

## TOPIC HIGHLIGHT

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# Recent trends in the surgical management of inflammatory bowel disease

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## Abstract

Surgery is required in the vast majority of patients with Crohn's disease (CD) and in approximately one-third of patients with ulcerative colitis (UC). Similar to medical treatments for IBD, significant advances have occurred in surgery. Advances in CD include an emphasis upon conservatism as exemplified by more limited resections, strictureplasties, and laparoscopic resections. The use of probiotics in selected patients has improved the outcome in patients with pouchitis following restorative proctocolectomy for UC. It is anticipated that ongoing discoveries in the molecular basis of IBD will in turn identify those patients who will best respond to surgery.

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**Key words:** Crohn's disease; Ulcerative colitis; Ileal pouch anal anastomosis; Laparoscopic colectomy

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## INTRODUCTION

Significant strides have been made toward more effective medical management of inflammatory bowel disease (IBD) over the past several decades. Surgery, however, is still an essential component of the current multi-modality approach to both Crohn's disease (CD) and ulcerative colitis (UC). The current surgical approach to CD, with its emphasis on bowel conservation, was born out of decades of surgical experience. Early published series on the surgical

management of ileal CD supported ileocolostomy with exclusion, the so-called "Berg" or "Mount Sinai" operation, as a safe and often therapeutic surgical approach. Concern that the remaining bypassed segment of diseased intestine placed the patient at risk for recurrent symptomatic CD and adenocarcinoma as well as an incidence of stump blow-out influenced a shift towards resectional techniques. Efforts to resect disease with margins free of microscopic disease gave way to a more conservative approach with the realization that radical resection did not result in lower rates of disease recurrence<sup>[1]</sup>. The addition of strictureplasty techniques to the surgical armamentarium has furthered this trend towards surgical conservatism.

In contrast, the history of the surgical management of UC is marked by a shift from non-resectional strategies to the current emphasis on near-total resection of the colon and rectum. Early approaches to the surgical management of UC involved the construction of appendectomies to facilitate colonic irrigation or diverting ileostomies. The application of proctocolectomy with permanent ileostomy in UC addressed the morbidity associated with not resecting the diseased colon and became standard-of-care for most of the 20th century. The refinement of techniques for constructing a neo-rectum using the ileum in the 1980's led to the wide acceptance of total proctocolectomy with ileal pouch-anal anastomosis (IPAA) as a viable and often preferable surgical option.

Today, 70%-80% of patients with CD and 30%-40% of patients with UC ultimately require surgery. The current indications for surgery in both CD and UC are well described and will be reviewed in this article. In addition, we will focus on more recent developments in the surgical and peri-operative management of IBD including the increasingly broad application of laparoscopic techniques, multimodality therapy for anorectal CD, and the use of post-operative probiotics therapy after IPAA.

## CROHN'S DISEASE

The surgical approach to CD is dictated, in large part, by the anatomic distribution of the disease. CD of the distal ileum with a varying degree of colonic involvement is present in 40% of patients. Isolated small bowel disease, isolated colonic, and isolated perineal and anorectal disease are present in 30%, 20%-25%, and 5%-10% of patients respectively. Gastroduodenal disease is not uncommon and has been endoscopically documented in 20% of

CD patients, usually with concomitant ileal disease. Symptoms related to gastroduodenal disease, however, are uncommon, and gastroduodenal disease necessitating operative intervention is rarer still<sup>[2]</sup>.

Irrespective of its anatomic distribution, CD can be classified on the basis of histopathologic and pathophysiologic criteria. The three major subtypes of CD are fibrostenotic disease, which presents with varying degrees of intestinal obstruction, fistulizing disease, and aggressive inflammatory disease. The former two often require operative intervention, while the latter is primarily managed medically.

Operative intervention for CD is indicated when medical therapies fail to adequately alleviate symptoms, or when patients develop one of several complications of the disease; specifically, these include fistula, abscess, obstruction, and malnutrition. Persistent symptoms which compromise quality of life despite several months of aggressive medical management, or recurrent symptoms following repeated attempts to taper aggressive therapies are well described indications for surgery. Adverse reactions to medical therapies, most often steroids, sometimes prompt a more aggressive surgical approach to the control of CD symptoms as well.

Fistula formation is a common component of CD but is infrequently an isolated indication for surgery. Fistulas may be accompanied by abscesses, inflammatory masses, obstructive symptoms, and in rare cases peritonitis, all of which may prompt surgical intervention. Enterocutaneous fistulas and peri-anal or perineal fistulas may significantly compromise quality of life. Operative intervention to alleviate symptoms is often warranted even if these fistulas do not constitute a significant threat to a patient's physical well being. Enterocutaneous fistulas are frequently discovered during surgical exploration for other indications. The presence of these fistulas does not mandate surgical repair unless they result in significant sequelae of malabsorption; namely malnutrition, dehydration or extremely frequent bowel movements. Enterovaginal and enterovesical fistulas may necessitate surgery if they are associated with significant symptomatology, vaginosis or urinary tract infections.

