

# Operative Management of Small Bowel Crohn's Disease

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## Historical aspects

When Crohn, Ginzburg, and Oppenheimer first described “regional enteritis,” they believed that a cure for this disease could only be possible with complete surgical resection. High morbidity, mortality, and recurrence rates led to a trend toward bypass surgery, however. This procedure carried a lower mortality rate but could be complicated by the development of an infected mucocele or a cancer in the bypassed segment. There was therefore a return to resectional surgery.

Over the last 25 years, there have been moves toward more conservative surgery (stricturoplasty and conservative resection), nonsurgical management (percutaneous drainage of abscesses, endoluminal dilatation of strictures, antibiotic management of microperforations), and an exploration of the usefulness of minimal access surgery (laparoscopic or laparoscopic assisted).

## Frequency of surgical intervention

Surgery is an important component of management of Crohn's disease, with studies showing that 70% to 90% of patients require surgical intervention at some point in the course of the disease [1,2]. The need for surgery depends on site and duration of disease. In patients who have ileocecal disease, the probability of requiring surgery within 5 years of onset is 75% and reaches 90% after 10 years of symptoms. For patients who have ileal disease

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only, the probability of requiring surgery is 50% at 5 years and 70% at 10 years [3]. Patients who have small bowel Crohn's disease and raised antibody concentrations to microbial antigens have an increased risk for requiring small bowel surgery [4]. Seiderer and colleagues [5] have shown that genotyping (identification of CARD15 variant 1007fs) can predict the need for surgery in patients who have Crohn's disease and symptoms suggestive of small bowel strictures.

### **Philosophy of surgical approach**

Crohn's disease is now considered a panenteric disease and is therefore not curable. Surgery carries with it a relatively high rate of major complications and recurrence, and a variable amount of diarrhea and metabolic upset because of a shortened bowel [6,7]. These observations have led to a philosophy of reserving surgery for patients who experience complications of their disease or in whom medical therapy has failed or not been tolerated.

There is an alternative philosophy of the use of surgery at an earlier stage in the course of the disease before serious septic complications develop [8]. This approach is based on the complication rates following surgery for non-complicated Crohn's disease (12%) being much lower than those encountered when operating on advanced Crohn's disease (49%) when the disease is usually complicated by abscess or fistula formation [8].

### **Indications for surgery**

Many patients require surgery for complications of their disease, most commonly recurrent intestinal obstruction because of strictures and perforations (abscesses, fistulas, free perforation) and less commonly because of major hemorrhage, failure to thrive, cancer, obstructive uropathy, and extraintestinal manifestations. The ileocecal region and small bowel are the most common sites requiring surgery. Duodenal involvement occurs in only 1% to 3% of patients who have Crohn's disease, with surgery being required for strictures, fistulas, or bleeding.

#### *Intestinal obstruction*

Intestinal obstruction is a frequent primary indication for surgery; it may be caused by a single narrow stricture (Fig. 1) or a series of strictures and present acutely or with chronic symptoms [9]. Acute small bowel obstruction usually follows ingestion of high-residue, indigestible fiber products, such as raw fruits or vegetables. This type of obstruction usually resolves with non-operative management. Surgery is indicated when an obstructive episode fails to resolve, when there are frequent bouts of obstruction, or when the obstruction is associated with a septic response, an intra-abdominal mass,



Fig. 1. Small bowel series showing recurrent stricture proximal to ileocolonic anastomosis.

fistula, or malnutrition. Surgery usually involves a resection, or rarely ileostomy formation or internal bypass. Chronic obstruction is typified by recurring episodes that do not respond to long-term medical therapy and usually require elective surgery. Surgery generally involves a resection, but one or more strictureplasties are an option if the patient has had previous intestinal resections or has multiple strictures.

#### *Alternatives to surgery for intestinal strictures*

Endoscopy and hydrostatic balloon dilatation of strictures has been used as an alternative to either resection or strictureplasty in selected patients who have short (<10 cm) solitary small bowel (or colonic) primary or anastomotic strictures. Dilatation is usually used for strictures in the terminal ileum that are not complicated by fistula or abscess formation and that can be accessed at colonoscopy. High technical success rates (66% to 100%) have been reported [10,11]. Complications (8% to 25%) include hemorrhage and perforation [11,12]. Repeat dilatations are necessary in 60% of patients [11]. Primary strictures tend to be longer, associated with more ulceration, and have a higher risk for perforation and recurrence after

dilatation than is described with anastomotic strictures [12]. Endoscopic stricture dilatation would therefore seem to have more of a role for solitary (recurrent) strictures at an ileocolonic anastomosis.

Postdilatation intralesional steroid injections have also been described that were associated with a reduced recurrence rate [13]. Bickston and colleagues [14] have reported an undernourished patient who had small bowel obstruction attributable to a Crohn's stricture of the terminal ileum that was successfully treated by insertion of a metallic enteral endoprosthesis.

### *Intra-abdominal abscesses*

Up to 25% of patients who have Crohn's disease present with intra-abdominal abscesses at some point in their life [15]. Abscesses can develop because of a local perforation, in association with a fistula, or postoperatively because of intra-abdominal contamination or anastomotic leakage. Abscesses can be classified as intraperitoneal, interloop, intramesenteric, or retroperitoneal.

