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REVIEW

Ileal reservoir with ileo-anal anastomosis: Long-term complications

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Summary Coloproctectomy with ileo-anal anastomosis (CP-IAA) has been in use for 30 years. This intervention is the standard technique when surgery is indicated for familial adenomatous polyposis (FAP) and for ulcerative colitis (UC). Although the surgery is safe with mortality of less than 1%, it is associated with a morbidity of 18—70%. We thought a literature review about long-term complications would be enlightening. Pouchitis is the most common complication; it occurs in 70% of patients over 20 years follow-up; small bowel obstruction affects 25% of patients and pelvic sepsis occurs in 20—30% within 10 years. CP-IAA can impact the patient's sexual life due to erectile and ejaculatory dysfunction, dyspareunia, and incontinence of stool during sexual intercourse. Nevertheless, patients with long-standing UC describe an overall improvement in their sexual function after surgery. The failure rate varies from 3.5 to 15%; major causes of failure are sepsis, unrecognized Crohn's disease, and poor functional results. Cases of dysplasia and cancer have been reported in the reservoir, but more particularly when there is retained colonic glandular mucosa. The transitional zone should be monitored whenever there are risk factors for colon neoplasia. The relatively high morbidity of CP-IAA should not overshadow the good functional results of this technique.

Introduction

Coloproctectomy with ileal anal anastomosis (CP-IAA) was developed 30 years ago by Parks and Nicholls and has become the standard intervention in the surgical treatment of familial adenomatous polyposis (FAP) and ulcerative colitis (UC).

It allows treatment of both colonic and rectal components of disease, reduces cancer risk, and preserves the natural pathway of defecation, while maintaining good continence.

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The procedure has been gradually standardized; almost all teams now use a J-shaped reservoir pouch (superior functional results compared to S- or W-shaped reservoirs). The anastomosis is either hand-sewn or mechanically stapled (most common technique) after mucosectomy.

The surgery has a mortality rate below 1% [1,2] but is accompanied by significant morbidity ranging from 18—70% in the literature (complication rates vary with the duration of follow-up) [1—4].

The long-term complications include pouchitis, cuffitis, small bowel obstruction, chronic pelvic sepsis, vaginal fistula, anal stenosis, impaired sexual function, incontinence, and failure, as well as late development of desmoid tumors, dysplasia, and cancer.

Complications

Pouchitis

Pouchitis is a non-specific inflammation of the ileal reservoir. This is the most common long-term complication after CP-IAA. Its incidence increases with duration of follow-up; the Mayo Clinic reported frequencies of 20% at 1 year, 32% at 5 years, 59% at 10 years, and 70% at 20 years [3]. It occurs almost exclusively in patients operated for UC; it occurs in only 5% of CP-IAA performed for FAP [1,5].

The evolution and severity of pouchitis are variable. There may be a single episode, recurrent episodes (over three episodes of acute pouchitis), or chronic pouchitis (progression over 4 weeks despite medical treatment) [6].

The clinical picture of pouchitis is associated with increased frequency of bowel movements, painful defecation, tenesmus, incontinence, abdominal pain, rectal bleeding and low-grade fever, or, at times, fever spikes with malnutrition and dehydration [6].

The diagnosis is confirmed by endoscopic appearance and biopsy. Sandborn et al. have developed the Pouchitis Disease Activity Index (PDAI) score combining clinical, endoscopic and etiological findings [7]. A score $\geq$7 indicates pouchitis. Use of these criteria will also help to eliminate the two other entities in the differential diagnosis, i.e., cuffitis and irritable pouch syndrome (Table 1). The difficulty of establishing an accurate diagnosis of pouchitis also explains the variability in reporting of this complication in the literature.

