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Classification and Management of Disorders of the J Pouch

Priscila Santiago, MD[1], Edward L Barnes, MD, MPH[2], Laura E. Raffals, MD, MS[1].

Author affiliations:

[1]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; [2]Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Corresponding Author

Laura E. Raffals, MD, MS

Division of Gastroenterology and Hepatology

Mayo Clinic

200 First St SW, Rochester, MN 55905

Phone: 507-266-0873

raffals.laura@mayo.edu

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ABSTRACT

Total abdominal proctocolectomy with ileal pouch-anal anastomosis (IPAA) for ulcerative colitis (UC) is associated with substantial complications despite the benefits of managing refractory and/or neoplasia-associated disease. For the purpose of this review, we focused on the diagnosis of some of the most common inflammatory and structural pouch disorders and their respective management. Pouchitis is the most common complication, and it is typically responsive to antibiotics. However, chronic antibiotic refractory pouchitis (CARP) has been increasingly recognized and biologic therapies have emerged as the mainstay of therapy. Crohn's like disease of the pouch (CLDP) can affect up to 10% of patients with UC after IPAA. Medical options are similar to CARP therapies, including biologics with immunomodulators. Studies have shown higher efficacy rates of biologics for CLDP when compared with CARP. In addition, managing stricturing and fistulizing CLDP is challenging and often requires interventional endoscopy (balloon dilation and/or stricturotomy) and/or surgery. The implementation of standardized diagnostic criteria for inflammatory pouch disorders will help in advancing future therapeutic options. Structural pouch disorders are commonly related to surgical complications after IPAA. We focused on the diagnosis and management of anastomotic leaks, strictures, and floppy pouch complex. Anastomotic leaks and anastomotic strictures occur in approximately 15% and 11% of UC patients after IPAA, respectively. Further complications from pouch leaks include the development of sinuses, fistulas and pouch sepsis requiring excision. Novel endoscopic interventions and less invasive surgical procedures have emerged as options for the management of these disorders.

Introduction

Total abdominal proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the surgical procedure of choice for medically refractory ulcerative colitis (UC) and UC-related neoplasia. Despite overall satisfactory long-term outcomes, surgery with IPAA is associated with significant morbidity (1-3). Structural and inflammatory pouch disorders are common, and pouch failure with subsequent pouch excision or permanent diversion can occur in up to 10% of cases (4, 5). Pouchitis is the most common complication, with an estimated 40% incidence rate within one year of IPAA surgery in initial studies (6, 7), and an 80.2% 30-year cumulative probability (8). In addition, a recent study using a large administrative claims database found a 48% cumulative incidence of pouchitis within 2 years of IPAA (9). Despite the burden of inflammatory pouch conditions, we lack reliable risk stratification tools and approved therapies for an effective management. In this review, we aim to provide an overview of the most relevant inflammatory and structural disorders of the pouch and their management, along with an insight of future research directions of pouch conditions.

Inflammatory pouch disorders

Idiopathic pouchitis

The clinical presentation of pouchitis is variable, ranging from a spectrum of asymptomatic disease to increased stool frequency, urgency, incontinence, and cramps (10). However, severity of symptoms does not correlate with endoscopic disease activity, and pouchoscopy is the most important tool for an accurate diagnosis (Figure 1) (11). In most patients, the etiology of pouchitis is likely multifactorial, hence the classification of idiopathic pouchitis. The proposed pathogenesis includes postsurgical altered bowel anatomy and fecal stasis, leading to dysbiosis and maladaptive mucosal changes that perpetuate inflammation in genetically susceptible individuals (12, 13). When pouchitis has a specific causative factor, it is classified as secondary pouchitis, which encompasses infectious pouchitis, ischemic pouchitis, autoimmune-associated pouchitis, nonsteroidal anti-inflammatory drug (NSAID) induced pouchitis, and radiation-induced pouchitis. Further investigation of these etiologies is important, as up to 30% of patients with chronic antibiotic resistant pouchitis (CARP) have detectable secondary causes of pouchitis (10, 14).

Idiopathic pouchitis is characterized by diffuse inflammation of the pouch body, with sparing of the afferent limb, which helps distinguishing the disease from secondary causes of pouchitis. Endoscopically, the loss of the "owls' eye" configuration of the J pouch, a pouch body with decreased distensibility, and the presence of a mucosal ridge and inflammatory polyps can suggest chronic pouchitis (12). Biopsies confirming acute on chronic inflammation aid the diagnosis, however, histology alone is not diagnostic of pouchitis (15). The management of acute idiopathic pouchitis involves antibiotics as the first-line therapy (Table 1). The most frequently used antibiotics are metronidazole or ciprofloxacin for 2 weeks. Nevertheless, multiple other antibiotics are effective, including amoxicillin/clavulanic acid, rifaximin, and trimethoprim/sulfamethoxazole (16, 17). Most patients will present with antibiotic-responsive pouchitis, which is characterized by < 4 episodes per year with each episode responding to a 2-week course of antibiotics (10, 12).

In our practice, we use metronidazole 500 mg twice daily or ciprofloxacin 500 mg twice daily for 2 weeks as first-line antibiotics. For those who respond to the regimen (antibiotic-responsive), we repeat antibiotics as needed to treat specific episodes of pouchitis in the future. However, if patients develop recurrent symptoms at the end of the second week or have incomplete response, we start the second antibiotic (metronidazole or ciprofloxacin) for an additional 2 weeks. If patients have recurrence of symptoms in less than 3 months, we usually repeat antibiotics for 2 weeks and add a slow taper for the subsequent 2 weeks.

