

## TOPIC HIGHLIGHT

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# Surgery for inflammatory bowel disease

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## Abstract

Despite the new and ever expanding array of medications for the treatment of inflammatory bowel disease (IBD), there are still clear indications for operative management of IBD and its complications. We present an overview of indications, procedures, considerations, and controversies in the surgical therapy of IBD.

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## ULCERATIVE COLITIS

Approximately 25%-35% of ulcerative colitis patients will ultimately require surgery for either a complication of the disease or inadequate control of symptoms<sup>[1,2]</sup>. While most of these surgeries can be done in the setting of an elective operation, a minority will require emergent or urgent treatment. A number of options are available in the

surgical management of ulcerative colitis, many of which may require more than one operation. Each procedure is associated with its own benefits and drawbacks, so a thorough understanding of each procedure, and its indications, is important.

## EMERGENT OR URGENT OPERATION FOR ULCERATIVE COLITIS

### Indications

Worsening signs and symptoms of colitis, including numerous bloody stools per day, fever, elevated heart rate, anemia, elevated sedimentation rate, radiographic evidence of colonic distension, and abdominal distension with tenderness on exam<sup>[3]</sup>, can predict the need for surgery. In most cases, acute flares of severe colitis respond to medical therapy. Up to 80% of patients with severe colitis will avoid an operation<sup>[4,5]</sup>. Failure to improve within a few days following an initial stabilization period, or worsening colitis should trigger consideration for operative intervention. Most studies define 48-96 h as an adequate trial of medical therapy in which significant improvement should occur<sup>[6,7]</sup>. One study of 49 patients with severe colitis cites an 85% colectomy rate if patients are still having 8 bowel movements per day, or 3-8 bowel movements per day with a C-reactive protein of > 45 mg/mL, despite 3 d of medical therapy<sup>[7]</sup>. Further, patients with an incomplete response within 7 d of medical management (as defined by four or more bowel movements per day or visible blood in the stools) had a 60% chance of continuing colitis symptoms and a 40% chance of colectomy within 1 year<sup>[7]</sup>.

The diagnosis of toxic megacolon, defined by a transverse colon diameter exceeding 6 centimeters, in ulcerative colitis has been reported in 7%-17% of patients requiring hospitalization and is thought to have a lifetime incidence of 0.5%-2.5%<sup>[8]</sup>. A European study looking at 796 patients showed that the mortality rate from toxic megacolon was only 0.2% in ulcerative colitis patients over a 4-year follow-up<sup>[9]</sup>. However, this accounted for 50% of all ulcerative colitis patient deaths over the same period. As such, most surgeons consider the development of toxic megacolon in ulcerative colitis, particularly in the context of perforation, progressive colonic dilatation, massive hemorrhage or hemodynamic instability, to be an indication for emergent colectomy<sup>[8,9]</sup>. However, severely ill patients can have toxic symptoms without dilatation that still warrants urgent surgical intervention. Greenstein has published a series of 7 ulcerative colitis patients diagnosed

with colonic perforation in the absence of colonic dilatation<sup>[10]</sup>. Six of them did not display classic signs of perforation including peritonitis and rebound tenderness. Impending perforation is extremely difficult to predict. The authors speculated that this lack of symptoms may have been due to the use of high-dose steroids. Patients with signs of actual or impending perforation should receive emergent surgery. The associated mortality rate of perforation in ulcerative colitis patients is between 27% and 57%<sup>[10]</sup>.

As might be predicted, the development of hemodynamic instability or multi-organ failure is also predictive of a poor outcome and warrants resuscitation and emergent operation. Caprilli cited a 72.7% mortality rate in ulcerative colitis patients developing multi-organ dysfunction<sup>[11]</sup>. They suggest that early signs of multi-organ dysfunction, including disproportionate tachycardia, tachypnea, oliguria, jaundice, hypoxemia and mental confusion, should prompt an aggressive therapeutic approach including ICU admission and early colectomy.

### **Surgical options**

Surgical management of ulcerative colitis in the emergent setting is aimed toward removing the inflamed bowel while minimizing morbidity, and a total abdominal colectomy and end ileostomy is the procedure of choice<sup>[12]</sup>. This procedure removes the majority of diseased bowel while avoiding the complications associated with both pelvic dissection and an enteric anastomosis.

A number of studies have shown that total abdominal colectomy with end ileostomy is a safe procedure in the emergent setting with a post-operative complication rate of 23%-33% and low mortality in the absence of a perforation (0%-4%)<sup>[13,14]</sup>. Some debate has centered on the management of the rectal stump. One study suggested that exteriorization of the stump, either by bringing it up into the subcutaneous tissues or by creating a formal mucous fistula, may decrease the incidence of pelvic septic complications and facilitate future pelvic dissection<sup>[15]</sup>. They found a 12% rate of pelvic abscess with an intraperitoneal rectal stump compared to a 4%-7% abscess rate when the stump was exteriorized. However, Karch and colleagues published a pelvic sepsis rate of only 2.6% (3 of 114 patients) in patients with an intraperitoneal stump<sup>[16]</sup>. One of these three patients responded well to transanal drainage prompting the authors to suggest that routine transanal drainage of the rectal stump may be warranted. Forty-one consecutive patients in this series underwent routine transanal drainage with no incidence of pelvic sepsis peri-operatively<sup>[16]</sup>.

Another advantage of this procedure is that after the abdominal colon is resected, the specimen undergoes histopathological assessment to confirm the diagnosis of ulcerative colitis. Surprisingly, the number of patients found to have Crohn's disease instead of ulcerative colitis after this procedure is appreciable. In a recent review of patients undergoing emergent total abdominal colectomy, of the 52 patients with ulcerative colitis, 13% had their diagnosis altered post-operatively (5 diagnosed with Crohn's disease and 1 with indeterminate colitis)<sup>[14]</sup>. Thus, in a

patient with indeterminate colitis, this may be the preferred surgical option to further define the diagnosis.

