

Five patients of this series presented with bilateral carotid stenosis and stenosis of the dominant (or unique) vertebral artery, requiring a complex revascularization, consisting of: simultaneous bilateral carotid endarterectomy + re-implantation of the vertebral artery into the common carotid artery. The arterial lesions and the surgical solutions are illustrated in figure 7, as follows:

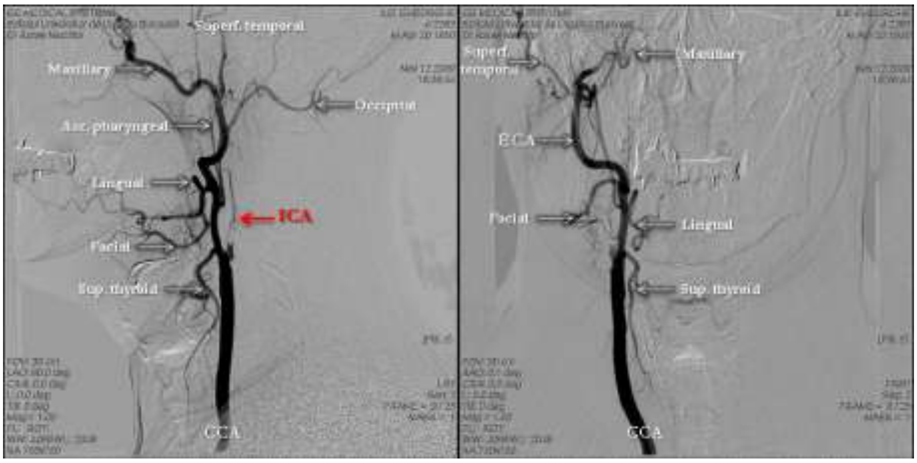


Figure 7a demonstrates a severe stenosis of the right carotid artery at the level of its bifurcation and a pre-occlusive stenosis of the origin of the right internal carotid artery. There is a faint filling of the distal cervical and intracranial portion of the right internal carotid artery

Figure 7b demonstrates the angiographic aspect of the left carotid artery, with a tight stenosis at the very origin of the left internal carotid artery

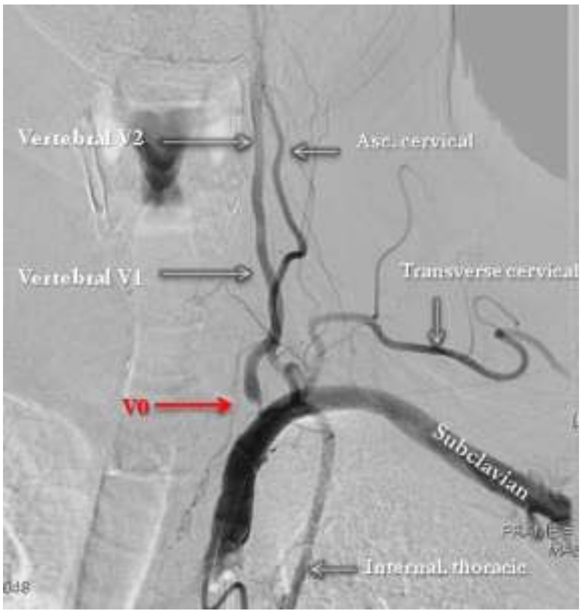


Figure 7c illustrates the severe stenosis at the origin of the left vertebral artery

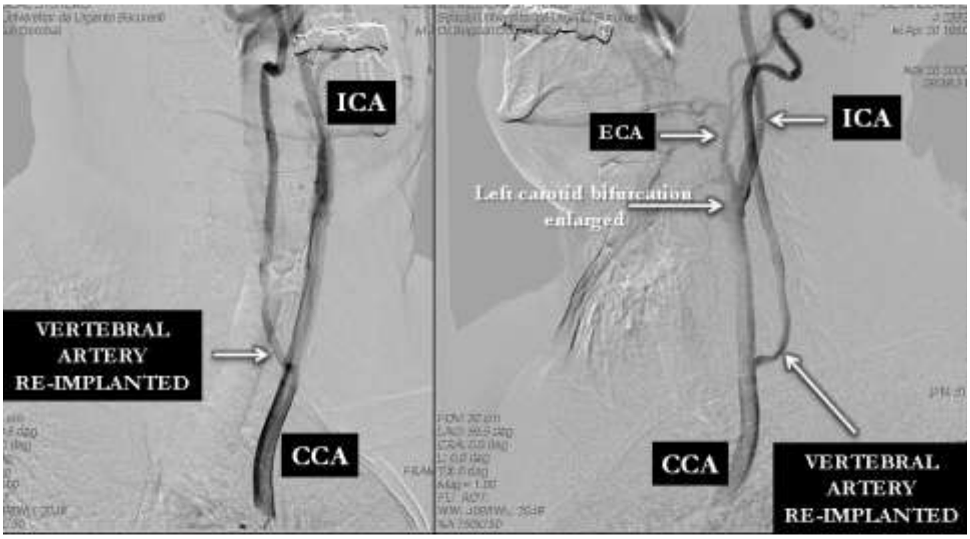


Figure 7d: completion angiogram. Contrast medium injected into the left common carotid artery (the right side not shown) in an oblique (left panel) and lateral view (right panel). The re-implanted left vertebral artery is filled concomitantly with the remainder carotid system; there is no stenosis or kinking of the re-implanted vertebral artery. The left carotid bifurcation is enlarged (best visible in the right panel, lateral view)

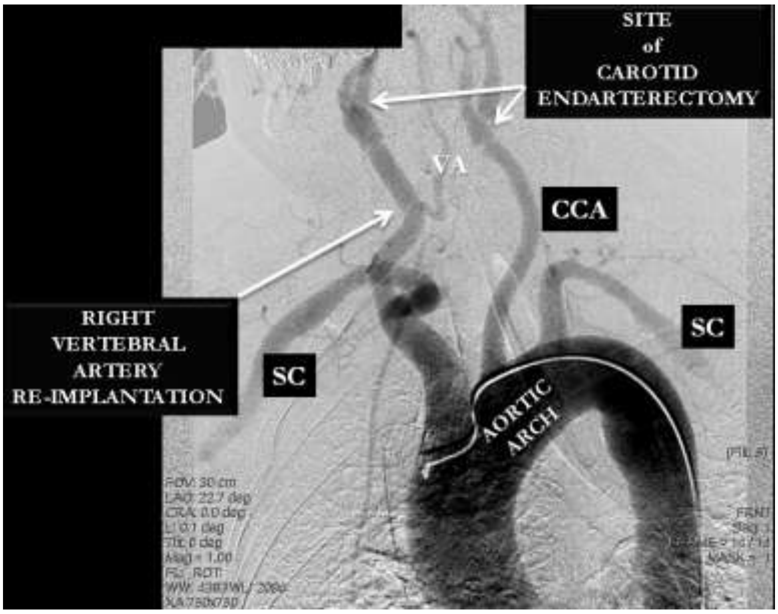
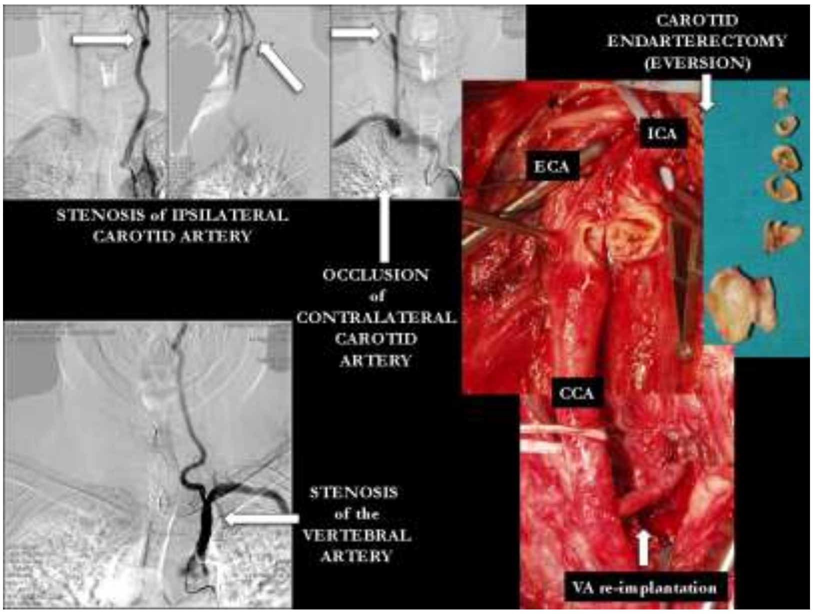


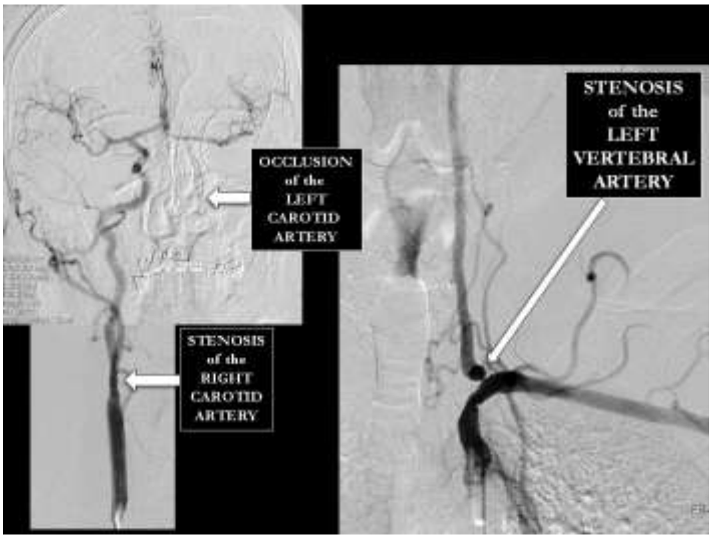
Figure 7e: completion angiogram in a patient with similar lesions, but with a re-implanted right vertebral artery. Note the enlarged carotid bifurcations, and the absence of the left vertebral artery

Figure 8: VERTEBRAL ARTERY STENOSIS + IPSILATERAL CAROTID STENOSIS.



Angiographic and intraoperative aspect in the case of a patient with left vertebral artery stenosis, ipsilateral (left) carotid artery stenosis and contralateral (right) internal carotid artery occlusion. The stenosis of the left carotid artery was moderate, but with an ulcerated plaque. The left internal carotid artery represented however, the sole vascular supply for the anterior part of the cerebral circulation. The left vertebral artery was also stenosed, as well as the left subclavian artery. The surgical solution comprised: the re-implantation of the left vertebral artery into the left common carotid artery + endarterectomy of the left carotid bifurcation (eversion technique). The intraoperative aspect and the excised carotid plaque – are all depicted in the right panels. The operation was performed under loco-regional anesthesia.

Figure 9: VERTEBRAL ARTERY STENOSIS + CONTRALATERAL CAROTID ARTERY STENOSIS.



The case illustrated hereby, had a left vertebral artery stenosis, left carotid artery occlusion and contralateral (i.e. right) carotid artery stenosis.
Figure 9a: angiographic aspect of the arterial lesions. The right carotid artery is moderately stenosed but with ulcerated plaque. The right internal carotid artery represents the sole arterial source vascularising the anterior cerebral system (note the bilateral filling of the anterior and middle cerebral arteries in the left panel). The left internal carotid artery is occluded. The left vertebral artery is severely stenosed; the left subclavian artery depicts numerous stenoses in its initial portion.

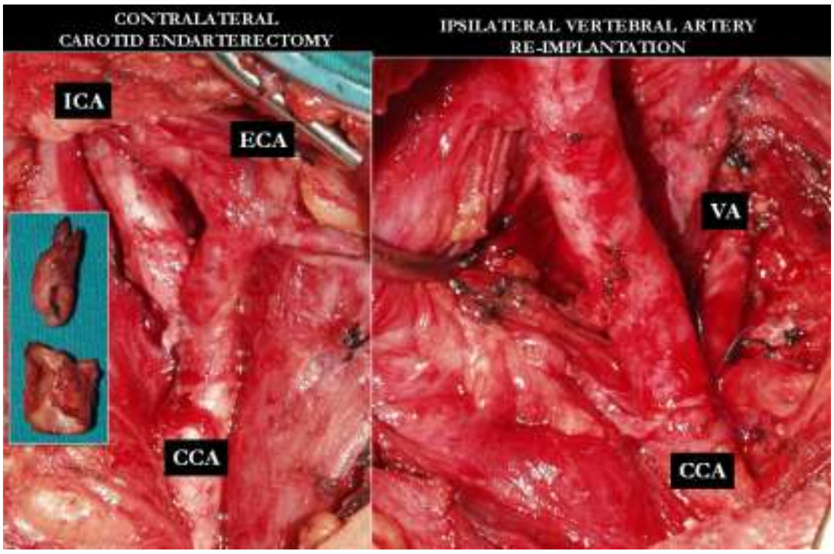


Figure 9b: intraoperative aspect. The surgical solution consisted in endarterectomy of the right carotid bifurcation (left panel) and re-implantation of the left vertebral artery into the left common carotid artery (right panel) – under loco-regional anesthesia. The aspect of the excised plaque is also demonstrated.

Figure 10: MULTIPLE NECK VESSEL ARTERIAL DISEASE + LOWER LIMB

A case with multiple and complex arterial lesions in the neck vessels + lower limbs, is presented.

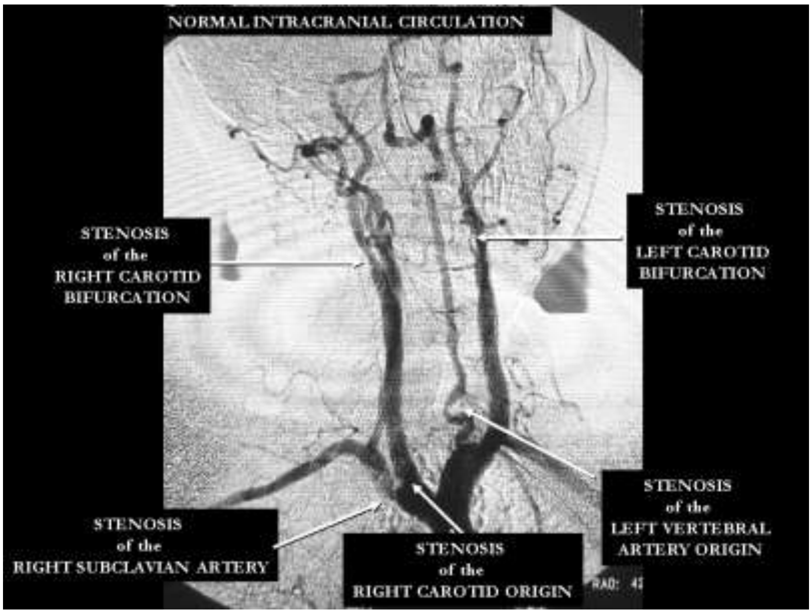


Figure 10a: angiographic aspect of the neck vessels, demonstrating stenosis of the right subclavian and of the right common carotid artery, stenosis of the right carotid bifurcation, stenosis of the left carotid bifurcation, stenosis of the left vertebral artery at its origin and absent right vertebral artery.

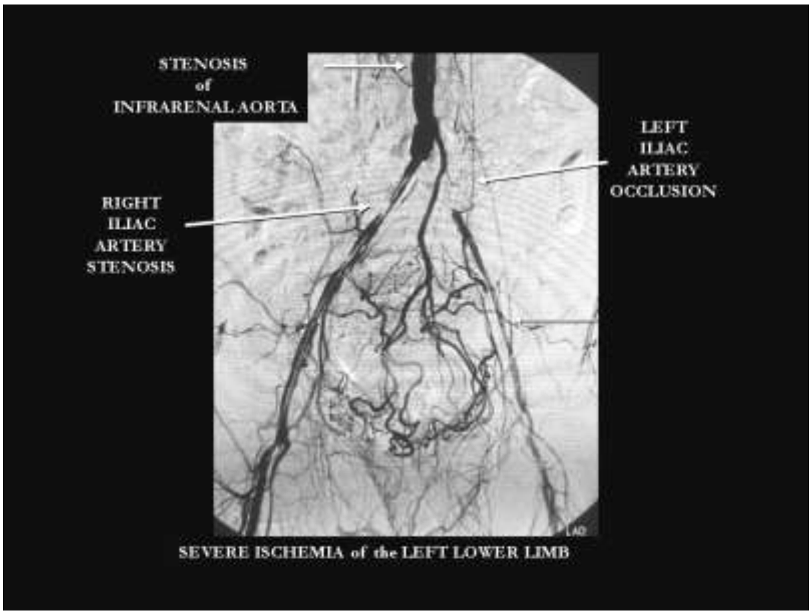
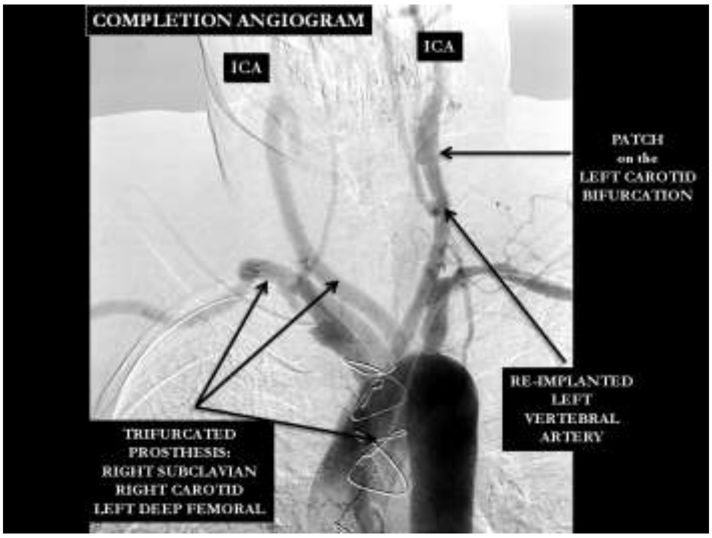
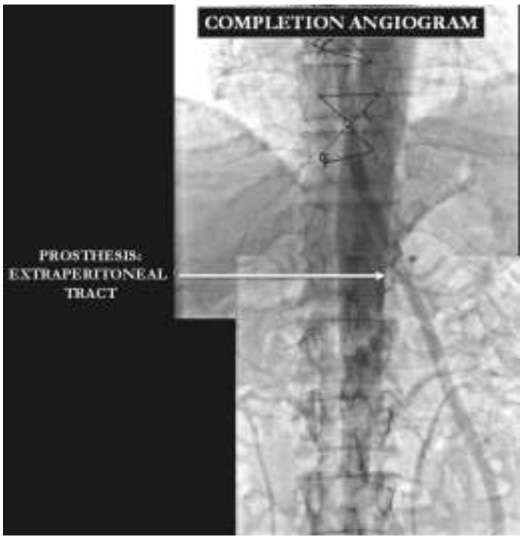


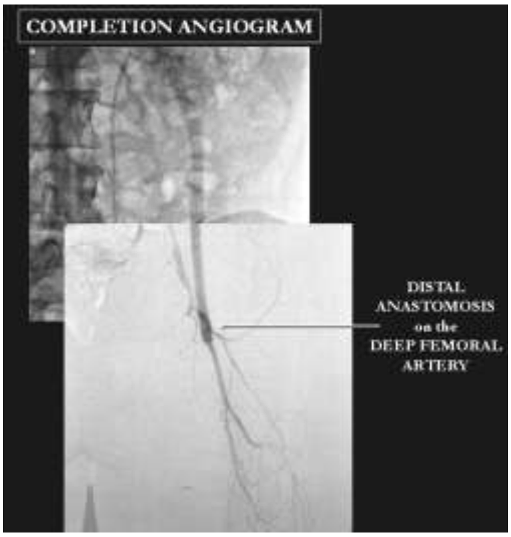
Figure 10b: angiographic aspect of the inferior aortic system. The patient had stenoses of the infrarenal aorta, multiple stenoses of the right iliac artery and occlusion of the left iliac artery

Figure 10c: completion angiogram. The common trunk of a trifurcated prosthesis was inserted on the ascending aorta (median sternotomy and pericardiotomy). The branches were anastomosed as follows: one branch to the right subclavian artery, the second branch to the right carotid bifurcation, the third branch, was tunnelled transdiaphragmatically, extraperitoneally and was anastomosed to the left deep femoral artery **(and is shown in figure 10d).** The left carotid bifurcation was treated by endarterectomy and patch enlargement, while the left vertebral artery was re-implanted into the left common carotid artery.





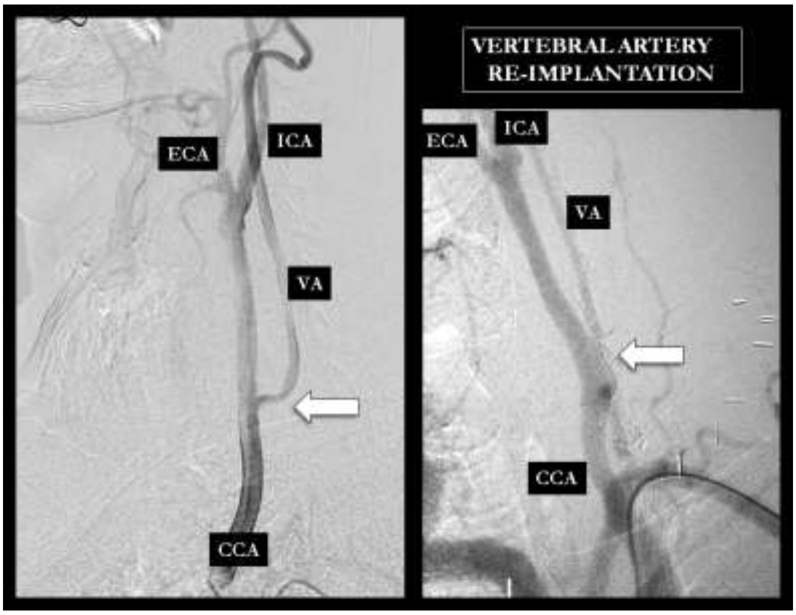
10 d)



10 e)

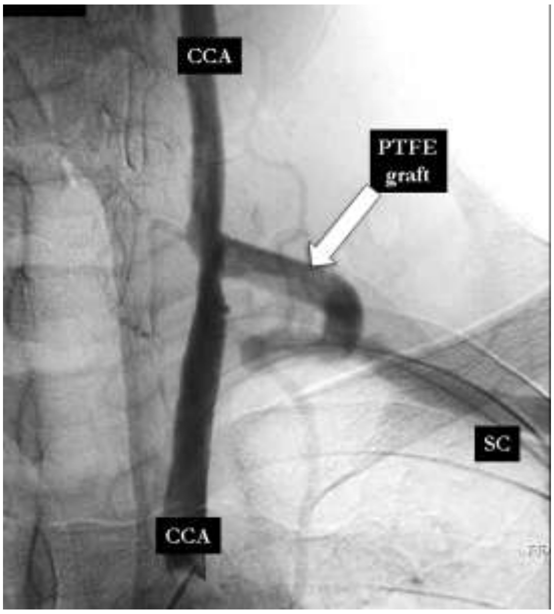
Figure 10d and **e:** angiographic images of the third branch of the prosthesis, as it travels across the diaphragm and through the extraperitoneal space, to be eventually anastomosed with the left deep femoral artery.

Figure 11: VERTEBRAL ARTERY RE-IMPLANTATION



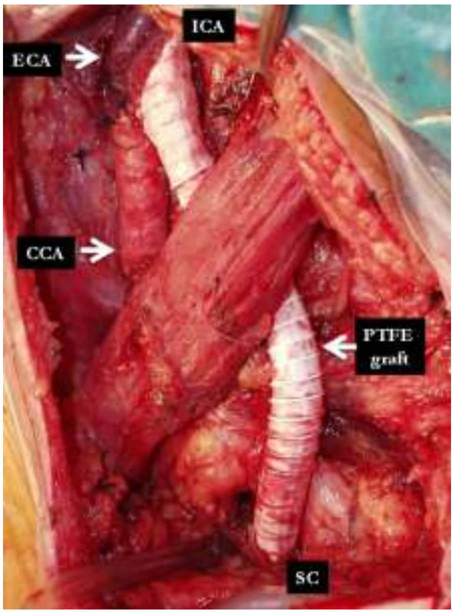
Angiographic image of re-implanted vertebral arteries into the common carotid arteries. Left panel: *latero-terminal anastomoses; right panel, latero-lateral anastomoses* between the common carotid and the vertebral artery, respectively. CCA = *common carotid artery*. ICA = *internal carotid artery*. ECA = *external carotid artery*. VA = *vertebral artery*.

Figure 12: COMMON CAROTID-TO-VERTEBRAL ARTERY BYPASS



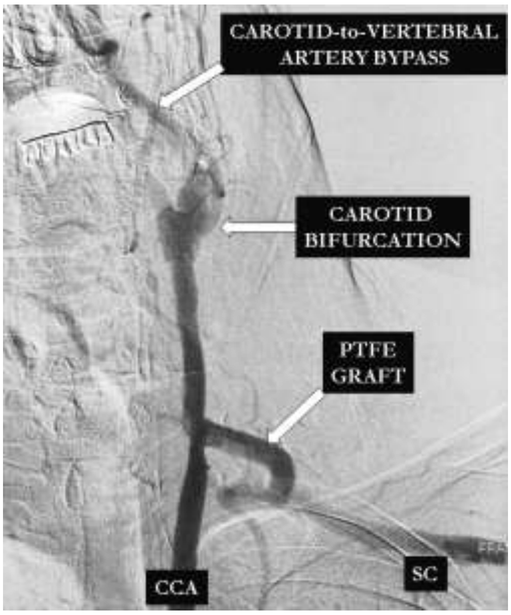
Angiographic image demonstrates an occluded left subclavian artery (SC) and the bypass between the common carotid artery (CCA) and the former. In our case series, a 6 mm. PTFE graft was used, whenever a re-implantation of the subclavian artery was rendered difficult either by the quality of the vessels or in patients with a short neck.

Figure 13: ENDARTERECTOMY OF CAROTID BIFURCATION AND CAROTID-TO-SUBCLAVIAN ARTERY BYPASS



Intraoperative aspect upon completion of the surgical procedure consisting of left carotid endarterectomy and bypass between the endarterectomised bifurcation and the subclavian artery, using a 8 mm. Armed PTFE graft. The graft is tunnelled underneath the sternocleidomastoid muscle. The common carotid artery (CCA), the carotid bifurcation (ECA and ICA) and the subclavian artery (SC) were approached through a longitudinal cervical incision, slightly curved inferiorly at supraclavicular level. The distal portion of the graft functions as an angioplasty patch over the carotid bifurcation. Note also that the subclavian artery was approached in its second/third segment, without the need of cutting the anterior scalene muscle. The anastomoses of the PTFE graft was performed first on the subclavian artery.

Figure 14: ENDARTERECTOMY OF CAROTID BIFURCATION + CAROTID-TO-SUBCLAVIAN ARTERY BYPASS + CAROTID-TO-SUBOCCIPITAL VERTEBRAL ARTERY BYPASS



Completion angiogram in the case of a patient with multiple arterial lesions on the left side, consisting of: subclavian artery occlusion, stenosis of the carotid bifurcation and occlusion of the vertebral artery. The vertebral artery remained patent at the level of the suboccipital portion (V3 segment). The surgical solution included: 1. Common carotid-to-subclavian artery bypass, using a 8 mm. PTFE graft; 2. Carotid endarterectomy and patch angioplasty (PTFE patch); 3. Revascularization of the vertebral artery through a saphenous vein bypass between the surgically enlarged carotid bifurcation and the suboccipital vertebral artery (V3).

14a

14b

Figure 14a depicts the general view of the operation
Figure 14b shows in detail the area of the former carotid bifurcation that actually became a "neo-carotid trifurcation".

The carotid bifurcation and the suboccipital vertebral artery were approached through a single upper cervical incision, while the common carotid and the subclavian artery, through a single supraclavicular incision.

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LIST OF TABLES

Comparison between conventional and endovascular surgery in the treatment of cervical carotid artery stenosis*)

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Stroke is the third leading cause of death following heart diseases and cancer, but also has additionally costs for the society in the form of disability and long term care. For these reasons stroke prevention continues to challenge the best efforts of all the specialists involved in this pathology. Extra cranial carotid occlusive disease is responsible for one third of the patients who have a cerebrovascular event. Our paper tries to define the role of angioplasty and stenting (CAS) in comparison with the open carotid revascularization (CEA), which remains the "gold standard" of our day's therapy.

Reported 30-day outcomes for CEA from randomised clinical trials

Study, publication date	Population	Study period	No. of procedures	Mortality %	Combined event rate, † %
Symptomatic					
ECST, 1998	Symptomatic, 0-99% stenosis	1981-1994	1745	1.0	7.0
NASCET, 1999	Symptomatic, 30-99% stenosis	1987-1996	1415	1.1	6.5
VA Symptomatic, 1991	Symptomatic, 50-99% stenosis	1988-1991	90	3.3	5.5
Asymptomatic					
ACAS, 1995	Asymptomatic 60-99% stenosis	1987-1993	721	0.1	1.5
VA Asymptomatic, 1990	Asymptomatic 50-99% stenosis	1983-1987	203	2.0	4.5

A number of major randomized clinical trials have informed vascular surgeons that CEA performed to treat hemodinamically significant carotid stenosis, symptomatic or asymptomatic, is an operation justified by a firm evidence base (figure 1).

Figure 1

CEA can be done in three ways:

1. classical endarterectomy with direct suture or patch of enlargement: syntetic (Dacron, PTFE, polyuretan) or vein;
2. eversion technique and
3. bypass surgery with prosthetic material or vein graft.

Indications for CEA are [1]: TIA – 45.3%, Amaurosis 23.1%, Stroke – 30.7%, Asymptomatic – 8.6%. The items that raise the stroke risk of carotid stenosis (NASCET)

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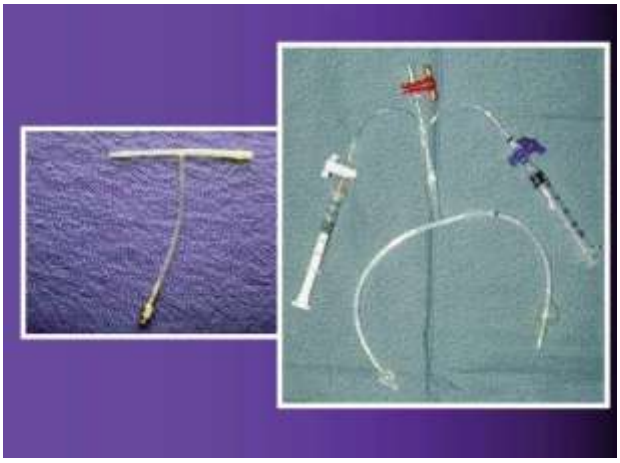
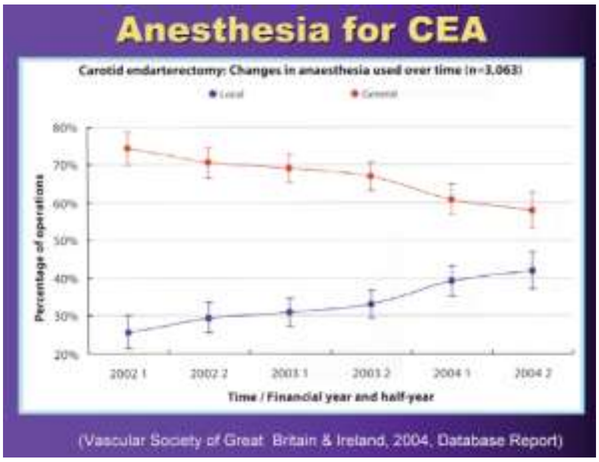
are: stenosis > 70%, stenosis + thrombus, stenosis + contra lateral occlusion, stenosis + distal lesions (siphon), ulcerative plaques. Contralateral occlusion, symptomatic - 10% or asymptomatic - 21%, put the patients in the high risk group even if they are asymptomatic. The co-morbidities are also important, especially the coronary association. In patients with instable angina and severe carotid stenosis is currently preferred the synchronous procedures, even if they rises the combined event rate (17.4% at 30 days) [8]. In patients with stable angina, previous CEA is recommended.



Taking in account the policy of shunting (routine, selective or never shunting) an overview of the randomized trials by the Cochrane Collaboration has failed to show that anyone strategy is better than another [2] there is a consensus that routine/ selective shunting is preferable (figure 2).

Figure 2

Selective users argue that shunts are necessary in 10-15% of patients [1] (potential intimal damage and secondary thrombembolism due to shunts). The most commonly used shunts are Javid, Brenner and Pruitt- Inahara.

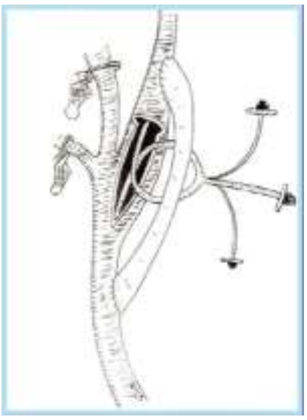


Carotid surgery has traditionally been performed under general anesthesia. More recently, loco regional anesthesia gains interest because of neurological monitoring. The vascular society of Great Britain and Ireland reported 32.8% of loco regional anesthesia and 67.2%of general anesthesia. However the trend is to increase the loco regional anesthesia (figure 3).

Figure 3

The timing after a cerebrovascular event is very important. A 4-6 weeks delay is a common practice (justified by NASCET, ECST trials). The joint Study of Extra cranial Artery Occlusion reported that surgery is contraindicated in patients with acute cerebral vascular events due to carotid artery occlusion. Recent data confirms that surgery is contraindicated at any time interval in patients with recent carotid artery occlusion.

Ballota et all, Gaseki et all. showed in patients with TIA or no disabling stroke no increase in operative morbidity and mortality rate when CEA was performed less then 30 days from the index event [7]. This data are supported by our studies also [4]. An overview of the randomized trials by the Cochrane Group showed that a policy of routine patching is preferable to routine primary closure and confers a reduction in the rate of per operative stroke (1.6% vs. 4.2%) and thrombosis (0.3% vs. 3.9%). Late stroke (2.2% vs. 5.9%) and restenosis (4.5% vs. 13%) were also reduced. There is no evidence that patch type (prosthetic or vein) alters outcome. Vein patches are susceptible to central rupture (1%), but prosthetic patches are vulnerable to 1% incidence of infection.



When carotid bypass is necessary, both prosthetic material or saphenous vein may be used and there is no randomized trial evidence that either is preferable. We prefer to use reversed saphenous vein harvested from the groin (figure 4).

Figure 4: Vein by-pass with shunting

Eversion endarterectomy (EEA) is a method first described by DeBakey in 1959 and then developed by Kieny (France) in 1959 and D. Raithel (Germany) in 1987. This technique is useful especially for primary carotid reconstructions, but cannot be used in redo surgery (fig. 5).

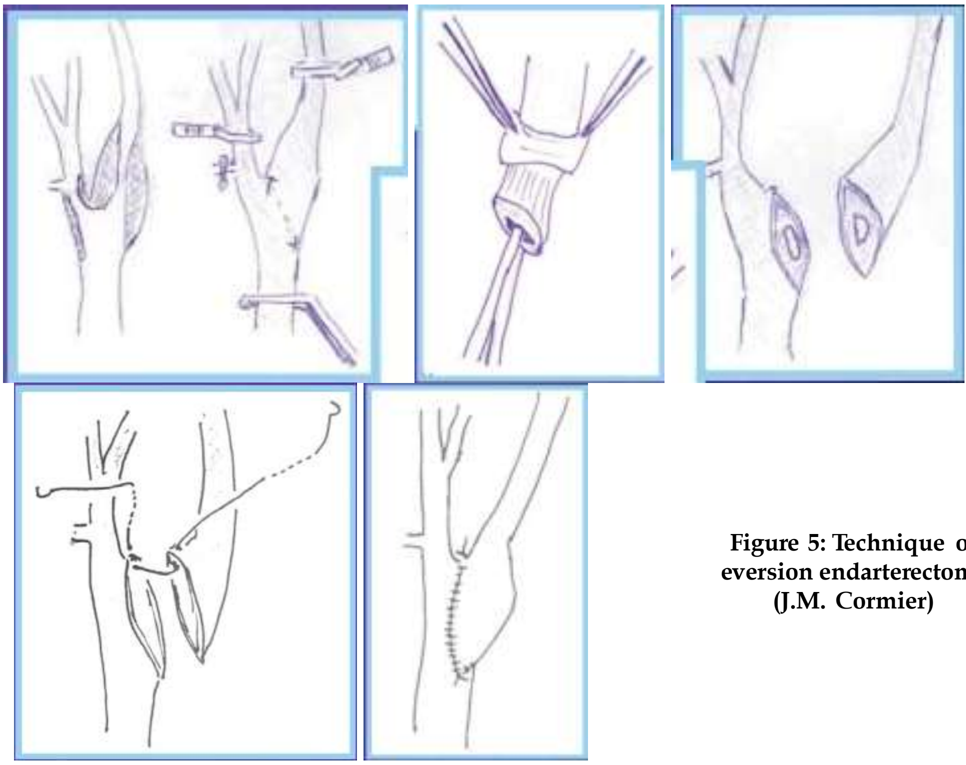


Figure 5: Technique of eversion endarterectomy (J.M. Cormier)

What are the advantages? No patch material required, the correction of an elongated ICA is easier and the occlusion time of the carotid artery is shorter than in classic CEA. EEA can reduce restenosis rate from 12.3% (Raithel) or 13.5% (Kieny) - rates for CEA to 1.9% (Kieny) - rate for EEA. The combined rate of morbidity and mortality was 4% in CEA and 1.35% in EEA (Entz, 1996), results confirmed by other authors (Raithel, Balzer) [11].

It has been generally accepted that restenosis after CEA can be categorized into 3 frames: residual stenosis (<2 months), early restenosis (<2 years), and late (>2 years) [Becquemin, 2006). Residual stenosis results from technical problems; early restenosis reflects intimal hyperplasia while late restenosis are due to the developing of the atherosclerosis. The average is about 8.5% at 5 years. Despite of restenosis rate, symptoms appeared in only 0.7% of patients, with only 5.9% requiring operation at 5 years (ACAS).
In high risk patients for endarterectomy (Prior CEA, Neck surgery, Radiation, Contralateral occlusion), carotid artery stenting (CAS) is superior to CEA (SAPHIRE study) [12]: 30 days cumulative percent of morbid-mortality is 5.8 in stent group and 12.6 in surgical group. This issue is confirmed by the FDA indications for CAS in 2004 [2].

The problem of CAS is restenosis. The rate of restenosis have been reported in different series between 2 and 8% [17].

Restenosis is defined as a stenosis more than 80% in duplex scan. It can be located proximal of the body of the stent, central body of the stent, and distal. It is symptomatic in only 7% of cases [17].

In stent restenosis (ISR) may be managed by endovascular techniques; however the results obtained may be suboptimal particularly in the long term [16]. The surgical approach is also difficult because of the fibrosis of the surrounding tissues, the requirement for distal internal carotid artery dissection and clamping and removal of the stent.

The endovascular procedures which can be used are: balloon angioplasty alone, angioplasty and stent and angioplasty with cutting balloon. Some teams reported very good results without per procedural complications and absence of significant restenosis at one year [13].

More aggressive approaches are currently at the investigational level and include intravascular brachytherapy, antiproliferative therapy with drug coated stents and biodegradable stents [13].

The factors identified with the developing of ISR are: female gender, elevated creatinine level, elevated cholesterol level. The surgical treatment is carotid endarterectomy with plaque and stent removal.

An alternative to CEA is the arterial bypass using saphenous vein graft or PTFE grafts.

Our results differ between two periods of studies:

- 1992-1999 = 1256 operated cases with a 3.3% cumulative percent morbi-mortality and
- 2000-2005 = 510 cases with a 0.8% cumulative percent. Between 2000 and 2005 we have performed 78 cases of CAS with 0% mortality and 2.5% morbidity; we have used routinely autoexpandable stents and cerebral protection devices.

We present our protocol which permitted us to reduce the postoperative events.

Preoperative evaluation included duplex scan and angiography of extra cranial and intracranial vessels. All the patients have cardiac evaluation: clinical, EKG, cardiac echocardiography and if necessary coronarography. Coronaropathy was managed according to a define algorithm, in collaboration with cardiologists and anestheologists. All patients were operated under general anesthesia and monitored with radial catheter and digital EKG. Systemic heparin was used (0.5 mg/kgc). Selective shunting was routinely used. Postoperatively the patients were monitorised in the ICU for 24 hours and usually discharged from the hospital at the 3rd day postoperatively. Maximal BP was kept below 160 mmHg. Pre- and postoperative evaluation by a neurologist was performed.

In our experience intrastent restenosis (ISR) appears in 5% of cases (figure 6).

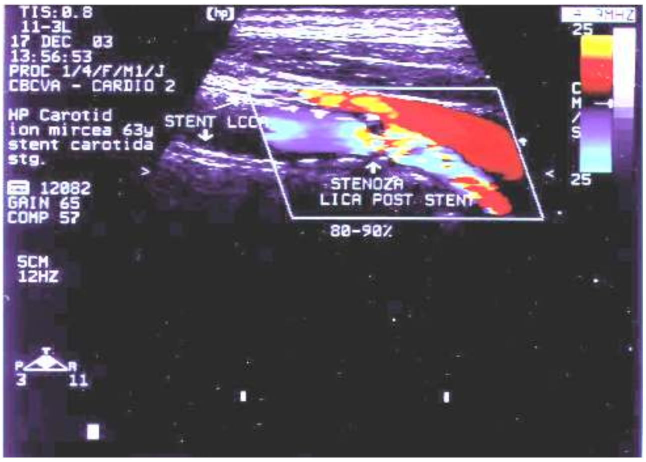


Figure 6: Color Doppler showing intrastent restenosis

We performed CEA with in bloc removal of the plaque and stent, using Brenner shunt for cerebral protection and dacron patch of enlargement. Intimal hyperplasia showed to be the predominant mechanism leading to ISR.