Obstruction is a relatively common indication for surgery. The specific character of obstructive symptoms is largely dependent upon the site of obstruction. Most commonly, terminal ileal narrowing causes chronic crampy abdominal pain associated with oral intake, often resulting in malnutrition. Additional less common indications for surgery in CD include acute hemorrhage, malignancy, and fulminant colitis<sup>[3]</sup>.

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## SMALL BOWEL DISEASE

As stated previously, indications for operative intervention for CD of the small bowel include obstruction and fistula, particularly when accompanied by abscess or an inflammatory mass. When small bowel resections are undertaken, anastomoses should be constructed between segments of bowel grossly free of active disease. In the setting of multiple strictures, strictureplasty may allow for conservation of bowel length. Conventional strictureplasty

involves the longitudinal incision of a stenotic segment of bowel with subsequent transverse closure of the enterotomy to increase lumen diameter. Resection and strictureplasty are often used in conjunction with the former technique applied to longer stenotic segments and the latter technique applied to shorter stenotic segments. Strictureplasty techniques aimed at addressing longer stenotic segments have been described in the recent surgical literature and are being applied with increasing frequency<sup>[4]</sup>.

The operative management of small bowel fistulas is a complex subject; the surgical approach is dictated by the structures involved. Generally, fistulous tracts are transected, diseased intestine is resected, the contents of the tracts are evacuated, and necrotic tissue is debrided. In the setting of enterocutaneous fistulas, the opening at the skin is typically excised and allowed to close secondarily. When fistulas involve intra-abdominal organs free of Crohn's disease, the opening in the non-diseased organ is debrided and closed primarily<sup>[5]</sup>.

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## COLONIC DISEASE

Complications of segmental CD of the colon may be addressed with segmental resection. Diffuse disease may require proctocolectomy with ileostomy, or total abdominal colectomy with ileorectostomy if the distal rectum is free of disease. In the setting of toxic colitis, total abdominal colectomy with construction of an ileostomy and Hartmann pouch is the preferred approach. In principle, the management of fistulous disease of the colon is similar to that described for fistulous disease of the small bowel. Colon with gross disease should be resected. Fistulous tracts to the colon from a diseased small bowel are typically managed with small bowel resection, excision and primary closure of the colonic opening.

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## ANORECTAL DISEASE

Typical manifestations of anorectal CD include fissures, fistulas, abscesses, and anal canal stenosis. Perianal disease resulting in fistulas and abscesses is frequently treated in stages. Perianal sepsis from abscess formation is addressed with incision and drainage. Subsequent abscess formation may be prevented by placement of seton drains. Fistulotomy and rectal advancement flaps are additional options in the management of chronic fistulas. Fistulotomy is specifically applicable to low fistulas. Rectal advancement flaps are less frequently successful in the CD population and candidates for these approaches must be carefully selected. The absence of significant rectal mucosal disease is a prerequisite for successful advancement flap coverage. The construction of a diverting ostomy may render active disease quiescent and is a useful option in selected patients with debilitating perianal or perineal disease who are poor candidates for a larger operation. Finally, proctectomy and proctocolectomy are appropriate options for patients with persistent, severe disease<sup>[6]</sup>.

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## ULCERATIVE COLITIS

In contrast to CD, UC may be cured with surgery. The

specific indications for surgical intervention fall into two broad categories: emergent and elective. Emergent indications include massive hemorrhage, toxic colitis, toxic megacolon, and intestinal perforation. Elective indications include the inability of medical therapy to alleviate symptoms, severe malnutrition, the presence of dysplasia, and cancer.

## EMERGENCY INDICATIONS

Toxic colitis, characterized by diffuse abdominal tenderness, tachycardia, fever, and leukocytosis is initially treated with fluid resuscitation, intravenous steroids and antibiotics. Surgery is indicated if clinical parameters do not improve with medical therapy in 48 to 72 h. The operation of choice in this setting is a subtotal colectomy and ileostomy with Hartmann pouch or rectal mucous fistula. Pelvic dissection is avoided to allow for a subsequent safe conversion to a proctocolectomy. Toxic megacolon is a variant of toxic colitis characterized by severe dilation of the colon. Toxic megacolon may be acutely managed with a subtotal colectomy and ileostomy. Construction of a skin-level transverse colostomy for decompression and a loop ileostomy for diversion has been described as an alternative approach in this setting. Colonic perforation is typically managed with a subtotal colectomy and ileostomy. Massive hemorrhage is similarly treated with a subtotal colectomy and ileostomy following proctoscopic confirmation that the majority of the bleeding is proximal to the rectum.