More extensive and definitive procedures for ulcerative colitis are often technically feasible at the time of an emergent operation. However, proctectomy is rarely required for symptomatic relief at the time of an emergent surgery and residual rectal inflammation can be treated medically<sup>[17]</sup>. Furthermore, these patients are often nutritionally deplete, anemic, and on high-dose steroids which increases the risk for an anastomotic complication. As such, we believe the safest approach is to salvage the patient and avoid proctectomy in the emergent setting. Interestingly, a significant proportion of patients, particularly in the elderly, may elect not to reverse their ileostomy. In Hyman's series of 52 ulcerative colitis patients undergoing emergent surgery, 20 patients elected not to reverse the ileostomy, choosing either completion proctectomy or no further surgery<sup>[14]</sup>.

## **ELECTIVE OPERATION FOR ULCERATIVE COLITIS**

### **Indications**

Failure of medical management remains the most frequent indication for elective surgery in ulcerative colitis<sup>[12]</sup>. Intractability may be defined by inadequate control of symptoms despite optimal medical management, chronic disability due to disease, or control of symptoms with therapy associated with high probability of long-term morbidity such as steroids. Growth failure in the pediatric population may be considered a consequence of intractable disease and is an indication for surgery<sup>[18]</sup>.

Risk of malignancy is also an indication for elective operation. A meta-analysis by Eaden cites an overall cancer incidence of 3.7% in ulcerative colitis patients, increasing to 5.4% in patients with pancolitis. This incidence rises with a longer duration of disease symptoms. Cancer risk in ulcerative colitis patients is 2% at 10 years, 8% at 20 years and 18% at 30 years<sup>[19]</sup>. As such, surveillance colonoscopy has been suggested in ulcerative colitis patients despite a paucity of clear evidence that this process increases survival. At present, practice guidelines of the American Society of Colon and Rectal Surgeons<sup>[12]</sup> suggest that patients with pancolitis undergo surveillance endoscopy after 8 years of disease symptoms and those with left-sided disease undergo surveillance endoscopy after 15 years of symptoms. The consensus of experts is that 4 quadrant biopsies should be taken every 10 cm<sup>[20]</sup>.

While an established carcinoma is an absolute indication for surgery, the management of dysplasia is somewhat more controversial. High grade dysplasia and dysplasia-associated lesions or masses (DALM) have a high incidence of synchronous cancer and are generally considered indications for surgery. A systemic review by Bernstein reported that 42% of patients with high-grade dysplasia and 43% of patients with DALM had synchronous cancers at the time of immediate colectomy<sup>[21]</sup>. However, a high rate of inter-observer variability in the pre-operative diagnosis of dysplastic lesions in ulcerative colitis patients has cast some doubt on this data. Variability in the diagnosis of low

or high-grade dysplasia may be as high as 60% even among experts<sup>[22]</sup>. It has been noted that pathologists may alter their diagnosis over time with experience or with new knowledge in the field<sup>[21]</sup>.

Several studies have suggested that adenoma-like DALMs may not be associated with as aggressive a natural history as previously believed and can be treated with endoscopic resection. Odze and colleagues published a series of 34 ulcerative colitis patients found to have either adenoma-like DALM or sporadic adenoma who were compared to 49 non-ulcerative colitis patients with sporadic adenoma. Their findings suggested that the rates of recurrent adenoma after endoscopic resection were similar in both groups and that ongoing surveillance endoscopy was adequate<sup>[23]</sup>.

The treatment of low-grade dysplasia in the absence of a DALM is even more ambiguous as the natural history of these lesions is not well understood. Several studies have suggested a high incidence of synchronous cancers in the presence of low-grade dysplasia as well as a significant rate of progression to high-grade dysplasia<sup>[21]</sup>. As such, many colorectal surgeons advocate for colectomy with a diagnosis of low-grade dysplasia. However, Befrits has shown over an average endoscopic follow-up of 10 years that progression of low-grade dysplastic lesions to high grade dysplasia or cancer in the absence of a DALM did not occur in 60 patients<sup>[24]</sup>. Lim and colleagues have also published a series of 160 chronic ulcerative colitis patients of whom 40 were diagnosed with low-grade dysplasia on colonoscopy. Over a 10-year follow-up, 10% of low-grade dysplasia progressed to high-grade dysplasia or cancer. However this rate of high-grade dysplasia or cancer in previously diagnosed low-grade dysplasia patients was not found to be significantly different from ulcerative colitis patients without dysplasia. The authors suggested that surveillance endoscopy for low-grade dysplasia was a reasonable option. As stated above, part of the discrepancy in reported rates of progression to high-grade dysplasia or cancer may be due to the lack of standardized pathological definitions for low grade dysplasia in ulcerative colitis<sup>[22]</sup>.

The management of a stricture in the context of low-grade dysplasia is more clear cut as up to 20%-24% of strictures are malignant<sup>[25]</sup>. Biopsies of strictures are inadequate to rule out malignancy and, as such, strictures in general should be considered an indication for surgery<sup>[12]</sup>. Strictures in the setting of ulcerative colitis may also be indicative of Crohn's disease and thus, operative treatment should be adjusted accordingly.

Elective surgery should also be considered for treatment of severe extra-intestinal manifestations of ulcerative colitis. Monoarticular arthritis, uveitis, and iritis are often ameliorated by colectomy while primary sclerosing cholangitis, ankylosing spondylitis and sacroiliitis are not improved<sup>[26]</sup>. The utility of colectomy for control of cutaneous manifestations such as erythema nodosum and pyoderma gangrenosum is uncertain as the response to surgery is variable<sup>[26]</sup>.

### **Surgical options**

A number of surgical procedures may be considered for

the treatment of ulcerative colitis, each with its own set of benefits and drawbacks. When selecting a procedure, the surgeon must consider a number of factors including pre-existing bowel dysfunction, patient stability, the presence of cancer and other medical comorbidities. Primary goals include removal of all diseased colon and rectum, elimination of cancer risk and restoration of normal bowel function. However, accomplishment of these goals may result in increased morbidity and decreased quality of life. As such, selection of an appropriate procedure is largely dependent on patient expectations and requires an ongoing dialogue between the patient, gastroenterologist, and surgeon.

Total proctocolectomy with end ileostomy remains the operative standard against which all other resections for ulcerative colitis are compared<sup>[12]</sup>. This operation removes all disease and eliminates the risk of colorectal cancer. It also eliminates issues of bowel function such as defecatory frequency, urgency and night waking and is generally associated with few dietary restrictions. It is still the procedure of choice for those with impaired anal sphincter function, or a distal rectal cancer. Other candidates include those patients who do not wish to undergo a restorative procedure and hope to have a single operation<sup>[27]</sup>.