No major complications occurred. The postoperative follow up (by duplex scan) was 12 months. The patients remained asymptomatic and without recurrent restenosis.

In conclusion, CAS is not opposite to CEA, but a complementary method, witch is indicated to treat high risk patients. The use of cerebral protection devices is strongly recommended. CEA remains the "gold standard" for all the other patients who are candidates for revascularization. The use of a well defined protocol may help to significantly reduce morbidity and mortality rates of open carotid surgery.

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Simultaneous bilateral carotid endarterectomy - mid-term results in 22 patients*)

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Abstract

Background*: The surgical treatment of bilateral carotid stenotic lesions in the neck is usually performed as a staged procedure. In selected cases, however, a simultaneous bilateral approach is indicated. We present our initial experience with simultaneous bilateral carotid endarterectomy (SBCE) in a number of 22 consecutive patients.*

Materials and Methods: *Twenty two consecutive patients operated in our clinic, for bilateral symptomatic and/or severe carotid stenosis, were included in the study. All patients had a neurological and cardiologic clearance pre-operatively; Doppler ultrasound diagnosis was performed in all patients, aided by 4-vessel angiogram in 10 patients. Simultaneous bilateral carotid endarterectomy way performed under general anesthesia, with no shunting and with patch closure in all but 3 sides (3 different patients).*

Results: *No deaths was recorded in our series. Only one neurological event developed post-operatively (parietal cortical ischemia causing left arm paresis). All patients performed well and pre-operative symptomatology resolved.*

Conclusion: *The simultaneous bilateral carotid endarterectomy represents a safe procedure, in selected patients. In spite of the more demanding intra- and post-operative measures, it can be performed as a safe procedure with short- and mid-term results. Further studies and longer-term follow-ups are however needed on larger series of patients.*

Key words: *carotid endarterectomy, cerebrovascular disease, simultaneous revascularization, vascular surgery*

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Introduction

Carotid artery disease can be located at either extracranial, intracranial or both levels. The major morbid lesions can be approached medically, percutaneously or surgically. These therapeutic strategies are not mutually exclusive, but complementary, as revealed for example by the combined (endovascular and surgical) approaches.

Surgery comprises various techniques: bypass, re-implantation or carotid endarterectomy (CEA). As dictated by the lesion(s) and symptomatology, CEA can be performed either unilateral or bilateral. Bilateral CEA is usually performed as a staged procedure. The simultaneous bilateral carotid endarterectomy (SBCE) is rarely performed. In the medical literature, only 13 studies belonging to 11 authorities were published so far, comprising a number of 235 patients (Table 1).

Table 1: SBCE international statistics

Year	Author	No. of cases
1969	Young et al.	2
1974	Sensening	3
1975	Pillone et al.	1
1976/1985	Clauss et al.	37
1978	Ketonen et al.	80
1990	Toung et al.	1
1992	Pizetti	85
1996/2000	Dimakakos et al.	17
2001	Farsak et al.	6
2005	Tsukahara et al.	2
2008	Portinos et al.	1
Total	11 authorities	232 patients

We hereby present our initial experience with simultaneous bilateral carotid revascularization, including simple SBCE or SBCE plus associated procedures.

Materials and methods

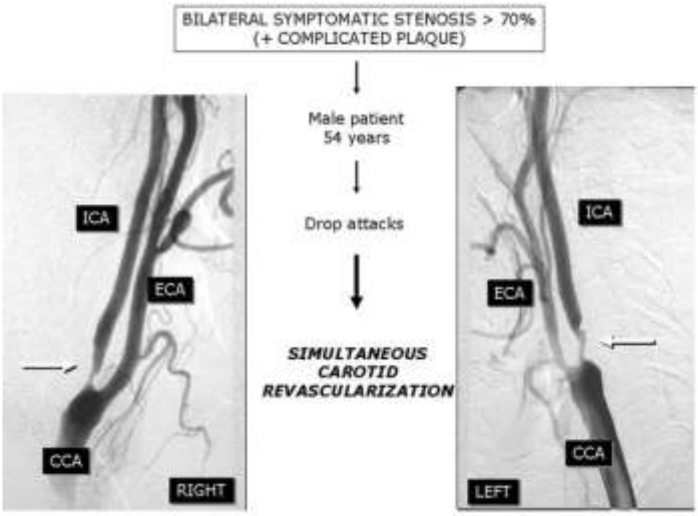
A number of 22 consecutive patients operated in our clinic, were included in the study. Patient demographics are presented in Table 2.

Table 2: Patient demographics

Patient no. and age (years)	Sex M = male, F = female	Associated diseases	Associated surgical procedures	Complications
1. GN, 64	M	IHD, AHT		
2. AM, 59	M	AHT, previous stroke, right amaurosis	direct closure on one side	neck hypoesthesia
3. CE, 65	F	repetitive TIAs, AHT	direct closure on one side	neck hypoesthesia
4. PG, 64	M	previous stroke, AHT. IHD (three-vessel disease)		cervical hematoma

5. MI, 71	M	previous stroke, AHT		cervical hematoma
6. RN, 53	M	previous stroke, AHT, IDDM	direct closure on one side	
7. PP, 56	M	previous stroke, AHT	common carotid-to-internal carotid bypass on one side	
8. TN, 54	M	Previous TIAs, AHT		
9. FS, 69	F	previous stroke, AHT		transitory right arm weakness - resolved
10. BD, 68	M	AHT, TIAs		cervical hematoma
11. CV, 52	M	AHT, previous stroke, IHD		neck hypoesthesia
12. AE, 52	F	AHT, previous stroke		neck hypoesthesia
13. SM, 54	F	AHT, TIAs, subclavian steal syndrome	left carotid-to-subclavian bypass	
14. DC, 71	M	AHT, TIAs, NIDDM		cervical hematoma
15. II, 75	M	AHT, TIAs, IHD		
16. BT, 61	M	AHT, IHD		
17. BV, 69	F	AHT, IHD, previous strokes		Right parietal cortical ischemia with left arm paresis
18. TA, 53	M	AHT		
19. PS, 51	M	AHT, previous stroke	right common carotid-to-internal carotid bypass	
20. NV, 75	F	AHT, previous bilateral strokes, mixed dementia, Atrial fibrillation		
21. ES, 61	M	AHT, IDDM, IHD	right common carotid-to-internal carotid bypass	
22. VI, 51	M	AHT, previous stroke	ascending aorta-to-bilateral internal carotid bypass	

Abbreviations	• **AHT**	- *Arterial hypertension,*
	• **IDDM**	- *Insulin-dependent diabetes mellitus,*
	• **NIDDM**	- *Non insulin-dependent diabetes mellitus,*
	• **IHD**	- *Ischemic heart disease*



Patients underwent a thorough pre-operative diagnostic evaluation including cardiologic and neurological clearance. All patients had a pre-operative Doppler examination of the cerebral (extracranial and intracranial) vessels; in 10 patients a 4-vessel angiogram was additionally performed (Figure 1).

Figure 1: Angiographic findings in a 54-years old male patient, with bilateral severe carotid stenosis and drop attacks

The surgical interventions were performed under general (total intravenous) anesthesia, maintaining a systemic blood pressure between 130-150 mm Hg. Stump pressure monitoring allowed us to refrain from the use of any shunting procedure. Patients were routinely placed in a semi-seated position (heads up); cerebrospinal fluid drainage was performed in 2 patients with associated severe vertebro-basilar stenotic lesions. The surgical approach consisted in 2 oblique cervical incisions in 13 patients (Figure 2) or a single transversal cervical incision in the remainder 9 patients (Figure 3, next page).

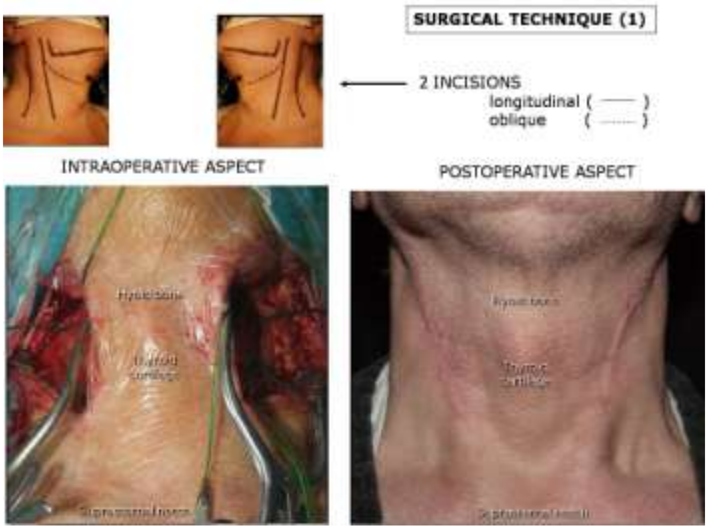


Figure 2: Surgical technique (1). Both carotid bifurcations are exposed through either 2 longitudinal or 2 oblique incisions. Bleeding and hematoma occur less with this approach, although the scar may appear more disturbing to the patient

Figure 3: Surgical technique (2). Exposure of both carotid bifurcations through a single transverse cervical incision, placed between the hyoid bone and the thyroid cartilage respectively. Esthetic results are better, while the risk of cervical hematoma is high

Both carotid bifurcations were carefully exposed, with minimal dissection and minimal manipulation in order to avoid embolization. Prior to clamping, 5,000 IU unfractioned heparin was administered and heparin was not reversed at the end of the procedure. The highest degree stenotic carotid side was approached first (or as dictated by the morphology of the arterial circle of Willis). Clamping times (for each side) varied between 22 and 30 minutes. A longitudinal postero-lateral arteriotomy, was performed, going beyond the stenotic lesion both at proximal and distal levels (measuring usually between 4-5 cm.). In 4 sides, the surgical approach included exposure of the internal carotid artery higher in the neck, by cutting the stylohyoid and digastric muscles and carefully dissecting the posterior aspect of the parotid artery, preserving the facial nerve and especially its marginal mandibular branch. CEA comprised the origin of the external carotid artery too. The thickened internal carotid endartery was tacked with separate U-stitches, avoiding thus the development of intimal flaps. In all sides, the arteriotomy was closed with the aid of a synthetic PTFE patch – except in 3 sides, where a direct closure was applied. De-airing and purging was performed in the usual manner. Bilateral wound drainage was performed with 24-French sylastic tubes connected to mild suction. Drainage was maintained for 24-48 hours. Wound closure was performed in two layers (subcutaneous and intradermal). Patients were extubated by the end of the procedure, at the time when a first neurological examination was completed. A strict control of the blood pressure and cardiac rhythm by continuous monitorization was necessary for at least the first 24 postoperative hours. Fluid ingestion was allowed after the first 6 hours. Normal food ingestion was allowed the very next day as was patient mobilization. Postoperative in-hospital stay lasted between 4-7 days. After discharge control and follow-up, included neurological examination and Doppler ultrasound monitoring starting 1-2 weeks after discharge, and subsequently, at 6 months interval.

Results

In our series the follow-up extended between 2-24 months. Mortality was nil. Neurological complications included a parietal cortical infarction with left arm paresis in a patient with unstable, ulcerated bi-carotid plaques and intractable pre-operative transient ischemic attacks. Supraclavicular and chin hypoesthesia was noted early in 4 patients, with symptomatology disappearing by 2 months. No cranial nerve damage was observed in our series. To note, 4 patients who were on dual antiplatelet therapy (aspirin + clopidogrel) developed cervical edema and hematoma with dysphagia and dyspnea – lasting less than one week. All patients were discharged with healed surgical wounds, on antihypertensive and antiplatelet drugs, plus statins. One patient presenting permanent atrial fibrillation was additionally anticoagulated.

Discussion

The surgical indications, for the staged CEA regards both the degree of stenois, the plaque morphology and the presence of symptoms. Staged CEA is usually indicated for bilateral symptomatic carotid stenosis > 70% or for ipsilateral symptomatic stenosis of > 70% and contralateral asymptomatic stenosis of > 80% [1, 2].

The idea of performing the simultaneous carotid endarterectomy (SBCE), results from the possible risk and hazard of a cerebral infarction while waiting for the second operation versus the risks of having both procedures performed during the same hospital admission – these aspects must be carefully weighted by the surgeon and by the patient.

The well-known "pro's" favoring the SBCE [3, 4], include: the increased danger that might arise from a double anesthetic/surgical procedure, especially in higher risk patients (but who, however must have a life expectancy of more than 5 years); the risk of contralateral intra-plaque bleeding with intra-operative heparin administration; the difficulty of obtaining patient's acceptance for a second anesthetic/surgical procedure; the lower incidence of cerebral damage after SBCE.

Taking into account the afore mentioned details, the general indications for the SBCE are presented in Table 3. [5-8].

Table 3. SBCE - Indications

Bilateral symptomatic stenosis > 70% + intraplaque hemorrhage
Ipsilateral symptomatic stenosis > 70% plus contralateral asymptomatic stenosis > 80% + plaque ulceration/hemorrhage
Bilateral asymptomatic stenosis > 80% + bilateral plaque hemorrhage
Bilateral asymptomatic stenosis + other surgical procedures (coronary revascularization)

Some further precautions must be taken for the performing of the SBCE: the morphology and the flow through the arterial circle (Willis) [9], as revealed by the transcranial Doppler examination or by the angiogram. The SBCE is usually performed under general anesthesia, although some authorities performed the procedure under loco-regional anesthesia. The SBCE represents a longer and technically demanding procedure, with longer carotid clamping times and comprising important hemodynamic shifts.

The cited complications more specific for the SBCE include: cervical hematoma, superficial cervical plexus lesions with neck hypoesthesia, tongue ischemia (with bilateral lingual artery interruption), lesions of the cranial nerves (hypoglossal, superior laryngeal and recurrent laryngeal) and the cerebral hyperperfusion syndrome.

Cervical hematoma was present in 4 of our patients, actually in those who were on dual antiplatelet therapy for unstable pre-operative neurological status. The neck hypoesthesia was only transitory in 4 patients. We conclude that the single cervical transversal incision interferes less with neck skin innervation but predisposes in the mean time to the development of hematomas. In our series, we had no cranial nerve lesions. We advocate the intra-operative identification of the hypoglossal nerve and of the main trunk of the vagus nerve. In order to avoid lesions to the superior laryngeal branch, we limit the dissection of the carotid bifurcation strict to the peri-adventitial layer and as distal as possible from the glomus. In our last 7 patients, we also routinely infiltrated the glomic area with a local anesthetic.

The most severe complication is represented by the post-endarterectomy cerebral hyperperfusion syndrome [10-12]. This may appear in 2-15% of cases, however less after CEA than after carotid (or vertebral) artery angioplasty and stenting [13-16]. The favoring conditions include disturbances of the cerebral microcirculation and the existence of multiple lacunar infarcts. The syndrome has a very high mortality rate, between 30-60%. The detection of patients at risk is usually performed with the aid of the transcranial Doppler examination, the acetazolamide test and SPECT. The general precautions that must be taken include the evaluation of the intracerebral anastomoses (arterial circle anatomy and function), the measurement of internal carotid stump pressure and the strict control of the arterial pressure.

We also advocate the routine use of patch closure of carotid arteriotomy, as this technique is less likely than direct closure to produce ipsilateral stroke, transient post-operative ischemic attacks and recurrent carotid stenosis [17].

Final remarks

The simultaneous bilateral carotid endarterectomy represents a feasible and safe procedure, in selected higher-risk patients, in whom, a clear benefit is to be expected from this demanding procedure, and in whom, also, there is a life expectancy of more than 5 years. Longer follow-ups are obviously needed together with a pertinent and thorough clinical judgement, as performed by a teamwork in which the neurologist, the cardiologist the surgeon and the anesthesiologist share equal weight. We are confident our experience with the SBCE is both significant as number of patients treated and stimulating for further research.

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Cerebral hyperperfusion syndrome – a complication of carotid revascularization*)

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Abstract

The cerebral hyperperfusion syndrome (CHS) is a relatively new clinical entity, several its manifestations being integrated in other pathology categories over the past years. It is specific for cerebral revascularization and has a unique pathophysiological mechanism.

We studied the actual literature, in a review intended to clarify this chapter of carotid revascularization complications. Our experience in this field is presented and compared, summarized in a prospective study, conducted over a period of 4 years, from 2005-2008, which included the postoperative clinical evaluation of 247 patients with carotid revascularization.

As a result of this literature review, we defined the CHS, underlined its causative pathological mechanisms, contoured the clinical manifestations and proposed therapeutic maneuvers, both preventive and curative. We also presented the reported risk factors for the development of CHS, adding our own observations, and described the imagistic diagnostic possibilities. In our series, the incidence of this complication is lower than reported in literature, so we emphasize our treatment protocol which allowed us to reach this level of complications. Prophylaxis is the most efficient treatment, and it is achievable through an adequate education of the medical personal with minimal financial implications in order to assure a faster recovery in carotid postrevascularization.

Keywords: *cerebral hyperperfusion, carotid surgery, revascularization*

Rezumat

Sindromul de hiperperfuzie cerebrală (SHC) este o entitate clinică relativ nouă conceptual, diferitele manifestări ale sale fiind integrate de-a lungul timpului în alte categorii de patologie. Este specific pentru revascularizarea cerebrală şi are mecanism fiziopatologic unic. Am studiat literatura curentă cu intenția de a clarifica acest capitol al complicațiilor revascularizării carotidiene. Experiența noastră în acest domeniu este reprezentată şi comparată, sumarizată într-un studiu prospectiv, cuprinzând o perioadă de 4 ani, din 2005-2008, bazată pe evaluarea clinică postoperatorie a 247 pacienți cu revascularizare carotidiană.

Ca şi rezultat al acestei evaluări, am definit SHC, subliniind mecanismul patogen, am conturat manifestările clinice, respectiv am propus manevre terapeutice, atât preventive, cât şi curative. Am mai prezentat factorii de risc în SHC, adăugând observațiile noastre, respectiv am

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descris posibilitățile diagnosticii imagistice. În lotul nostru incidența acestei complicații este mai mică față de datele din literatura de specialitate, subliniind eficiența protocolului nostru de tratament care ne-a permis atingerea acestei rate a complicației. Profilaxia este cel mai eficient tratament, este posibilă prin educarea adecvată a personalului sanitar cu implicații financiare minime, în scopul asigurării unei recuperări postrevascularizație carotidiană cât mai rapide.

Cuvinte cheie: *hiperperfuzie cerebrală, chirurgie carotidiană, revascularizare*

The cerebral hyperperfusion syndrome (CHS) is a relatively new clinical entity, several its manifestations being integrated in other pathology categories over the past years. Its common denominator which led to the description of this particular syndrome are represented by physiopathological mechanisms that competed to accomplish a fairly heterogeneous clinical image.

CHS is typical for both for surgical (carotid endarterectomy CEA) and endovascular (carotid stenting CAS) carotid revascularization.

For the first time Sundt described this syndrome, dated from 1981 (7). He characterized this syndrome in the association of an increased cerebral perfusion with a clinical triad represented by: ipsilateral migraine headache, seizures, focal neurological deficits in the lack of cerebral ischemia after CEA.

The specific phisiopathological element of this syndrome is represented by the alteration of vascular self-regulation at the level of the revascularized territory, situation which based on elevated pressure of cerebral perfusion is capable to determine a wide variety of symptoms. Whether in the mild cases local metabolic disturbance, the alteration of the hematoencefalic barrier occur, the gravity increase assumes more severe injuries, starting from the primarily cerebral edema becoming generalized till a more complex and infaust event, conferring exceptional gravity to the case, meaning intracerebral hemorrhage.

The definition of cerebral hyperperfusion syndrome is difficult, forasmuch from a clinical point of view it is characterized by an extremely varietal image. Due to this reason we consider as relevant the definition based on the determinant physiopathological mechanism. CHS represents the clinical context ulterior of a carotid revascularization intervention (CEA or CAS) characterized by the alteration of the hematoencefalic barrier at the revascularized territory without any other known pre-existent or concomitant detectable cause.

The physiopathology of CHS is based on the exhaustion of the self-regulating vascular capacity in the cerebral circulation on the affected territory. This self-regulation system represents the main compensating mechanism in balancing the modifications of the cranial blood debit, accomplished by the reactivation of the local arterioles, especially by humoral regulation. This exhaustion is due to a long term vasodilatation, necessary for the circulatory compensation in case of a cerebral perfusion deficit (carotid stenosis), in a linear ratio with the grade of the deficit (15). The ascendant factors on the cerebral micro vascular self-regulation are dominated by the grading of the deficit of the cerebral blood debit. The duration of this deficit is as well as important, however in the carotid atherosclerotic pathology we might consider as an irrelevant factor, as in most of the cases it is about a long period of time, ages in developing carotid stenosis. The duration factor is only important in rare cases when an acute occlusion or stenosis develops (non-stenotic atherosclerotic plaque complicated by thrombosis, trauma).

The cranian blood flow deficit is influenced by the degree of the ipsilateral carotid stenosis, the controlateral occlusion or stenosis, the frail collateral debit, vertebrobasilar circulatory failure (1, 13, 16-19). Any significant stenosis hemodynamic (> 50%) on an extra cranial axe produces compensatory modifications in the cranial microcirculation (19).

The main molecular mechanisms that generate alteration are represented by the increase in nitric oxide during the decrease of cerebral blood flow, respective the increase of free radicals during reperfusion. These humoral mediators aggress the self-regulating capacity in different moments, on the other hand determining an extreme vasodilatation, respective directly affecting the vascular endothelia (12). There are studies (20, 21) which demonstrate the increase of lipid degradation products due to induced peroxides by free radicals (malon dialdehyde, diene conjugates, lipoperoxides) in jugular veins after declamping the internal carotid artery during CEA. It also has been concomitant observed an existence of an increase of biomarkers with neuronal affectation (neuron-specific enolase = NSE and S-100B) after CEA in the jugular torrent (37).

Other factors that contribute at the appearance of this syndrome are represented by: systemic hypoperfusion, intra- and postprocedural cerebral microemboli, the stimulation or interruption of carotid glomus efferents.

Systemic hypoperfusion determines an implicit decrease of cerebral blood flow. This systemic hypoperfusion might install after CEA or CAS as well. During CEA in general anesthesia, the anesthetic induction represents a critical moment. Also, the instrumental handling of the carotid glomus might induce bradicardia respective hypotension. According to this, the surgeon must thwart these manifestations, mainly by strongly cooperating with the anesthetist, respective through simple and concrete actions at the right time. Infiltrating the intercarotid space with 3-5 ml 1% lidocaine during the procedure represents a classic solution. The exclusively instrumental maneuvers, the less "palpation" of the carotids are some other techniques. Similarly with the "no touch" concept described by Turnbull for oncologic surgery, we propose avoiding maneuvering the carotid, bypassing excessive vagal stimuli, respectively avoiding mobilization of emboli from the level of the atherosclerotic plaque. The exact anatomic diagnosis of the lesion preoperatively, early heparinization, sectioning the efferents of carotid glomus (Hering nerve) are amongst other adjuvant maneuvers.

During CAS, using dilatation balloons influences mechanically the baroreceptors at the level of the internal carotid artery and carotid glomus, able to determine an immediate vagal reaction, leading to bradicardia and hypotension.

Cerebral microemboli are frequent; especially din case of CAS (30). Their existence is also documented postprocedure by transcranial Doppler. This is an important monitoring procedure in order to improve and control the quality of cerebral revascularization through CEA or CAS. Although several times clinically mute, these microemboli can generate a CHS, explaining intracerebral hemorrhage after CAS.

Sectioning the efferents of the carotid glomus or carotid glomectomy associated with eversion CEA might generate an intra- or postoperative instability, usually marked by arterial hypertension, situation which obviously increases cerebral hyperperfusion, becoming an adjuvant factor of CHS. In extreme cases, with high blood pressure values, it might become a trigger factor for CHS. For this reason, monitoring the perioperatory blood pressure is a key element for a successful carotid revascularization.

The clinical manifestations of CHS are extremely various. Understanding the phisiopathologycal mechanisms at the base of this syndrome is essential to identify the symptoms at patients with carotid revascularization. The symptomatology is widely various, due to localization, extension and severity of hemodynamic disturbances in cerebral circulation. The most frequent symptoms summoned in literature are (1):

- Temporal-spatial disorientation
- Confusion
- Migraine type headache
- Focal seizures
- Motor disturbances (hemiparesis, hemiplegia)
- Aphasia
- Nausea
- Intracerebral haemorrhage
- Physiological disturbances
- Hemianopsy
- Ataxy

Based on our experience the most frequent symptoms were (following the incidence):

- Persistent headache
- Temporo-spatial disorientation
- Physiological agitation
- Nausea, vomiting
- Troubled consciousness (torpor, obnubilation)

In our case study no sensorial or motor disturbances were described.

The debut of this symptomatology is relative, from a few hours till several weeks. Seemingly CAS is associated with the symptomatology of CHS much earlier than CEA, the first 12 hours vs. the 6^{th} day postop (apex) (23). The migraine type ipsilateral headache, confusion, temporo-spatial disorientation are the most frequent symptoms (2, 4, 5, 8, 16, 22).

The imagistic diagnosis is important to sustain cerebral hyperperfusion, respective for the differential diagnosis with other perioperatory complications of the revascularizating procedures. Although hyperperfusion is not a synonym of CHS, it represents an important factor in the genesis of this syndrome. The available imagistic techniques today allow the evaluation of the degree of cerebral perfusion (marking hyper/hypoperfusion), cerebral vascular reactivity, respective the positive/differential diagnosis of cerebral lesions.

Highlighting cerebral hyperperfusion is possible through SPECT (single photon emission CT), multi-slice dynamic susceptibility contrast MRI or PWI (perfusion weighted MRI)(17,18,24,57,67). Due to their high cost there is a lack of substantial data.

Cerebral vascular reactivity might be evaluated through SPECT after administrating acetazolamide, however the usage of this substance at a transcranial Doppler examination is more cost efficient. In order to achieve vasodilatation inhalation of CO2 might be useful or the apnea test, followed by measuring the velocity and blood flow in the middle cerebral artery, we might detect an exhausted microvascular system. The disadvantages of the transcranial Doppler examination are due to the characteristic subjectivism of the exploration, the difficulty to obtain an echographic window, the multiple anatomic variations (the standard anatomy of the poligone of Willis at the maximum of 54% of the population) and controlateral stenosis with a significant redistribution of the cerebral debit (9,30,31,26-29).

The incidence of CHS in literature is different for CEA respective CAS, however, without statistical significance. Moulakakis et al. publishes a metaanalysis of the existent data in literature regarding the incidence of CHS post CEA, respective post CS (2003-2008) (1).

	CHS	Intracerebral hemorrhage
EAC	0.40%-14.0%, average 4.53%	0 – 1.0%, average 0.48%
CAS	0.44%-11.7%, average 3.65%	0 – 4.5%, average 2.08%

The incidence at our institution, prospectively evaluated on 247 patients, exclusively with CEA in general anaesthesia with different surgical approach, was represented by 7 patients, meaning 2.83%. The patients were evaluated in days 1 and 2 postop. regarding the complaints, consciousness and possible neurological manifestations. 5 of these patients (2.02%) presented postop. headaches of high intensity, ipsilaterally the surgical intervention, not responding to specific pain management, however with propitious reaction to cerebral depletive drugs (diuretics), respectively to the dropping of arterial blood pressure. The other two patients (0.81%) presented a more complex symptomatology, associating temporo-spatial disorientation to the headaches, respective troubled consciousness, nausea and vomiting. None of the patients presented motor disturbance (hemiparesis, hemiplegia).

In our casuistry, among the 5 patients with mild CHS, 2 of them beneficiated of bilateral CEA under shunt protection, respective amongst the 3 being operated unilateral, in 2 cases intravascular shunt had been utilized. Patients who presented an advanced form of CHS in our allotment had undergone bilateral CEA in the same surgical session, representing 20% of the total of those 10 patients who suffered bilateral CEA in this period.

Thereby, we add another risk factor for CHS, represented by bilateral CEA in the same surgical session, reason why in our institution bilateral CEA became a "relative" counter-indication.

It is important for the treatment of CHS above all to be preventive. The most important aspect is represented by the knowledge of this possible complication in order of an efficient prevention.

The foreground is represented by surgical maneuvers meant to reduce the risk of pressure instability, emboli, described above. Monitoring the blood pressure has to be correct, if possible in an invasive manner, until its stabilization and the reintroduction of the chronic treatment of hypertension, managing promptly the pressure values. This procedure has to be done aggressively, keeping the values at a normal or mild low range (6, 13, 35, 36). Transcranial Doppler monitoring of cerebral blood flow is also a useful technique (3, 5).

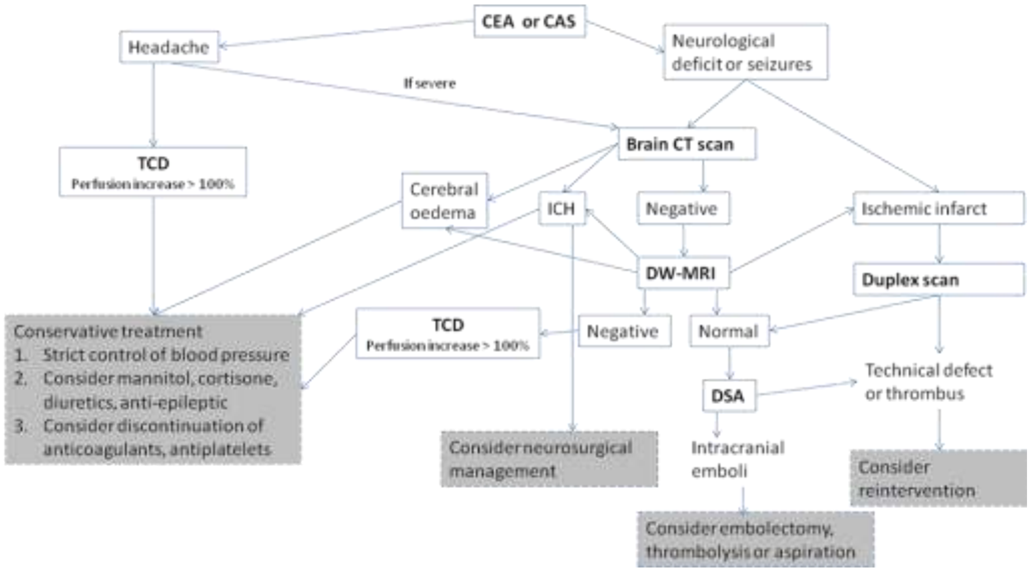
CHS risk factors

Preoperative	Perioperative	Postoperative
Hypertensive microangiopathy	Intraoperative distal carotid pressure < 40 mmHg	Postoperative hypertension
Diabetes mellitus	High doses of volatile anesthetic agents (halogenated hydrocarbon)	Use of anticoagulant and antiplatelet therapy
Age > 80 years	Perioperative cerebral infarction	
Recent contralateral EAC (< 3 months)	Intraoperative ischemia	
Severe contralateral internal carotid artery stenosis with poor collateral circulation	Refractory peritoperative cerebral hyperperfusion	
Contralateral internal carotid occlusion		
Incomplete poligone of Willis		
Alterated cerebrovascular reactivity at testing with acetazoamide		

(*Modified after* **Moulakakis et al. (1)**

Sedation, hyperventilation (general anesthesia), mannitol, hypertone saline are all to be useful in treating cerebral edema (9, 24, 33, 34). Corticotherapy was utilized in treatment of CHS (9, 24, 33, 34).

The curative treatment of CHS is actually the treatment of the generated complication, mainly cerebral edema, intracerebral hemorrhage, epileptic seizures, and so on. A subservient algorhytm in diagnosis and treatment in case of unfavourable neurological evolution of a patient after surgical or endovascular carotid revascularization is presented as it follows:



After **Moulakakis et al. (1)**

The prevention protocol in our institution is based on the concepts represented above. Although there are limitations due restricted financial resources, by using judgematical the available materials and investigations leads to a very good cost-efficient ratio regarding prevention in CHS:

- The correct indication of revascularization (CEA vs. CAS)
- A complete and correct preoperatory diagnosis
- A possibly exact anatomic-lesion diagnosis
- Highlighting the risk factors for CHS
- Avoiding bilateral CEA
- Using intravascular shunt
- "no touch" surgery before carotid clamping
- Using pharmacological protection: preoperatory antiagregation and statins, intraoperatory anticoagulation (heparin 1 mg/kg, without postoperator antagonisation)
- Avoiding intra- and postoperator blood pressure variations, prompt and energetic treatment of hypertension
- Continuous postop monitorization of the patients in the first 3 days
- Ambulatory reevaluation of the patient after 14 days postop.
- The notification of the attending physician about the possible postoperative complications.

Conclusions

CHS is a redoubtable complication of carotid revascularization. Its manifestations are various, but the base is the same phisiopathological concept. It is essential to distinguish the risk factors and incipient symptoms. Prophilaxis is the most efficient treatment, and it is achievable through an adequate education of the medical personal with minimal financial implications in order to assure a faster recovery in carotid postrevascularisation.

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The use of a well defined protocol can keep combined mortality - neurological morbidity rate of carotid surgery under 1%*)

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Abstract

Objective: *to evaluate the results of carotid bifurcation surgery (CBS) performed using a well defined protocol.*

Design: *prospective non randomized clinical study.*

Materials and methods: *From January 1999 to October 2004, all patients admitted for CBS were managed according to precise pre, per and postoperative protocol. Preoperative evaluation included duplex scan and angioscan or MRI of extra and intracranial vessels and brain. Cardiac evaluation included clinical evaluation, ECG and cardiac echography. Coronaropathy was managed according to a defined algorythm, in collaboration with cardiologists and anesthesiologist. All patients were operated upon under general anesthesia, and monitored with radial catheter and digitalized ECG. The precise level of carotid bifurcation was identified and marked using duplex scan in the operating room. Systemic heparin was routinely used (0.5 mg/kg). Selective shunting was based upon preoperative data and subjective evaluation of reflux. Perioperative control arteriography was routinely performed. Postoperatively, all patients were observed and monitored during 24 hours in their own room using the same monitoring process. Maximal blood pressure was kept under 160 mmHg. Anticoagulation used Aspirin and low-molecular weight heparin. Daily ECG and troponine I titration were routinely performed during three days. Pre and postoperative neurological evaluation by a neurologist was performed since September 2003. 261 procedures were performed in 243 patients (56% asymptomatic). A shunt was used in 25% of the procedures. Endarterectomy and prosthetic patch closure was used in 196 procedures (75%), and eversion endarterectomy or bypass in 65 (25%).*

Results: *There was no mortality. Two patients had a stroke, one permanent due to a perioperative embolus, and one, regressive in few days, due to hyperperfusion. Three patients had a cervical hematoma. Combined neurological morbidity and mortality rate was 0.8%. Five patients had myocardial ischemia (2 cardiac infarcts) and 4 a coronary bypass (1) or angioplasty (3).*

Conclusion: *the use of a well defined protocol may help to significantly reduce morbidity and mortality rates of carotid surgery.*

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Introduction

A number of major randomized clinical trials have informed that carotid endarterectomy is an operation justified by a firm evidence base. The obsessive attention to operative detail improves the results from surgery and enhances the benefit of carotid endarterectomy to the population. Despite that carotid endarterectomy (CEA) confers significant benefit over "best medical therapy", the paradox remains that the operation carry out to prevent stroke is associated with a small, but important risk of stroke in the perioperative period. However, the debate as to how stroke and other cardiovascular complications might be prevented following CEA remains largely refereed.

When performing a carotid endarterectomy, surgeons may use a number of ancillary techniques, such as different types of anaesthesia, shunting, patching or anticoagulation. Randomized controlled trials have been performed to try and assess the effect of these techniques, but the relatively low risks of stroke and death due to carotid endarterectomy mean that very large patient sample sizes are required to get reliable results.

Moreover, the decision to use any one ancillary technique is rarely made in isolation and is likely to affect the decision to use another. The reasons and thresholds for selecting a particular technique may differ between individual surgeons. Secondly, it is important to determine the inter-relations between uses of the different techniques. To what extend might randomization to the use of one technique (e.g. shunting) influence the use of another ancillary technique (e.g. patching)?

We evaluate the results of carotid bifurcation surgery (CBS) performed using a well defined protocol.

Material and methods

Patient population

From January 1999 to October 2004, 261 consecutive, primary or repeat CEA procedures were performed in 243 patients. Patients included 172 men (66%) and 89 women (34%), ages 54 years to 92 years (mean, 63.27). Associated risk factors included hypertension in 240 (91%) patients, smoking in 203 (77%); coronary artery disease in 210 (80.4%), diabetes in 15 (5.7%), and chronic renal insufficiency in 2 (0.7%). The 163 patients with symptomatic disease had ipsilateral ICA stenosis 60% or greater at duplex ultrasound scanning. 82 patients underwent staged bilateral CEA.

Preoperative assessment

Duplex ultrasound imaging is the initial investigation because it is non-invasive, free of risk and accurate in determining degree of stenosis, in assessing plaque density and detecting plaque stenosis.

MRA or CT complement duplex provide images of the arch, great vessel origins, distal ICA, and intracranial circulation. Furthermore, MRA data acquires assessment of the brain parenchyma along with assessment of the cerebral circulation.

CT scanning gives anatomic detail and resolution as standard contrast angiography.

Despite the traditional contrast angiography as the "gold standard", this technique we don't use any more.

Cardiac evaluation included clinical evaluation, ECG and cardiac echocardiography. Coronaries disease was managed according to a defined algorithm, in collaboration with cardiologists and anesthesiologists.

Surgical technique

All patients were performed under general anaesthesia. The precise level of carotid bifurcation was identified and marked using duplex scan in the operating room. We used a perioperative monitoring with radial catheter and digitalized ECG. Systemic heparin was routinely used (0.5 mg/kg). Selective shunting was based upon preoperative data and subjective evaluation of reflux. A shunt was used in 25% of the procedures. Endarterectomy and prosthetic patch closure was used in 196 procedures (75%), and eversion or bypass in 65 (25%). The lumen of the endarterectomy zone was inspected by loupe magnification. Heparin was not reversed following flow restoration. Perioperative quality control assessment by arteriography was routinely performed. All patients didn't stop aspirin preoperatively.

Postoperative monitoring

After recovery from anesthesia, the patient was transferred to the recovery area of the operating theatre for 3-hour period.

Postoperative assessment

All patients were observed and monitored during 24 hours in their own room using the same monitoring process. Maximal blood pressure was kept under 160 mmHg. Anticoagulation used Aspirin and low-molecular weight heparin. Daily ECG and troponine I titration were routinely performed during three days. Pre and postoperative neurological evaluation by a neurologist was performed since September 2003.All patients discharged after 3 days post-operative.

Results

There was no mortality. Two patients had a stroke, one permanent due to a perioperative embolus, and one, regressive in few days, due to hyperperfusion. Three patients had a cervical haematoma. Combined neurological morbidity and mortality rate was 0.8%. Five patients had myocardial ischemia (2 cardiac infarcts) and 4 a coronary bypass (1) or angioplasty (3).

The mean length of surgery (skin to skin) was 80 min (95% range = 40-150). The mean carotid artery occlusion time for all patients was 25 min (range from 17 min to 42 min). For the patients in whom a shunt was used, the mean occlusion time was 5 min.

Discussions

In the five decades since CEA was first introduced, the debate about how to reduce the operative risk has been totally dominated by "single issue" subjects. More importantly, more useful has practices and strategies from a protocol. We chose to evaluate the role of monitoring, partly because there was evidence that implementation of such a protocol might improve outcome. Our hypothesis was that implementation of a monitory program should reduce the operative risk by preventing technical error.

The diagnostic of carotid disease is usually made from the history and physical examination. Once carotid disease is suspected, detailed assessment carry out using duplex scanning. But the quality of duplex scanning is depending on the ultrasound technologist's experience. Second, duplex has no capability to image the arch, great vessel origins, distal ICA, or intracranial vasculature. We used like complement MRA or CT scanning data, allowing detailed assessment of the brain parenchyma. We don't require evaluation by contrast angiography, because it has a potential morbidity and variability in interpretation.

It knows that the most important benefit of CEA under LRA (loco-regional anaesthesia) may be the potential for significantly reducing early cardiovascular morbidity, especially hypertension (Naylor). All own patients were carrying out under beta-blockers and we prefer general anaesthesia. However, there aren't contra-indications for CEA under general anaesthesia. The choice/dose of antiplatelet agent, like low dose aspirin, reduce vascular death and non-fatal stroke, MI and aspirin was not be stopped prior to surgery. Combination aspirin and Clopidrogel therapy should generally be avoided, but the patients receiving chronic Clopidrogel, we did not stop this medication.

The most enduring single-issue subject, however, remains the role of shunting. Few surgeons advocate a policy of "never" shunting, so that the battle lines are drawn between the "routine" and "selective" shunting. Selective shunting was based upon pre-operative data and subjective evaluation of reflux. We have had one stroke using this technique of evaluation, due to a perioperative embolus.

In summary, the introduction of an integrated program of monitoring in the carotid endarterectomy has been associated with a mortality and neurological morbidity rate under 1%.