Abscesses may present as a tender abdominal mass but clinical features may be indistinguishable from an exacerbation of the disease. CT and ultrasound scanning may aid the diagnosis; however, abscesses may only be confirmed at laparotomy in up to 50% patients [16]. Surgery is often difficult in patients who have abscesses because they may be nutritionally depleted, steroid dependent, or immunocompromised. Surgery usually involves resection of bowel and drainage of abscesses. Anastomosis may be considered if there are local and systemic factors that are conducive to healing of an intestinal anastomosis [17] but a temporary stoma and later restoration of intestinal continuity is often necessary.

Interloop abscesses are usually found at the time of resection when bowel loops are separated. Intramesenteric abscesses may be drained by intraoperative needle aspiration. It has been recommended that the involved segment should be excluded by bringing both ends to the skin surface as mucous fistulas and performing enteroenterostomy between proximal and distal segments, rather than risk peritoneal contamination and difficulty with the vascular pedicle by performing intestinal resection at that stage [18].

### *Alternatives to surgery for intra-abdominal abscesses*

If the patient is hemodynamically stable and the abscess has been diagnosed preoperatively, percutaneous drainage is an option. Intraperitoneal, pelvic, and retroperitoneal abscesses may all be suitable for percutaneous drainage under CT (Fig. 2) or ultrasonographic guidance. This may change a two-stage procedure (initial resection and stoma; later restoration of intestinal continuity) to a one-stage procedure with definitive resection and anastomosis [19]. Not all patients may need a subsequent resection [20]. A sinogram should be performed by way of the drainage catheter a week later to investigate for enteric communication. If no enteric communication is demonstrated, the catheter can be removed and the patient followed for

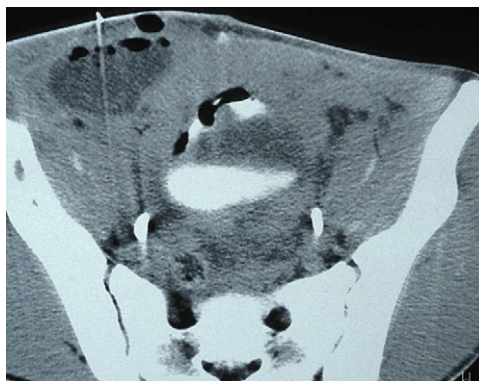


Fig. 2. CT scan showing percutaneous drainage of Crohn's-related abscess in right iliac fossa.

recurrence. If the abscess cavity had an enteric communication, complete resolution is unlikely without resection. Garcia and colleagues [21] studied 51 patients who had intra-abdominal abscesses complicating Crohn's disease and found that fewer patients developed recurrent abscesses after initial surgical drainage and resection (12%) than patients treated by percutaneous drainage alone (56%). Gutierrez and colleagues [22] compared percutaneous drainage with open surgical drainage in 66 patients who had intra-abdominal abscesses in Crohn's disease. They found no difference in time to resolution of infection. One third of the patients treated with percutaneous drainage required surgery within 1 year.

### *Free perforation*

Free perforation is a rare complication of Crohn's disease and typically occurs during an acute exacerbation of chronic disease just proximal to a strictured intestinal segment. Urgent laparotomy is required, with resection of the involved segment being preferred to simple closure with suture because associated mortality is reduced 10-fold to approximately 4% [23].

### *Fistulas*

Fistulas are commonly found (35%) in patients operated on for Crohn's disease but were the primary indication in only 6.3% of patients [24]. Patients may present with fistulas but they are more commonly recognized as postoperative complications (leak from anastomosis or strictureplasty site). Fistulas may be classified as internal (enteroenteric, enterovesical, or enterovaginal) or external (enterocutaneous). The same patient may have several types of fistula.

Enteroenteric fistulas are the most common internal fistula and may cause few symptoms unless associated with obstruction or intra-abdominal abscess. An enteroenteric fistula is an indication for surgery when it causes

a bypass of a sizable portion of intestine with consequent diarrhea and malabsorption. Treatment is by primary resection and anastomosis in most cases, unless the patient is poorly nourished or there is excess intraoperative blood loss or unresolved sepsis. Surgical resection involves resection of the fistula source—which is most often the terminal ileum (with anastomosis)—and performing a wedge excision and closure of the adjacent segment that has been secondarily involved [18]. For ileosigmoid fistulas, simple suture closure of the sigmoid may be vulnerable to leakage; limited sigmoid colonic resection and anastomosis is recommended [18].

Enterovesical fistulas may present with pneumaturia or repeated urinary tract infections. Diagnosis is by cystogram, cystoscopy, or CT scan. Surgery is the appropriate treatment and involves separation of the small bowel from the bladder, intestinal resection with anastomosis, and débridement and closure of the bladder, leaving a urinary catheter in for 10 days. Cystography before catheter removal can be used to confirm bladder integrity.

Enterovaginal fistulas usually occur in patients who have undergone a hysterectomy. They are treated by surgical resection and anastomosis of the fistula source and débridement and closure of the vagina with omental interposition between the intestinal anastomosis and vaginal closure [18].

