

# ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Diseases

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## Complications of IBD-related Pouch Surgery

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**G&H** What are the indications for colonic resection and pouch surgery, and how do they affect the way surgery is performed?

**BS** The main indication for pouch surgery is in those patients with medically refractory ulcerative colitis (UC). This designation includes all patients with either left-sided UC or pancolitis who have persistent symptoms of bloody diarrhea and urgency, anemia, or hypoalbuminemia, despite oral or intravenous administration of corticosteroids.

Another group of surgical candidates are patients with steroid-dependent UC. These patients' symptoms can be controlled with corticosteroid administration, but the patients have developed significant, sometimes irreversible, adverse effects from chronic steroid use. They may not tolerate, or their disease may be refractory to, steroid-sparing agents such as azathioprine or 6-mercaptopurine.

With the recent approval of the biologic agent infliximab (Remicade, Centocor) by the United States Food and Drug Administration, physicians have another therapeutic option in both of these groups of patients. Individual physicians and practices have their own thresholds for trial of infliximab and for sending patients for colectomy. Some will stop medical therapy at the steroid-dependent stage and go straight to surgery. Some will recommend surgery at the steroid-refractory stage. The decision to try infliximab in these cases, in an attempt to avoid or delay the surgery, is dependent on physician practice, patient demographics, patient preference, local

expertise on restorative proctocolectomy, and is often determined on a case-by-case basis.

The third indication for pouch surgery is in patients with dysplasia or cancer developed from underlying UC. Surgery in these patients is performed slightly differently. These patients often require hand-sewn anastomosis combined with mucosectomy or removal of the rectal cuff mucosa instead of a standard, stapled pouch-anal anastomosis without mucosectomy.

For patients with Crohn's disease (CD) or Crohn's colitis, pouch surgery is contraindicated because CD will most likely recur after the pouch surgery. Those patients who have segmental involvement of the colon can undergo partial colectomy. If their CD involves the whole colon, they are candidates for a Brooke ileostomy. Patients with indeterminate colitis that cannot be classified as either CD or UC by a combined clinical, endoscopic, radiographic, and histologic evaluation can undergo restorative proctocolectomy with ileal pouch-anal anastomosis.

**G&H** Are there patient factors besides disease state that can be used to predict outcomes in pouch surgery?

**BS** Multiple studies have been performed to identify risk factors associated with pouchitis, CD of the pouch, or dysplasia. Smoking has been shown to have a protective role for the development of pouchitis, but it is a risk factor for CD of the pouch. If the patient has primary sclerosing

cholangitis (PSC) or other extraintestinal manifestations (such as arthropathy), the patient will have an increased risk for pouchitis. Investigators have also found that patients with backwash ileitis or pancolitis and regular use of nonsteroidal anti-inflammatory drugs (NSAIDs) are at risk for pouchitis. Among biomarkers, patients with preoperative thrombocytosis (high levels of platelets) are at increased risk for pouchitis, as are those positive for perinuclear antineutrophil cytoplasmic antibody (pANCA) and those with the *NOD2* genetic mutation or polymorphism. Data have also shown that antibodies against *Saccharomyces cerevisiae* (ASCA) may impart increased risk of CD of the pouch.

### G&H What is the symptomatic characterization of patients with postsurgical pouch complications?

**BS** Pouch disease can be roughly classified into five broad categories.

1. Surgery-related complications: leak, abscess, sepsis, sinus, anastomotic stricture
2. Inflammatory disease: pouchitis, CD of the pouch, cuffitis
3. Functional disease: irritable pouch syndrome, anismus
4. Dysplastic/neoplastic conditions: cancer or dysplasia in the pouch or the anal transitional zone
5. Systemic disease: anemia, bone loss, renal stones, vitamin B12 deficiency

