



Lisa M. Cannon and Alessandro Fichera

Key Concepts

- Despite significant advances in medical management, surgery for Crohn's disease remains a vital component of many treatment paradigms.
- Optimal timing of surgery is critical in order to achieve the best outcome.
- Preoperative patient optimization is of critical importance.
- The surgeon treating Crohn's disease should be familiar with bowel-sparing principles and properly apply them while not compromising long-lasting remissions.
- Different anastomotic configurations should be considered based on severity and location of the disease.
- For all the abovementioned aspects, Crohn's disease requires a multidisciplinary approach to achieve optimal and lasting outcomes.
- Risk stratification should guide postoperative medical management.

Introduction

Medical therapy and our understanding of the pathophysiology of Crohn's disease have advanced during the last two decades. Surgical treatment has become less invasive, selective, and targeted. Now more than ever, it must be properly timed and planned. Patients affected by the disease ought to be managed in the context of a multidisciplinary approach. Surgery should be performed by properly trained surgical teams, and like our gastroenterology colleagues, many colorectal surgeons have subspecialized to become "surgical

IBDologists" working in the context of a specialty medical home (SMH). It has been shown that an IBD SMH significantly reduces unplanned care and disease activity and increases patient quality of life [1].

Changing Trends in the Surgical Management of Crohn's Disease

Crohn's disease is not cured by surgery; however, surgery retains an important role in disease management. The goals of a well-timed surgical intervention are to relieve symptomatic complications such as obstruction or fistula, improve quality of life, preserve small bowel, and minimize treatment interruptions in order to reduce risk of surgical recurrence.

Significant advances in medical therapy including the advent of immunomodulators and biologic therapies have altered the natural history of Crohn's disease. The need for surgery based on time from diagnosis has declined compared to patients managed in earlier decades. For example, in a population-based cohort of patients diagnosed with Crohn's between 1955 and 1989, 73% of patients overall required surgery: 44% at 1 year, 61% at 5 years, and 71% at 10 years after the diagnosis [2]. In a cohort of patients diagnosed from 2003 to 2004 and followed to 2011, 29% of patients required surgery: 14.6% at 1 year, 24.6% at 5 years, and 28.5% at 7 years after diagnosis [3]. Comparably numbers are seen in other studies based on decade. Interestingly, the largest drop in need for surgery predates the introduction of biologics and appears reflective of the increased use of corticosteroids. Immunomodulators and biologics have likely decreased the need for surgery, but the attributable impact is hard to measure. Improved diagnostic modalities in this same timeframe have led to earlier diagnosis and initiation of therapy, and treatment paradigms have shifted to individualized and risk-stratified medical management algorithms. Both of these evolutions have likely decreased the rate of complicated surgical disease.

L. M. Cannon (✉)
University of Rochester Medical Center, Department of Surgery,
Division of Colon and Rectal Surgery, Rochester, NY, USA
e-mail: lisa_cannon@urmc.rochester.edu

A. Fichera
Colon and Rectal Surgery, Baylor University Medical Center,
Department of Surgery, Dallas, TX, USA

After recovery from intestinal resection, health-related quality of life improves as early as 2 weeks after surgery and remains high in the long term. Postoperative complications and disease recurrence may limit improvement in quality of life [4]. Overall, patients are satisfied with their surgery and generally wish they had undergone surgery earlier in their disease course [5].

Indications for Surgery

The indications for operative management of Crohn's disease are varied and listed in Table 48.1. Free perforation, toxic colitis, and major hemorrhage are true surgical emergencies; these are far less common than the host of nonemergent Crohn's complications that require individualized surgical decision-making.

Failed Medical Therapy

Despite the introduction of entirely new classes of Crohn's therapies in the past decade, failure of medical management remains a common indication for surgical intervention. The phrase "failure of medical therapy" carries multiple meanings. Some patients are unable to achieve acceptable symptom control despite aggressive medical therapy; the patient is transitioned to the next medical agent or combination of agents until all options have been exhausted. Other patients may be able to achieve good symptom control but suffer side effects or reactions to the medications. In pediatric inflammatory bowel disease, growth retardation is a manifestation of failure of medical therapy as well. Steroid-refractory patients are those who have active disease despite prednisolone up to 1 mg/kg/day for a period of 4 weeks. Steroid-dependent patients are those who are unable to reduce their steroid dose below the equivalent of prednisolone 10 mg/day without disease reactivation or who have relapse within 3 months of stopping steroids [6].

Table 48.1 Operative indications for Crohn's disease

Failure of medical management
Pediatric growth retardation
Bowel obstruction
Free perforation
Penetrating disease/fistula/phlegmon/abscess
Cancer/dysplasia
Toxic colitis
Bleeding

Bowel Obstruction

Several Crohn's phenotypes can lead to bowel obstruction; taken together, about one-quarter of Crohn's disease surgery is secondary to obstructive symptomatology. Untreated and poorly controlled Crohn's disease causes progressive transmural intestinal injury. Histologic examination of a Crohn's stricture reveals thickening of the muscularis mucosa and muscularis propria with fibrotic change, as well as increased volume and density of the submucosa [7]. There is a slow evolution, and the bowel slowly accommodates to the progressive obstruction. The patient experiences intermittent abdominal pain, bloating, and progressive food intolerance. Eventually intervention is necessary due to acute or chronic obstruction or intolerable symptoms as the occlusive disease progresses. Currently no antifibrotic therapies for stricturing disease exist. Other etiologies of Crohn's disease-related obstruction include anastomotic stricture and neoplasm.