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Part 11.

VARIA

Names and Facts in the History of Vascular Surgery*)

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Vascular surgery techniques are an ever presence in medicine: control of bleeding, controlled bleeding, treatment of superficial varicose veins. Indirect vascular operations on the autonomous nervous system are a recent acquisition. Vascular reconstructive surgery is the most recent and exciting chapter; it represents the basis for spectacular organ transplantation. A very close relation is established with angiology and radiology and special relationship exists today between vascular surgery and other medical specialties like haematology and nephrology. The history of surgery is in large part a record of its technical advances and the development of surgical control of the arterial system represents one of the most important of its achievements. Of significance is the fact that within the past several decades vascular surgery has reached a high level of accomplishment. Direct operations on arteries and the use of autografts, arterial prosthesis, and extracorporeal circulation form the basis for many brilliant surgical procedures (1).

The 20th Century has produced such a plethora of discoveries and advances that in some way the face of medicine has changed out of all recognition. The rapid progress in this era was reinforced by enormous improvements in communication between scientists through the world. Through publications, conferences and - later - computers and electronic media, they freely exchanged ideas and reported on their endeavors. No longer was it common for one individual to work in isolation. Although specialization increased teamwork become the norm.; it consequently has become more difficult to ascribe medical accomplishment to particular individuals. In the years following world war II insights derived from all biology altered basic concepts of the disease process; new discoveries in biochemistry and physiology opened the way for more precise diagnostic tests and more effective therapies; and spectacular advances in biomedical engineering enabled the physician and surgeon to probe into the structures and functions of the body by noninvasive imaging techniques like ultrasound (sonar), computerized axial tomography (CAT) and nuclear magnetic resonance (NMR). With each new scientific development, medical practices of just a few years earlier become obsolete (2).

Modern surgery has evolved from one of the most despised branches of medicine into one of the most respected, most powerful and best compensated areas of medical

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specialization (3). Three seemingly insuperable obstacles beset the surgeon in the years before the mid-19th century: pain, infection, and shock. Once these were overcome, the surgeon believed that he could burst the bonds of centuries and become the master of his craft. There is more however, to anesthesia, than putting the patient to sleep; infection, despite first antisepsis (destruction of microorganisms present) and later asepsis (avoidance of contamination) is still an ever present menace, and shock continues to perplex physicians. But the 20th century, surgery has progressed further, faster, and more dramatically than in all preceding ages (4).

Abdominal surgery has been the spearhead of surgical advance in the XXth century. In the abdomen have been workout and proved changes which have than made the platform for advance in other spheres. No doubt the glamour and perhaps the impetus have moved to other subdisciplines (5). Vascular surgery may be defined as the surgery of the arteries, the veins and the lymphatic, together with certain related procedures such as amputations for ischemia and fasciotomy for acute vascular occlusions; there is also a close association between vascular surgery and organ transplantation, because the success or failure of an organ transplant procedure depends in no small measure upon the vascular anastomoses between the host and the transplanted organ (6). Surgery of the arteries Arteries diseases is one of the oldest chapters of the surgical pathology: trauma and aneurysms are known from over 2000 years (7). Hemostasis is recorded in ancient Chinese literature. During the era of Hippocrates, ligation of vessels was rarely practiced, and amputation was done only through a gangrenous extremity at a site where the vessels were thrombosed to assure that significant bleeding did not occur (8).

Celsus recommended amputation at the line of demarcation, but again most of the vessels at this level were thrombosed. At that time he advocated limited use of ligatures of Celtic linen. In about 100 A.D. Archigenes was more doing and advanced the scope of amputation significantly by proposing that it be performed for gangrene, necrosis, cancer, and certain callous tumors. Antyllus contributed by recommending surgical treatment of aneurysms by proximal ligation of the arteries (1).

Ambroise Paré, one of the most notable surgeons of the European Renaissance, regarded by some medical historians as the father of modern surgery, rediscovered the ligation and used it, rather than the hot iron, to control hemorrhage in amputation the leg of an officer wounded at the siege of Danvillliers, in 1552. He initiated the beginning of the standard use of the ligatures to control arterial bleeding. He was also the first to suggest syphilis as a cause of aneurysm formation (swelling of blood vessels). The origin of prosthetics as a science is attributed to him too (9, 10, 11).

In the 18th Century, John and William Hunter made important contributions to vascular surgery that has prevailed until today. Their studies of aneurysm formation, pathology, and treatment laid the foundation for many modern surgical concepts. After Galen second-century writings grouped aneurysms either of the true or false type they defined true and false aneurysms. William, in addition, was the first to describe the arterio-venous aneurysm or fistula. Later, John developed a successful operation for popliteal aneurysm based on his meticulous laboratory investigations. John Hunter had a particular interest in coronary artery disease, and was the first to determine that fatty plaque was deposited before vascular calcification occurred. He was the "skillful anatomist" who demonstrated pathologic coronary vessels for William Heberden's classic description of angina pectoris presented in 1772. Hunter too suffered from angina, and once said "my life is in the hands of any rascal who chooses to annoy and tease me" (12).

In the progress of vascular surgery, the events between 1888 and 1967 represent the period of most significant development beginning with Matas introduction of endoaneurysmorrhaphy and extending to the popularization of vein grafts to bypass coronary artery obstruction by Favaloro (13).

For centuries, surgeons had brought the techniques of amputation, incision and drainage to bear the problems not amenable to "diet or drugs". The philosophy of removal began to be supplanted by the concept of repair. This was nowhere more apparent than in the nascent field of vascular surgery, where simple ligation of an injured vessel after entailed significant tissue loss secondary to gangrene. In the presence of an aneurysm there was the additional danger of rupture and almost certain death from hemorrhage, since collateral vessels frequently supplied the aneurysm and were not included in the usual ligation procedure. Therefore, when Rudolph Matas reported the technique of endoaneurysmorrhaphy in 1902, 14 years after his first clinical application of the procedure, a great advance was achieved.

The next logical step was resection af a segment of artery and primary reanastomosis of the severed ends. This was accomplishd in 1895 by Zoege von Manteuffel and in the following years Murphy of Chicago achieved the first successful repair of an arteriovenous fistulaaneurysm with restoration of normal circulation pathways (14, 15, 16, 17).

Allexis Carrel received in 1912 Nobel Prize for Physiology or Medicine for developing a method of suturing blood vessels and who laid the groundwork for further studies of transplantations of blood vessels and organs. He also investigated preservation of tissue outside the body and the application of the process to surgery. His strain of chick heart tissue was kept alive for more than 30 years (18). In 1906 Carrel and Guthrie first reported successful implantation of venous autografts into the arterial system of dogs (19). This soon was followed by the clinical use of the popliteal vein for arterial reconstruction after popliteal aneurysm excision by Goyanes in 1906.

The first successful arterial allograft was reported by Hoepfner in 1903 (20). The following year Lexer inserted a segment of saphenous vein for reconstruction of an axillary-brachial aneurysm following trauma (21, 22). In 1923, Leriche called attention to the symptoms produced by chronic occlusion of the terminal aorta and iliac vessels. Atherosclerotic obstruction of the area of the aortic bifurcation with superimposed thrombosis of the stenotic area are usually found. Unlike saddle embolus or sudden thrombosis ischemia manifestations are typically present for months or years before the sufferer seeks medical attention (23, 24). He published a series of observations of a syndrome occurring in relatively young men consisting of bilateral intermittent claudication, diminished or absent femoral pulses and sexual impotence. He termed this syndrome, which has subsequently come to bear his name "aortitis terminalis" and suggested that the ideal treatment would be excision and reestablishment of vascular continuity by means of an arterial graft (25). The pioneering work of Murray in the intraoperative use of Heparin and the work of Moniz and dos Santos, and colleagues in establishing the technique of arteriography then combined with the concept of arterial substitutes initiate the modern era of clinical vascular grafting (26, 27, 28, 29). In 1924, Brook injected sodium iodide into a patient's femoral artery producing the first arteriogram. One should remember the role of W.C. Röntgen who is the recipient of the first Nobel Prize for Physics in 1901 for his discovery of X-rays, which heralded the age of modern physics and revolutionized diagnostic medicine (30).

In 1947 J. Cid dos Santos was the first to perform the procedure of thrombo-endarterectomy in the way we use this technique today. In 1948 Kunlin introduced the procedure of femoropopliteal bypass grafting using an autogenous vein (6). In 1951 Dubost and col. reported for the first time the successful resection af an aneurysm of the abdominal aorta and its replacement by an arterial homograft (31). Thoracic aneurysm was attacked by DeBakey and Bahnson H.T. (32, 33).

In 1952 Voorhees, Jaretzki and Blakemore were the first to report the use of porous plastic cloth tubes to bridge arterial defects using Vinyon-N prosthetic arterial substitute (34). Extra-anatomic arterial reconstruction is devised to circumvent complex vascular problems when conventional anatomic procedures necessary for the relief of severe ischemia were deemed impossible or too hazardous to perform. Freeman and Leeds applied this concept in 1949 using the superficial femoral artery as a donor to transport blood to the controlateral femoral artery through a subcutaneous transabdominal pathway (35, 36).

The first successful embolectomy was performed by Georges Labey and reported by Mosey and Dumont in 1911. They stated that to be acceptable it is important that "the operation should be undertaken without delay, that the embolus be aseptic and easily accessible, that the patient be young and his arteries healthy". Obviously, these principles were then and still are today most applicable to ideal situation. Because of the pioneering efforts of Eivar Key of Sweden this procedure gained increasing acceptance (37). It was not until 1963 that a most notable advance in the performance of arterial embolectomy was achieved by the introduction of the balloon catheter by Fogarty et al. (38, 39, 40, 41, 42).

Today vascular disease management is in the midst of a revolution in clinical practice namely catheter-based intervention. Angioplasty led to the evolution of stents, which spawned stent grafts. Currently the stent is no longer simply a passive mechanical scaffold, but is being developed as a drug delivery platform. Catheter delivered devices will pharmacologically or genetically produce temporary and perhaps permanent changes in the biology of the vessel wall. The names of new endovascular pioneers must be added including Ch Dotter (endoluminal recanalization), A. Gruentzig (ballon angioplasty), J. Palmaz (endoluminal stent) and J. Parodi (stent graft) (43).

SECOND PART

Surgery of the veins

The pathophisiology of venous disease is in many respects more complex then that of arterial disease. With the exception of aneurysm formation, obstruction is responsible for nearly all the physiologic aberration characteristic of arterial disease. Venous pathophisiology, however, involves both obstruction and valvular insufficiency (1). Moreover the disability from venous disease includes not only regional problems but also those that follow the escape of thrombi into the pulmonary circulation (2, 3, 4). Together with the copious network of venous collaterals, the low intraluminal pressure, the collapsible nature of the venous wall, and the intermittency of venous flow, definition of the features of venous pathophysiology provide a real challenge (5). Varicose veins with their associated symptoms and complications constitute the most common vascular disorder of the lower extremities (6).

Proof that physicians have always been concerned with venous problems is found as early as 1550 A.D. in the Eber's Papyruses, which describes certain serpentine windings on the legs (7). Wisdom of the ancients, no doubt the product of experience, admonishes the novice not to cut into these because of operation causes hemorrhage and death (the head to be laid on the ground). Eleven hundred years later, the same advice was repeated by Hippocrates. He discussed their treatment at length 2500 years ago (8).

In the first century after Christ, Galen of Pergamum perpetuated the Hippocratic therapy of "humors", and belief that black bile would be trapped by a healing ulcer. It is to his credit that Galen described the use of silk ligatures and advised that varicose veins be removed. Similarly, Celsus advised ligation and excision of bleeding varices. Many of Galen's belief permeate the writings of the next 1500 years and these teach us nothing. Some wisdom surfaces however: the cause of varicosities was attributed to the weight of stagnant blood that pressed the walls of the veins, causing elongation, tortuosity, and dilatation, that is still believed to be true. Another pertinent in the modern era is found in the words of Fernel: "it (the varix) comes also from a blow, from a contusion, from excessive effort" (9). Marianus Sanctus related varicosities to the child bearing, but also said they were caused by ".standing to much before kings" (10).

Aullis Cornelius Celsus (121-201 A.D.) describes the operation for varices. The byzantynes paid special attention to varicosis surgery from the early period of the empire. The famous fourth-century physician Oribasius meticulously described a number of surgical methods of confronting varicosis, same of which derived from the texts of earlier Greek surgeons, to which he added his own keen observation (11).

Ancient Roman surgeons already performed surgical resection. French surgeon of the Middle Age Guy de Chauliac, described, in Chirurgica Magna, bandaging for ulcers and cautery or surgical resection for varicose veins. The most remarkable texts were those of Ambroise Pare in the 16-th Century, using all these techniques for surgical teaching while abandoning many treatments based on concepts of diseases on imbalance of "humors". Hieronymi Fabricii ab Aqua-pendente describes venous valves in 1603 - "De venarum osteolis" (12).

By the beginning of the 19-th Century, principles of surgical care of varicosities had been set down (13, 14). All that was needed for refinement of care was development of aseptic surgery and invention of the hypodermic syringe. Techniques of ligation, extraction (stripping), removal by dissection, sclerosis, and compression bandaging were all in use (15).

Over the intervening centuries, numerous modes of therapy including puncture, avulsion, excision, cautery, ligation, resection, injection and stripping were advocated with variable degrees of success. Although current methods, surgical as well as nonsurgical, have proved generally therapeutic, the search for an effective mean of prevention and the proved cure for this common malady continues (16).

The end of 19-th century was the start of new surgical progress with Trendelenburg, Delbet and Mocquot development of sclerotherapy (17). Sclerotherapy of varicose veins began in Europe soon after Pravaz devised the hypodermic syringe in 1851. Injection therapy had become widely accepted in most European countries as the best form of treatment after Linsey of the Tubingen Clinic in 1911 discovered that bichloride of mercury used as a sclerosing agent was less toxic when injected intravenously than were previously used agents.

Although early practitioners had performed ligation or local excision of varicose veins, it was not until the advent of general anesthesia and aseptic surgical therapy that a more extensive and definitive operation could be undertaken with success.

In 1884, Madelung of Germany, in a radical surgical procedure, excised the greater saphenous vein through a long incision over the medial aspect of the leg and thigh. In 1905, Keller, in the United States, first reported the removal of varicose veins, without extensive incision: a wire was passed through the lumen of the saphenous vein, and the vein was pulled or stripped by inverting the vein on itself. Homans, in 1916, emphasized that ligation of the saphenophemoral junction was a vital step in the prevention of recurrence of varicosities, since tributaries to a patent proximal saphenous segment would often allow refilling of distal varicosities. Linton, in the late 1930', emphasized the pathologic contribution of incompetent perforating veins for venous insufficiency and devised an operation to separate the deep and superficial venous systems by dividing these perforating veins (5).

Surgery of the lymphatics

Aristotle and the anatomists Herophiles and Erasistratos are said to have observed aspects of the lymphatic system between 348 and 250 A.D. Knowledge about these recordings is hearsay; non of the works of the Alexandrian school of Medicine come directly to us. In the sixteenth century, Vesalius, professor of anatomy and surgery at Padua, named the thoracic duct "vena alba thoracis" because of its content of milky fluid; his contemporary Eustachius also described the equine thoracic duct. In 1627, Aselli of Pavia, illustrated lymphatics in the mesentery of fed dogs. The Parisian Pequet observed in 1651 that intestinal "lacteals' emptied into the receptaculum chyli, thence drained into the thoracic duct, eventually emptying into "the whirlpool of the heart". Rudbeck of Uppsala described liver lymphatics as "vasa serosa".

In 1653, Bartholin named the vessels "lymphatics" (18). In 1774, William Hewson, after resigning from the Hunterian School, published an important anatomic treatise entitled: "The Lymphatic System in the Human Subject and Other Animals" (19). In the nineteenth century, the role of the lymphatics was illuminated by Claude Bernard's global concept of a mammalian requirement for maintenance of a constant "internal milieu" bathing all cells (20). By the late nineteenth century, Starling had clarified the relationship between the hydrostatic pressure of the blood in the capillaries and the colloid osmotic pressure of the plasma proteins (21). In the twentieth century, from 1930 to 1941, Dinker and collegues measured protein flux from the capillaries to the tissues, showing that blood capillaries were leakier than hitherto believed (22). Lymphangiographic studies by Kinmonth (1955) have shown states of hyperplasia, dilatation or aplasia of lymphatic vessels with dermal back-flow of lymph (23).

Kondoleon (1912) attempted to establish communications between the diseased lymphatics and the deep muscle compartment by excising strips of fascia as windows into the muscle compartment (24). Charles (1912) advocated excision of the diseased skin and subcutaneous tissue down to the fascia and resurfacing by split thicken skin grafts (25). Thomson (1962) has exended Kondoleon's plan and incoroporated principles of Sistrunk's flap operation to produce an effective procedure, the buried dermis flap (26, 27).

Surgical therapy of the lymphatic system has yet to fulfill the Hunterian prophecy as it has for the heart and arteries. While neither modest nor generous, Hunter was a forceful man. He said: "if we mistake not, in a proper time the lymphatics will allow to be the greater discovery both in physiology and pathology that anatomy has suggested, since the discovery of the circulation" (22).

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Microsurgery

It was developed in the twentieth century as a culmination of achievements in vascular surgery by combining techniques of vascular surgery with an operating microscope, fine instruments, microsuture and new operative strategy and techniques. It was in 1960 that Jules Jacobson, a vascular surgeon, described microsurgical anastomoses in vessels as small as 1,4 millimeters using a microscope used by ear, nose and throat surgeons for surgery on the middle year; he was the first to use the term "microvascular surgery". In 1964 Harry Bunke reported the first successful rabbit ear replantation to the Plastic Surgery Research Council Meeting in Kansas City, Kansas. This was a milestone in the development of the field of microsurgery because it was the first report of an amputated part successfully reattached using blood vessels millimeter in size - this size was considered critical because it approximated the size of vessels in finger and major vessels supplying muscles and skin. In 1966 he reported in a second landmark paper the transplantation of a monkey great toe to hand using microsurgery. These two studies opened the door to replantation of amputated body part and to microsurgical tissue transplantation (28).

Vascular access

Despite the development of more sophisticated machinery, the use of hemodialysis continued to be limited and its shunts were rather disappointing. The development of external shunts by Quinton et al. in 1960 broke this impasse. In 1966 Appel thought of using a surgically produced arteriovenous fistula as a source of access to dialysis. In order to construct an arteriovenous fistula, a suitable artery and vein have to be in proximity. Unfortunately this anatomic configuration was not always present in these sick patients. The most common problem was the absence of a good vein. A natural solution to this problem was to interpose an autologous or synthetic tube graft between an artery and a vein. This was the origin of the graft arteriovenous fistula (29).

Ambulatory or same-day surgery

It is performed in a physician's office or clinic. It involves operations that use minimally invasive techniques, require less extensive cutting, and use anesthesia that clears rapidly from the body (30).

Laparoscopic techniques

They have changed the face of many surgical specialties; although more studies are needed to further define the role of laparoscopy, in vascular surgery present indications can be found in those patients with TASC III and IV occlusive lesions and in patients with abdominal aortic aneurysms who are candidate to tube grafts or aortobifemoral bypass. With further refinements in technology (anastomotic stapling device, robotics) and techniques, laparoscopy should replace many open surgeries presently done for aorto-iliac disease but will also have to be considered for treatment of mesenteric disease (31).

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Today operations are less invasive and vascular surgeons are cooperating more and more intensively with other medical disciplines especially radiologists. Examples are endovascular treatment of abdominal aortic aneurysms in which and endoprosthesis is inserted via minute incisions in the groin by the vascular surgeon and an interventional radiologist together. In addition interventions such as percutaneous transluminal angioplasty and stenting as well as new diagnostic possibilities (e.g. MRA) strengthen the cooperation with radiologists. The multidisciplinary approach is also extremely important in other areas. Vascular surgeon team up with internal medicine specialists (diabetes, hypertension, lipid metabolism disorders, thrombotic syndromes, etc.), rehabilitation specialists and podotherapists (in case of diabetic foot and amputation) vascular laboratory technicians (diagnostics and follow-up by means of Doppler and duplex techniques) and neurologists (cerebro-vascular diseases). In the vascular centers, patients are treated effectively by a multidisciplinary team that draw up a plan for diagnosis and treatment (32, 33).

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The Aortic Root*)

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MOTTO
"It is my own belief that the aortic root would be best understood if divorced from the concept of annulus"
(R.H. Anderson)

Part 1: Clinical and surgical anatomy

Abstract

The aortic root represents a region of major interest both from the diagnostic and for the surgical points of view. The major advances in cardiology and surgery require a thorough knowledge of this important region consisting of various interdependent elements. Static, bidimensional and older views should be abandoned "parri passu" with the acquisition of new details. This review presents an update of the anatomy of the aortic root with special reference for the clinician and surgeon and it represents the first part of a work addressed to these categories of specialists. This critical review puts an accent on the main relations of the aortic root, describes the structures that form this entity, brings in discussion such concepts as "anatomical annulus" and "surgical annulus" and demonstrates from a practical standpoint the hidden or less known details regarding the aortic root. Images belong to the author's collection and were specially chosen to satisfy this purpose.

Key words: *Aortic root, Aortic valve, surgical anatomy, Aortic valve repair*

Introduction

The aortic root represents the integral of various structures supporting the aortic valve. The aortic root indicates a clinical-anatomical concept (1) and it includes structurally and functionally interconnected elements of clinical and surgical relevance: the origin of the aorta from the left ventricle (i.e. the distal left ventricular outflow tract - LVCT), the ventriculo-aortic junction *("the anatomical annulus")*, the aortic sinuses together with the interleaflet triangles and the supravalvar crest *("the sinutubular*

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junction"). From a clinical and practical point of view, the proximal part of the ascending aorta should be also added to these elements.

A thorough knowledge of these intricate elements is necessary for a proper diagnostic interrogation and in order to choose the most suited surgical solution in the individual patient.

Location and main relations of the aortic root

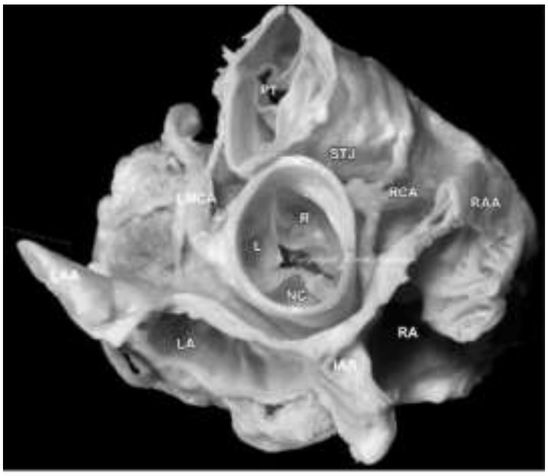
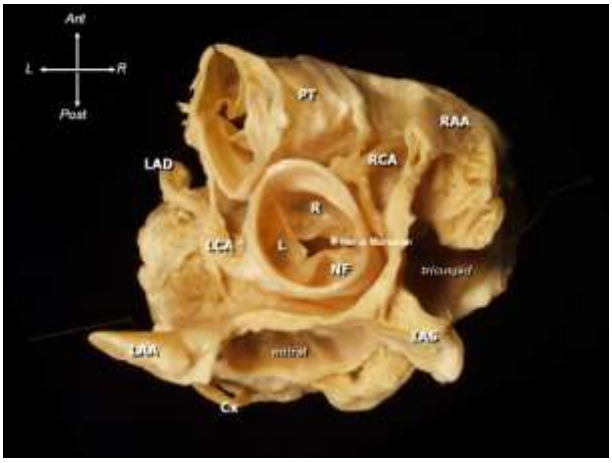


Figure 1: Basal view of the heart

Due to the fact that the left ventricular inflow and outflow parts make an acute angle and that the anterior leaflet of the mitral valve separates the two afore mentioned compartments and also due to the fact that the right ventricle winds around the left, the aortic root is the centrally-located element of the heart. It establishes relations with practically all the remainder cardiac structures (2) (Figure 1).



Both atria were opened. Atrial appendages were left in place. Note the principal relations of the aortic root and valve with surrounding structures. The interatrial septum was cut to the level of the fossa ovalis which is left in place. In depth, the position of the inter-atrial septum corresponds to the right fibrous trigone of the heart

Compared to the pulmonary root, the aortic root in normal hearts doesn't have an infundibulum (2, 3) and it takes origin from ventricular myocardium only from approximately 2/3 of its circumference. The remainder roughly 1/3 takes origin from the fibrous continuity between the aortic and mitral valves, including the left and right fibrous trigones. The muscular origin is actually septal in nature, as the interventricular septum is not a planar structure but it follows the general winding disposition of the right ventricle around the left (Figure 2).

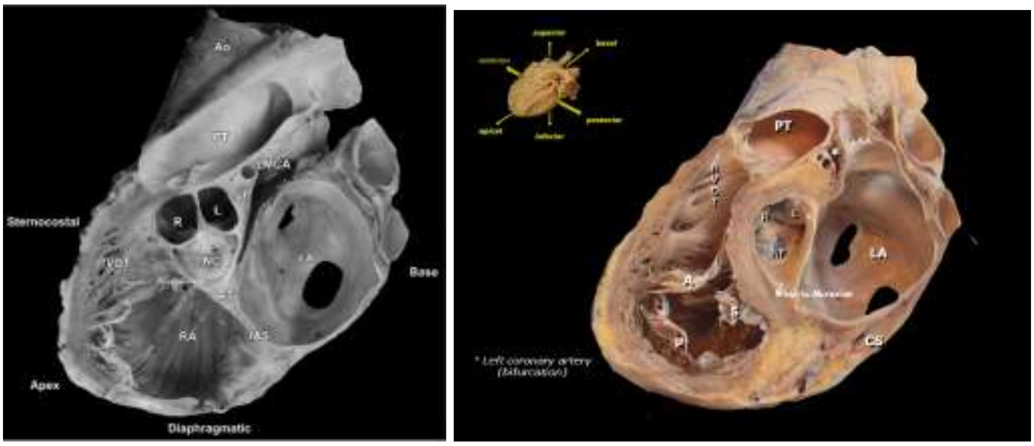


Figure 2: Longitudinal section through the heart

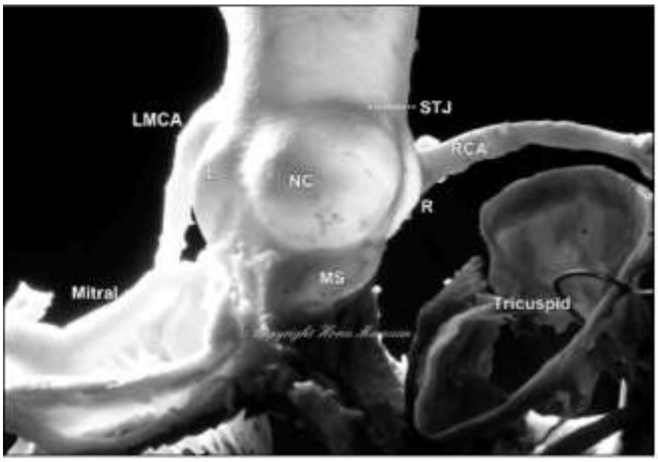
This image depicts the relations of the aortic root as viewed from the left side after performing a section parallel to the cardiac long axis. For a better orientation, the main aspects of the cardiac silhouette were mentioned. The origin of the aorta between the right and left trigones, is fibrous in nature (corresponding to the NC and L aortic sinuses). Opposite, and in correspondence with the RVOT, the origin is muscular. Note the winding right ventricle around the left and the non-planar structure of the septum.

Ventricular muscle has a complex disposition and some controversy still remains regarding the actual disposition of the fibers, fascicles and the very existence of an unique myocardial helical band (4). However, the left and right trigones are not only part of the cardiac fibrous skeleton but they are also circumscribed and embedded into the myocardial mass. A complex system of left ventricular trabeculae fixes the aortic root to the apical part of the left ventricle, and indirectly, by means of the mitral subvalvar apparatus, to the left ventricular free wall. The only portion of the aortic root less covered by adjacent cardiac structures is the left sinus ("left coronary sinus") with the origin of the left coronary artery. The left auricle ("left atrial appendage") covers only in part this area. The main relations of the aortic root are depicted in Figure 1 and Figure 2.

Description

Distal to its "origin" the aortic root shows a series of important elements (5). The continuation between the LVOT and the aorta as a vessel is called "the ventriculo-aortic junction". The term denotes the level at which the ventricular myocardium is replaced by arterial wall. Compared to the pulmonary root, the term is not applicable to the part of fibrous origin. The mitral-aortic curtain (or continuity) is a pentagonal area, bordered by the left and right trigones, by the left and non-coronary sinuses of the aorta and it merges distally with the interleaflet triangle between the afore mentioned sinuses. An imaginary line continuing the circumferential junction between the left ventricular myocardium and the aorta, would intersect the mitral-aortic curtain in such a way that the nadir of the aortic left and non-coronary sinuses would be placed "underneath" this line. This "annulus" is the so-called "anatomical annulus" - a notion less applicable than in the case of the pulmonary root.

The insertion of the aortic sigmoid leaflets follows a crenated (or crown-shaped) profile traveling the distance between the LVOT and the supravalvar crest. The aortic leaflet material is interrupted at the level of the three commissures, in contrast with the atrioventricular valves. This crenated line is the so-called "surgical annulus" of the valve. The sewing of cardiac prosthesis follows this very line but this actually creates a distortion of the aortic wall, due to the fact that the prosthesis has a planar sewing ring.



The crenated insertion line represents the hemodynamic ventriculo-aortic junction: everything proximal (i.e. "*underneath*") this line, is "ventricular" while everything distal (i.e. "*above*") this line, is "*aortic*". The sinuses are "aortic" and the interleaflet triangles are "ventricular" (Figure 3).

Figure 3: Advanced dissection of the heart. Posterior view

This image demonstrates the intimate structure of the aortic root. The three sinuses are well visible (L, R and NC). The interleaflet triangles between the sinuses are also visible, except the anteriorly-located triangle between the right and left sinuses. The triangle between the L and NC sinuses merges inferiorly with the mitral-aortic curtain. The triangle between the NC and R sinuses in continuous with the membranous septum (MS) of which the tricuspid valve was retracted

Thus, the interleaflet triangle between the left and right aortic cusps, corresponds to the pulmonary root (the outlet septum); distally, closer to the commissure, this corresponds to the pericardial cavity between the two major arterial trunks. The interleaflet triangle between the left and non-coronary aortic cusps corresponds to the pericardial transverse sinus and the left atrium. It merges "inferiorly" with the mitral-aortic curtain.

The interleaflet triangle between the non-coronary and right aortic cusps shows even more complex relations: the inferior part incorporates to the membranous septum which is divided by the insertion of the tricuspid valve into a interventricular and respectively, an atrioventricular part. Superiorly, the apex of this triangle (which is continuous with the atrioventricular part of the membranous septum), separates the LVOT from the right part of the pericardial transverse sinus.

The three commissures are joined at the level of the supravalvar crest (sinutubular junction). The integrity of this structure is a "sine qua non" for the normal functioning of the aortic valve. Effacement of the commissures leads to aortic insufficiency in spite of normal aortic cusps. The surgical techniques of aortic repair envisage the reconstruction of the normal shape and dimensions of this "ring".

In the human species, there is a normal asymmetry of the aortic sinuses, with R > NC > L. Thus, the plane of the "anatomical annulus" and the plane of the "sinutubular junction" are not parallel but they form an angle called "the aortic tilt angle" of 5.47° (1). This, together with some local structural differences, might explain the different involvement of the aortic sinuses in morbid conditions as aortic aneurysms and dissection.

Clinical and surgical applications

The coordinated action of all the structures forming the aortic root is necessary for the proper function and adaptation of the aortic valve.

The aortic root has a wider part corresponding to the sinuses; proximal and distal to these, the root is narrower. Ultrasound examination includes measurements at various levels. Correct measurements are highly important. Usually, measurements are performed at the bottom ("nadir") of the sinuses, at the widest point of the sinuses and at the level of the sinutubular junction. Great attention must be offered to the points of reference: if measurements were taken from the basal attachment of one leaflet to the homologous point of the adjacent leaflet (as frequently shown in bidimensional diagrams), this would not measure the full diameter of the outflow tract but a secant across the root; similarly, for the widest points of the sinuses or the sinutubular junction (Figure 4).

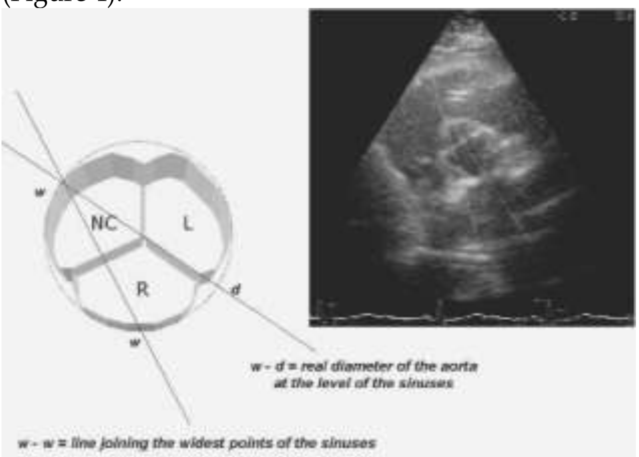


Figure 4: Pitfalls in measuring the aortic diameters

An imaginary measurement of the diameter at the level of the widest points of the sinuses. Should the echographist measure the distance between the widest point s of two adjacent sinuses (w-w), a secant will be obtained and not the true diameter (w-d) at this level (see also text for details)

The diameter of the sinutubular junction is statistically smaller than the diameter of the anatomical annulus.

Various morbid conditions affect the aortic root differently. Restoration of the normal shape and dimension in circumferential and longitudinal directions (6) is not an easy task and this requires a periodical feed-back with data on larger series both in the living patient, in normal individuals and comparisons with anatomical studies.

Apparently some areas were less considered or overlooked: pathologic dilatation of the aortic root includes the interleaflet triangles (7) too and surgical approaches should address these areas as well. The mitral-aortic curtain (the intertrigonal space) allegedly doesn't dilate, although recent studies deny this assertion (8, 9).

Compared to the atrioventricular valves, the aortic valve has no subvalvar apparatus and the proper functioning of the cusps require a proper environment (10). The surgical techniques which envisage restoration and plasty of the aortic root must obey some basic principles: the aortic valve must be preserved and resuspended in as near normal environment as possible; all abnormal tissue that can be excised, should be excised; any remaining abnormal tissue must be secured to prosthetic material; the sinuses of Valsalva and the sinutubular junction must be reestablished.

Conclusion

A good understanding of the structure and function of the aortic root is essential for a complete diagnosis and for choosing the proper surgical technique. The function and integrity of the aortic valve, although structurally apparently simpler when compared to the atrioventricular valves, depends more on the adjacent elements and on the hemodynamic factors. The concept of "annulus" or of various "annuluses" can sometimes be limiting and even misleading and should be if not discarded, at least included into broader concepts such as the one that the 13/CT in continued by the aorta within few centimeters, that between the distal LVCT and the ascending aorta, the sinuses represent the dilated part of the aorta which is crossed by the crown-shaped insertion of the cusps. Measurements at various well-determined levels can reveal morbid conditions even in the incipient phase and can guide the surgical therapy.

Further research and more complex models of normal and altered physiology of the aortic root are needed, as many new elements are continuously added (11-14).

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Part 2: Surgical perspective

Abstract

The aortic valve is considered into the broader concept of aortic root or aortic valvar complex. Numerous elements function in a coordinated manner driven by the hemodynamic factors. In spite of an apparently simpler organization when compared to the atrioventricular valves, the approach toward the aortic root requires a more detailed diagnostic approach and for a more selected surgical solution. New interesting and useful details are offered by a multitude of studies, both in basic research and respectively, in the clinical series. This review presents the main criteria, indications and surgical solutions with special emphasis to aortic repair, valve-sparing techniques and offers a paradigm for the interdisciplinary dialogue.

Key words: *Aortic root, Aortic valve, Aortic valve repair, Aortic valve replacement, Surgical technique*

Introduction

The more recent successful and widely accepted repair of the atrioventricular valves together with the significant progress in myocardial protection and the reduced rate of complications in redo cardiac operations, have encouraged a new interest in aortic reconstruction. Most of the techniques described and applied nowadays, have been intermittently used over the last 40 years; many of the earlier failures being however related to technical problems and often clouded by the need of simultaneous mitral surgery.

A major step forward was taken with the advent and development of echocardiography which has allowed a superior diagnostic evaluation and has contributed to the better understanding of the main mechanisms of aortic disease and that represents the most valuable diagnostic tool in the follow up of the patients.

Anatomic and functional background

A careful analysis of the lesions encountered, is mandatory The aortic valve must be considered into the larger concept of "aortic root" or "aortic valvar complex" which includes the distal left ventricular outflow tract (LVOT), the basal ring (BR), the sinuses of Valsalva and the interleaflet triangles, the sinutubular junction (STJ) and the proximal tract of the ascending aorta. The functional significance of each of these components was already discussed in the first part of this review (1, 2).

In man, the aortic sinuses have a normal asymmetry (probably of hemodynamic significance): R > NC > L (right > non-coronary > left). An aortic tilt angle (of 5.47°) between the planes of the BR and of the STJ results. The valve cusps are correspondingly of different sizes (3). The three sinuses differ in their distensive capacity with: R > L > NC (4). This very pattern is manifested and holds true both in radial as well as in longitudinal direction. The functional significance of the sinuses of Valsalva can be resumed by the fact that they induce powerful vortices that facilitate valve closure, reduce leaflet stress, reduce the regurgitant fraction from 23% to 4% and probably induce a washing effect within the sinuses, preventing thrombosis (5, 6). These effects contribute to the proper coronary flow.

The importance and surgical relevance of the aortic sinuses has been recently demonstrated and has lead to the implementation of new techniques (7, 8). Re-creation of the sinuses allows a more physiologic function of the aortic cusps and contributes to their longer-standing resistance. As stated previously (4), the sinuses distend in longitudinal direction too and the ideal aortic prosthesis should have this characteristic added. Implantation of larger coronary buttons is recommended in order to avoid anastomotic complications but in the mean time, such circumferential sutures alter the distensibility of the aortic sinuses.

The aortic valve cusps have however a more complex structural organization (9, 10) and further research will undoubtedly will endow the surgeon with new important details (11).

Etiology and particularities

Aortic root pathology can be classified by using multiple criteria. Lesions can be located at the various levels of the aortic root complex (Table 1). Lesions can manifest predominantly as stenotic, insufficient or mixed (the major causes of aortic insufficiency are presented in Table 2).

Table 1: Aortic root pathology - Major categories

Aortic root pathology			
Level	**Etiology**	**Characteristics**	**Pathology**
Subvalvar (25-30%)	Subaortic membrane/tunnel	Stenosis (annulus-like or tunnel-like)	Diffuse of localized forms Circumferential narrowing from the basal ring to 1-3 cm. proximal
	Accessory mitral valve tissue	Stenosis (crescent-like stenosis)	Abnormal valvar tissue that bulges into the left ventricular outflow tract
	Abnormal insertion of the AML	Stenosis	AML inserted on the septum directly or by abnormal chordae Cleft AML with abnormal chordae into the LVOT Parachutte mitral valve
	Deviation of the outlet septum Restrictive bulboventricular foramen	Coarctation of the aorta *Interrupted aortic arch* *Single-ventricle complexes*	Both static and dynamic components of the obstruction Presence of SAM helps in the differential diagnosis
	Shone complex	*Subvalvar aortic stenosis* *Supravalvar mitral ring* *Parachute mitral valve* *Coarctation of the aorta*	
	Hypertrophic cardiomyopathy	*Primary cardiac muscle disease** *Aortic valve usually normal*	
Valvar (70%)	Unicuspid acommissural	Stenotic from birth	Dome-shaped valve Pinpoint opening
	Unicuspid unicommissural	Stenotic	Eccentric orifice Two raphes present
	Bicuspid	Stenotic	Leaflets equal in size or discrepant
		Insufficient	Alterations of the aortic wall Left-right orientation Antero-posterior orientation

	Tricuspid	Stenotic	Gelatinous, thick leaflets
		Insufficient	May become stenotic late in life
		Mixed forms	Calcifications
	Quadricuspid	Insufficient	
Supravalvar (<5%)	Williams-Beuren syndrome (AD)	- Supravalvar aortic stenosis - Mental retardation - Elfin facies - Dysplasia and hypoplasia of dentition - Osteosclerosis (skull and metaphyses) - Failure to thrive - Hypercalcemia (in infancy) - Associated lesions: peripheral pulmonary stenosis, generalized arteriolar narrowing	Hourglass deformity Fibrous membrane Diffuse narrowing (tubular, hypoplastic type) Non-stenotic supravalvar aortic membranes or bands**

** Stenosis of the LVOT may also occur secondary to metabolic and other disorders: glycogen storage disease, rhabdomyoma, endocardial firboelastosis*

*** Strands crossing the aorta far distal to the aortic valves; possible of aortic origin - remnants of the fifth aortic arch. Other forms of aortic stenosis associated with complex cardiac malformations are not discussed in this manuscript: conoventricular malalignement (ventricular septal defects with interrupted aortic arch), complete transposition of the great arteries with ventricular septal defect, atrioventricular canal defects, restrictive bulbo-ventricular foramen in single-ventricle hearts, ventricular inversion, hypoplastic left heart syndrome or complex.*

Table 2: Main causes of aortic regurgitation

Congenital (rare)
Aortic-left ventricular tunnel (the most frequent cause in children)
Supravalvar aortic stenosis
Subvalvar aortic stenosis with jet lesion on the aortic valve
Quadricuspid aortic valve (late presentation)
Congenitally stenotic bicuspid aortic valve
Ventricular septal defect (supracristall VSD)
Rheumatic
Post-interventional (aortic balloon valvotomy)
Annuloectasia
Infective endocarditis
Virus arteritis
Trauma
Autoimmune (relapsing chondritis, Wegener granulomatosis)
Aneurysm of sinus of Valsalva / aneurysm of the aortic root
Aorto-left ventricular tunnel
Aortic aneurysm and dissection

The diameter at the level of the BR is greater than at the level of the STJ (12). The importance of this detail in the disease process and its surgical relevance have been known for almost 20 years (13). Moreover, these measurements should be referred to the body surface area (BSA) in the individual patient (14).

