Academy of Romanian Scientists *Volume 12, No. 2, 2023, pp. 73 - 80*
Annals Series on Biological Sciences ISSN 2285 – 4177

ORIGINAL PAPERS

Correlations Between Galectin and Clinically Relevant Biochemical Parameters Involved in the Diagnosis and Control of Heart Failure

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Abstract. *Galectins belongs to the Lectin family and fulfil various roles. Among them, Galectin-3 is involved in inflammatory processes associated with cardiovascular diseases. Biomarkers have become essential in the management of cardiovascular disease and their potential clinical applications continue to grow. Of great interest is the knowledge of Galectin-3 as a novel biomarker involved in cardiac fibrosis and remodeling, as well as its clinical application in heart failure.*

Keywords: Galectin, Cardiovascular Diseases, Heart Failure.

DOI 10.56082/annalsarscibio.2023.2.73

Introduction

In relation to cardiovascular diseases and their association with metabolic dysfunctions, it is important to focus research on biological markers with clinical relevance involved in the diagnosis and control of cardiac diseases. Among these, heart failure is correlated with the epidemiological dimensions of major cardiovascular diseases. It is therefore necessary to develop an effective and optimal therapeutic approach to cardiovascular pathology and to identify biological markers that can provide additional values to standard methods of assessment and diagnosis. The correlation of several specific markers for inflammation, dysfunction or cardiac fibrosis and their association may thus

improve the clear assessment of risk stratification in addition to traditional cardiovascular assessment methods.

Cardiovascular disease is a class of diseases with a very high incidence worldwide. According to Suthahar et al., 2018, a major cause of cardiovascular disease is atherosclerosis. One of the primary categories of cardiovascular disease is heart failure. According to Daniels et al., 2007, these represent a complex clinical syndrome expressing certain degrees of impairment of the heart's pumping function, a function essential for providing the body's metabolic needs (McMurray, JJ et al., 2012).

The study was carried out in the "Sfântul Apostol Andrei" Emergency Clinical County Hospital Constanta and the "Dr. Alexandru Gafencu" Emergency Military Clinical Hospital, Constanta for patients admitted to the Cardiology Department.

The patients are over 18 years of age, and the study takes into account the research issues, which involve clinical and paraclinical evaluation of which laboratory analyses are part, with respect to the rules according to Law no.206/2004 on good conduct in scientific research, technological development and innovation (Lupu et al., 2023), as well as respect for informed consent and confidentiality.

The topic addressed, a topical theme, may be of major theoretical and applied importance.

Part I. The current state of knowledge.

Biomarkers have become essential in the management of cardiovascular disease and their potential clinical applications continue to grow. Of great interest is the knowledge of Galectin-3 as a novel biomarker involved in cardiac fibrosis and remodeling, as well as its clinical application in heart failure.

Clinical studies have suggested the prognostic value of the biomarker Galectin-3, a marker of fibrosis in heart failure (French, B., et al., 2016). It is a carbohydrate-binding protein with implications according to recent studies in inflammation, immunity and cancer and mediates the progression of heart failure (Hristenson, RH et al., 2016).

Heart failure is a common diagnosis among cardiovascular diseases, and according to Fang J, et al. (2008), despite adopted guideline-based therapies (angiotensin, beta-blockers, etc.), this condition is a significant impact factor for healthcare systems, this is among the group of diseases with the highest rate of readmission, the financial values for this are significant (Fang J, et al. 2008).

Galectins are defined as a family of proteins based on conserved β-galactoside binding activity localized within their characteristic carbohydrate recognition domains (Stowen, S., et al., 2022).

Role of Galectin in fibrosis and the inflammatory process.

Galectin-3 is a protein that has been directly implicated in the inflammatory process and subsequent fibrosis in several organ systems (deFilippi, R., C., 2010), including the heart.

According to Klyosov, A., el al. (2008), Chronic inflammation leading to fibrosis with loss of tissue architecture and subsequent organ failure is a massive problem in healthcare. Tissue fibrosis represents the last common pathway of chronic tissue injury. Inflammation is normally a beneficial protective response to tissue injury that promotes healing or repair of damaged tissues (Klyosov, A., el al., 2008). However, chronic inflammation with scar tissue formation and organ failure is a characteristic feature of the pathogenesis of many human diseases and results in major morbidity and mortality worldwide as stated by Neuberger, J., et al., 2000, Simplson K., et al., 1999 and El Nahas, A., et al., 2005, cited by Klyosov, A., et al., in 2008.