Once the diagnosis of obstruction has been established, the relative contribution of fibrosis and inflammation is assessed. CT or MR enterography is the current standard for assessing the small intestine. CT enterography findings of tissue inflammation include mucosal hyperenhancement, mesenteric fat stranding ("comb sign"), and mesenteric hypervascularity. However, CT enterography is not as successful at identifying degree of fibrosis, and upstream dilation is not reliable at distinguishing inflammation from fibrosis. On multivariate analysis, mesenteric hypervascularity was the only CT radiologic finding that predicted fibrosis. This highlights the pathophysiologic continuum between inflammation and fibrosis [8]. MRI findings indicative of inflammation include T2 hypersignal, mucosal enhancement, presence of ulceration, and blurred margins. A homogenous pattern of enhancement, and the percent of enhancement gain over time, can discriminate severe fibrosis deposition. Again, most lesions have a mixed pattern of fibrosis and inflammation [9].

Inflammatory stenoses are likely to respond to medical therapy, while fibrotic strictures typically require surgery. For localized ileocecal disease with obstruction, surgery is indicated if the patient does not respond to a trial of medical management with bowel rest and intravenous corticosteroids; upfront surgical management is indicated if clinical and radiologic findings suggest marked fibrosis with low levels of inflammation (Fig. 48.1). Ileocectomy for Crohn's disease has a high rate of disease control. Retrospective studies performed even prior to the era of biologic therapy indicated that over half of patients never require another surgery [10]. Though postoperative endo-

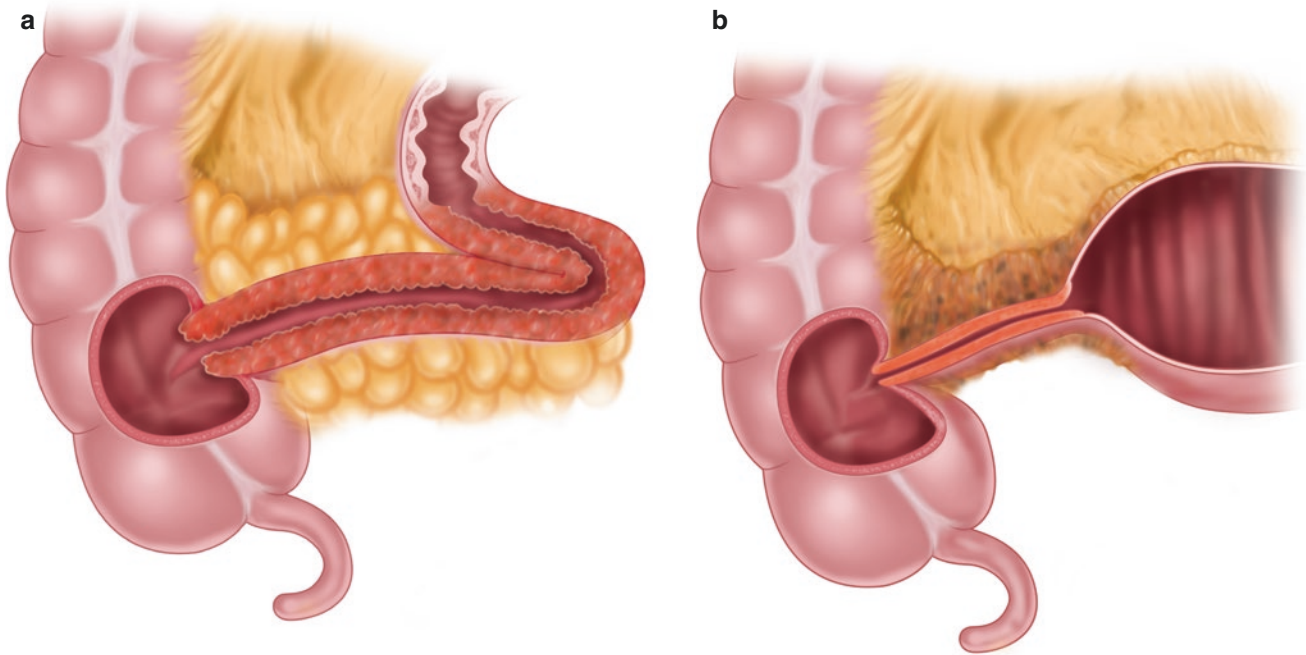


Fig. 48.1 (a, b) Crohn's-related bowel obstruction (a). Active inflammation with creeping fat, mural thickening, and luminal narrowing representing active disease which may respond to medical therapy. (b)

Fibrotic change with luminal narrowing and upstream dilation, representing fibrotic stricture that is unlikely to respond to medical therapy

scopic recurrence is the rule, aggressive postoperative medical management paradigms based on endoscopic, disease-related, and patient-related risk stratification enable many patients to avoid the disease progression that led to their initial operation [11].

Endoscopic balloon dilation is an alternative therapeutic option for bowel obstruction due to stricturing disease in some patients and has been shown to delay and even prevent the need for surgery when successful. The ideal candidate for this procedure is a patient with a single short-segment (<4 cm) fibrostenotic stricture or a patient with an anastomotic stricture. The stricture should not be associated with marked angling of the bowel lumen and be without associated fistula or abscess [12]. Dilation diameter should be at least 14 mm; dilation to 16–18 mm is associated with the need for less frequent follow-up procedures; dilation of small bowel strictures to greater than 20 mm may contribute to increased rates of perforation and bleeding [12, 13]. Multifocal stricturing disease is an independent risk factor for clinical failure of balloon dilation [14].

In a recent pooled analysis, Bettenworth evaluated 1463 patients with Crohn's disease who underwent over 3000 balloon dilation procedures. Overall technical success was achieved in 89% of cases. Anastomotic strictures com-

prised 62% of the procedures. At 2-year follow-up, three-quarters of patients had required re-dilation, and half had undergone surgical resection. Major adverse events including perforation, bleeding, and sepsis occurred in 2.8% of patients and highlight the need for a skilled and capable endoscopist in close communication with the surgical team [15].

