Therapeutic Endoscopy in Postoperative Pouch Complications

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Abstract

Ileal pouch-anal anastomosis (IPAA) or "J"-pouch as it is commonly referred to, is the treatment of choice in patients with medically refractory ulcerative colitis. IPAA can have infectious, inflammatory, and mechanical complications. Currently, there are no Food and Drug Administration-approved medical therapies for these complications. Surgery that may be eventually required can have significant morbidities due to the complexity of IPAA. Endoscopy is fast emerging as a leading modality of treatment for some of these pouch complications. Endoscopy in adjunct with medical treatment can help manage the majority of pouch-related disorders and improve the outcome.

Keywords
- ileal pouch-anal anastomosis
- Crohn's disease
- ulcerative colitis

Ulcerative colitis (UC) is a chronic disease of the colon and rectum characterized by relapsing and remitting inflammation episodes. Although medical therapy remains the primary treatment, surgery may be required in patients with acute severe colitis who become refractory to medical therapy. UC-associated severe complications (such as colonic perforation, life-threatening colonic hemorrhage, or toxic megacolon) may warrant emergent surgery.[1] Colectomy is also indicated in colitis-associated neoplasia. Restorative total proctocolectomy (TPC) was first described by Sir Alan Parks and Nicholls of St. Mark's Hospital in 1978.[2] TPC with ileal pouch-anal anastomosis (IPAA) has become the surgical treatment of choice for patients with refractory UC, UC with histology-proven neoplasia, or patients with familial adenomatous polyposis (FAP).[3] Two commonly fashioned configurations are J- and S-pouches. The J-pouch is created using two loops of the small intestine, each measuring approximately 15 to 18 cm in length. The pouch body is typically handsewn or stapled to the rectal cuff or anal transition zone (ATZ). The long-term efferent limb complications in patients with J-pouches are less frequent than those with S-pouches. Additionally, the J-pouch requires a shorter intestine length, is efficient, and is easier to create. However, the J-pouch or S-pouch can also be associated with a variety of structural, inflammatory, and functional complications.

The etiology of pouch complications can be classified as mechanical, inflammatory, or functional (►**Table 1**). Mechanical complications include anastomotic strictures, anastomotic leaks resulting in pelvic abscess or sepsis, fistulae, sinuses, pouch prolapse, pouch volvulus, pouch septae, afferent limb, or efferent limb syndrome.[4] Inflammatory complications include pouchitis, cuffitis, and Crohn's disease (CD). Those mechanical or inflammatory complications are the common causes of pouch failure, leading to permanent fecal diversion, pouch excision, or surgical pouch redo. Common ileal pouch disorders and associated complications are summarized in ►**Table 1**. We present a thorough review of different therapeutic endoscopic modalities available to address these mechanical complications post IPAA.

Pouch Stricture

Approximately 5 to 38% of patients with IPAA develop pouch strictures,[5–7] and these can significantly impair pouch

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Table 1 Classification of ileal pouch disorders and associated complications

Surgical and mechanical	Anastomotic leaks Pelvic sepsis and abscess Pouch sinuses Pouch fistulae Strictures Afferent limb syndrome and efferent limb syndrome infertility and sexual dysfunction Portal vein thrombi Pouch prolapse, twisted pouch bleeding, sphincter injury or dysfunction
Inflammatory and infectious	Pouchitis Cuffitis Crohn's disease (CD) of the pouch Proximal small-bowel bacterial overgrowth inflammatory polyps
Functional	Irritable pouch syndrome Anismus Pseudo-obstruction
Dysplastic and neoplastic	Dysplasia or cancer of the pouch Dysplasia or cancer of the anal transition zone (ATZ)
Systemic and metabolic	Anemia bone loss vitamin B12 deficiency

function and outcome. Anastomotic strictures typically develop 6 to 9 months post-IPAA[8] and cause frequent watery stools, urgency, dyschezia, or excessive straining, or a sensation of incomplete evacuation. The most common locations for stricture are at the pouch-anal anastomosis (pouch outlet), the junction of neo-terminal ileum and pouch body (pouch inlet), and the stoma closure site. The main causes of stricture formation include inflammation of the pouch,[9] prepouch ileitis, CD of the pouch, surgery-associated ischemia, medications such as nonsteroidal anti-inflammatory drugs,[10] and "kinking" of the pre-pouch ileum. Long-term use of anti-TNF biologics has also been proposed as a risk factor, especially in patients with CD, although not specifically studied in patients with IPAA.[11,12] However, it is also important to consider de novo CD as an underlying cause of pouch strictures.[13]

Strictures in IBD have been classified based on underlying disease process, length, degree, location, and associated conditions.[14] The management of pouch strictures can be challenging, as their mechanical or fibrotic nature makes them not amenable to medical therapy. Although medical therapy, such as the use of mesenchymal stromal cells as an antifibrotic agent, has been investigated to treat CD strictures[15] the mainstay of therapy remains endoscopic and surgical interventions. Herein we discuss some of the most commonly performed endoscopic interventions including endoscopic balloon dilation (EBD) and endoscopic stricturotomy (EST).