Enterocutaneous fistulas usually occur postoperatively as a result of anastomotic breakdown or at a later stage because of recurrent disease (Fig. 3). Most open onto the anterior abdominal wall through a previous incision. Spontaneous fistulas may develop in close proximity to an



Fig. 3. Small bowel series showing multiple strictures and enterocutaneous fistulas to midline wound and to right iliac fossa.

ileostomy in 1% of patients and usually indicate a short stricture or recurrent disease. The fistula itself is not an indication for surgery; initial efforts are directed toward elimination of sepsis, protection of the skin, restoration of nutrient and electrolyte deficiencies, and establishment of fistula anatomy before planning a definitive procedure [25]. Early surgery (defunctioning ileostomy) may be necessary for an early postoperative fistula.

All fistulas are initially associated with sepsis, although discharge through the abdominal wall may satisfactorily drain the sepsis. CT and ultrasound scans may aid identification and percutaneous drainage of any associated abscess. Surgical drainage of the abscess may be necessary if the abscess cavity is inaccessible or multiloculated, and for those patients who show persistent sepsis despite percutaneous drainage. The surrounding skin needs to be protected at an early stage to prevent contact dermatitis. This procedure may be possible with a stoma bag or require wound drainage bags and suction. Nutritional support needs to be considered at an early stage with the options being oral/enteral nutrition with a high-protein, low-residue feed (if the fistula site is distal), or parenteral nutrition or fistuloclysis (feeding into distal bowel by way of fistula site) if the fistula is proximal. Proton pump inhibitors and somatostatin analogs are often used in an attempt to reduce gastric acid production and pancreatic secretion, respectively. Definition of the fistula tract usually involves oral contrast studies (small bowel series or small bowel enema), fistulography, and CT scanning.

Definitive surgery should be delayed for at least 3 months to allow time for spontaneous closure and for resolution of obliterative peritonitis. Fistulas are unlikely to close if they are associated with recurrent disease, distal obstruction, or persistent infection, or if there is mucocutaneous continuity or discontinuity of bowel ends. A decision may be made not to operate if the fistula has a low output and the operative risk is high. Surgery involves complete mobilization of the bowel, resection of the fistulizing segment, and anastomosis.

#### *Alternatives to surgery for fistulas*

Prolonged parenteral nutrition may be necessary to correct undernutrition before surgery can be contemplated. Immunosuppressants, such as azathioprine, 6-mercaptopurine, and cyclosporine, have all been evaluated in the setting of enterocutaneous fistulas. Favorable results have been reported for the use of 6-mercaptopurine for external and internal fistula: almost 40% of fistulas closed after a 6-month period of treatment [26,27]. There is a high recurrence rate following withdrawal of treatment, however. Long-term treatment with oral cyclosporine produces an improvement in enterocutaneous fistulas in 40% of patients [28,29], but side effects are common and there is a tendency for the fistulas to recur when the drug is withdrawn.

Infliximab has been evaluated in patients who have Crohn's disease and enterocutaneous fistulas. The ACCENT-1 study showed a rapid response to three infusions of infliximab in 46% of patients, but the duration of the

effect was limited to only 3 to 4 months [30]. The ACCENT-2 study treated 306 patients who had actively draining enterocutaneous fistulas with three infliximab infusions [31]. Sixty-nine patients responded (22%) and these patients were then treated with further infusions of infliximab (or placebo) every 8 weeks. At the end of the trial the response rate (discontinuation of fistula drainage in more than 50% fistulas) to infliximab was 46% compared with a response rate to placebo of 23%; complete response rate (all fistulas closed) was 36% for infliximab and 19% for placebo. The most common side effect was abscess formation in association with the fistula.

### *Failed medical treatment*

Medical therapy is initiated for most patients suffering from disease symptoms unless presentation mandates emergency surgery. Medical therapy is considered to have failed if:

- Symptoms cannot be controlled with the maximum possible doses
- Disease progresses (worsening symptoms or new complications) while on maximum medical therapy
- Significant treatment-related side effects occur
- There is noncompliance with medication

Failure of medical therapy has been found to be the most common indication for surgery in some series.

### *Hemorrhage*

Massive hemorrhage is an uncommon indication (0.9%–1.4%) for surgery. Other causes, such as coagulopathy and peptic ulcer, need to be excluded. Surgery is indicated in patients who are hemodynamically unstable, those who continue to bleed after receiving four to six units of blood, and those who have recurrent major hemorrhage. Preoperative or intraoperative mesenteric angiography may aid in localizing the bleeding source, especially if there is multisite disease [32,33]. The involved segment requires resection with or without anastomosis depending on hemodynamic stability. If there is difficulty in identifying the responsible segment, wide resection may be necessary. One third of patients who have Crohn's disease experience recurrent hemorrhage, usually within 3 years of the original episode.

### *Alternatives to surgery for massive hemorrhage*

Mesenteric angiography and intra-arterial infusion of vasopressors [34] or embolization [35,36] have been recently used in an attempt to avoid surgical resection.