Perforation

Free perforation in Crohn's disease is a rare occurrence. It is typically associated with toxic colitis or complete obstruction due to multifocal small bowel stricturing disease. If the perforation is associated with small bowel strictures, it is usually immediately proximal to a completely obstructing stricture, when a more proximal stricture has created a relative closed loop obstruction. This is best treated with resection and primary anastomosis if the patient's condition allows. In the setting of an obstructing colonic stricture, the site of perforation is more commonly the cecum; this is best treated with total abdominal colectomy and ileostomy. The extent of distal resection may be tailored somewhat to the site of the stricture if the distal colon and rectum are free of disease. Toxic colitis leading to perforation is managed with total abdominal colectomy and ileostomy.

Penetrating Disease: Fistula and Abscess Formation

Approximately 11–16% of adult patients have penetrating intestinal disease manifestations [16–18]. Risk factors for penetrating disease include a number of serologic and genetic markers and tobacco [19]. Transmural inflammation of the bowel wall promotes phlegmon, abscess, or fistula formation to a nearby organ or viscera. Hirten characterized the relative frequency of fistula formation by location; 29% are entero-colonic, 18–24% enteroenteric, 6–16% enterocutaneous, 4–9% rectovaginal, and 2–8% enterovesical, and rarely enterosalpingeal and enterogastric. The originating site is usually the ileocecal region and terminal ileum [17]. Only fistulas that are symptomatic require intervention (Fig. 48.2). When surgery is indicated, the diseased segment of bowel requires resection, but often the targeted organ or bowel can be primarily repaired or a small patch excision and transverse closure performed. Penetration to the retroperitoneum can cause a psoas abscess, which requires special mention. These cavities are prone to epithelialize and become a recalcitrant source of recurrent abscess and usually require surgical intervention. After resection of the diseased bowel, the psoas abscess cavity may be unroofed and curetted; an omental pedicle flap may facilitate healing.

Patients with small abscesses or phlegmon should typically be initiated on antibiotic therapy. When a phlegmon is associated with active inflammatory disease, it is safe to administer antibiotics in combination with corticosteroids. Felder examined 24 patients with Crohn's disease and palpable inflammatory mass treated with high-dose corticosteroids. Two-thirds of patients resolved their phlegmon completely, and in the remaining 1/3, it reduced in size by greater than 50%. Though 58% of the patients did require resection for persistence or recurrence of symptoms, most were performed in the elective setting [20].

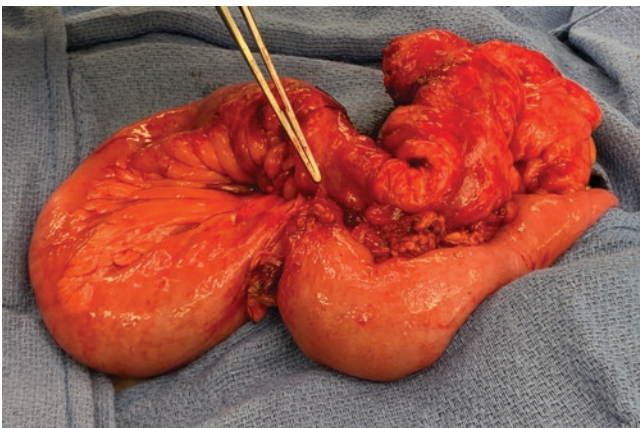


Fig. 48.2 Enteroenteric fistula. The targeted loop of otherwise normal bowel is in the foreground. (Reproduced with permission from F Michelassi, MD)



Fig. 48.3 Crohn's interloop abscess found during operative exploration. (Reproduced with permission from F Michelassi, MD)

Intra-abdominal abscess in the setting of active disease often presents a management dilemma (Fig. 48.3). Patients with accessible abscesses greater than 3 cm in average diameter should usually undergo percutaneous drainage and be initiated on antibiotic therapy. The technical success of percutaneous drainage is >90% [21, 22]. A meta-analysis by Clancy performed in 2016 of 333 patients from 6 studies compared the outcomes of primary surgery versus percutaneous drainage alone. Intra-abdominal abscess was defined as extra-luminal fluid collections identified on various imaging modalities [23]. Primary surgical resection was performed in 184 (55%) patients, and percutaneous drainage was performed in 149 patients (45%). There was a significantly higher rate of recurrent abscess in the percutaneous drainage group (OR 6.54), and the pooled proportion of these patients requiring subsequent surgery was 70.7%. The proportion of patients who underwent initial surgery and required surgery for recurrence was 17.9%.

Patients whose abscess resolves both clinically and radiologically with percutaneous drainage may present more of a therapeutic dilemma; it is unclear whether they should all proceed to elective resection. There is much interest in identifying patients who may be able to avoid surgery in the setting of successful percutaneous drainage or medical management. The prior meta-analysis suggested that up to 30% of patients undergoing percutaneous drainage can avoid surgery [23]. The MICA trial is prospectively examining predictive factors of anti-TNF response in luminal Crohn's disease complicated by abscess formation. This trial is sponsored by the Groupe d'Etude Therapeutique des Affections Inflammatoires Digestives (GETAID).

There are a number of studies that have examined percutaneous drainage as a bridge to surgery for Crohn's-related abscess. Müller-Wille examined the influence of preoperative percutaneous abscess drainage on postoperative septic complications. Twenty-five of the patients with spontaneous

intra-abdominal abscess were treated with percutaneous abscess drainage (48%) on average 37 days (range 6–83 days) before surgery. The rate of postoperative septic complications was significantly lower in the group who underwent preoperative intra-abdominal abscess drainage (25% versus 69%) [24].