Endoscopic Balloon Dilation

EBD has been extensively used to treat fibrostenotic strictures of the pouch or nonpouch CD,[16–21] and has emerged as a safe and effective treatment modality. Navaneethan et al performed a meta-analysis of 13 studies, including 1,163 patients with CD who underwent EBD. Overall, 1,571 strictures were dilated from 1,163 patients, with the majority of them (69%) being anastomotic (ileo-colonic and ileo-rectal). The remaining (31%) were primary CD strictures including, 17.5% in the ileal region (including the neo-terminal ileum and the ileocecal valve), 9% in the colon, 2% in the rectum, and 2% in the upper GI tract, predominantly in the duodenum. The authors concluded that EBD had immediate technical success in 89% and surgery-free rate in 67% of the patients during a median follow-up of 15 to 70 months. Major adverse events, including perforation/hemorrhage requiring interventions or blood transfusion/abscess or fistula or sepsis, were found in 4% of the patients and there was no mortality as a direct consequence of the procedure.[22]

Pouch-anal anastomotic strictures are common and usually respond well to digital and instrumental dilatation, such as Hegar dilatation, in which patients can be taught to perform independently. Fazio et al[23] published a case series of 141 patients in whom the strictures were dilated using a bougie either in the theater or in an outpatient clinic. While three patients went on to revision of their pouch, there were no other complications reported during a mean follow-up time of 35 months (range 1–125 months). Hultén[24] reported the largest case series where nine out of 13 patients underwent successful balloon dilatation for their pouch-anal anastomotic stricture. While four patients needed surgical revision, there were no complications reported. Another study reported outcomes in 50 patients who were treated with either surgical dilatation under anesthesia, digital dilatation, or no treatment. A total of 26 patients underwent dilatations under anesthesia, 12 underwent digital and endoscopic dilatation, and three had no treatment. While all procedures needed repeated attempts, success was achieved in 37/50 patients.[25] A large case series on 100 fibrotic and 100 nonfibrotic strictures that were treated with either surgical or bougie dilations showed that 95/100 nonfibrotic strictures and 45/100 fibrotic strictures respond to bougie dilatation. Additionally, 55 fibrotic strictures and five nonfibrotic strictures that underwent bougie dilation ended up requiring surgical intervention. Clinical failure, defined as permanent ileostomy, occurred in 0.5% of patients after a median follow-up of 6.5 years (range 2–15 years). No complications were reported in both studies.[8] Overall, available published data suggests that pouch-anal anastomotic strictures respond to bougie dilatation and Hegar dilators. These strictures often require repeat dilatations, and in the event of failure of simple dilatation, surgical therapies including stricturoplasty, circular stapler resection, or pouch revision may need to be considered.

Several studies have also reported the clinical success of EBD for pouch inlet strictures. A study by Kirat et al included nine patients, reported a 66.7% success with balloon dilation after a mean follow-up of 1 year (range 0.14–2.5 years). Four out of nine patients required repeat dilatations, with three of the nine patients requiring pouch excisions.[26] In a small study of 20 patients who underwent 88 endoscopic dilations,

technical efficacy was observed in 98% of procedures, and clinical improvement after EBD was observed in 95% of patients. A median of 3.5 dilatations per patient (2.0–7.0) was performed, and after a median follow-up of 3.0 years (2.1–3.5), only one patient had stricture-related pouch failure. The smallest and largest median balloons sizes were 12 mm (12–15) and 18 mm (15–20), respectively. Fifteen percent of patients had more than one stricture, the median diameter was 10 mm (7.5–11.7), and the most frequent location of stricture was the pouch-anal anastomosis. Notably, during the follow-up period, no significant complications related to dilation were observed. There were no hospitalizations, pouch/intestinal perforations, gastrointestinal bleeding requiring transfusion, urgent interventional endoscopy, or surgical intervention.[27]

Shen et al reported a case series of 19 patients with pouch inlet and outlet strictures dilated using an 11 to 18 mm through the scope balloon. In all patients, mean stricture scores immediately after EBD were significantly improved. While one patient required revision of their pouch following intervention due to persistent symptoms, no post-procedure complications were reported.[28] A follow-up study by the same group reported on the treatment of 150 mixed pouch strictures, including 96 pouch inlet strictures, 73 pouch outlet strictures, 33 afferent limb strictures (above the pouch inlet), and two pouch body strictures. While some strictures required repeat dilation, overall, 646 strictures were dilated. Technical success, as measured by the ability to pass the scope through the stricture, was achieved in 97.8% of cases. The 5-, 10- and 25-year pouch continuity retention rates were 97.0, 90.6, and 85.9%, respectively. Perforation was reported in 2 patients who required urgent laparotomy and diverting ileostomy. While there were four post-procedure bleeding events requiring hospitalization and blood transfusion, there was no procedure-related mortality (►**Fig. 1A–C**).[29]

Wu et al compared pouch survival in patients with pouch strictures undergoing either surgical stricturoplasty or EBD. Pouch survival was defined as the avoidance of permanent diversion, complete pouch redo, or pouch excision in patients undergoing either technique. In total, 151 patients had EBD, and six patients had surgical stricturoplasty. The 5-year overall pouch survival rates were 83 and 82% for patients with stricturoplasty and endoscopic dilation, respectively. While one patient in the stricturoplasty group developed a deep anastomotic leak/sinus requiring a redo pouch procedure, there was no difference between the two procedures regarding the overall severe complication rate.[30]