### *Malignancy*

Cancer is an uncommon complication of small bowel Crohn's disease (0.3%) and may be multifocal and poorly differentiated. The risk for small

bowel cancer is increased 12- to 60-fold in patients who have small bowel Crohn's disease compared with the general population [37]. Predisposing factors include long duration of disease, early age of onset, smoking, diffuse disease, and bypassed intestinal segments [38]. Bypassed segments are impossible to keep under surveillance and are therefore best resected. Concern about the potential to develop cancer at the site of longstanding strictures has led to the recommendation that stricture biopsies should be undertaken when strictureplasty is being performed [39,40]. The presence of a neoplasm may be suggested in a patient who has longstanding Crohn's disease who develops an unresolving obstruction [41]. In most patients who have small bowel cancer complicating Crohn's disease, the neoplasm is found incidentally at surgery. Surgical resection is indicated but the outcome is poor [41] with a mean survival of 6 months for small bowel cancers [38].

### *Obstructive uropathy*

The right ureter may be compressed or obstructed by an ileocecal phlegmon or an associated abscess with consequent hydronephrosis. Urinary symptoms are often absent and the obstructive uropathy is frequently diagnosed by CT scanning. The obstructive uropathy is usually relieved by intestinal resection [42]. If the ileocecal segment is densely fixed in position, a proximal defunctioning ileostomy may be necessary to allow the inflammation to reduce, with a subsequent resection [42].

### *Failure to thrive*

Growth retardation is seen in 26% of children affected by Crohn's disease [43]. This finding may be attributable to malabsorption, nutritional deficiencies, and corticosteroid therapy. If a prepubertal patient remains undernourished despite adequate medical therapy and nutritional supplementation, operative intervention is recommended. Surgery for growth retardation is not beneficial after the onset of puberty.

### *Gastroduodenal disease*

Symptomatic gastroduodenal disease occurs in 0.5% to 4% of patients who have Crohn's disease and is usually associated with disease at other sites. The most common indications for intervention are strictures, hemorrhage, and fistulas. Duodenal strictures may be bypassed (gastrojejunostomy), subjected to strictureplasty (depending on their site), or dilated (hydrostatic balloon). Strictureplasty may be preferable to bypass because it decreases the chances of stomal ulceration and diarrhea. Hemorrhage is usually managed by upper gastrointestinal endoscopy and adrenaline injection, rarely necessitating duodenotomy and underrunning of the bleeding source. Fistulas generally arise from small bowel disease and therefore surgical intervention includes small bowel resection (and anastomosis) and

closure of the duodenum. Pettit and Irving [44] have recommended that it is safer to close this secondary duodenal defect with the aid of a jejunal serosal patch, or to use a Roux-en-Y duodenojejunostomy.

### **Preparation for surgery**

Preparation for surgery entails counseling of the patient; documentation of extent of disease and presence of sepsis; consideration of bowel preparation, antibiotic, and venous thromboembolism prophylaxis (subcutaneous heparin, compression stockings); correction of fluid, electrolyte, and nutritional deficiencies; review of medication (corticosteroids and immunosuppressants); and marking of possible stoma sites.

Counseling of the patient includes discussion of disease extent, indications for surgery, alternatives to surgery, possible findings at surgery, intraoperative assessment and decision making (extent of resection, use of stricturoplasty, formation of stoma), postoperative pain relief, expected discharge date, possible complications (bleeding, intra-abdominal and wound infections, intestinal injury, anastomotic leakage, fistula formation, respiratory atelectasis and infection, venous thromboembolism, incisional hernia, adhesive intestinal obstruction) and long-term outcome (possibility of recurrent disease, need for adjuvant therapy, symptomatic consequences of intestinal resection, nutritional deficiencies).

The extent of disease can be documented by small bowel series, colonoscopy (or barium enema), gastroscopy (if there are upper gastrointestinal symptoms), or isotope-labeled white cell scanning. It is wise to repeat studies preoperatively if the most recent imaging is more than 1 year old. There is evidence that newer modalities (enteroscopy, CT enterography, wireless capsule endoscopy, magnetic resonance enteroclysis) may improve detection of intestinal disease and strictures [45–49]. Blood tests (C-reactive protein, white cell count), CT scanning, and isotope-labeled white cell scan may also give useful information about the presence of septic complications [50,51].

Bowel preparation should be considered if there is any suggestion of colonic involvement, but may not be possible or well tolerated if there are obstructive symptoms. Prophylactic antibiotics (third-generation cephalosporin and metronidazole) should be given at induction and for up to 24 hours. A treatment regime (5 days of antibiotics) may be necessary if there is significant intraoperative contamination.

Patients who have small bowel Crohn's disease may be undernourished because of oral intake failure and malabsorption. Common nutritional disturbances are weight loss, hypoalbuminemia, anemia, and deficiencies of zinc, selenium, iron, vitamin A, vitamin D, and folic acid. Severely undernourished patients may benefit from preoperative nutrition support by either enteral or parenteral nutrition.

Stoma sites are best marked by specialist stoma care nurses who discuss the site with the patient considering visibility at the summit of the infraumbilical fat pad, within the surface markings of rectus abdominis muscle, and remote from old scars, skin creases, and bony prominences.

Drugs need to be reviewed so that anticoagulants are omitted; immunosuppressants may also need to be discontinued if there is leukopenia, and corticosteroids may need to be given to cover the perioperative stress in patients at risk for adrenal suppression (systemic steroid therapy within the last 6 months). No relationship between perioperative use of infliximab or immunosuppressants and the development of postoperative complications has been found [52].