Similarly, Zhang demonstrated that intra-abdominal abscess, not penetrating behavior, is associated with poorer outcome after resection. In this study, 288 patients, 180 of whom had penetrating behavior including 54 with intra-abdominal sepsis, underwent surgical resection. Patients with intra-abdominal sepsis, not penetrating behavior alone, were more likely to have postoperative septic complications, superficial surgical site infection, and stoma formation [25]. Percutaneous drainage may improve the nutritional and general medical conditional of the patient and enable a less invasive operation. Given that penetrating disease is a risk factor for recurrence, initiation of prophylactic therapy is typically recommended after intestinal resection [6].

Cancer and Dysplasia

Patients with Crohn's disease are at increased risk of developing both intestinal and non-intestinal cancers, compared to the general population. Colorectal cancer is the cause of 1 in every 12 deaths of patients with inflammatory bowel disease [26]. Colitis-associated cancer has many of the molecular alterations also found sporadic colorectal cancer, but with different timing and frequency. For example, loss of adenomatous polyposis coli (APC) functions occurs early in sporadic colon cancer and late in colitis-associated cancer. In contrast, loss of p53 function occurs early in colitis-associated cancer [27]. Development of cancer in chronic colitis is accelerated by inflammatory activity [26]. Patients with Crohn's disease have a twofold to threefold increase in colorectal cancer compared to the general population. The mean age at diagnosis is 51.5 years, about 20 years earlier than the general population [28]. The risk of cancer is also associated with disease duration; the cumulative risk of colorectal cancer in Crohn's disease is 2.9% at 10 years, 5.6% at 20 years, and 8.3% after 30 years with the disease [27]. With equivalent disease duration, the risk of colorectal cancer in Crohn's disease appears to be lower than that of ulcerative colitis, but this may be informed by differences in disease distribution [28].

Colorectal strictures in the setting of Crohn's disease are particularly associated with an increased risk of cancer. Yamazaki analyzed 132 patients with 175 strictures identified between 1959 and 1980. A total of ten malignant strictures were identified in nine patients, three with ileocolic and six with colonic disease. The frequency of cancer in patients with a stricture was 6.8% [29]. The authors further observed that all of the malignant strictures were short-segment. A group out of Hungary similarly analyzed 640 patients with

Crohn's disease over a 30-year period, including 62 patients with ileocolic or colonic strictures. The group observed a 6.5% rate of colorectal cancer in those patients with stricture. The authors observed that all four patients with stricture-associated colorectal cancer were male smokers [30].

The surgical management of colitis-associated dysplasia in Crohn's disease follows the same principles as ulcerative colitis and is reviewed elsewhere in this textbook.

Toxic Colitis

Up to 50% of cases of toxic colitis from IBD may be attributed to Crohn's colitis. Severe colitis is defined by Truelove and Witt as six or more bloody bowel movements daily, temperature greater than 37.8 °C, heart rate greater than 90 beats per minute, anemia with a hemoglobin less than 10.5 g/dL, and an elevated erythrocyte sedimentation rate greater than 30 mm/h. These criteria, combined with imaging demonstrating dilation of the colon and a disturbed or absent haustral pattern, constitute toxic megacolon. The medical management of toxic colitis is covered in another section of this textbook. When surgery is required due to clinical deterioration or failure to respond to rescue therapy, total abdominal colectomy with end ileostomy is indicated, with or without mucous fistula. The extent of resection and surgical management in the setting of medically refractory colitis is reviewed later in this chapter, under operative considerations for colonic and rectal disease.

Bleeding

Acute severe gastrointestinal hemorrhage is a rare complication of Crohn's disease, with an incidence of 1–2%. There are few studies that describe the epidemiology of this condition. Bleeding does not always correlate with disease activity. The site of bleeding can be duodenal, jejunoileal, ileocolic, or colic. Surgery is typically successful when the site of bleeding has been localized. In those that resolve without surgery, recurrent hemorrhage is not rare [31–33].

A patient with Crohn's disease presenting with acute gastrointestinal bleeding should be initially managed using the usual resuscitative algorithms for gastrointestinal bleeding, including nasogastric lavage to begin the process of source localization. In contrast to ulcerative colitis where bleeding is due to widespread mucosal ulceration, hemorrhage in the setting of Crohn's disease is more often due to a focal erosion into an intestinal vessel or occasionally an inflammatory pseudopolyp. Source localization therefore is extremely important to minimize unnecessary bowel resection should surgery be required. Up to 30% of patients with Crohn's disease and hemorrhage will have a bleeding duodenal ulcer and positive gastric lavage should trigger upper endoscopy [34]. Colonoscopy within 24 hours of bleeding can successfully locate the bleeding source 60–78% of the time [31, 32]; endoscopic control is not often successful, but will localize

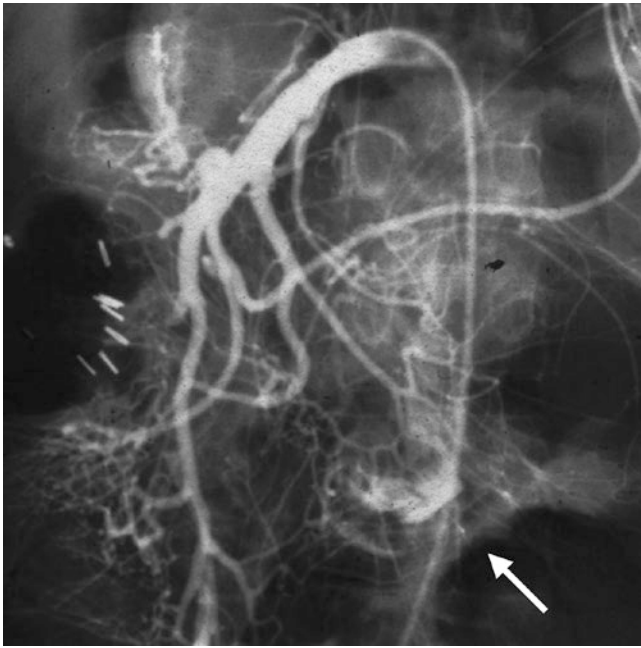


Fig. 48.4 Contrast extravasation (arrow) seen on angiography from an intestinal segment in a patient with Crohn's disease. (Reproduced with permission from F Michelassi, MD)

the site for guided resection. CT angiography and traditional mesenteric angiography have also been successfully utilized for source localization (Fig. 48.4). When mesenteric angiography localizes bleeding, methylene blue injection can be used to identify the segment of involved bowel so that it may be readily identified during operative exploration. This approach will typically stain a 10–40 cm segment of bowel for resection [35].