The pathophysiology of pouchitis is still poorly understood and involves multiple factors (bacterial overgrowth, colonic metaplasia, primary underlying disease, immune dysfunction). Fecal stasis caused by the reservoir may result in bacterial overgrowth. This flora produces volatile fatty acids, which damage the mucosa of the reservoir. Moreover, the presence of colonic metaplasia results in modification of colonic mucus and contributes to bacterial overgrowth and inflammation of the pouch. The primary illness may also play a role in this inflammation; it most commonly occurs in patients with UC [1,5]; in this population, pouchitis occurs more commonly when there are extra-intestinal manifestations of UC [9,10]. These various mechanisms alter the lining of the reservoir and promote inflammation due to an imbalance between pro- and anti-inflammatory cytokines [11,12].

The first-line treatment of pouchitis is the administration of antibiotics (oral or trans-anal) such as metronidazole or ciprofloxacin. Probiotics (VSL#3) find a place in the treatment of chronic forms of pouchitis and in maintaining remissions [13—15]. For refractory or recurrent pouchitis, the same treatments as those for inflammatory bowel disease (5 amino salicylate, budesonide, inhibitors of xanthine oxidase inhibitors) may be useful [16].

The development of pouchitis is highly variable. Sometimes it occurs as a single episode while in other cases there are multiple recurrences or it becomes chronic with a major impact on patient quality of life [17].

Cuffitis

This is an inflammation involving the band of retained rectal mucosa which most often after persists after stapled anastomosis in the tissue between the bottom of the reservoir and the top of the anal canal. Its frequency is estimated at about 9% [18]. Diagnostic features are summarized in Table 1.

Patients with cuffitis are also at increased risk of developing mucosal dysplasia and cancer (5% at 10 years) [19].

Irritable pouch syndrome

Described by Shen et al. in 2002, this syndrome is encountered in 46% of patients who present with clinical features of pouchitis but whose PDAI score is below 7 (Table 1) [20]. This clinical entity is related to the irritable bowel syndrome and its treatment involves similar treatments with good results [8].

Small bowel obstruction

As with any major abdominal surgery, CP-IAA exposes patients to the risk of small bowel obstruction. Indeed, it is one of the most common complications after such surgery; 25% of patients will be hospitalized for symptoms of intestinal obstruction and half of these will require surgical remediation [21]. The major causes of obstruction include stenosis of the diverting ileostomy, volvulus, internal hernia, adhesive bands, and anastomotic stricture [21,22]. Laparoscopy seems to decrease the occurrence of adhesion formation and thereby the risk of bowel obstruction; so too does use of anti-adhesion films although these are rarely used at present [23,24].

Infectious complications

The prevalence of septic complications is 6—37% in various series [25—28]. They most typically occur following different types of fistula (anastomotic, vaginal, perineal) [29]. Septic complications are a major determinant of long-term success of CP-IAA, since they adversely affect the functional outcome and increase the risk of failure [25,30—33]. Farouk et al. showed that poor functional results were due to reduced pouch compliance, dysmotility, and alterations of the pelvic floor caused by fibrosis secondary to resolving pelvic sepsis [34].

Several risk factors have been identified: age <50 years, severe pouchitis, hemoglobin below 10 g/dl, corticosteroid use and anastomotic tension; the use of a protective ileostomy appears to protect against these risks [25,35].

Patients with FAP are at lower risk of septic complications than patients with UC; this is probably due to immunosuppression associated with UC and its treatment. However, once septic complications arise, there is no difference in terms of failure between these two categories of patients [27,30,36—38].

Fistulas developed between the reservoir and the vagina in 3—16% of patients [39]. They may originate from the anastomosis, the reservoir or anal crypt glands; the principal risk

Table 1 Distinction between pouchitis, irritable pouch syndrome.