## ELECTIVE INDICATIONS

Severe persistent symptoms that compromise quality of life are an indication for surgical resection as are complications of long term steroid dependence. Malnutrition and growth retardation are common indications for resection in the pediatric population. Finally, dysplasia or colorectal cancer detected by colonoscopy mandate surgical resection.

Surgical options for chronic ulcerative colitis include proctocolectomy with ileostomy, proctocolectomy with continent ileostomy, and proctocolectomy with IPAA. Proctocolectomy with ileostomy remains an important surgical option with curative potential in UC and relatively low morbidity when compared to proctocolectomy with IPAA. In healthy individuals who are motivated to maintain fecal continence and are willing to accept the potential associated morbidity, restorative proctocolectomy with IPAA is the procedure of choice. Though the necessity of a temporary diverting ileostomy has been called into question by some investigators, the majority of experienced surgeons routinely divert patients undergoing IPAA for a period of two to three months. The construction of continent ileostomies was more popular prior to the refinement of IPAA techniques. Continent ileostomies are prone to failure from valve slippage and this approach is only applicable in highly selected patients. Conversion to a continent ileostomy may be appropriate in patients with an IPAA who develop septic complications but are uncomfortable with the realities of a conventional ileostomy<sup>[7]</sup>.

**Table 1 Advances in the surgical management of IBD**

Crohn's disease
Laparoscopic ileocecal resection
Multi-modality approach to anorectal CD
Ulcerative colitis
Laparoscopic restorative proctocolectomy
Probiotics

## ADVANCES IN THE SURGICAL MANAGEMENT OF IBD

### Crohn's disease

The role of laparoscopy in the surgical management of CD has been the focus of considerable investigation over the past decade. Several non-randomized trials suggested equivalent morbidity and mortality following laparoscopic or open ileocecal resection. Benefits of the laparoscopic approach, such as shorter length of hospital stay and lower rates of post-operative bowel obstruction, were suggested in some series. More definitive data in the form of two published prospective randomized trials have shed further light on these topics. In the study published by Milsom *et al*<sup>[8]</sup>, 60 male patients were randomized to either laparoscopic or conventional ileocolic resection. Serial pulmonary function tests (PFT's) were measured post-operatively and were used as an objective surrogate for recovery. While the laparoscopic group's PFT's normalized more rapidly than did those of the conventional surgery group, the return of GI function and length of hospital stay was not significantly different between the two groups<sup>[8]</sup>. In the study reported by Maartense *et al*<sup>[9]</sup>, sixty patients were randomized to either laparoscopic-assisted or open surgery. Importantly, post-operative care of the enrolled patients, regardless of which operation they received, was standardized. The primary outcome parameter was post-operative quality of life as measured by responses to two standardized questionnaires during a three month follow-up period. Secondary outcomes included operating time, morbidity, hospital stay, post-operative morphine requirement, and costs. Median operating time was longer (115 min *vs* 90 min,  $P < 0.003$ ), median hospital stay was shorter (5 d *vs* 7 d,  $P = 0.008$ ), and costs were lower in the laparoscopic group when compared to the open surgery group. Quality of life did not differ between the two groups<sup>[9]</sup>. In summary, there is no demonstrable difference in outcomes after open and laparoscopic ileocecal resection. Evidence is somewhat contradictory with regards to recovery time, but there is some evidence suggesting a more rapid recovery following laparoscopic ileocecal resection (Table 1).

As stated previously, 70%-80% of patients with CD eventually require surgery. Unfortunately, rates of disease recurrence remain high with a median time of ten years between a first and second bowel resection. A number of studies have proposed lower rates of disease recurrence after bowel resection when side-to-side stapled anastomoses are performed as opposed to hand-sewn end-to-end anastomoses. The widespread observation that disease recurrence invariably affects

bowel proximal to the prior anastomosis has led some surgeons to hypothesize that some element of relative obstruction at the anastomosis contributes to the pathogenesis of proximal disease. If this is the case, it follows that techniques allowing for a larger, more widely patent, anastomosis might lower recurrence rates. A number of retrospective, and non-randomized prospective studies suggest longer intervals of time prior to second resections when the stapled technique is employed<sup>[10]</sup>. A multicenter randomized trial is ongoing to investigate these observations.