Surgical Considerations

Crohn's disease cannot be cured by surgical therapy, and thus surgery, like medical treatment, should be considered palliative. It is paramount to keep in mind the recurrent and chronic nature of the disease that is typically diagnosed in a young patient population with a long life expectancy. The pendulum has swung from an emphasis on margin-negative resection to bowel-sparing approaches largely based on a landmark paper from Fazio. The authors randomized 152 patients undergoing ileocolic resection to 2 groups in which the proximal line of resection was 2 cm (limited resection) or 12 cm (extended resection) from the macroscopically involved area. They showed that there was no difference in recurrence rates between the two groups; further, recurrence rates did not increase when microscopic disease was present

at the resection margins [36]. Similar to medical treatment, the goal of surgical treatment of Crohn's disease is to provide long-lasting symptomatic relief while avoiding excessive morbidity. Complete extirpation of microscopic disease should not be the primary goal of surgery, as this does not produce cure and is frequently counterproductive. Rather, treatment of complications and relief of disease-related symptoms coupled with bowel preservation should be the main aims of surgical treatment.

To avoid excessive loss of small intestine, nonresectional techniques such as strictureplasty may be required. On the other hand, in patients with isolated Crohn's colitis, especially if multifocal and associated with perianal disease, a more aggressive approach is often indicated [37–39]. Understanding the natural history of different patient cohorts is key to optimal decision-making.

Nutritional Support and Total Parenteral Nutrition

Exclusive enteral nutrition has been shown to induce remission in the pediatric Crohn's population and to be as effective as systemic corticosteroids in inducing remission both in newly diagnosed and established patients. In fact, intestinal healing was significantly more likely among patients receiving exclusive enteral nutrition compared to corticosteroids (OR = 4.5 [95% CI 1.64,12.32]) in a recent meta-analysis [40]. In the adult patient population, exclusive enteral nutrition is not as effective in inducing remission, but it may be useful for maintaining remission in patients with quiescent Crohn's disease [41].

In the adult literature, nutritional support has been evaluated primarily for preoperative optimization. Crohn's disease patients are at increased risk for malnutrition, which can result in adverse clinical outcomes. In a recent study from China, 59.0% of screened patients were deemed to be at risk for malnutrition [42]. If we consider that surgical patients have failed medical management, that percentage is probably even higher in the operative cohort. Crohn's disease patients with serious nutritional deficits, based on weight loss >10% in the last 3–6 months, body mass index <18.5 kg/m, or albumin levels <30 g/L, have been shown to benefit from intensive enteral or parenteral nutritional support, thereby reducing the risk of surgical site infections and postoperative septic complications [43]. Malnutrition has been shown to be an independent risk factor for postoperative morbidity and mortality irrespective of immunosuppressive and biologic therapy [44]. The duration of preoperative nutritional support depends on the urgency of the operation and the suitability of the gastrointestinal tract for enteral administration [45, 46].

Overview of Operative Considerations

Minimally Invasive Surgery

Crohn's disease may present both real and perceived challenges to a minimally invasive surgical approach. A Crohn's-related inflammatory mass and secondary phlegmon can increase the risk of bowel injury during minimally invasive manipulation and dissection. Thick, inflamed mesentery may be difficult to divide with a vessel-sealing device. With limited tactile feedback, it may be difficult to determine whether a fistula requires resection versus debridement and repair. Despite these challenges, evidence has accumulated in favor of a tailored approach to minimally invasive surgery (MIS) in Crohn's disease.

Milsom and Maartense both conducted prospective randomized trials in selected Crohn's patients undergoing ileocecectomy, concluding that MIS patients enjoy improved postop pulmonary function, morbidity, and reduced length of stay [47, 48]. Analysis of long-term outcomes in these two trial populations supported improved body image perception and cosmesis, as well as a decreased risk of bowel obstruction and hernia [49, 50]. Evidence does not support the concern that diminished tactile feedback will lead to missed strictures or increased disease recurrence due to incomplete resection [51]. MIS approaches for complex Crohn's disease, defined as reoperative disease, presence of phlegmon, abscess and/or fistula, or immunosuppressed state, can be accomplished with acceptable outcomes, albeit with generally higher conversion rates [52–55].

Robotic MIS for Crohn's disease is technically feasible. Like the laparoscopic approach, morbidity and length of stay are reduced compared to open approach [56], but operative times are longer [57]. The conversion rate is lower than with laparoscopy in some series [58]. All in all, there is not yet a clear demonstrated advantage of robotic over laparoscopic MIS in Crohn's disease [59].

The general advantage of MIS versus open approach in Crohn's disease is no longer disputed. Widespread acceptance of MIS approach is cultivating advanced near-term technologies and techniques, such as single-incision surgery and intracorporeal anastomosis. Inability to deliver a foreshortened Crohn's mesentery through a small extraction site in order to perform an extracorporeal anastomosis makes intracorporeal anastomotic technique enticing and may reduce the surgical site infection rate [60]. Heimann demonstrated that it may be possible to decrease and possibly eliminate incisional hernia in Crohn's disease patients undergoing bowel resection using an intracorporeal anastomosis and small (<4 cm) transverse extraction incision [61]. Tou described a robotic-assisted strictureplasty, and Scaringi illustrated a robotic approach to stricturing disease that is in

essence a nonresectional, intracorporeal, side-to-side isoperistaltic anastomosis [62, 63]. Further studies and long-term analysis are needed to understand how these techniques may influence disease recurrence.

