



Endoscopic therapy for pouch problems: Can we avoid surgery?

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ABSTRACT

While restorative proctocolectomy and ileal pouch-anal anastomosis significantly improves patients' quality of life, the reconstructive surgery is often associated with various structural, inflammatory, and functional disorders. Those disorders have been traditionally managed with surgery. However, the past two decades have witnessed a growing role of endoscopic management of strictures, prolapse, anastomotic leaks, sinuses, fistulae, and polyps. The main advantages of endoscopic therapy are its less invasiveness in nature and better tolerance over surgery. Endoscopic sinusotomy is at least as effective as surgical pouch redo for a majority of pouch presacral sinuses, while carrying a lower risk for procedure-associated complications.

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Introduction

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) has become the surgical treatment of choice for refractory ulcerative colitis (UC), colitis-associated neoplasia (CAN), and familial adenomatous polyposis. The gold-standard surgical procedure significantly improves patient's quality of life. On the other hand, this reconstructive surgery is often associated with structural (such as strictures and anastomotic leaks) and inflammatory sequelae (such as pouchitis, cuffitis, and Crohn's disease [CD] of the pouch). Surgical re-intervention has been the standard practice for the management of those structural complications.

The past two decades have witnessed endoscopic therapy emerging as a major treatment modality for some structural disorders of the ileal pouch. Currently there are four main areas which are amenable for endoscopic therapy: (1) strictures and obstructions; (2) fistulae; (3) acute and chronic surgical leaks; and (4) pouch neoplasia.

Strictures and obstructions

Strictures are common in patients with IPAA as well as in those with continent ileostomies. In addition, pouch surgery can be associated with other forms of obstructions, such as pouch prolapse or

intussusception, afferent limb syndrome, efferent limb syndrome, pouch septum, and twisted pouch.

Strictures

Due to the reconstructive nature of pouch surgery, pouch strictures are common. In a large study of 3707 cases from Cleveland Clinic led by the late Dr. Victor Fazio, he showed that the cumulative frequencies of small bowel obstruction and strictures were 5% and 5.2%, respectively, as early complications; and 12.9% and 11.2% respectively, as late complications.¹ The common locations of strictures are anastomosis, pouch inlet, and prior stoma site (especially with end-to-end anastomosis). For these problem in the past, surgical options were the mainstay of treatment and pouch strictures were treated with surgical resection with anastomosis or strictureplasty.²

Nonsurgical approaches for ileal pouch strictures have been explored. These mainly consist of digital and instrument (bougie and Hegar dilators and endoscopic balloon) dilations for anastomotic strictures.³ Our group at The Cleveland Clinic first described endoscopic balloon dilation (EBD) of various forms of pouch strictures in 19 patients (Fig. 1).⁴ The cohort included 11 patients with concurrent Crohn's disease of the pouch (CDP), 5 with cuffitis, and 3 with pouchitis ($n = 3$), with a total of 14 inlet and 14 outlet strictures. EBD was successfully performed and achieved improvement in symptomatology and quality-of-life (QOL). There were no complications with the procedure. During a mean follow-up of 6.10 ± 5.83 months, one patient with CD failed the endoscopic therapy and underwent pouch resection.⁴ We further expanded the cohort ($n = 151$) with addition of a treatment arm for strictures in a strictureplasty ($n = 16$). We found that 51 patients (31%) had multiple pouch strictures and 100 (60%) patients had inlet strictures. The mean length of the pouch strictures

Abbreviations: CAN, colitis-associated neoplasia; CD, Crohn's disease; CDP, Crohn's disease of the pouch; EBD, endoscopic balloon dilation; EMR, endoscopic mucosal dissection; ESt, endoscopic stricturotomy; FPC, floppy pouch complex; IPAA, ileal pouch-anal anastomosis; IQR, interquartile range; QOL, quality of life; UC, ulcerative colitis