	Pouchitis	Irritable pouch syndrome	Cuffitis
Definition	Non-specific inflammation of the ileal reservoir	Clinical picture of pouchitis with a PDAI score <7 and absence of cuffitis	Inflammation of the rectal mucosa without pouchitis
Symptoms	Increase in stool frequency, anorectal pain, tenesmus incontinence, abdominal pain, rectal discharge, low-grade fever	Increase in stool frequency, anorectal pain, tenesmus, incontinence, abdominal pain	Increase in stool frequency, anorectal pain, tenesmus incontinence, abdominal pain, rectal discharge, extra-abdominal manifestations of UC
Endoscopic appearance	Mucosal edema, bleeding, friability, ulceration, mucosal hemorrhage	Normal	Inflammation of the rectal mucosa
Histologic appearance	Acute inflammation, chronic ulceration, crypt hyperplasia, villous atrophy	Normal	Ulceration, erythema, leukocyte infiltration
PDAI	≥7	<7	

McGuire et al. [8].
PDAI: Pouchitis Disease Activity Index; UC: ulcerative colitis.

factors are operative trauma, sepsis or undiagnosed Crohn's disease [38,40,41].

Several techniques for treatment have been proposed. Inferior transposition of a trans-anal ileal flap resulted in cure in 50% of cases [42]. This technique is only practicable if the reservoir can be mobilized; unfortunately, these fistulas are often associated with chronic sepsis leading to cicatricial fixation of the reservoir. In this case, an abdominal approach is preferable; this permits advancement of the anastomosis and treatment of the vaginal defect at the same intervention. Burke et al. have proposed a trans-vaginal approach, which offers the advantage of avoiding sphincteric lesions while providing a good vaginal repair [43].

Nevertheless, the recurrence rate is high (30—60%) and, in severe cases, can lead to the need for a diverting ileostomy with local fistula drainage, or even to a permanent ileostomy (14%) [29,31,39].

Anal stenosis

In the Mayo Clinic series of 1884 patients who underwent proctocolectomy with ileo-anal anastomosis (IAA) from 1986 to 1996, 11.2% of patients developed anal stenosis; of these stenoses, 86.4% were supple and resolved with dilation [44]. Stricture was more common after manual anastomosis than after stapled anastomosis (12% vs. 4%) or if there were technical difficulties such as tension on the reservoir.

Anal dilatation was effective in 95% cases where stenoses were pliable, but in only 45% of cases with fixed fibrous strictures. In addition to dilatation, re-operative intervention was necessary in 12% of stenoses. Surgery consisted of either excision of the stenosis with lowering of a mucosal flap or in refashioning of the pouch with a new anastomosis. A complementary end-ileostomy was performed if there were other coincident complications (fistulas, abscesses, chronic pelvic sepsis) [44].

Sexual function

The consequences of surgery on the patients' sexual life are an underappreciated and under-reported aspect of rectal surgery. Yet 4—20% of patients (regardless of gender) suffer from sexual dysfunction after surgery [45,46].

In the male, the principal problems are erectile dysfunction and retrograde ejaculation. Sexual problems in women are more difficult to define; surgery's impact is best appreciated by systematic study of alterations of sexual desire, arousal, orgasm, and satisfaction as well as by evaluation of vaginal dryness and the presence or absence of dyspareunia. Thus, Ogilvie et al. showed that nearly one in two women suffer from sexual dysfunction after IAA [47].

To reduce the rate of these complications, several avenues have been explored such as the surgical approach and the plane of dissection. Even though it is well established that dissection along the planes defined for total mesorectal excision results in preservation of the hypogastric nerves, dissection in close contact with the rectal wall is recommended for UC and FAP as long as there is no evidence of mucosal dysplasia or cancer. However, studies published to date have shown no difference in the incidence of sexual problems whether the plane of dissection was in the mesorectal plane or in contact of the rectal wall [48]. Investigations comparing laparoscopic with open surgery did not show any difference in terms of sexual dysfunction [49].

In spite of these specific complications, overall sexual life is improved after CP-IAA. In the series published by Chapman et al., 27.8% of patients said they had a better sex life 10 years after surgery [45]. Kelly et al. reported that 40% of patients reported suffering from sexual dysfunction before surgery vs. 12% after surgery [50]. This marked post-surgical improvement is certainly due to improved quality of life and simplification of medical therapy after surgery for patients with UC.