A particular form of aortic root pathology is represented by the sinus of Valsalva aneurysm (Tables 3 and 4). Dilatation of more than one aortic sinus is classified as aneurysm of the aortic root and asks for amore complex surgical approach. Within the wide spectrum of disease, the dilatation of the aortic sinuses represents probably the first step. The inter-leaflet triangles also dilate (15) with consequent dilatation at the level of the BR. This is reflected by the fact that the most efficient surgical solutions are represented by those in which the BR is reshaped and fixed, either by circumclusion or by fixation to prosthetic material. Aneurysm of the aortic root can be accompanied by dilatation at the level of the STJ. Some authors make a clear distinction between the simple dilatation of the aortic root and the effacement of the STJ (16).

Table 3: Sinus of valsalva aneurysm. Simplified scheme for classification

Sinus	**Clinical aspects**				**Chamber of termination**					
	Acquired	**Congenital**	**Ruptured**	**Non-ruptured (protruding onto)**	**RA**	**RV**	**LS**	**LV**	**PA**	***Peri-cardium***
Left	+		+			+				
Right										
NC										

Table 4: Sinus of valsalva aneurysm - Acquired forms

Atherosclerosis			
Infection	**Primary (mycotic, endocarditis)**	**Secondary periaortic abcess (tuberculosis, pancreatitis) syphilis (luetic aortitis)**	
Inflamatory	**Autoimmune**	**Scleroderma, Periarteritis nodosa, Reiter's syndrome, lupus, ankylosing spondylitis, juvenile rheumatoid arthritis**	**Aortic valve and coronary arteries may become involved**
	Takayasu, Giant cell artheritis, Kawasaki disease, Behcet's disease		
Traumatic	**Penetrating Blunt Surgical Procedural**		
With late presentation, ethiologic classification might become difficult			

Indications for surgery

The main indications for surgery are given in Tables 5, 6 and 7. Particular cases should stimulate detailed analyses and interdisciplinary communications especially between the echographist, surgeon and anesthesiologist. Mixed lesions or associated valvar or coronary disease, render the therapeutic choice more difficult.

Moreover, the choice for a particular surgical technique and a particular type of aortic valve prosthesis or repair (Table 8) is influenced and depends by several inter-related factors such as: patient's age, concomitant disease (valvar, coronary), the presence of atrial fibrillation, the center's experience with implantation of a particular type of prosthesis, the preference of the referring cardiologist, attending surgeon and the patient. Often, more than one type of prosthesis or technique appears to be suitable for the individual patient and the decision is made rather arbitrarily (17).

Table 5: Aortic valve stenosis - Criteria for surgery

Area	**< 0.75 cm$^{2*)}$**
Pressure gradient	**dP max**
	dP medium
Transvalvar flow	**Doppler velocity**
	> 4-5 m/s
Symptoms	**Present (angina, dyspnea, syncope)**
	Absent
LV systolic dysfunction	**EF < 50%**
Abnormal response to exercise	**Dobutamine challenge test**

*) The normal aortic valvar area = 3-4 cm^2. An area of less than 0.75 cm^2 is generally regarded as severe stenosis, but it may still be adequate for small patients (small BSA).

Table 6: Aortic stenosis - Main surgical indications

Severe aortic stenosis plus:	**Symptoms**
Severe aortic stenosis in patients needing:	**CABG**
	Surgery on the aorta
	Surgery on other valves
Moderate aortic stenosis in patients needing:	**CABG**
Severe aortic stenosis in asymptomatic patients with:	**LV systolic dysfunction**
	Abnormal response to exercise (*hypotension*)

Table 7: Aortic insufficiency - Main surgical indications

NYHA III-IV	**LVEF > 50%**
NYHA II	**LVEF > 50% but diminishing at serial examinations**
Angina (Canadian class II-IV)	**± Coronary artery disease**
Asymptomatic or symptomatic patients with:	**LVEF 25-49%**
Asymptomatic patients with:	**LVEF > 50% but with dilating LV:**
	LVESD > 55 mm and LVEDD > 75 mm
Patients needing	**CABG**
	Surgery on other valves
	Surgery on the aorta

In patients with aortic regurgitation, other ethiologies should be also considered: hypertension, cardiomyopathy, coronary artery disease

Table 8: Aortic valve replacement

Contraindications	Complications	Special points	Cost/Efficiency
	Mechanical valve		
Absolute contraindications for anticoagulation Women of child-bearing age	Perioperative morbidity and mortality. Mechanical failure. Thromboembolism (4% per year). Endocarditis. Bleeding. Complications are higher in older patients	Long-term durability is proven specially in bileaflet mechanical valves	Cost of surgery is high but operation is effective when compared with any other therapeutic measures. Less likely to require a reoperation
	Stented bioprosthetic valve		
In patients with life expectancy of > 10-15 years, unless cases with contraindication to anticoagulation	Perioperative morbidity and mortality. Endocarditis. Structural failure (especially in young subjects and renal failure). Approximately 30% of grafts fail within 10-15 years after implantation	No need for anticoagulation. Higher risks related to reoperation. Surgical difficulties in small or bicuspid aortas. Excision difficult in redo operations.	Frequent need for reoperation: higher costs.
	Stentless bioprosthetic valve		
Significant aortic root dilatation	- Perioperative morbidity and mortality and endocarditis: less than with other valves. - Structural failure (long-term data still not available)	- No need for anticoagulation. - Better hemodynamics, specially indicated in patients with small aortas. - Durability uncertain (maybe more than stented valves). - Surgical procedure more complicated	Need for reoperation: higher costs.

Homograft			
No specific contraindications	Structural failure and endocarditis might be less than with other valves	Limited supply. Durability uncertain. Failure rate 10-20% at 10-15 years. More complex surgical technique. Specially in women of child bearing age and younger patients	When specially indicated, costs do not represent a limiting factor
Autograft - Ross procedure			
- Coronary artery disease. - Still debated in Marfan, rheumatic pathology, bicuspid aortic valve	- Dilatation of the neo-aorta and aortic insufficiency. - Need for homograft exchange. Endocarditis less frequent	- Limited supply of homograft. - Surgically demanding. - Specially indicated in young patients and women of child bearing age, patients with endocarditis	see above

Indications for valve-sparing operations

As in the case of the atrioventricular valves, the repair techniques addressed to the aortic complex envisage the preservation of the patient's own valve while stabilizing the lesion, slowing the disease process, postponing the need for valve replacement - elements which allow a better quality of life (especially by eliminating the need for anticoagulation), permit the completion of the growth process (in children), or offer the possibility for pregnancies (in women of child-bearing age).

Aortic valve repair represents a palliation but it can be of extreme benefit in selected patients. In this respect, another category needs to be specially referred: acute aortic dissection. The classical patient with aortic dissection comprising the ascending aorta, arch and descending tract, would theoretically need a Bentall approach and subsequent extension with the elephant trunk technique. Another surgical approach can be proposed: valve-sparing procedure (e.g. T. David), treating the arch but leaving the descending tract of the aorta for subsequent evaluation. The patient is not given anticoagulation and under anti-hypertensive therapy, the remaining dissection can be transformed into a chronic dissection thus, the thrombosis of the false lumen is facilitated.

The role of the repair techniques in endocarditis is limited, due to the presentation of the disease, usually as acute aortic insufficiency, with annular destruction and abcesses. In such cases, root replacement with a stentless valve, homograft or Ross procedure are the techniques of choice.

Surgical technique

The principles for the surgical repair are presented in Table 9.

Table 9: Surgical principles for aortic valve repair 27

<table>
<tr><td colspan="3">Valve-sparing operations. Principles
Aortic valve must be preserved and resuspended in as normal environment as possible
All abnormal tissue that can be excised must be excised
Any remaining abnormal tissue (valvar or annular) must be secured to prosthetic material
The sinuses of Valsalva and sinutubular junction must be reestablished</td></tr>
<tr><th>Cusp morbidity</th><th>Major cause</th><th>Surgical solution</th></tr>
<tr><td rowspan="3">Normal</td><td>Annular dilatation</td><td>Circumclusion</td></tr>
<tr><td>Dilatation at STJ</td><td>Commissural plication
Reshaping of the STJ</td></tr>
<tr><td>Cusp perforation or rupture</td><td>Suture
Patch closure</td></tr>
<tr><td>Increased</td><td>Elongation of the free edge</td><td>Triangular resection
Resuspension
Commissural resuspension*</td></tr>
<tr><td rowspan="4">Reduced</td><td>Commissural fusion</td><td>Commissurotomy</td></tr>
<tr><td rowspan="3">Thickened leaflet</td><td>Unrolling / Thinning
Enhancement of the STJ</td></tr>
<tr><td>Cusp extension**</td></tr>
</table>

* *for example in aortic root dilatation*
** *all three cusp remnants are equal*

The classification is extrapolated from the original scheme proposed by Carpentier in the case of mitral valve disease, this representing the first step toward the standardization of such surgical procedures. Nevertheless, larger series are still needed for a validation of these principles and surgical gestures.

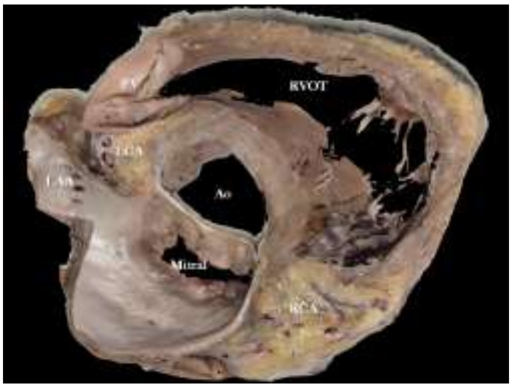
• **BR ("annular") level.** In case of stenosis, two classical techniques are applied: Nicks and Monouguian (18, 19). These techniques do not interfere with the vascularization of the aortic root but allow only limited enlargements (not more than one size). More extensive enlargements are obtained at the level of the outlet septum, but the vascularization of the septum can be altered (20). In case of aortic insufficiency annular circumclusion or fixation to prosthesis, are the techniques of choice.

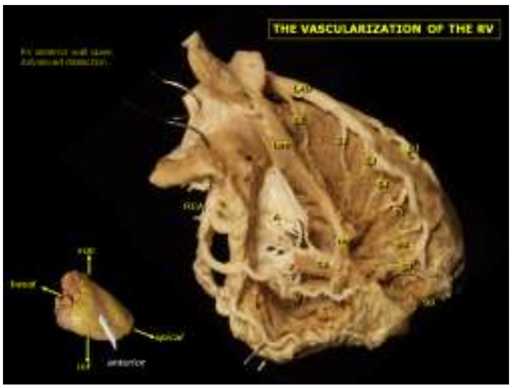
• **Aortic sinuses.** Stenosis can be addressed by the patch aortoplasty (one sinus), the Doty extended aortoplasty (two sinuses) or Brom repair (three sinuses). Such techniques have the major disadvantage of not creating physiologically-distensible neo-sinuses of Valsalva. Dilation of the aortic sinuses "per se" is not regarded by some authorities as a cause of aortic insufficiency if not accompanied by effacement of the STJ or dilatation of the BR (16). But more recent studies reveal the functional importance of the sinuses of Valsalva (21) and the importance of re-creation of the sinuses, for example as revealed by new technical achievements (22).

• **Sinutubular junction.** Re-shaping the STJ, and adapting it to the BR and to the patient's BSA represent important steps both in valve-sparing operations and in replacements using the root technique. Circumclusion of the STJ has been abandoned and replaced by commissural plication or re-shaping by using prosthetic material.

• **Special situations.** Repair may be more difficult in cases with eccentric aortic regurgitation (23). Re-modeling of the aortic sinuses, re-shaping and fixation of the STJ is performed in the Jena technique: commissures are re-suspended, the sinuses of Valsalva are re-modeled by J or U-shaped mattress sutures and supravalvar prosthesis is inserted (24).

However, the dilated aortic root shows particular mechanical properties (25) with a non-linear stress-strain behavior. The aortic wall behavior is anisotropic with different elastic properties at the media and adventitia level. Surgical procedures and planning should take into account these changes with disease: aortic root and valve repair are precluded by the intrinsic changes in the wall. Contrary to what has been accepted so far, changes into the very structure of the aortic wall precede the formation of aneurysms (26). This represents an important detail regarding the operative approach in the way that the results of the surgical repair might be clouded, limited or contra-indicated by intrinsic modifications of the aortic wall. Larger series, histopathologic and longer-term follow-ups will be needed in order to delineate better the indications and the techniques of the procedures to be applied. Special points to be addressed are the Marfan syndrome, the bicuspid aortic valve and rheumatic disease.





List of abbreviations and Legend (to all figures):

Ao	*= ascending aorta*
BR	*= basal ring (imaginary line uniting the nadir of the aortic cusps)*
BSA	*= body surface area*
IAS	*= interatrial septum*
L	*= left aortic (left coronary) sinus*
LA	*= left atrium*
LAA	*= left atrial appendage (left auricle)*
LMCA	*= left main coronary artery (left main trunk)*
LT	*= left fibrous trigone of the heart*
LVOT	*= left ventricular outflow tract*
MS	*= membranous septum*
NC	*= non-coronary sinus (non-facing sinus) / non-coronary cusps and sinuses of the aorta*
PT	*= pulmonary trunk*
R	*= right aortic (right coronary) sinus*
RA	*= right atrium*
RAA	*= right atrial appendage (right auricle)*
RCA	*= right coronary artery*
ROVT	*= right ventricular outflow tract*
RT	*= right fibrous trigone of the heart*
STJ	*= sinutubular junction (supravalvar crest)*

Conclusions

In spite of its apparent simplicity, the aortic valve is included and functions in a more complex *millieu* in which all the constituting elements work in a coordinated manner. New studies are still needed in order to understand the functional anatomy of the aortic root and to select the best surgical solutions.

Aortic valve repair and reconstruction represent palliative measures but they can be the ideal solution in well-selected patients, in spite of their limitation in time. As much important as the surgical anatomy of the diseased valvar complex, is the status of the left ventricle which can be irreversibly compromised under the long-standing stresses induced either by the disease process or by incomplete surgery. A well-indicated and performed aortic valve repair should promote the reversal of ventricular alterations.

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Does EuroSCORE relate to direct costs in open heart surgery?*)

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Abstract

The aim of this study is to determine if the additive EuroSCORE algorithm can predict cardiac care unit stay and direct costs of cardiac surgery. We evaluated all patients who underwent open heart surgery at our institution between July 1, 2005 and November 24, 2005. EuroSCORE was collected prospectively for all cases. Direct variable costs (disposable materials and drugs) were calculated for the surgery and cardiac care unit stay for each patient. The postoperative complications, the duration of postoperative ventilator support, length of stay in cardiac care unit (CCU-LOS) were studied. Values are given as mean ± standard deviation. Univariate linear regression analysis was used to test the correlation between the EuroSCORE and either costs, duration of ventilator support or CCU-LOS. Of the 133 patients enrolled 63.2% were males, mean age 55.9 ± 12.5 ys. The mean CCU-LOS was 4.4 ± 5.7 days and the mean duration of post-operative ventilator support was 29.3 ± 97.8 hours. According to EuroSCORE, 55 patients (41.4%) were at low, 41 (30.8%) at medium, and 37 (27.8%) at high risk. The relationship EuroSCORE vs. direct costs is, respectively: EuroSCORE 0-2 = 2155 ± 658 euro; 3-5 = 2421 ± 1086; ≥ 6 = 3381 ± 3380. Costs were correlated with preoperative assessed risk with a correlation coefficient of 0.424 ($p < 0.001$). CCU-LOS and the duration of postoperative ventilator support were correlated with EuroSCORE with a correlation coefficient of 0.266 ($p < 0.01$) and 0.175 ($p < 0.05$), respectively. In our study is a strong correlations between the EuroSCORE algorithm and both direct costs and CCU-LOS. This indicates that preoperative prediction of CCU-LOS and costs may be used in clinical practice.

Key words: *EuroSCORE, risk assessment, cardiac surgery, intensive care unit stay, cost assessment*

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Rezumat

Scopul studiului este de a determina dacă algoritmul EuroSCORE are valoare predictivă cu privire la durata şederii în unitatea de terapie intensivă cardiacă şi la costurile directe ale chirurgiei cardiace. Am evaluat toţi pacienţii care au suferit intervenţii chirurgicale cardiace în instituţia noastră între 01 iulie 2005 şi 24 noiembrie 2005. EuroSCORE a fost calculat prospectiv la toţi pacienţii. Costurile variabile directe (consumabilele de unică folosinţă şi medicamentele) au fost calculate pentru intervenţia chirurgicală şi pentru şederea în unitatea de terapie intensivă pentru fiecare pacient. Au fost studiate complicaţiile postoperatorii, durata ventilaţiei mecanice, durata şederii în serviciul ATI. Valorile sunt exprimate ca medii ± deviaţia standard. Analiza prin regresie univariată liniară a fost utilizată pentru a testa gradul de corelare între EuroSCORE şi costuri, durata ventilaţiei mecanice şi/sau durata şederii în ATI. Din cei 133 pacienţi înrolaţi 63,2% au fost bărbaţi, cu vârsta medie 55,9 ani ± 12,5 ani. Durata medie a şederii în ATI a fost de 4,4 ± 5,7 zile iar durata medie a suportului ventilator postoperator a fost 29,3 ± 97,8 ore. Conform EuroSCORE 55 de pacienţi (41,4%) au fost catalogaţi ca având risc mic, 41 (30,8%) risc mediu, iar 37 (27,8%) risc mare. Relaţia EuroSCORE/ costuri a fost: EuroSCORE 1 - 2 = 2155 ± 658 Euro; EuroSCORE 3 - 5 = 2421 ± 1086 Euro; EuroSCORE ≥ 6 = 3381 ± 3380 Euro. Costurile s-au corelat cu riscul operator apreciat preoperator prin EuroSCORE cu un coeficient de corelare de 0,424 ($p < 0,001$). Durata şederii în ATI şi durata ventilaţiei mecanice postoperatorii s-au corelat de asemenea cu EuroSCORE cu un coeficient de corelare de 0,266 ($p < 0,01$) şi, respectiv, 0,175 ($p < 0,05$). În studiul nostru există o corelaţie puternică între algoritmul EuroSCORE şi costurile directe şi durata şederii în ATI. Acest fapt arată că predicţia preoperatorie a duratei de şedere în ATI şi a costurilor poate fi utilizată în practica clinică.

Background

Risk stratification and outcomes analysis will have an increasing role in cardiac surgery. The methods of risk analysis are straightforward but are in their early stages. The goal of risk adjustment in the analysis of outcomes is to account for the contribution of patient-related risk factors, in order that patient outcomes can be used as an indicator of the quality of care rendered by physicians and hospitals. The future will undoubtedly see refinements in risk-adjustment methods and increasing use of these techniques at all levels of health care delivery, including the distribution of health care financial resources (1, 2, 3).

The EuroSCORE staging system is a large-scale used system used to assess operative risk in cardiac surgery (4). The EuroSCORE model strongly correlates to in-hospital operative mortality in cardiac surgery (5).

Purpose

It is however not proven whether the EuroSCORE staging system predicts the costs, duration of intensive care unit stay and duration of mechanical ventilation. The aim of this study is to determine whether the EuroSCORE staging system can predict duration of mechanical ventilatory support, cardiac care unit length of stay and direct costs in patients undergoing cardiac surgery.

Materials and methods

Our study is prospective and observational. We enrolled all open heart surgery patients operated on between July 1, 2005 and November 24, 2005. The data collected were: The EuroSCORE parameters, Direct variable costs (disposable materials and drugs), Duration of ventilator support (DVS), Cardiac care unit length of stay (CCU-LOS).

Statistical analysis

The values are given as mean ± standard deviation. Univariate linear regression was used to test the correlation between EuroSCORE and either cots, CCU-LOS and DVS.

Results

Of the 133 patients enrolled 63.2% were males, mean age 55.9 ± 12.5 years. The mean CCU-LOS was 4.4 ± 5.7 days and the mean duration of postoperative ventilator support was 29.3 ± 97.8 hours.

We assessed a predominantly male population, with a high incidence of non-CABG as surgical procedure: in 57% of patients a non-CABG surgical procedure was performed. 10.5% of patients were operated in an emergency setting. The overall mortality was 3%.

Table 1: Population characteristics according to EuroSCORE assessment

EuroSCORE variables	No pts = 133	%
Female	50	37.60
Mean age (years)	55.1±12.4	
Chronic pulmonary disease	22	16.50
Vascular peripheral disease	6	4.51
Cerebrovascular disease	2	1.50
Infectious endocarditis	4	3.00
Critical preoperative state	12	9.00
Unstable angina	8	6.00
Pulmonary artery pressure > 60 mmHg	17	12.70
Creatinine > 2mg/dl	27	20.30
Intervention other than CABG	76	57.00
Thoracic aortic surgery	6	4.50
Post infarction ventricular septal rupture	1	0.70
Previous MI (< 90 days)	8	6.00
LVEF < 30%	1	0.75
Re-operation	7	5.20
Emergency	14	10.50
30-days mortality	4	3.00

Table 2: Grouping of patients according to EuroSCORE

Parameters	EuroSCORE		
	0-2	3-5	> 6
No pts (%)	55 (41.4%)	41 (30.8%)	37 (27.8%)
CCU-LOS (days)	2.8 ± 1.3	5.0 ± 8.1	6.2 ± 6.3
DVS (hours)	9.3 ± 4.2	36.3 ± 123.9	44.7 ± 81.6
Direct costs (€)	2155 ± 658	2421 ± 1086	3381 ± 3380

The patients were balanced according to the SuroSCORE: 41.4% were staged as low risk (EuroSCORE 0-2), 30.8% were staged as intermediate risk (EuroSCORE 3 - 5) while 27.8% were staged as high risk (EuroSCORE > 6).

The relationship EuroSCORE vs. direct costs is, respectively: EuroSCORE 0-2 = 2155 ± 658 euro; 3-5 = 2421 ± 1086; > 6 = 3381 ± 3380. Costs were correlated with preoperative assessed risk with a correlation coefficient of 0.424 (p < 0.001). CCU-LOS and the duration of postoperative ventilator support were correlated with EuroSCORE with a correlation coefficient of 0.266 (p < 0.01) and 0.175 (p < 0.05), respectively.

Conclusions

In our study we found a strong correlation between the EuroSCORE staging system and both direct costs and CCU-LOS. This indicates that pre-operative prediction of CCU-LOS and costs may be used in clinical practice.

The EuroSCORE model can be used to predict direct perioperative costs and identify patients with different levels of resource consumption.

Table 3: Correlation between EuroSCORE staging and CCU-LOS, DVS and direct costs

Correlation coefficient	p	
CCU-LOS vs. EuroSCORE	0.266	< 0.010
DVS vs. EuroSCORE	0.217	< 0.050
Direct costs vs. EuroSCORE	0.424	< 0.001

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The cardiopulmonary by-pass and the neuroprotection*)

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Abstract

The development of extracorporeal circulation and perfusion's techniques let us improve the complexity of the open-heart surgery procedures. In the same time we become more interested in improving the techniques of protection for the organs found under the risk of imbalance between oxygen supply and demand. The increase of patients' mean age and also the increase of the neurological dysfunction's incidence after ECC determined us to develop pharmacological and non-pharmacological techniques in order to improve the neuroprotection. The current review tries to set up the new concept of strategies for neuroprotection in cardiac surgery.

Rezumat

Dezvoltarea tehnicilor de circulație extracorporeală şi perfuzie au permis creşterea complexității intervențiilor chirurgicale cardiace. Totodată, s-a născut preocuparea îmbunătățirii strategiilor de protecție a organelor aflate sub riscul imbalantei aport/consum de O2. Creşterea mediei de vârstă a pacienților şi a incidenței disfuncției neurologice post CEC au impus dezvoltarea strategiilor farmacologice şi nonfarmacologice în vederea îmbunătățirii neuroprotecției.

The development of extracorporeal circulation and perfusion's techniques represented the necessary support for improving and increasing the complexity of cardio-vascular surgeries' techniques, during the last 50 years.

Thus, in the last decades, there were done complex surgical procedures like the correction of severe congenital heart malformations, complex adult surgeries (change of one or two valves and/or CABG under cardiopulmonary by-pass) and transplant of heart and/or lungs.

Once the techniques of ECC were largely used the next problem was to achieve the best biocompatibility (at structural and physiological level) between the heart-lung machine, its circuits and the human body.

The basic principles of the ideal ECC are:

- providing the necessary oxygen supply for each organ, in real time;
- decreasing the systemic inflammatory respond. The idea of "organ protection" comes from these basic principles and it supposes the usage of drugs and technique

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procedures in order to maintain at least the each organ functionality (ideally is to maintain the morfo-functionality of the organs).

Certainly, at the beginning the attention was guided to the myocardial protection which was considered the most vulnerable organ during the cardiac surgery. Later, once the surgical techniques were improved, the average age of the patients increased and the operations became much more complex, it was discovered the significant increase of other organs dysfunction after ECC (kidney, mesentery, brain and lungs). Obviously, the attention was focused on discovering the causes and therapeutically methods in order to decrease the incidence of these complications [1, 2].

The lonely neurological dysfunctions after ECC represents the most frustrate complication because of its socio-economical and emotional impact on both family and society.

A cardiac surgery, which was done without complications on lungs, kidneys or mesentery, can't be considered a therapeutically success if the patient remains dependent on family and society because he has irreversible neurological damages (Figure 1) [1, 3, 4].

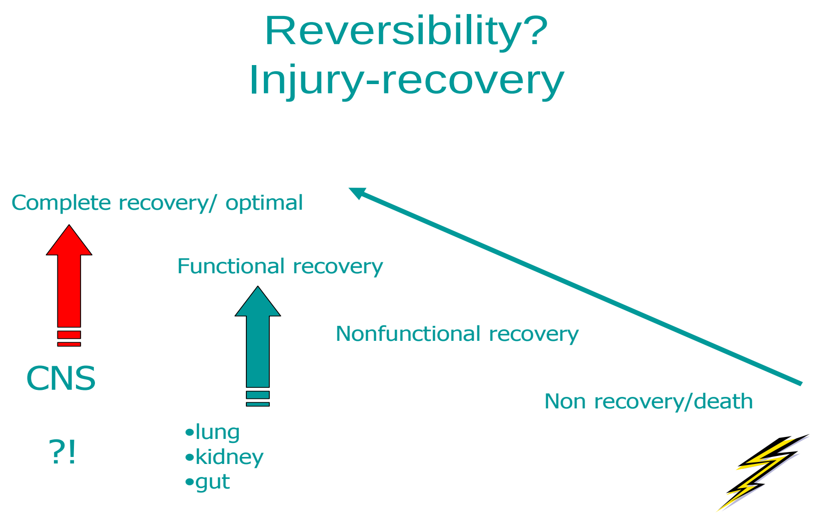


Figure 1

The damage of any tissue goes to the structural and functional loss of that zone. The recovery process (healing) is initiated immediately after injury (the healing mechanisms are genetically coded and they are already initiated just before the injury is done). Certainly, the recovery process may not be possible (no recovery), that will mean the complete loss of that tissue (structurally and functionally loss), or it may recover completely (the ideal situation). Between the two limits there are different tissue recovery grades:

• morphological but not functional recovery;

• functional recovery but with morphological damages.

For lungs, kidneys and mesentery the functional recovery is enough even if the healing process damages the morphological structure. The optimum recovery for CNS (without residual lesions) supposes a whole structural and morphological recovery (there is no perfect functional recovery without structural recovery). So the idea of reversibility of the damage – recovery mechanism is not recognized for CNS [1, 3]. The interfering between economically, social and family psycho-emotionally problems are enormously for a patient with severe CNS dysfunctions, changing a therapeutically success in a failure which affects not only the patient life but also the life of the family. Also, the mortality immediately after surgery is higher at the patient with CNS damages (see table 1) and the stroke patients survival versus non-stroke patients survival is lower (see figure 2) [3, 5, 8].

Table 1: Stroke incidence related to type of surgery (Johns Hopkins Hospital 1994-2004)

Type of surgery	% stroke	% stroke identified in first 48 h postop.
CABG	4.1	84
valve	3.1	65
CABG + valve	7.9	76
CABG + others	7.2	80
Aortic root surgery	8.7	83
others	3.6	59

Stroke and Encephalopathy After Cardiac Surgery: The Search for the Holy Grail; Stroke, 2006; 37; 284-285; originally published online Dec 22, 2005;

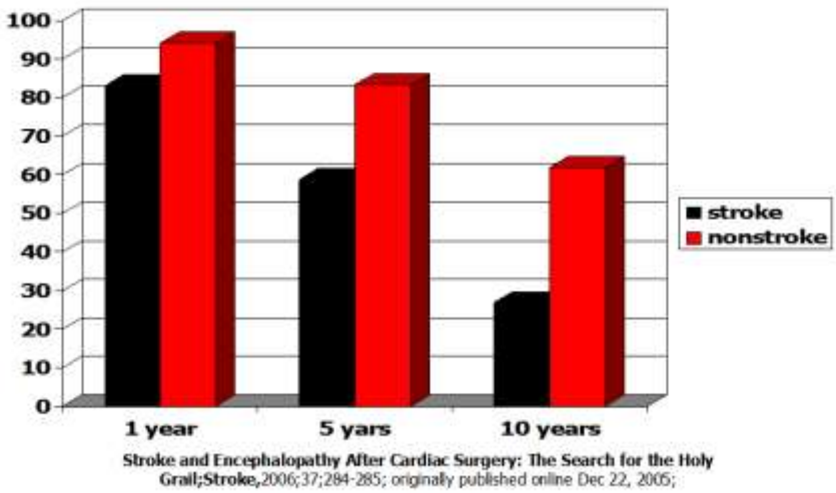


Figure 2: Surviving CABG stroke vs. non stroke [Johns Hopkins Hospital 1994-2004]

The statistical data reveal an incidence of the CNS between 1-80%, from which stroke is 1–5…8% and neurocognitiv deficiency is 25–80% [3, 5, 7]. The large variation interval of the reported incidence might be ascribed to the next causes:

- the type of cardiac surgery
- definition
- the show-down method
- the type of the study
- the moment of inspection.

The evaluation for the postoperative neurocognitive insufficiency reveals the constantly decrease incidence up to one year after surgery and, paradoxically, a significant increase at 5 years after surgery. There are some ongoing studies that try to explain this behavior of the incidence, and the preliminary results show a big question mark for the consequence of statines on CNS (figure 3) [6, 9, 12, 15, 33].

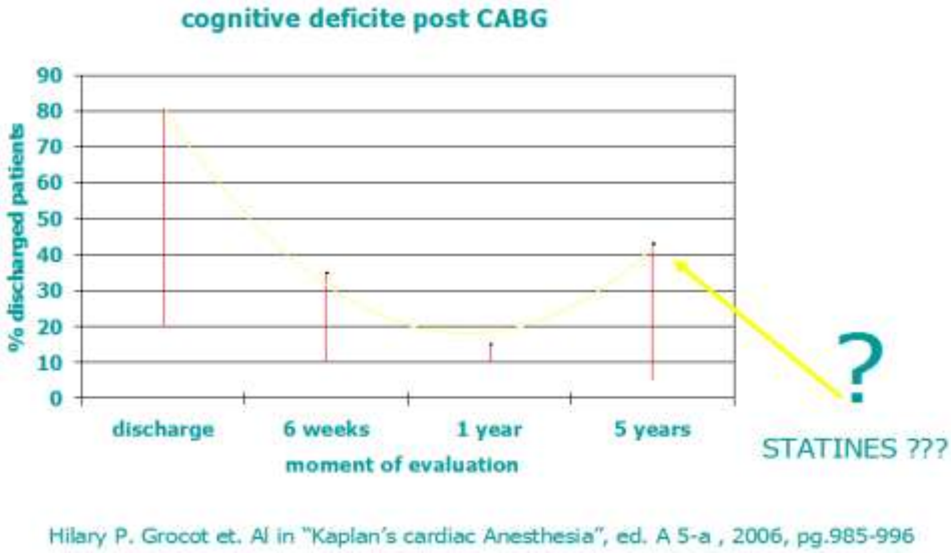
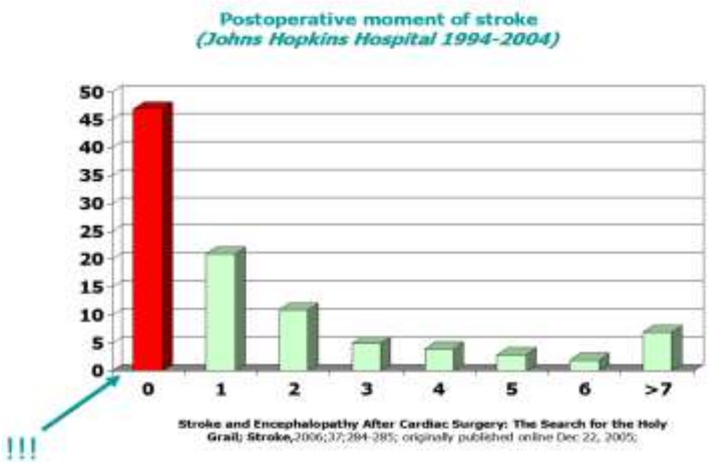


Figure 3: CNS injury incidence



The connection between ECC and the developing of the severe CNS dysfunction is sustained by the statistics which prove the appearance of stroke in the first 24 hours after surgery at almost 50% of the patients (Figure 4) [4, 8, 11, 15].

Figure 4: Postoperative moment of stroke (Johns Hopkins Hospital 1994-2004)

I. Definition

In order to exactly quantize the incidence, the causes and the therapeutically strategies for the neurological dysfunction after ECC it was attempted to compel by using guidelines the way to identify the complication' kind:

• **Type I:**
- nonfatal stroke
- AIT
- stupor /coma at the discharging moment from hospital
- death by stoke / hypoxic encephalopathy

• **Type II*:**
- impairment of the intellectual level
- memory problems
- obfuscation
- nervousness
- disorientation

* without focal signs The Roach Classification, *ACC/AHA guidelines for CABG* published in Br. J Anaesth 84:337, 2000 in a *Multicenter Study of Perioperative Ischemia* from Arrow Smith et. Al - "*central nervous system complications of cardiac surgery*" [11, 23, 28, 31]

II. Neurological evaluation methods (Stroke)

There are various methods in order to evaluate the neurological status, but the most used are:

• Clinical Examination Scale Following Acute Cerebral Infarction (NIH Stroke Scale, NIHSS)
• The Toronto Stroke Scale
• The Copenhagen Stroke Scale
• The Scandinavian Neurological Stroke Scale (SSS)
• The European Stroke Scale which is the most used scale in Europe.

Some other evaluation methods and details for those above can be found at the web address *www.medal.org.*

Even it is the most used scale, the European Stroke Scale has numerously usage impediments and the most important are:

• the consciousness level is influenced by the analgesic / sedative drugs and in this way it is a lower collaboration between patient and the person who examines him
• presence of orotraheal tube makes impossible the oral communication.

The assignation of a consensus method for the neurological evaluation of the neurocognitive dysfunction is much more difficult that seems. Below there are some basic principles for that kind of evaluation based on generally valuable truths: [17, 21, 32].

• after cardiac surgery there is temporary or persistent neurological alterations at different stages in a variable proportion of patients,
• some patients have a previous neurocognitive alteration so each patient should be investigated before operation in order to establish the basic level,

• each neurocognitive alteration that exist after surgery must be interpreted on the existing data before surgery,
• the neurocognitive evaluation tests must take into account the physical limits imposed by surgery itself, as follow:
  • testing cognitive domain,
  • the test must be sensitive and reproducible,
  • the necessary time for doing the test,
  • the existing parallel forms of the test,
  • the physical effort for covering the test,
  • the tests must not be prejudiced by race or sex of the patient,
  • because of the complexity of the neurological alterations a single test will never be sufficient for a fair evaluation,
  • the evaluation may be influenced by the environment, mental status and pharmacological factors,
  • the same experienced examiner will test all the patients from a center.

There are a lot of tests for neurocognitive evaluation after ECC, and they could be found at the web address www.medal.org

III. Risk factors for neurological alteration after ECC

Based on statistical data from many randomisated trials some attempted to identify the risk factors associated with the development of the neurological alteration after ECC. The most important factors are shown in the next tables: [13, 17, 19, 25]

Table 3: Risk factors associated with neurological alteration after cardiac surgery

Risk factor	Type I	Type II
Proximal atherosclerotic aorta	4.52 [2.52-8.09]	
Previous Neurological diseases	3.19 [1.65-6.15]	
IABP use	2.60 [1.21-5.58]	
Diabetes mellitus	2.59 [1.46-4.60]	
Medical history of Arterial hypertension	2.31 [1.20-4.47]	
Medical history of pulmonary disease	2.09 [1.14-3.85]	2.37 [1.34-4.18]
Medical history of unstable angina	1.83 [1.03-3.27]	
Age	1.75 [1.27-2.43]	2.20 [1.60-3.02]
TAS> 180 mmHg at admission		3.47 [1.41-8.55]
Alchool abuse		2.64 [1.27-5.47]
Prior CABG		2.18 [1.14-4.17]
Aritmia in the surgery day		1.97 [1.12-3-46]
Antihypertensive drugs		1.78 [1.02- 3.10]

Table 4: Risk factors for neurocognitive alteration type I

• diabetes mellitus
• arterial hypertension
• before cerebrovascular diseases
• atherosclerotic aorta
• handling the ascendant aorta
• complex surgery
• ECC > 2h
• hemodynamicaly instability before surgery
• Hiperglycemia, Hyperthermia, Hypoxemia

Table 5: Risk factors for neeurocognitive alteration type II

• low cognitive status before surgery
• educational type
• age
• diabetes mellitus
• ECC time (> 2h)

While the patients average age increased and the incidence of postoperative myocardial infarction and low cardiac output syndrome remained increased, the last 20 years of cardiac surgery practice have demonstrated that the incidence of neurological alteration after ECC has significantly increased, proving an obviously relationship between the age of the patients and the type of alteration (Figure 5).

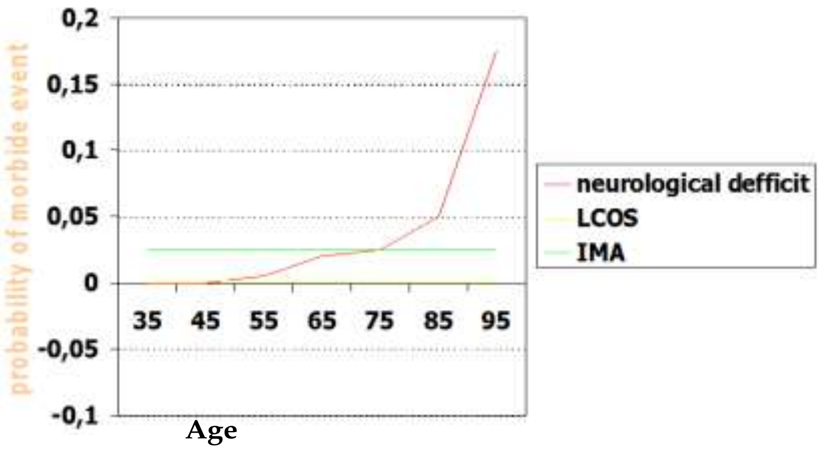


Figure 5: Age influence on cardiac and neurological morbidity

IV. Risk scales

Once the related factors for the increased possibility of developing neurological dysfunction after ECC were identified, the medical practice required the imagining of a mathematical algorithm in order to predict and to quantize the possibility of progressing to this kind of complication.[12, 17, 20, 22]

Such risk scales may be found on the web address www.medal.org

V. Physiopathological mechanisms

The presumptive cerebral physiopathological mechanisms responsible for neurological dysfunction after ECC are:

1. Hypoxia
2. Local homeostasis alteration
3. Edema
4. The SIRS mediators
5. Other causes

VI. Expected causes

1. Brain embolus

The brain embolus probably represents the most frequent cause of neurological dysfunction after ECC. Intuitively it is supposed that:

• macro-emboli (ruptured atheroma plaque) produce stroke
• micro-emboli (solid particles or gas bubbles) produce neurocognitive dysfunction

The emboli resources are:

• the mobilization of the atheromatous plaque by handling the aorta
• the novo creation of emboli by blood interaction with the lung-heart machine circuits
• the air aspiration from operating field
• the injection of air bubbles in the extracorporeal circuit
• the insufficiency of arterial line filters

The existence of micro-emboli is observed with:

• Echo Doppler
• brain histological analysis (millions of micro-emboli = small capillary arteriolar dilatations)

2. Global Brain Hypo-perfusion

Global brain hypo-perfusion was supposed the cause of neurological dysfunction even in the beginning of ECC. Intuitively, the decrease of TAMs and systemic flow determine the brain alteration. The multicenters random studies proved that this mechanism is responsible for stroke and not for neurocognitive dysfunction.