### **Surgical approach**

Surgical assessment and resection for Crohn's disease can now be performed laparoscopically—or with laparoscopic assistance—and by the traditional open approach. Laparoscopic surgery offers the possibilities of less postoperative morbidity, a faster recovery of pulmonary and intestinal function, better cosmesis, less narcotic use, shorter length, reduced costs of hospital stay, and reduced time to resumption of work. For patients who have Crohn's disease, laparoscopic surgery may also reduce intra-abdominal adhesions and abdominal wall injury seen in patients requiring repeated surgery. A laparoscopic approach can be used in Crohn's disease to create stomas, for ileocolonic resection, small bowel resection, and strictureplasty [53]. Concerns regarding the use of the laparoscopic approach have been a risk for underestimating the extent of the disease and an inability to complete the operation because of the presence of a thickened mesentery, inflammatory masses, abscesses, and fistulas.

The laparoscopic approach for ileocolonic resection usually involves mobilization of the terminal ileum and right colon; this can be performed medial to lateral or vice versa. The ileocolic pedicle is usually divided at an early stage to release the affected bowel from the retroperitoneum. A small 4- to 8-cm midline incision allows exteriorization of the specimen, control of remaining mesenteric blood vessels, bowel division, and extracorporeal anastomosis. Total intracorporeal resection and anastomosis have been described [54,55]. Extracorporeal resection and anastomosis may be safer and more rapid, however, and allows reliable examination of the total small bowel [53].

There is evidence of reduced surgical stress and faster recovery of pulmonary function after a laparoscopic approach. The laparoscopic approach was found to have no effect on recurrence rate or quality of life [56–58]. Lowney and colleagues [56] found that all disease recurrences were at the preanastomotic site, which did not substantiate the hypothesis that occult segments of disease were being missed as a result of the laparoscopic

approach. Bergamaschi and colleagues [59] reported a reduced incidence of obstructive episodes over a 5-year period despite a similar preanastomotic recurrence rate; this may be because of a lower rate of adhesion formation and a reduced rate of ventral hernias.

Tilney and colleagues [60] in a meta-analysis showed that there was no significant difference in blood loss, anastomotic leak rate, or incidence of wound or chest infection, bowel obstruction, or formation of intra-abdominal abscesses between open and laparoscopic approaches in Crohn's disease. The operative times were significantly longer in the laparoscopic group. The laparoscopic group had a faster return of intestinal function and a shorter duration of hospital stay, however.

There is a large variation in the reported conversion rates for laparoscopic surgery for Crohn's disease (2%–40%). The conversion rate is likely to depend on patient selection, time constraints, and surgeon experience [61]. In a prospective study involving 69 consecutive patients, Alves and colleagues [62] found that recurrent episodes of Crohn's disease and the presence of intra-abdominal abscesses or fistulas were independent risk factors for conversion. Conversion was not found to increase morbidity or mortality, however [62], and therefore some authors believe that the presence of a mass or fistula are not contraindications to a laparoscopic approach [2,63]. The benefits of a laparoscopic approach begin to be lost when large incisions are needed for resection and anastomosis, which is more likely to be the case with larger, complex masses [2,64]. When a laparoscopic approach was used for recurrent Crohn's disease, the conversion rate (21%) and morbidity (10%) were higher than for those who had no prior surgery [65]. A laparoscopic approach may still be recommended if conversion is necessary; these patients do as well as those undergoing primary open surgery [66].

A fast-track multimodal rehabilitation approach has now been applied to open ileocolonic resections for Crohn's disease with a reduction in hospital stay and low morbidity and readmission rates [67]. This type of approach achieves similar rates of recovery of intestinal function and duration of hospital stay to those published using a laparoscopic approach. The main advantages of laparoscopic surgery over open surgery thus may be cosmesis and a reduction in wound complications because of the smaller size of the wounds [68].

### **Principles of open laparotomy for Crohn's disease**

Consideration is necessary regarding positioning of the patient, maintaining body temperature, intraoperative venous thromboembolism prophylaxis, choice of incision, and intraoperative assessment and decision-making. The choice regarding position is between supine or modified lithotomy positions. The argument in favor of a modified lithotomy position is that any portion of the bowel can be involved and a sigmoid colon

resection (and anastomosis) may be necessary. An infraumbilical midline skin incision gives good access to the small bowel and the ileocecal region and avoids potential stoma sites in the right and left iliac fossae. The midline incision can be reopened for recurrent disease, but may need to be extended to gain access if there is small bowel adherent to the existing scar.

A full exploration of the abdominal cavity is necessary to identify sites of disease and length of normal small bowel. It is not uncommon to find that the disease is more extensive than preoperative imaging had suggested. Sites of disease can be identified by visual inspection (fat wrapping, inflammatory changes, wall thickening, mesenteric thickening, adherence to adjacent organs), palpation (induration, thickening of the mesenteric edge, luminal narrowing), and intraoperative endoscopy [69,70]. Strictures may be identified by palpation or by the use of intraluminal Foley catheter, bougie, ball bearing, or plastic sphere. Bleeding sites may be identified by intraluminal endoscopy or intraoperative mesenteric angiography.

Intraoperative decision making involves whether to resect, perform strictureplasty, bypass, or defunction by stoma. Decisions regarding resection include the extent of resection, the margins of resection beyond the disease margins, preservation of the ileocecal valve, and type of anastomosis (stapled or hand-sewn; end-to-end, end-to-side, or side-to-side).