Endoscopic Stricturotomy

Another therapeutic endoscopic modality that has been successfully used for the treatment of strictures in the gastrointestinal tract, is needle knife or insulated tip knife stricturotomy.[31–33] EST can be performed by various tools ranging from needle knife, hook knife (Olympus, United States), to IT Nano knife (Olympus, United States) (►**Fig. 1**). In patients with long, fibrotic strictures refractory to multiple endoscopic balloon dilatation therapy, endoscopic needle knife stricturotomy has been attempted (►**Fig. 2A–C**). In a study by Shen et al 10 patients underwent EST, six of whom managed to maintain a functional pouch at follow-up.[29] Furthermore, in a subsequent analysis of 85 patients by Lan and Shen all patients, who had a diagnosis of pouch or nonpouch inflammatory bowel disease (IBD) and developed

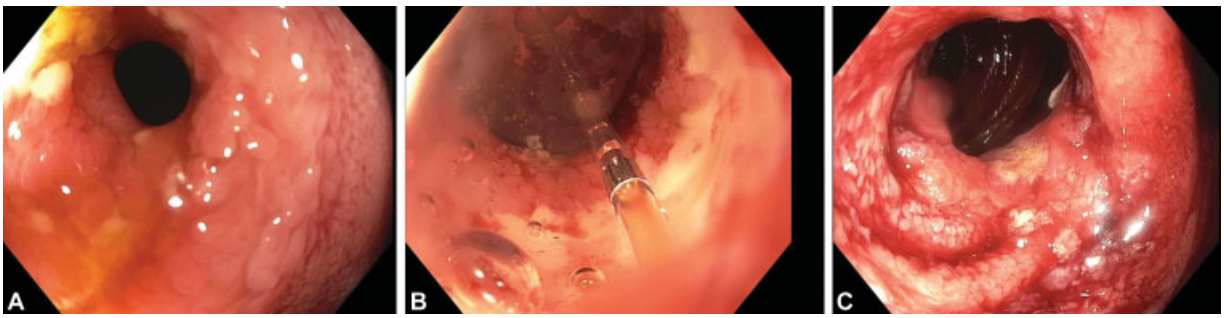

Fig. 1 (**A**) Non-traversable fibrotic stricture. (**B**) Endoscopic balloon dilatation of the stricture. (**C**) Post endoscopic balloon dilatation.

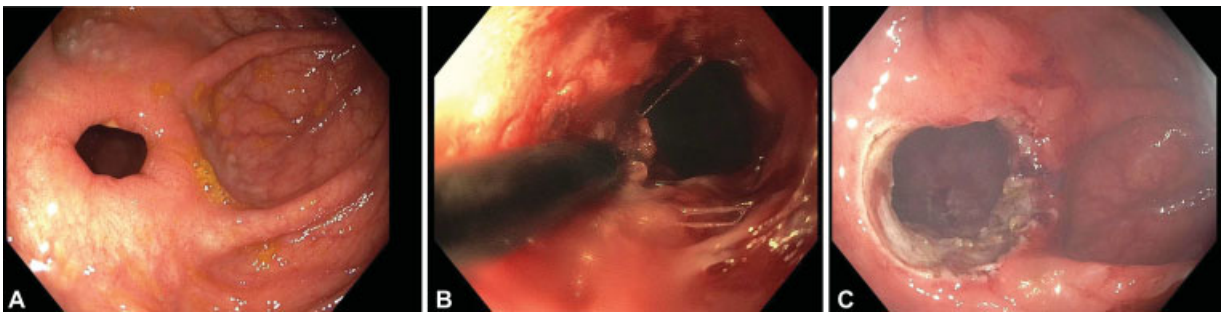

Fig. 2 (**A**) Non-traversable fibrotic stricture. (**B**) Endoscopic stricturotomy using Olympus Nano knife. (**C**) Post endoscopic appearance of the stricture.

a primary (disease-related) or secondary (anastomosis-related) fibrotic stricture, were included. A total of 127 strictures were treated, and the median length of the stricture was 1.5 cm (range 1.0–2.0), while 52 (41.6%) were endoscopically nontraversable. Technical success, as assessed by successful passage of the scope through the stricture, was achieved in all patients. During the median follow-up of 0.9 years and a median of two treatments, 13 (15.3%) patients required stricture-related surgery. There were 77 (60.6%) patients who required additional EST, EBD, or both. Overall, in 272 procedures, 10 (3.7%) adverse events occurred, including nine with delayed bleeding and one hospitalization due to perforation.[34]

Another recent study evaluated the efficacy and safety of EST compared with EBD in the treatment of pouch inlet strictures. A total of 200 patients with IBD-related strictures, of which 40 (20.0%) were treated with EST and 160 (80.0%) with EBD, were included. The median length of strictures in both groups was approximately 2.0 cm. Symptom improvement was recorded in 11 (42.3%) patients treated with EST and 16 (13.2%) treated with EBD. The subsequent surgery rate was comparable between the two groups (9 [22.5%] vs. 33 [20.6%], $p = 0.80$) during a median follow-up of 0.6 years (range 0.4–0.8) versus 3.6 years (range 1.1–6.2). The overall surgery-free survival was also comparable ($p = 0.12$). None of the patients in the stricturotomy group developed pouch failure, while nine patients (5.6%) had pouch failure in the EBD group ($p = 0.17$). Procedural bleeding was seen on three occasions (4.7% per procedure) in patients receiving endoscopic stricturotomy and perforation was seen on three occasions (0.8% per procedure) in patients receiving EBD ($p = 0.02$).[35]

