

POUCHITIS AFTER ILEAL - POUCH ANAL SURGERY – A SHORT OVERVIEW

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Abstract. *Restorative proctocolectomy is widely used for ulcerative colitis and familial adenomatous polyposis coli. Pouchitis represent the specific late complication after ileal pouch surgery. It is more frequent in patients with ulcerative colitis and may have a negative impact on long-term functional outcome. The diagnosis is based on clinical signs and should be confirmed by pouch endoscopy with biopsy. The prevention and treatment of pouchitis remains a challenging issue. Most of the patients with acute pouchitis can be conservatively managed using antibiotics. Probiotics appears to be an effective alternative to antibiotics in chronic pouchitis.*

Keywords: ileal pouch surgery; complications; functional outcome

Rezumat. *Proctocolectomia totală restaurativă este utilizată în prezent pe scară largă în tratamentul recto-colitei ulcero-hemoragice și al polipozei adenomatoase familiale. Pauchita sau inflamația rezervorului ileal reprezintă complicația specifică acestui tip de procedeu chirurgical. Este mai frecvent întâlnită la pacienții operați pentru recto-colită ulcero-hemoragică și poate avea un impact negativ asupra rezultatelor funcționale la distanță. Diagnosticul este sugerat de manifestările clinice dar trebuie confirmat de examenul endoscopic al rezervorului ileal, cu biopsierea mucoasei. Prevenția și tratamentul pacienților cu pauchită reprezintă o piatră de încercare. Majoritatea pacienților cu pauchită acută pot fi tratați conservator, cu rezultate bune, utilizând antibiotice. Probioticele par a fi o alternativă eficientă față de antibiotice în tratarea pauchitei cronice.*

Cuvinte-cheie: *proctocolectomie restaurativă; complicații; rezultate funcționale*

Introduction

Restorative proctocolectomy is considered nowadays the gold standard of the surgical treatment for ulcerative colitis (UC) and familial adenomatous polyposis coli (FAP) (1). It consists of removal of the entire colon and rectum but with the preservation of the anal sphincters; the digestive continuity is realized through interposition of an ileal pouch, with ileal-pouch anal anastomosis. Anal

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mucosectomy is mandatory for patients with FAP, while in patients with UC a small part of the anal mucosa (1-2 cm) can be preserved with the reason to mitigate the possible damages of the internal anal sphincter and to allow a stapled ileal-pouch anal anastomosis (2). Nevertheless, mucosectomy can be a demanding procedure, especially in patients with active rectal lesions of UC (3).

For FAP prophylactic colectomy is recommended in all cases due to the almost 100% risk of colo-rectal malignancies. Indeed, the most frequent cause of mortality in patients with FAP without colectomy, is represented by the malignancies of the colon and rectum (4). The presence of colonic malignancy at the time of surgery for FAP does not preclude a good postoperative outcome regarding both oncological and functional results (5). However, prophylactic colectomy does not exclude future development of extracolonic malignancies in FAP (4).



Figure no.1:
Macroscopical appearance of UC: hemorrhagic colitis, ulcerations and pseudopolyps (operative specimen: colectomy)

For UC, the main indications for elective surgery are inefficiency of the medical treatment or steroid dependence, along with the presence of severe dysplasia or malignancies. Acute complications of UC (i.e., acute attack, toxic megacolon, perforation, massive hemorrhage) represent the indications for surgery in an emergency setting (6). In our experience, surgery for UC was indicated mostly for patients with complicated disease (acute or chronic complications) (*Figure no.1*) (6).

Nowadays, ileal-pouch anal surgery is performed with almost nil mortality (1;7). However, even in experienced centers, the postoperative morbidity is still high, up to 50% of patients (7). The most frequent early postoperative complications are represented by pelvic sepsis and small bowel obstruction (1).

Pouchitis (inflammation of the reservoir) represents the specific late complication after restorative proctocolectomy (2). Most of the patients with pouchitis can be conservatively managed but in a small number of patients it is necessary to remove the ileal pouch (1). Thus, the development of pouchitis after ileal pouch surgery may jeopardize the functional outcome of the patient (8). Chronic pouchitis has been proven to have a negative impact on quality of life after ileal

pouch surgery for UC (9) and may increase the risk of dysplasia (10). Nevertheless, a correct diagnosis and treatment for pouchitis after ileal pouch surgery is of utmost importance.

Epidemiology, pathogenesis and risk factors

It appears that pouchitis is more frequent in patients operated for UC than in patients with PAF. Thus, pouchitis may occur in the ileal pouch in up to 60% of patients with UC, especially in the first years after restorative proctocolectomy (11). The prevalence of pouchitis increases over time (8). In our experience, the prevalence of pouchitis after ileal pouch surgery was 8% (mainly patients with UC) and in one patient the removal of the ileal reservoir was imposed by the intractable disease (1). However, in our series almost two third of the patients were operated for FAP (1) and this feature may explain the reduced incidence of this late complication. These data are consistent with a recent study that showed an incidence of only 5% for pouchitis at one year after ileal pouch surgery for FAP (12).