3. Temperature Variations

The accidents of cardio-respiratory arrest in severe hypothermia, followed by efficient resuscitation without neurological deficiencies, brought to the utilization of hypothermia in cardiac surgery in order to protect the organs which suffer of oxygen imbalance during ECC.

Moderate hypothermia was largely used until '90s, when the concern for postoperative bleeding, high risk for infections etc determined the establishment of the normothermia ECC guidelines. This therapeutically method is still used in many hospitals in pediatric cardiac surgery.

The temperature monitoring during ECC (central temperature, peripheral temperature, the gradient of temperature) are part from the standard of care.

The monitoring of central temperature is realized by measuring it in rectum or urinary bladder or in the pulmonary catheter. The brain temperature (which is different of central temperature) is monitoring in nasopharynx or on the tympanic membrane [19, 24, 27].

The esophagus temperature may give us mistaken information because of the mechanical ventilation.

The re-warming period is the most critical one because of the risk of a too quick re-warming and of a reheating, hyperthermia being extremely harmful.

The principles that must be followed during the re-warming period are:

- after profound hypothermic circulatory arresting it must initiate hypothermic reperfusion
- $\Delta t < 10°C$ blood/ central temperature
- the re-warming stops when central temperature is around 35°C
- hyperthermia is detrimental = "second injury"

4. The systemic inflammatory response

Another possible cause for the neurological dysfunction is the triggering of SIRS. The systemic inflammatory response represents the organism reaction to the contact between immune system cells and the non-physiological heart-lung machine's circuits. It's not exactly knew if SIRS or micro-embolus particles generate the stimulus for pro-inflammatory especially cyclooxygenase ARNm up-regulated gene.

5. The brain edema

Any kind of tissue reacts specifically to the aggression, by altering the membrane permeability and increase in liquid volume in extra-vascular and extra cellular space. Particularly, the brain is an incompressible tissue, so any increase in its volume goes to a fast increase in intracranial pressure with very serious physiopathological consequences. The developing mechanisms for brain edema during ECC are:

- cytotoxic - global hypoperfusion
- hyponatremia - hemodilution
- retrograde stasis - wrong position of the venous cannula.

It is not clear if the brain edema is determined by a primary neurological injury or that is the edema's consequence. Anyway, there is no doubt that the final result for both of them is the neurocognitive dysfunction.

6. The dysfunction of the blood - brain barrier

The dysfunction of the blood / brain barrier represents one of the possible mechanisms for the neurological dysfunction after ECC. The studies realized with acid aminoisobutiric 14C and fluorescent albumin have proved that:

- the maximal peak for the dysfunction is at 2 h after CEC
- the dysfunction is secondary to ischemia, SIRS Etc.

7. The pharmacological causes of the neurological dysfunction

Actually, the pharmacological causes of the neurological dysfunction are not really proved. They were noticed in the necrosis of the neonatal brain.

8. Genetic causes

It is possible to exist a relationship between the genetic causes and the neurocognitive dysfunction after ECC [12, 15, 33].

There are some genetic variations:

- ε 4 allele apolipoprotein gene (high risk for Alzheimer, head injury)
- PLA2 receptor (protrombogen / coronary artery, cerebral artery)
- other causes.

Neuroprotective Strategies

1. The decrease of the emboli

The decrease of the emboli is realized by:

- using circuits with a high degree of biocompatibility
- avoiding the usage of intra-pericardium suction pumps
- increasing the performance of the arterial filters
- paying attention in the solutions' infusion in the cardiotomy reservoir
- keeping the surgery field in a CO_2 atmosphere
- using an aortic canulla with an apex distal situated of the outlet of the neck vessels
- using the cell saver

2. The management of the atherosclerotic aorta

The atherosclerotic aorta is evidenced by using:

- transesophagian echo
- epiaortic echo.

The strategies for the management of the athero-sclerotic aorta are:

- minimal handling of the atherosclerotic aorta or the "no touch technique"
- the identification of the aortic clamping zone
- special canullas for protecting the brain circulation
- avoiding the partial clamping of the aorta

3. Continuous vs. pulsatil perfusion flow

Even from the beginning of the ECC, the use of continuous flow was a controversial issue, because it delivers a non-physiological blood flow to the organs.

Later it was believed (intuitively, because of the similitude with the human body circulation) that the pulsatil flow is the answer for the perfusionists' problems, but it was proved (by analyzing SvO_2 in different critical organs) that there is not always a perfect match between the demand and the supply of oxygen, even if it is using a pulsatil flow.

Computer controlled pulsatil perfusion (jugular SvO2) seems to be the optimal solution even if the statistical analyses of the first data from two studies didn't proved a significant mortality decrease.[21]

4. The management of acid - base equilibrium

• α - stat ↔ CMRO2 ~ CBF (in adults)
• pH stat ↔ it is used in a single case - congenital heart disease

5. The management of temperature

The neuroprotective effect of temperature:

• metabolic - ↓t with 1°C → ↓CMRO2 with 6-7%
• nonmetabolic:
  - blockage of glutamate release
  - ↓Calcium influx
  - ↓Protein synthesis
  - ↓protein-kinase C activity
  - ↓depolarization
  - ↓ROS
  - suppress the NO synthetase

Since the '90s, the trend in adult cardiac surgery is to realize ECC in normothermia. In order to estimate the impact of normothermia on the organ protection it was initiated "The Warm Heart Investigators Trial", and the neurological effects were studied by Emory University and Duke University [23, 25, 27]. The results are:

• the normothermic perfusion do not cause neuro-cognitive dysfunction (the results of the two universities are congruent)
• stroke is more frequent in normothermia (Emory University) and has the same incidence (Duke University) - so the results are disjunctive.

The rewarming period supposes a slow temperature increase, keeping a gradient between central and peripheral temperature of max 3-5°C.

6. Mean systolic blood pressure during ECC

About the blood pressure value during ECC, in order to realize a good brain perfusion, there are controversial issues. The pump's flow is calculated by nomograms (sex, age, BMI), in order to obtain a cardiac index of ~ 2.4 $l/min/m^2$. The changes of systemic vascular resistance make us need drugs in order to modify it, thus the patient blood pressure must be between 50 and 100mmHg (+10-15 mmHg in patients with arterial hypertension, old age patients, patients with atherosclerotic aorta).

7. The management of glycemia

Hyperglycemia is associated with an increase in the neurological dysfunction incidence after ECC. Ideally, the glycemic blood level at critical patient from ICU must be maintained between 110-140 mg/dl. The medical practice has proved that this glycemic level is impossible to realize during ECC in patient with high resistance to insulin, because he needs the administration of high dosages of insulin and in this way it is a high risk for hypoglycemia immediately after ECC.

Today, the perioperator glycemic management is:

• maintain normoglycemia before and after ECC (110 - 150 mg/dl)
• stop oral antidiabetic drugs 48h before surgery
• Glycemia > 180 - 200 mg/dl during ECC.

The adverse effects of hypoglycemia are:

• anaerobic conversion from glucose to lactate
• release of neuro-cytotoxic aminoacids during ischemia.

8. The pharmacological neuroprotection

There is a therapeutic window between injury and cell death. This window is the time target of this kind of protection. The area target is the "penumbra" zone which contains the reversible damaged cells, but not dead. The purpose of the neuroprotective drugs is to "protect" against the second injury during reperfusion and to reduce the metabolic demand (Figure 6) [26, 28].

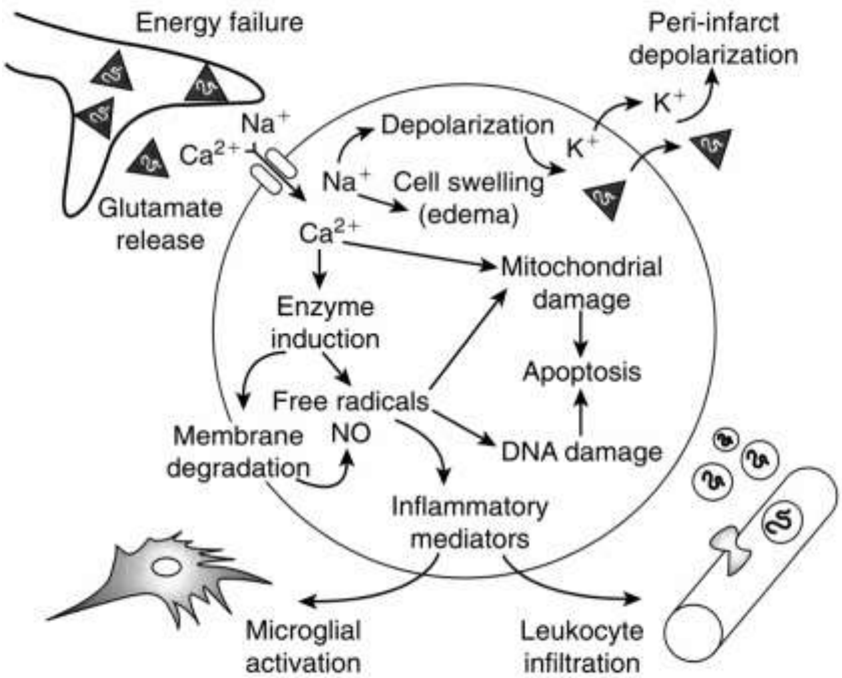


Figure 6: Cerebral ischemic cascade. A simplified overview of central nervous system events that occur after energy failure in the ischemic brain. (From Dirnagl U, Iadecola C, Moskowitz M: ***Pathobiology of ischemic stroke: An integrated review.*** **Trends Neurosci 22:391, 1999)**

There were many studies using many drugs but none was approved by the US FDA or other regulatory agencies. There are many ongoing trials designed to test the neuroprotective effect.

1. Thiopenthal was the first studied drug. Nussmeier et al concluded that "*burst suppression dose*" do not reduce stroke morbidity after CABG. In addition, Pascoe et al. stated that thiopenthal is not neuroprotective in "open chamber cardiac surgery". However, during the time it was observed that this drug offers some neuroprotective effect and, on can speculate that the cerebral vasoconstriction and reducing the sum of embolies is the neuroprotective effect.

2. Propofol reduces the cerebral oxygen demand in the same fashion like thiopenthal and has an antioxidant effect. "Burst suppression" dose do not influence the neurologic postoperative outcome.

3. Aprotinine remains the only drug obviously proved to decrease the mortality after cardiac surgery. The effect is represented by inhibit the activity of serine proteases. The neuroprotective effect is assumed by reducing of new potential embolic material.

4. The N metyl D aspartate (NMDA) receptor antagonist (dextromethorphan, remacemide and S (+) ketamine) were used for neuroprotection in many trials. None has prevailed the effect in clinical human studies in order to reduce the incidence of stroke or neurocognitive deficiency.

5. Intravenous lidocaine, because of its properties as a sodium channel blocking agent and potential anti-inflammatory effects, has been investigated as a neuroprotectant in cardiac surgery. In a study of 55 patients undergoing valvular surgery, a lidocaine infusion (1 mg/') was begun preinduction and maintained for 48 h after surgery. Neurocognitive testing was performed preoperatively and 8 days, 2 months and 6 months postoperatively. Compared with placebo, neurocognitive out-come 8 days after surgery was significantly better in the lidocaine group (p = 0,025). However, a much larger double blind, randomized trial in cardiac surgery failed to replicate the finding. Lidocaine cannot be recommended as a clinical neuroprotective agent in cardiac surgery.

6. β-blockers has been predominantly use toward the prevention of adverse miocardial events. The neuroprotective effect of carvedilol is under investigation in a large trial.

7. Lexiphant Platelet activating factor (PAF) antagonists have demonstrated neuroprotective effects in experimental models of cerebral ischemia. PAF is tought to modulate postischemic injury by the release of cellular lipids and free fatty acids that may result in cellular injury and cerebral edema. There is no clear neuroprotective effect of this drug.

8. Corticosteroids have long been considered as potential cerebroprotective agents in part due to their ability to reduce the inflamatory response. Inflammation is considered an important factor in propagating ischemia mediated brain injury. However, with the exception of spinal cord injury, they have never been demonstrated to posses any significant clinical neuroprotective properties.

Conclusions

Clinical strategies that may decrease neurologic complications in cardiac surgery:

1. early and aggressive control of hemodynamic instability

2. perioperative glycemia < 200 mg/ dl
3. routine epiaortic scanning before manipulation of ascending aorta
4. avoidance of manipulation of ascending aorta in severe atheromatosis
5. maintenance of adequate cerebral perfusion pressure
6. full dose aprotinin in high risk patients

Strategies to decrease impact of cardio-pulmonary by-pass on neurological complications:

1. Avoidance of reinfusion of unprocessed blood
2. Use of cell saver
3. Monitoring of cerebral venous pressure via a proximal central venous pressure catheter or the introducer port of a pulmonary artery catheter
4. Management of alpha stat pH during moderate hypothermic CPB
5. Avoidance of arterial inflow temperature > 37 °C
6. Use of CBP circuitry incorporating membrane oxygenator and 40 micron arterial line filter
7. Use of surface modified and reduced area CPB circuitry

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Adverse drug reactions. Heparin-induced thrombocytopenia*)

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Abstract

Heparin induced thrombocytopenia *(HIT) is a serious, potentially life-threatening complication of treatment with unfractioned heparin or other heparin products. Paradoxically, its morbidity derives principally from venous and arterial thrombosis and embolism even in the face of thrombocytopenia. HIT is caused by the development of an IgG antibody that recognizes multi-molecular complexes of platelet factor 4 and heparin. Although various factors have been associated with a high risk for the development of HIT, this syndrome has occurred with all types of heparin, all routes of heparin administration, and all heparin dose levels. For patients with strongly suspected or laboratory confirmed HIT, heparin should be stopped and full dose anticoagulation with an alternative commenced. The recommended alternatives of heparin are danaparoid, a heparinoid, or direct thrombin inhibitors, such as lepirudin, argatroban and bivalirudin.*

Heparin is in widespread use as anticoagulant for the prophylaxis and therapy of thrombo-embolism. Recently, an audit in the German health system found heparin to be the leading drug inducing adverse reactions (1). The most frequently reported event was heparin induced thrombocytopenia (HIT), a serious, potentially life-threatening complication of treatment with unfractioned heparin (UFH) or other heparin products (2).

What is HIT?

HIT is an unpredictable immune-mediated reaction to heparin/platelet factor 4 complex where heparin administration is associated with: thrombocytopenia, the generation of heparin-dependent antibodies (typically Ig-G), and paradoxical high risk for thrombosis causing significant morbidity and mortality (3). The odds ratio for risk of thrombosis for HIT is higher than all other known congenital and acquired risk factors for thrombosis (4).

Pathology

The pathophysiology of HIT represents a link between immune system and hemostasis. HIT is caused by the development of an IgG antibody that recognises multi-molecular complexes of platelet factor 4 (PF4) and heparin (5). Heparin, depending on the chain length and degree of sulphation of the glycosaminoglycan induces conformational

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changes in the PF4 (neoepitopes). The HIT antibodies recognise these neoepitopes on the PF4 complexed with heparin on the platelet surface. The new IgG-PF4-heparin complexes induce platelet activation and generation of pro-thrombotic microparticles. The clinical presentations of these events are thrombocytopenia and the seemingly contradictory occurrence of arterial or venous thrombosis (6).

Thus, the development of HIT antibodies may create a vicious cycle of progressive platelet activation, vascular injury and thrombosis with serious consequences including death. It is important to know that not all patients who develop HIT antibodies develop clinical HIT (7). The analogy of the "iceberg" can be used in considering the diagnosis of HIT (figure 1): the patients with clinical features of the syndrome (thrombocytopenia and associated thrombosis) represent the "tip above the water"; sensitive HIT antibodies assays will detect both these individuals and many others, i.e. the "body below the water" who have sero-converted on heparin therapy but who do not have the HIT syndrome. It remains unclear as to what regulates the progress from sero-conversion (development of antibodies) to the full expression of the HIT syndrome.

HIT and associated thrombosis occurs in the subset of patients with platelet-activating anti-PF4/H antibodies

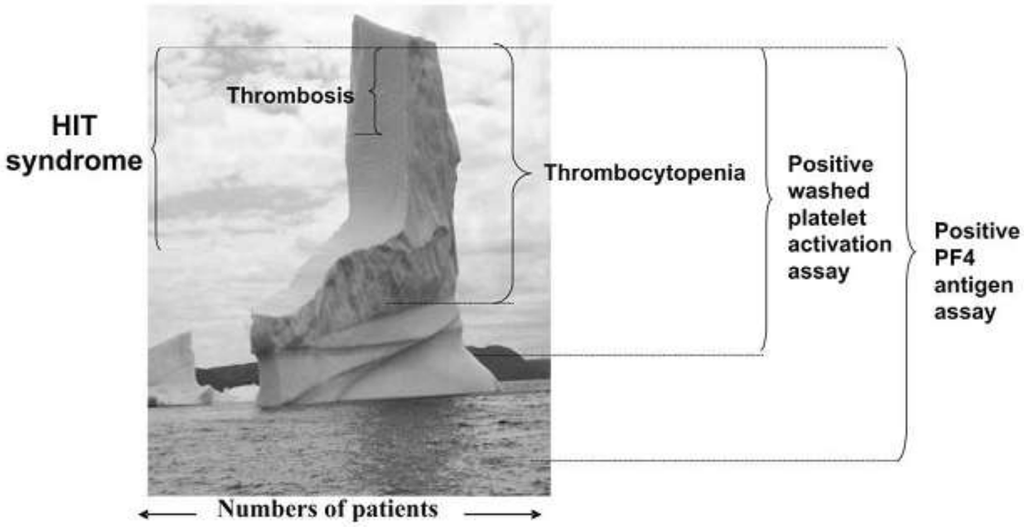

Figure 1: The "iceberg model" of HIT (modified from ref 7)

PF4 can also bind the endothelial heparan sulphate and the complexes with HIT antibodies might lead to endothelial injury with subsequent tissue factor expression and thrombin generation (2).

Incidence

HIT is occurring in up to 5% of patients treated with unfractioned heparin (UFH) (8). The incidence of HIT is greater with bovine than with porcine heparin (9). Up to 1%

incidence of HIT is reported with the use of low molecular weight heparin (LMWH) (10). The frequency of HIT is greater in surgical than in medical patients and it is lower still in pregnancy. These considerations suggest that routine platelet count monitoring for HIT is appropriate in at least some clinical situations (9).

HIT has been documented after administration of heparin line flushes, as well as during both high- and low-dose treatment (8).

Clinical presentation

The classic presentation of HIT is the development of thrombocytopenia 5 to 14 days after starting heparin (11). In patients who have received heparin in the previous three months the onset of thrombocytopenia can be more rapid due to pre-existing antibodies (2). Occasionally, HIT can occur after more than 14 days of heparin exposure or after cessation of heparin administration (delayed onset of HIT) (3).

Thrombocytopenia in HIT is defined as a platelet count of less than 1500000/µL, but HIT should also be considered when a patient's platelet count falls by greater than 30-50% during treatment (2). Severe thrombocytopenia (less than 15 000/µL) is unusual (11).

Half of the patients who develop HIT have associated thrombosis (HITT), such as: venous thromboses, pulmonary embolism, stroke, myocardial infarcts, mesenteric or peripheral infarctions, resulting in necrotic tissue and amputations (2). The ratio of venous to arterial thrombotic events is approximately 4:1 (9). In a large retrospective study, pulmonary embolism occurred in about 25% of all patients with HIT, which was more frequent than all arterial thrombotic events combined (12).

Patients who present HIT without thrombosis (isolated HIT) have a high risk of subsequent thrombosis if heparin is not stopped and an alternative anticoagulant given in therapeutic doses (11). Careful Doppler evaluation looking for thromboses is worthwhile (9).

Some patients who receive subcutaneous injections develop skin lesions (skin necrosis or erythematous plaques) at the injection site (2).

Rapid onset of HIT may be clinically manifest as acute inflammatory cardio-respiratory, neurological, or other unusual symptoms and signs within 30 minutes following an intravenous UFH bolus (2).

Laboratory tests

Laboratory tests for HIT diagnosis comprise 1) platelet activation assays using aggregometry or a variety of platelet activation endpoints and 2) immunological assays (ELISA) using PF4 as the antigen (7). The latter have a high sensitivity, 80-100%, for the heparin-PF4 antibodies but the specificity is low as they are more likely to detect clinically insignificant antibodies (11). Diagnostic specificity is greater with the washed platelet activation assays which, unfortunately, are technically demanding.

Diagnosis

HIT is a clinico-pathological syndrome, i.e. the diagnosis is based on both clinical and laboratory pre-requisites. In patients receiving heparin and having a fall in the platelet count HIT is suspected on clinical grounds. The diagnosis of HIT is made based on the clinical estimate of the probability of HIT together with the result of laboratory assays. The features helpful in estimating the probability of HT are: the degree of thrombocytopenia, the timing of the onset, the presence of new or progressive thrombosis, and the likelihood of an alternative diagnosis (2). A scoring system based on these features has been proposed to assess the clinical probability of HIT (table 1).

Table 1: Diagnosis – pretest probability: the 4 T's (from ref. 11)

Points: Score 0, 1 or 2 for each of 4 categories:

	2	1	0
Thrombocytopenia	> 50% platelet count fall to nadir e 20	30-50% platelet count fall to nadir 10-19	< 30% platelet count fall to nadir d 10
Timing of fall in platelet count or other sequelae	Onset d 5-10 or < 1 day (if heparin exposure within 30 day)	> day 10, or timing unclear, or < day 1 with recent heparin 31-100 day	Platelet count fall < day 4 (without recent heparin exposure)
Thrombosis or other sequelae	New thrombosis; skin necrosis; post-heparin bolus acute systemic reaction	Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis not confirmed	None
Other cause for thrombocytopenia	No other cause for platelet count fall is evident	Possible other cause is evident	Definite other cause is present

If this probability of HIT is high, heparin should be stopped and an alternative anticoagulant started whilst laboratory tests are performed. It is recommended to consider only the quantitative results (ELISA) to determine the post-test probability of HIT (11).

A number of conditions should be considered in the differential diagnosis of HIT. The most frequent causes of thrombocytopenia are presented in table 2.

Table 2: Differential diagnosis of thrombocytopenia

Pregnancy
Antiphospholipid syndrome
Immune thrombocytopenic purpura (ITP)
Hypersplenism
Cancer-associated DIC
Drug-induced thrombocytopenia (other than heparin)
Sepsis
Hemodilution post-surgery
DIC (multiple causes besides HIT)
Post-transfusion purpura
Thrombolytic therapy
GP IIb/IIIa inhibitor
Use of IABP

Management

Early diagnosis and treatment of HIT to prevent sequelae mandate routine platelet count monitoring for patients receiving heparin in which the risk of HIT is considered to be > 0.1% (9). Depending on the estimated risk, this should be done every other day or every 2 to 3 days until day 14 or until heparin is stopped (table 3).

Table 3: Recommendation for platelet count monitoring during heparin therapy (from ref. 9)

	Platelet count monitoring	
Patient population	**Yes/No**	**Frequency**
Risk for HIT common (>1%)		
Receiving therapeutic dose UFH	Yes	min. alternate day → 14 d
Receiving post-op prophylactic dose UFH	Yes	min. alternate day 4 - 14 d
Starting UFH/LMWH & have received UFH in last 100 d or exposure uncertain	Yes	baseline value-repeat in 1 d
Systemic reaction after UFH bolus	Yes	immediate – compare with pre-bolus value
Risk for HIT infrequent (0.1-1%) Medical/Obstetric UFH; Post-op LMWH; Post-op UFH 'flush'; LMWH after UFH	Yes	every 2 -3 days, 4 - 14 d
Risk HIT < 0.1% Medical/obstetric patients on LMWH	No	-

For patients with strongly suspected or confirmed HIT heparin should be stopped and full dose anticoagulation with an alternative commenced. The recommended alternatives of heparin are danaparoid, a heparinoid, or direct thrombin inhibitors (DTI) such as lepirudin, argatroban and bivalirudin (6). The evidence for the efficacy of non-heparin anticoagulants for HIT is not based on large prospective randomized trials, due to the overall infrequent occurrence of HIT and the clinical heterogeneity of affected patients. Clinical decisions should be made following considerations of the risks and benefits of treatment with alternative anticoagulants.

Danaparoid is a heparinoid which inhibits activated factor X (FXa) and to a much lesser degree thrombin (11). It is equivalent to lepirudin in the treatment of HIT and HITT when is administered in high dosage (13). However, there is ongoing controversy over the appropriate dose of danaparoid in patients with uncomplicated HIT and the need of anti-FXa activity monitoring. The DTI are a new group of potent anticoagulants. They do not require anti-thrombin to bind heparin. Instead, they bind one or more of the active sites of thrombin directly and do so wherever thrombin exists (6). The use of lepirudin in the treatment of HIT has been extensively reviewed. At doses adjusted to achieve an APTT ratio of 1.5-2.5 it reduces the risk of limb amputation because of thrombosis, death or new thrombosis in patients with HIT and HITT (14). The major risks of lepirudin administration are represented by major hemorrhage, directly related the

APTT ratio, lepirudin levels and serum creatinine levels, and severe anaphylaxis, more common in previously exposed patients (6).

Argatroban is a synthetic DTI cleared by hepato-billiary system with a 40-50 minute half life (6). Its efficacy has been documented in patients with HIT (15). Use of argatroban is a good option in patients with impaired renal function.

Bivalirudin is another option for the management of patients with HIT. It has been tested extensively in percutaneous coronary interventions (16). Besides the rapid renal elimination (half-life of approximately 25 minutes) the drug is cleaved by proteases and thrombin itself, providing an elimination mechanism independent of special organ function.

Vitamin K antagonists should be used only when platelet count has recovered and during overlapping alternative anticoagulation until the INR is therapeutic for two consecutive days (11).

For patients who do not have active bleeding prophylactic platelet transfusions are relatively contraindicated (9).

Safe management of patients with HIT requiring cardiac surgery mandates a fast-acting anticoagulant, with reliable point-of-care monitoring of the effects and rapid reversal of them. Bivalirudin appears to fulfill these criteria (17) but further studies are necessary to confirm this. The combined use of UFH with a potent inhibitor of platelet aggregation is another alternative strategy (11). Delay in surgical intervention may be possible and even desirable in patients with non-acute presentations. Patients with previous HIT who are antibody negative and who require cardiac surgery should receive intra-operative UFH in preference to other anticoagulants which are less validated for this purpose (9).

In conclusion, HIT is considered a common immunologic adverse drug reaction. Patients exposed to heparin products, which develop thrombocytopenia, should not be overlooked. Thrombosis, not bleeding, fatal thrombosis or embolism is not uncommon. Increased awareness of the HIT syndrome might reduce morbidity and mortality. Because the incidence of this complex syndrome appears to be increasing it is vital that medical teams define, review, and prepare protocols well before an actual emergency presents itself. With recent introduction of new direct thrombin inhibitors, further options for the treatment of patients with HIT are available.

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Recommandations concernant le monitorage et les dispositifs de sécurité pour la circulation extracorporelle en chirurgie cardiaque*)

Avant-propos

La médecine connaît un développement accéléré de nouvelles technologies, à visée préventive, diagnostique et thérapeutique, qui conduisent les décideurs de santé et les praticiens à faire des choix et à établir des stratégies, en fonction de critères de sécurité, d'efficacité et d'utilité.

L'Agence nationale d'accréditation et d'évaluation en santé (ANAES) évalue ces différentes stratégies, réalise une synthèse des informations disponibles et diffuse ses conclusions à l'ensemble des partenaires de santé. Son rôle consiste à apporter une aide à la décision, qu'elle soit individuelle ou collective, pour:

- *éclairer les pouvoirs publics sur l'état des connaissances scientifiques, leur implication médicale, organisationnelle ou économique et leur incidence en matière de santé publique;*
- *aider les établissements de soins à répondre au mieux aux besoins des patients dans le but d'améliorer la qualité des soins;*
- *aider les professionnels de santé à élaborer et à mettre en pratique les meilleures stratégies préventives, diagnostiques et thérapeutiques selon les critères requis.*

Ce document répond à cette mission. Les informations qui y sont contenues ont été élaborées dans un souci de rigueur, en toute indépendance, et sont issues tant de la revue de la littérature internationale que de la consultation d'experts dans le cadre d'une étude d'évaluation des technologies et d'évaluation économique.

Alain COULOMB,
Directeur général

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Sommaire

Liste des abréviations

ACT	-	*activated clotting time* (temps de coagulation activé)
BIS	-	*bispectral index scale* ou échelle d'index bispectral
CEC	-	circulation extracorporelle
CIVD	-	coagulation intravasculaire disséminée
CO_2	-	dioxyde de carbone
DSC	-	débit sanguin cérébral
ECG	-	électrocardiogramme
ECMO	-	extracorporeal membrane oxygenation
FiO_2	-	fraction inspirée d'oxygène
GDS	-	gaz du sang
HNF	-	héparine non fractionnée
SaO_2	-	saturation artérielle en oxygène
SFAR	-	Société française d'anesthésie-réanimation
SvO_2	-	saturation du sang veineux mêlé (artère pulmonaire) en oxygène
$SvjO_2$	-	saturation du sang veineux jugulaire interne en oxygène
TCA	-	temps de céphaline avec activateur
TP	-	temps de prothrombine

Résumé

Objectif: Proposer des recommandations françaises sur le monitorage et la sécurité de la circulation extracorporelle (CEC) en chirurgie cardiaque.

Conclusions et résultats:

(i) Technique invasive et complexe s'intégrant dans un contexte périopératoire caractérisé par des interactions permanentes entre les équipes d'anesthésie réanimation, de chirurgie et de perfusion.

(ii) Risque de survenue d'incident dans 1/138 CEC avec une proportion d'incidents graves de 1/1 453 CEC selon une enquête américaine; pas de données françaises.

(iii) Aucune étude clinique n'avait pour objet l'évaluation de l'impact du monitorage sur la morbidité et la mortalité liées à la CEC.

(iv) Enquête française de 2003 montrant une hétérogénéité des pratiques.

(v) Élaboration de 41 recommandations de grade C, regroupées en 3 thèmes majeurs: prérequis et recommandations générales, dispositifs et mesures de sécurité et enfin paramètres surveillés.

Méthode: L'Anaes a interrogé, de façon systématique sur le sujet, les banques de données Medline, Embase, Pascal, les sites Internet utiles et recherché la littérature grise à partir de 1993. La sélection a été réalisée selon le niveau de preuve et la qualité méthodologique des études.

Les recommandations ont été élaborées par la méthode du consensus formalisé par un groupe de travail (14 experts), puis soumises à un groupe de lecture (33 experts) pluridisciplinaire.

Les professionnels médicaux et paramédicaux de la CEC, de l'anesthésie-réanimation, de la chirurgie cardiaque, de l'ingénierie biomédicale et de la gestion du

risque composant ces deux groupes avaient été proposés par les sociétés savantes des spécialités concernées.

Perspectives: Définir la formation initiale et continue ainsi que le statut des professionnels de la CEC.

Préciser les responsabilités respectives des professionnels (perfusionnistes, chirurgiens, anesthésistes-réanimateurs) impliqués dans la réalisation et les suites de la CEC.

Synthèse et perspectives

Contexte

La circulation extracorporelle (CEC) en chirurgie cardiaque est une technique invasive et complexe. Il n'existe pas à l'heure actuelle de données françaises sur la morbidité et la mortalité liées à la CEC. Une enquête réalisée aux États-Unis mettait en évidence la survenue d'un incident pour 138 CEC, avec un risque d'incident grave, c'est-à-dire pouvant conduire au décès du patient, pour 1 453 CEC. L'hétérogénéité des pratiques a été reconnue comme un facteur d'erreurs dans les systèmes complexes. En France, la conduite, le monitorage et la sécurité de la CEC ne bénéficient actuellement d'aucune recommandation.

Objectifs

À la demande du groupe d'étude en perfusion, l'Anaes a élaboré des recommandations concernant le monitorage, la surveillance et les règles de sécurité de la CEC, afin de contribuer à une amélioration de la qualité des soins. Il s'agit d'une étape initiale qui n'a pu aborder tous les aspects de la question.

Méthode

L'analyse critique de la littérature clinique a été faite à partir de publications de langue française et anglaise. La recherche bibliographique a été faite à partir de 1993.

Le rapport réalisé par l'Anaes a été discuté par un groupe multidisciplinaire de 14 personnes lors de trois réunions. Avant la dernière réunion, un deuxième groupe de 33 experts a relu le document et a coté les recommandations élaborées par le groupe de travail, selon la méthode d'obtention d'un consensus formalisé.

Les professionnels médicaux et paramédicaux de la CEC, de l'anesthésie-réanimation, de la chirurgie cardiaque, de l'ingénierie biomédicale et de la gestion du risque composant ces deux groupes avaient été proposés par les sociétés savantes des spécialités concernées (Collège français de perfusion, Société française de chirurgie cardio-thoracique, Société française d'anesthésie-réanimation, Société française de gestionnaires de risques en établissement de santé).

Résultats de l'analyse de la littérature clinique

Aucune étude clinique ayant pour objet l'évaluation de l'impact du monitorage sur la morbidité et la mortalité liées à la CEC n'a été retrouvée.

Plusieurs enquêtes, dont une française, ont fourni des informations sur les pratiques de monitorage et de sécurité pendant la CEC. Dans l'enquête française, sur les 66 centres réalisant des CEC pour la chirurgie cardiaque, 48 centres avaient répondu. L'enquête montrait une hétérogénéité des pratiques de monitorage et de surveillance de la CEC. Cette hétérogénéité peut être responsable d'une diminution du nombre de paramètres monitorés et de la qualité de la surveillance pendant la CEC par rapport à la période pré et post-CEC.

Les éléments suivants ont fait l'objet d'une analyse de la littérature avec comme objectif principal d'assurer une continuité de la surveillance de la CEC entre la période pré et post-CEC:

- pression;
- oxygénation;
- anticoagulation;
- température;
- fonction cérébrale;
- glycémie;
- dispositifs de sécurité (électrique, prévention de l'embolie gazeuse, pompes de CEC, valves antiretour, etc.)

Les particularités de la CEC néonatale et pédiatrique ont été prises en compte.

Proposition de recommandations

L'analyse de la littérature n'apportant qu'un faible niveau de preuve scientifique, les recommandations ont été obtenues par un consensus formalisé.

Dans l'élaboration des recommandations, le groupe de travail a suivi comme principe la nécessité d'assurer une continuité de la surveillance pendant toute la période opératoire, dans laquelle s'intègre l'anesthésie ainsi que la CEC avec mise en place, réalisation et retour aux fonctions cardio-respiratoires des patients.

Les recommandations ainsi établies ont été soumises au vote d'un autre groupe pluridisciplinaire de 33 experts, représentant toutes les modalités d'exercice (public universitaire et non universitaire, privé) et les différentes régions de France. Le vote du groupe de lecture avait atteint une médiane supérieure ou égale à 8 pour toutes les recommandations. Les commentaires et votes du groupe de lecture ont été discutés et intégrés lors d'une dernière réunion du groupe de travail.

Les recommandations ont été regroupées en 3 grands thèmes: prérequis et recommandations générales, paramètres surveillés et dispositifs et mesures de sécurité. Elles ont recueilli l'avis unanime du groupe de travail à l'exception des propositions concernant l'utilisation de filtre artériel et de valves antiretour qui avaient obtenu un accord de la majorité du groupe de travail.

Proposition de 41 recommandations fondées sur un accord professionnel fort (grade C)

Perspectives

Le groupe de travail et le groupe de lecture ont conjointement souligné la nécessité de continuer ce travail, destiné à améliorer la sécurité des patients qui bénéficient d'une CEC, en se fixant comme perspectives la définition:

- de la formation initiale et continue ainsi que du statut des professionnels de la CEC;

- et des responsabilités respectives des professionnels (perfusionnistes, chirurgiens, anesthésistes-réanimateurs) impliqués dans la réalisation et les suites de la CEC.

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Introduction

La circulation extracorporelle (CEC) en chirurgie cardiaque est une technique invasive et complexe qui s'intègre dans un contexte périopératoire caractérisé par des interactions permanentes entre les équipes d'anesthésie-réanimation, de chirurgie et de perfusion. La complexité de la CEC ainsi que les interactions entre de multiples intervenants pourraient être à l'origine d'incidents et d'accidents graves.

L'expérience clinique accumulée en France, ainsi que plusieurs publications réalisées par des perfusionnistes, anesthésistes-réanimateurs et chirurgiens français impliqués dans la pratique de la CEC (1-4) ont mis en évidence une grande hétérogénéité des pratiques, des mesures de sécurité et de monitorage pendant la CEC. L'hétérogénéité des pratiques est reconnue comme un des facteurs capables d'augmenter le risque lié aux procédures complexes (5). Il est probable que l'hétérogénéité des pratiques de CEC contribue aux incidents et aux accidents de la CEC (6).

Ces travaux ont souligné la nécessité de rédaction de recommandations concernant la surveillance et le monitorage pendant la CEC afin d'en améliorer la sécurité. La rédaction de telles recommandations en France s'inscrit dans une démarche déjà entreprise aux États-Unis, au Canada et dans plusieurs pays européens. De surcroît, dans la mesure où pendant la CEC l'anesthésie se poursuit, il est indispensable que les normes de sécurité et de monitorage pendant la CEC soient harmonisées avec celles de la période pré et post-CEC.

L'objectif de ce travail est de proposer des recommandations sur les CEC dites conventionnelles (pompes à galets, circuits ouverts). Les CEC appelées non conventionnelles (pompes centrifuges, systèmes clos, etc.) n'ont pas été spécifiquement abordées à cause de l'hérérogénéité des circuits, du relatif manque de recul mais aussi parce que les grands principes de sécurité et de monitorage sont en grande partie similaires (par exemple monitorage de l'anticoagulation, prévention des embolies gazeuses, etc.). Le document comporte également des recommandations qui tiennent compte de la spécificité de la CEC néonatale et pédiatrique.

Les professionnels du groupe de travail et du groupe de lecture qui ont contribué à la rédaction du présent document sont conscients du fait que l'amélioration des conditions de sécurité de la CEC est un processus complexe et ambitieux qui comprend, en plus de la définition et de l'application des normes de sécurité et de monitorage, la formation initiale et continue des perfusionnistes ainsi qu'une meilleure définition des interactions et des responsabilités des équipes impliquées dans la réalisation de la CEC. Ces thèmes ne seront pas abordés dans ce document mais devront faire l'objet d'un travail complémentaire.

Ce document n'est pas un livre de chirurgie cardiaque, ni d'anesthésie-réanimation en chirurgie cardiaque, ni de circulation extracorporelle, domaine dans lequel les lecteurs peuvent consulter deux ouvrages récents[1].

Contexte

I. PROGRÈS DE LA CHIRURGIE CARDIAQUE

Les progrès techniques de la chirurgie cardiaque, des techniques de protection myocardique ainsi qu'une meilleure connaissance de la physiopathologie des complications péri-opératoires ont entraîné une diminution de la morbi-mortalité et, de ce fait, permis une extension des indications chirurgicales vers le très jeune âge (néonatalogie) ainsi que vers les patients très âgés (octogénaires et au-delà). Malgré l'extension des indications opératoires il n'y a pas eu d'augmentation de la morbi-mortalité.

L'amélioration des techniques de protection myocardique est perçue comme une avancée majeure dans l'extension des indications de chirurgie cardiaque. Débutée en 1950 (7) par l'hypothermie qui diminue les besoins en oxygène, la protection myocardique s'est poursuivie en 1955 (8) avec l'arrêt électromécanique hyperkaliémique. En 1964 Bretschneider proposait les premières solutions cristalloïdes froides (pour revue voir (9)); de nombreuses autres seront proposées par la suite. À partir de 1978 la cardioplégie au sang froid (10) puis chaud (11) se généralise en utilisant des voies d'apport antéro ou rétrogrades et une perfusion continue ou intermittente.

Plusieurs revues récentes ont montré que la cardioplégie au sang enrichi en potassium pouvait mieux préserver la fonction myocardique surtout chez des patients ayant une dysfonction systolique ventriculaire gauche, à la phase aiguë d'une ischémie myocardique, en présence d'une hypertrophie myocardique ou lors d'une transplantation cardiaque (12, 13). D'autres revues ont souligné l'intérêt de la cardioplégie normothermique (14). Enfin, des travaux récents suggèrent l'intérêt de la cardioplégie tiède (29-33°C) (13).

En fonction des stratégies thérapeutiques de chaque équipe, telle ou telle technique de protection myocardique peut être choisie. Chacune peut trouver sa justification pour autant que les conditions de délivrance soient clairement définies, et que soient contrôlés débits, pression, température, et efficacité (silence ECG, éventuellement température myocardique).

II. PROGRÈS EN ANESTHÉSIE

Les progrès de la chirurgie cardiaque et de la CEC se sont accompagnés de progrès dans le domaine de l'anesthésie et de la réanimation. En plus des impératifs liés aux progrès techniques, la Société française d'anesthésie-réanimation (SFAR) a eu une politique active d'amélioration de la sécurité en anesthésie. Le taux de mortalité imputable strictement à l'anesthésie a diminué régulièrement depuis plusieurs années

[1] **Gravlee GP, Glenn P.** - *Cardiopulmonary bypass: principles and management*. 2nd ed. Philadelphia: Lippincott Williams and Wilkins; 2000 et **Janvier G, Lehot JJ.** - *Circulation extracorporelle: principes et pratique*. Paris: Édition Arnette; 2004.

comme résultat d'une politique visant à améliorer la surveillance et le monitorage per et périopératoires (15). Le taux de mortalité ajusté sur l'état de santé des patients[2], strictement ou partiellement imputable à l'anesthésie, est de 1/250 000 pour les patients classe ASA 1, de 1/8 000 pour les patients classe ASA 3 et de 1/1 666 pour la classe ASA 4 (15). Les patients de chirurgie cardiaque sont dans leur majorité en classe ASA 3.