In conclusion, EST and EBD are effective and safe in treating patients with pouch inlet or afferent strictures. EBD, while may be less effective than surgical stricturoplasty,[30] is also less invasive. It appears that the overall surgery-free survival is comparable between the two approaches. While there is a higher rate of delayed postprocedural bleeding with EST, EBD appears to have a higher risk of perforation. It is crucial to note that the length of stricture may affect the response to endoscopic therapy. Stricture length < 4 to 5 cm is associated with a lower risk of surgical intervention,[22] while length > 5 cm is associated with shorter surgery-free survival.[36] In recently published consensus guideline by The Global Interventional IBD Group, states that while EST is technically feasible, its application in IBD strictures warrants investigation and expansion. It may be particularly useful in treating severe fibrotic strictures or strictures of the distal bowel close to the anal sphincter, with the advantage of giving the endoscopist full control of depth and location of electroincision.[37]

Pouch Fistulas

Fistulae represents one of the advanced phenotypes in IBD and can occur in patients with CD or UC after restorative proctocolectomy with IPAA.[38] A recent population-based database analysis estimated that there were more than 76,000 prevalent cases of fistulizing CD in United States in 2017. The most common type of fistulae was anal in 8.1%, rectovaginal in 1.1%, enterocutaneous in 0.3%, and internal in 2.2% of patients. Ileal pouch fistulas may appear after IPAA, with a reported frequency ranging from 4 to 16%.[39] If left untreated, these can lead to complex fistulas, abscesses, and pouch failure in 21 to 30% of patients with IPAA.[40]

In the management of fistulas, the key endoscopic therapies have evolved around the closure of fistula tracks with endoscopic clips (through the scope as well as over the scope clips) and fistula tract drainage in addition to biological therapies and surgical modalities.

Table 2 Studies on fibrin glue injection

Author	Patients(n)	Success	Follow-up
Parades et al 2010	30	17/30 (57%)	1 mo
Vitton et al 2005	14	10/14 (71%)	3 mo
Grimaud et al 2010	34	13/34 (38%)	2 mo

Traditional Therapy

Some other treatment modalities for fistulas include injection of fibrin glue and stem cells. Fibrin glue, a mixture of fibrinogen and calcium, can be injected directly into a perianal fistula, sealing off the tract by forming a thrombin clot. Initially used in conjunction with other surgical procedures such as an endorectal advancement flap, fibrin glue has been studied as a monotherapy in patients with perianal CD. Most of the initial studies on fibrin glue were conducted on patients with cryptoglandular perianal fistulas, but studies on patients with CD have shown healing rates in the range of 30 to 80%. The injection procedure has historically been performed in the operating room, along with examination under anesthesia. Summary of studies reporting on fibrin glue injection and mesenchymal stem cell (MSC) therapy in CD-related fistulas is summarized in ►**Table 2**

Endoscopic Fistulotomy

Endoscopic fistulotomy (EFt) has proven to be successful for the treatment of pouch fistulas. The principle of EFt is to incise and open up the fistula tract to the bowel lumen or skin tunnel, incorporating the fistula track into the bowel or skin, thereby help to drain the fistula, thereby preventing the formation of an abscess (►**Fig. 3A,C**). It is useful in patients with short (<3 cm), superficial (<2 cm thick), simple fistulas, such as; ileum-to-cecum fistula, perianal fistulas, and pouch-to-pouch body fistula. A series of 29 patients who underwent EFt was recently reported by Kochhar et al.[40] In this series, 26 patients had IPAA, and three had an ileocolonic resection for CD. Of these, 21 patients (72.4%) had an underlying diagnosis of UC, whereas seven (24.1%) had a preoperative diagnosis of CD, and one (3.4%) had indeterminate colitis before pouch surgery. The initial technical success reported was 100%. Nineteen patients (34.4%) needed only one endoscopic session. Five patients (48.2%) required one additional endoscopic session for fistula treatment,