Several interesting observations and advances have been reported regarding the operative treatment of anorectal CD. As mentioned previously, the placement of a draining seton is of considerable utility in the management of perianal fistulas. Perianal fistula recurrence following the removal of draining setons, however, is common. A combined medical and surgical approach to anorectal disease has been widely advocated. Specifically, the use of infliximab therapy in combination with examination under anesthesia and seton placement is supported by retrospective data published by Regueiro and Mardini<sup>[11]</sup>, and by Topstad *et al.*<sup>[12]</sup>. Irrespective of pharmacologic and surgical intervention, anorectal fistulizing disease remains a difficult problem as evidenced by the 44% rate of fistula recurrence after combined seton placement and infliximab therapy cited in Regueiro and Mardini's study. Surgical diversion is an often effective, if relatively radical, strategy for severe, medically refractory anorectal disease. Galandiuk *et al.* reviewed their extensive experience in treating patients with anorectal CD. They identified the presence of anal canal stenosis and concomitant colonic CD as predictors of the need for permanent fecal diversion<sup>[13]</sup>.

### Ulcerative colitis

Laparoscopic surgery for UC has attracted considerable interest in recent years. Several case series and case-control studies established the feasibility of laparoscopic restorative proctocolectomy with ileal pouch anal anastomosis<sup>[14]</sup>. One randomized study comparing hand-assisted laparoscopic and open surgery for both UC and familial adenomatous polyposis has been published<sup>[15]</sup>. Maartense *et al.* randomized sixty patients and documented their post-operative recovery at three months after surgery as measured by two standardized quality of life questionnaires. Secondary parameters included post-operative morphine requirement, operating time, morbidity, hospital stay and costs. Recovery in the two groups was equivalent. The laparoscopic operation took longer and was more costly<sup>[15]</sup>. At the current time, there is little evidence to suggest a benefit to laparoscopic restorative proctocolectomy as compared to the open operation with the exception of cosmesis. Interest in this approach, however, both in the medical and patient communities, remains great. With increased experience the role for this operation will, presumably, become more clearly defined.

Morbidity associated with restorative proctocolectomy with IPAA remains significant. Pouchitis is the most common long-term complication following IPAA. This syndrome, most often characterized by increased stool frequency, urgency, and abdominal discomfort, remains

poorly understood. The efficacy of antibiotic therapy in the majority of patients suggests an infectious etiology. Promising data supporting probiotic maintenance therapy for relapsing pouchitis after initial treatment with antibiotics was published by Gionchetti *et al.*<sup>[16]</sup>. Forty patients were randomized to receive a probiotic called VSL#3 containing viable lyophilized bacteria including four strains of *Lactobacillus*, three species of *Bifidobacterium* and *Thermophilus*, or placebo. Over a nine month follow-up period, 15% of patients treated with VSL#3 compared to 100% of patients treated with placebo relapsed<sup>[16]</sup>. Similarly impressive results for VSL#3 were published by Mimura *et al.*<sup>[17]</sup> VSL#3 has also been studied as prophylaxis against pouchitis during the first year following IPAA in a randomized prospective study. Of 20 patients randomized to VSL#3, 2 (10%) developed pouchitis within 12 months. Comparatively, 8 of 20 patients randomized to placebo (40%) developed pouchitis<sup>[18]</sup>. These results warrant further study of probiotics in the prevention of, and as maintenance therapy following initial therapy for, pouchitis.

### CONCLUSION

Surgery remains an important component of the multimodality treatment of IBD, required in 70%-80% of patients with CD and 30%-40% of patients with UC. Operative intervention for CD is indicated when symptoms are refractory to medical therapies, or when patients develop complications of the disease. Emergent indications for surgical intervention in UC include massive hemorrhage, toxic colitis, toxic megacolon, and intestinal perforation. Elective indications include refractoriness to medical therapy, severe malnutrition, the presence of dysplasia, and cancer. During the last decade significant efforts have been made to apply laparoscopic techniques to the surgical management of IBD. Additionally, significant advances in medical therapy have been made which promise to impact positively on outcomes following surgical interventions. The role of laparoscopy in the surgical management of CD has been the focus of considerable investigation. No significant difference in outcomes after open and laparoscopic ileocecal resection has been demonstrated but shortened recovery time following laparoscopic resection has been suggested in some studies. Except for improved cosmesis, there is little evidence to suggest a benefit to laparoscopic restorative proctocolectomy as compared to the open operation. Morbidity associated with restorative proctocolectomy with ileal pouch anal anastomosis (IPAA) remains significant. Pouchitis is the most common long-term complication following IPAA. Probiotic maintenance therapy for relapsing pouchitis after initial treatment with antibiotics and as prophylaxis against pouchitis during the first year following IPAA is promising and further investigations are warranted.

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