While total proctocolectomy with end ileostomy is generally a safe procedure, it is still associated with significant morbidity. The most common complications include stoma-related issues such as parastomal herniation, skin excoriation and stomal stenosis<sup>[28,29]</sup>. A prospective analysis of 104 ulcerative colitis patients with total proctocolectomy and end ileostomy cited a 24% rate of stoma revision over 8 years<sup>[29]</sup>. The majority of these revisions were for stenosis or regression of the stoma. Small bowel obstructions are also a frequent complication but can often be treated conservatively<sup>[28]</sup>. Other morbidities associated with this operation that are intrinsic to pelvic dissection include sexual dysfunction, infertility, altered bladder function, and delayed perineal wound healing<sup>[30]</sup>. Interestingly, despite the fact that these patients live with a permanent stoma, they have a remarkably similar quality of life to age- and sex-matched patients with restorative procedures<sup>[31]</sup>.

As a result of patient's dissatisfaction with having a permanent end ileostomy and need to wear an appliance, Kock advocated the continent ileostomy in the 1960s and 1970s<sup>[32]</sup>. The terminal ileum is intussuscepted within a proximal ileal pouch forming a continent nipple valve. This procedure is performed with decreasing frequency due to significant rates of failure of the continence mechanism as well as the success of restorative proctocolectomy. A study of 96 Kock pouches showed an overall failure rate (that is, conversion to conventional ileostomy or ileal pouch-anal anastomosis) of 29% at 29 years. Fifty-nine percent of patients required a revision of their Kock pouch with 19% requiring more than 1 revision. However, it was noted that the 71% long-term success rate of Kock pouch was similar to that of restorative proctocolectomy<sup>[33]</sup>.

Although it is considered an option for the elective treatment of ulcerative colitis in a certain selection of patients, total abdominal colectomy with ileorectal anastomosis is not a common procedure. It may be

appropriate in the context of minimal rectal involvement or indeterminate colitis. A Swedish study of 51 ulcerative colitis patients treated by total colectomy with ileorectal anastomosis demonstrated that 29 patients (57%) ultimately failed this procedure and required completion proctectomy or restorative proctocolectomy<sup>[34]</sup>. Most (23 of 29 patients) failed due to ongoing rectal inflammation and diarrhea, but dysplasia was detected in 3 patients necessitating proctectomy.

Currently, the most frequent elective procedure performed for ulcerative colitis is the restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA). Its greatest benefits are removal of disease up to the anal transition zone, maintenance of a normal pathway for defecation, and avoidance of a perineal wound and permanent stoma. Disadvantages of IPAA include the need for a second operation to close the diverting loop ileostomy, the need for continued surveillance of the residual anal transition zone<sup>[27]</sup>, and ongoing management of bowel function.

IPAA is an appropriate procedure for most patients with ulcerative colitis. Two large, retrospective cohort studies from the Cleveland Clinic and Mayo Clinic have shown that it is a relatively safe and durable procedure with a low perioperative mortality rate of 0.2%-1.0%<sup>[35,36]</sup>. However, the morbidity of this procedure is still considerable. In the peri-operative period, the incidence of anastomotic separation has been cited between 5% and 10%<sup>[35-37]</sup>. The need for aggressive therapy is often unnecessary in the immediate post-operative period as routine pelvic drainage and diverting ileostomy obviate the need for surgical or radiologic management. In this setting, reversal of the ileostomy should be delayed until there is both clinical and radiographic evidence of complete resolution of the anastomotic separation.

A relatively common complication often associated with anastomotic dehiscence is ileal pouch-vaginal fistulas which occur in 3%-16% of IPAA performed in women<sup>[38]</sup>. The spectrum of disease may range from relatively asymptomatic leakage of gas, to debilitating soilage and pelvic sepsis. Pelvic sepsis secondary to anastomotic dehiscence is thought to be the major contributor to the development of these fistulas. However, other causative factors may include anal cryptoglandular disease and vaginal injury during rectal dissection. Treatment is associated with a high failure rate. A recent study of 22 patients with pouch-vaginal fistula repairs cited a 50% recurrence rate after surgery. Combined abdominoperineal approaches were associated with a significantly higher success rate than local perineal repairs (52.9% *vs* 7.9%). Overall, 21% of patients required pouch excision for non-functional pouches and recurrent fistulas<sup>[39]</sup>.

The most frequent long-term complication of IPAA is pouchitis, a non-specific inflammation of the ileal pouch that occurs in 24%-48% of IPAA patients depending on the length of follow-up<sup>[35,36]</sup>. Presenting symptoms include cramping, fever, chills, perineal pain and an increase in stool frequency. The mainstay of treatment is antibiotics such as ciprofloxacin or metronidazole. Patients can develop antibiotic-dependent or antibiotic-resistant

pouchitis that requires escalation of treatment and a small fraction may need to be treated with pouch excision<sup>[40]</sup>.

Recent studies have suggested that fertility following IPAA is significantly decreased<sup>[41,42]</sup>. A Canadian study comparing 153 females with ulcerative colitis who had IPAA with 60 females who were medically managed showed an infertility rate of 38.6% which is 3 to 4 times higher than that in the normal population<sup>[41]</sup>. A history of post-operative small bowel obstruction, pelvic sepsis, or greater number of abdominal operations was not found to increase infertility. This is somewhat surprising as the etiology of decreased fertility following IPAA is suspected to be related to the presence of post-operative adhesions in the pelvis which may cause obstruction of the fallopian tube<sup>[42]</sup>.

The most common long-term complications of the pouch are related to altered bowel function<sup>[43,44]</sup>. A number of studies have suggested that IPAA patients have, on average 6 stools during the day with 1-2 stools overnight. Occasional daytime fecal incontinence may occur in 31%-45% of patients and this rate increases to 40%-59% at night. Up to 55% of patients use an undergarment pad to absorb seepage and 45% of patients will require bulking agents or anti-diarrheal medications to help regulate their bowels. A recent meta-analysis by Hueting and colleagues evaluated 43 observational studies encompassing 9317 patients. Severe and urge incontinence rates were reported at 3.7% and 7.3% respectively<sup>[45]</sup>. They found a pouch failure rate of 6.8% at a median follow-up of 36.7 mo increasing to 8.5% with follow-up over 60 mo.