Chronic antibiotic dependent pouchitis

Pouchitis represents a disease spectrum, with an estimated 17% of patients with acute pouchitis developing chronic pouchitis (1). Chronic antibiotic dependent pouchitis (CADP) is defined as ≥ 4 episodes of pouchitis per year or persistent symptoms requiring long-term antibiotics to maintain disease remission (10). In patients with CADP, the mainstay of therapy is chronic suppressive and rotating antibiotics to reduce the chances of antibiotic resistance (18). Occasionally, a combination of antibiotics is needed to induce and maintain remission. Probiotics such as the 8-strain combination have shown limited efficacy given non-durable effects and adverse events (19). Future research directions will include alternative antibiotic-sparing therapies including dietary interventions for these patients who require chronic antibiotic therapy. In our practice, we use the lowest possible dose of the antibiotic to maintain remission. We also use the strategy of alternating 2 weeks on antibiotics with 2 weeks off

antibiotics at the lowest doses. The most frequently prescribed antibiotics in our practice are ciprofloxacin and metronidazole, and amoxicillin-clavulanate or vancomycin as third options.

Chronic antibiotic refractory pouchitis

A minority of patients can develop CARP, which is defined as failure to respond to a 4-week course of a single antibiotic, needing > 4 weeks of therapy with 2 or more antibiotics, 5-aminosalicylates, steroids or immunomodulators (10). In this subset of patients, it is essential to rule out the secondary causes of chronic pouchitis. Given the challenging management, new biologic and small molecule therapies used in IBD are being explored for the treatment of CARP.

In a meta-analysis of anti-TNF studies to treat CARP or Crohn's-like Disease of the pouch (CLDP), the long-term clinical remission rate in CARP was 37% vs 57% in CLDP (P = 0.57). The remission rate after anti-TNF induction was 10% in CARP vs 64% CLDP (P = 0.06), suggesting that anti-TNF therapies have higher efficacy in CLDP (20). In a multicenter cohort of 83 patients treated with vedolizumab for chronic pouchitis and CLDP, clinical response and endoscopic response rates of 70.0% and 48.7% respectively were achieved among patients with chronic pouchitis (21). In a single center analysis by Verstockt *et al*., clinical remission was achieved in 43.5% of patients using infliximab for CARP, and in 38.5% and 60.0% among patients treated with adalimumab and vedolizumab, respectively (22). Similarly, a systematic review on ustekinumab efficacy reported a pooled clinical response rate of 63% and a pooled clinical remission rate of 10% in 3 studies that included CARP patients (23-26). Most recently, the EARNEST trial was the first randomized double-blind placebo (PBO)-controlled study to evaluate a biologic for chronic pouchitis. A total of 102 patients were randomized to IV vedolizumab or PBO, and 31.4% of vedolizumab vs 9.8% of PBO patients achieved mPDAI remission at week 14 (P=0.013), with similar adverse event rates between groups (27).

In our experience, we use advanced immnunosuppressive therapies with biologics or small molecules for both CARP and CLDP. Our main strategy when treating these patients is to choose an advanced therapy that the patient was not exposed to prior to colectomy.

Crohn's-like disease of the pouch

It is estimated that 10% of patients with UC or indeterminate colitis will develop CLDP after IPAA (28). The most relevant endoscopy clues are the presence of fistulas involving the perineum or small

bowel but not associated with an anastomosis, pre pouch ileitis, and strictures in the pre pouch ileum and pouch (Figure 2) (28). However, there remains heterogeneity in standard diagnostic criteria for the disease, which continues to be poorly understood and difficult to treat (29). In the setting of fistulas, it can be challenging to differentiate CLDP versus chronic anastomotic leak. In addition, histology is of limited utility as only 10% to 12% of patients with CLDP will have granulomas on biopsy (30). CLDP can be classified as inflammatory, fibrostenotic or penetrating, and it is associated with an increased risk of complications including pouch failure (29, 30).

The data on treatment options for CLDP is mainly originated from retrospective cohorts with weak quality of evidence (31-33). Pharmacologic options are similar to CARP therapies, including biologics with adjunctive therapy of immunomodulators, antibiotics, and/or steroids. In addition, the management of stricturing or fistulizing disease usually requires endoscopy (balloon dilation, stricturotomy) and/or surgery with pouch excision in refractory cases (15). Recent consensus statements offered several recommendations for the treatment of this challenging condition (34), with biologic therapy remaining a mainstay of therapy in the current era.

Several studies have demonstrated that biologics have higher efficacy rates in CLDP when compared with CARP (20, 21, 25, 26). Anti-TNF agents for CLDP have shown a clinical remission rate after induction of 64%, and 57% on long-term maintenance (20). In addition, systematic review data on ustekinumab showed that 85% of patients had clinical response, 27% clinical remission, and 67% endoscopic response (26). Finally, vedolizumab is also promising, with an observed clinical response rate of 72.2% and endoscopic response rate of 56.9% (21).

PSC-associated pouchitis

Patients with PSC and IBD who undergo IPAA are at increased risk of pouchitis and progression to chronic pouchitis. In a study of 182 PSC/UC patients with pouchitis, PSC was strongly associated with chronic pouchitis when compared with a matched non-PSC cohort (68.1% vs 34.1%, $P < 0.001$). Furthermore, PSC-pouchitis was associated with moderate-to-severe pouch inflammation, pre pouch ileitis, and an increased risk of antibiotic-dependent and antibiotic-refractory pouchitis (35). In a recent meta-analysis, patients with PSC-IPAA demonstrated a 4-fold increase in odds of developing pouchitis compared to patients undergoing IPAA for UC alone (36). Endoscopic findings include diffuse inflammation of the pouch body and a long segment of ileitis, with higher endoscopic PDAI scores when

compared to non-PSC pouchitis (37). Therefore, patients who are found to have a long segment of inflammation in the afferent limb should be investigated for PSC (37). Evidenced-based treatment recommendations are lacking; thus, management is mainly based on expert clinical practice. Initiation of antibiotics is usually the first step; however, most patients will require long-term suppression with antibiotics and rotating antibiotics. In our practice, the preferred antibiotic is vancomycin twice daily used chronically for suppression. For refractory disease, clinical experience has demonstrated similar rates of response to immunomodulators and biologics when compared with non-PSC pouchitis (15, 35).