### **Bypass, stoma, resect, or strictureplasty**

Bypass operations were introduced in the 1950s because of an associated reduced mortality rate, but have largely been abandoned because of the risk for continued disease activity and malignancy. A bypass procedure is still an option if an ileocolonic phlegmon is densely adherent onto iliac vessels or ureter, however, with a definitive resection being performed a few months later when the acute inflammation has subsided.

An ileostomy may be formed to defunction distal disease in association with a resection when an anastomosis is unsafe (undernourished patient, systemic steroid therapy, intra-abdominal sepsis), or if there is a simultaneous resection of colon and rectum. There is a significantly lower early recurrence rate after formation of ileostomy than after anastomosis [71].

Strictureplasty was introduced by Katariya and colleagues [72] who applied the technique to tuberculous strictures of the small intestine, to preserve intestinal length and reduce the risk for developing a short bowel syndrome in patients who would otherwise have undergone massive resection for these strictures. Lee and Papaioannou [73] applied the technique to patients who had Crohn's strictures of the small bowel. Since then strictureplasty has been used in patients who have short fibrous Crohn's strictures, in whom the technique has been shown to conserve intestinal length, relieve obstructive symptoms, promote weight gain, and enable reduction or withdrawal of steroid therapy. Strictureplasty has also been performed on recurrent strictures at ileocolonic anastomoses [74].

Sites of strictureplasty generally heal well with a low incidence of suture line breakdown; this may be because the blood supply to the involved segment of bowel remains untouched. There is radiologic, endoscopic, histopathologic, and operative evidence that active Crohn's disease regresses at the site of strictureplasty, especially when a large anastomosis has been performed [75,76]. The Cleveland Clinic [77] has reported a 5-year recurrence rate of 28% in a series of 698 strictureplasties in 162 patients with the recurrent strictures being found at the previous strictureplasty site in only 5% of patients. Because of the concern that a cancer may complicate a longstanding stricture and go unrecognized, it has been recommended that an intraoperative full-thickness biopsy should be taken from stricture sites during strictureplasty.

Indications for strictureplasty are: patients who have symptomatic fibrous strictures in the presence of diffuse disease, previous extensive intestinal resections (> 100 cm) or recent resection (within 1 year). Contraindications to strictureplasty are: patients who have small bowel perforation, malnutrition, or hypoalbuminemia; and strictures that are all located within a short segment, are very long (> 20 cm), or are found at the site of a fistula, an acute inflammatory mass, or in close proximity to a segment that needs to be resected.

Strictureplasty can be performed by several different techniques. Heinecke-Mikulicz and Finney are the two most commonly performed, Heinecke-Mikulicz strictureplasty being used for strictures less than 10 cm in length and Finney for strictures of 10 to 20 cm. In the Heinecke-Mikulicz technique, a linear antimesenteric incision is made through the stricture and extending for 3 cm on either side followed by closure of the wound transversely with a single-layer interrupted suture. In the Finney method, the strictured bowel is arranged in a U shape and the stricture is opened on the antimesenteric margin and closed side-to-side. Tichansky and colleagues [75] have reported a lower reoperation rate in patients whose strictures were subjected to Finney rather than Heinecke-Mikulicz strictureplasty.

With regard to resection, the main debate has focused on whether patients should have a limited or extensive resection and on the influence of microscopic involvement of the resection limits on subsequent recurrence. Berman and Krause [78] reported a lower recurrence rate after radical resection (29%) when compared with a conservative procedure (84%) after a 7.5- to 9.5-year follow-up. A large randomized controlled trial comparing limited (2 cm) and extended (12 cm) margins showed no relationship between recurrence and resection margins, however [79]. Hamilton and colleagues [80] compared recurrence rates in patients who underwent resection based on visual inspection with those in whom the resection margin was based on frozen section evaluation. There was no difference in clinical recurrence rates or reoperation rates after 10 years of follow-up. Glehen and colleagues [81] have reported that small bowel length (as measured at laparotomy) is significantly shorter in patients who have Crohn's disease

than in controls. Limited resection is therefore the procedure of choice; frozen section evaluation of resection margins does not influence recurrence rates.

Anastomoses may be performed by hand-sewn or stapled techniques and a variety of configurations have been described (end-to-end, end-to-side, and side-to-side). Stapled anastomoses have been reported to be associated with a lower morbidity [82], lower anastomotic leak rate [83], and lower reoperation rate [82], but these findings were not reported in all studies. Concerns about the use of staplers are related to a greater risk for bleeding in thickened bowel in patients who have undergone resection and anastomosis for chronic intestinal obstruction. Indeed, this thickened proximal bowel wall may exceed the specifications of the stapling device and therefore hand-sewn anastomosis may be safer. A hand-sewn anastomotic technique that is interrupted and single layer is less likely to cause luminal narrowing and is therefore preferred.

Regarding configuration of the anastomosis, a standard end-to-end anastomosis produces the narrowest lumen and so may make anastomotic recurrence more likely to be symptomatic. A retrospective study showed fewer symptomatic recurrences and lower operation rate in patients treated by a wide-stapled anastomosis compared with end-to-end sutured anastomosis [82]. Most studies have shown no effect of anastomotic configuration on recurrence rate, however.