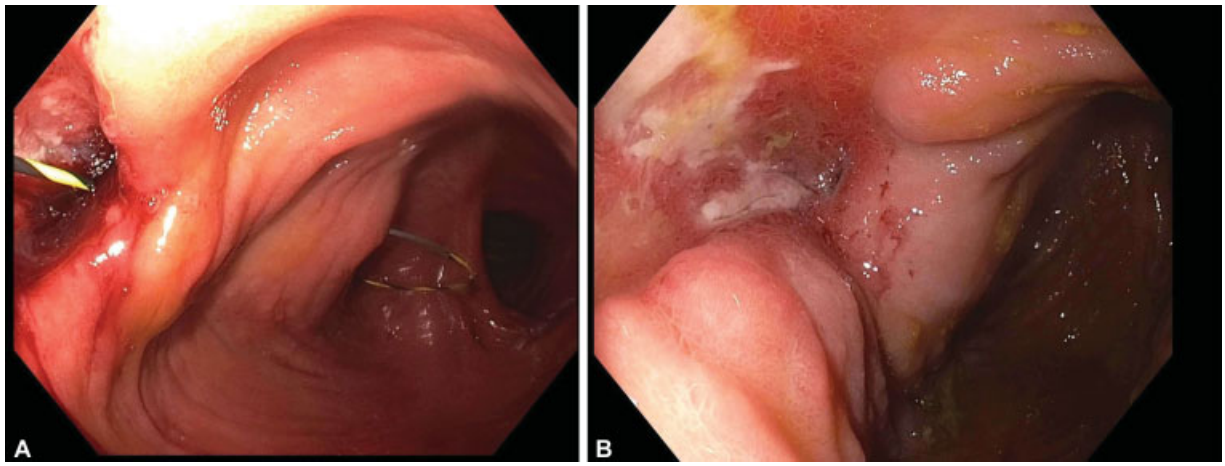

Fig. 3 (**A**) Pouch body fistula tract depicted by guidewire. (**B**) Post endoscopic fistulotomy healing of pouch fistula.

whereas five patients (17.2%) required two additional sessions. The mean (±SD) number of endoscopic sessions for the successful healing of the fistula was 1.9 ± 0.7. The median time between repeat fistulotomies was 90 days (range 23–591 days). EFt was clinically successful in 26 patients (89.6%), whereas three (10.4%) patients eventually required surgery to manage their fistulas. Twenty-two patients (75.8%) had immediate symptom improvement after the procedure. Patients with symptoms secondary to abscess formation responded the earliest, with a resolution of symptoms. The median follow-up time after the procedure was 390 days. There were no immediate adverse events after the outpatient procedure, and all patients were discharged home the same day after routine post-procedural observation. While no perforations were observed, one patient (3.4%), developed significant bleeding.[41]

More recently, Lan et al presented preliminary data comparing Eft and redo pouch surgery in the management of pouch-to-pouch fistula. Their study included 59 patients, 40 of whom underwent Eft and 19 underwent redo surgery. Complete resolution of the fistula was achieved in 29/37 (78.4%) patients, partial healing was seen in 8/37 (21.6%) patients with EFt while initial complete healing was obtained in all patients receiving redo surgery. During a follow-up of 1.4 years, subsequent surgery was needed in four (10.0%) patients with Eft and four (21.1%) patients with initial redo surgery ($p = 0.45$). While the rate of adverse events in the EFt group was significantly lower than that in the surgery group (5.6 vs. 68.4%, $p < 0.001$), surgery-free survival was comparable between the two groups.[42]

Endoscopic Clipping

The other endoscopic treatment that has been described in the literature is endoscopic clipping, using either through-the-scope clips or over-the-scope clips (OTSC). The OTSC system (Ovesco Endoscopy AG, Tübingen, Germany) was initially developed for hemostasis and leakage closure in the gastrointestinal tract during flexible endoscopy. These "bear claws" apply high compression forces on the tissue and facilitate stable closure.[43]

A case series of 10 cases with refractory anal fistulas ($n = 10$), including six with perianal CD, showed clipping to be technically successful in all patients, and permanent fistula closure was achieved in seven patients (70%) with a median follow-up of 72 days.[44] A case report showed successful endoscopic needle-knife sinusotomy and OTSC system in a symptomatic patient with a pouch-to-pouch fistula, from the tip of the "J" to the anastomosis.[45]

A recently published white position statement paper from the Global Interventional IBD Group suggested that while endoscopic closure of a primary fistula opening from CD with clips is not recommended, it may be attempted in an anastomotic leak-associated fistula.[37]

Stem Cell Therapy

The use of allogeneic[46,47] and autologous[48–50] adult MSCs to induce fistula healing in patients with perianal CD has also been studied. MSCs are commonly isolated from adipose tissue or bone marrow and have been shown to down-regulate the immune system and promote tissue repair. This technique is still undergoing clinical trials, in patients with fistula secondary to CD. Although these modalities have been described in the management of CD-related fistulas, however, studies suggesting their use to manage IPAA-related fistulas are lacking.

Pouch Anastomotic or Suture Line Leaks

Anastomotic leaks are reported in up to 17.1% of primary IPAA procedures with "J" configuration.[51] The tip of the "J" consists of the distal ileum, which is sealed with a linear stapler with or without additional reinforcement sutures. The tip of the "J" is one of the two most common locations for leaks, with the other being the anastomosis.[52] While no algorithm of treatment for IPAA leaks has been universally accepted, fecal diversion and drainage of pelvic sepsis are considered standard options. Patients would be subsequently followed-up, waiting for spontaneous healing. The redo pouch-anal anastomosis could be an option for early onset of anastomotic dehiscence, although a

reoperation carries a higher risk of intra- and postoperative complications.

