A Comprehensive Approach to Pouch Disorders

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Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the surgical procedure of choice for patients with medically refractory ulcerative colitis (UC) or indeterminate colitis, UC with colonic dysplasia or neoplasia, and familial adenomatous polyposis. In general, patients experience good function outcomes and quality of life with an IPAA. Although pouchitis is the most well-recognized and frequent complication after IPAA, a number of additional inflammatory, postsurgical, structural, neoplastic, and functional complications may occur, resulting in pouch dysfunction. We herein provide a comprehensive review of pouch function and an approach to diagnosis and management of pouch complications.

Key Words: ileal pouch-anal anastomosis, pouch dysfunction, pouchitis

INTRODUCTION

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA), first described in 1978 by Parks and Nicholls,[1] has become the surgical procedure of choice for patients with medically refractory ulcerative colitis (UC) or indeterminate colitis, UC with colonic dysplasia or neoplasia, and familial adenomatous polyposis (FAP).[2] This procedure allows for the removal of the affected colon and rectum while maintaining gastrointestinal continuity without a permanent stoma, leading to improvement of symptoms and avoidance of medications in UC, substantial reduction in the risk of dysplasia and colon cancer, and improvement in health-related quality of life.[3, 4] Although most patients experience good functional outcomes after IPAA,[5] a number of early and late complications may occur, resulting in pouch dysfunction. These include inflammatory, infectious, postsurgical, structural, functional, and dysplastic or neoplastic complications of the pouch (Table 1).

POUCH ANATOMY

To properly care for patients with an IPAA, a basic understanding of pouch anatomy is important. A number of pouch configurations have been developed and utilized since the IPAA was first introduced, including pouches with 2 (J), 3 (S), and 4 (W) limbs of small intestine to form the ileal reservoir.[6] J pouches have a smaller volume compared with S pouches (305 mL vs 420 mL, respectively) but require only 30 to 40 cm of ileum for construction compared with 50 cm required for an S pouch or W pouch.[7] Perioperative complication rates are similar among the various configurations,[8] although S and W pouches are more technically demanding to construct. Due to an additional 2 to 3 cm of mesenteric reach achieved with an S pouch, this configuration can be considered when excessive mesenteric tension is of concern. However, difficulty with evacuation and need for pouch intubation are more common with the S configuration, limiting its utility and maintaining the notion that a J configuration is preferred for reliable function and ease of construction.[8, 9]

NORMAL POUCH FUNCTION

It is important to educate patients that normal pouch function is not the same as life with a healthy colon. However, patients generally experience good pouch function after IPAA with an average of 5 to 6 bowel movements per day and 1 to 2 per night beginning 12 months after IPAA completion.[5, 10, 11] Patients may experience higher stool frequency and looser stools within the initial 6 to 12 months as they adapt to the IPAA. This is an important point to emphasize when counseling FAP patients before IPAA as they may be less accustomed to increased stool frequency compared with those with UC. Leakage of stool and mucous may also be present in this initial postoperative period. If so, a barrier ointment should be used for skin protection as skin breakdown can cause significant discomfort.

Fortunately, after this 12-month adaptation period, stool frequency stabilizes over time with only a slight increase after 20 to 30 years.[5, 11] Within the first 5 years after IPAA, most patients have good daytime fecal continence. However, as sphincter strength decreases over time, fecal incontinence becomes more common, affecting up to 40% to 50% of patients after 20 to 30 years.[11] Dietary modifications with stool thickening foods (eg, applesauce, bananas, breads, pasta, rice,

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TABLE 1. Classification of Pouch Dysfunction

Inflammatory	Postsurgical or Mechanical	Functional	Neoplastic

• Idiopathic pouchitis
• Secondary pouchitis
  • CD of the pouch
  • PSC-associated
  • Ischemic
  • Infectious
  • NSAID-associated
  • Radiation-induced
• Cuffitis
	• Leak
	• Pelvic abscess
	• Pouch sinus
	• Pouch fistula
	• Anastomotic stricture
	• Small bowel obstruction
	• Afferent limb syndrome
	• Efferent limb syndrome
	• Pouch prolapse
	• Pouch volvulus
		• Dyssynergic defecation
		• Reduced pouch compliance
		• Irritable pouch syndrome
			• Dysplasia or carcinoma of the ileal pouch
			• Dysplasia or carcinoma of the anal transition zone
			• Pouch adenomas (FAP)

and peanut butter), stool bulking agents (eg, psyllium or methylcellulose) given in the form of a slurry (1 tablespoon of agent mixed with 4 ounces of water or yogurt), and antidiarrheal medications (eg, loperamide or diphenoxylate/atropine) may be helpful in situations of high frequency, seepage, or incontinence. Overall, patients experience great satisfaction after IPAA and excellent quality of life (QoL) as it relates to general health, energy, relationships, work, and social activity. In fact, QoL improves 12 months after restorative proctocolectomy and becomes indistinguishable from the general population.[12, 13]

POUCH EVALUATION

Disorders of the pouch may present with a wide range of symptoms, including increased stool frequency, urgency, incontinence, hematochezia, abdominal pain, and perianal pain being among the most common.[14, 15] Due to their nonspecific nature, symptoms alone are insufficient to make a definitive diagnosis.[14] Thus, appropriate investigation of pouch disorders relies on various diagnostic tests and procedures, including endoscopy, histology, imaging, labs, stool tests, and/or assessment of pouch function with anorectal manometry (ARM) and balloon expulsion testing (BET) (Fig. 1).

Endoscopy

Endoscopy is the mainstay of pouch evaluation, especially for suspected inflammatory, mechanical, and dysplastic pouch complications. During pouchoscopy, it is important to correctly identify pouch landmarks, including the afferent limb and pouch inlet, tip of the J (in J pouches), efferent limb, pouch outlet, and rectal cuff (Fig. 2).[16] Images should be captured from each of these areas for appropriate documentation. For inflammatory pouch disorders, pouchoscopy provides valuable information on the configuration and distensibility of the pouch body, the severity and extent of inflammation, and the presence of prepouch ileitis, inflammatory polyps, or cuffitis.[16] Pouchoscopy also allows for assessment of postsurgical or mechanical complications including strictures, fistulae, and sinus tracts.