Table 2 Causes of failure after ileo-anal anastomosis (IAA).

Causes of failure related to primary diagnosis
Unrecognized Crohn's disease: recurrent abscess, fistula, mediocre functional result
FAP: desmoid tumors
UC: persistent sepsis
Patients with colon cancer: tumor recurrence

Prudhomme et al. [44].
FAP: familial adenomatous polyposis; UC: ulcerative colitis.

Fertility

A significant proportion of females undergoing CP-IAA are of childbearing age; these patients can successfully carry a pregnancy to term. Pregnancy entails no particular increase in complications (pouchitis, occlusion, sepsis) [51]. However, several studies have shown that there is a significant risk of reduced fertility [51—54]. Patients should be clearly informed of this risk when consent is obtained before this surgical procedure.

Vaginal delivery is safe and does not increase the rate of anal incontinence [51,55]. There is therefore no reason to prefer cesarean section for these patients other than for obstetrical indications.

It is possible that laparoscopy, by reducing the incidence of pelvic adhesions, may play a protective role in fertility, but no study has clearly demonstrated this theoretical advantage.

Incontinence

One of the main interests of coloproctectomy with reservoir and IAA is to allow patients to have satisfactory continence of stool while avoiding the disagreeable inconveniences of an ileostomy. But the anatomical modifications result nonetheless in a significant alteration in the frequency of stool evacuation with an average of six daytime and two nocturnal bowel movements [3].

In 72.3% of patients, complete continence was achieved at 5 years; most of the remaining patients had an average of three to seven episodes of incontinence per week while 3.6% of patients had total incontinence [56]. When patients suffer from incontinence, its severity tends to decrease over time [56]. Achievement of complete continence is more likely for patients with stapled vs. hand-sewn anastomosis (8.7% incidence of incontinence for stapled anastomosis vs. 35.7% after manual anastomosis) [56].

Failure

Failure is defined as the need to excise the reservoir or the need for a permanent ileostomy. The rate ranges from 3.5 to 15% in the literature [1,32,57]. The causes of failure are listed in Table 2.

To reduce this failure rate, several teams have developed techniques to salvage the reservoir. Dehni et al. have proposed two different surgical approaches. The trans-anal approach is used preferentially for low-lying fistulae and for anastomotic strictures as long as the reservoir is of satisfactory size and the stricture is not fixed and fibrotic. The abdominoperineal approach is used when the above-mentioned conditions are not met [58]. Baixauli et al. have proposed reconstruction of the anastomosis [59]. In this case, the complication rate is higher than for the initial intervention.

Table 3 Major risk factors for desmoid tumor in patients with Familial Adenomatous Polyposis (FAP) [62].

Risk factors for desmoid tumors
Family history of desmoid tumors
Presence of an osteoma or epidermal cysts
Mutation of the APC gene between codons 1444 and 1578
Female gender

Desmoid tumors

Desmoid tumors may occur sporadically or as part of the syndrome of FAP. Patients with FAP carry a thousand-fold increased risk of developing desmoid tumors [60]. In 75% of cases they occur after colectomy [61].

The main risk factors for desmoid tumors in patients with FAP are listed in Table 3.

Desmoid tumors occur more commonly in the abdomen (mesentery and abdominal wall in 90%) or less commonly (in <10%) in extra-abdominal locations (along the belt line or in the neck) [63,64]. Their progression is highly variable: in 50% of cases, the tumor remains stable, in 30% of patients there is an alternation of growth and regression, in 10% of cases there is spontaneous regression, and in 10% of tumors show rapid growth [65,66].

These tumors are often asymptomatic and their mode of abdominal presentation is quite varied: bowel obstruction, increased abdominal girth, mesenteric ischemia, abscess, fistula, gastrointestinal perforation, or compression of adjacent organs [63].