Endoscopic Vacuum-Assisted Closure

Endoscopic vacuum-assisted closure is a technique based on continuous negative pressure applied to the wound with sponge, resulting in effective drainage of fluid and healing of the tissue. In 2008, Weidenhagen et al described a novel approach to treat anastomotic leaks after anterior rectal resection using Endosponge, a vacuum-assisted treatment designed specifically for small leaks.[53] It is an open-pored polyurethane sponge, connected to a vacuum suction bottle to create a constant negative pressure, which is placed endoscopically in the presacral cavity. The procedure replicates the advantages of vacuum-assisted therapy for complex wounds, allowing a progressive reduction in the size of the cavity while draining the contaminated fluids. The procedure showed promising results and was subsequently applied to other conditions as well.[54–56] In 2014, Gardenbroek et al described the first application of Endosponge after IPAA leaks.[57] The approach was different from the previously reported technique. The sponge was changed every few days until the presacral cavity was judged clean. Subsequently, the dehiscence was sutured over a vacuum drain that was removed on postoperative day 3. The surgical procedure was performed in the operation room under general anesthesia after a median of 15 days. While the modified technique allowed a reduction in the length of in-hospital stay, it had the drawback of the need for another surgical procedure under general anesthesia.

Rottoli et al reported a case series of eight patients diagnosed with anastomotic leak following surgery for UC refractory to medical treatment in seven cases and FAP in one case. The patients were treated with vacuum-assisted closure therapy. All UC patients underwent a three-stage IPAA procedure. The FAP patient underwent restorative proctocolectomy with IPAA and loop ileostomy formation (two-stage IPAA). In all cases, a J-pouch and loop ileostomy were fashioned at the time of IPAA surgery. The FAP patient had a mucosectomy and handsewn suture, while a stapled anastomosis was performed in the rest of the cases. Seven patients had a diagnosis of an anastomotic leak during the initial hospitalization for pouch surgery. In one case, the leakage became evident after the ileostomy closure, although there were no suspicious findings on preoperative pouchoscopy and contrast enema. One patient experienced anal bleeding, while in three others, a discharge of pus *per anus* was observed. In four cases, the presence of a pelvic abscess was confirmed at the scan, and a CT-guided drainage was successfully positioned. The drainage was removed at the first Endosponge procedure, after a median of 3 days (range 2–4) from the insertion. The Endosponge treatment started at a median of 6.5 (range 1–15) days after the diagnosis of the leakage and lasted for a median of 12 (range 3–32) days. The device was replaced a median of 3 (1–10) times. The median length of hospital stay after the first application of the treatment was 15.5 (6–48) days. Overall, the median length of hospital stay (including the postoperative stay from the pouch surgery in seven cases and the closure of ileostomy in one case) was 32 (16–72) days. The complete healing of the leak was documented after a median of 60 (24–90) days from the first treatment with no need for any additional surgical procedure. All patients but one had their ileostomy reversed at a median of 2.5 (1–6) months from the endoscopic confirmation of healing. At a median follow-up time of 11.6 (6–18) months after confirmation of the healing of the anastomotic leak, no recurrence was documented. No patients reported incontinence to feces or gas.[58]

Endoscopic Clipping

The use of OTSC has been described for the treatment of pouch/anastomotic leaks. Lian et al described a case of a 58-year-old female with a history of UC and three-staged TPC and handsewn IPAA, who presented with worsening diarrhea. Her pouchoscopy showed a normal pouch body, inlet, and outlet, anal transitional zone, and afferent limb. However, an ulcerated lesion was found in the tip of the "J." A leak from the tip of the "J" was suspected and confirmed with a soft guidewire via endoscopy operating channel. The leak from the tip of the "J" was further confirmed by pouchogram with contrasted watery soluble enema. A 12–6t-sized OTSC (or "Bear Claw") and OTSC Anchor 220tt (Ovesco Endoscopy USA, Campbell, California, United States) were used, and the leak defect was completely closed. Kochhar et al published a case series of 12 patients with chronic leak at the tip of the "J," with a mean time from the pouch construction to diagnosis of the leak being 7.5 ± 4.9 years. All 12 patients had a successful deployment of OTSC during endoscopy, and eight (66.6%) were successfully treated. No excessive bleeding or perforation was observed. Ten patients (83.3%) had a repeat pouchoscopy within 1 year after the index therapeutic pouchoscopy; two patients were followed up as outpatients with no additional pouchoscopy. Six patients (50.0%) had complete healing on initial follow-up, five (41.6%) had a recurrent leak identified on subsequent pouchoscopy, and one (8.3%) developed a new leak at a different site other than prior treatment site. The latter six patients underwent repeat endoscopic therapy, five patients had reapplication of OTSC, and one patient was attempted with endostitch (Apollo endosurgery, United States) after failed OTSC. Of these, two more patients achieved complete healing of the leak, while four (33.3%) patients had a persistent leak requiring surgery. There were no immediate post-procedure complications, and all patients were discharged home the same day after routine post-procedural observation. One (8.3%) patient, however, developed a presacral spinal abscess 14 days after deployment of OTSC and was treated with drainage surgery, pouch revision, and long-term intravenous antibiotics.[59]

In conclusion, endoscopic vacuum-assisted closure can be attempted in an anastomotic leak after distal bowel surgery in patients with IBD and OTSCs may be attempted in patients with a larger anastomotic or suture-line leak, in the absence of an abscess.