There are numerous studies reporting an important role of galectins in the pathogenesis of fibrosis, but there are also mentions of protective roles. It is important to understand the level of understanding of tissue immune cell-fibroblast interactions and to understand the molecular mechanisms by which targeted antifibrotic therapeutics can then be developed. Of the galectin group (shown in a previous study to be a compex of about 15 in the same family), Galectins 1 and 3 are the ones primarily studied for their role in tissue fibrosis.

Galetin in the context of cardiac biomarkers.

It is important that Galectin testing can provide important information for patients at the onset of heart failure even without symptoms or even stratify some risk in those who would only present predisposition or risk factors. According to deFilippi, C., et al. (2010) the focus of much research is the possibility that inhibition of the pro-fibrotic actions of Gal-3 may be a target for prevention or treatment of CHF.

According to Hogas et al., 2017, Galectin-3 in clinical trials has been shown to be an independent prognostic factor for cardiovascular assessment in patients without heart failure and in those at high risk, having the best predictive value (Hogas, S et al., 2017).

Also, in the literature, according to Rubattu S., et al., 2019, NT-proBNP and BNP have been shown to be of great importance in the diagnosis of heart failure, both in assessing severity and prognosis.

According to a study by Novartis, cited by Rubattu S., et al., 2019, plasma BNP concentration increased with the severity of heart failure. Plasma levels of BNP and NT-proBNP have prognostic values in patients with cardiovascular

disease, and a reduction in BNP and NT-proBNP levels predicts an improvement in clinical symptoms (Rubattu, S., et al., 2019)

Part II. Own experimental research.

II.1. Materials and methods used.

The study was conducted in the first half of 2023, in the County Emergency Hospital "St. Apostle Andrew" Constanta and in collaboration with the Military Emergency Hospital "Dr. Alexandru Gafencu" Constanta for a number of 21 adult patients aged between 46 and 89 years, all with diagnosis of heart failure established at admission (a percent of about 10% of patients taken in the study) or with diagnosis of old heart failure (about 90% of patients taken in the study). Patients in the current study were divided by age group into three groups (group I - patients aged 40-55 years, group II - patients aged 56-70 years and group III - patients aged 71 years and over). Also, another grouping was done for diagnostic classes of heart failure (HF), namely one group representing 9.52% of patients with HF class I and class II, and the second group representing the remaining 90.47% of patients with HF class III and class IV.

Values of specific inflammatory markers, cardiac markers, biochemical parameters known in paraclinical analysis for cardiovascular diseases were taken in the study, and especially values for Galectin-3 were determined.

Correlations were made between each of the parameters of interest for the current study and Galectin-3 levels.

Table 1. Characteristics and groups of patients with C.I.

Number of subjects	21
Mean age	74.61
Gender	
M	16
F	5
Social env.	
U	14
R	7
Groups NYHA Classification	
Class I	0
Class II	2
Class III	4
Class IV	15
Diabetics	5
Kidney diseases	9
Liver diseases	4

The Arhitect assay is a chemoluminescence-based assay (CMIA technology), a quantitative assay for the determination of Galectin-3 in human serum and EDTA plasma. The results obtained for Galectin-3 were classified and grouped according to the recommended risk categories as follows:

- Low risk = levels above 25.9 ng/ml
- Medium risk = levels between 17.8 - 25.9 ng/ml
- High risk = levels between 3- 17.8 ng/ml

II.2. Results and discussion

Tabel 2. Pearson Correlations

Correlations

		INR	TropT	CKMB	K	TGO	GAL
INR	Pearson Correlation	1	.063	.133	.143	.064	.490*
	Sig. (2-tailed)		.785	.564	.537	.782	.024
	N	21	21	21	21	21	21
TroponinaT	Pearson Correlation	.063	1	-.165	-.108	.172	-.254
	Sig. (2-tailed)	.785		.475	.640	.456	.267
	N	21	21	21	21	21	21
CKMB	Pearson Correlation	.133	-.165	1	.454*	.428	.297
	Sig. (2-tailed)	.564	.475		.039	.053	.192
	N	21	21	21	21	21	21
K	Pearson Correlation	.143	-.108	.454*	1	.205	.359
	Sig. (2-tailed)	.537	.640	.039		.373	.111
	N	21	21	21	21	21	21
TGO	Pearson Correlation	.064	.172	.428	.205	1	-.015
	Sig. (2-tailed)	.782	.456	.053	.373		.948
	N	21	21	21	21	21	21
GAL	Pearson Correlation	.490*	-.254	.297	.359	-.015	1
	Sig. (2-tailed)	.024	.267	.192	.111	.948	
	N	21	21	21	21	21	21

*. Correlation is significant at the 0.05 level (2-tailed).