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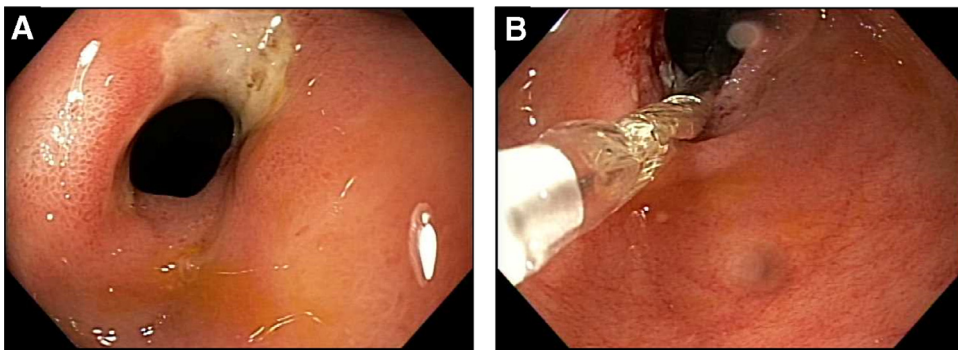


Fig. 1. Endoscopic balloon dilation. A. Ulcerated stricture at end-to-end anastomosis at prior ileostomy site; B. Balloon dilation to 20 mm.

was 1.2 ± 0.6 cm. During a mean follow-up of 4.1 ± 2.6 years, 92 patients (55%) had recurrent strictures and 21 (13%) developed pouch failure. The strictureplasty group had a significantly longer time interval between the procedure and pouch stricture recurrence or pouch failure than the EBD group. However, patients in the two groups had comparable overall pouch survival rates and stricture-free survival rates. The two groups had a comparable rate of procedure-associated complications.² EBD is not a difficult procedure and can safely be performed in an outpatient setting utilizing conscious sedation. The targeted balloon size is 18–20 mm. However, strictures at the pouch inlet and anastomosis often recur after EBD, which require exploration of other treatment modalities.

Endoscopic stricturectomy (ESt) is another modality that has been developed by our group. In 85 patients with IBD-related strictures, including 53 with ileal pouch strictures (Fig. 2). The technique was technically feasible and effective. In a total of 272 needle knife or insulated tip knife ESt procedures, 10 (3.7%) adverse events occurred, including 9 with delayed bleeding and one hospitalization due to perforation.⁵ In a separate study of 185 patients with ileocolonic anastomosis in CD, including 21 treated with ESt and 164 with EBD, we were able to achieve immediate technical success in 100% of patients treated with ESt and 90% of patients with EBD. We also found that those treated with ESt had higher symptomatic and endoscopic improvement rates than EBD. Subsequent salvage surgery for refractory strictures was needed in 2 (9.5%) patients with ESt and 55 (33.5%) with EBD ($p = 0.03$), a median of 0.8 (interquartile range [IQR]: 0.1–1.6) year and 4.0 (IQR: 0.8–6.9) years, respectively. We reported none in the ESt group and 5 procedure-associated perforation in the EBD group. Four procedure-associated, transfusion-required bleeding episodes occurred in the ESt group and none in the EBD group.⁶ We also recently reported that the efficacy of ESt vs. surgical resection in ileocolonic anastomotic strictures in CD was comparable, with a significantly lower rate of procedure-associated complications.⁷ We have extrapolated that the outcomes for ESt (vs.

EBD or surgical resection) for pouch strictures should be comparable. Both EBD and ESt have been recommended in a position statement from the Global Interventional IBD group, a special interest group, devoted to standardizing the endoscopic treatment of IBD (including pouch disorders).⁸ At The Cleveland Clinic Pouch Center, ESt has become the first-line endoscopic therapy for pouch-anal anastomosis stricture. The main advantage of ESt over EBD, bougie or Hagar dilators are the endoscopist's full control of the location and depth of electroincision. This is particularly important to minimize iatrogenic injury when treating strictures near the anal sphincter and adjacent organs, such as vagina and prostate.

Both EBD and ESt have limitations. Most patients require repeat endoscopic treatments. In addition, pouch patients with a long stricture (>4–5 cm) have a suboptimal response to EBD or ESt. One additional conservative treatment for refractory, long, and straight strictures could be placement of a self-expandable metallic stent.⁹