### **Intraoperative challenges**

During the course of laparotomy for Crohn's disease, the surgeon may encounter an inflammatory mass, an unexpected abscess, an internal fistula, thickened mesentery, enlarged lymph nodes, or multisite disease. It is usually easier to deal with these situations if the affected bowel and associated mass can be delivered into the wound. The challenge then is to separate non-diseased bowel from diseased bowel without causing injury to normal bowel or to its vascular supply. This is usually achieved by a combination of blunt and sharp dissection.

For ileocolonic fistulas, the terminal ileum is usually the offending segment. Intraoperative colonoscopy may help to determine whether the colon is diseased (and therefore requiring resection) or secondarily affected. For ileo-ileal fistulas, the secondary site may be débrided and primarily sutured. For ileo-colonic fistulas, the secondary site can be treated by wedge excision or limited resection.

The mesentery of the ileocecal region affected by Crohn's disease is usually thickened and friable; care is needed during division to prevent significant blood loss or the development of a large mesenteric hematoma. It is often difficult to fashion convenient pedicles to ligate and it is usually safer to serially clamp the mesentery and to ligate using sutures. If diffuse

jejunoileal disease is encountered, the site and extent of the disease should be documented but only disease that is currently causing a complication should be dealt with surgically to avoid major intestinal resection and the development of short bowel syndrome.

### **Outcome of surgery**

Outcome of surgery can be classified according to mortality, morbidity, quality of life, and recurrence. In the Mount Sinai experience, postoperative (30-day) mortality rate was 3.2% with sepsis the most common cause [84]. In a long-term study, sepsis and severe electrolyte imbalance attributable to short bowel syndrome were the most common causes of death related to Crohn's disease [85]. Major postoperative complications occur in 10% to 20% of patients, the most common complications being bowel obstruction, intra-abdominal and wound infections, anastomotic leakages, and fistulas [6,75,84]. Serious postoperative complications are more likely if there is pre-existing intra-abdominal sepsis or preoperative immune suppression because of steroid use [6]. Post-strictureplasty intestinal hemorrhage may occur in as many as 10% of patients and if it is persistent may require surgery. Preoperative mesenteric angiography may help identify the source and avoid having to open or resect multiple intestinal segments that had been subjected to strictureplasty.

Later complications of small bowel resection for Crohn's disease include cholelithiasis; urolithiasis; fluid, electrolyte, mineral, and vitamin deficiencies; undernutrition; and diarrhea. Short bowel syndrome is unavoidable in a small percentage of patients who have Crohn's disease as a result of recurrent resection of affected small intestine and inflammatory destruction of remaining small bowel [86]. Agwunobi and colleagues [87] reported that most patients who had Crohn's disease developed intestinal failure as a result of multiple unplanned laparotomies for intra-abdominal sepsis (61%), with extensive primary surgery (17%) and uncomplicated sequential resection (22%) causing the remainder. Short bowel syndrome can be classified according to the anatomic configuration (jejunum-jejunostomy; jejunum-jejunocolonic anastomosis) and results in a variable degree of intestinal failure. Patients who have moderate intestinal failure require parenteral fluid and electrolyte supplementation; those who have severe intestinal failure require parenteral administration of fluid, electrolytes, and nutrition. Patients on home parenteral nutrition are at risk for severe complications, such as line-related sepsis, venous thromboembolism, and metabolic liver and bone disease.

Many patients who have Crohn's disease have physical and mental limitations on their quality of life, with depression reported in 33% to 100% of patients. Low quality-of-life scores with active disease improve to normal when remission is obtained by surgery [88]. Thaler and colleagues [57] found

that quality of life was significantly reduced in patients who had Crohn's disease at long-term followup irrespective of surgical approach (laparoscopic versus open).

### **Recurrent disease after surgery**

Surgery aims to overcome complications of Crohn's disease or to improve quality of life when medical treatment has failed, but does not cure Crohn's disease because of its panenteric nature. After intestinal resection and anastomosis, recurrence rates increase progressively with time after the surgery [89]. The risk for recurrence depends on the age of patient at initial surgery, site of the disease, extent of disease, disease pattern (stricturing or perforating), and postsurgical behavior (cigarette smoking). There is controversy regarding the effect, if any, of anastomotic configuration on the risk for recurrence.

Recurrence can be defined as endoscopic, radiologic, symptomatic, or requiring reoperation. Following ileocecal resection with anastomosis for terminal ileal disease, longitudinal endoscopic studies have shown that inflammation typically recurs within 12 months of resection [90]. The relevance of endoscopic recurrence has been queried; however, there is evidence that endoscopic recurrence often predicts later symptomatic recurrence and that endoscopic severity predicts future disease activity [91].

Overall, the risk for recurrence following intestinal resection and anastomosis is in the region of 29% to 35% at 5 years, 52% to 55% at 10 years, 60% to 75% at 15 years, and rising to 94% at 25 years [7,89]. The presence of a symptomatic recurrence does not mandate surgery. The rates of recurrence requiring re-resection have been reported to be 25% to 35% at 5 years and 40% to 70% at 15 years [92,93]. The risk for recurrence is higher for ileocolonic disease (50% at 5 years, 53% at 13 years) than for ileal disease [3,92], and higher for perforating disease than nonperforating disease [94]. An effect of disease pattern on recurrence rate has not been a universal finding, however [95].