Single-incision laparoscopic surgery utilizes only one abdominal incision and an incisional platform through which a 5-mm camera and two working instrument ports are inserted. A number of small studies support the safety of this approach in Crohn's disease, but there is no clear benefit over conventional laparoscopy [64].

IBD surgeons should tailor the approach to the individual patient and be willing to utilize a hybrid or open approach if there is a lack of progress in complex cases. The hybrid approach is attractive when circumstances prohibit a fully MIS procedure. If a Crohn's terminal ileal phlegmon is fixed to the retroperitoneum, the surgeon can mobilize the proximal bowel and distal colon in order to limit the incision required to complete the procedure. If the mesentery is noted to be too thick and unwieldy for laparoscopic vessel sealers, it may be possible to perform minimally invasive mobilization and then divide this mesentery extracorporeally using more traditional clamp and suture ligation technique [65].

Enhanced Recovery Pathways

Very little disease-specific data exists supporting the application of enhanced recovery pathways (ERPs) after colorectal resection in inflammatory bowel disease. A recent review identified only a dozen English-language studies on ERPs that included any proportion of patients with IBD in their analysis, and only 28.9% of the total number of patients within these studies had a stated surgical indication of IBD [66]. Most studies did not provide important IBD-specific demographic information such as biologic therapy, steroids, or immune modulations. Still, all available evidence to date suggests that application of ERPs to patients undergoing colorectal surgery for IBD is safe and likely leads to decreased length of stay without an increase in the rate of readmission or morbidity. Inflammatory bowel disease is a known risk factor for prolonged length of stay, and this should be taken into account when setting postoperative expectations for recovery [67].

Perioperative Medical Management

In steroid-treated and steroid-dependent patients, concern over postoperative adrenal insufficiency and adrenal crisis has traditionally led to the liberal utilization of stress-dose steroids in the perioperative setting. Truong noted that much of the evidence around dosing, duration, and indications for steroid supplementation is poorly supported and anecdotal [68]. The dose and duration of steroid therapy do not correlate with the degree and duration of hypothalamic-pituitary-

adrenal (HPA) axis suppression. Recovery of HPA axis function after cessation of steroid therapy can be as short as 2 days and as long as 1 year, which is the basis for recommending stress-dose steroids for a patient who has required steroid therapy within the past year [69].

As perioperative high-dose steroids are associated with impaired wound healing, reducing or omitting stress-dose steroids in Crohn's disease surgery is desirable. In a small pilot study, Zaghiyan did not administer any perioperative steroids to IBD patients who had received steroids within the year but were not on steroids at the time of surgery. All cases of hypotension, bradycardia, and tachycardia spontaneously resolved without the need for fluid bolus, vasopressor, or steroid administration [70]. Further studies support the notion that steroid-treated patients can be maintained on their usual preoperative steroid dose in the perioperative period. Patients who have been treated with steroids within the year probably do not need precautionary perioperative steroid supplementation at all. High "stress-dose" perioperative steroids are unnecessary and may increase perioperative risk [71, 72].

There is a dose-dependent relationship between steroid use and infectious complications. The highest risk of complications occurs in patients on >40 mg prednisolone or equivalent [73, 74]. If the surgery is elective or semi-elective, an attempt to wean steroids should be undertaken, with the goal to have patients off steroids for 1 week prior to surgery [75]. If complete cessation is not possible, an attempt to wean to their lowest possible dose, with a target of less than 20 mg prednisolone or equivalent, is recommended [6].

There have been few studies examining whether immunomodulator use leads to increased complications. Patients on 6-mercaptopurine/azathioprine (6-MP/AZA) alone do not have an increase in complication rates, and concurrent use of 6-MP/AZA and corticosteroids does not further elevate complication rates as compared to the known risk of corticosteroids alone [73]. In a recent review, Rosen did not find any literature suggesting an increased complication rate with methotrexate. Discontinuing immunomodulator therapy prior to surgery appears unnecessary. These medications are typically held on the morning of surgery and resumed as per the gastroenterologist treatment plan [76].

Since the approval of infliximab in 1998 for treatment of inflammatory bowel disease, biologic therapy has vastly advanced medical treatment options for Crohn's disease. The influence of biologic therapy on surgical timing, morbidity, and intraoperative surgical decision-making is a ripe area of clinical interest. Tumor necrosis factor- α (TNF α) is a central cytokine in the pathogenesis of IBD, and anti-TNF α therapies including infliximab, adalimumab, and certolizumab pegol are some of the most successful Crohn's therapies available.

Table 48.2 Risk factors for postoperative septic complications in patient with Crohn's disease undergoing surgical resection [79, 154, 155]

Corticosteroid use
Malnutrition/hypoalbuminemia
Anemia/acute blood loss
Emergency surgery
Anti-TNF α therapy
Vedolizumab therapy
Penetrating disease/fistula/intraoperative abscess
Recurrent disease
Smoking

Several studies had sought to describe the relationship between anti-TNF α therapy and postoperative outcomes, with mixed results. Interpretation of the impact of biologics is complicated by drug pharmacokinetics and associated drug levels, as these medications are typically protein-bound and prone to be lost in the stool in patients with active disease. One study showed that 50% of patients on anti-TNF α at the time of surgery did not have detectable drug levels immediately preoperatively [77]. Complications do not appear to correlate with anti-TNF α serum trough levels [78]. There are several, heterogeneous, retrospective, and prospective studies that either support or refute the hypothesis that anti-TNF α therapy leads to a significant increase in postoperative complications. Thought leaders in this area recommend considering biologic therapy as one of the several risk factors (Table 48.2) that negatively influence postoperative complications.