Other forms of obstruction

There are other disorders which can cause partial bowel obstruction or symptoms of dyschezia or incomplete evacuation. Floppy pouch complex (FPC) is a newly described cluster of pouch disorders in which patients have a redundant afferent limb, afferent limb syndrome (angulation of the afferent limb) or pouch prolapse.¹⁰ Due to the mechanical features, medical therapy has a limited role in the management of these structural problems. Surgical treatment for pouch prolapse has been explored, with mesh pexy,¹¹ repair, and revision. In our 3176-case Pouch Registry at Cleveland Clinic, 11 were found to have pouch prolapse (0.3%) with 7 having full-thickness prolapse and 4 mucosal prolapse. Two patients with mucosal prolapse were managed conservatively and two required mucosal excisions. Three patients developed pouch failure with conversion to continent ileostomies.¹² In a survey study of 269 colorectal surgeons or trainees, 35 respondents reported that they had taken care of 83 patients with prolapse of the

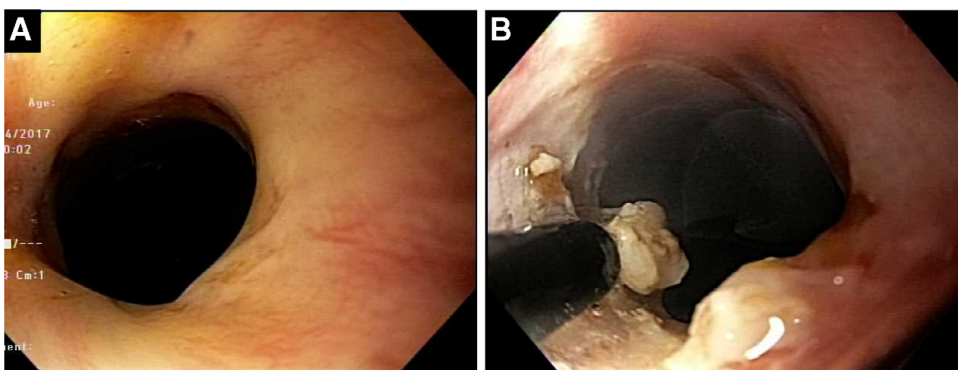


Fig. 2. Endoscopic stricturectomy. A. Tight pouch-anal anastomosis stricture; B. Electroincision in action.

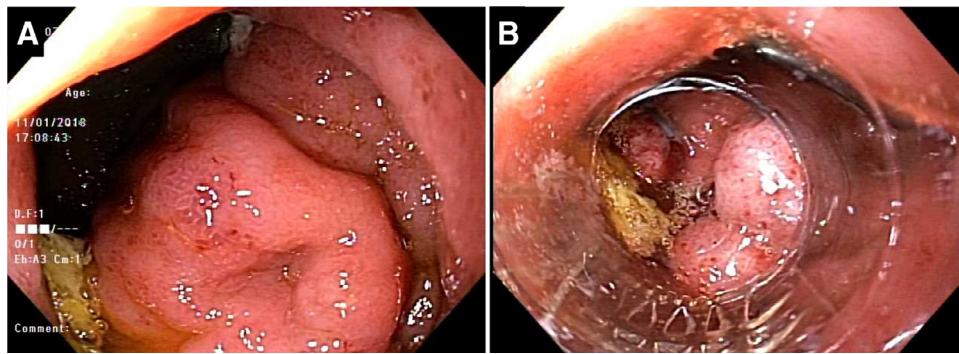


Fig. 3. Endoscopic banding of pouch prolapse. A. Mucosal prolapse at the anterior wall of distal pouch blocking the outlet of the pouch; B. Banding ligation of the prolapse.

ileoanal pouch. Fifty-two patients required surgery which included a combination of transanal repair, abdominal pouchpexy, and transabdominal revision or excision. All pouches except one were salvaged.¹³

At Cleveland Clinic, we have developed a novel banding technique to treat mucosal prolapse of the pouch with promising outcomes.¹⁰ This endoscopic procedure is minimally invasive and can be performed in an outpatient setting. The procedure involves submucosal injection of 50% dextrose and ligation with rubber bands. Approximately 70%–80% of patients reported some degree of improvement in dyschezia and incomplete evacuation symptoms (Fig. 3).