Smoking increases the risk for recurrent disease as defined on endoscopy, by symptomatology, and in those requiring reoperation [96]. The 6-year recurrence-free rate after surgery is 60% for nonsmokers, 41% for ex-smokers, and 27% for smokers. The likelihood of recurrence correlates with the number of cigarettes smoked and the duration of smoking and is especially high in female smokers who have small bowel disease [97].

Crohn's disease tends to recur in the proximal limb of an ileo-ileal or ileocolonic anastomosis, although as many as one third of recurrences occur separately from it [98]. Fewer recurrences occur at strictureplasty than at resection sites [98]. When disease recurs, old notes and radiologic studies need to be reviewed and an up-to-date assessment made of remaining small and large bowel using contrast examinations and colonoscopy. CT scanning

is useful if intra-abdominal sepsis is suspected and nuclear medicine imaging may help to determine whether symptoms are attributable to disease recurrence or postoperative adhesions.

Indications for surgery in patients who have recurrent disease are the same as for those who have primary surgery: failed medical therapy and acute or chronic complications. There is concern that reoperative surgery for Crohn's disease leads to the development of short bowel syndrome; this often leads to a more cautious approach and stricturoplasty is often favored. Resection is usually undertaken for intra-abdominal sepsis and fistula formation, however.

### **Postoperative advice and treatment**

Having achieved remission by surgical intervention, the next challenge is to maximize the period of symptom-free remission. Cessation of smoking is the postoperative intervention with the best evidence of effect on maintenance of remission, the relapse rate in ex-smokers being reduced by approximately 40% [96]. Esaki and colleagues [99] showed that postoperative enteral nutrition (>1200 kcal/day) reduced postsurgical recurrence, especially in patients who had penetrating disease and in those who had disease confined to the small bowel. There has been a lot of interest in prophylaxis against postoperative recurrence using aminosalicylates, antibiotics, corticosteroids, thiopurines, and probiotics. Many of the studies have used an endpoint of endoscopic recurrence to assess response to prophylactic treatment, rather than symptomatic recurrence, which would be a more useful clinical endpoint.

There have been several placebo-controlled trials of mesalazine as a prophylactic treatment with conflicting results. Meta-analysis has shown an advantage for Pentasa at a dose of 4 g/d, but only in patients who have isolated ileal disease [100]. Metronidazole (20 mg/kg/d for 3 months) reduces symptomatic and endoscopic relapse at 1 year [101]. The side-effect profile (nausea, vomiting, rashes, peripheral neuropathy) means that this antibiotic cannot be used long-term, however. With regard to steroids, prednisolone was found to have no prophylactic effect. Budesonide (6 mg/d) reduced endoscopic but not clinical recurrence at 1 year in patients who had inflammatory disease but not in those who had fibrostenotic disease [102]. Budesonide at a 3-mg dose was no better than placebo in preventing endoscopic recurrence in patients after ileal or ileocecal resection, however [103].

Thiopurines (azathioprine and 6-mercaptopurine) are effective steroid-sparing agents in active Crohn's disease but have a significant range of side effects and require regular toxicity monitoring. Studies in children (1 mg/kg/d) and adults (50 mg/d) have shown that 6-mercaptopurine is more effective than aminosalicylates (or placebo/no medication) in preventing postoperative recurrence [104,105]. Domenech and colleagues [106]

found that azathioprine was more effective than aminosalicylates in reducing clinical and endoscopic recurrence rates after surgical resection. Two other studies found no difference in efficacy between azathioprine (at a dose of 2 mg/kg/d or 50 mg/d) and aminosalicylates in preventing postsurgical recurrence [107,108]. Alves and colleagues [109] have shown that immunosuppressive drugs (one of azathioprine, 6-mercaptopurine, or methotrexate) reduce the rate of postoperative recurrence and the need for further surgery after a second ileocolonic anastomotic recurrence.

Trials assessing probiotic therapy have shown that neither *Lactobacillus G* nor *Lactobacillus johnsonii* LA1 was more effective than placebo in maintaining remission following intestinal resection [110,111].

Rutgeerts [112] has stratified postoperative patients into those at low (nonsmoker, first operation, and fibrostenosis) and high (female smoker, smoker; at least one previous operation; perforating disease and extensive disease) risk for recurrence. For patients at higher risk who have exclusively ileal disease, Pentasa at a dose of 4 g/d is a reasonable choice with minimal side effects. For patients who have extensive disease needing repeated operations, or with perforating disease, treatment with a thiopurine (azathioprine at 2–2.5 mg/kg/d or 6-mercaptopurine at 1–1.5 mg/kg/d) would seem a pragmatic approach.

## Summary

Despite advances in medical treatment, most patients who have Crohn's disease of the small intestine need surgery at some point during the course of their disease. Surgery is currently indicated for intractable disease and complications of the disease (strictures, abscesses, fistulas, hemorrhage). There is increasing interest in nonsurgical and minimal access strategies of dealing with complicated disease, however. These new approaches may enable postponement of surgery to a more favorable time, or conversion of a two-stage procedure involving a stoma to a one-stage resection with anastomosis. A continuing challenge is prevention of disease recurrence postoperatively.

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