Despite these morbidities, IPAA is an exceptionally durable and well tolerated procedure which results in markedly improved quality of life. A study of 1895 patients suggested that quality of life and quality of health following IPAA was similar that of the general population<sup>[44]</sup>. In patients under 65, social, work and sexual restrictions were experienced in only 11%-17% of those who had an IPAA. Interestingly, 98% stated that they would have the surgery again or recommend it to someone else with ulcerative colitis<sup>[44]</sup>. In addition, health-related quality of life has been found to be closely linked to pouch function<sup>[46,47]</sup>. Carmon and colleagues also found that elderly patients tended to have worse quality of life as well as pouch function<sup>[47]</sup>.

## CONTROVERSIES IN THE SURGICAL MANAGEMENT OF ULCERATIVE COLITIS

### Age

A debatable issue is whether IPAA should be offered to elderly patients, mainly due to increased incidence of anal sphincter dysfunction and comorbidities in this cohort. Several groups have shown that IPAA is feasible in the elderly<sup>[44,48]</sup>. The Cleveland Clinic published their series of 17 IPAA patients over the age of 70 and found similar functional outcomes to younger patients<sup>[49]</sup>. However, while continence in the first 10 years of IPAA remains relatively stable, it is uncertain whether this deteriorates with time, particularly in the elderly. Delaney and colleagues have shown that incontinence and night

seepage in patients over 65 approach rates of 67% and 60%, respectively<sup>[44]</sup>. However, the authors are quick to note that these decreased levels of perfect continence do not seem to translate into a decreased quality of life or satisfaction with the surgical outcome. While it seems that chronologic age alone should not be a contraindication to IPAA, older patients must be appropriately motivated and well-informed regarding the potential problems of IPAA.

### **Hand sewn vs stapled anastomosis**

Another debate centers on the need to perform a mucosectomy to remove the last 1-2 cm of rectal mucosa and, thus, require a hand sewn ileal pouch anal anastomosis. This approach was the only technique available until the advent of the circular staplers in the early 1990s. Most surgeons quickly switched to using a double-stapled anastomosis for ileal pouches due to the ease of this technique. This involves leaving the distal 1-2 cm of rectal mucosa intact, transecting the rectum above the anorectal junction with a stapler, and performing the anastomosis with the circular stapler. Because this method avoids a mucosectomy, the abundant nerve supply to the anal transition zone is preserved and sphincter injury is minimized. Additionally, double-stapled techniques are associated with less tension on the anastomosis<sup>[12]</sup>. With increasing experience, it was felt that "mucosectomy" led to unnecessary anal sphincter and nerve damage with minimal benefit in terms of disease control. A meta-analysis of 4183 patients (2699 hand sewn with mucosectomy and 1484 with stapled IPAA) showed no significant difference in the rate of post-operative complications<sup>[50]</sup>. While the frequency of bowel movements and use of anti-diarrheal medications did not differ in the two groups, the incidence of nocturnal seepage and usage of pads favored stapled IPAA. Further, manometric measures suggested that resting and squeeze pressures were significantly reduced in the hand sewn population<sup>[50]</sup>.

Detractors of double-stapled approaches will cite the potential for ongoing rectal cuff inflammation and the consequent risk of malignancy. However, a recent review of the literature cites a total of only 17 reported cases of cancer in the pouch or anastomosis<sup>[51]</sup>. In 12 cases, dysplasia or cancer was present in the original resection specimen. All 17 patients had a diagnosis of ulcerative colitis for at least 10 years at the time of the IPAA cancer diagnosis. The authors recommended surveillance starting at 10 years after disease onset. In post-IPAA patients, they recommended more intensive surveillance with biopsies in patients with cancer or dysplasia in the original specimen<sup>[51]</sup>.

### **Routine proximal diversion**

Routine diversion of the fecal stream by loop ileostomy following IPAA is also a debated issue. Ileostomies are thought to minimize both postoperative septic complications and morbidity associated with anastomotic leak<sup>[52]</sup>. However, many surgeons believe that routine diverting loops ileostomy is counterproductive. First, loop ileostomies are associated with some morbidity including poor body image, leakage, and skin breakdown. A second

procedure to reverse the ileostomy, with its associated cost and morbidity, is also required. It has been suggested that routine diversion is not needed in carefully selected patients depending on patient, disease, and operative factors<sup>[53]</sup>. A relatively healthy, well-nourished patient, who is not anemic, or on high dose steroids would be a candidate<sup>[53]</sup>. Intraoperative factors, such as healthy-appearing, well-vascularized small bowel, low blood loss, hemodynamic stability, and a tensionless anastomosis, may allow for omission of a diverting loop ileostomy<sup>[53]</sup>.

Using these criteria for omission of a diverting loop ileostomy, Remzi retrospectively studied 2002 IPAA patients (1725 diverted by ileostomy and 277 undiverted)<sup>[53]</sup>. While a single stage procedure was associated with a higher incidence of post-operative ileus, he found no significant differences in septic complications, quality of life or functional outcomes in the two groups. This contrasts an earlier report from the same institution that rates of septic complications are increased, particularly in patients taking high doses of steroids<sup>[52]</sup>. Another report has suggested that the routine omission of a diverting loops ileostomy is associated with an increased risk to life<sup>[54]</sup>. As such, Remzi and others have suggested that only carefully selected patients are suitable for one-stage restorative proctocolectomy.

## **LAPAROSCOPIC PROCEDURES FOR ULCERATIVE COLITIS**

All operations for ulcerative colitis can be performed laparoscopically, including subtotal colectomy, total proctocolectomy and restorative proctocolectomy. Earlier reports in the mid-1990's demonstrated significantly longer operative times without a benefit in post-operative ileus or length of stay (traditional rationales for minimally invasive procedures)<sup>[55]</sup>. Further, it was shown that postoperative morbidity and transfusion requirements were higher in laparoscopic procedures<sup>[56]</sup>.