Ischemic pouchitis

The diagnosis of ischemic pouchitis is suggested by endoscopic findings of asymmetric inflammation with sharp demarcation of margins. Inflammation distribution is usually restricted to specific areas such as staple lines, afferent limb, or distal pouch (15, 38). The pathogenesis is thought to be related to surgical factors and mesenteric tension leading to an hypoperfusion state, especially in males and obese individuals (38, 39). Therefore, most patients do not respond to conventional antibiotic therapy. Severe cases might benefit from hyperbaric oxygen therapy and/or pouch redo surgery (39).

Infectious pouchitis

Clostridioides difficile infection (CDI) is one of the most concerning infections of the pouch. A high index of suspicion for CDI should be kept, as the typical risk factors for CDI might not be present (12, 40). A study based on administrative data from hospitalized IBD patients with pouchitis found that the frequency of CDI was 2.6% in admitted patients (41). In addition, the prevalence of CDI in a retrospective cohort of 198 patients with CADP and CLDP was 9.1%, which is comparable to the general IBD population (42). Patients with CDI of the pouch might exhibit more systemic symptoms and higher recurrence rates than non-IPAA patients. However, CDI of the pouch is typically responsive to antibiotics (43-45). Fecal microbiota transplantation (FMT) has been used for refractory cases and was shown to be effective for eradication of CDI in a study by Lan et al. However, recurrence of CDI was common (38.5%) after initial successful treatment (46). Cytomegalovirus can also be an etiology of secondary pouchitis, especially in patients who are on immunosuppressive medications. The infection is treated similarly to cytomegalovirus colitis with ganciclovir or valganciclovir, which seems to be effective with favorable pouch outcomes (47).

Cuffitis

Classic cuffitis represents the recurrence of UC in the rectal mucosa ("cuff"). This is most commonly seen as a complication of IPAA surgery with stapled anastomosis preserving the anal transition zone as opposed to hand-sewn anastomosis with mucosectomy (15, 48). The stapled anastomosis requires the presence of 1-2 cm of rectum, which remains as an area at future risk of inflammation and malignancy. Although clinical symptoms of cuffitis can mimic pouchitis, the presence of tenesmus and small bloody bowel movements suggests cuffitis. Therefore, endoscopy is essential for the diagnosis and typically shows inflammation in the rectal cuff. Management consists of using topical mesalamine or steroids (53). Recent consensus statements recommended topical mesalamine as first-line therapy, which can be used for induction and maintenance (34). Expert experience has also found some benefit to tacrolimus suppositories for refractory cuffitis.

Structural pouch disorders

Structural pouch disorders are most often related to surgical complications after IPAA. For the purpose of this review, we will focus on anastomotic leaks, fistulas, strictures, and floppy pouch complex, highlighting the afferent limb syndrome (Table 2).

Anastomotic leaks

Anastomotic leakage occurs in approximately 15% of patients after IPAA (49). Leaks are most commonly located in the pouch-anal anastomosis, in the tip of the J, and in the pouch body along the staple line (Figure 3) (10). Patients usually present within 2 weeks of surgery with symptoms related to pouch sepsis, which has been described as the most common indication for pouch excision (50-52). However, small anastomotic leaks can go unrecognized for months or years. Computerized tomography scan, MRI of the pelvis, and soluble contrast enema can aid in the diagnosis, along with pouchoscopy (10). Management includes percutaneous drainage of the leak; however, surgery is often needed for repair (10, 52). Endoscopic over-the-scope clipping has been used for closure of the tip of the J leak as a novel technique to avoid surgery. In a series of 12 patients, 67% achieved complete closure of the leak with the procedure (53). In addition, Wasmann et al. have described successful experience managing anastomotic leakage by endo-sponge assisted early surgical closure. This approach was associated with

preservation of pouch function and preclusion of pouch failure, likely related to the quick control of the leakage and sepsis (54). Complications from undiagnosed anastomotic leaks include the development of pouch sinuses and fistulas as a sequela (10).

Pouch-related fistulas

Pouch-related fistulas (PRF) arise in up to 5-12 percent of patients after IPAA (55, 56). They can involve various areas such as the bladder, vagina, small bowel, abdominal wall, and skin (57). As previously discussed, chronic anastomotic leaks and pelvic sepsis can lead to the development of sinuses and fistulas. Another etiology for PRF is CLDP. Specifically, the presence of an anastomotic fistula without a previous history of anastomotic leak and/or the late formation of fistulas after ileostomy takedown should raise suspicion for CLDP (10). In addition, a history of complex anovaginal fistulizing disease with perianal lesions corroborates a diagnosis of CLDP. Other risk factors for the development of fistulas include surgical technique problems and cryptoglandular disease (55, 58, 59).

PRF are associated with increased morbidity and high pouch failure rate. In a recent retrospective review of 97 patients who were treated for PRF at Mayo Clinic, 79% had at least one definitive surgical procedure, with a median of 2 and a maximum of 10 (59). Only 28% had resolution of the PRF, with a long interval to resolution (median 2.8 years). Of the remaining 70 patients (72%) who did not achieve resolution, 48 (51%) had pouch failure, with 42 requiring pouch excision and diversion, and 6 requiring diversion.

The management of PRF is challenging and includes heteregeneous surgical approaches. A recent systematic review and meta-analysis studied surgical outcomes of 641 patients with IPAA surgery and pouch-vaginal fistula, which is the most common type of PRF (56). Interventions to repair vaginal fistulas included fistulotomy, fistula plug, redo IPAA, seton placement, abdominal revision of the pouch, transanal ileal pouch advanced flap, and transvaginal repair. Despite these interventions, the overall fistula recurrence was 50%, pouch failure rate was 19%, and pouch excision rate was 20% (56).