Histologic evaluation of biopsies obtained during pouchoscopy provides further information regarding the presence of granulomas, viral inclusion bodies (for CMV infection), and dysplasia. However, the role of histology in accurately grading the degree of acute or chronic inflammation is limited.[14, 16] Furthermore, acute inflammatory changes (ie, polymorphonuclear leukocyte infiltration, crypt abscesses, and mucosal erosions) are nonspecific, whereas changes of chronic inflammation (ie, mononuclear cell infiltration and villous blunting) are commonly seen in asymptomatic patients, likely as an adaptive response to fecal stasis.[14]

Imaging

Abdominal and pelvic imaging may include computed tomography (CT) or magnetic resonance (MR) enterography, pelvic MRI, water-soluble contrast pouchogram, and MR or barium defecography. Computed tomography and magnetic resonance enterography provide information regarding the presence of abscesses, strictures, and inflammation of the pouch or small bowel.[16] Enterography offers the advantage of better visualization of the small bowel compared with conventional CT or MR. In contrast to CT, pelvic MRI allows for more accurate assessment of complex perianal disease, chronic sinus tracts, and length of the remaining rectal cuff.[14] A water-soluble contrast pouchogram, or gastrografin enema, may provide useful information regarding the pouch anatomy and shape, whereas barium or MR defecography allows for a more dynamic assessment of pouch function.[14]

Examination Under Anesthesia

With both diagnostic and therapeutic capabilities, examination under anesthesia (EUA) is an important tool when evaluating pouch complications. Examination under anesthesia is useful in diagnosing Crohn's disease (CD) of the pouch and can provide valuable information regarding the presence and location of various structural abnormalities, including strictures, leaks, sinuses, and fistulae.[14] This is especially important for patients who are not able to tolerate an unsedated exam due to physical or psychological discomfort.[14] Although data is limited in patients with an IPAA, much of what we know regarding the use of EUA in patients with an intact colon can be extrapolated

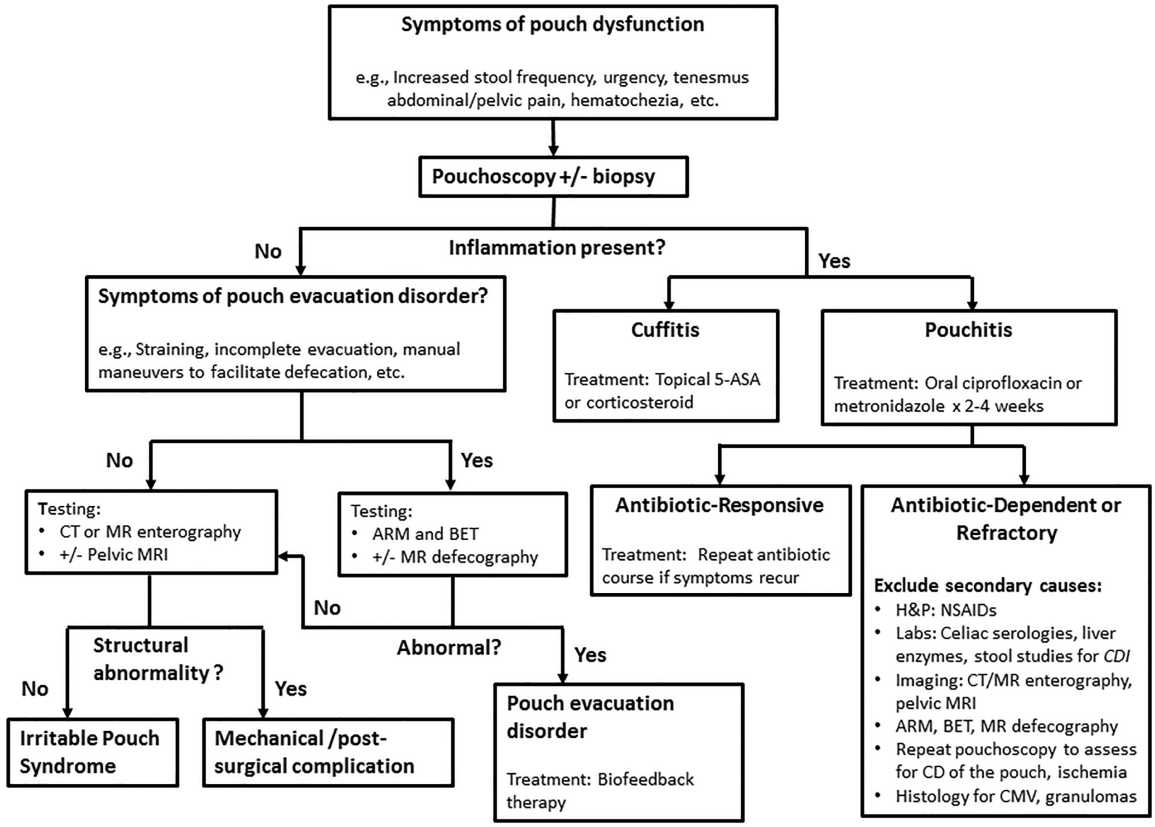

FIGURE 1. Diagnostic and management algorithm for pouch dysfunction. Stepwise approach for evaluation and management of patients presenting with of pouch dysfunction.

to the IPAA population. For example, EUA combined with either MRI or endoscopic ultrasound was shown to increase the diagnostic accuracy of perianal fistulae in Crohn's disease to 100%.[17] Lastly, EUA allows for certain therapeutic interventions, including sinus tract debridement.[18]

Laboratory Evaluation

Laboratory assessment is especially important in patients with chronic pouchitis to exclude secondary causes of pouchitis. This may include liver enzymes to screen for the presence of primary sclerosing cholangitis (PSC), celiac serologies to rule out concomitant celiac disease, and stool testing for *Clostridium difficile* infection (CDI). Depending on the circumstances, further lab evaluation may be useful to investigate for the presence of anemia, vitamin B_{12} deficiency, and vitamin D deficiency.[14] Inflammatory markers, such as C reactive protein (CRP), although nonspecific, may also be helpful when evaluating pouch inflammatory disorders.