Le niveau de sécurité (< 1 décès/105 anesthésies) atteint en anesthésie a été comparé avec celui obtenu dans d'autres systèmes complexes comme l'aviation civile (15). Ce niveau de sécurité est obtenu seulement dans les systèmes complexes qui ont adopté le modèle des acteurs équivalents (15) qui implique la rédaction et l'application des normes de sécurité incluant la présence médicale et paramédicale ainsi que le monitorage minimum (16).

L'incidence des accidents graves (séquelles persistantes ou décès) dans la plus large enquête réalisée aux États-Unis sur la pratique de la CEC (6) est de 1/1 453 CEC. Comme la CEC comporte des risques supplémentaires par rapport à celui de l'anesthésie il est impossible de comparer directement les taux de mortalité strictement et partiellement imputables à l'anesthésie en France (15) à ceux rapportés par l'enquête de Mejak et al. (6). Il est possible néanmoins de formuler l'hypothèse qu'une politique active visant à améliorer la surveillance et le monitorage pendant la CEC peut contribuer à diminuer l'incidence des complications liées à la CEC. Dans la littérature sur la CEC on note d'une part une amélioration et une sophistication, généralisées à presque tous les pays, de la surveillance et du monitorage utilisés (17) et d'autre part une diminution de l'incidence des accidents graves liés à la CEC (6) (mais il n'y a pas d'études de corrélation, pas de relation statistique étudiée, pas de relation de cause à effet démontrée).

III. PROGRÈS DES TECHNIQUES DE CIRCULATION EXTRACORPORELLE

Les techniques de circulation extracorporelle ont progressé pour aboutir maintenant à plusieurs types de circuits avec dans chaque cas de nombreuses variantes (18). Le moteur des progrès des techniques de CEC a été la nécessité de diminuer les doses d'héparine non fractionnée, la réaction inflammatoire, la charge embolique et les autres effets secondaires de la CEC. Des traitements complexes des matériaux qui composent les circuits de CEC (circuits pré-héparinés) ont contribué à améliorer la biocompatibilité. La complexité des techniques modernes de CEC a entraîné l'apparition de dispositifs de monitorage et de sécurité de plus en plus nombreux.

[2] Estimé par la classification de y American Society of Anesthesiologists (ASA), avec classe 1: patient en bonne santé jusqu'à la classe 4: patient ayant un risque vital à court terme.

Méthode générale

I. RECHERCHE DOCUMENTAIRE

I.1. Sources d'informations

I.1.1. Bases de données bibliographiques automatisées

- Medline (National library of medicine, États-Unis);
- Embase (Elsevier, Pays-Bas);
- Pascal (CNRS-INIST, France).

I.1.2. Autres sources

- Cochrane Library (Grande-Bretagne) *http://www.update-software.com/clibng/cliblogon.htm*
- National guideline clearinghouse (États-Unis) *http://www.guideline.gov;*
- HTA Database (International network of agencies for health technology assessment -INAHTA) *http://www.inahta.org;*
- BDSP (Banque de données en santé publique, Rennes);
- Internet: moteurs de recherche.

I.2. Stratégie de recherche

La stratégie d'interrogation de Medline, Embase et Pascal précise les termes de recherche utilisés pour chaque sujet ou type d'étude et la période de recherche.

Les termes de recherche sont soit des termes issus d'un thesaurus (descripteurs du MESH pour Medline) soient des termes du titre ou du résumé (mots libres).

Ils sont combinés en autant d'étapes que nécessaire à l'aide des opérateurs « ET » « OU » « SAUF ».

Une présentation synthétique sous forme de tableau reprend les étapes successives et souligne les résultats en termes de:

- nombre total de références obtenues;
- nombre d'articles analysés;
- nombre d'articles cités dans la bibliographie finale.

Tableau 1. Stratégie de recherche documentaire.

Type d'étude/ sujet	Termes utilisés	Période de recherche	Nombre de références
Recommandations		1993-2003	M; E: 78
Étape 1	*Extracorporeal circulation OU Cardiopulmonary bypass*		
ET			
Étape 2	*Guideline* OU Practice guideline OU Health planning guidelines OU Recommendation [titre] OU Consensus development conferences OU Consensus development conferences, NIH OU Consensus conference [titre, résumé] OU Consensus statement [titre, résumé]*		

Méta-analyses, revues de littérature		**1993-2003**	**M; E: 36**
Étape 1			
ET			
Étape 3	*Instrumentation OU Method OU Standard OU Adverse effects*		
ET			
Étape 4	*Étape 4 Meta analysis OU Meta analysis [titre] OU Review literature OU Systematic review OU Review effectiveness [titre]*		
Analyses de la décision médicale		**1997-2003**	**M; E: 71**
Étape 1			
ET			
Étape 3			
ET			
Étape 5	*Medical decision making OU Decision support techniques OU Decision trees OU Decision analysis [titre] OU Patient selection*		
Monitorage de la CEC: études contrôlées		**1997-2003**	**M; E: 196**
Étape 1			
ET…			
Étape 6	*Instrumentation OU Method OU Standard OU Mortality OU Monitoring, Intraoperative OU Monitoring, Physiologic OU Safety management OU Risk management OU Hypothermia, Induced/method OU Perfusion/method OU Algorithms OU Point-of-Care Systems OU Alarm monitoring OU Biological monitoring OU Drug monitoring OU Ion monitoring OU Signal detection OU Safety OU Online monitoring*		
ET			
Étape 7	*Controlled clinical trial OU Randomized controlled trial * OU Single-Blind method OU Single blind procedure OU Double-blind method OU Double blind procedure OU Random allocation OU Randomization OU Random* [titre] OU Controlled study OU Major clinical study OU Cross-over studies OU Crossover procedure*		
Risques de la CEC: études contrôlées		**1997-2003**	**M: 15**
Étape 1			
ET …..			
Étape 7			
ET			
Étape 8	*Equipment Failure OU Risk OU Risk factors OU Risk assessment*		
Littérature francophone		**1998-2003**	**P: 78**
Étape 9	*Circulation extracorporelle*		
	Nombre total de références obtenues		**623**
	Nombre total d'articles analysés		**474**
	Nombre d'articles cités		**126**

M: *Medline*; **E:** *Embase*; **P:** *Pascal*

II. GRILLE DE SÉLECTION DES ÉTUDES ET MÉTHODE D'ANALYSE

Il existe peu d'études randomisées portant sur la CEC (circuits pré-héparinés), le monitorage (ACT versus ACT/héparinémie, température). Elles ont été toutes été analysées mais les résultats de ces études ne sont pas contributifs pour répondre aux objectifs de ce document.

Pour connaître l'état des pratiques de surveillance et de monitorage pendant la CEC dans le monde et en France, la principale source de documentation est représentée par les enquêtes. Toutes les enquêtes de pratiques retrouvées par la recherche bibliographique ont été retenues.

L'analyse des données cliniques a été réalisée en utilisant le guide méthodologique «Analyse de la littérature et gradation des recommandations» (19) de l'Anaes.

III. GROUPE DE TRAVAIL ET DE LECTURE

L'analyse de la littérature réalisée par l'Anaes a été présentée à un groupe de travail multidisciplinaire de 14 personnes et a été discutée au cours de trois réunions.

L'élaboration des recommandations a été fondée sur l'obtention d'un consensus formalisé. Les recommandations ont été proposées par le groupe de travail. Elles ont ensuite été soumises, par courrier, à un deuxième groupe pluridisciplinaire de 33 experts, le groupe de lecture. Il leur était demandé une cotation de 1 (pas d'accord) à 8 (tout à fait d'accord). La médiane des votes pour chaque recommandation ainsi que les commentaires du groupe de lecture ont été discutés et intégrés lors d'une dernière réunion du groupe de travail.

Les membres du groupe de lecture ont également relu le document selon une grille leur demandant leur avis sur sa lisibilité, l'exhaustivité des informations scientifiques, la présentation de la méthode de travail et la cohérence des conclusions et recommandations.

Les personnalités associées à ce travail ont été proposées par les sociétés savantes et représentaient les spécialités suivantes: anesthésistes-réanimateurs, chirurgiens cardiaques, perfusionnistes, ingénieurs biomédicaux et gestionnaires de risque.

Argumentaire

I. DONNÉES DISPONIBLES

La définition d'une stratégie de monitorage minimum en période périopératoire et pendant la CEC devrait être basée sur des preuves obtenues par des études méthodologiquement solides.

Aucune étude clinique ayant pour objet l'évaluation de l'impact clinique du monitorage en CEC n'a été retrouvée.

En l'absence d'études, les recommandations sur la surveillance et le monitorage ont été basées sur:

- la nécessité d'assurer la continuité avec le monitorage anesthésique;

• les objectifs (définis par le groupe d'experts) du monitorage pendant la CEC;
• les enquêtes de pratiques concernant la surveillance et le monitorage pendant la CEC réalisées en France et dans d'autres pays;
• les recommandations concernant la surveillance et le monitorage minimum pendant la CEC rédigées dans d'autres pays;
• et les avis des experts qui ont constitué le présent groupe de travail.

II. LES OBJECTIFS DU MONITORAGE

Selon les experts du groupe de travail, les objectifs du monitorage pendant la CEC sont de:

• s'assurer de la persistance de l'homéostasie et de détecter rapidement d'éventuelles anomalies, avant l'apparition des signes cliniques;
• recueillir suffisamment d'informations pour permettre de faire rapidement le diagnostic étiologique des anomalies afin d'apporter les mesures correctrices adéquates.

Le groupe de travail a considéré qu'il était nécessaire d'harmoniser les principes et les objectifs du monitorage et de la surveillance pendant la CEC avec ceux de la période péri-opératoire, caractérisée par une complémentarité (pouvant être à tort perçue comme une redondance) des paramètres monitorés.

III. ENQUETES DE PRATIQUES

Les propositions concernant l'amélioration de la sécurité pendant la CEC doivent tenir compte:

• de l'analyse des pratiques et des recommandations élaborées pour la surveillance et le monitorage de la CEC dans d'autres pays;
• de la situation actuelle dans les centres qui pratiquent des CEC en France (stratégie de surveillance pendant la CEC, types de moniteurs utilisés);
• des incidents et accidents les plus fréquents qui surviennent pendant la CEC ou qui sont considérés comme conséquences directes de la CEC, en prêtant une attention particulière aux situations pour lesquelles une amélioration de la surveillance et du monitorage pourrait aboutir à diminuer leur fréquence.

III.1. Limites des enquêtes de pratiques

À cause des modifications importantes des pratiques de CEC (par exemple abandon des oxygénateurs à bulles et adoption quasi systématique des oxygénateurs à membrane au début des années 90) (17), l'analyse des enquêtes de pratiques cliniques pour la CEC, antérieures à 1990, a été considérée comme peu contributive au document actuel.

Les rares informations existant en France sur la surveillance et le monitorage de la CEC ont été analysées.

III.2. État des lieux pour la surveillance et le monitorage pendant la CEC à l'étranger

Les moniteurs utilisés pendant la CEC aux États-Unis dans l'enquête de Mejak et al. (6) étaient (pourcentage de perfusionnistes utilisant ce type de monitorage):

- mesure de pression sur la ligne artérielle (94,3%);
- dispositif d'asservissement et d'arrêt de la pompe principale (artérielle) en cas d'augmentation de la pression dans la ligne artérielle (35,1%);
- pièges à bulles sur le circuit de cardioplégie (88,4%);
- détecteur de bulles sur la ligne artérielle (87,8%);
- dispositifs d'asservissement et d'arrêt de la pompe principale (artérielle) en cas de détection de bulles dans la ligne artérielle (63%);
- détecteur de niveau sur le réservoir veineux (70,4%);
- dispositifs d'asservissement et d'arrêt de la pompe principale (artérielle) en cas de baisse du niveau en dessous de la limite fixée (34,4%).

Le monitorage continu concernait:

- la saturation du sang veineux en oxygène (SvO2) (75,2%);
- la valeur de l'hématocrite (54,4%);
- le monitorage continu des gaz du sang (GDS) (35,9%);
- la saturation artérielle en oxygène (SaO2) (13,2%).

Les dispositifs de sécurité utilisés rapportés dans l'enquête de Mejak et al. (6) étaient (pourcentage de perfusionnistes utilisant ce type de monitorage):

- les manivelles en cas de panne électrique (99,2%);
- les filtres sur la ligne artérielle (98,5%);
- les dispositifs de mesure de la pression sur la ligne de cardioplégie (97,3%);
- les filtres sur l'alimentation en gaz (94,5%);
- les systèmes de purge unidirectionnelle sur la ligne artérielle avec filtres artériels (91,8%);
- des valves unidirectionnelles pour la décharge ventriculaire gauche (83%).

D'autres dispositifs de sécurité étaient utilisés, comme:

- le filtre sur le circuit de CEC lors de l'amorçage du circuit (81,3%);
- la présence d'une seconde console de CEC dans le site opératoire (99,2%);
- la liste de vérification (check-list) avant la CEC (94,5%);
- la présence d'une source de lumière de secours (sur batterie) au-dessus de la console de CEC (91,4%);
- une source additionnelle (bouteille indépendante du circuit de l'hôpital) d'oxygène (90,8%);
- une batterie de secours pour la pompe artérielle (84,7%);
- un analyseur de la fraction inspirée d'oxygène (FiO2) (53,4%).

III.3. État des lieux pour la surveillance et le monitorage pendant la CEC en France

Une enquête sur la surveillance et le monitorage pendant la CEC a été réalisée et publiée en France (20). Sur les 66 centres médico-chirurgicaux contactés qui pratiquaient la chirurgie cardiaque avec CEC au moment de l'enquête, 48 ont répondu. Les dispositifs de monitorage étaient utilisés pour mesurer les paramètres suivants:

- la pression en aval de l'oxygénateur (21% des centres);
- la pression en amont et en aval de l'oxygénateur (2 centres sur 48);
- la température du patient; un seul site de température pour 7 centres et plus d'un site pour 40 centres (1 centre ne mesurait pas la température du patient); les sites de mesure de la température étaient par ordre décroissant de fréquence: rectal, œsophagien, vésical, nasopharyngé et tympanique;
- la température des lignes artérielle et veineuse (90%);
- la température du circuit d'eau (moins de 56%);
- la température au niveau du circuit de cardioplégie (44%);
- la FiO_2 (44%);
- la SvO_2 et l'hématocrite (98%);
- la pression partielle en CO_2 à la sortie de l'oxygénateur (29%);
- les gaz du sang en continu (25%);
- les gaz du sang en discontinu par les autres 75% des centres (100% des centres mesuraient les gaz du sang avec une fréquence inconnue).

Parmi les autres mesures de surveillance et de sécurité rapportées par les centres:

- la check-list pré-CEC était utilisée par 80% des centres;
- une alarme de niveau sur le réservoir veineux était utilisée systématiquement dans 52% des centres mais 24% des centres n'utilisaient jamais ce type de monitorage. Pour les centres qui utilisaient une alarme de niveau sur le réservoir, 85% asservissaient le débit de la pompe principale à l'alarme de niveau bas du réservoir;
- un détecteur de bulles était utilisé par 38% des centres sur la ligne artérielle et par 6% des centres sur le circuit de cardioplégie;
- l'enquête ne comportait pas de questions sur l'utilisation des filtres artériels ou le filtrage pré-CEC.

Une part importante avait été accordée dans l'enquête de Charrière et al. (20) au monitorage cérébral pendant la chirurgie cardiaque et la CEC. Sous cette appellation de monitorage cérébral, il faut distinguer d'un côté le monitorage de la « profondeur de l'anesthésie » par l'EEG spontané ou évoqué et de l'autre les vraies approches de monitorage de fonction cérébrale dont la mesure du débit sanguin cérébral (DSC) par Doppler transcrânien ou de la saturation veineuse jugulaire interne en oxygène ($SvjO_2$) ou la saturation cérébrale en oxygène (par la spectrométrie en proche infrarouge). Ces deux dernières techniques ont pour objectif la mesure de la tolérance cérébrale à une éventuelle diminution du DSC.

III.4. Enquête de pratiques de la CEC en chirurgie cardiaque pédiatrique

Il existe peu d'enquêtes de pratiques de CEC pédiatriques et il n'en existe aucune en France. En 1996 Groom et al. (21) ont publié la plus complète, réalisée en 1994 sur 110 centres exclusivement nord-américains. Les auteurs soulignaient l'utilisation exclusive d'échangeurs gazeux à membrane, l'utilisation dans 96,1% des cas d'un filtre artériel et dans 92,3% des centres de l'ultrafiltration. Sur le plan de la sécurité 84,8% des centres utilisaient un détecteur de bulles, 66,7% un détecteur de niveau, et 48,5% un analyseur des gaz arrivant à la CEC.

Une étude plus récente (22) ne concernait que 17 centres pédiatriques. Ce rapport est issu d'une enquête avec 52% de réponses au questionnaire et montre une amélioration des pratiques de monitorage et de sécurité par rapport à 1994. Les réponses portant sur 7 721 patients pédiatriques ayant bénéficié d'une CEC montrent que le taux d'incidents était plus important en pédiatrie que chez les adultes, avec un incident pour 83 interventions (1,2%) responsable de dommages graves dans 15% des cas dont 2 décès, soit 0,023% de décès dus à la CEC. Les incidents rapportés sont d'abord liés à la coagulation (1/429 cas), à la neutralisation de l'héparine (1/483), à une défaillance de la pompe (1/858), à un problème de canulation artérielle (1/1 103), à la présence d'air dans le circuit (1/1 287), à la défaillance de l'oxygénateur (1/1 286), à une rupture ou une déconnexion (1/1 544). Les autres incidents rapportés sont exceptionnels.

Les dispositifs de sécurité pour les CEC pédiatriques consistaient en:

- filtre artériel (88% des centres);
- purge avec valve unidirectionnelle sur le filtre artériel (72%);
- filtre sur la ligne de cardioplégie (100%);
- valve unidirectionnelle sur la décharge gauche (76%);
- un circuit complet prêt en salle (76%);
- piège à bulles sur la ligne de cardioplégie (100%);
- détecteur de bulles sur la ligne artérielle (94%);
- détecteur de niveau sur le réservoir veineux (71%);
- détecteur de bulles sur la ligne artérielle avec arrêt automatique de la pompe (82%);
- détecteur de pression sur la ligne de cardioplégie avec arrêt automatique de la pompe (53%);
- détecteur de pression sur la ligne artérielle avec arrêt automatique de la pompe (53%);
- détecteur de niveau sur le réservoir veineux avec arrêt automatique de la pompe (47%).

Le monitorage rapporté comportait la mesure:

- de la pression sur la ligne de cardioplégie (94% des centres);
- de la pression sur la ligne artérielle (100%).

L'enquête rapportait également le monitorage en continu de:

- la saturation veineuse et de l'hémoglobine (86% des centres);
- la mesure des gaz du sang (76%).

L'enquête rapportait aussi l'utilisation de divers autres dispositifs de sécurité ou de monitorage comme:

- les manivelles pour les pompes (100% des centres);
- la check-list pré-CEC (94%);
- la bouteille d'oxygène de secours (88%);
- la source de lumière de secours sur batterie (100%);
- la batterie pour la pompe artérielle (76%);
- l'analyseur de FiO2 (65%).

III.5. Discussion des enquêtes de pratiques

Un élément important qui doit être pris en compte lors de l'analyse des résultats des enquêtes de Charrière et al. (20) et de Mejak et al. (6) est qu'elles rapportent le pourcentage de perfusionnistes ou de centres qui utilisent un type de monitorage. Ce pourcentage n'est pas superposable au pourcentage de patients qui bénéficient de ce monitorage. Par exemple, l'utilisation du moniteur BIS® (Aspect Medical System, Newton, MA, États-Unis) était rapportée par 42% des centres dans l'enquête de Charrière et al. (20). Le nombre de moniteurs et de capteurs commercialisés en France par Aspect Medical System, pour la période analysée par l'enquête, suggère que 42% des centres disposaient d'un faible nombre de moniteurs BIS® et que nettement moins des 42% des patients pris en charge dans les centres qui ont participé à l'enquête ont bénéficié de ce type de monitorage. Cette affirmation est confortée par les résultats d'une enquête française réalisée en 2001 et publiée en 2004 qui a montré que sur les trois jours de déroulement de l'enquête moins de 5% des patients avaient bénéficié d'une monitorage par le moniteurs BIS® (23).

Il existe des différences entre les pratiques françaises et nord-américaines de CEC. Elles concernent surtout le monitorage plus fréquent aux États-Unis de la pression au niveau de différents sites du circuit de CEC (en amont et en aval de l'oxygénateur, sur le circuit de cardioplégie) ainsi que l'utilisation plus fréquente de dispositifs comme les filtres artériels, les valves unidirectionnelles, les détecteurs de bulles, la présence de consoles de CEC de secours, de batteries de secours, etc.

Les deux enquêtes citées mettent en évidence une hétérogénéité des pratiques de CEC. L'hétérogénéité des pratiques en France reflète, comme le soulignent Charrière et al. (20), l'absence de recommandations des sociétés savantes.

L'hétérogénéité des pratiques a été mise en avant comme facteur d'erreurs dans les systèmes complexes (5). Il est probable qu'elle contribue aux incidents et aux accidents de la CEC (6). Les efforts pour diminuer l'hétérogénéité des pratiques ont probablement contribué à la diminution de la morbidité et de la mortalité en anesthésie (15).

IV. BILAN DES INCIDENTS/ACCIDENTS LIES À LA CEC

Les définitions légales françaises des incidents et accidents médicaux ont été formulées dans le document de l'Anaes de 2003 (24). Dans ce document figurent les notions d'accident (risque patent), de complications non évitables, de presque accident (*near-miss;* situation qui aurait conduit à l'accident si des conditions favorables n'avaient pas permis de l'éviter), d'incidents (événements fortuits, peu importants en soi et n'ayant pas engendré de conséquences).

Dans l'enquête de Mejak et al. (6) un incident était défini comme une anomalie qui n'a pas eu de conséquences immédiates sur le patient mais a nécessité des mesures de correction. Un accident était défini par une anomalie qui a laissé des séquelles malgré la correction ou qui a entraîné un allongement de l'hospitalisation.

Le plus souvent, les conséquences des incidents/accidents liés à la CEC ont été analysées à court terme (délai souvent non précisé mais estimé à 30 jours postopératoires).

IV.1. Résultats

Il n'existe pas de données françaises sur l'incidence des incidents et accidents liés à la CEC.

Il existe dans la littérature anglo-saxonne plusieurs enquêtes sur l'incidence des incidents et des accidents liés à la CEC. L'enquête la plus récente reflète de manière plus fidèle les pratiques actuelles et a analysé le plus grand nombre de patients (6). L'incidence des incidents dépend du nombre d'items présents dans les questionnaires (1 incident/1 000 CEC avec 5-15 questions versus 1/138 avec 20 questions versus 1/35 avec 72 questions) (6).

Dans l'enquête de Mejak et al. (6) réalisée dans 1 012 centres de chirurgie cardiaque (79% des centres ont répondu ce qui représente 671 290 interventions de chirurgie cardiaque avec CEC) aux États-Unis entre juillet 1996 et juillet 1998, il a été mis en évidence qu'un incident survenait pour 138 CEC. Un accident grave pouvant aller jusqu'au décès pouvait survenir pour 1 453 CEC. L'incidence des accidents graves pouvant conduire au décès a diminué de 1/1 000 CEC en 1986 à 1/1 453 CEC dans l'enquête de Mejak et al. (6). Les auteurs font l'hypothèse (sans pouvoir apporter des preuves) que la diminution de l'incidence des accidents graves/décès pourrait être en relation avec l'amélioration des techniques de monitorage et des procédures de sécurité (6).

Les incidents les plus fréquents dans l'enquête de Mejak et al. (6) étaient les problèmes de coagulation (1/771 CEC) et les réactions à la protamine nécessitant la ré-héparinisation et le démarrage d'une autre CEC (1/783 CEC).

La liste des autres incidents répertoriés par l'enquête de Mejak et al. (6) est présentée dans le tableau 2.

Tableau 2. Incidents de la CEC (modifié d'après Mejak et al., 2000) (6).

Incident	Survenue		Conséquences graves		Décès		*Modification possible par le monitorage et/ou un dispositif de sécurité* *
Anomalies de l'hémostase	1/783		1/4	829	1/13	700	Oui
Réaction à la protamine	1/771		1/9	872	1/29	187	?
Panne de l'échangeur thermique	1/1	809	0		0		?
Air présent dans le circuit de CEC	1/1	849	1/335	645	0		Oui
Présence de thrombus visible dans le circuit pendant la CEC	1/2	283	1/223	763	1/55	941	Oui
Dissection aortique	1/2	291	1/11	987	1/16	373	Oui
Dysfonction de l'oxygénateur	1/2	459	1/335	645	0		Oui

Changement d'oxygénateur en urgence	1/4	662	0		0		Oui
Défaillance mécanique d'une pompe de CEC	1/2	582	0		0		?
Utilisation des manivelles	1/3	356	1/95	899	0		Oui
Déplacement de la canule aortique	1/3	709	1/111	882	1/671	290	Oui
Panne électrique avec mise en route du générateur de secours	1/4	118	1/671	290	0		Oui
Rupture d'une tubulure ou déconnexion	1/4	144	1/223	763	1/335	645	Oui
Défaillance électrique ou mécanique de la console de CEC	1/4	475	0		1/671	290	?
Réaction transfusionnelle	1/6	159	1/67	129	1/167	823	?
Embolie gazeuse par la ligne de cardioplégie	1/7	716	1/223	763	1/671	290	Oui
Erreur de cardioplégie	1/8	497	1/671	290	1/671	290	?
Erreur d'administration des médicaments	1/8	606	1/223	763	0		?
Changement de circuit à cause d'un problème de contamination	1/23	148	1/671	290	1/335	645	?
Embolie gazeuse à partir des lignes de décharge	1/24	863	1/223	763	1/335	645	Oui
Embolie gazeuse massive	1/29	187	1/111	882	1/111	882	Oui
Fuite d'eau dans le circuit de CEC	1/37	294	1/671	290	0		Oui
Erreur transfusionnelle	1/61	026	0		1/335	645	?

* **Note:** *Avis du groupe de travail*

IV.1.1. Incidents et accidents liés à l'utilisation des CEC avec pompes centrifuges

Les incidents et accidents liés à l'utilisation des CEC avec pompes centrifuges ont fait l'objet de peu de publications (25). Il a été montré qu'un dysfonctionnement lié à l'utilisation des pompes centrifuges avait été signalé pour 3 763 utilisations (soit 93 incidents pour 350 000 utilisations). Parmi les 93 incidents le rapport (25) fait part de 5 décès et de 3 patients ayant des séquelles graves. L'incidence des incidents/accidents liés à l'utilisation des CEC avec pompes centrifuges est certainement sous-estimée car de nombreuses complications n'avaient pas été rapportées (25). Ces résultats suggèrent que l'incidence des incidents et accidents rapportés avec les CEC qui utilisent des pompes centrifuges est comparable à celle des CEC conventionnelles.

IV.1.2. Incidents liés aux problèmes d'alimentation électrique (défaillances électriques) des consoles de CEC

Tous les appareils électriques liés à la console de CEC ou au monitorage pendant la CEC doivent avoir un marquage CE et respecter les normes de sécurité électrique en vigueur en France. La réglementation impose, pour les secteurs sensibles de l'hôpital, dont les blocs opératoires font partie, des systèmes et procédures permettant d'assurer la continuité des soins en cas de défaillance de l'alimentation principale (arrêtés du 7 janvier 1993 et du 03 octobre 1995) (26,27). Le décret 2001-1154 du 05 décembre 2001 (28) impose aux exploitants de dispositifs médicaux de mettre en œuvre, selon les types d'appareils, des maintenances et des contrôles de qualité internes et externes. Le matériel de CEC, faisant partie de la catégorie de marquage CE classe II b, est visé par l'obligation de maintenances préventives.

En dehors de ces principes, il existe peu de travaux sur ce sujet dans la littérature internationale et pratiquement pas en France.

Dans l'enquête de Mejak et al. (6) une défaillance électrique de l'alimentation principale avec mise en route de l'alimentation de secours a été observée avec une incidence de 1/4 118 CEC; un seul cas sur 671 290 a eu des conséquences graves pour le patient. Une enquête complémentaire sur le même collectif de patients (671 290 patients) souligne le fait qu'il a été nécessaire de faire tourner la pompe principale de la CEC à l'aide d'une manivelle 200 fois et que dans 7 cas, la panne électrique a eu pour conséquence un allongement de la durée de séjour (22). L'incidence des défaillances électriques est faible. Pour un centre de chirurgie cardiaque qui réalise 800 interventions avec CEC/an une panne électrique risque de survenir une fois tous les 5 ans.

Hargrove et al. (29) estiment, sur une série de 3 500 CEC, que les défaillances électriques ont une incidence de 1/1 000 CEC. La description détaillée des défaillances électriques par Hargrove et al. est intéressante car elle explique des défaillances en chaîne de l'alimentation centrale, de l'alimentation auxiliaire et des piles de courant continu. Hargrove et al. décrivent des pannes du générateur de secours liées à une rupture du piston, à un défaut de refroidissement du générateur ainsi qu'une panne liée à un survoltage qui s'est accompagnée de la destruction de nombreux appareils électriques dans les salles d'opération.

IV.2. Avis du groupe de travail sur les incidents et accidents liés à la CEC

Le caractère rétrospectif de l'enquête permet de faire l'hypothèse que le nombre réel d'incidents/accidents graves est en réalité plus important. L'incidence des incidents et accidents rapportée par Mejak et al. (6) ne peut être analysée qu'en tenant compte du pourcentage élevé de perfusionnistes qui utilisent les dispositifs de sécurité cités plus haut. L'incidence des incidents/accidents liés à la CEC est relativement faible. Pour cette raison, compte tenu du nombre moyen d'interventions de chirurgie cardiaque réalisé dans chaque centre en France qui est d'environ 700 par an (20), même les incidents les plus fréquents comme la survenue d'une anomalie de la coagulation ou d'une réaction à la protamine peuvent passer « inaperçus » dans un seul centre en l'absence d'un recueil prospectif des incidents/accidents. De la même manière, le faible nombre d'incidents/accidents rend presque illusoire la réalisation de toute étude prospective randomisée destinée à montrer le bénéfice d'une technique ou d'une stratégie de monitorage pendant la CEC.

Les anomalies de l'hémostase rapportées dans l'enquête de Mejak et al. (6) ne peuvent pas être analysées correctement à cause de l'absence des définitions. Il s'agit d'incidents survenus pendant la CEC ou en tant que conséquence de la CEC. De surcroît, l'interprétation de ces résultats est difficile en l'absence d'informations sur les techniques de monitorage de la coagulation, les protocoles d'administration de l'héparine /protamine, les stratégies d'hémodilution et de transfusion.

L'incidence élevée des accidents survenus lors de l'administration de la protamine est difficile à analyser en l'absence d'informations sur les modalités d'administration de ce médicament. Compte tenu des mécanismes impliqués dans les accidents à la protamine (30), certains effets sont en relation avec une administration trop rapide, d'autres avec une vraie réaction anaphylactique. Un monitorage plus sophistiqué n'aurait permis d'éviter un accident pour aucune de ces situations.

Plusieurs incidents comme la survenue d'une dissection aortique ou d'une défaillance de l'oxygénateur pourraient être plus facilement diagnostiqués avec un monitorage des pressions au niveau de la ligne artérielle.

L'entretien du matériel de CEC (consoles, pompes, etc.) et la calibration des moniteurs et des dispositifs de sécurité doivent bénéficier du même niveau d'attention que le monitorage. Certains incidents peuvent probablement être évités par un entretien plus efficace des consoles de CEC (défaillances mécanique et électrique).

Certains incidents ne peuvent probablement pas être évités avec une sophistication du monitorage (accidents allergiques à la protamine ou à l'aprotinine par exemple).

Il est indispensable d'avoir un raisonnement du type « nombre de patients qu'il faut monitorer pour éviter un incident » et à partir de cette approche faire une estimation du coût d'un incident/accident évité. Le coût estimé du circuit de CEC et celui lié à la perfusion dans sa totalité ne représentent aux États-Unis que 10% du coût global d'une chirurgie cardiaque (31). Comme il a été justement souligné, les modifications des techniques de perfusion peuvent avoir un impact mineur sur le coût de la perfusion mais beaucoup plus important pour le coût global de la chirurgie (31). La gestion d'un certain nombre de composantes de la CEC peut aboutir à diminuer le degré d'hémodilution ou l'administration excessive d'héparine; par exemple en rajoutant des filtres artériels, il est possible de diminuer la réaction inflammatoire, en rajoutant des médicaments comme l'aprotinine la réaction inflammatoire peut être diminuée. L'ensemble de ces modifications rajoute un surcoût. Néanmoins, les effets bénéfiques de ces mesures supplémentaires doivent être estimés sur des paramètres mesurés après la CEC (besoins transfusionnels diminués, moindre immunosuppression car moins de transfusions homologues, atténuation de la réaction inflammatoire, diminution de l'eau extravasculaire pulmonaire, extubation plus rapide, etc.).

V. LES DIFFÉRENTS PARAMÈTRES MONITORÉS

V.1. Continuité de la surveillance et du monitorage entre la période pré-CEC, l'institution de la CEC, le déroulement de la CEC, le sevrage de la CEC et le retour aux fonctions cardio-respiratoires des patients

❏ Données disponibles

La Société française d'anesthésie-réanimation (SFAR) a publié en 1994 des normes de surveillance et de monitorage minimum pour la période peropératoire et pour la période de surveillance postinterventionnelle (16).

Les recommandations de la SFAR concernent la présence du personnel médical et paramédical et la surveillance du patient et de l'appareil d'anesthésie. La surveillance du patient porte sur l'oxygénation, la ventilation, la circulation, la « profondeur de l'anesthésie » et la curarisation. La SFAR recommande que chaque site d'anesthésie dispose d'un moniteur électrocardiographique (ECG), d'un appareil de mesure automatique de la pression artérielle, d'un oxymètre de pouls, d'un capnographe et d'un analyseur de gaz anesthésique.

Les recommandations de la SFAR concernant la surveillance des patients en cours d'anesthésie devraient continuer à s'appliquer à la période de la CEC car l'anesthésie continue pendant toute cette période.

Pour éviter la diminution du niveau et de la qualité de la surveillance des patients pendant la CEC, il est souhaitable qu'en plus des paramètres de surveillance et de monitorage minimum recommandés par la SFAR (et des paramètres supplémentaires adaptés à l'état clinique du patient pour la chirurgie cardiaque), des paramètres spécifiquement liés aux techniques de CEC soient surveillés et monitorés.

Il a été souligné que le monitorage des fonctions vitales pendant la CEC était peu différent du monitorage des fonctions vitales pendant la période peropératoire en général (32) et que la période de la CEC n'occupe qu'une partie de la période opératoire. Le choix et la mise en place du monitorage sont habituellement sous la responsabilité du médecin anesthésiste qui partage ces informations avec l'équipe chirurgicale, l'équipe de perfusion et l'équipe paramédicale.

Selon les recommandations de l'Australasian Society of Cardio-Vascular Perfusionists, le déroulement de la CEC dans les meilleures conditions de sécurité pour les patients est la responsabilité conjointe du médecin anesthésiste-réanimateur, du chirurgien et du perfusionniste (33).

❏ Avis des experts

Le groupe de travail estime qu'il est indispensable que les trois principaux intervenants, le chirurgien, le médecin anesthésiste et le perfusionniste aient une stratégie commune concernant le monitorage peropératoire et per-CEC. Il est également indispensable que pendant toute la durée de la CEC le médecin anesthésiste, le chirurgien et le perfusionniste soient présents dans la salle d'opération (33).

V.2. Monitorage des pressions

Le monitorage de la pression de perfusion systémique est indispensable pour la période per-anesthésique (16) et en chirurgie cardiaque le monitorage de la pression artérielle est réalisé par cathétérisme artériel.

La CEC per se nécessite des sites supplémentaires de monitorage des pressions.

- Le monitorage de la pression dans le territoire cave supérieur par l'intermédiaire des cathéters veineux centraux, associé à l'analyse des signes cliniques, est utile pour l'estimation du retour veineux en même temps que l'analyse du volume présent (stable, en augmentation ou en diminution) dans le réservoir veineux (32). Il permet d'estimer la pression de perfusion cérébrale. Il ne permet pas d'estimer le retour veineux dans le territoire cave inférieur.
- Le monitorage de la pression en amont et en aval de l'oxygénateur permet de calculer le gradient de pression à travers l'oxygénateur et d'évoquer une défaillance de l'oxygénateur (32).
- Le monitorage de la pression sur la ligne artérielle, en aval de l'oxygénateur, permet de détecter un problème de canulation aortique (malposition de la canule aortique), de dissection aortique, de coude ou de clamp sur la ligne artérielle. Certaines consoles de CEC sont équipées de dispositifs qui permettent l'arrêt de la pompe à galets en cas de surpression sur la ligne artérielle. Les mesures de la pression en amont et en aval de l'oxygénateur apportent des informations complémentaires. Si un seul site de mesure est choisi, ceci pourrait aboutir une perte d'informations lorsque le perfusionniste doit trouver la cause des anomalies observées.
- Le monitorage de la pression dans la ligne d'administration de la cardioplégie permet de détecter les problèmes de canulation (sinus coronaire pour les cardioplégies rétrogrades).
- D'autres sites de monitorage de la pression peuvent être nécessaires en fonction des techniques chirurgicales (territoire jugulaire en cas de perfusion rétrograde par exemple).

Particularités de la mesure des pressions en chirurgie cardiaque pédiatrique

La littérature est très pauvre sur ce sujet. Une étude descriptive sur 21 enfants montrait que la mesure de la pression dans l'artère radiale sous-estimait de façon significative la pression de perfusion par rapport à la mesure au niveau de l'artère fémorale, particulièrement à la fin de la CEC (34).

La mesure de la pression de perfusion lors de la délivrance de la cardioplégie est souhaitable dans tous les cas mais devient essentielle au cours de la CEC néonatale (35).

V.3. Monitorage multimodal de l'oxygénation

Dans le contexte de l'anesthésie, le monitorage multimodal a pour objectif de détecter des anomalies de la ventilation et de l'oxygénation et de faire rapidement le diagnostic étiologique de ces anomalies (16).

Le monitorage de la ventilation et de l'oxygénation pendant la CEC s'inscrit dans le même cadre conceptuel. L'analyse de la FiO_2 permet de détecter rapidement une anomalie de l'alimentation en gaz de l'oxygénateur. L'analyse du CO_2 au niveau de l'évent de l'oxygénateur permet d'analyser rapidement l'adéquation entre le débit de gaz et la production de CO_2 pour éviter l'hypo et l'hypercapnie qui peuvent modifier les débits sanguins régionaux, notamment le débit sanguin cérébral. Il n'existe pas en France de dispositifs de monitorage du CO_2 expiré destinés spécifiquement aux oxygénateurs des CEC. Le monitorage des gaz du sang artériel et veineux pendant la CEC permet d'estimer les performances de l'oxygénateur, la consommation en O_2 et la production de CO_2 du patient (32).

V.4. Monitorage en continu de la PO2 pour la CEC en chirurgie cardiaque néonatale

Les travaux expérimentaux et cliniques montrent depuis au moins deux décennies les effets toxiques de l'oxygène en période néonatale (36). Plus le nouveau-né est prématuré, plus le risque de bronchodysplasie pulmonaire, de rétinopathie, d'entérocolite nécrosante et de persistance du canal artériel est important (37). La toxicité de l'oxygène est liée à la production de radicaux libres dont l'une des principales sources est le système xanthine-hypoxanthine oxydase. Il a été possible de mesurer ce stress oxydatif en mesurant l'oxydation des protéines sur les aspirations bronchiques de nouveau-nés ventilés (38). Chez les enfants de très petit poids, une PaO_2 de 5,5kPa suffit à obtenir une saturation artérielle de 90%, permettant de réduire la FiO_2 et par conséquent la toxicité induite par l'oxygène (39). La toxicité de l'oxygène dépend de la durée d'exposition, de la concentration et de la pression d'exposition (40).

V.5. Monitorage de la SvO2

Le monitorage de la SvO2 permet d'estimer l'adéquation globale entre le transport et la consommation d'oxygène (32) et de détecter, tardivement, une anomalie de ventilation ou d'oxygénation. Ce paramètre intégratif est le témoin d'une anomalie physiologique qui peut avoir plusieurs causes. L'analyse des informations fournies par le monitorage des autres paramètres de circulation et de ventilation permet de faire le diagnostic étiologique de la dysfonction.