Strictures

Strictures are commonly formed after IPAA surgery and most frequently observed after a handsewn anastomosis (60). Despite a reported rate of 38% of stricture frequency in a consecutive series (61), more recent studies observed stricture formation in up to 11.2% of the patients (1, 60). Typical locations include the pouch-anal anastomosis, mid-pouch, and pouch inlet (Figure 4) (10, 62). They can be fibrotic or nonfibrotic (inflammatory) in nature (60). Strictures can be due to ischemia, intraoperative technical difficulties, NSAIDs use, or CLDP (10, 62, 63). Complications from strictures include bowel obstruction, evacuation disorders, pouch dilatation and bacterial overgrowth (63). Management varies depending on etiology and location. While pharmacologic therapy is available for inflammatory CD strictures of the pouch, most cases require endoscopic or surgical procedures with dilation or stricturotomy. Severe cases might require proximal diversion and stricture resection with redo pouch formation or pouch excision (10, 63). Preferential therapies based on stricture location have been proposed by Segal and colleagues (63). Pouch-anal anastomosis strictures have good response to digital and Hegar dilatation, however multiple dilations might be required. Mid-pouch strictures are usually managed with endoscopic balloon dilation and surgical revision. Finally, pouch inlet strictures are usually responsive to endoscopic balloon dilation in addition to medical therapy when an underlying inflammatory process exists (63).

Floppy pouch complex and Afferent limb syndrome

Floppy pouch complex (FPC) is defined as the presence of pouch prolapse, afferent limb syndrome, enterocele, redundant loop and folding pouch visualized on pouchoscopy, Gastrografin pouchogram or defecography (64, 65). Given that the term encompasses different clinical phenotypes, each disorder has specific findings and management; nonetheless, the presentation might be similar among the phenotypes. The most common subtypes of FPC are afferent limb syndrome and pouch prolapse (66). Although the pathogenesis remains unclear, risk factors include a low body mass index with low peripouch fat area, thin pouch wall, female sex, and a family history of IBD (65-67). Diagnosis is facilitated by dynamic contrasted pelvic defecating studies and high index of suspicion during pouchoscopy. Treatment involves behavioral changes with avoidance of excessive straining, physical therapy retraining of the pelvic floor muscles with biofeedback therapy, modification of stool

consistency, endoscopic procedures (e.g. mucosal banding or excision of pouch prolapse), and definitive surgical interventions (65).

Afferent limb syndrome refers to a distal small bowel obstruction caused by acute angulation, prolapse, or intussusception of the afferent limb at the pouch inlet (Figure 5) (10, 64). Patients classically present with recurrent obstructive symptoms (68-70). Other symptoms include dyschezia, straining, incomplete evacuation, abdominal pain, bloating, and constipation (65). Radiographic imaging can help showing dilation of the small bowel proximal to the pouch inlet, with reflux of contrast enema to the distal small bowel. An endoscopic clue is a challenging intubation of the afferent limb given the sharp angulation at the level of the afferent limb and pouch (64). Management is typically surgical with laparotomy and ileopexy/pouchopexy, however pouch excision might be required (68-70).

Future directions

Despite the progress in elucidating some of the processes in the pathogenesis of inflammatory pouch disorders, there is an unmet need for improved biomarkers that can help assessing disease activity and predicting disease complications. Fecal calprotectin has emerged as a non-invasive test that was useful in distinguishing inflammatory from non-inflammatory pouch disorders (71, 72). When compared to the gold standard of pouchoscopy, calprotectin proved effective in ruling out inflammatory pouch disorders when < 100 µg/g (AUC 0.90) and ruling in inflammatory pouch conditions when ≥ 350 µg/g (AUC 0.90)(71). Furthermore, stool bile acids are a potential marker for chronic pouchitis, as studies have shown decreased levels of secondary bile acids in chronic pouchitis and a differential composition of bile acids among patients with normal pouches, chronic pouchitis, and chronic pouchitis with PSC (73, 74). Similarly, the composition of the pouch microbiome is correlated to the presence vs. absence of pouchitis, and further studies might leverage the pouch microbiome composition as a risk predictor for complications.

Future research is also needed to develop and validate standardized tools for disease assessment. The PROP-RD study has implemented standardized strategies in the evaluation of pouchitis, which can help with accurate measurements and refinement of treatment (75, 76). In addition, the Chicago Classification of Pouchitis is a novel system based on the endoscopic patterns of inflammation, leading to the description of 7 unique pouch phenotypes with contributing factors and prognosis (77).

Further validation of such instruments will aid in the evaluation of the effect and safety of new therapies in clinical trials.

Ultimately, these improved methods of risk stratification markers and disease assessment will enable studies of early interventions to prevent inflammatory conditions of the pouch, which are critically needed. Furthermore, expanding the basic and translational research on the microbiome, metabolome, and inflammatory pathways of pouchitis might open doors to new prophylactic and therapeutic interventions for pouch disorders.

Summary

Complications from IPAA surgery can be broadly classified as inflammatory and structural disorders, which were reviewed here, in addition to functional and neoplastic conditions. The implementation of standardized diagnostic criteria and outcome assessment for pouchitis will aid in advancing knowledge and future therapeutic options. Indeed, there is an unmet need for the development of new treatments for pouch related diseases, especially in CADP and CARP. Furthermore, structural disorders associated with the IPAA surgery are common, especially anastomotic leaks and strictures. Current advances in endoscopic therapies and less invasive surgery techniques emerge as novel options for the management of these disorders.

Figures and table legends

Figure 1. Summary of different endoscopic, imaging, and scoring tools used in the evaluation of pouch disorders. CTE: computed tomography enterography; MRE: magnetic resonance enterography; CD: Crohn's like disease; ATZ: anal transition zone; PDAI: Pouchitis Disease Activity Index; mPDAI: modified PDAI.