With better experience and technique, the increased morbidity of laparoscopic procedures for ulcerative colitis has decreased<sup>[57]</sup>. Marcello and colleagues have published a series using only experienced surgeons who have performed more than 700 laparoscopic colorectal procedures of which at least 100 were total abdominal colectomies<sup>[58]</sup>. The study compared 20 consecutive laparoscopic restorative proctocolectomies with 20 conventional procedures. While a significant increase in operative time was noted in the laparoscopic group (100 min), many of the previously cited morbidities associated with laparoscopic procedures, including blood loss and post-operative infection, were not significantly different from the open group. The length of stay in hospital was also shorter (7 d *vs* 8 d). A few subsequent studies have confirmed Marcello's findings<sup>[59,60]</sup>. Further, recent analysis of functional outcomes including number of bowel movements, stool consistency, incontinence, need for anti-diarrheal medications, and dietary restrictions has not revealed a significant difference between laparoscopic and conventional IPAA<sup>[60]</sup>.

A randomized, prospective study by Milsom has shown that laparoscopic resection in ileocolic Crohn's disease is associated with less blood loss, fewer respiratory

complications, faster return of bowel function and shorter hospital stay<sup>[61]</sup>; no similar study has been performed for laparoscopic procedures in the treatment of ulcerative colitis. Part of the problem is the lack of agreement on the optimal technique for laparoscopic IPAA which makes a comparative study with the open procedure difficult<sup>[57]</sup>. As discussed, there is also a steep learning curve associated with laparoscopic IPAA; most recent published results involve very experienced surgeons. It may be difficult to attain this experience outside of dedicated colorectal centers with a high volume of laparoscopic inflammatory bowel disease cases. While the current data suggest that laparoscopic IPAA may be a safe and effective treatment in the hands of an experienced surgeon, there are insufficient studies to recommend its general use. Further, despite improvements in technology, increased operative times may pose a barrier in institutions where operating room time is at a premium<sup>[57]</sup>.

## CROHN'S DISEASE

While advances in the medical management of Crohn's disease have decreased the need for surgery, it is estimated that between 70% and 90% of Crohn's patients will need a surgical intervention at some point during their disease<sup>[62]</sup>. The panenteric nature of Crohn's disease results in a variety of presentations depending on both the location of the disease as well as the disease behavior. Nonetheless, as Crohn's disease cannot be cured, the indications for surgery remain relatively straight-forward: failure of medical management and complications of the disease process. The specific surgical managements available are often multiple and selection of the most appropriate modality is dependent on several patient and disease factors.

## CROHN'S DISEASE: SMALL BOWEL

### Indications

Failure of medical management remains the most common indication for surgery in most series of patients with small bowel Crohn's disease<sup>[63,64]</sup>. Failure is defined by (1) symptoms that cannot be controlled or progress with maximum medical therapy, (2) problems with treatment side effects, and (3) inability of patient to maintain compliance with a medical regimen. Extra-intestinal manifestations (EIM) of disease are another indication for surgery and may occur in as many as 25% of Crohn's patients<sup>[65]</sup>. Disorders of the skin, mouth, eye and joints are common in colonic disease and tend to parallel disease activity. As such, surgical resection of diseased bowel tends to ameliorate these EIMs. Hepatic, vascular, hematologic, pulmonary, cardiac and neurologic system EIMs tend to act independently of intestinal disease. Other disorders such as nephrolithiasis and cholelithiasis are actually complications of disease secondary to altered intestinal absorption. As such, surgical resection may improve these conditions.

Intestinal obstruction represents a frequent complication of small bowel Crohn's disease<sup>[63,64]</sup>. Acute obstruction can occur due to a primary stricture or series of strictures.

Healthy, non-diseased, bowel may be mechanically obstructed as part of an inflammatory mass or fistula. Acute obstructions are more likely to be the result of active inflammation and will often resolve with medical management<sup>[66]</sup>. Conversely, chronic obstruction, which is usually the result of a fixed fibrostenotic lesion, tends to require surgical management<sup>[66]</sup>. Surgery usually involves a resection of the diseased segment, but other options include intestinal bypass, creation of ileostomy, or stricturoplasty (discussed below).

Fistulas with associated abscess or stricture are another common complications of small bowel Crohn's that requires surgery<sup>[63,64]</sup>. In a study of 1379 patients, Michelassi found fistulas in 35% of surgically managed patients. However, fistula was the primary surgical indication in only 6.3% of patients<sup>[67]</sup>. Enterointeric fistulas are the most common type of fistula and may be relatively asymptomatic unless a large segment of intestine is bypassed or complications of obstruction arise. Broe and colleagues published that 40% of patients with fistula initially managed non-operatively eventually required surgery within 1 year, usually secondary to medical intractability<sup>[68]</sup>. The surgical management of enterointeric fistulas generally involves resection of the primary site that has active disease and simple debridement and primary closure of the secondary site that is usually normal. Enteral fistulas to the vagina and urinary bladder often require surgery and treatment adheres to similar principles of primary site resection with repair of the secondary site. Ileal-sigmoid fistulas may represent an exception to this rule. Fazio and colleagues have shown that primary repair of a sigmoid defect is vulnerable to breakdown, particularly when the sigmoid is involved in a phlegmon<sup>[69]</sup>. They suggest that a minimal sigmoid resection can be performed with minimal morbidity<sup>[69]</sup>.

Enterocutaneous fistulas deserve special mention as these fistulas will occasionally respond to medical therapy. The most promising trials to date have evaluated the use of infliximab. The ACCENT-1 trial suggested a rapid response to 3 infusions of infliximab in 46% of patients, but the duration of effect was short-lived (only 3-4 mo)<sup>[70]</sup>. The follow-up ACCENT-2 trial showed that the duration of effect could be sustained in 46% of patients with maintenance doses of infliximab every 8 wk<sup>[71]</sup>. Surgical principles for the management of enterocutaneous fistulas parallel that for other types of fistulas. Those patients with short fistula tracts, exposed bowel mucosa, and high outputs will generally require operative intervention, but this should be delayed until the patient's health and nutritional status have been optimized.