Fistulae

Fistula formation in patients with IPAA is a detrimental complication, often resulting from suture line or staple line leak or development of CDP. Types of fistula include: perianal fistula, pouch-to-pouch fistula or pouch-to-afferent limb fistula, and enterocutaneous fistula (often from anastomotic leak or leak at the tip of the “J”). While CDP-associated fistulae can be managed medically, pouch fistula with or without abscess has been managed surgically. Surgical modalities include fistulotomy, incision and drainage, bowel resection, mucosal or muscle flaps, redo pouch, or fecal diversion. Salvage surgical procedures often are associated with postoperative complication or postoperative recurrence. Our group at Cleveland Clinic has developed various novel endoscopic techniques to address some of these fistulae.^{14,15}

The tip of the J leak can be associated with an abscess and is one of the causes for pouch failure. We have used the endoscopic over-the-scope-clip system to treat 12 patients with a tip of the “J” of IPAA (Fig. 4). Eight patients (67%) achieved complete closure of the leak and 4 patients (33%) had a persistent leak and required surgical intervention.¹⁶ We also developed endoscopic fistulotomy for the treatment in 29 patients with IBD-associated fistulae, including 7 (24%)

with fistulae from of the “J” to the anastomosis, 14 (48%) pouch-pouch body or anastomosis fistulae, and 1 (3%) afferent limb-to-proximal pouch body fistula. For the 29-case cohort, 26 (90%) achieved a persistent complete healing and complications were rare with one having post-procedural bleeding (Fig. 5).¹⁷ Endoscopic fistulotomy can also be performed in patients with perianal fistula.^{15,18} Endoscopy may also be used for seton placement.^{15,18}

Endoscopic management is an emerging field for IBD-associated fistulae. A position paper from the Global Interventional IBD Group has been published on this topic.⁸ In many patients, endoscopic approaches can be attempted first before salvage surgery.

Surgical leaks

Pouch sinus is defined as a *chronic* blind tract resulting from chronic pouch-anal anastomotic leak and abscess, which occurs in 2.8%–8% of patients undergoing IPAA.^{19,20,21} The common location of sinus is the presacral space. Patients with acute, asymptomatic leaks may heal spontaneously, with a reported healing rate of 53%–95%.^{20,21,22,23} Surgical treatment for acute sinus includes debridement of the sinus, unroofing of the cavity, or the use of fibrin glue.^{20,21,22,23} The reported overall healing rate of surgery ranged from 60% to 100%.^{7,8,19,20,24} Other surgical options include pouch advancement and pouch redo.²⁵ The main disadvantages of the surgical approaches are postoperative complications and postoperative recurrence.

Our Interventional IBD Unit at Cleveland Clinic has explored endoscopic options for the treatment of pouch sinus. We described endoscopic sinusotomy, a novel treatment modality for a pouch sinus (Fig. 6).²⁶ Subsequently, we conducted a case-controlled study comparing endoscopic sinusotomy ($n = 141$) and redo pouch surgery ($n = 85$) in the treatment of symptomatic pouch sinuses. We were able to achieve complete healing of sinuses in 75 patients (53%) and partial healing in 23 (16%) treated with endoscopic sinusotomy. In contrast,

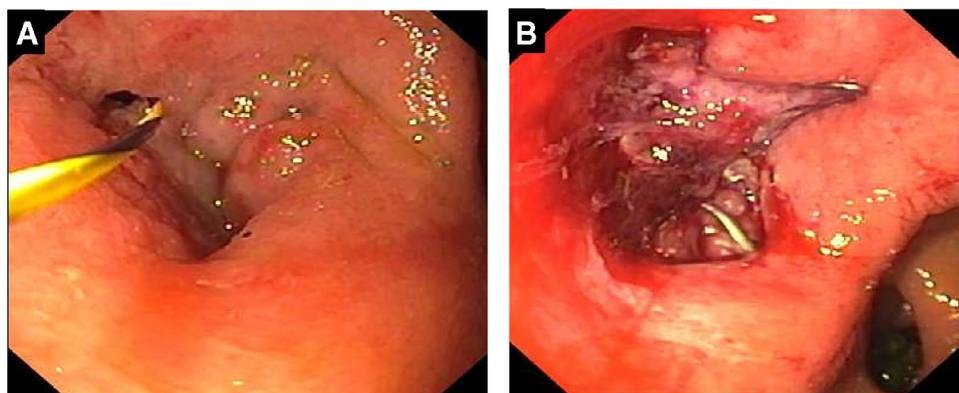


Fig. 4. Endoscopic clipping of a leak at the tip of the “J”. A. The leak detected by a soft-tip guidewire. B. Deployed over-the-scope clip on the leak.