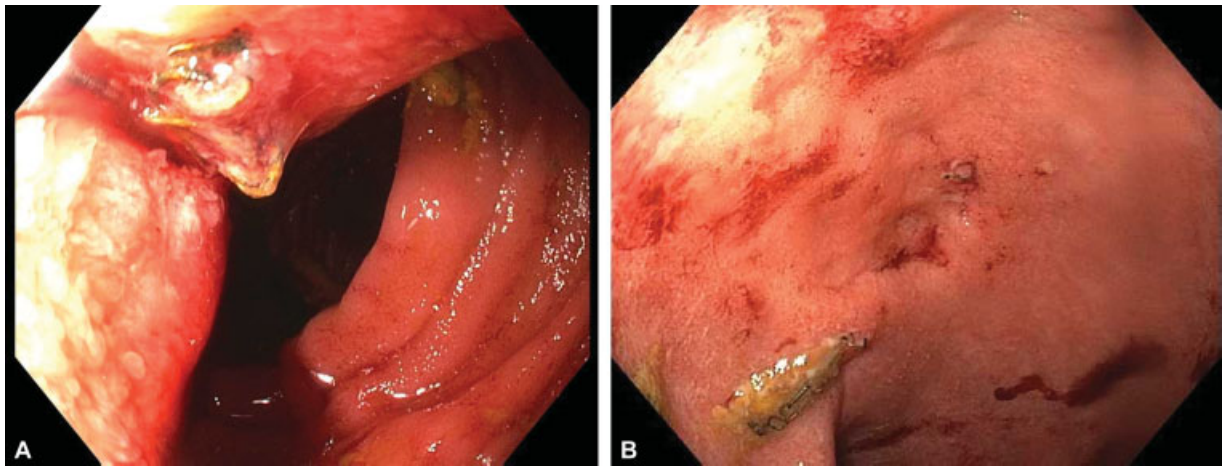

Fig. 4 (**A**) Pouch sinus. (**B**) Post endoscopic sinusotomy depicted by healed sinus tract.

Pouch Sinus

Pouch sinus is defined as a chronic blind tract resulting from chronic pouch-anal anastomotic leak and abscess, which occurs in 2.8 to 8% of patients undergoing IPAA.[60,61] Traditionally, patients with pouch sinuses have been managed with a conservative or operative approach, including observation, proximal fecal diversion, drainage or surgical closing of the sinus, mucosal advancement flaps, redo pouch surgery, or pouch excision.[60,62–64] Debridement of the sinus combined with unroofing of the tract[63] or the application of fibrin glue has been reported.[65] Chronic persistent pouch anastomotic sinus could result in pouch failure, which has been traditionally treated with surgical pouch redo or permanent diversion.[61,66] Pouch redo surgery while promising, is technically challenging with a high rate of postoperative adverse events.[67]

Endoscopic Sponge Placement

Endoscopic therapy for pouch sinus has previously involved marsupialization and local vacuum sponge treatment. Abild et al reported seven patients with chronic presacral sinus who underwent endoscopic stapled marsupialization. This procedure was successful in six patients. Of the six patients, two developed fistula during the follow-up, and the remaining four had complete healing without recurrence.[68] The placement of a sponge using the endoscopy was also shown to play a role in the management of pouch sinus.[69,70] However, these techniques for managing pouch sinus are based on a simple description of the experience from a single institution, with an added disadvantage of a small sample size. Particularly, potential risks and benefits associated with the healing of pouch sinus have not been studied.

Endoscopic Sinusotomy

Endoscopic approach with needle-knife unroofing for treating pouch sinus, first described in 2010[71,72] was further described by Wu et al in 2013.[73] They conducted a historical cohort study from a prospectively collected database, including a total of 65 patients. All pouch sinuses were identified by pouchoscopy with or without imaging modalities (pouchogram) or examination under anesthesia. Pouchogram was performed with water-soluble gastrografin enema. Complex pouch sinuses were defined as multiple sinuses or compartmentalized sinuses. The primary outcomes of this study were partial and complete healing. Complete healing was defined as the disappearance of the sinus tract or complete epithelialization of the sinus cavity (i.e., conversion of the sinus to a diverticulum) on endoscopy and/or radiographic imaging (►**Fig. 4A,B**). Partial healing was defined as at least a 50% reduction in the length or size of the sinus. The median interval from colectomy to the diagnosis of pouch sinus was 4.0 years. Pouch sinus was located at the anastomosis in 59 patients (90.8%), at the mid pouch suture line in four patients (6.2%), and at the tip of "J" in two patients (3.1%). The mean depth of the pouch sinus was 4.4 ± 1.8 cm. Twenty patients (30.8%) had complex pouch sinuses. After a median of 2.0 needle-knife therapies during a follow-up period of 1.1 years (range 0.4–2.8), 28 patients (43.1%) with pouch sinus experienced a complete response, 27 (41.5%) had a partial response, and 10 (15.4%) had persistent sinus. Fifty-three patients (81.5%) maintained a functional pouch at the last follow-up. The causes for pouch failure in this population included pouch sinus with or without anastomotic leak ($n = 7$, 10.8%), the late development of CD of the pouch ($n = 3$, 4.6%), and chronic antibiotic-refractory pouchitis ($n = 2$, 3.1%). The authors performed multivariate analysis and showed that a longer duration from colectomy to the diagnosis of pouch sinus and complex sinuses were inversely associated with the healing of pouch sinuses, whereas the increased sessions of needle-knife therapy improved the healing of the pouch sinuses. Finally, only one patient (1.5%) developed a procedure-related adverse event, which required hospitalization for continuous pouch bleeding.