The pathogenesis of pouchitis remains unknown (13). Several pathogenic theories, such as genetic predisposition, inflammation due to the presence of some bacterial antigens or immunological mechanisms were proposed to explain the development of pouchitis (13). Recently, it was suggested that the presence of Bacteroidaceae spp and Clostridiaceae spp may be associated with inflammation of the pouch mucosa while Enterococcaceae spp may have an active role in maintaining the immunologic homeostasis within pouch mucosa (14). An increased IgG4+ plasma cell infiltration of the pouch mucosa was associated with chronic pouch inflammation and concurrent autoimmune disorders (15). Deficiency of short chain fatty acids in stool was also associated with development of acute pouchitis (16).

Several clinical factors were associated with an increased risk for development of pouchitis (11):

- Severe UC
- Pancolitis (17)
- Diagnosis of UC at young age
- Extraintestinal manifestation of UC, including primary sclerosing cholangitis
- Male gender (14)
- Non-steroidal anti-inflammatory drugs.
- Depression (18)
- A long follow-up period after ileal pouch surgery (17)

Other factors, such as smoking and acute colitis appears to be correlated with a decreased risk for pouchitis (11).

Patients with indeterminate colitis are more likely to develop continuous pouch inflammation after ileal pouch surgery, particularly those with a preoperatively positive antibody reactivity profile (19).

In summary, pouchitis is by far more frequent after ileal pouch surgery for UC and, although the pathogenesis is not clearly understood, several clinical factors are considered as risk factors.

Diagnosis

The diagnosis of pouchitis is based on clinical and endoscopic features. The clinical features of pouchitis are represented by diarrhea (usually an increased number of semiformed or liquid stools per day, sometimes with associated mild rectal hemorrhage) accompanied by abdominal pain, tenesmus and urgency or even anal incontinence (20). Some patients may also present with fever.

From clinical point of view, pouchitis can be classified according to (11;21):

- Disease activity:
 - Remission
 - Mild disease
 - Moderate disease (increased stool frequency, urgency, infrequent incontinence)
 - Severe disease (dehydration, frequent incontinence)
- Symptoms duration:
 - Acute disease (less than 4 weeks)
 - Chronic disease (more than 4 weeks)
- Disease pattern of evolution:
 - Infrequent disease (1-2 acute episodes)
 - Relapsing disease (more than 3 acute episodes)
 - Continuous disease
- Response of the disease to antibiotics:
 - Responsive disease
 - Dependence to medication of the disease
 - Refractory disease.

Investigations in a patient suspected of pouchitis should include as mandatory endoscopy with mucosal biopsy of the ileal pouch (8). In a patient with pouchitis, endoscopic examination of the ileal reservoir (pouchoscopy) may show an ileal pouch with intense oedema, a granular and friable mucosa, with decreased vascularization and, sometimes, ulcerations and hemorrhage (22). The final diagnosis of pouchitis is established by the pathologist showing histological signs of acute inflammation: infiltration of the mucosa with neutrophils, ulceration of the mucosa and crypt abscess (11).

In clinical practice, the differential diagnosis of pouchitis should be made with other diseases such as Crohn's disease, infection of the reservoir with Cytomegalovirus or Clostridium difficile, pelvic septic complications (**Figure no.2**), inflammation of the remnant anal mucosa (cuffitis), ischemic changes of the reservoir or anal sphincter dysfunctions (11). Sometimes, the symptoms of pouchitis are considered to be a result of reactivation of UC at the level of the terminal ileum.



Figure no.2:
*Pelvic abscess (arrow) after ileal pouch surgery
(computed tomography examination of the pelvis)*

Moreover, in a small number of patients the final pathological examination of the operative specimen (recto-colectomy) revealed a Crohn disease or indeterminate colitis instead of UC. In these former cases it was noticed an increased rate of complications at the level of the ileal pouch, mainly represented by symptoms mimicking pouchitis or even fistulization of the reservoir to vagina or tegument (entero-cutaneous or perianal fistulas) (3). In these patients usually the inflammatory lesions are also present at the pre-pouch ileum. Cuffitis can be diagnosed by endoscopic examination with biopsy of the remnant rim of mucosa at the level of anal canal. The presence of cuffitis does not exclude the presence of pouchitis (21).

Contrast X-ray of the pouch (pouchogram) and magnetic resonance imaging is a useful tool in detection of strictures or fistulas at the level of the ileal pouch, perianal fistulas and pelvic septic collections. Thus, although it is not a diagnostic tool for pouchitis, it may exclude other causes of symptoms mimicking pouchitis, such as pelvis sepsis related to ileal reservoir fistula or ileal-pouch anal dehiscence. Some surgical teams recommend the routine use of pouchogram before closing the loop ileostomy after ileal pouch surgery but, based on our own experience, we recommend this procedure only selectively, in patients who postoperatively developed pelvic septic complications.