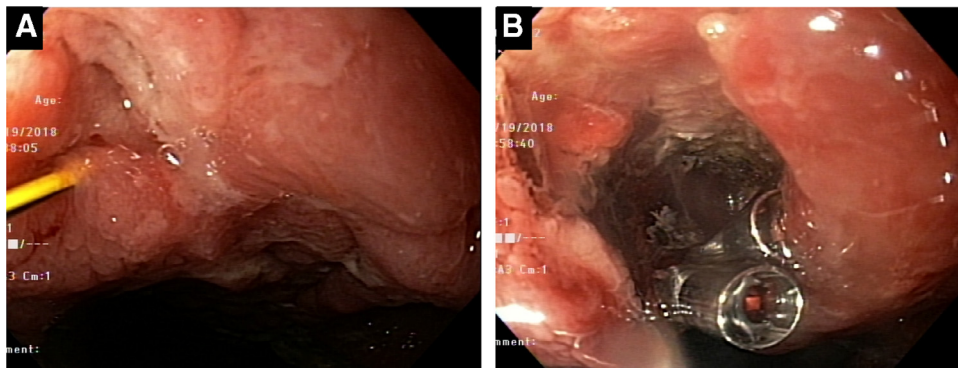


Fig. 5. Endoscopic sinusotomy. A. Deep presacral sinus detected by a soft-tip guidewire. B. Sinusotomy followed by placement of endoclips along the electroincised edges, to prevent reformation of the sinus.

an initial complete healing, defined as the absence of anastomotic leak before ileostomy closure was achieved with surgery in 80 patients (94%) with redo surgery. However, recurrence of the sinus after complete healing was documented in 17 (23%) with the endoscopic therapy and 28 (33%) with surgery ($p = 0.15$). Furthermore, subsequent surgery was required in 34 (24%) after endoscopic therapy and 18 (21%) after redo surgery ($p = 0.70$). Recurrence-free and surgery-free survival curves after index procedures were comparable between the 2 groups. However, the frequency of adverse events in the endoscopy group was lower than in the surgery group (3% vs 44%, $p < 0.0001$).²⁷ Therefore, we endoscopic sinusotomy can be considered as the first-line of therapy for a pouch sinus, with surgical approach as a backup.⁸

Pouch neoplasia

Chronic mucosal inflammation can be associated with formation of inflammatory polyps, which can cause symptoms of bleeding, diarrhea, and dyschezia. In a study of 1094 UC patients from Pouch Center at Cleveland Clinic, 96 (9%) were found to have pouch polyps. The median size of the polyps was 1.2 (IQR: 1.0–2.0) cm. Ninety-three patients (97%) had inflammatory-type polyps and 3 (3%) had polyps with low-grade dysplasia or indefinite for dysplasia.²⁸ Despite the fact that a majority of pouch polyps are benign, we recommend that large (>1 cm) or symptomatic polyps be removed with endoscopic polypectomy or endoscopic mucosal resection (EMR) (Fig. 7).

Pouch neoplasia is not common. The best data to date comes from two large cohorts. A study of 3,203 pouch patients with underlying IBD from Cleveland Clinic showed the cumulative incidence for pouch dysplasia was 0.8%, 1.3%, 1.5%, 2.2%, and 3.2% at 5, 10, 15, 20, and 25 years after pouch construction, respectively.²⁹ A 1,200-case cohort study of from the Dutch Pathology Registry showed that 25 (1.8%) developed pouch neoplasia, including 16 adenocarcinomas. The cumulative incidence for pouch neoplasia (i.e. dysplasia or cancer) at

5, 10, 15, and 20 years were 1.0%, 2.0%, 3.7%, and 6.9%, respectively.³⁰ The location of pouch neoplasia was mainly at anal transitional zone or cuff. The risk factors for pouch neoplasia are a pre colectomy diagnoses of CAN in the colon or rectum.^{29,30}