Functional Assessment

As noted previously, MR and barium defecography are useful in assessing pouch function when there is suspicion of a functional or pouch evacuation disorder. Anorectal manometry and BET are also commonly used in this situation, although data with regard to what constitutes normal and abnormal values for ARM and BET in patients with an IPAA are lacking.[19]

POUCH DYSFUNCTION

Inflammatory and Infectious Complications

Patients with an ileoanal pouch are susceptible to a number of inflammatory complications, of which pouchitis is the most frequent long-term inflammatory complication after IPAA. Pouchitis is a rather nonspecific term that encompasses a variety of different causes and should be further classified as idiopathic or secondary.[20] Secondary causes of pouchitis are many and include infections, ischemia, Crohn's disease (CD) of the pouch, PSC-associated pouchitis, radiation, and medications, especially nonsteroidal anti-inflammatory drugs (NSAIDs). Secondary causes of pouchitis are important to consider, as up to 20%–30% of patients who present with chronic pouchitis may have an identifiable secondary cause.[21]

Idiopathic Pouchitis

Traditionally, it has been recognized that up to 50% of UC patients who undergo proctocolectomy with IPAA experience

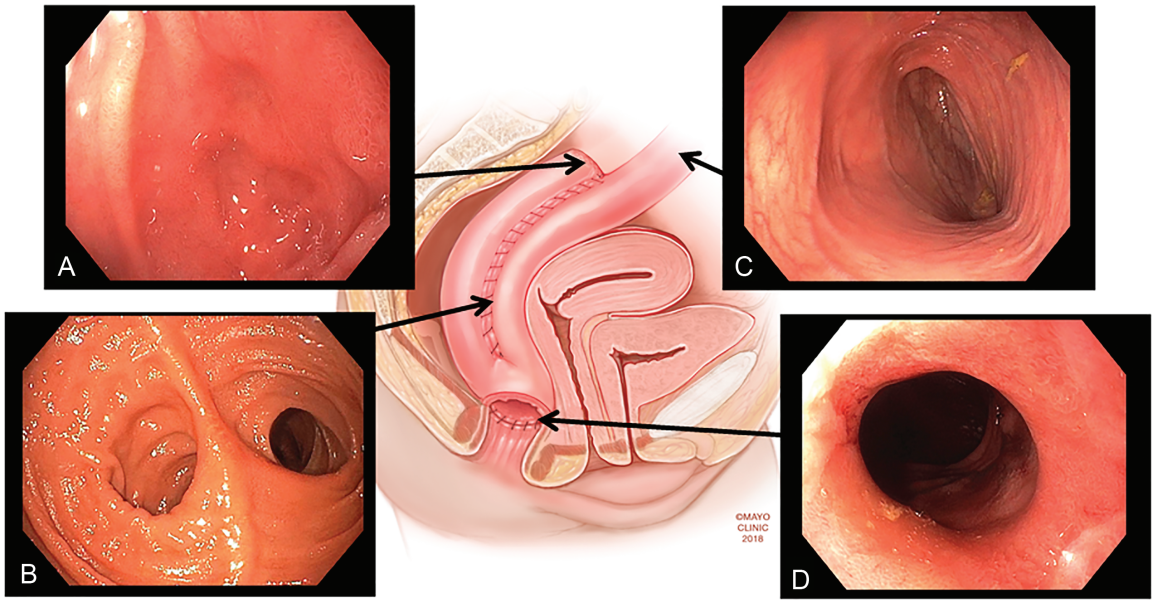

FIGURE 2. Normal pouch anatomy. Cross-sectional view of a normal J pouch configuration with endoscopic views of (A) the tip of the J pouch, (B) "owls' eye" appearance in the pouch body, (C) afferent limb just proximal to the pouch body, and (D) anal transition zone leading to rectal cuff.

at least one episode of pouchitis.[2, 22] However, recent data suggest that up to 80% develop at least 1 episode of pouchitis at 30 years after IPAA.[11] In contrast, patients with FAP have been thought to only rarely develop pouchitis. More recent studies, however, suggest that pouchitis is a more frequent complication in FAP than previously recognized, occurring in approximately 20% of patients.[13, 23]

In the vast majority of pouchitis cases, inflammation of the ileal pouch reservoir is considered idiopathic. The pathogenesis of idiopathic pouchitis remains unclear but is thought to result from an abnormal mucosal immune response to alterations among mucosal and luminal microflora in genetically susceptible patients.[16, 24] Pouch microbiota are believed to play an important role in the pathogenesis of pouchitis. This is supported by the observation that pouchitis occurs only after restoration of the fecal stream through the pouch and that antibiotics are the most effective treatment.[25] Fecal stasis due to altered bowel anatomy during construction of the ileal pouch promotes alteration of commensal bacteria, or dysbiosis.[16] Postsurgical complications, including anastomotic strictures or pouch evacuation disorders, may further promote fecal stasis. Dysbiosis and exposure to an increased microbial load promotes colonic metaplasia of the ileal mucosa. This, in turn, activates the innate and the adaptive mucosal immune systems, which have been shown to be altered in patients with pouchitis compared with those with a healthy pouch.[26] Together, these changes create an environment susceptible to the development of inflammation, leading to pouchitis.

Certain genetic and individual risk factors for pouchitis have also been identified. Polymorphisms in the interleukin (IL)-1 receptor antagonist and NOD2/CARD15 have been associated with increased risk for pouchitis.[16, 20] Individual risk factors include extensive UC before IPAA, the presence of backwash ileitis, extraintestinal manifestations of UC—especially PSC—concurrent autoimmune disorders, and NSAID use.[20, 27]

Pouchitis may be further classified based on duration of pouch-related symptoms as either acute (<4 weeks) or chronic (≥4 weeks). Response to antibiotic treatment is another important distinguishing factor that allows for classification into antibiotic-responsive, antibiotic-dependent, and antibiotic-refractory phenotypes.[16] It is important to emphasize that pouchitis is a spectrum of disease, ranging from acute, antibiotic-responsive to chronic, antibiotic-refractory disease.

Patients with pouchitis may present with a variety of pouch-related symptoms, including increased stool frequency, urgency, tenesmus, incontinence, nocturnal seepage, blood per ani, abdominal cramping, and pelvic discomfort. Occasionally, more systemic manifestations such as fevers, chills, and weight loss may be present. Given the nonspecific nature of symptoms, the diagnosis of idiopathic pouchitis cannot be made from symptoms alone. Rather, characteristic endoscopic and histologic findings are required to accurately diagnose idiopathic pouchitis and to rule out secondary causes. Several scoring systems have been developed to aid in the diagnosis of pouchitis, including the 18-point Pouchitis Disease Activity Index (PDAI), consisting of symptom, endoscopy, and histology subscores.[28] However, the PDAI and other scoring systems have been most useful as research tools.