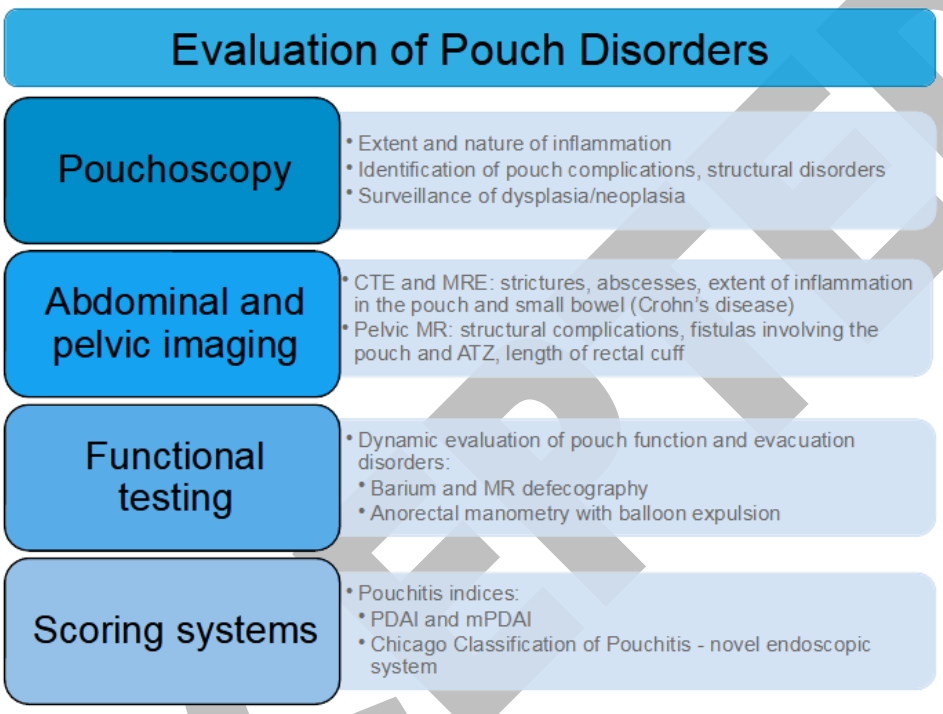
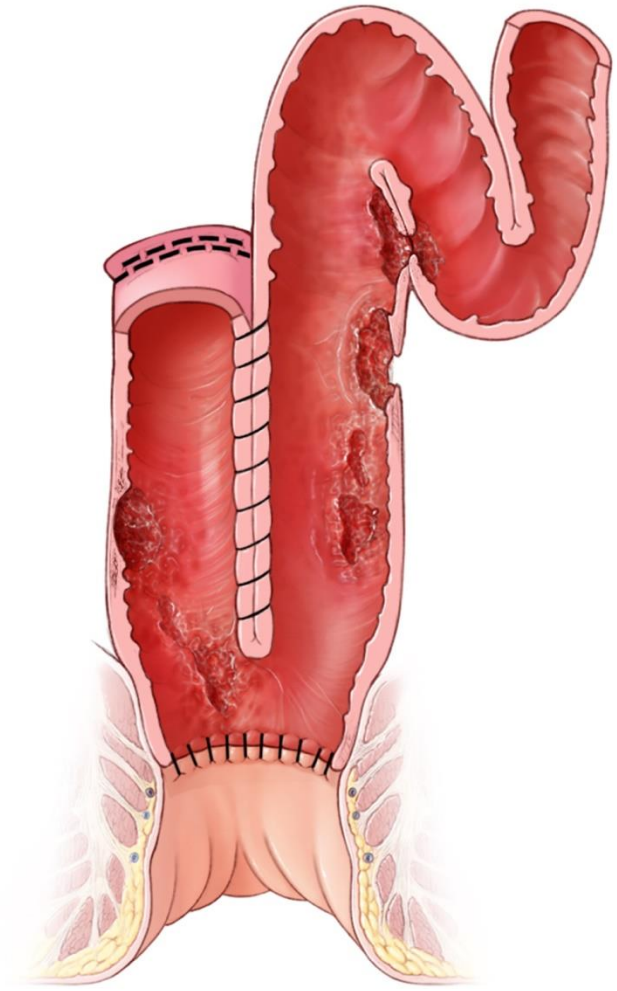


Figure 1. Summary of different endoscopic, imaging, and scoring tools used in the evaluation of pouch disorders.

Figure 2. Crohn's like disease of the pouch, depicting pouch inflammation, pre pouch ileitis and fistulas in the small bowel.



Crohn's like disease of the pouch

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Figure 3. Anastomotic leaks, including the tip of the J (1), pouch body (2), and pouch-anal anastomosis (3).