With regard to symptoms, patients may have different categories of disease but similar clinical presentations such as diarrhea, abdominal cramps, urgency, and pelvic discomfort. These symptoms often overlap, but there are “characteristic” symptoms that indicate specific problems. Fistula drainage is likely due to a surgical complication or CD of the pouch. Major bleeding symptoms are indicative of cuffitis, a variant of residual UC. Some patients have partial bowel obstruction symptoms due to strictures and adhesions. However, for the most part, symptoms are not specific and in order to make a correct diagnosis, symptom assessment needs to be combined with endoscopic, histologic, and radiographic examination. Additional diagnostic modalities should be considered if surgery-related complications and CD of the pouch are suspected. We have found that retrograde contrast enema with gastrografin is useful in delineating pouch leak, stricture, fistula, or abscess. Suspected perianal fistula, sinus, abscess, or sepsis can be confirmed with pelvic magnetic resonance imaging, which is preferred to computed tomographic enterography. In patients with suspected

CD or persistent anemia, small bowel capsule endoscopy can be safely performed.

### G&H Once diagnosis has been established, what are the medical options for management of pouchitis?

**BS** Medical management for patients with pouchitis is primarily antibiotic-based. First-line therapy consists of either ciprofloxacin or metronidazole. Other possible drugs include rifaximin (Xifaxan, Salix) and tinidazole. For simple pouchitis, a 2-week course of a single antibiotic agent is recommended. For refractory pouchitis, 4 weeks with a combination of two antibiotics can be prescribed. If pouchitis patients fail the latter regimen, prognosis is generally not good, as these patients often have an even poorer response to next-line therapies with anti-inflammatory drugs, corticosteroids, or immunomodulators. Pouch failure in this group of patients is high.

Although some pouchitis patients are antibiotic-refractory, the main challenge in treatment of pouchitis is antibiotic dependency. These patients are fine while on antibiotics, but off therapy they have symptoms. Further, with the initial episode of pouchitis, nearly every antibiotic agent works. As pouchitis recurs, patients often gradually lose response to the antibiotic agents or become dependent. Thus, the current need is for agents that can be utilized for maintenance of long-term remission.

The novel agent AST-120 (Ocera), which is a form of activated charcoal, has been tried in an open-label fashion on a cohort of 9 patients with pouchitis. The initial response rate was approximately 50%, which is encouraging. VSL#3 is a probiotic agent that has also been used as primary or secondary prophylaxis in pouchitis. In European studies, the efficacy rate for this agent was 80–90%. However, in a postmarketing open-label trial in the United States, a much lower rate of efficacy was reported.

### G&H When medical therapies are no longer effective, what are the next steps for patients with pouchitis?

**BS** There are several remaining surgical options for these patients. The fecal stream can be diverted with the creation of a temporary ileostomy that allows the pouch to heal. Afterward, some patients may elect to retry the internal pouch. Others may prefer permanent diversion, with or without pouch resection. In a small subgroup of patients, the ileal pouch-anal anastomosis or pelvic pouch can be converted to an abdominal pouch or continent ileostomy (Kock pouch procedure).

## G&H Are there other postsurgical concerns in pouch patients that require monitoring?

**BS** In my opinion, pouch patients require endoscopic surveillance for dysplasia and cancer of the pouch and anal transitional zone. Two recent articles in the literature have suggested that routine surveillance pouch endoscopy is not necessary. However, this year at the American College of Gastroenterology meeting, our group will make an oral presentation describing our experience of 2,500 UC patients who have undergone pouch surgery, where 9 developed adenocarcinoma of the pouch and/or anal transitional zone. Some of these patients progressed, starting with low-grade dysplasia, progressing to high-grade, and ultimately to cancer. Others seemed to develop cancer without going through dysplasia stages. With this in mind, my recommendation is that endoscopic pouch surveillance is necessary, particularly in patients with colonic dysplasia or cancer before colectomy, PSC, chronic pouchitis, cuffitis, CD of the pouch, or a family history of cancer. Whether or not endoscopic surveillance of the pouch is adequate and will lead to cancer-related deaths for these patients has not been determined. However, it is currently the only strategy available.

### Suggested Reading

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