When the diagnosis of pouchitis is suspected, pouchoscopy should be performed to confirm the diagnosis. As discussed previously, all pouch landmarks must be identified, and careful attention should be given to determine the severity and extent

of mucosal inflammation. Endoscopic findings in idiopathic pouchitis typically consist of diffuse inflammation throughout the pouch body, with sparing of the afferent limb (Fig. 3a).[29] Endoscopy is the most accurate method for grading the degree of inflammation. Severity of inflammation may range from mild pouch erythema, edema, increased granularity, or loss of vascular pattern to more severe changes consisting of friability, hemorrhage, ulcerations, and erosions.[30] Prepouch ileitis may also be present and can mimic CD of the pouch or PSC-associated pouchitis. Some changes may be specific to chronic pouchitis, including loss of the "owls' eye" configuration of the J pouch, inflammatory polyps, and poor dispensability of the pouch.[16]

Biopsies are routinely obtained during pouchoscopy, although histology has a limited role in grading the degree of inflammation compared with endoscopic evaluation.[16, 26, 30] In idiopathic pouchitis, histologic assessment may show acute inflammatory changes, including neutrophil infiltration, ulceration, and crypt abscesses,[16] which are often superimposed on a background of chronic inflammatory changes, consisting of chronic inflammatory cell infiltrate, villous atrophy, and crypt hyperplasia. These chronic histologic findings alone are not diagnostic of pouchitis as they likely represent adaptive changes to fecal stasis of the ileal reservoir.[16, 31] Various histologic features, including granulomas or viral inclusions, may point to secondary causes of pouchitis.

Treatment depends upon an accurate diagnosis and classification of pouchitis. For most cases of acute idiopathic pouchitis, antibiotics are the mainstay of therapy. In clinical practice, first-line therapy includes ciprofloxacin (500 mg twice daily) or metronidazole (500 mg 3 times daily) for 2 to 4 weeks. In one small randomized controlled trial comparing ciprofloxacin and metronidazole in acute pouchitis, ciprofloxacin led to a greater reduction in total PDAI scores and was associated with fever adverse events.[32] Alternative antibiotic regimens may include rifaximin, tinadazole, trimethoprim/sulfamethoxazole, or amoxicillin/clavulanic acid, although evidence to support use of these antibiotics is limited.[33, 34] For those who do not respond to initial monotherapy, combination therapy could also be considered.[35–38]

Of all patients with pouchitis, 5%–19% will develop chronic pouchitis, some of whom ultimately progress to pouch failure.[13, 16] Treatment of chronic pouchitis depends upon the response to antibiotics and remains largely empiric given a lack of quality data. Those with antibiotic-dependent pouchitis respond to antibiotics but have frequent relapses if antibiotics are withdrawn. Treatment options include prolonged courses of low-dose antibiotics or alternating antibiotic regimens to minimize risk of antibiotic resistance. Given the black-box warning regarding the risk of serious tendinopathy, prolonged use of fluoroquinolones should be avoided. Those who do not respond to antibiotics have chronic antibiotic-refractory pouchitis. In chronic antibiotic-refractory pouchitis, secondary causes of chronic pouchitis must be considered (Table 1).[39] Once secondary causes have been excluded, pharmacotherapy options

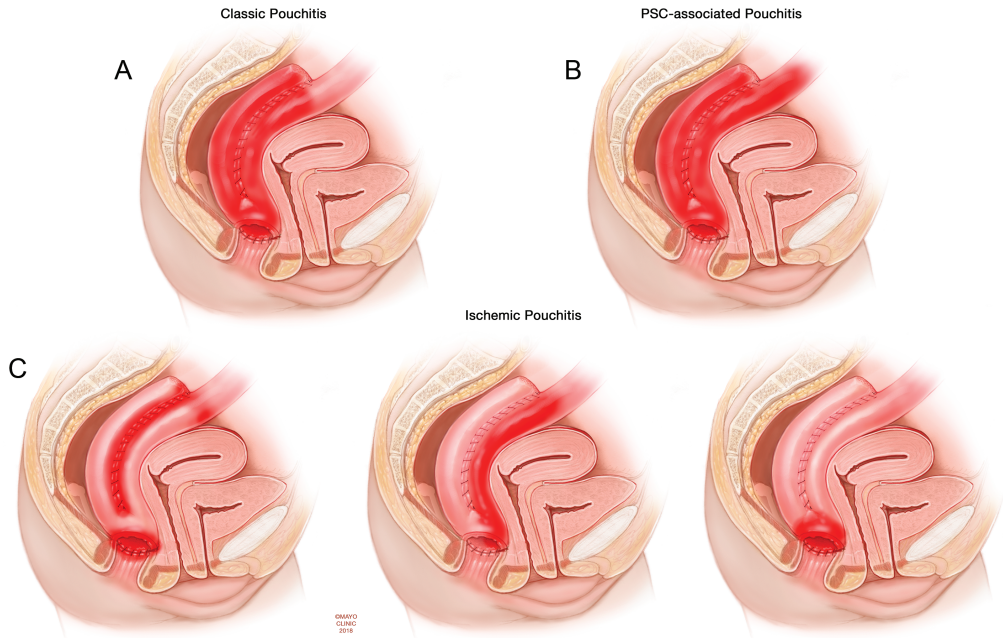

FIGURE 3. Patterns of pouchitis. Distribution of pouch and ileal inflammation: (A) classic (or idiopathic) pouchitis—diffuse inflammation throughout the pouch body with sparing of the afferent, (B) PSC-associated pouchitis—diffuse inflammation throughout the pouch body with involvement of a long segment of the afferent limb, and (C) ischemic pouchitis—asymmetric distribution of inflammation seen only along the suture line, the afferent limb with relative sparing of the efferent limb, or the distal pouch.

are similar to the treatment of UC, including topical or oral 5-aminosalicyates (5-ASAs), topical or oral corticosteroids, immunomodulators, and biologics. Although evidence to support 5-ASA preparations is mostly anecdotal,[40, 41] the relative safety of this class of medications makes it an appealing option. Corticosteroids may be considered when antibiotics fail, with 1 small study showing a benefit of oral budesonide 9 mg/day in inducing remission.[42] Multiple observational studies and case reports have described benefit with biologics, including infliximab, adalimumab, vedolizumab, and ustekinumab.[43–46]