A reasonable elective strategy is to delay surgery by 4 weeks (allowing for washout period of two half-lives) from the last anti-TNF α dose. If this is not possible due to the patient's clinical circumstances, temporary diversion may be considered if the patient has two or more risk factors [79].

Vedolizumab, a monoclonal antibody to $\alpha 4\beta 7$ integrin, has been approved for medical treatment of Crohn's disease since 2015. Literature is also conflicted regarding the influence of postoperative septic complications in patients receiving vedolizumab therapy. Vedolizumab has been associated with an increased rate of postoperative surgical site infections [80]. A reasonable strategy is to delay surgery by 6 weeks (two half-lives) from the last vedolizumab dose and, if this is not possible, consider temporary diversion if the patient has additional risk factors for septic complications. Ustekinumab, a monoclonal antibody targeting interleukin-12 and interleukin-23, does not appear to increase the risk of postoperative septic complications [81].

Anastomotic Type

Different anastomotic techniques in Crohn's disease may be compared based on safety (i.e., anastomotic leak rates) and risk of recurrence. When looking at leak rates, one very

important component that is hard to factor in is the surgeon's experience with the applicable technique. With the advent and wide acceptance of the surgical staplers, many are less facile at sewing the anastomosis, and that may result in higher complication rates for the hand-sewn technique.

Despite anastomotic construction being a critical aspect of Crohn's disease management, there is limited level 1 evidence in the literature. Muñoz-Juárez [82] performed the first case-controlled comparative analysis of 138 patients divided evenly into wide-lumen stapled side-to-side anastomoses and hand-sewn end-to-end anastomoses. Clinical recurrence occurred in 16 (24%) of the side-to-side anastomosis group and in 39 (57%) of the end-to-end anastomosis. The cumulative surgical recurrence rates at 5 years were 11% after side-to-side anastomosis and 20% after conventional end-to-end anastomosis ($p = 0.017$). A 2007 meta-analysis [83] comprising only 8 studies with 661 patients who underwent 712 anastomoses compared the outcomes of end-to-end anastomoses (53.8%) and other types of anastomotic configurations (46.2%), including stapled side-to-side in the vast majority. There were no significant differences between the groups regarding overall complications, anastomotic recurrence, or surgical anastomotic recurrence. When comparing only side-to-side and end-to-end anastomosis, a lower leak rate as well as reduction in postoperative complications was demonstrated in the side-to-side anastomosis group. However, there was no difference in overall recurrence or surgical recurrence rates. These data were confirmed in a subsequent Cochrane review by Choy [84].

Two more recent systematic reviews [85, 86], however, demonstrated no difference in anastomotic leak rates between side-to-side and end-to-end anastomotic configurations. In terms of surgical recurrence, Guo [85] reported no differences between the two anastomoses, while Feng [86] reported superiority of the side-to-side anastomosis. The results from these reviews should be interpreted with caution given the retrospective nature of most studies included in each analysis.

In 2009, the first randomized study comparing anastomotic type, the CAST trial [87], was published. Patients were randomized to either side-to-side anastomosis or end-to-end anastomosis. A total of 139 patients were included, and after a mean follow-up of 11.9 months, the endoscopic recurrence rate was 37.9% in the side-to-side anastomosis group and 42.5% in the end-to-end anastomosis group ($p = 0.55$). The symptomatic recurrence rate was also similar between the two groups (22.7% and 21.9%, $p = 0.92$). In 2013, another prospective, randomized trial from Germany was planned with a primary endpoint to investigate whether stapled side-to-side anastomosis resulted in lower recurrence rates compared to hand-sewn end-to-end anastomosis. The secondary endpoint was early postoperative complications. The study was terminated early due to insufficient patient

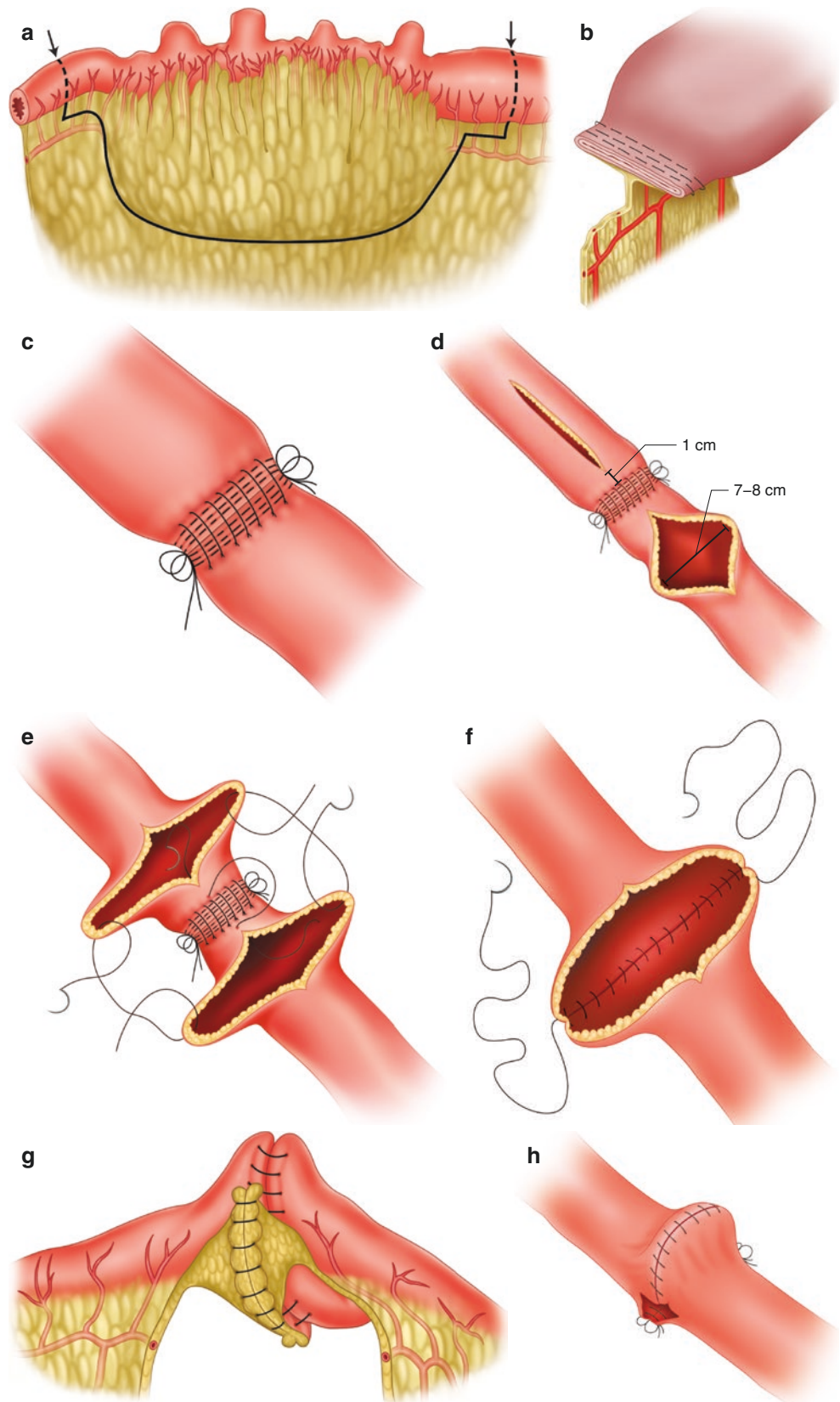
recruitment; while they did not have an adequate number of patients to draw conclusion for the primary endpoint, there was no difference in terms of postoperative complications, length of surgery, and length of hospital stay between the two techniques [88].