V.6. Monitorage de l'anticoagulation

L'analyse des données de Mejak et al. indique que les anomalies de l'hémostase (définitions non fournies par les auteurs), pendant ou après la CEC, sont les incidents les plus fréquemment rapportés par l'enquête qu'ils ont menée (6). La stratégie de monitorage des effets des médicaments anticoagulants dépend des objectifs définis, concept qui a été développé par Bélisle (41). Ces objectifs, du plus simple vers les plus compliqués, sont:

- éviter la coagulation en masse du circuit de CEC et la présence de thrombi visibles au niveau du circuit de CEC ou dans le champ opératoire;
- atteindre une anticoagulation estimée comme « efficace » par la mesure d'un paramètre physique considéré comme étant étroitement corrélé à un paramètre clinique (risque très faible voire nul de thrombose du circuit) (42);
- optimiser l'anticoagulation pour diminuer la consommation des facteurs de la coagulation, les pertes sanguines et les besoins transfusionnels.

V.6.1. Éviter la coagulation du circuit de CEC

Cet objectif, purement clinique, est implicite et ne nécessite aucun monitorage en plus de l'administration d'une dose d'anticoagulant (le plus souvent l'héparine non fractionnée ou HNF) ajustée au poids. Il existe encore en France des centres de chirurgie cardiaque qui ne font appel à aucun monitorage pour mesurer les effets des traitements anticoagulants. Compte tenu de la variabilité inter et intra-individuelle des relations dose-concentration d'HNF et concentration d'HNF-effet anticoagulant mesurées par un test de coagulation, le monitorage de l'effet anticoagulant de l'HNF pendant la CEC est indispensable. Les mesures de l'effet anticoagulant de l'HNF doivent être réalisées après l'administration de l'HNF avant le début de la CEC, ensuite régulièrement pendant toute la CEC et après l'arrêt de la CEC et l'administration de protamine (41).

V.6.2. Atteindre une anticoagulation estimée efficace

Il s'agit de l'objectif le plus souvent ciblé. Pour atteindre cet objectif il est nécessaire d'avoir recours à la mesure de l'effet anticoagulant de l'HNF par la mesure d'un temps de coagulation. Il existe plusieurs principes et plusieurs techniques pour chaque principe de mesure du temps de coagulation.

Le principe le plus utilisé est la mesure d'un temps de coagulation du sang total après la mise en contact du sang avec un activateur. Ce temps de coagulation activé (activated clotting time ou ACT abrégé en anglais pour ne pas le confondre avec l'abréviation française TCA ou temps de céphaline avec activateur) peut être mesuré par différentes méthodes de détection du caillot. Comme les activateurs diffèrent et les méthodes de détection de formation du caillot sont différentes, il n'est pas possible de fixer une valeur unique d'ACT applicable à tous les types de mesures et à tous les types d'appareils. Une équivalence entre les différents types d'appareils et méthodes de mesure de l'ACT a été proposée par Bélisle (41) à partir des données de la littérature.

La principale limite de l'ACT est que, dans un certain nombre de situations, relativement fréquentes en pratique clinique courante, l'allongement de l'ACT n'est pas dû à l'effet anticoagulant de l'héparine mais à des facteurs confondants comme l'hypothermie, l'hémodilution excessive, etc. (41, 42). Il a été suggéré que dans ces situations, le monitorage à la fois de l'ACT et de la concentration d'héparine (soit par titration directe héparine-protamine, soit par la mesure de l'activité anti-Xa) pouvait mettre en évidence les situations où l'allongement de l'ACT n'était pas en relation avec l'effet anticoagulant de l'héparine (41, 42).

Tous les centres doivent utiliser, pour tous les patients qui bénéficient d'une CEC, le monitorage de l'ACT sur sang total par une des techniques disponibles sur le marché en tenant compte des équivalences proposées entre les différents appareils (41) pour fixer la limite inférieure de l'ACT qui correspond à une anticoagulation considérée comme adéquate (41). Cette limite inférieure devrait idéalement être documentée dans chaque centre (41) sur des critères cliniques (présence de thrombi au niveau de l'oxygénateur; survenue de complications thrombotiques pendant la CEC, saignement en relation avec une coagulopathie de consommation, besoins transfusionnels) ou des critères intermédiaires (dosage dans le plasma de complexes protéiques qui témoignent de la génération de thrombine comme par exemple les complexes thrombine-antithrombine).

Le changement du type d'HNF, voire du lot, pourrait nécessiter une réévaluation de la limite inférieure d'anticoagulation. Une telle démarche, bien que théoriquement souhaitable, n'a jamais été entreprise en France et ne le sera probablement jamais à cause du coût excessif d'une telle approche.

En plus des éléments cités plus haut, la limite inférieure de l'ACT doit être définie en fonction: (i) du type de moniteur et d'activateur utilisé; (ii) du coefficient de variation de la mesure (étudié dans les conditions cliniques d'utilisation et non celui rapporté par le fabricant); il a été proposé (41), par mesure de sécurité, de rajouter le double de la valeur du coefficient de variation à la valeur minimum prédéfinie pour augmenter la marge de sécurité; il a également été proposé, lorsque le coefficient de variation de la mesure dépasse 15%, de réaliser les mesures en double et de retenir seulement la valeur la plus basse (41).

Plusieurs auteurs ont souligné l'importance de l'accès, dans un délai raisonnable, aux résultats du dosage de la concentration d'HNF par un des deux tests cités plus haut, considérés comme un dosage fonctionnel de l'héparine (41, 42) et non pas comme un dosage «massique». Les limites méthodologiques liées à la mesure au laboratoire de l'activité anti-Xa doivent être connues (41).

Le problème du monitorage de l'effet anticoagulant de l'HNF pendant la CEC a récemment été revu par un groupe d'experts français (43). Ces auteurs ont souligné que les données de la littérature ne permettaient pas d'analyser les avantages de l'utilisation de l'ACT versus l'activité anti-Xa pour monitorer l'effet anticoagulant de l'HNF. Le groupe de travail qui a élaboré le présent document considère que l'utilisation de l'activité anti-Xa pour le monitorage de l'effet anticoagulant de l'HNF, à la place de l'ACT, pendant la CEC, poserait des problèmes majeurs liés (i) aux délais trop longs (de 30 à 60 minutes minimum) avant l'obtention des résultats lorsque cet examen est réalisé au laboratoire central; (ii) à la nécessité d'avoir accès à cet examen de laboratoire 24 heures sur 24. La mesure de l'activité anti-Xa par des appareils aux sites de soins poserait également des problèmes majeurs de surcoûts et de gestion des stocks des réactifs pour un bénéfice clinique qui n'est pas démontré (44).

Pour les situations, rares, où l'HNF ne peut pas être utilisée comme anticoagulant pendant la CEC, un monitorage adéquat devrait être utilisé, adapté à chaque type/stratégie d'anticoagulation utilisés (45).

V.6.3. Optimiser l'anticoagulation pour diminuer la consommation des facteurs de la coagulation, les pertes sanguines et les besoins transfusionnels

Ces objectifs thérapeutiques ne sont pas suffisamment étayés par les résultats de la littérature pour permettre, dans l'état actuel des connaissances, de recommander l'utilisation d'un monitorage sophistiqué pour tous les patients. Des revues de la littérature sur ce sujet ont été publiées (46,47). La diminution du saignement périopératoire et des besoins transfusionnels homologues passe aussi par l'utilisation de l'aprotinine ou d'autres antifibrinolytiques (48,49), la gestion des aspirations de sang à partir du champ opératoire (50); l'utilisation des circuits de CEC pré-héparinés (31) avec un bénéfice plus important en faveur des circuits pré-héparinés avec liaisons covalentes (31). Dans l'état actuel des connaissances et compte tenu du surcoût et des problèmes de formation à l'utilisation de plusieurs types de moniteurs d'anticoagulation pendant la

CEC, le groupe de travail estime que cet objectif doit faire l'objet d'études complémentaires.

V.6.4. Particularités du monitorage de l'anticoagulation en chirurgie cardiaque pédiatrique

La sensibilité des patients pédiatriques à l'héparine est plus faible que celle de l'adulte, et les niveaux requis d'anticoagulation plus variables entre les différents types d'interventions chirurgicales. Cette variabilité accrue est liée à une hémodilution plus importante, une utilisation plus fréquente de l'hypothermie, mais également au métabolisme hépatique et aux conséquences de certaines cardiopathies (polyglobulie). En dessous d'un an, il existe une grande disparité entre la concentration d'héparine sur sang total et l'activité anti-Xa (51). L'étude de 16 centres britanniques prenant en charge plus de 3 000 patients pédiatriques par an montre que l'objectif de la surveillance de l'anticoagulation se fait sur l'ACT qui doit être entre 400 et 700 secondes et surveillé en moyenne toutes les 20 minutes (extrêmes de 15 à 60 min) (52). Dans ces conditions, le monitorage de l'anticoagulation en CEC pédiatrique doit être particulièrement attentif et ne peut pas se limiter à la mesure de l'ACT. Les situations complexes nécessitent le recours à des tests d'hémostase plus complets (51).

Lors de la neutralisation de l'héparine par la protamine, les complexes héparine-protamine sont particulièrement actifs sur la vasomotricité pulmonaire et le myocarde de l'enfant, réclamant une attention particulière pour éviter tout excès de protamine (53). L'utilisation de plus en plus fréquente de l'aprotinine en CEC pédiatrique (51) (81% des centres dans l'étude de Codispoti et al. au Royaume-Uni (52)) encore étayée par la mise en évidence récente de son efficacité par Mössinger et al. (54) aboutit aux mêmes recommandations que pour le patient adulte sur l'utilisation préférentielle de l'ACT au kaolin plutôt qu'à la celite (55).

V.7. Monitorage de la température

Les problèmes liés au choix du site de monitorage de la température per-CEC sont nombreux (32) et la controverse entre les avantages et les risques des CEC en normothermie versus hypothermie persiste. Une méta-analyse publiée par la Cochrane Library (56) montre que l'hypothermie per-CEC pourrait avoir un effet bénéfique en diminuant l'incidence des complications neurologiques mais un effet délétère si d'autres types de complications sont pris en compte.

V.7.1. Les sites de mesure de la température pendant la CEC

Ils peuvent être classés en:

- sites de mesure sur le patient; ces sites peuvent être divisés en sites centraux (censés refléter la température du cortex cérébral, elle-même le reflet de la température de l'hypothalamus, responsable de la thermorégulation) (32,57) et sites périphériques;
- sites de mesure sur le circuit de CEC et au niveau du générateur thermique.

Sites de mesure au niveau du patient

Les deux sites, cités dans la littérature comme étant le plus souvent utilisés pour le monitorage de la température pendant la CEC, sont le nasopharynx et la vessie (58). D'autres sites sont l'œsophage, la trachée, le sang dans l'artère pulmonaire, le rectum, le tympan. Chaque site a des avantages et des inconvénients (32) liés au fait que certains ne reflètent pas la température du cortex cérébral, d'autres ont un temps de réponse qui est trop long (32,57). Le choix d'un site de mesure de la température pendant la CEC doit être fait en fonction des objectifs. Les principaux objectifs sont les suivants. Pendant la phase de refroidissement, il faut s'assurer que la température cérébrale est suffisamment basse pour permettre l'allongement de la tolérance à l'ischémie. Dans ce cas, il faut choisir les sites de mesure qui reflètent le mieux la température cérébrale. Ces sites sont le tympan, le nasopharynx et l'œsophage (32). Pendant la phase de réchauffement, les objectifs sont: (i) éviter une hyperthermie cérébrale. Les trois sites cités précédemment permettent une estimation de la température cérébrale (32); (ii) éviter une hétérogénéité du processus de réchauffement dont témoignerait par exemple un température nasopharyngée proche de 37°C et une température vésicale ou rectale plus basse (32). Le risque d'un réchauffement incomplet est un rebond d'hypothermie (afterdrop) (32).

L'enquête de Charrière et al. (20) a montré qu'en France, le monitorage de la température sur deux sites n'était pas respecté par 8 centres sur les 48 ayant répondu. En France, les sites le plus souvent utilisés (ordre de décroissance) sont rectal, œsophagien, vésical, nasopharyngé et tympanique.

Sites de mesure au niveau du circuit de CEC et du générateur thermique.

À cause des problèmes liés à la solubilité des gaz en fonction de la température et afin d'éviter la génération d'embols gazeux, il est nécessaire d'éviter un gradient entre la température du générateur thermique et celle du sang veineux supérieur à 10°C. Par ailleurs, il est nécessaire d'éviter une hyperthermie cérébrale, facteur favorisant les complications neurologiques après la CEC (59).

V.7.2. Particularités du monitorage de la température en chirurgie cardiaque pédiatrique

L'importance du monitorage de la température en CEC pédiatrique est d'autant plus grande que de nombreuses interventions sont encore pratiquées en hypothermie, parfois profonde, afin de permettre l'arrêt circulatoire et protéger le cerveau. L'absence de littérature sur le meilleur site de mesure de la température ne permet pas de recommander un site plutôt qu'un autre, même si Kern et al. (60) ont montré que la mesure de la température du sang veineux jugulaire interne était le reflet le plus fidèle de la température cérébrale. Les sites nasopharyngé et tympanique restent les plus utilisés pour refléter la température cérébrale et le site œsophagien celle du cœur. La mesure de la température vésicale fournit des informations sur la température centrale tant que la diurèse est conservée.

V.7.3. Discussion du monitorage de la température

Compte tenu des limites concernant la fiabilité de la température nasopharyngée pour estimer la température cérébrale (58), afin d'éviter une hyperthermie cérébrale (59), il a été suggéré de monitorer la température du sang au niveau de la ligne artérielle et de ne pas dépasser une température de 37,5°C pour les CEC à plein débit et de 38°C pour les CEC partielles (32). À cause du risque de défaillance de mesure de la température sur un seul site, lorsqu'une CEC en hypothermie est effectuée, il est recommandé de monitorer la température dans au moins deux sites qui reflètent la température centrale (32). Le monitorage de la température sur trois sites (nasopharynx, œsophage, artère pulmonaire) est recommandé pour les arrêts circulatoires en hypothermie profonde (57). En normothermie, la mesure de la température au niveau d'un seul site peut être suffisante.

V.8. Monitorage de la fonction cérébrale pendant la CEC

Les complications neuropsychologiques après chirurgie cardiaque de l'adulte concernent de 1-5% des patients pour les complications de type I (accidents vasculaires cérébraux ou AVC constitués, coma) et de 30-60% pour les complications de type II (troubles neuropsychologiques) (61-63). Pour les patients qui ont bénéficié d'une chirurgie de revascularisation myocardique avec CEC, l'incidence des AVC constitués documentés sur des critères cliniques était de 1,63% sur un collectif de 503 478 interventions chirurgicales (64).

L'incidence des complications de type II dépend:

- des types de tests neuropsychologiques utilisés;
- du délai entre la chirurgie cardiaque et le moment où les tests ont été pratiqués;
- du seuil adopté pour définir une modification cliniquement significative des tests neuropsychologiques utilisés (65).

Il existe très probablement une augmentation de l'incidence des complications neurologiques liée spécifiquement à la CEC car il a été démontré sur des travaux rétrospectifs qu'à scores de gravité préopératoire comparables, les patients qui bénéficiaient d'une chirurgie de revascularisation myocardique sans CEC avaient une moindre incidence des complications neurologiques (incidence des AVC à 1,25%) que ceux opérés avec une CEC (incidence des AVC à 1,99%; $p < 0,001$) (66). Les résultats de cette étude rétrospective qui a porté sur 118 140 patients n'ont pas été confirmés par une méta-analyse (67) qui a porté sur un faible nombre d'études et de patients. La diminution de l'incidence des complications neurologiques en l'absence de la CEC a été mise sur le compte d'une diminution de la charge embolique cérébrale (68).

Ces problèmes seront abordés ici seulement dans la perspective du monitorage. Les résultats de l'enquête de Charrière et al. (20) peuvent être interprétés de la façon suivante:

Les anesthésistes français utilisent le monitorage des effets corticaux des médicaments anesthésiques (appelé communément monitorage de la « profondeur de l'anesthésie »).

Le moniteur BIS® (Aspect Medical System Inc, Natick, MA, États-Unis), bien que basé sur l'analyse du tracé EEG, n'est pas un moniteur de fonction cérébrale et ne peut pas se substituer au monitorage de l'EEG classique. Ce moniteur explore un seul hémisphère, avec seulement deux électrodes, et les médecins anesthésistes-réanimateurs ne sont pas formés pour analyser et interpréter le tracé EEG.

L'anesthésie pour chirurgie cardiaque est réputée comme étant associée à un risque plus élevé de mémorisation explicite (69) que d'autres types de chirurgie. La CEC représente une partie de l'anesthésie où le monitorage de la profondeur de l'anesthésie est plus difficile (70). Un des objectifs cliniques des moniteurs de « profondeur d'anesthésie » est de détecter les patients qui, surtout pendant la CEC, ont une hypotension artérielle qui inciterait à diminuer les doses/concentrations de médicaments hypnotiques alors que le niveau d'hypnose est insuffisant (risque de réveil et/ou de mémorisation explicite) (70).

Deux études récentes (71,72) ont montré que l'utilisation du moniteur BIS® pour surveiller le niveau de conscience pendant l'anesthésie diminuait de 80% l'incidence de la mémorisation explicite qui est de 1-2 cas pour 1 000 anesthésies générales en l'absence d'un tel monitorage (69). Sur la base de ces deux études, la Joint Commission on Accreditation of Healthcare Organizations (JCAHO; www.jcaho.org) (73) a publié le 7 octobre 2004 une note d'information concernant l'incidence de la mémorisation explicite peropératoire et cite une recommandation de la FDA selon laquelle l'utilisation du moniteur BIS® peut être associée à une réduction de l'incidence de la mémorisation explicite pendant l'anesthésie. Il s'agit d'une information de grande importance mais pour l'instant aucune société savante n'a recommandé l'utilisation systématique des moniteurs de profondeur de l'anesthésie. Le groupe d'experts estime que les recommandations concernant l'utilisation systématique des moniteurs de profondeur d'anesthésie doivent s'inscrire dans un cadre plus large que l'actuel document.

Les autres types de moniteurs de la fonction cérébrale utilisés

Ils ont pour objectifs de mesurer la tolérance corticale à une diminution du DSC. Un type de monitorage est communément accepté pour une indication précise: il s'agit de l'EEG pour s'assurer de l'existence d'un tracé isoélectrique lors de l'arrêt cardio-circulatoire en hypothermie profonde (74). Les autres types de moniteurs: les potentiels évoqués, la spectrométrie en proche infrarouge ou la saturation en oxygène au niveau du bulbe jugulaire (SvjO2) ne peuvent pas être recommandés dans l'état actuel des connaissances comme un monitorage de routine. Le monitorage continu de la SvjO2 est celui dont la technologie est utilisée en routine clinique avec des performances diagnostiques correctes et une compréhension de la signification physiologique et physiopathologique du paramètre mesuré (75-81). Dans la mesure où aucune société savante de perfusion, de chirurgie ou d'anesthésie n'a formulé de recommandations concernant le monitorage cérébral, les auteurs de ce rapport considèrent aussi qu'il n'existe pas suffisamment de preuves pour recommander une stratégie ou une technique de monitorage cérébral pendant la chirurgie cardiaque avec CEC.

Il est important de souligner le fait que les moniteurs de fonction cérébrale destinés à être utilisés pendant la CEC ont été développés dans un cadre conceptuel selon lequel la cause des complications neurologiques de type I (et probablement celles de type II) était une hypoperfusion cérébrale. Dans ce cadre conceptuel, la détection d'une diminution du DSC (mesure de la vélocité au niveau de l'artère cérébrale moyenne par Doppler) et/ou celle de la mauvaise tolérance d'une diminution du DSC (tracé EEG, SvjO2) étaient les principaux objectifs du monitorage. Plusieurs travaux récents suggèrent que l'hypoperfusion cérébrale (diminution du DSC) ne serait responsable que d'environ 25% des accidents neurologiques de type I. La principale cause de complications neurologiques de type I lors de la chirurgie cardiaque serait la charge embolique, surtout athéromateuse, liée à la présence de plaques d'athérome au niveau de l'aorte (82). Des recommandations récentes de l'American Heart Association/ American College of Cardiology sur la pratique de la chirurgie des pontages coronariens ont désigné le dépistage de l'athérome aortique par échographie épi-aortique comme la principale stratégie capable de diminuer les complications neurologiques de type I après chirurgie cardiaque (83).

Particularités du monitorage de la fonction cérébrale en chirurgie cardiaque pédiatrique

Il existe de nombreuses publications concernant les complications neuropsychologiques survenant après chirurgie cardiaque pédiatrique. Les travaux publiés par le groupe de Boston qui suit un groupe de 172 nouveau-nés opérés de 1988 à 1992 (84-88) ainsi que ceux provenant d'autres groupes (89) sont souvent cités. Une étude récente (90) montre que la plupart des nouveau-nés opérés avec CEC présentent des complications cérébrales. Les raisons de ces lésions sont à la fois multiples et d'origine mal connue (91-93). La surveillance de l'oxygénation du tissu cérébral semble intéressante mais le manque de spécificité et de précision des moyens actuels (saturation veineuse jugulaire en oxygène et spectroscopie dans le proche infrarouge) ne permet pas encore de recommander une méthode de monitorage de la fonction cérébrale. Dans certaines circonstances, la surveillance de l'EEG a permis d'alerter sur une diminution du débit sanguin cérébral (94) mais présente les mêmes inconvénients que pour les patients adultes. Les seules recommandations validées sont, en cas d'utilisation de l'hypothermie profonde, de monitorer les temps de refroidissement et de réchauffement qui doivent durer autour de 20 minutes pour le refroidissement et être précédés pour le réchauffement d'une recirculation froide de 10 minutes (95-97). Malgré un faible effectif (n = 18) Shaaban et al. (98) ont montré l'efficacité de la spectroscopie dans le proche infrarouge pour monitorer la désaturation cérébrale survenant lors du réchauffement de CEC hypothermique. Le coût et la difficulté d'interprétation des résultats ne permettent cependant pas de recommander l'utilisation en routine de la spectroscopie dans le proche infrarouge au cours des CEC pédiatriques.

V.9. Autres types de monitorage pour la CEC en chirurgie cardiaque néonatale. Arguments concernant la mesure en discontinu des concentrations plasmatiques de calcium ionisé

Le calcium ionisé est abaissé chez le nouveau-né transfusé, en CEC, au cours d'un sepsis, d'une transplantation cardiaque ou hépatique. Au cours de la CEC, des diminutions importantes du calcium ionisé peuvent induire une instabilité hémodynamique. La mesure du calcium total ne permet pas d'identifier ces taux anormalement bas du calcium ionisé (99). La CEC peut induire fréquemment, et ce d'autant plus que l'enfant est jeune, des alcaloses métaboliques responsables de taux anormalement bas de calcium ionisé (100). La concentration de citrate fait fluctuer le taux de calcium ionisé au cours de la CEC pédiatrique, rendant nécessaire le contrôle du calcium ionisé pour maintenir la fonction cardiaque et diminuer les lésions de reperfusion (101). La normalisation du calcium ionisé dans le volume d'amorçage d'une

ECMO néonatale permet d'obtenir une meilleure stabilité hémodynamique au démarrage de la CEC (102).

V.10. Mesure répétée de la glycémie

La CEC hypothermique est responsable de larges variations de la sécrétion d'insuline et de l'homéostasie du glucose (103,104). La suppression de l'apport glycémique lors du jeûne préopératoire fait courir le risque d'hypoglycémie grave (105), faisant recommander la mesure de la glycémie particulièrement chez le nouveau-né au cours de la CEC (106,107). Récemment, de Ferranti et al. (108) ont publié les résultats d'une étude prospective randomisée concernant 171 nouveau-nés opérés d'une transposition des gros vaisseaux. Les auteurs ont montré que l'hypoglycémie post-CEC était corrélée à la survenue de convulsions à l'EEG et au ralentissement d'un retour à la normale de l'EEG. Dans la même étude, de fortes concentrations de glucose n'étaient associées à aucune complication. Les auteurs concluent qu'il faut éviter l'hypoglycémie et que l'hyperglycémie n'est pas délétère chez les nouveau-nés et enfants bénéficiant d'une CEC avec arrêt circulatoire (108).

V.11. Dispositifs de sécurité associés à la console de CEC

Les détecteurs de niveau bas sont installés sur le réservoir veineux pour alerter le perfusionniste que le niveau de liquide/sang dans le réservoir est en dessous d'une limite fixée. En fonction du niveau fixé et du débit de la pompe de CEC, le temps disponible pour éviter une embolie gazeuse peut varier de quelques secondes à quelques minutes (32). Il est communément accepté que le niveau minimum dans le réservoir doit correspondre à 25% du débit systémique (L/min) afin de permettre un temps de réaction de 15 secondes (32). Il est habituel que le détecteur de niveau bas soit couplé à un dispositif qui permet l'asservissement avec régulation et ensuite l'arrêt de la pompe principale.

V.12. Utilisation des filtres artériels

L'utilisation des filtres artériels a été rapportée par 98,5% des perfusionnistes dans l'enquête de Mejak et al. (6). L'enquête française (20) ne comportait pas de questions sur l'utilisation de ce dispositif.

Le problème de l'utilisation des filtres artériels doit être analysé dans le contexte des filtres des circuits de CEC en général. Des filtres micropore peuvent être utilisés au niveau de la ligne artérielle, du réservoir de cardiotomie, de l'arrivée des gaz au niveau de l'oxygénateur, lors de l'administration des produits sanguins, avant la CEC (après l'amorçage de la pompe mais avant la connexion du circuit de CEC au patient et sur le circuit de cardioplégie) (18). La plupart des circuits de CEC modernes sont dotés d'un filtre micropores au niveau des réservoirs veineux.

L'utilisation des filtres artériels a comme objectifs de diminuer voire d'éliminer (i) les microembols particulaires; (ii) les microembols gazeux et (iii) les embolies gazeuses macroscopiques (109). Un quatrième objectif a été rajouté, qui est celui de filtrer les leucocytes impliqués dans la réaction inflammatoire de la CEC (18).

Si un filtre artériel est mis en place, il est recommandé de pouvoir court-circuiter le filtre par une tubulure qui est habituellement clampée mais qui peut être utilisée si le filtre est obstrué (18). Pour que le filtre artériel puisse jouer son rôle de diminution de la charge embolique gazeuse macroscopique il est nécessaire qu'il dispose d'un système type «auto-venting» ou alors d'un système de purge qui comporte une valve unidirectionnelle et qui relie le filtre au réservoir veineux (18). Les caractéristiques et les performances des filtres artériels proposés par les fabricants peuvent être différentes (109).

Les filtres artériels, quelles que soient leurs caractéristiques techniques, sur des tests réalisés ex vivo, permettent de diminuer d'au moins 98% la charge microembolique et de 95% la charge embolique gazeuse macroscopique (109). Cette diminution de la charge embolique est observée en l'absence d'effets secondaires notables (18). Les inconvénients potentiels liés à l'utilisation des filtres artériels sont :

(i) le surcoût;

(ii) l'augmentation du volume mort;

(iii) une dé-aération plus difficile pouvant représenter une source additionnelle d'embolie gazeuse;

(iv) une augmentation de l'hémolyse et de la destruction plaquettaire ainsi qu'une activation du complément (18).

À cause de la diminution de la charge embolique sans effets secondaires majeurs, certains auteurs considèrent les filtres artériels comme étant le dispositif le plus important pour l'amélioration de la sécurité de la CEC (109). En même temps, il a été souligné que la diminution de la charge embolique ne devait pas être confiée exclusivement à l'utilisation des filtres artériels (109). D'autres mesures comme la diminution du débit de gaz, de la pression des aspirations, le positionnement correct des canules veineuses et la vigilance de la part des équipes de chirurgie, de perfusion et d'anesthésie-réanimation doivent contribuer à la diminution de la charge embolique.

Il est indispensable d'analyser les données de la littérature concernant la réduction de la charge embolique par l'utilisation des filtres artériels en tenant compte du fait que la plupart des publications qui sont citées, y compris récemment (18), datent de l'époque des oxygénateurs à bulles (109-111) et n'ont pas analysé les effets des filtres artériels sur la diminution de la charge embolique dans le contexte des autres filtres cités plus haut (au niveau du réservoir de cardiotomie par exemple). Des recommandations récentes de l'American Heart Association/American College of Cardiology sur la pratique de la chirurgie des pontages coronariens (83) citent l'utilisation du filtre artériel sur les circuits de CEC comme un des éléments qui peuvent contribuer à la diminution de l'incidence des complications neurologiques de la chirurgie cardiaque.

L'analyse critique de la littérature suggère que les filtres artériels remplissent leur rôle de diminution de la charge embolique particulaire et gazeuse bien que leur effet bénéfique sur la diminution de la morbidité et de la mortalité n'ait pas été établi formellement. Le filtre artériel n'est pas en lui-même un dispositif de monitorage mais un élément de sécurité. L'utilisation conjointe d'une alarme de niveau, d'un détecteur de bulles et d'un filtre artériel sur les CEC conventionnelles, bien que potentiellement coûteuse, correspond à des niveaux de sécurité complémentaires et non redondants. Compte tenu des conséquences graves liées à une augmentation de la charge embolique particulaire et gazeuse (microscopique et macroscopique) (25), la complémentarité des dispositifs de monitorage et de sécurité est souhaitable. Cette approche de complémentarité des dispositifs aboutissant à ce qui peut être interprété (probablement à tort) comme une redondance des dispositifs de monitorage et de sécurité a également été retenue par les sociétés savantes des autres pays (33, 112, 113).

Utilisation des valves antiretour

Des valves unidirectionnelles sont habituellement utilisées au niveau de la ligne de décharge ventriculaire gauche et au niveau de la purge qui relie le filtre artériel au réservoir veineux (18). L'utilisation de ces valves est justifiée à cause des accidents publiés (25).

V.13. Particularités pédiatriques concernant divers éléments liés à la CEC

V.13.1. Circuits traités

Malgré une littérature abondante sur l'utilisation de circuits pré-héparinés pour améliorer la biocompatibilité en CEC pédiatrique, il n'est pas possible de recommander l'utilisation systématique de ces circuits. La plupart des études montrent une diminution de certaines composantes de la réaction inflammatoire (114-117) mais sur de faibles nombres de patients (n = 40) et avec des études ciblées seulement sur un nombre limité de composantes de la réaction inflammatoire, phénomène beaucoup plus complexe. Ozawa et al. (118) retrouvent néanmoins une efficacité clinique des circuits traités, dans une étude randomisée chez 34 enfants. Horton et al. (119), dans une étude réalisée chez 200 patients pédiatriques, ne retrouvent pas de différences significatives liées au type de circuit de CEC sur un critère de jugement qui comprend plusieurs marqueurs de l'inflammation. L'effet de ces circuits préparés sur la coagulation chez l'enfant n'a pas fait l'objet d'études sérieuses.

V.13.2. Mélangeurs gazeux

Bien que ces dispositifs n'apparaissent dans aucun rapport ou étude, il est important de recommander des mélangeurs gazeux adaptés au faible débit de gaz utilisé; en effet, les mélangeurs gazeux adultes sont instables aux débits utilisés en néonatologie < 1 L/min.

V.14. Dossier de CEC

Le dossier de CEC est un élément du dossier du patient selon les recommandations de l'Anaes (120). Il est une réalité aux États-Unis et l'AmSECT a rédigé des recommandations concernant sa réalisation (113). Un tel dossier existe en France dans certains centres et la nécessité de sa généralisation a été soulignée par les perfusionnistes lors des réunions professionnelles (1).

Propositions de recommandations

I. MÉTHODOLOGIE

Toutes les recommandations ont été fondées sur un accord professionnel fort (grade C)

Comme l'analyse de la littérature n'apportait qu'un faible niveau de preuve scientifique, les recommandations ont fait l'objet d'un consensus formalisé.

Elles ont été élaborées par le groupe de travail. Les recommandations publiées par plusieurs sociétés savantes de pays européens, des États-Unis et du Canada, sur les normes minimales de surveillance et de monitorage pour la période de la CEC, ont servi de modèles (33, 75, 112, 113). Certaines recommandations concernant le monitorage n'ont pas pu être faites car les dispositifs de monitorage n'ont pas été spécifiquement adaptés à la CEC (par exemple, monitorage du CO_2 au niveau de l'évent de l'oxygénateur).

Suite aux deux premières réunions du groupe de travail, 53 propositions de recommandations ont ainsi été adressées par voie postale à un deuxième groupe multidisciplinaire de 33 experts proposés par les sociétés savantes concernées. Il était demandé au groupe de lecture de voter la pertinence de chaque recommandation. La cotation allait de 1 (pas du tout d'accord) à 9 (tout à fait d'accord): 1à 3 correspondait à un désaccord; 4 à 6 à une indécision et 7 à 9 à un accord.

Les médianes du vote du groupe de lecture ont toutes été supérieures ou égales à 8. Tous les commentaires adressés par le groupe de lecture ont été colligés et discutés lors d'une dernière réunion du groupe de travail qui a permis de consolider les recommandations.

Les 41 recommandations issues de ce consensus ont ainsi été adoptées à l'unanimité par le groupe de travail sauf 2 recommandations: la recommandation 31 sur le filtre artériel et la recommandation 41 sur les valves antiretour. Ces 2 recommandations avaient recueilli la majorité du vote du groupe de travail et de ce fait ont été retenues.

II. PRÉREQUIS ET RECOMMAN DATIONS GÉNÉRALES

1) Les consoles de CEC, les générateurs thermiques, les moniteurs et les autres dispositifs utilisés pendant la CEC ou en relation avec la CEC doivent être calibrés, maintenus et entretenus selon les spécifications des fabricants. Le décret 2001-1154 du 05 décembre 2001 (28) impose aux exploitants de dispositifs médicaux de mettre en œuvre, selon les types d'appareils, des maintenances et des contrôles de qualité internes et externes. Le matériel de CEC, faisant partie de la catégorie de marquage CE classe II b, est visé par l'obligation de maintenances préventives.

2) Tous les appareils électriques présents en salle d'opération doivent respecter les normes de sécurité électrique et posséder le marquage CE.

3) La réglementation impose, pour les secteurs sensibles de l'hôpital, dont les blocs opératoires font partie, des systèmes et procédures permettant d'assurer la continuité des soins en cas de défaillance de l'alimentation principale (arrêtés du 7 janvier 1993 et du 03 octobre 1995) (26, 27).

4) Les moniteurs de l'anticoagulation, les appareils de mesure des gaz du sang et d'autres appareils délocalisés doivent respecter les normes en vigueur concernant la biologie délocalisée.

5) Des protocoles de calibration, d'entretien et de surveillance microbiologique des générateurs thermiques doivent être disponibles.

6) Des protocoles de conduite de CEC doivent être rédigés et facilement disponibles dans chaque centre.

7) La liste de vérification (check-list) de CEC doit être réalisée systématiquement avant le départ en CEC.

8) Il est recommandé que les alarmes soient à la fois sonores et visuelles.

9) Du matériel de remplacement permettant de continuer la CEC (en cas de défaillance des consoles de CEC) doit être disponible au niveau du bloc opératoire.

III. PARAMÈTRES SURVEILLÉS

Pendant toute la durée de la CEC, les informations fournies par les moniteurs (pressions, ECG, température, etc.) doivent être accessibles (écrans répétiteurs) aux équipes d'anesthésie, de chirurgie et de perfusion.

III.1. Monitorage de la fonction cardio-vasculaire, spécifiquement lié à la CEC

Il est recommandé de monitorer en continu les paramètres suivants:

10) Le tracé ECG (minimum 2 dérivations avec un cordon ECG à 5 brins). Le monitorage automatisé du segment ST est souhaitable.

11) La pression artérielle systémique (systolique, diastolique, moyenne) avec valeurs et formes des courbes.

12) La pression veineuse centrale avec valeurs et formes des courbes.

13) La pression au niveau de la ligne artérielle du circuit de CEC (en aval de l'oxygénateur). Dans certaines situations il peut être utile de monitorer la pression en amont de l'oxygénateur. Les informations fournies par la mesure de la pression en amont et en aval de l'oxygénateur sont différentes (ceci concerne plus particulièrement les pompes à galets). Lors de certaines CEC néonatales, le calibre extrêmement réduit de la canule artérielle (< 1 mm) peut créer une perte de charge très importante rendant difficiles la mesure et l'interprétation du monitorage de la pression au niveau de la ligne artérielle.

14) La pression au niveau de la ligne d'injection de la cardioplégie (en pédiatrie) et pour la cardioplégie rétrograde chez l'adulte.

III.2. Monitorage de la fonction respiratoire, spécifiquement lié à la CEC

Il est recommandé de monitorer en continu les paramètres suivants:

15) Le débit de gaz frais vers l'oxygénateur à l'aide d'un rotamètre (ou débitmètre électronique). Pour les centres qui font des CEC pédiatriques, il est nécessaire de disposer de dispositifs adaptés à la pédiatrie.

16) La fraction inspirée en oxygène (FiO2) des gaz frais en utilisant un analyseur d'oxygène dédié à la console de CEC, avec une alarme de baisse de la FiO2.

17) La saturation veineuse (SvO2) sur la ligne veineuse du circuit de CEC. La mesure de l'hémoglobine est associée à la mesure de la SvO2.

18) La pression partielle en oxygène (PaO2) (en néonatologie).

III.3. Monitorage de la température

Il est recommandé de mesurer:

19) La température du patient au niveau d'au moins deux sites centraux en hypothermie et au niveau d'un seul site central en normothermie. Le monitorage d'un site reflétant la température cérébrale est recommandé pour les arrêts circulatoires en hypothermie profonde.

20) La température du sang au niveau de la ligne artérielle et de la ligne veineuse du circuit de CEC.

21) La température de l'eau au niveau du générateur thermique.

III.4. Monitorage biologique (discontinu)

La fréquence avec laquelle les paramètres énumérés sont mesurés doit être dictée par le contexte clinique. Le groupe de travail n'est pas parvenu à un accord sur les fréquences minimales de mesure pour chacun des paramètres. Il est recommandé de mesurer les paramètres suivants:

22) Les gaz du sang. Certains paramètres (par exemple la PaO2) peuvent également être mesurés en continu.

23) La concentration d'hémoglobine ou l'hématocrite. Ce paramètre peut être également mesuré en continu.

24) Kaliémie.

25) Glycémie.

26) Calcémie ionisée chez les nourrissons.

III.5. Monitorage des effets anticoagulants de l'héparine non fractionnée (HNF) pendant la CEC

La variabilité inter et intra-individuelle de la réponse à l'HNF (mais aussi aux autres anticoagulants plus rarement utilisés pour assurer l'anticoagulation pendant la CEC) est telle, qu'il est indispensable de surveiller les effets des médicaments anticoagulants pendant la CEC.

27) Tous les centres doivent disposer d'un moniteur par salle qui permet de s'assurer de l'efficacité de l'anticoagulation. Le dosage de la concentration de l'HNF (mesure de l'activité anti-Xa) ne permet pas, s'il est effectué seul, d'estimer l'efficacité de l'anticoagulation dans toutes les situations.

28) Le monitorage de l'anticoagulation doit être réalisé avant l'administration de l'HNF, 5 minutes après administration d'HNF et avant le début de la CEC (si l'intervalle entre ces deux moments est supérieur à 15 minutes), puis régulièrement (toutes les 30 minutes ou plus fréquemment si nécessaire) pendant la CEC.

IV. DISPOSITIFS ET MESURES DE SÉCURITÉ RECOMMANDÉS

IV.1. Protection contre l'embolie gazeuse

Il est recommandé d'utiliser les dispositifs suivants:

29) Un détecteur de niveau bas pour les réservoirs veineux (en dehors des systèmes clos actuels) muni d'une alarme.

30) Un détecteur de bulles d'air sur la ligne artérielle muni d'une alarme. Le dispositif de détection des embols gazeux devrait être placé sur un site du circuit qui permet, une fois les embols gazeux détectés, de procéder à une dé-aération rapide du circuit avec le minimum d'effets sur le patient.

> **NB**: Pour les CEC réalisées en circuit dit ouvert, à la fois le détecteur de niveau bas et le détecteur d'embols gazeux devraient être utilisés.

31) Un filtre artériel*.

> * **Note:** Recommandation retenue à la majorité du groupe de travail

IV.2. Sécurité électrique

Les éléments de sécurité suivants sont recommandés:

32) Alarme de défaut d'alimentation électrique de la console de CEC.

33) Source d'énergie (onduleur ou batterie chargée) capable de fournir suffisamment d'énergie pendant une heure pour la pompe artérielle et l'éclairage indépendant de chaque console.

34) Source de lumière indépendante qui doit rester allumée en cas de défaillance de l'éclairage dans la salle d'opération. Cette source de lumière peut être soit intégrée à la console de CEC soit être une source indépendante fonctionnant sur batterie.

IV.3. Éléments de sécurité liés aux pompes de CEC

35) L'inversion volontaire des pompes à galets doit nécessiter deux manœuvres séparées pour éviter les manipulations involontaires.

36) Chaque module de pompe doit afficher le débit de la pompe.

37) La pompe artérielle doit pouvoir être asservie par:

- des dispositifs d'alarme de niveau bas;
- des systèmes qui détectent une surpression dans la ligne artérielle ou la ligne de cardioplégie;
- des dispositifs de détection des embols gazeux.

Si la pompe artérielle est asservie par les dispositifs mentionnés, la pompe de cardioplégie doit pouvoir être asservie à la pompe artérielle.

38) Une manivelle permettant de faire tourner la pompe principale de CEC doit être disponible.

IV.4. Autres mesures de sécurité

39) Une source indépendante (bouteille) d'oxygène doit être disponible Les bouteilles de réserve doivent être vérifiées régulièrement et après chaque utilisation.