In 1994 Sandborn et al proposed a standard, objective and reproducible scoring system for pouchitis in order to assess the severity of the disease (22). Accordingly, acute pouchitis was defined as a score of ≥ 7 (22), while remission is defined as a score less than 3 (20). This scoring system is based on clinical, endoscopical and histological data, as shown in **Table 1**.

Table 1. Pouchitis disease activity index (PDAI) according to Sandborn et al (22)

<i>Clinical features</i>		<i>Endoscopic features</i>	
Stool frequency:			
➤ Usual	0	➤ Edema	1
➤ 1-2/ day more	1	➤ Granularity	1
➤ ≥ 3 / day more	2	➤ Friability	1
Rectal bleeding:		➤ Loss of vascular pattern	1
➤ None or rare	0	➤ Mucus exudates	1
➤ Daily	1	➤ Ulceration	1
Urgency/ abdominal cramps:		<i>Histological features (acute)</i>	
		➤ Polimorph infiltration:	
➤ None	0	- Mild	1
➤ Occasional	1	- Moderate + crypt abscess	2
➤ Usual	2	- Severe + crypt abscess	3
Fever:		➤ Ulceration per low-power field (average)	
➤ Absent	0	- < 25%	1
➤ Present	1	- $\geq 25, \leq 50\%$	2
		- > 50%	3

In summary, the diagnosis of pouchitis in a patient with previous ileal pouch surgery is suggested by clinical signs and should be confirmed by endoscopy with ileal pouch biopsy.

Treatment

Most of the patients with acute symptoms of pouchitis will respond to conservative treatment. However, up to 60% of these patients will experience at least one recurrence of the symptoms and up to 10% of patients will develop chronic pouchitis (11). Antibiotics and probiotics are the main tools for the treatment of pouchitis.

In clinical practice, the most widely used antibiotics in the treatment of pouchitis are represented by ciprofloxacin and metronidazole. Metronidazole is preferred in acute pouchitis while in chronic pouchitis ciprofloxacin is preferred due to a decreased incidence of side effects (11). However, a randomized clinical trial showed that ciprofloxacin (1 g per day, 2 weeks) has the same efficacy in the treatment of acute pouchitis as metronidazole (20 mg/ kg per day, 2 weeks) but with significantly less side effects, suggesting ciprofloxacin as first choice therapy (23). Moreover, some randomized studies showed that ciprofloxacin is more effective than metronidazole at inducing remission in acute pouchitis (24). We also used, in our patients with acute pouchitis, ciprofloxacin as first-line therapy, with good results in most of the cases (data not shown).

Probiotics have been proven as an effective therapy in chronic pouchitis due to the impact on the flora of the ileal pouch (11). Probiotics are living microorganisms that exert health benefits ingested in a specific amount (25). A recent meta-analysis suggested that probiotics may have a benefit in maintaining remission of patients with pouchitis, although the dose and timing of administration are not clearly defined (25). Probiotics may also play a role in prevention of pouchitis after ileal pouch surgery (24). The probiotic compound VSL#3 seems to be effective at preventing first episode or active pouchitis and to maintain remission after an acute episode (20).

Other therapies such as anti-inflammatory (i.e., mesalamine and sulfasalazine) or immunosuppressive drugs (i.e., azathioprine) are reserved for antibiotic-refractory pouchitis (11). Infliximab, a monoclonal antibody that targets tumour necrosis factor alpha was reported as an effective treatment on short- and mid-term outcome in patients with chronic refractory pouchitis. However, a large number of patients could not complete the treatment (26).

Although treatment of acute pouchitis appears to be quite simple, the therapy of chronic pouchitis remains a great challenge. Thus, the therapeutic strategy for those patients with chronic refractory pouchitis includes several options (21):

- Antibiotics in a prolonged course
- Therapy maintenance with the most effective antibiotic in the lowest clinically effective dose
- Cycles of multiple antibiotics at one week intervals



Figure no. 3:
Ileal J pouch excised
(operative specimen)

As it was already mentioned, only a small number of patients with pouchitis will not respond to medical therapy, requiring excision of the ileal pouch. However, chronic pouchitis represents one of the main cause for late-onset pouch failure (i.e., pouch excision, revision or permanent diverting ileostomy) (27). Pouch excision is necessary in about 1% of patients with pouchitis (**Figure no.3**) (20).

In summary, ciprofloxacin is the first-line therapy for acute pouchitis, while probiotics such as VSL#3 are effective for prevention and maintenance of remission after an acute episode.

Conclusion

Pouchitis represents a specific, late complication after ileal pouch surgery, mostly in patients with UC. The diagnosis is suggested by clinical signs but should be confirmed by the endoscopy with biopsy of the ileal pouch. The majority of the patients who develop pouchitis will respond to medical therapy and only a small number of cases will need ileal pouch excision.

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