A follow-up study with 109 patients was performed in 2018. Nine patients had fecal diversion at the diagnosis of pouch sinus. A total of 102 patients (93.6%) had pre-procedural documentation of symptomatology and 84 (82.4%) of patients were symptomatic at the time of sinus diagnosis. Sinus was located in the presacral area of the pouch-anal anastomosis in 101 (92.7%) patients. The length of the pouch

was recorded in 100 patients, with a median length of 4.8 cm. Complex sinus was documented in 38 patients (34.9%). Patients underwent a median of 2.0 sessions of needle-knife sinusotomy (range1.0–3.0). Symptomatic improvement was documented in 79/102 (77.5%) patients after the initial procedure. At the latest endoscopy, complete healing of the sinus was documented in 54 (49.5%) patients and partial healing in 20 (18.3%). Symptomatic improvements were seen in 44/54 (81.5%) patients with complete healing and 15/20 (75.0%) patients with partial healing. Recurrent sinus occurred in 14 (25.9%) patients who had had complete healing of the sinus after a median interval of 10.4 (range 6.0–15.5) months. One patient was treated with loop ileostomy and later had surgical pouch redo. The other 13 patients were treated with additional needle-knife sinusotomy sessions, and six of the 13 patients reported complete healing after a single session. Procedure-associated complications were encountered in six (1.8% per procedure) occasions. One patient (0.3% per procedure) with sinus at the tip of the "J," who responded to the first procedure, developed perforation at the second sinusotomy and required urgent single-port diverting loop ileostomy and perforation repair.[74]

Another study conducted in 2019, compared endoscopic sinusotomy (ESi) to redo pouch surgery. The study included 226 patients (ESi, $n = 141$; redo surgery, $n = 85$). The authors concluded that complete healing of the sinus was achieved in 75 patients (53.2%) and partial healing in 23 patients (16.3%) with ESi, and an initial complete healing (i.e., no anastomotic leak before ileostomy closure) was obtained in 80 patients (94.1%) receiving redo surgery. Sinus recurrence after complete healing was seen in 17 patients (22.7%) treated with ESi and 28 patients (32.9%) treated with surgery ($p = 0.15$). Subsequent surgery was needed in 34 patients (24.1%) with ESi therapy and 18 patients (21.2%) with initial redo surgery ($p = 0.70$). Kaplan-Meier recurrence-free and surgery-free survival after initial procedures showed no statistical difference between the two groups. The rate of adverse events in the ESi group was significantly lower than that in the redo pouch surgery group (2.5 vs. 43.5%, $p < 0.0001$). The authors concluded that ESi is a feasible, effective, and safe procedure for ileal pouch patients with chronic anastomotic sinus. It may be considered as the first-line therapy in appropriate patients with asymptomatic or symptomatic chronic pouch sinus because of its similar surgery-free survival rate and reduced adverse event rate to redo pouch surgery. Redo pouch surgery had a higher immediate healing rate and should be considered in those who continue to have symptomatic chronic pouch sinus after ESi therapy.[75] A subsequent study investigating the risk factor for recurrent pouch sinus after the endoscopy or surgical therapy showed that an excessive gain in BMI, i.e., >10% increase from baseline after initial successful pouch sinus treatment, was associated with an increased risk for sinus recurrence. They reported that excessive BMI gain (OR 3.0, 95% CI 1.0–9.0) and CD of the pouch (OR 2.9, 95% CI 1.0–8.1) were independently associated with sinus recurrence. The authors concluded that weight control may help decrease the risk for recurrence of pouch sinus.[76]

In conclusion, ESi may be attempted as the first-line therapy in experienced hands for patients with persistent pouch sinuses. The endoscopist should always anticipate perforation or bleeding and be ready to manage the same when it occurs. The backup plan, such as endoscopic clipping or surgical intervention, should be readily available whenever needed.

Conclusion

IPAA will continue to remain the mainstay of surgical treatment for medically refractory UC. As the number of IPAA patients increases with time we will also see a higher risk of complications related to IPAA. Although the quest to find medications for the management of these complications always remains, it is unlikely we might have a therapy available soon. Redo IPAA surgery is technically challenging and is not widely available. Hence, endoscopy will continue to be a mainstay of treatment for patients with IPAA and its complications. As the field of endoscopy improves, so will the management of these said complications.

Abbreviations

Anti-TNF	Anti-tumor necrosis factor
ATZ	Anal transition zone
CD	Crohn's disease
EBD	Endoscopic balloon dilation
EST	Endoscopic stricturotomy
EF	Endoscopic fistulotomy
FAP	Familial adenomatous polyposis
IPAA	Ileal pouch-anal anastomosis
IBD	Inflammatory bowel disease
MSCs	Mesenchymal stem cells
OTSC	Over-the-scope clip
TPC	Total proctocolectomy
TTSC	Through-the-scope clip
UC	Ulcerative colitis

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Conflict of Interest
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