40) Le générateur thermique devrait disposer d'un système de sécurité empêchant une augmentation de la température au-dessus de 42°C ou une baisse de la température en dessous de 3°C. Des alarmes de température excessive doivent être présentes sur le générateur thermique.

41) Des valves antiretour sont recommandées au niveau:

- de la décharge ventriculaire gauche;
- du système de purge qui relie le filtre artériel au réservoir veineux*.

*** Note:** *Recommandation retenue à la majorité du groupe de travail*

Perspectives

Le groupe de travail, en faisant une synthèse de l'expérience accumulée par les professionnels de la perfusion et des remarques du groupe de lecture, propose deux types de perspectives.

I. PERSPECTIVES TECHNIQUES

I.1. État des lieux actuel du monitorage et des mesures de sécurité de la CEC en France

L'application en pratique clinique courante des recommandations actuelles doit être précédée d'une réflexion sur les surcoûts et les difficultés éventuelles.

Le groupe de travail propose d'évaluer, pour tous les centres français qui effectuent des CEC, la différence entre leur niveau actuel de monitorage et de sécurité et les recommandations actuelles. Cette évaluation pourrait permettre une estimation du surcoût entraîné par l'application de ces recommandations et pourrait permettre de définir, en fonction du surcoût, le délai accordé aux centres qui pratiquent des CEC, pour la mise en conformité avec les recommandations.

I.2. Établir un dialogue avec les fabricants de matériels de CEC afin d'harmoniser certains dispositifs de monitorage et de sécurité

Le groupe de travail et le groupe de lecture ont souligné la nécessité d'établir un dialogue avec les fabricants de circuits et de dispositifs de CEC.

Le dialogue, initié et suivi par le Collège français de perfusion, devrait aborder en priorité les dispositifs de monitorage (FiO_2, CO_2 expiré), les modifications nécessaires aux circuits pour permettre l'administration des gaz halogénés pendant la CEC, les procédés de décontamination et de stérilisation. Le monitorage du CO_2 au niveau de l'évent de l'oxygénateur pourrait fournir des informations concernant l'adaptation du débit ventilation-perfusion plus rapidement par rapport à la mesure discontinue des gaz du sang. Les centres français qui mesurent en continu ce paramètre font appel à des systèmes improvisés. Il serait nécessaire que les constructeurs aient une réflexion commune pour la mise en place de dispositifs de mesure fiable du CO_2 au niveau de l'évent des oxygénateurs.

L'administration des gaz anesthésiques pendant la CEC représente une priorité pour le groupe de travail, dans le contexte de plusieurs travaux qui ont montré un effet cardioprotecteur cliniquement important des agents halogénés par rapport aux anesthésiques intraveineux (121-123).

I.3. Rédaction de recommandations de monitorage minimum et de sécurité pour les CEC dites non conventionnelles

Les CEC dites non conventionnelles sont souvent utilisées dans le contexte de la CEC en chirurgie cardiaque (124) ainsi qu'en dehors du bloc opératoire (oxygénation extracorporelle, assistance ventriculaire) (125,126). Le développement de la CEC en dehors du contexte de la chirurgie cardiaque a été à l'origine de l'apparition et du développement aux États-Unis et au Canada de Départements de perfusion dont les missions dépassent la CEC pour chirurgie cardiaque.

I.4. Entamer une réflexion sur la prévention/gestion de la réaction inflammatoire induite par la CEC

La réaction inflammatoire induite par la chirurgie cardiaque et la CEC est probablement responsable d'une grande partie des complications postopératoires. Le groupe de travail souligne l'intérêt d'étudier ce problème et de proposer des mesures destinées à diminuer l'activation de la réaction inflammatoire et ses complications.

I.5. Rédaction de rapports d'incidents/accidents liés à la CEC (en dehors des vigilances légales)

En plus des vigilances légales, le groupe de travail propose d'étudier la faisabilité de la mise en place d'une base de données nationale des incidents mineurs ou majeurs liés à la pratique, avec ou sans conséquences pour les patients, avec:

- description détaillée de l'incident/accident;
- causes possibles;
- résultats;
- actions entreprises;
- recommandations pour éviter la survenue de nouveaux incidents/accidents.

Le groupe de travail est conscient des difficultés de ce projet mais estime qu'il s'agit pratiquement du seul moyen qui pourrait permettre d'analyser l'impact de l'application des recommandations du présent document.

II. PERSPECTIVES GÉNÉRALES: DÉFINIR LA FORMATION INITIALE ET CONTINUE DU PERFUSIONNISTE

Les professionnels du groupe de travail et du groupe de lecture ont souligné que l'amélioration des conditions de sécurité des CEC passe non seulement par une amélioration du matériel de CEC, du monitorage et des éléments de sécurité, mais également par une amélioration de la formation initiale et continue des perfusionnistes. Cet aspect est indissociable du statut des perfusionnistes. Le Collège français de perfusion a fait plusieurs propositions qui ont reçu l'accord de la majorité des professionnels pour définir le statut des perfusionnistes.

Les experts souhaitent la définition d'un statut du perfusionniste qui comprenne la définition de la formation initiale, avec la collaboration des professionnels et des institutions concernées (ministères, Cnamts et autres organismes).

ANNEXE I - PROPOSITIONS DE CHECK-LISTS

1. Proposition de check-list selon le Collège français de perfusion

DATE:	IDENTIFICATION PATIENT:	CEC n°

Matériel à usage unique:		
	Dates de péremption	☐
	Témoins de stérilité	☐
	Intégrité des emballages	☐
	Conformité schéma	☐
	Étiquettes traçabilité collées	☐

Console CEC:		
	Branchement secteur	☐
	Relais batterie	☐
	Présence manivelle	☐
	Clamps fonctionnels	☐
	Chariot CEC complet	☐

Générateur thermique:		
	Branchement secteur	☐
	Pompe fonctionnelle	☐
	Contrôle niveau eau	☐
	Connexion échangeur thermique	☐
	Absence de Fuite	☐
	Contrôle Chaud/Froid	☐

Fluides médicaux:		
	Branchement ALR/O_2	☐
	Absence de fuites	☐

Monitorage:		
	Chronomètres fonctionnels	☐
	Pressions calibrées	☐
	Mesures en lignes calibrées	☐
	Sondes de températures connectées	☐

Montage CEC:		
	Occlusivité des pompes	☐
	Artérielle	☐
	Cardioplégie	☐
	Aspirations	☐
	Mobilité des galets	☐
	Sens de rotation des galets	☐
	Centrifuge: zéro débitmètre	☐
	Détecteur de niveau connecté	☐

Détecteur de bulles connecté	☐
Oxygénateur fixé	☐
Connexion ligne de gaz	☐

Contrôle ultime:		
	Vérification du circuit	☐
	Débullage	☐
	Absence de fuites	☐
	Sens de rotation des galets	☐
	Vérification pompe centrifuge	☐
	Vérification détecteur de niveau	☐
	Monitorage des pressions	☐
	Contrôle débit des gaz	☐
	Pousse-seringues fonctionnels	☐
	Mise en route générateur thermique	☐
	Injection héparine	☐
	Act post-héparine	☐
	Démarrage CEC possible	☐

NOM ET SIGNATURE DU PERFUSIONNISTE		OBSERVATIONS

2. Proposition de check-list selon Y American Society of Extra-Corporeal Technology (AmSECT3)

Patient	- Identité - Analyse du dossier patient - Vérification de la procédure chirurgicale - Vérification des contraintes liées à l'anesthésie (allergie, etc.)
Stérilité	1. Intégrité et stérilité du pack de CEC (date d'expiration) 2. Vérification de l'absence de fuite au niveau du générateur thermique
Pompes	1. Speed control opérationnel 2. Fonctionnement correct de pompes à galets 3. Vérification de l'occlusion 4. Débitmètres placés correctement et calibrés
Électricité	1. Cordon d'alimentation électrique correctement fixé
Alimentation en gaz	1. Tuyaux d'alimentation en gaz correctement fixés 2. Mélangeur/rotamètre fonctionnels 3. Tuyaux et connecteurs sans fuites 4. Évent de l'oxygénateur non obstrué
Les tubulures du circuit	1. Connexions sécurisées 2. Direction/sens des tubulures corrects 3. Absence de coudes dans les tubulures 4. Valves unidirectionnelles placées correctement 5. Déaération et absence de fuites 6. Perméabilité de la ligne artérielle vérifiée
Cardioplégie	1. Solution de cardioplégie vérifiée 2. Circuit de cardioplégie déaéré et sans fuites
Systèmes de sécurité	1. Alarmes fonctionnelles et activées 2. Filtre artériel/pièges à bulles déaérés 3. Réservoir de cardiotomie « vented »
Monitorage	1. Capteurs de température en place et calibrés 2. Moniteurs de pression de la pompe calibrés 3. Capteurs d'oxygène calibrés 4. Analyseur de FiO_2 calibré
Contrôle de la température	1. Source d'eau connectée et fonctionnelle
Accessoires	1. Clamps disponibles 2. Médicaments dans des seringues correctement étiquetées 3. Sang disponible 4. Seringues pour les prélèvements sanguins disponibles
Anticoagulation	1. Vérification du fait que l'héparine (et la dose) a été injectée 2. Vérification de la valeur du test utilisé pour le monitorage de l'effet anticoagulant de l'héparine
Autres éléments de sécurité	1. Manivelle disponible 2. Source de lumière de secours sur batteries disponible 3. Circuit identique disponible en réserve
Protocoles écrits pour la prise en charge des complications « catastrophiques »	- Embolie gazeuse massive - Défaillance de l'oxygénateur - Rupture d'une ligne (tubulure) de CEC - Panne de courant électrique globale - Défaillance (arrêt) de la pompe principale - Défaillance du générateur thermique

[3] http: //www.amsect.org/general/checklist.html

ANNEXE II - PROPOSITION DE CONSTITUTION D'UN DOSSIER DE CEC

Les propositions suivantes sont faites en tenant compte des recommandations récentes faites par l'Anaes concernant le dossier médical (120). Le dossier de perfusion doit contenir:

- **des informations générales**
- **certains paramètres**
- **le volume des produits d'expansion volumique**
- **les médicaments administrés dans le circuit de CEC**

Informations générales

- Identité du patient (numéro admission)
- Âge
- Sexe
- Poids
- Taille
- Surface corporelle
- Groupe sanguin
- Allergies
- Résultats biologiques préopératoires
- Rappel du diagnostic et des antécédents du patient significatifs pour la CEC
- Date de la CEC
- Intervention chirurgicale
- Nom du/des perfusionniste(s)
- Nom du/des chirurgien(s)
- Nom du/des anesthésiste(s)
- Commentaires

Les numéros de lot du matériel à usage unique utilisé

- Oxygénateur
- Réservoir veineux
- Tubulures/filtre artériel
- Circuit de cardioplégie
- Circuit utilisé pour l'ultrafiltration
- Têtes des pompes centrifuges et débitmètre

Les paramètres suivants doivent être notés avec une fréquence qui doit être définie par les procédures locales adaptées aux situations spécifiques ou figurer dans le dossier du patient en fonction des établissements

- Débit de perfusion
- Pression artérielle (systolique, diastolique ou seulement moyenne)
- Pression veineuse centrale
- Résultats des gaz du sang
- Saturation en oxygène du sang veineux
- Concentration de potassium
- Les valeurs d'ACT et la technique de mesure utilisée
- Au moins une valeur de température en indiquant son site de mesure
- D'autres valeurs de température provenant d'un deuxième site

• Débit de gaz et fraction inspirée en oxygène des gaz qui alimentent l'oxygénateur
• Diurèse

Volume d'ultrafiltration

• Le type et volume des produits d'expansion volémique utilisés au cours de la CEC
• Le volume et la composition des liquides de cardioplégie

Médicaments injectés dans le circuit de CEC

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The venous oxygen saturation in critically ill cardio-vascular patients*)

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Abstract

Mixed venous saturation and central venous saturation have been used for a long time in evaluation and management of critically ill patient. Experimental studies showed than there is a good correlation between SvO_2 and $ScvO_2$: a low SvO_2 mirrors a low $ScvO_2$, even if the absolute values are different. It is now clear that absolute values as well as the trend for the two parameters could be used as an alarm setting or a therapeutic target with the goal of optimizing tissue perfusion. We try in this work to remember notions of physiology, explaining the changes in this two parameters in different hemodynamic states, and we offer the results of many studies as guidelines.

Rezumat

Saturația în oxigen a sângelui din artera pulmonară şi cea a sângelui din vena cavă, reprezintă doi parametri utilizați în evaluarea statusului hemodinamic al pacientului critic. Studiile experimentale au demonstrat că există o bună corelație între cei doi parametri, evoluând în timp în acelasi sens, chiar dacă valorile absolute diferă. Atât valorile instantanee, cât şi evoluția lor pot fi utilizate ca nivel de alarmă sau țintă terapeutică în vederea optimizarii perfuziei tisulare. În această lucrare am punctat câteva noțiuni de fiziologie, explicând modificările în diferite situații hemodinamice şi oferim concluziile a numeroase studii ca şi protocoale de lucru.

Introduction

Mixed venous saturation (SvO_2-blood from the pulmonary artery) and central venous oxygen saturation ($ScvO_2$-blood from the superior vena cava) are two parameters which have been used for a long time in evaluation and management of critically ill patient. However, there are controversies concerning the significance of measured values for the assessment of the patient and judgment of the adequacy of the therapy.

These two parameters can be measured intermittently (blood sampling and analysis) or continuously, using special catheters (Swan-Ganz or adapted central venous catheters) and monitors (Vigilance-Edwards, Space-Labs Ultraview, Intelivue Philips, etc).

Continuous SVO_2 monitoring allows the minute-to-minute assessment of total tissue oxygen balance (i.e., the relationship between oxygen delivery and oxygen consumption).

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Physiolocical elements regarding SvO_2 and $ScvO_2$

The major determinants of oxygen content are oxygen delivery (DO_2) and oxygen content (VO_2).

Oxygen delivery is the product of cardiac output and arterial oxygen content (CaO_2). DO_2 represents the quantity of oxygen delivered by the arterial perfusion to the tissues per unit of time.

$$\mathbf{DO_2 = CO \times CaO_2}$$

As a consequence, the determinants of CO (preload, after load, contractility, heart rate and rhythm) and the ones of arterial oxygen content (CaO_2) - hypoxemia, oxygenotherapy, anemia or carbon monoxide poisoning, can modify the relationship between DO_2 and VO_2. The consumption of DO_2 is dependent on the factors affecting cellular breathing.

According to the Fick principle there is a direct relationship between the two determinant factors of CaO_2 (DO_2 and VO_2)

$$\mathbf{CvO_2\ (ml/dl) = CaO_2\ (ml/dl) - VO_2/DC\ (ml/min)}$$

Rearranging the equation,

$$\mathbf{SvO_2 = SaO_2 - VO_2\,/\,DC \bullet Hb}$$

SVO_2 varies directly with cardiac output, Hb, and SaO_2, and inversely with VO_2. The normal SVO_2 is 75%, which indicates that under normal conditions, tissues extract 25% of the oxygen delivered. An increase in VO_2 or a decrease in arterial oxygen content (SaO_2 x Hb) is compensated by increasing CO or tissue oxygen extraction.

When the SVO_2 is less than 30%, tissue oxygen balance is compromised, and anaerobic metabolism ensues.

A normal SVO_2 does not ensure a normal metabolic state but suggests that oxygen kinetics is either normal or compensated.

The cellular needs for oxygen are more difficult to evaluate, but under physiological conditions oxygen consumption equals oxygen demands.

Oxygen demands ascribe the quantity of oxygen that is necessary at the tissue level for aerob metabolism. When oxygen demand is greater than oxygen delivery anaerob metabolism and lactic acidosis take place. Oxygen demand cannot be measured directly in clinical practice, but indirect indicators of anaerob metabolism (as lactic acid) show that oxygen needs exceed oxygen delivery (1, 2).

The uncompensated raise of oxygen consumption (as in sepsis, septic shock, fever, strenuous exercise) or uncompensated fall of cardiac output (low/inadequate cardiad output states), haemoglobin concentration or SaO_2 *(ALI/* ARDS, cardiogenic pulmonary oedema) leed to SvO_2 diminution. Similarly, DO_2 in excess for VO_2 leads to a raise in SvO_2.

SvO_2 as a balance between pulmonary function, haemodinamic status, oxygen transporter (Hb) and tissue oxygen consumption makes this parameter an invaluable tool in evaluation of critically ill patient (1).

Every time SvO_2 is low the practitioner must evaluate all four determinants and identify and correct the cause (table 1) (2).

Table 1

Factors that affect DO_2	Factors that affect VO_2
Cardiac output	***Cytopathic hypoxia***
- exercise	- sepsis / septic shock
- hypovolemia	- cyanid poisoning
- cardiac failure / shock	
CaO2	↑ ***consumption***
- hypoxemia	- fever
- anemia	- convulsions
- oxygenotherapy	- sepsis/septic shock
- carbon monoxide poisoning	- exercise
	↓ ***consumption***
	- anaesthesia
	- sedation
	- hypothermia

It must be remembered that SvO_2 /$ScvO_2$ are global indicators of tissue oxygenation and major regional disturbances can be present without being reflected in SvO_2 /$ScvO_2$ values.

The normal values and the relationship between SvO_2 and $ScvO_2$

There are only few studies that measured those parameters in healthy volunteers, and the values were: SvO_2 78.4% (±2.6) and $ScvO_2$ 76.8% (±5.2) (3, 4). For premedicated patients, spontaneously breathing atmospheric air ScvO2 was 69%, and after volume administration was 72%.

It is now considered that physiologic values for $ScvO_2$ and SvO_2 are between 70 and 80%. For patient hospitalized but not critically ill values as low as 65% are considered normal.

There is no direct relationship between SvO_2 and $ScvO_2$ because of physiologic/ metabolic (DO_2 and VO_2 are different in the upper and lower parts of the body, the kidney receives 25% of the cardiac output) and anatomic reasons (coronarian venous return, directly intracardiac, which is proportional with myocardial work).

As we say, in healthy volunteers $ScvO_2$ is slightly lower than SvO2, but this is changed in haemodynamic instability.

In critical, but stable patients, $ScvO_2$ is similar with SvO_2 (54.7 vs 56.9%). In patients with heart failure the relationship is changed $ScvO_2 = SvO_2$ (61.8 vs 58.2%). This is even more pronounced in shock state (58 vs 47.5%) (5, 6).

This change can be explain by the redistribution of cardiac output in conditions of haemodynamic instability thus, venous blood from the lower part of the body is less desaturated than the one from the upper part, so $ScvO_2$ is lower than SvO_2. In hypodynamic states (hypovolemia or low cardiac performance), there is a shift of blood from the organs rich in alfa receptors (muscles, skin, digestive tract) to organs that lack those receptors (brain, heart), maintaining in this way the integrity of organs that are more sensible to hypoxia. The consequence is that blood from inferior vena cava is more desaturated than one from superior vena cava, so $ScvO_2$ is greater than SvO_2.

Experimental studies showed thar there is a good correlation between SvO_2 and $ScvO_2$: a low SvO_2 mirrors a low $ScvO_2$ and vice versa, even if the absolute values are different. However, what is more important is that the trend of $ScvO_2$ is similar with that of SvO_2 in critically ill patients (7-9).

It is now clear that absolute values as well as the trend for the two parameters could be used as an alarm setting or a therapeutic target with the goal of optimizing tissue perfusion. Intraoperative values of SvO_2 are routinely well above normal.

This is presumably due to the increased FiO_2 and the anesthetic-induced decreased metabolism or the inability of tissues to extract oxygen. Under general anesthesia, patients may have mixed venous saturations near or above 90%.

At that level, small changes in the partial pressure of oxygen in the pulmonary artery will not be indicated by discernable changes in the saturation.

At a normal mixed venous partial pressure oxygen of 40 torr and saturation of 75%, small changes in the oxygen tension will be easily noted with the corresponding changes in the saturation. The patients in poor cardiovascular condition may not have abnormally high venous saturations while undergoing anesthesia and surgery.

Thus, changes in the cardiovascular status of our patients are easily reflected by changes in the mixed venous saturation.

Clinical significance of SvO_2 and $ScvO_2$ in cardiovascular critically ill patient

• the "most" critical cardiovascular patient is of course the one in cardiorespiratory arrest, and there are studies that show that a high $ScvO_2$ during resuscitation is a good marker for correct resuscitation and, more important, a good predictor for spontaneous and efficient cardiac recovery and survival. A value of $ScvO_2$ > 72% has a positive predictive value of 70% (10-13).

• The utility of $SvO_2/ScvO_2$ in patients with heart failure/cardiogenic shock post myocardial infarction was studied since late 60' (1, 5, 14-29). The conclusions are:

- $SvO_2/ScvO_2$ changes correlate with the severity of myocardial dysfunction
- the trend under treatment reflects cardiac output response to therapy
- $ScvO_2$ of 60% can reflect occult heart failure
- $ScvO_2$ of 45% means cardiogenic shock

• For the high-risk non-cardiac surgery patient there are studies which show that $ScvO_2$ values under 65% are associated with poor prognosis (30).

• In cardiac surgical patients:

- SvO_2 changes appear sooner than that of heart rate or arterial pressure and are in close relationship with cardiac output. Values under 65% are associated with greater morbidity (31-33).
- Studies suggest that intra/postoperative changes in SvO_2 reflects better VO_2 changes than cardiac output because of special conditions of these patients (34).
- We published four studies which demonstrate the predictive value of SvO_2 in optimizing therapy in patients after coronaro-aortic bypass grafting whom necessitate mechanical support (intra-aortic balloon pump - IABP) and we

demonstrate that a value greater than 60% has a survival predictive value of 90% and a value under 60% is 96%predictive for death (35-38).

$ScvO_2$ and SvO_2 in clinical practice: clinical studies-results

SvO_2

There are only a few studies that tried to determine, under a therapeutic algoritm, a target SvO_2 that could improve the critically ill prognosis.

Gattinoni showed that, for critically ill patients after general surgery, haemodinamic therapy for a SvO_2 greater than 70% or optimization of cardiac index to supranormal values does not reduce morbidity or mortality in these patients (39).

Another study showed that trying to obtain a SvO_2 value greater than 65% does not improve the prognosis for patients who underwent vascular surgery (40).

The target: SvO2 >70% and serum lactate < 2mMol/l during the first postoperative hours where successfully used in cardiac surgery: morbidity 1.1% vs. 6.1% (p < 0,01) control group, and 6 vs 7 days of hospitalization (41).

$ScvO_2$

An interesting algorithm based on combination of CVP, MAP, $ScvO_2$ was proposed and validated by Rivers in the early goal directed therapy of septic shock. In this study there were randomized 263 patients: one group with standard therapy and one group with a target ScvO2 greater than 70% before going into the ICU. The results changes the management of septic shock: 30.5 vs 46.5% mortality in the control group (29). Plus, further studies showed that continuous monitoring of ScvO2 was a good parameter to alert the physician in case of a perturbation in oxygen balance. This parameter also favorises a good and adapted therapeutic intervention (42).

On the other hand is the study of Varpula who demonstrate that after the period of initial stabilization, the SvO2 of the patient in septic shock cannot be estimated by ScvO2 (43).

Conclusions

Monitoring SvO_2 and $ScvO_2$ is important and usefull in cardiovascular critically ill patients. The normal values for both parameters are between: 70-80%. Every time ScvO2 or SvO2 is low, we have to asses all four determinants: pulmonary function, haemodinamic status-cardiac output, oxygen transporter (Hb) and tissue oxygen consumption then we have to identify and correct the cause.

However we will keep in mind that SvO_2 and $ScvO_2$ are global indicators of tissue oxygenation and major regional disturbancies can be present without being reflected in SvO_2 or $ScvO_2$ values.

Monitoring SvO_2 or $ScvO_2$ is still an invasive method but in the future we will be able to measure in a noninvasive manner even regional tissue oxygen saturation (a new technology produced by Hutchinson Technology that noninvasively and quantitatively measures tissue oxygen saturation - StO_2 - directly in the muscle tissue using near infrared light).

Guidelines for using $ScvO_2$ - in cardiovascular critically ill patients

a) a resuscitated patient for cardiorespiratory arrest must achieve a $ScvO_2$ greater than 72% in order to have a good outcome

b) in patients with heart failure:

- keeping a $ScvO_2$ > 60% - is a "sit belt"
- $ScvO_2$ < 45% is a "landmark" for cardiogenic shock

c) high-risk surgery associated with $ScvO_2$<65% poor prognosis

We can conclude that a value of $ScvO_2$ >65% seems to be safe and desirable in critically ill patients, including those cardiovascular, but with the exception of septic patient who needs a $ScvO_2$ greater than 70%.

Guidelines for using SvO2 - in cardiovascular critically ill patients

a) postoperative period in cardiac surgery

- SvO_2 < 65% - means a high risk morbidity
- a good target is SvO_2 > 70% plus serum lactate < 2 mmol/l
- SvO_2 > 60% when using IABP is mandatory

b) in ICU postoperative septic patient SvO_2 is more reliable than $ScvO_2$.

We can conclude that a value of more than 60% seems to be safe and reliable in all critically ill patients, including those cardiovascular, with the exception of the cardiac surgical patient who needs SvO_2 > 70% in the first 8 postoperative hours.

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Troubles psychiques (anxiété et dépression masquée) dans la chirurgie à coeur ouvert*)

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Abstract

Pre- and post-operatory investigations on 575 patients who underwent open heart operations, led us to conclude that anxiety and masked depression presents some particularities which render them different from those met in other surgical specialties presenting direct implications in postoperatory evolution. Patients were aged 4 to 62 years, the female gender representing 77.5%. Neurology complications were 4.6% and psychical ones 36.8%, nearly half of them being anxieties and masked depressions. By knowing these two entities, almost identical though, a big step forward was performed in the detection of the patients with high anxiogène potential, of the sequels of some cerebral affections, and also in preventing unexpected decompensations. As a conclusion we recall the principal risk factors, which may generate psychical complications, but also the measures of psychiatry prophylaxy that are to be applied, bearing in mind preexistent elements, the apparition of new psychical troubles, but also the decompensation of the ancient ones.

Kev words: *Open heart surgery, anxiety, depression, circadian fluctuations of symptomatology.*

Résumé

Les observation pré et postopératoires sur un nombre de 575 malades ayant subi une intervention à coeur ouvert, ont conduit à la conclusion que l'anxiété et la dépression masquée présentent des particularités qui les différencient de celle rencontrées dans d'autres spécialités chirurgicales à implications directes sur l'évolution postopératoire. L'âge des malades qui font l'objet de cette étude était compris entre 4 et 62 ans, les femmes y étaient pour 77,5%. Les complications neurologiques ont eu un pourcentage de 4,6%, les complications psychiques de 36,8%, dont près de la moitié ont été l'anxiété et la dépression masquée. Connaître ces deux entités, qui ont des particularités communes, d'ailleurs, représente un pas important dans le dépistage des malades à potentiel anxiogène élevé, les séquelles de certaines affections cérébrales,

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mais aussi en ce qui concerne la prévention d'éventuelles décompensations. En conclusion, les auteurs citent à nouveau les principaux facteurs de risque, qui peuvent générer des complications psychiques, ainsi que les mesures de prophylaxie psychiatrique qui seront nécessairement mises en application, compte tenant des éléments préexistants, l'apparition de nouveaux troubles psychiques, mais aussi la décompensation de ceux plus anciens.

Mots clés: *Chirurgie à coeur ouvert, Anxiété et Dépression, Fluctuations circadiennes de la symptomatologie.*

Introduction

La chirurgie cardiaque comporte divers éléments stressant le patient, qui ne se limitent pas à l'acte opératoire, les réactions émotives commençant dès la phase où apparaît la maladie cardiaque, puis quand le problème de l'intervention se pose, et jusqu'à la décision opératoire proprement dite.

L'acte opératoire, de même, est stressant.

L'opération cardiaque, surtout celle à coeur ouvert, comporte de nombreuses manoeuvres anesthésiques, des manipulations inter-opératoires, la réanimation intense, des problèmes de réhabilitation postopératoire.

La préparation de Pacte opératoire, la conscience qu'il (elle) sera opéré "au coeur", tout ceci, met le malade devant le plus dramatique moment de sa vie.

Le candidat à l'opération à coeur ouvert présente un déficit circulatoire cérébral chronique, qui peut induire un état de dépression approfondie, avec l'aggravation de l'état somatique. En résumé, ce type de malade est un grand invalide, qui assiste, conscient mais impuissant, à son inexorable évolution vers une fin fatale.

Matériel et Méthode

Un groupe de 575 malades ayant subi l'intervention à coeur ouvert ont été étudiés. Lâge des malades allait de 4 à 62 ans, les femmes représentant 77,5% des malades. Les complications neurologiques ont été de 4,6%, celles psychiques étant de 36,8%, dont plus de la moitié étaient des états anxieux ou des dépressions masquées. Pour trouver les facteurs responsable des complications psychiques, nous avons développé la recherche psychiatrique pre-, intra- et postopératoire, tout en insistant sur deux des troubles les plus fréquents, à savoir: la dépression masquée et l'anxiété.

Après avoir étudié ces deux entités psychiques, dont les manifestations sont presque semblables d'ailleurs, et à implications directes sur l'évaluotion postopératoire, nous avons décidé d'accorder un temps plus prolongé à l'anamnèse, tout en insistant sur l'examen psychiatrique, l'étude de la personnalité du malade, l'EEG, en grandissant le nombre des contacts avec les malades, avant et après l'opération, également.

Résultats

L'anxiété et la dépression masquée présentent en chirurgie vasculaire des particularités qui leur sont propres, les différenciant donc de celles rencontrées dans d'autres spécialités chirurgicales. La systématisation de ces notes distinctives, qui doit mettre en relief et appliquer ces différences, a mené à la conclusion que le patient auquel on propose une intervention à coeur ouvert, l'accepte, apparemment, le plus souvent sans aucune hésitation. Sur les 575 que nous avons surveillés, nous n'avons rencontré que deux cas où l'insistance de la famille a joué un rôle décisif, les autres patients ayant eux même assumé cette responsabilité et ses conséquences. Les malades candidats à l'intervention à coeur ouvert ont à leur disposition une information médicale, qu'ils comprennent et qu'ils interprètent selon leur niveau social. A tout ceci viennent s'ajouter les observations et les faits qu'ils apprennent pendant l'hospitalisation, ainsi que l'interprétation - souvent erronée - de certaines attitudes du personnel médical.

Tout ceci contribue à l'installation, graduellement, d'un état d'inquiétude qui peut évoluer vers une anxiété plus ou moins évidente. L'association de la dépression et surtout, de la dépression masquée, complique la symptomatologie clinique, compliquant très fort en même temps le travail de l'anesthésiste, qui se trouvera devant une périphérie "fermée, avec des vaisseaux invisibles et difficiles à aborder", l'induction de l'anesthésie nécessitant des doses plus fortes de médicaments, pour obtenir le résultat souhaité (1).

Le questionnaire subi par le malade a mis en évidence son attitude envers sa maladie, ses relations avec le milieu, l'intervention chirurgicale, par des réponses d'un caractère général: "c'est naturel de craindre une opération aussi grave" ou "on ne peut pas être tranquille si l'on sait à quoi s'attendre".

Ultérieurement nous avons constaté les principaux motifs d'inquiétude:

- la crainte que l'opération commencerait avant l'installation de l'anesthésie.
- est-ce que le sommeil anesthésique est assez profond pour qu'on ne sente rien?
- le coeur va-t-il pouvoir supporter tout ce qu'il devra subir?
- la circulation extracorporelle, n'est-elle par un risque? et si les appareils ne sont pas à la hauteur?
- peur de la douleur postopératoire
- et le principal motif d'anxiété, rencontré chez la majorité des malades étudiés, est la crainte que le coeur ne reprendrait plus son activité après l'opération.

L'étude de la personnalité de ces malades, a mis en évidence une personnalité dominée par un état permanent de tension avec des tendances névrotiques, un sentiment d'insécurité et d'infériorité. Nous avons remarqué une intense composante réactive, les malades se considérant "infirmes", aux "jours comptés". Nous avons décelé des formes légères de dépressions imperceptibles à l'examen clinique, mais aussi des dépressions intenses, avec des états agités, états d'inquiétude et même de confusion mentale. Notre statistique nous a fourni les renseignements suivants:

- 35% de personnalités normales ou comportant des signes discrets d'asthénie;
- 20% de personnalités psychasthéniques;
- 30% de personnalités à symptômes hystéroïdes ou hystériques;
- 5% de personnalités paranoïaques;
- 10% de personnalités pithiatiques. Sans être d'une fidélité absolue, l'EEG nous a offert des éléments concernant le débit sanguin cérébral, le métabolisme de la cellule nerveuse, le niveau de vigilance, informations extrêmement nécessaires pour les patients dont l'équilibre biologique est précaire et qui supportent une intervention chirurgicale de durée dans les conditions de CEC. Si pré opératoirement l'EEG nous a signalé la présence de l'épilepsie (deux cas), pendant l'opération nous avons constaté:

• l'aplatissement du tracé et l'apparition des ondes thêta et même delta, dues à l'hypothermie provoquée;
• la réduction significative des rythmes de base, tout en décelant des zones délimitées de tranquillité électrique (signe de localisation) au cas d'un accident vasculaire cérébral;
• silentium électif localisé, à aplatissement focalisé et asymétrie de rythme a - au cas d'une souffrance superficielle;
• enregistrement dans toutes les dérivations, symétriquement et synchroniquement, de la présence du rythme delta sinusoïdal ample, organisé en bouffée, comme le rythme thêta sinusoïdal - au cas de la souffrance cérébrale profonde.

Les limites de l'EEG apparaissent pourtant, dues au fait que les modifications survenues dans l'apport de sang et d'oxygène ne sont présentes que si elles sont assez importantes et notamment quand le gradient de pression artério-veineuse cérébrale descend sous 30 mmHg (2).

Pendant le travail nécessaire pour établir l'interdépendance de l'hémodynamique cérébrale et de l'apparition et du développement de certaines modifications neuropsychiques, au long de la surveillance des cas, nous avons rencontré postopératoirement ce qui suit (voir le figure 1) (3):

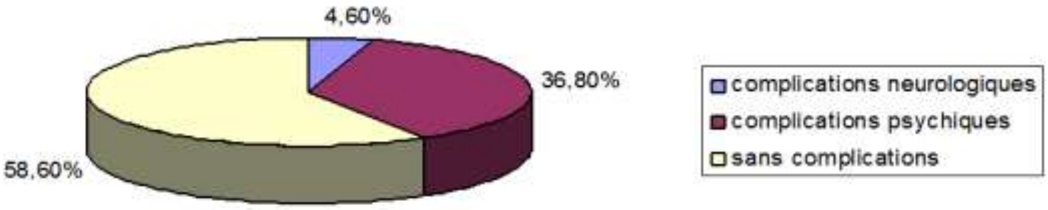

Figure 1

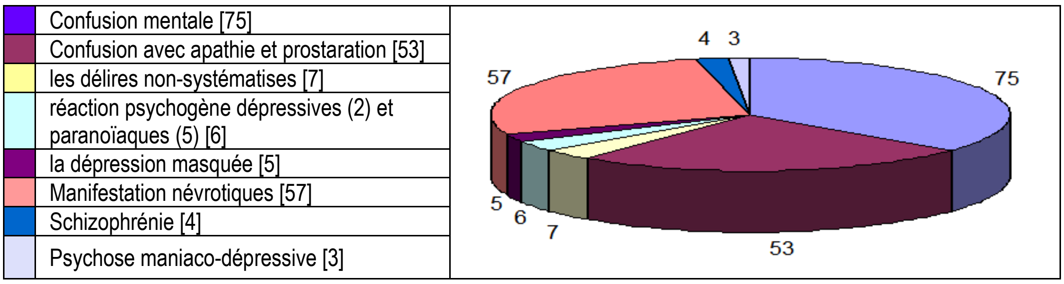

Figure 2

Quoiqu'une partie des troubles psychiques apparus après l'intervention à coeur ouvert aient été inclus dans le "délire post-cardiotomique" (4), à l'heure actuelle ce "délire" est reconnu comme apparaissant après un intervalle lucide de 2-5 jours après l'intervention chirurgicale. Nous avons classifié la présence du délire post-cardiotomique en trois groupes:

Groupe 1 - a inclus les symptômes de désorientation dans le temps et l'espace;

Groupe 2 - a inclus les hallucination de perception, le phénomène d'absence (l'impossibilité de reconnaître la famille ou les amis) ou l'impossibilité de connaître sa propre identité;

Groupe 3 - a inclus les hallucinations, les idéations, les produits de l'imagination paranoïde ou l'agitation.

Discussions

L'anxiété et la dépression masquée sont deux entités nosologiques très semblables, à implications directes dans l'évolution des malades opérés à coeur ouvert. A l'heure actuelle il n'y a pas de marqueur biologique ou pharmacologique à l'exception, paraît-il, de celui pour l'installation de la latence du sommeil. (5). Dans la pratique clinique usuelle, certains symptômes permettent d'orienter le diagnostic vers la dépression ou vers l'anxiété.

L'insomnie, dans la période de temps de la tombée de la nuit est plus fréquente dans les troubles anxieux, cependant que les réveils nocturnes et ceux de la fin de la nuit caractérisent les syndromes dépressifs. Nous signalons qu'il est important que les attaques nocturnes de panique soient clairement différenciées des insomnies. Les troubles de sommeil chez les sujets dépressifs, ne répondent pas de façon satisfaisante aux hypnotiques, mais disparaissent en général quand on applique un traitement à substances antidépressives.

La considération vis-à-vis de soi-même est très détériorée dans les syndromes dépressifs, mais beaucoup moins dans l'anxiété.

Les fluctuations circadiennes des symptômes et, surtout, la prédominance matinale des symptômes, définissent nettement la dépression.

La lenteur ideomotrice dans ses composantes comportementales et cognitives, paraît être Tune des dimensions essentielles du noyau dépressif. Sa présence dans des symptômes d'anxiété doit déterminer la suspicion du médecin et la recherche des éléments caractéristiques d'un trouble dépressif authentique.

Cette liste de symptômes, qui n'est pas exhaustive, peut offrir des points de repère au médecin mis en présence du problème tortueux du diagnostic "anxiété ou dépression?" (6). Cependant, entre les deux types de troubles il y a des rapports étroits. Les troubles anxieux se compliquent souvent d'épisodes dépressifs, et les dépressions sont accompagnées souvent d'anxiété.

Le dépistage et le traitement des deux entités psychiatriques modifient favorablement le tableau psychologique du malade opéré à cœur ouvert. Nous avons constaté que les malades qui présentent une anxiété modérée, une attitude raisonnable envers l'acte opératoire, ont ultérieurement une bonne évolution, sans complications, ou, s'ils en ont, elles sont de gravité mineure, à convalescence de courte durée. Les grands anxieux sortent difficilement de l'anesthésie, présentent de nombreuses complications postopératoires, surtout d'ordre psychique, et ont une convalescence prolongée. Les malades qui, avant l'opération, affichaient une attitude indifférente ou, disons, sans trop de crainte, ont eu certains traits de la personnalité de ceux qui appartiennent à la catégorie des malades à dépression masquée.

Les principaux facteurs de risque conduisant aux complications neuropsychiques ont dépendu de: l'âge du patient, la gravité de la maladie préopératoire, la présence des lésions organiques du cerveaux, la présence des lésions mitrales rhumatismales, la durée du pontage, l'insomnie et la durée du séjour dans la chambre de réanimation.

Pendant le traitement des troubles neuropsychiques il faut tenir compte que (7):

• l'association des barbituriques aux coagulants n'est pas recommandée aux vasculaires cérébraux, ceci pouvant induire des troubles de l'équilibre, de coordination, des états d'agitation, la tristesse, l'euphorie;

• il faut éviter l'association des barbituriques à la digitale, aux glucocorticoïdes, aux antidiabétiques oraux et aux tétracyclines;

• les phénothiazines de type chloredélazine, plégomazine et les neuroleptiques retard, peuvent donner des troubles vasculaires (thromboses) et la thioridazine peut induire des troubles de rythme cardiaque;

• en insuffisance respiratoire il faut éviter les tranquillisants;

• les thymoleptiques de la catégorie de l'antideprin, l'amitriptyline, le sinequan peuvent produire une hypotension artérielle, avec de possibles accidents vasculaires cérébraux, l'infarctus myocardique, le collapsus, des troubles du rythme cardiaque; Le lithium présente une cardiotoxicité réduite.

Conclusions

Dans la chirurgie à coeur ouvert le neuropsychiatre est l'un des membres de l'équipe médico-chirurgicale dont le rôle est actif pendant les trois phases que le malade subit pendant son hospitalisation, à savoir:

• pendant la période d'investigation il tâchera de déceler les éventuelles séquelles d'affections cérébrales, la présence d'une insuffisance cérébrale circulatoire, d'une épilepsie, de maladies psychiques, etc., proposant les mesures préparatoires nécessaires. D'accord avec le psychologue, il devra dépister les malades au potentiel anxieux élevé et tâcher de prévenir d'éventuelles décompensations. De plus, l'interventions à coeur ouvert étant extrêmement coûteuse, il faudra établir le quantum de responsabilité concernant la personne même et la capacité qu'a le malade d'apprécier correctement sa situation pendant toute la durée de sa vie;

• pendant l'intervention chirurgicale, il surveillera en clinique (surtout au moyen des encéphalogrammes) l'évolution du patient;

• post-opératoirement, l'équipe tout entière, assurera le traitement des affections préexistantes et interviendra activement dans la solution des éventuels problèmes neuropsychiques qui surviendront.

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