The prevention of pouchitis has been studied with results that are conflicting. Two small RCTs showed benefit of VSL#3, a Lactobacillus-containing proprietary probiotic, in both the primary and secondary prevention of pouchitis.[47, 48] However, this practice has not been widely adopted in clinical practice, due to lower response rates to VSL#3 in post-marketing, open-label studies.[16]

Crohn's Disease of the Pouch

In contrast to UC, a preoperative diagnosis of CD is generally considered a contraindication to IPAA due to increased risk of complications from recrudescent CD, including pouch dysfunction, fistula formation, and subsequent need for pouch excision.[14, 49] However, an IPAA can be offered to a select group of highly motivated patients with isolated Crohn's colitis without evidence of small bowel or perianal involvement. Pouch retention rates at 10 years in this select cohort reach 71% and give favorable functional results.[50] Crohn's disease may also be diagnosed inadvertently in colectomy specimens of patients with a preoperative diagnosis of UC or indeterminate colitis.[51] Nevertheless, most patients with CD of the pouch are those who develop de novo CD in the postoperative period, which may present months to years after IPAA.[52] In total, the cumulative frequency of CD of the pouch ranges from 2.7%–13%.[51, 52]

Although the pouch, prepouch ileum, and cuff are most affected, any part of the gastrointestinal tract may be involved. Similar to CD in nonpouch patients, CD of the pouch can be classified into inflammatory, fibrostenotic, and fistulizing phenotypes.[14, 51] Presenting symptoms are nonspecific and overlap with other pouch inflammatory disorders. Timing to onset of Crohn's symptoms is crucial in distinguishing de novo CD of the pouch versus a postoperative complication (eg, a leak, which results in a chronic fistula tract), with CD typically developing more than 6 to 12 months after IPAA completion.[49] Endoscopy is typically the first step in diagnosis. Endoscopic features suggestive of CD of the pouch include mucosal ulcerations, fistulae, and strictures involving the afferent limb or other parts of the small bowel in the absence of NSAIDs.[53] Despite somewhat limited utility in establishing the diagnosis, biopsies should be obtained for histology. Granulomas on histology are specific for CD of the pouch but present in only 10%–12%.[54] Radiographic evaluation with CT or MR enterography and CT or MRI of the pelvis can also be helpful to determine if there is evidence of proximal small bowel disease and to delineate disease extent, severity, and the anatomy of extraluminal complications of CD (eg, fistulizing disease).[51, 52]

Little data exist on the treatment of CD of the pouch, which may consist of medications, endoscopy (eg, balloon dilation of strictures), and surgery (eg, stricturoplasty or pouch excision).[51, 53] In general, pharmacologic therapy is similar to that of chronic pouchitis and consists of antibiotics, 5-ASAs, corticosteroids, immunomodulators, and biologics. The choice of medication depends in part on the specific phenotype, with fistulizing disease requiring the most aggressive treatment regimen.[52] A recent systematic review suggests antitumor necrosis factor (anti-TNF) agents are more efficacious in inducing remission in patients with CD of the pouch (64%) compared with refractory pouchitis (10%), highlighting the importance of distinguishing between these 2 entities.[44] Pouch excision is reserved for those who develop refractory symptoms related to CD of the pouch despite maximal treatment efforts; in fact, CD of the pouch is one of the leading causes of pouch failure.[51]

Psc-Associated Pouchitis

Up to 80% of patients with PSC have associated inflammatory bowel disease (IBD), with UC being most common.[55] Patients with PSC who undergo IPAA represent a unique population. These patients carry an increased risk of pouchitis, including chronic pouchitis.[56, 57] Thus, PSC-associated pouchitis has a distinct clinical phenotype and should be thought of as a separate entity from idiopathic pouchitis. Endoscopically, PSC-associated pouchitis is often associated with long-segment inflammation of the afferent limb in addition to diffuse inflammation of the pouch body (Fig. 3b).[16, 56] Thus, any patient with significant prepouch ileitis should be evaluated for PSC.[56] Additionally, PSC-associated pouchitis seems less responsive to antibiotic therapy. Experience at our institution has suggested efficacy of topical 5-ASAs, which should be consider as the next step in management if there is no response to a trial of antibiotics. Anecdotal data from other institutions has also suggested benefit of oral budesonide for the treatment of PSC-associated pouchitis.[26]

Ischemic Pouchitis

Ischemia has been implicated in a subset of patients with pouchitis, especially chronic antibiotic-refractory pouchitis. Ischemic pouchitis is thought to be driven by factors during surgery, including tension on vessels supplying the distal ileum, disruption of the ileocecal artery or distal branches of the superior mesenteric artery during colectomy that supply the distal ileum, tension of the mesentery, or torsion of the mesentery, all of which may result in relative hypoxia.[21] Males, obese patients, and those who gain excessive weight after IPAA may be more prone to mesenteric tension due to foreshortened mesentery.[21, 58] Supporting this theory is the lower observed rate of pouchitis in S pouches, a configuration with less mesenteric tension than

a J pouch.[58] Ischemic pouchitis can be distinguished endoscopically by asymmetric distribution of inflammation with sharp demarcation (Fig. 3c). This may include inflammation and ulceration confined to the distal pouch, along the suture line, or involving one limb of the pouch but not the other.[21, 58] Many patients with ischemic findings on endoscopy have minimal symptoms.[20] For those requiring treatment for more significant symptoms, antibiotics seem to be less effective. Redo pouch surgery may be necessary in more severe cases.[58, 59]

Infectious Pouchitis

Infectious causes of pouchitis, including *Clostridium difficile* infection (CDI) and cytomegalovirus (CMV), have been increasingly recognized. The true incidence of CDI in patients with an IPAA is unknown.[60] However, up to 10% of symptomatic IPAA patients tested positive for *C. difficile* in a single tertiary center study.[61] *Clostridium difficile* infection should be considered in any patient with recurrent or chronic pouchitis. Endoscopic findings are nonspecific with pseudomembranes occurring in a minority of patients.[61] Recommended first-line treatment for CDI of the pouch is oral vancomycin, as many patients will have already been exposed to metronidazole.[26, 61] Fecal microbiota transplantation (FMT) can be considered in refractory CDI of the pouch. However, FMT seems to be less effective and may be associated with higher recurrence rates (up to 40%) in patients with IPAA compared with the general population.[62] Cytomegalovirus infection can also lead to chronic pouchitis. As is similar for patients with IBD and an intact colon, immunosuppression may be a risk factor for CMV pouchitis.[63] Similar to CMV colitis, treatment consists of antiviral therapy with valganciclovir or ganciclovir and seems effective.[63] Although uncommon, multiple additional organisms have been implicated in cases of chronic pouchitis, including *Campylobacter, Salmonella,* and *Candida.*[21]