The life-time risk for developing an abscess in Crohn's patients is estimated to be around 25%<sup>[72]</sup>. Using radiographic techniques, abscesses can often be drained percutaneously. However, some controversy exists as to whether abscesses must eventually be followed up with surgical resection of the associated diseased bowel. One study has shown that abscesses recur more frequently when they are percutaneously drained compared to surgically drained abscesses (56% *vs* 12% respectively)<sup>[73]</sup>. However, Gutierrez and colleagues have shown in a study of 66 patients only one third of patients who were

percutaneously drained required surgery at 1 year follow-up<sup>[74]</sup>. Certainly, if an abscess contains enteric contents, it is less likely to resolve without surgical resection<sup>[62]</sup>.

Other less common indications for surgery in small bowel include perforation, bleeding and cancer. Free perforation is associated with a high mortality if not treated and surgical management should involve resection rather than repair<sup>[75]</sup>. Massive hemorrhage due to Crohn's is a rare indication for surgery<sup>[76]</sup>. Other more common sources of bleeding such as peptic ulcer disease or diverticulitis must be actively ruled out. Adenocarcinoma of the small intestine, while rare, is increased 12-fold to 60-fold compared to the general population<sup>[77]</sup>. Prognosis is generally poor due to the often advanced stage of disease at the time of diagnosis. Mortality rates at 1 year or 2 years have been reported to be 30%-60%<sup>[77]</sup>.

### Surgical options

Resection is the most commonly performed surgical procedure for small bowel Crohn's disease. In general, the panenteric nature of Crohn's disease has resulted in a surgical philosophy of conservatism. Recurrence rates tend to increase with the passage of time<sup>[78]</sup> and Crohn's disease patients may eventually require multiple resections, each increasing the risk of short-bowel syndrome and its associated metabolic morbidities. Of note, Glehen and colleagues have reported that Crohn's disease patients start out with shorter bowel than the normal population<sup>[79]</sup>.

A number of studies have investigated whether certain technical factors, including resection margin and configuration of anastomosis, influence the rate of recurrence. Two retrospective Swedish studies suggested that "radical" resection resulted in a much lower rate of resection and better quality of life in Crohn's patients. Krause and colleagues studied 186 patients with margins of uninvolved bowel of less than 10 cm or greater than 10 cm (a radical resection). They reported a 31% recurrence rate and better quality of life with radical resection compared to an 83% recurrence rate in the other group<sup>[80]</sup>. Softley and colleagues used a 4 cm histologic margin and found that impingement on this margin resulted in a ten-fold increase in recurrence<sup>[81]</sup>.

However, the best evidence available that large resection margins do not decrease the rate of recurrence is based on a study performed by Fazio<sup>[82]</sup> where 131 patients were randomized to resection with margins of either 2 cm of uninvolved bowel (75 patients) or 12 cm (56 patients). Although the rate of recurrence was lower in the group with more extensive resection (25% *vs* 18%), this difference did not achieve statistical significance. In Fazio's study, grossly normal resection margins were used. Hamilton and colleagues studied the role of frozen section examination of bowel wall at the resection margins during surgery and found there was no difference in reoperation or recurrence rates in Crohn's patients with disease-free margins that were detected histologically or grossly<sup>[82]</sup>.

The type of anastomosis performed in small bowel resections has also been speculated to affect recurrence rates. Since fibrostenotic disease is a described clinical phenotype of Crohn's disease by the Vienna Classification<sup>[83]</sup>, it was

thought that the larger lumen of a side-to-side anastomosis would be less likely to obstruct and require re-operation. Stapled anastomoses have been reported to have lower morbidity and recurrence rates<sup>[84,85]</sup>. Resegotti also reported lower anastomotic leak rates in stapled versus hand-sewn anastomosis<sup>[86]</sup>. However, it has been suggested that certain circumstances clearly favor hand-sewn anastomosis, particularly when joining thickened (but grossly disease-free) bowel which may exceed the specifications of a bowel stapler<sup>[62]</sup>.

Recurrence rates following resection remain high and although not all symptomatic recurrence requires surgery, it has been reported that surgical re-intervention occurs in 25%-35% of patients at 5 years and 40%-70% at 15 years<sup>[87]</sup>. However, several trials have been done to evaluate patient and disease factors as well as medication regimens which may decrease recurrence. Yamamoto has recently published a comprehensive systematic review of factors affecting Crohn's recurrence after surgery<sup>[88]</sup>. His review concludes that cessation of smoking seems to be the most consistent factor in reducing recurrence. While several other factors (including 5-ASA use, immunosuppressant drugs, wider anastomosis, and disease duration) may affect recurrence rates, further studies are still required<sup>[88]</sup>. Post-surgical recurrence in Crohn's disease is still largely unpredictable<sup>[89]</sup>.

When preservation of intestinal length is an issue, stricturoplasty represents an alternative to resection and can reduce the risk of short bowel syndrome. Indications for stricturoplasty include short fibrous strictures; diffuse involvement of the small bowel involving multiple strictures, a stricture in someone who has short bowel syndrome or a history of multiple prior small bowel resections, patients with a rapid recurrence of Crohn's disease manifested as obstruction, or patients with duodenal Crohn's disease. Stricturoplasties should not be done in patients with multiple strictures within a short segment, a long (< 20 cm) stricture, or stricture close to a site of resection<sup>[62]</sup>. Perforation, fistula and phlegmon at the site of stricture are also contraindications to stricturoplasty. The largest stricturoplasty experience published to date comes from the Cleveland Clinic in which 698 stricturoplasties were performed in 162 patients<sup>[90]</sup>. Their cited recurrence rate at 5 years was 28% which is similar to published rates of recurrence following resection. In addition to relieving obstruction, there have been reports of disease regression at sites of stricturoplasty<sup>[91]</sup>. Indeed, in the Cleveland Clinic series, documented recurrences only occurred at the previous stricturoplasty site in 5% of cases<sup>[90]</sup>. Fearnhead and colleagues have recently published a long-term follow-up of 479 stricturoplasties in 100 patients<sup>[92]</sup>. Over a mean follow-up of 85 mo, the overall morbidity rate was 22.6% with septic complications (leak, fistula or abscess) occurring in 11.3%. Obstruction occurred in 4.4% of patients while rate peri-operative mortality rate was 0.6%. Although bleeding from stricturoplasty sites has previously been cited as a potentially serious problem due to the presence of a suture line in diseased bowel, Fearnhead found a gastrointestinal hemorrhage incidence of only 3.8%<sup>[92]</sup>.