The indications for treatment of desmoid tumors depend entirely on their clinical impact. A wide variety of therapeutic options includes the use of non-steroidal anti-inflammatory drugs (NSAIDs), cytotoxic chemotherapy, surgery, or radiotherapy. The role of surgery must be debated in every case because of its high morbidity and mortality (hemorrhage, early death, short bowel syndrome) and the high rate of tumor recurrence [67].

There are numerous obstacles to the analysis of treatments of desmoid tumors: the tumors are very heterogeneous as is their progression, they are exceedingly rare, and only a few centers have enough experience to conduct comparative studies. Church et al. have proposed a classification for intra-abdominal desmoid tumors based on their

Table 4 Classification of desmoid tumors according to Church et al. [68].

Stage	
I	Asymptomatic, <10 cm in maximal diameter and not enlarging
II	Slightly symptomatic, <10 cm in maximal diameter and not enlarging
III	Moderately symptomatic or ureteral/intestinal obstruction, 10—20 cm in maximal diameter and slowly enlarging
IV	Severely symptomatic, rapidly changing, or >20 cm in maximal diameter

Table 5 Therapeutic options depending on the tumoral stage for intra-abdominal desmoid tumors [69].

	Stage I	Stage II	Stage III	Stage IV
Treatment options	Nothing or Sulindac®	Sulindac® or Sulindac® + anti-estrogen	Anti-estrogen + chemotherapy	Recourse to the most radical therapy possible

size and their clinical impact (Table 4) [68]. The same team proposed to use this classification for prospective studies of therapy based on tumor stage (Table 5) [69].

No commentary on the efficacity of these treatments can be made for lack of published comparisons, but this staging system developed by the team with the largest series of desmoid tumors offers the ability to tailor treatment for different clinical forms of desmoid tumors.

Dysplasia and cancer

In ulcerative colitis

Mucosal dysplasia of the ileal reservoir

Veress et al. found low-grade dysplasia in 3.4% patients in their series. They also observed that all these patients had a change of the lining of the reservoir that predisposed to dysplasia (so-called modification type C: villous atrophy with severe inflammation) [70]. However, this risk is quite low in the Veress' et al. series, (3/87 cases), in the series of Herline et al. (1/160 cases), and in that of Borjesson et al. (2/45 cases) [70—72].

Anal dysplasia

In theory, mucosectomy and manual anastomosis should eliminate the risk of development of dysplasia in residual colonic mucosa. Nonetheless, the risk of dysplasia persists at this level whether the IAA is performed mechanically or manually. Meanwhile the risk of dysplasia at the level of the reservoir is fairly low. Ziv et al. found low-grade dysplasia in eight patients in their series of stapled anastomoses, and O'Riordain et al. in eight patients in their series [73,74]. In any case, the risk of dysplasia seems to be increased in all cases where cancer or dysplasia was present pre-operatively [73,74]. In these cases, Ziv et al. have recommended mucosectomy with a hand-sewn anastomosis in order to leave as little residual anal mucosa as possible [74].

Cancer

In a review of the literature, Das et al. reported 20 cases of adenocarcinoma of the anorectal mucosa or of the reservoir after IAA [75]. Several risk factors for dysplasia and adenocarcinoma were identified: dysplasia or cancer in the proctocolectomy specimen, co-existence of sclerosing cholangitis, type C change of the reservoir mucosa [75].

They also suggest that patients meeting these criteria be monitored with annual endoscopy with multiple biopsies of the reservoir and the remaining part of the anal canal after the 10th year from diagnosis [75].

In familial adenomatous polyposis

Even after coloproctectomy, patients with FAP are at risk of developing adenomas either in the reservoir (8 to 62%) or the anal canal (10—31%) [76]. These adenomas are at risk of developing dysplasia or cancer.

In the reservoir

Parc et al. have shown that the risk of developing one or more adenomas increases with time [77]. It is therefore important to define a monitoring strategy, particularly as cases of evolution from adenoma to cancer have been reported [78—80]. Kartheuser et al. have therefore proposed annual endoscopy and, where appropriate, polypectomy or endoscopic destruction, treatment of polyps by Sulindac®, and excision of the pouch with permanent end-ileostomy for cancer [76].