Cuffitis

During IPAA formation, 1 of 2 anastomotic techniques is used: mucosectomy of the anal transition zone(ATZ) and hand-sewn anastomosis or a stapled anastomosis preserving the ATZ.[29] The stapled approach is generally preferred due to ease of technical construction and the improved functional outcomes due to preservation of the ATZ.[64] During the stapled approach, it is necessary to leave a 1–2 centimeter segment of rectum to allow transanal passage of the stapler head.[65] The tradeoff for improved function is the risk for the development of inflammation (cuffitis) or dysplasia of the residual rectal mucosa or ATZ.[29] Cuffitis refers to recurrence of UC in the residual "cuff" of rectal mucosa after IPAA. Symptoms may overlap with pouchitis, although bleeding is more common with cuffitis. The diagnosis of cuffitis requires endoscopic evidence of inflammation of the residual rectal mucosa to distinguish it from pouchitis, although the 2 may sometimes coexist. Most cases of cuffitis respond to topical therapy with 5-ASAs or corticosteroids.[29, 65] Oral antibiotics are generally not effective. In cases of medially refractory cuffitis, transanal mucosectomy with pouch advancement may be considered.[66]

POSTSURGICAL AND MECHANICAL COMPLICATIONS

A number of early and late postsurgical complications may occur after IPAA, leading to pouch dysfunction and morbidity. Some of the more common complications include anastomotic leaks, sinuses, abscesses, fistulae, strictures, small bowel obstruction, volvulus, efferent/afferent limb syndrome, and pouch prolapse. Some postsurgical complications, including strictures, fistulae, and abscesses, may also be seen in inflammatory pouch conditions, especially CD of the pouch. Distinguishing between postsurgical complications and CD of the pouch can be challenging but is important as treatment differs depending on the underlying etiology. The vast majority of postsurgical fistulae occur in the immediate post-IPAA period or within the first 3 months after ileostomy reversal, when the patient first starts using their pouch. Fistulae that develop more than 6–12 months after IPAA in the absence of a known postoperative leak or abscess suggests CD of the pouch.[67] The anatomic location also aids in the diagnosis. The presence of a fistula or stricture at the anastomosis suggests a postoperative complication, whereas fistulae arising from crypts of the anal canal or stricture of the pre-pouch ileum suggest CD of the pouch.[67]

Anastomotic Leaks

An anastomotic leak is defined as a separation in the anastomosis leading to extrusion of pouch luminal contents which can lead to both acute and chronic complications.[53] Early postsurgical anastomotic leaks may lead to a pouch abscess or pelvic sepsis, whereas long-term complications include the formation of strictures, sinuses, and fistulae.[64] Most leaks occur at the posterior pouch-anal anastomosis or the tip of the J (in J pouches); leaks along the common channel staple line in the body of the pouch are far less frequent (Fig. 4).[58, 64] Early postoperative anastomotic leaks (<90 days of completion of IPAA) have been reported in up to 4.8% of patients, with late leaks (≥90 days) occurring in 1.7%.[13] Early leaks most commonly occur at postoperative days 4–6 and present with signs of sepsis, pelvic pain, ileus, and/or enteric or bilious output from the drain adjacent to the anastomosis.[53, 64] Computed tomography with intravenous contrast and/or rectal contrast can aid in the diagnosis. Water-soluble contrast enemas could also be used, although they are less sensitive than CT.[64] In acute leaks, antibiotics should be initiated and CT-guided drainage performed if the patient is stable and fluid collection is amendable to percutaneous drainage.[64] Occasionally, a patient will require

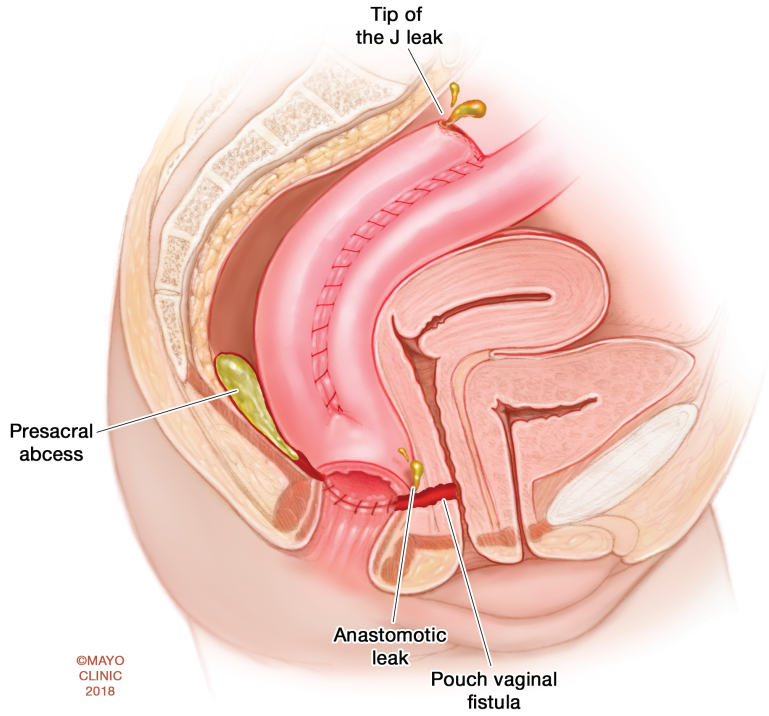

FIGURE 4. Postoperative pouch complications. Common sites of postoperative complications include leaks at the posterior pouch-anal anastomosis or the tip of the J (in J pouches); sinuses at the pouch-anal anastomosis that often extend into the pre-sacral space forming an abscess; and pouch-vaginal fistulae.