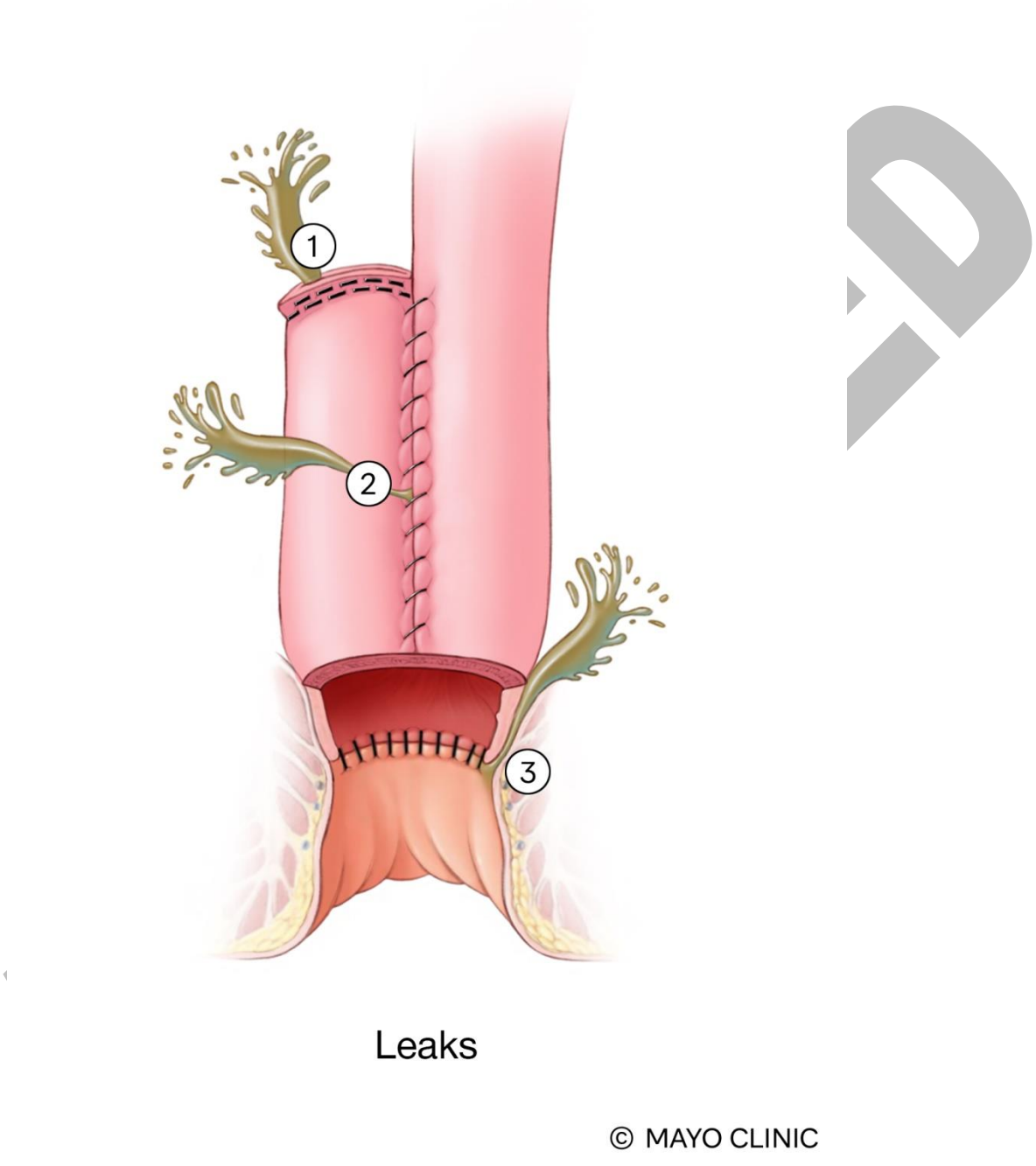
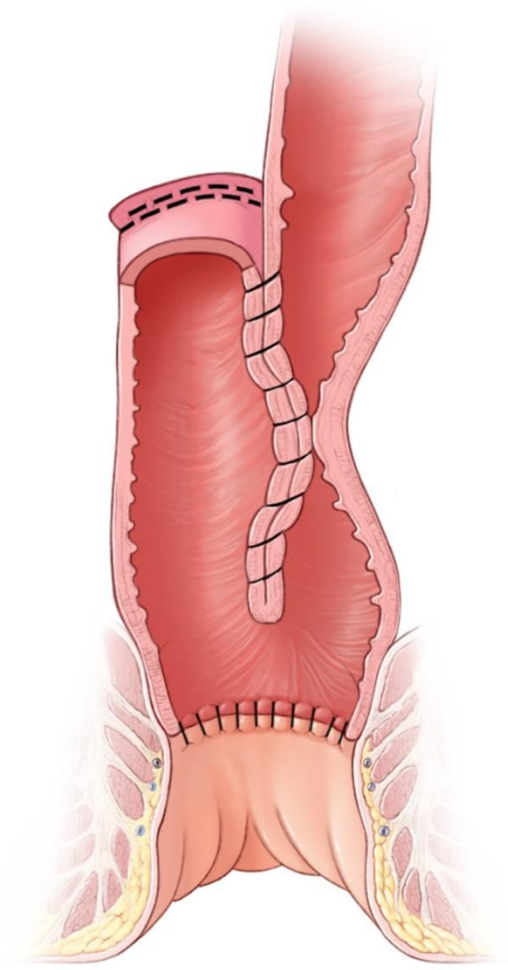


Figure 4. Common locations of pouch strictures, including a) pouch inlet, b) mid-pouch, and c) pouch-anal anastomosis.