One disadvantage of performing a stricturoplasty is

that a malignancy of the bowel can be missed. Several case reports have been published of adenocarcinoma arising from Crohn's-related stricture sites. To avoid missing a cancer in a longstanding stricture, it has been suggested that full-thickness biopsies should be taken for frozen section to aid the surgeon in the decision to perform either stricturoplasty or resection<sup>[93]</sup>.

Other surgical options for the treatment of small bowel Crohn's disease include bypass operations or ileostomy formation. Bypass operations have largely been abandoned due to the risk of malignancy and continued disease activity<sup>[62]</sup>. A role for bypass may be for temporary relief of obstruction when a future resection is planned<sup>[62]</sup>. An ileostomy may be required in Crohn's patients when enteric anastomosis is unsafe (sepsis, unstable patient, severe malnutrition, chronic immunosuppression) or when small bowel resection is done in conjunction with colonic or rectal resection.

## CROHN'S DISEASE: COLON

### Indications

Crohn's colitis occurs in approximately one quarter of Crohn's patients although colonic disease is most frequently seen in conjunction with terminal ileal disease<sup>[62]</sup>. As with small bowel Crohn's disease, indications for surgery in colonic Crohn's disease can be grouped into complications of the disease and failure of medical therapy. Indications specific to colonic disease include the development of dysplasia or colorectal cancer and toxic colitis. The treatment of obstruction and fistula of the colon may differ from that in the small bowel.

Obstruction from colonic strictures may be present in as many as 17% of patients with Crohn's colitis<sup>[94]</sup>. There is some evidence to suggest that benign strictures may be adequately treated by endoscopic balloon dilatation<sup>[95,96]</sup>. A recent series of 16 patients by Nomura showed 75% had symptomatic relief after an initial dilation with one third of patients requiring further dilations within two years<sup>[96]</sup>. All colonic strictures should be endoscopically biopsied as 7%-10% may contain malignancy<sup>[94]</sup>.

Despite earlier studies suggesting that the risk of colorectal cancer was lower than that seen in ulcerative colitis, the current literature suggests that the risk is equivalent<sup>[97]</sup>. Maykel and colleagues have published a retrospective analysis of 222 patients who underwent resection for colonic Crohn's disease<sup>[98]</sup>. Five cases of dysplasia (2.3%) and 6 cases of adenocarcinoma (2.7%) were identified. Of note, in only 3 of the dysplasia cases and 1 of the adenocarcinoma cases was the abnormality identified preoperatively. Consistent with previous reports, Maykel further identified older age at diagnosis of Crohn's disease, duration of disease (greater than 8 years) and extent of disease (pancolitis) as risk factors for the development of dysplasia or cancer<sup>[98]</sup>.

As with ulcerative colitis, surgery is indicated for a proven malignancy, high-grade dysplasia, or DALM in colonic Crohn's disease and the diagnosis and management of low-grade dysplasia is still controversial<sup>[99]</sup>. A recent Cochrane review suggests that surveillance endoscopy does

not necessarily improve survival despite the earlier detection of cancers<sup>[100]</sup>. Nonetheless, current recommendations for surveillance in Crohn's colitis mirror those for ulcerative colitis<sup>[19]</sup>.

Fistulous disease can also occur with Crohn's colitis. However, it is important when assessing fistulas involving the colon to determine the primary site of the fistula. Endoscopic evaluation of the colonic mucosa should be performed. Enterocolonic fistulas in Crohn's patients are often a result of primary small bowel disease with the colon only secondarily involved. In these circumstances, it is generally preferable to debride the colonic side of the fistula and close the defect rather than perform a colonic resection<sup>[101]</sup>. Despite the introduction of new medical therapies, such as infliximab, 50%-75% of patients with colonic fistulas will require surgery<sup>[102]</sup>.

Toxic colitis in Crohn's disease has a similar presentation to that in ulcerative colitis. Operative indications include perforation, lack of improvement with medical management, fulminant colitis, massive hemorrhage and hemodynamic instability. As with ulcerative colitis, the most common procedure for toxic colitis in Crohn's disease patients is subtotal colectomy and end ileostomy<sup>[62]</sup>.

### Surgical options

The extent of resection in patients with only segmental colonic disease is a subject of some debate. A recent meta-analysis of six studies encompassing 488 patients suggests that there is no significant difference in overall recurrence rate, complications or need for permanent stoma between segmental colectomy and total abdominal colectomy with ileorectal anastomosis, but time to recurrence was longer in the total abdominal colectomy group by 4.4 years<sup>[103]</sup>. This is in contrast to previous studies which actually suggested the more extensive procedure (total abdominal colectomy) was associated with a higher recurrence. Bernell published a review of 833 patients and found the 10 year recurrence rate of total abdominal colectomy and ileorectal anastomosis to be 58% compared to 47% in the segmental colectomy group<sup>[87]</sup>. Another study found similar recurrence rates in both groups, but better functional outcomes in the segmental colectomy group<sup>[104]</sup>. In patients with diffuse colitis and proctitis, total proctocolectomy has been associated with less medication use 1 year after operation as well as increased time interval to first recurrence when compared to total abdominal colectomy or segmental colectomy<sup>[105]</sup>. Tekkis has suggested that more extensive resection such as total abdominal colectomy may be more appropriate when 2 or more segments of colon are diseased<sup>[103]</sup>.

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) for Crohn's disease has most often occurred in the setting of a changed diagnosis following IPAA for ulcerative colitis or indeterminate colitis<sup>[62]</sup>. A majority of studies suggest that IPAA in Crohn's disease is associated with a significantly higher rate of morbidity (including pouch failure, incontinence, and pouchitis) than in ulcerative colitis<sup>[106,107]</sup>. Although a few authors have suggested that IPAA may be appropriate in highly selected patients with Crohn's disease<sup>[108,109]</sup>, the current literature



certainly does not support its general use in the Crohn's population.

## ANORECTAL CROHN'S DISEASE

### *Indications for surgery*

About 10%-15% of Crohn's disease patients will have disease limited to the anorectal area but up to 90% of all patients have some manifestation of anorectal disease<sup>[110]</sup>. Perianal disease, including fissures, fistulas and abscesses, can have both typical and atypical presentations. Damage of even a small amount of sphincter muscle can lead to severe morbidity.