In the anal canal

The risk of dysplasia and cancer increases depending on the amount of residual anal mucosa [76]. Kartheuser et al. have compiled several cases of adenoma and cancer. In the literature, systemic monitoring and treatment has been advocated: annual endoscopy with biopsy, destruction of small polyps, trans-anal excision of larger lesions and in proven cases of dysplasia, trans-anal mucosal stripping with advancement of the anastomosis, and abdominoperineal resection with end-ileostomy for established cancers [76].

Technical options

Several technical issues may influence the occurrence of complications following CP-IAA.

Mucosectomy vs. stapled anastomosis

Mucosectomy has the advantage of reducing the amount of remaining anal mucosa and thus reducing the risk of cuffitis in patients with UC, and reducing the risk of dysplasia and neoplasia. However, it seems to increase the risk of anal stenosis and anal sphincter injury [44,81].

A meta-analysis by Schluender et al. did not identify any difference in functional or manometric outcomes between the two techniques [82].

The role of ileostomy

Most teams create a protective ileostomy after CP-IAA, to facilitate the healing of the anastomosis and to decrease the risk of fistula or pelvic sepsis. However, ileostomy was its own intrinsic morbidity: high output, stomal retraction, parastomal hernia and/or stomal prolapse, abscess, fistula, increased risk of bowel obstruction, plus the risks of re-operation for ileostomy closure. Heuschen et al. and Sugerman et al. have both demonstrated superiority of single-stage surgery in their series [83,84]. Grobler et al. showed in a randomized study that there was no difference in complications related to the reservoir or IAA, whether or not a protective ileostomy had been performed, but the ileostomy led to an increase in ileostomy-specific complications [85].

Several criteria have been developed to identify patients who may be eligible for single-stage surgery: good general condition, good nutrition, young age, low co-morbidity, surgeon experience, good vascularization of the pouch, and absence of anastomotic tension [76]. This last criterion is considered the most important and almost unique element in the decision of the need for a diverting ileostomy [76,86].

Role of the laparoscopic approach

A recent review by the Cochrane Library shows that laparoscopic CP-IAA is feasible and safe, but its short-term benefits are limited, and there is need for further studies [87]. Lefevre et al. have similarly demonstrated the feasibility and the safety of the technique on a series of 82 unselected patients and that the choice of surgical approach did not alter morbidity or outcome of the intervention [88].

Laparoscopy has the potential to decrease postoperative adhesion formation and to preserve fertility. These advantages should be confirmed by comparative studies.

Conclusion

CP-IAA has passed its 30th anniversary. It is the standard therapy when surgery is indicated for UC or for FAP. While it is associated with a high morbidity rate, this should not obscure the patient's satisfaction at avoiding a permanent ileostomy.

HIGHLIGHTS

- CP-IAA has frequent morbidity, well and often described but poorly studied over the long-term.
- Pouchitis is the most common complication; its clinical manifestations and evolution vary with the duration of follow-up (ranging from a single episode to advanced chronic pouchitis requiring definitive ileostomy).
- Pelvic sepsis is the most dangerous complication because it is the major cause of failure despite various surgical re-interventions.
- The overall quality of sexual life for patients with UC is improved by surgery despite specific complications (dyspareunia, vaginal dryness, erectile dysfunction, retrograde ejaculation).
- Several cases of dysplasia or cancer have been reported involving residual colonic glandular mucosa, and also ileal mucosa within the reservoir; this makes periodic endoscopic surveillance advisable.
- Desmoid tumors may develop in patients with FAP. Their clinical presentation and evolution is unpredictable; staging is crucial to define therapeutic strategies.
- The place of laparoscopy is yet to be defined, especially in the prevention of long-term complications.

Conflict of interest statement

None.

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