Mid-pouch stricture

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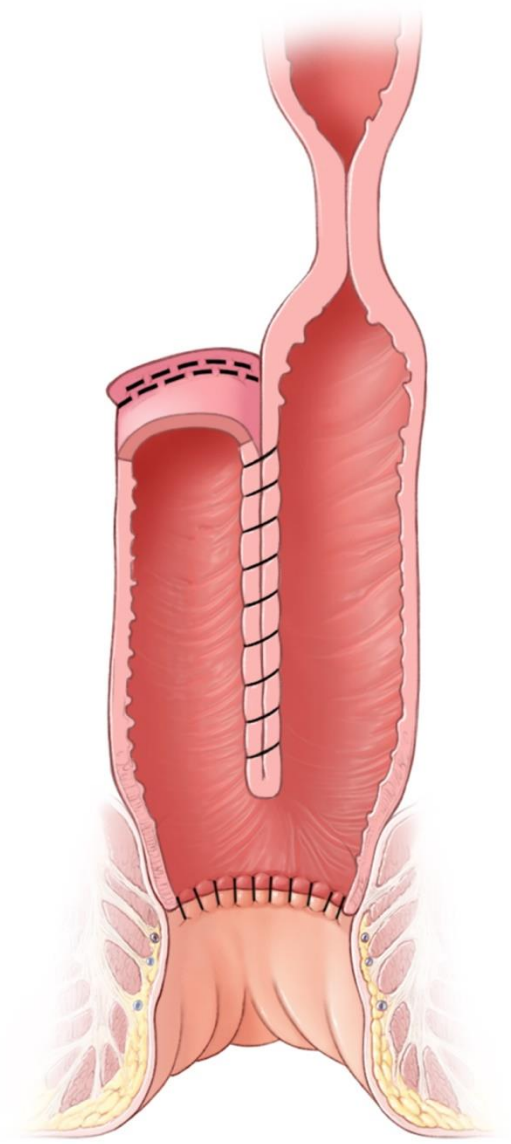
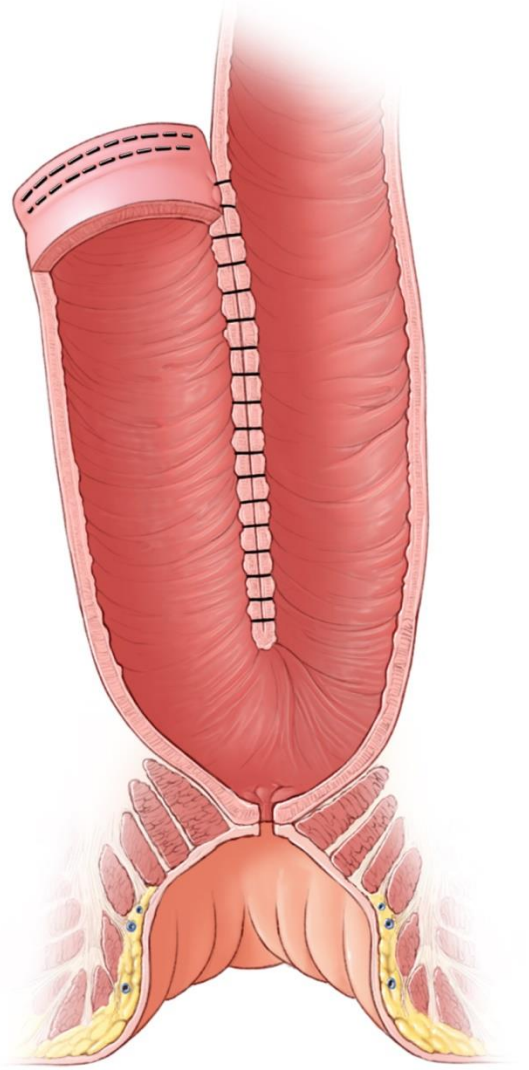


Inlet stricture



Pouch-anal anastomosis stricture

Figure 5. Afferent limb syndrome. Illustration of a sharp angulation of the afferent limb at the pouch inlet detected during pouchoscopy.