Anal skin tags and hemorrhoidal disease may present in up to 70% of patients with anorectal Crohn's<sup>[110]</sup>. These lesions are most often asymptomatic, but may present problems with hygiene, particularly in the context of a diarrheal illness. Patients being seen for potential surgical therapy of these problems should be counseled regarding the risk for non-healing wounds and loss of continence following surgery. Anal skin tags and hemorrhoidal disease are best treated conservatively<sup>[111]</sup>.

Anal fissures are a challenging problem in the Crohn's population. These fissures are often painless and do not necessarily present in the anterior or posterior midline. Often, there is concomitant disease or multiple fissures. While the initial therapy for fissures should be conservative (that is, fiber and fluid supplementation with local medications to aid in sphincter relaxation), some studies have shown that 50% of Crohn's patients will fail medical management<sup>[112]</sup>. Thus, if patients are suffering from significant symptoms of pain, these authors have advocated for a more aggressive approach including lateral sphincterotomy. Wolomir and colleagues published a series of 25 Crohn's patients who underwent sphincterotomy<sup>[113]</sup>. Twenty-two patients had completely healed their fissures within 2 mo and at an average follow-up of 7.5 years, there were no direct complications of sphincterotomy. However, given the risks of decreased continence with surgery, surgical management should be reserved for those with minimal active anorectal inflammation who have truly failed conservative management and have significant symptoms. Division of sphincter muscle should be minimal.

Anorectal abscesses and fistula-in-ano are common problems in the Crohn's population. Treatment of simple abscesses involves incision and drainage. It is important to place the incision as close to the anal verge as possible while still achieving adequate drainage as a fistula may form in the future. It is unclear whether fistulas from Crohn's disease are more common following abscesses or develop in the same way as those of a cryptoglandular origin. As such, Crohn's fistulas may erode deep into sphincter muscle or have complicated, blind tracts. Treatment of these fistulas is closely associated with the anatomy of the fistula, the amount of sphincter complex involved, as well as the status of the patient's fecal and gas continence. Furthermore, the surgeon must consider active disease elsewhere in the gastrointestinal tract and the potential for chronic diarrhea. Aggressive procedures which may

alter continence should be avoided. Treatment options include setons, fistula plugs and mucosal advancement flaps. While several authors have suggested that these procedures can be performed with similar success rates to identical procedures performed in non-Crohn's patients, these studies tend to lack appropriate follow-up<sup>[62]</sup>. There has been some suggestion that fecal diversion following a definitive procedure for fistula-in-ano may improve resolution rates<sup>[114]</sup>.

In rare cases, anorectal disease is insufficiently controlled by adequate drainage of infection and medical management. Assuming that Crohn's disease is still the primary diagnosis, these patients may be assessed for diversion with or without proctectomy<sup>[62]</sup>. While the vast majority of patients will respond to medical management or conservative surgical management such as seton placement, there is evidence that fecal diversion helps the resolution of peri-anal disease, at least temporarily<sup>[115]</sup>. As many as 80% of patients with peri-anal Crohn's manifestations will respond to diversion, but relapse may occur despite a stoma, and restoration of intestinal continuity occurs in a minority of patients<sup>[115]</sup>. A multivariate analysis performed by Galandiuk and colleagues suggest that colonic Crohn's disease and anal stenosis are risk factors for fecal diversion<sup>[116]</sup>.

## LAPAROSCOPIC PROCEDURES FOR CROHN'S DISEASE

The safety and feasibility of laparoscopic resections for treatment of Crohn's disease has been extensively studied<sup>[117]</sup>. Unlike ulcerative colitis, robust data is available for laparoscopic resection in Crohn's disease. Two randomized, controlled studies have been published suggesting that the laparoscopic ileocolic resection is associated with decreased morbidity and length of stay in the hospital<sup>[61,118]</sup>. Maartense further suggested that overall costs of laparoscopic resection were lower<sup>[118]</sup>. While operative times have decreased with increased experience, most studies still suggest significantly longer operative times when compared to open procedures.

## PREPARING THE IBD PATIENT FOR SURGERY

Preparation for surgery is a multidisciplinary approach. Surgery for inflammatory bowel disease differs from cancer surgery in several aspects. Surgery is generally elective and several treatment options are available. Medically intractability and unacceptable symptoms are subjective in nature. Pre-operatively, the patients may be severely malnourished or on high-dose immunosuppressants or steroids. Patients are generally younger and issues including future child-bearing, sexual function and body image have increased importance. Preparation for surgery requires close interaction between many health care team members (including surgeons, gastroenterologist, primary care physicians and enterostomal therapists) and the patient.

Counseling should include a discussion of the extent of disease, the specific indication for surgery,

and alternatives to surgery. A description of the surgical procedure should include risks and complications of the surgery, but also possible intra-operative findings and a discussion about how intra-operative decisions will be made. Particular attention should be made towards issues of bowel function and continence. It is important to assess the patient's expectations from surgery. As stated above, surgery is often elective, but still associated with significant morbidity. The specific surgical procedure or timing of the procedure should be modified, as possible, to reflect the needs of the patient.

Finally, we recommend that patients undergoing surgery for inflammatory bowel disease are referred to former patients who have had similar procedures. In our experience, previous patients are very willing to share their experiences, offer a different perspective and are usually helpful. If possible, we try to match patients according to sex, age and marital status.

## CONCLUSION

While the indications for surgery in IBD are relatively straight forward (intractability or complications), the precise timing and specific procedure(s) to be performed are often fraught with controversy. In ulcerative colitis, the correct diagnosis and management of low grade dysplasia is still a work in evolution. IPAA is the most common procedure performed, but may be contraindicated in certain populations such as the elderly. Other patient cohorts may be appropriate for single-stage IPAA. The performance of a mucosectomy (and its associated morbidity) may be indicated, particularly in those with rectal dysplasia or cancer. In Crohn's disease, the panenteric nature of the disease leads to significant recurrence rates. While surgical conservatism is the current general rule, several authors have advocated for a more aggressive approach in small bowel, colonic, and anorectal disease. In both ulcerative colitis and Crohn's disease, laparoscopic procedures seem to be associated with increased operative times, but could also result in decreased morbidity while providing similar functional results to open procedures.

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