Galectin-3 (ng/mL) correlates with INR ($r = 0.490$, $p = 0.024 < \alpha = 0.05$) Correlation is positive, low to moderate, statistically significant.

From the Pearson correlation profile analysis a direct correlation is observed between Gal-3and INR, CK-MB with K and TGO. This indicates a potential diagnostic or physiological adaptive remodeling index of the functional dynamics of the heart in patients with heart failure.

Table 3. Kendall Index correlation

Correlations

			INR	TropT	CKMB	K	TGO	GAL
Kendall's	INR	Correlation Coefficient	1.000	-.087	.102	.131	.029	.327*
		Sig. (2-tailed)	.	.586	.525	.413	.856	.040
		N	21	21	21	21	21	21
	TropT	Correlation Coefficient	-.087	1.000	.014	-.053	.106	-.076
		Sig. (2-tailed)	.586	.	.928	.739	.506	.629
		N	21	21	21	21	21	21
	CKMB	Correlation Coefficient	.102	.014	1.000	.300	.257	.158
		Sig. (2-tailed)	.525	.928	.	.060	.108	.318
		N	21	21	21	21	21	21
	K	Correlation Coefficient	.131	-.053	.300	1.000	.150	.168
		Sig. (2-tailed)	.413	.739	.060	.	.348	.290
		N	21	21	21	21	21	21
	TGO	Correlation Coefficient	.029	.106	.257	.150	1.000	-.010
		Sig. (2-tailed)	.856	.506	.108	.348	.	.952
		N	21	21	21	21	21	21
	GAL	Correlation Coefficient	.327*	-.076	.158	.168	-.010	1.000
		Sig. (2-tailed)	.040	.629	.318	.290	.952	.
		N	21	21	21	21	21	21

*. Correlation is significant at the 0.05 level (2-tailed).

Table 4. Spearman's rho correlation

Correlations

			INR	TropT	CKMB	K	TGO	GAL
Spearman's rho	INR	Correlation Coefficient	1.000	-.120	.113	.214	.039	.465*
		Sig. (2-tailed)	.	.603	.626	.353	.866	.034
		N	21	21	21	21	21	21
	TropT	Correlation Coefficient	-.120	1.000	.043	-.053	.161	-.142
		Sig. (2-tailed)	.603	.	.854	.821	.487	.540
		N	21	21	21	21	21	21
	CKMB	Correlation Coefficient	.113	.043	1.000	.417	.342	.190
		Sig. (2-tailed)	.626	.854	.	.060	.129	.410
		N	21	21	21	21	21	21
	K	Correlation Coefficient	.214	-.053	.417	1.000	.213	.259
		Sig. (2-tailed)	.353	.821	.060	.	.354	.256
		N	21	21	21	21	21	21
	TGO	Correlation Coefficient	.039	.161	.342	.213	1.000	-.051
		Sig. (2-tailed)	.866	.487	.129	.354	.	.827
		N	21	21	21	21	21	21
	GAL	Correlation Coefficient	.465*	-.142	.190	.259	-.051	1.000
		Sig. (2-tailed)	.034	.540	.410	.256	.827	.
		N	21	21	21	21	21	21

*. Correlation is significant at the 0.05 level (2-tailed).

In the case of the model under study, a relatively small number of correlations can be observed, the Pearson correlation index having a statistical significance

threshold of less than 0.05 for the correlation variants mentioned in Table 2.

Conclusions

1. The results of the study confirm the literature data and indicate statistically significant values and risk in the group of patients with chronic C.I. and classified as high risk.
2. Galectin levels are a significant indicator factor related to age, C.I. class according to NYHA classification
3. As a laboratory test, between paraclinical explorations and clinical assessment, Gal-3 can provide alongside established biomarkers an optimization of patient assessment and care.
4. Galectin levels are complementary to BPN and NT-proBNP and can be used in assessment and risk group stratification alongside specific analysis correlated with specific imaging investigations.

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