a washout with operative drains and conversion of a loop ileostomy to an end ileostomy to prevent intraluminal contents from reaching the pouch, which could otherwise occur to some degree with a loop ileostomy. In comparison, chronic leaks may be amendable to endoscopic therapy, including endoscopic needle-knife sinusotomy for presacral anastomotic sinuses or clipping devices to close leaks at the tip of the J.[58] However, chronic leaks often require transanal repair of the leak, pouch revision/reconstruction, or—rarely —pouch excision if all the aforementioned are unsuccessful.[68, 69]

Pouch Sinuses

Pouch sinuses, which consist of blind-ending tracts, most often develop as sequelae of anastomotic leaks and may occur in 2%–8% of patients undergoing IPAA.[70] The pouch-anal anastomosis is the most common site of sinuses, often with extension into the presacral space, as a leak is most frequently located in the posterior staple line where there is the greatest amount of tension on the anastomosis (Fig. 4).[53] Clinical presentations may range from asymptomatic to pelvic sepsis or recurrent pouchitis. Sinus openings can often be detected during careful pouchoscopy, although CT or MRI is typically needed to assess the extent of the sinus and to distinguish it from a fistula.[53] When small and asymptomatic, close observation may allow for adequate healing without specific intervention. When required, interventions may include incision and drainage, unroofing, primary closure of the sinus, placement of serial mushroom catheters, needle-knife sinusotomy, and diverting ileostomy. However, pouch failure can occur in up to 33%, requiring pouch reconstruction or excision.[70]

Abscesses

Pelvic abscesses after IPAA occur in up to 4.6% of patients in the early postoperative period (<90 days from IPAA completion).[2] Abscesses may form due to an anastomotic leak, but can also develop in the absence of an identifiable leak.[64] Perianal abscesses may also occur as postoperative complications due to surgically induced ischemia or a leak. Perianal abscesses from postsurgical complications typically develop early in the postoperative course compared with perianal disease associated with CD of the pouch.[64] For pelvic abscesses, nonsurgical management with antibiotics and/or percutaneous drainage is often effective. Rarely, patients require surgical drainage.

Pouch Fistulae

Fistulae may develop at any level of the pouch and can extend to the skin, abdominal wall, perineum, or any adjacent hollow organ, including the vagina, bladder, and small bowel.[64, 71, 72] After IPAA, 4.2% of patients develop a pouch-related fistula, with most occurring as a late complication.[13] Pouch-vaginal

fistulae are most common, occurring in nearly 6% of women. They may develop from an iatrogenic intraoperative injury when the posterior vaginal wall is caught in the circular EEA stapler used to create the IPAA or may occur as a late complication related to CD of the pouch.[53, 71] Occasionally, pouch-vaginal fistulae may result from a leak at the pouch-anal anastomosis or body of the pouch (Fig. 4).[64, 73] Unfortunately, treatment of pouch-vaginal fistulae is notoriously difficult, with patients often requiring multiple operative interventions, including pouch advancement, transvaginal repair, or pouch reconstruction. Despite the numerous attempts, pouch failure requiring a pouch excision occurs in 22% to 35%.[64, 73–75]

Strictures

Strictures of the pouch are common, occurring in approximately 16% of patients after IPAA.[13] Strictures commonly arise from surgery-related ischemia, anastomotic tension, pelvic sepsis, NSAID use, or CD of the pouch.[53, 58, 64] Strictures most commonly occur at the pouch-anal anastomosis but can also occur in the pouch body and afferent limb.[53, 64, 76] When in the afferent limb, CD of the pouch should be considered. Strictures commonly present with abdominal cramping, straining, tenesmus, increased stool frequency, or a sense of incomplete pouch evacuation. Strictures may be treated endoscopically via balloon dilation, which has been shown to be efficacious and safe.[76] For strictures refractory to balloon dilation, endoscopic needle-knife stricturoplasty, surgical stricturoplasty, and pouch advancement can be considered.[58, 77] At our center, select patients with anastomotic strictures at the ileoanal anastomosis are taught self-dilation of the anastomosis to maintain patency after endoscopic or surgical dilation.

Miscellaneous Mechanical Complications

Similar to abdominal and pelvic surgeries for other causes, postoperative ileus and small bowel obstructions are common after restorative proctocolectomy with IPAA. Other mechanical pouch complications, although relatively rare, may also occur and warrant prompt recognition. This may include afferent and efferent limb syndromes, pouch volvulus, and pouch prolapse.

Afferent limb syndrome is caused by a distal small bowel obstruction due to acute angulation, prolapse, or intussusception of the afferent limb in the absence of a stricture.[78] Diagnosis is typically made radiographically by finding the dilated small bowel proximal to the pouch inlet or endoscopically due to angulation of the pouch inlet with difficulty intubating the afferent limb.[53, 78] In contrast, efferent limb syndrome is often caused by an excessively long efferent limb, leading to complete or partial obstruction of the pouch outlet.[58, 79] This is most typically seen in patients with an S pouch.[79] In both afferent and efferent limb syndromes, surgical intervention is typically required to relieve the obstruction.[53, 79]

Pouch prolapse is a rare complication, occurring in 0.3% of patients after IPAA.[80] Prolapse of the distal pouch is most common, although prolapse at the pouch inlet may occur.[58] Prolapse of the pouch may consist of mucosal tissue only or full thickness prolapse. For mucosal prolapse only, stool bulking agents and biofeedback therapy, when associated with pelvic floor dysfunction, may be effective initial therapies.[80] Resection of redundant mucosal tissue may be required if symptoms persist. Full thickness prolapse requires transabdominal pouchopexy with fixation of the pouch to the sacrum.[80] Pouch excision with permanent end-ileostomy is reserved for recurrent or refractory cases.[64, 80]

Pouch volvulus is exceedingly uncommon, with only a few cases reported.[81] When radiographic findings suggest volvulus of the pouch, early intervention is necessary to prevent ischemia and necrosis. Pouchoscopy allows for assessment of the mucosa and an attempt at endoscopic pouch reduction.[81] Surgical intervention consists of pouchopexy if mucosa is viable or pouch excision with end-ileostomy if it is nonviable.[64]