The prognosis of pouch neoplasia appears to be poor. In a study of 44 patients with pouch neoplasia from Cleveland Clinic, 6 (27%) had persistence or progression in the 22 patients with an initial diagnosis of low-grade dysplasia of the pouch after a median follow-up of 9.5 (4.1–17.6) years. In 12 patients with high-grade pouch dysplasia, the disease either persisted or progressed in 3 (25%), during a median time interval of 5.4 (2.2–9.2) years. Of our 14 patients with pouch adenocarcinoma, 6 (43%) died during a median follow-up of 2.1 (0.6–5.2) years.³¹ It appears that surveillance pouchoscopy may not detect all pouch neoplasia at the dysplasia stage and some patients with cancer in the pouch may not have endoscopically visible lesions.²⁹ It is not clear whether image-enhanced endoscopy or deep biopsy can improve accuracy over conventional white light-guided mucosal biopsy. While endoscopic mucosal resection or endoscopic submucosal resection for dysplastic lesions of the pouch body, anal transitional zone or cuff may be technically feasible, their oncological benefits and risks are not clear. Since the prognosis of pouch cancer is poor and the cancer is not common, the natural history of pouch neoplasia is poorly studied and defined. We recommend that dysplastic lesions, especially flat or depressed lesions or non-liftable lesions, should be managed surgically.

Summary

Endoscopic therapy has provided valuable options for the management of ileal pouch disorders. EBD and ESt can be routinely performed for pouch strictures at various locations in the IPAA. Endoscopic band ligation can be attempted to treat those with mucosal prolapse. In eligible patients, endoscopic fistulotomy has the potential to provide a cure. Endoscopic sinusotomy may be considered as the first-line

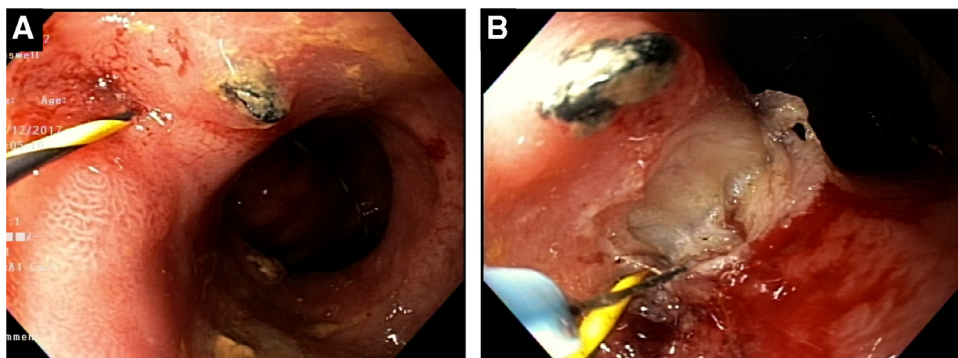


Fig. 6. Endoscopic fistulotomy A. Pouch-pouch fistula detected by a soft-tip guidewire. B. Fistulotomy with needle knife was performed over the guidewire.

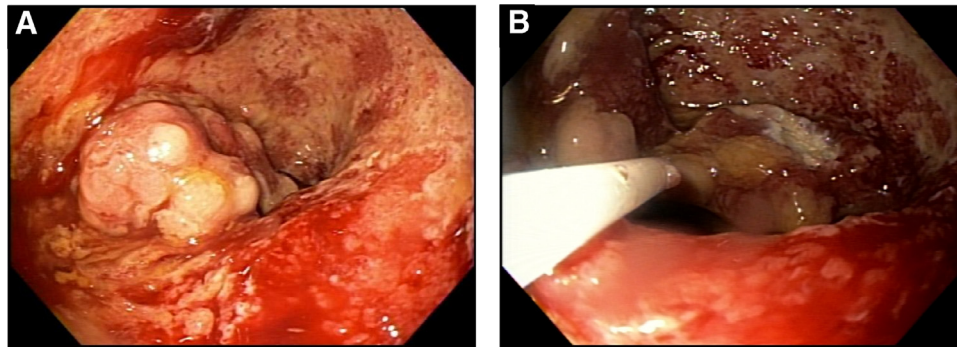


Fig. 7. Endoscopic polypectomy. A. Large pedunculated inflammatory polyp with severe pouchitis; B. Completion polypectomy with hot snare.

therapy for pouch sinus, due to its efficacy and minimal degree of invasiveness. However, we advocate that a multidisciplinary approach with medical, endoscopic, and surgical therapists collaborating is highly recommended for the management of complex ileal pouch disorders.

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Disclosure

No financial conflict of interest.

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