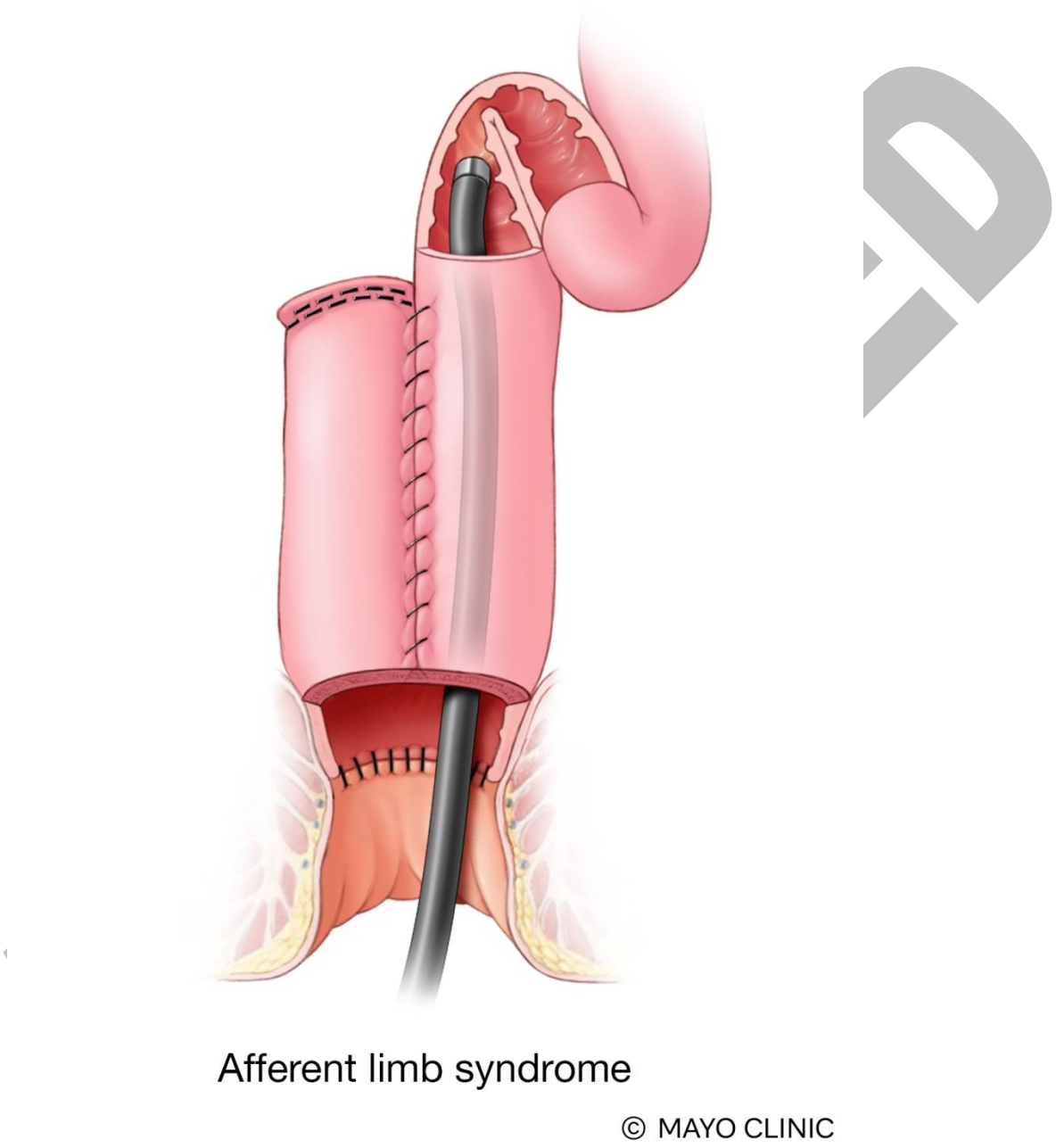


Table 1. Summary of the management options for inflammatory pouch disorders.

	Management	Notes
Idiopathic pouchitis	First line: antibiotics, most often ciprofloxacin or metronidazole. Other options: amoxicillin/clavulanic acid, rifaximin, tinidazole, trimethoprim/sulfamethoxazole	Acute pouchitis is usually responsive to a 2-week course of antibiotic monotherapy.
Chronic antibiotic dependent pouchitis	Chronically suppressive antibiotics (usually given as a single antibiotic for a certain period), with a rotating schedule. Limited efficacy for probiotics (VSL#3).	Some patients might need a combination of antibiotics given concomitantly for induction and/or maintenance.
Chronic antibiotic refractory pouchitis	First line: biologics, especially vedolizumab. Potential therapies: infliximab, adalimumab, ustekinumab, immunomodulators, 5-ASA, steroids.	Exclude secondary causes of pouchitis.
Crohn's like disease (CD) of the pouch	Pharmacology therapy is similar to CARP: biologics with adjunctive therapy of immunomodulators, steroids. Inflammatory CD of the pouch: • Anti-TNFs recommended for induction and maintenance. • Vedolizumab and ustekinumab can be used for induction and maintenance. • Immunomodulators can be used as monotherapy or combination with anti-TNFs. • Budesonide can be used for induction. Fibrostenotic or penetrating disease: • Pouchoscopy for balloon dilation and/or stricturotomy • Surgery • Pouch excision in severe cases.	Several biologics have higher efficacy rates in CD of pouch when compared with CARP.
PSC-associated pouchitis	Management is based on expert clinic practice.	Patients with PSC-IBD and IPAA are at increased risk

	• 1st line: Antibiotics; patients usually need chronic rotating antibiotics. • Refractory disease: immunomodulators and biologics • 5-ASA formulation (Pentasa)	of pouchitis and progression to chronic pouchitis, when compared with non-PSC. PSC-pouchitis is associated with more severe endoscopic pouch inflammation, pre pouch ileitis, and refractory pouchitis.
Ischemic pouchitis	Unlikely to respond to antibiotics. Severe cases might require hyperbaric oxygen therapy or pouch surgery.	Related to surgical factors / hypoperfusion.
Infectious pouchitis	CDI: responsive to conventional therapies for CDI. Bidirectional FMT can be effective in severe cases. CMV: ganciclovir or valganciclovir (similar to CMV colitis treatment)	Patients with pouchitis due to CDI might exhibit more systemic symptoms and higher recurrence rates than non-IPAA patients.
Cuffitis	First line: topical mesalamine (induction and maintenance) Other therapies: • Topical steroids for induction only, if failed topical mesalamine. • Tacrolimus suppositories if refractory (expert experience).	

PSC: primary sclerosing cholangitis; CARP: chronic antibiotic refractory pouchitis; Anti-TNF: anti-tumor necrosis factor alpha; IBD: inflammatory bowel disease, IPAA: ileal pouch anal anastomosis; CDI: *Clostridioides difficile* infection; FMT: fecal microbiota transplant; CMV: cytomegalovirus.

Table 2. Summary of the management options for structural pouch disorders.

	Management	Notes

Anastomotic leaks	• Percutaneous drainage
	• Surgery
	• Novel techniques:
	  ○ Endoscopic over-the-scope clip – for tip of the J leak
	  ○ Endo-sponge assisted early surgical closure	

Pouch-related fistulas	Management is mainly surgical, with multiple procedures often required: • Fistulotomy, fistula plug, seton placement • Abdominal revision of the pouch, re-do pouch, resection of retained rectum, mucosectomy, transanal ileal pouch advanced flap, transvaginal repair, etc. High pouch failure rates, requiring excision and diversion.	- High recurrence rates - Heterogenous surgical approaches, local vs. abdominal depending on location of fistula
Strictures	• Pharmacology therapy – if inflammatory stricture, such as CLDP • Digital and Hegar dilatation – for pouch-anal anastomosis strictures • Endoscopic balloon dilation – mid-pouch and pouch-inlet strictures • Stricturotomy (endoscopic or surgical) • Surgical revision – refractory cases	Management varies depending on etiology and location.

Floppy pouch complex	• Behavioral management
	  ○ Avoidance of excessive straining
	  ○ Modification of stool consistency
	  ○ Physical therapy with biofeedback therapy - retraining of the pelvic floor muscles
	• Endoscopic procedures
	  ○ Mucosal banding
	  ○ Excision of pouch prolapse
	• Definitive surgical interventions
		Defined as the presence of pouch prolapse, afferent limb syndrome, enterocele, redundant loop and folding pouch.

Afferent limb syndrome	Management is mainly surgical. • Laparotomy and ileopexy/pouchopexy • Pouch excision (refractory cases)	

CLDP – Crohn's like disease of the pouch.

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