FUNCTIONAL AND DEFECATORY DISORDERS OF THE POUCH

Dyschezia, or difficult defecation, is a common presentation in patients with IPAA.[19] Often, impaired pouch evacuation is secondary to a mechanical pouch complication, such as an anastomotic stricture or a pouch inflammatory disorder. However, in the absence of a mechanical or inflammatory cause, a functional defecatory disorder should be considered. Among patients with an intact colon, functional defecatory disorders are characterized by paradoxical contraction or inadequate relaxation of pelvic floor muscles (ie, dyssynergic defecation) and/or inadequate propulsive forces during attempted defecation.[82–85] Dyssynergic defecation is quite common in patients with chronic constipation and is thought to be driven by maladaptive learning of sphincter contraction in response to an undesirable stimulus.[82, 84, 85] Similar to those with an intact colon, patients with an IPAA may also develop dyssynergic defecation.[19] This may develop from maladaptive learning as a consequence of the voluntary holding of stool and recurrent recruitment of pelvic floor muscles in the setting of frequent defecation.[19] Surgery-related nerve damage and structural changes may also contribute.[86]

Patients with impaired pouch evacuation may present with a number of nonspecific symptoms including abdominal and/or pelvic pain, bloating, constipation, straining, incomplete evacuation, and incontinence. Interestingly, patients with IPAA and nonrelaxing pelvic floor dysfunction (N-RPFD), or dyssynergic defecation, are more likely to develop chronic pouchitis.[19] This may be attributed to an increase in fecal stasis due to impaired pouch evacuation.

Dyssynergic defecation in patients with an intact colon is often diagnosed by ARM and BET, which are also frequently used in IPAA patients with suspected pouch evacuation disorders. However, these tests have not been validated in the IPAA population. Moreover, the altered anatomy in IPAA makes

interpretation challenging. Khanna et al showed that paradoxical contractions during manometric evaluation and failed balloon expulsion were more common in those with a functional pouch disorder compared with patients with an inflammatory or structural pouch disorder.[86] In another study, nearly 75% of IPAA patients with symptom suggestive of a pouch evacuation disorder met criteria for N-RPFD.[19] Most met criteria based on failed balloon expulsion (78%), with only 21% meeting criteria based on abnormal ARM.[19] Magnetic resonance and barium defecography are also useful diagnostic tests for evaluating functional defecatory disorders of the pouch, as they provide valuable information regarding pouch empting dynamics and exclusion of pouch outlet obstruction.[87]

Biofeedback therapy has become the mainstay of management for dyssynergic defecation; this aims to improve the relaxation of anal and pelvic floor muscles during defecation.[88] Previous RCTs have demonstrated the efficacy of biofeedback therapy compared with both standard therapy (ie, diet, exercise, and/or laxatives) and sham biofeedback in patients with dyssynergic defecation and in patients with intact colons.[89, 90] Limited observational data in the IPAA population also suggest biofeedback to be effective for dyssynergic defecation of the pouch.[19, 91]

Irritable Pouch Syndrome

Irritable pouch syndrome (IPS) is a functional pouch disorder, analogous to irritable bowel syndrome (IBS) in patients with an intact colon, first described by Shen et al in 2002.[92] Multiple factors may contribute to the development of IPS, including visceral hypersensitivity, enterochromaffin cell hyperplasia, and psychosocial factors.[93–95] Patients with IPS have been found to have a lower threshold for perception of gas, urge to defecate, and pain.[29, 94] Symptoms of IPS may overlap with structural or inflammatory pouch conditions, including pouchitis and cuffitis. Thus, IPS is a diagnosis of exclusion characterized by increased bowel movement frequency with a change in stool consistency, abdominal pain, and perianal or pelvic discomfort in the absence of a structural or inflammatory pouch disorder based on endoscopic and histologic assessment.[29, 53, 92] Treatment is largely empiric. Pharmacotherapy may include antispasmodics (eg, hyoscyamine or dicyclomine), antidiarrheal agents (eg, loperamide, diphenoxylate/atropine, or cholestyramine), and tricyclic antidepressants (eg, amitriptyline or nortriptyline).[29, 53]

POUCH DYSPLASIA AND NEOPLASIA

In patients with UC and FAP, colectomy substantially reduces the risk of developing colorectal cancer. Although rare, dysplasia and neoplasia may develop within the residual rectal mucosa (anal transition zone) and the ileoanal pouch. A recent systematic review of IBD patients with IPAA showed a cumulative incidence of pouch dysplasia and carcinoma of 3.0% and 2.7%, respectively, after 20 years.[96] Of all cancers that develop in the pouch, most are adenocarcinoma (84%), although lymphoma and squamous cell carcinoma have also been described.[97] Of those who develop adenocarcinoma after IPAA for UC, nearly two-thirds develop at the anal transition zone, with the remainder developing from the pouch mucosa.[98] Interestingly, while the rectal cuff is at theoretical increased risk of dysplasia, large studies actually report no difference in malignancy among patients who underwent a hand-sewn anastomosis with mucosectomy versus stapled anastomosis.[99]

Surveillance strategies for development of pouch dysplasia or carcinoma should be based on risk stratification, with the presence of colorectal dysplasia or carcinoma before colectomy being the most dominant risk factor.[96, 100] Of 49 cases of pouch carcinoma in IBD patients, 28 (57.1%) had prior colorectal neoplasia.[98, 100] Additional risk factors have been identified, including longer duration of IBD before colectomy, PSC, chronic pouchitis or cuffitis, and CD of the pouch.[97] It is generally agreed that patients with colorectal dysplasia or neoplasia before colectomy should undergo annual surveillance pouchoscopy with biopsies.[97, 100] However, there is no published evidence based guidelines regarding pouch surveillance, largely due to variability in practice among providers and low numbers of pouch dysplasia cases. Regular endoscopic evaluation should be considered for other high-risk IBD pouch populations (eg, those with PSC or chronic pouchitis), although the optimal surveillance frequency is less clear given lack of data. In patients with FAP who undergo IPAA, the risk of adenoma recurrence within the ileal pouch is as high as 44%–65%.[101, 102] Thus, these patients require lifelong surveillance with yearly pouchoscopies to detect and remove any adenomas.

SUMMARY

Overall, patients who undergo proctocolectomy with IPAA experience good long-term functional outcomes and quality of life. However, a number of early and late adverse sequelae can occur, which include inflammatory, postoperative, mechanical, functional, and neoplastic pouch disorders. It is important to be familiar with these various pouch complications to properly evaluate, diagnosis, and manage patients who present with pouch dysfunction.

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