In 2011, Kono [89] developed a new hand-sewn antimesenteric functional end-to-end anastomosis with the intent of reducing surgical recurrence in CD. The rationale behind this anastomotic configuration is centered on preservation of the mesenteric vascularization and innervation and a posterior supporting column created by suturing the two staple lines together in order to maintain the three-dimensional structure. In the original paper, the authors performed Kono-S anastomosis in 69 CD patients and compared this group with a historical cohort of 73 CD patients. They found significantly lower endoscopic recurrence rates in the Kono group than in the conventional one, with a lower probability of anastomotic surgical recurrence in the Kono group at 5 years (0% vs 15%; $P < 0.0013$) [89].

In brief, a small window in the mesentery is created at the level of the proximal and distal resection margins. The mesentery is divided using a tissue-device close to the intestinal wall to preserve vascularization and innervation [89]. At this point, the bowel is divided transversely, placing the stapler perpendicular to the intestinal lumen and the mesentery, so that the mesentery is located in the middle of the staple lines. The corners of the two stapled lines are imbricated and reinforced with 4/0 silk Lembert sutures, and the two stumps are approximated by tying together the corresponding corner sutures. The two stapled lines are now sewn together with interrupted 4/0 silk sutures spaced apart, thus creating the so-called supporting column. At this point, an antimesenteric longitudinal enterotomy (or colotomy) is performed on each stump to allow a transverse lumen of 7 cm on the small bowel or closer to 8 cm on the colon, starting no more than 1 cm away from the staple line. The anastomosis is now completed by closing the longitudinal opening transversely in two layers (Fig. 48.5).

This anastomotic configuration has been evaluated in two large multicenter studies [90, 91] and more recently in a prospective randomized trial [92]. Kono reported only 2 surgical anastomotic recurrences in the Kono group with a follow-up of 65 months and a 5 and 10 years' surgical recurrence-free survival rate of 98.6% [90]. Shimada reported a surgical recurrence rate of 3.4% in the Kono-S group versus 24.4% in the end-to-end group, as well as an increased risk of anastomotic leak in the end-to-end group (17.3% vs 5.1%). Kono-S anastomosis had a significantly lower risk of anastomotic surgical recurrence at 1 year (OR 0.14). The 5-year surgery-free survival rate on the anastomosis site (95.0%) was significantly higher with the Kono-S than with the end-to-end anastomosis (95% vs 81.3%; $P < 0.001$) [91]. The first published randomized controlled trial (RCT) [92] confirmed the

Fig. 48.5 Kono-S anastomosis. **(a)** Resection of diseased segment preserves mesentery at resection margin. **(b)** Transverse division of bowel with orientation of mesentery perpendicular to staple line. **(c)** Creation of supporting column. **(d)** Longitudinal enterotomy. **(e, f)** Transverse two-layer anastomosis. **(g, h)** Posterior and antimesenteric view of completed Kono-S anastomosis. (Courtesy of T. Kono, MD)



early reports showing lower rates of endoscopic recurrence, reduced severity of endoscopic scores, and lower rate of clinical recurrence in favor of the Kono-S anastomosis.

The mesentery has been thought by some to be involved with the initiation and recurrence of the disease as early ulcers develop typically on the mesenteric side of the bowel with the corresponding “creeping fat.” A recent report from Ireland [93] compared wide excision of the mesentery with the conventional closer division in 64 patients. They reported surgical recurrence rates of 40% and 2.9% in favor of the wide excision group ($p = 0.003$). This study has several limitations. The conventional group was a historical control with longer follow-up, postoperative medical prophylaxis of recurrence was not standardized, and there is no data on anastomotic technique. In summary, there is no definitive evidence supporting superior safety of one anastomotic technique over the other. In regard to the risk of recurrence, the role of radical mesenteric excision and the promising results reported with the Kono-S anastomosis will require further study.

Disease Recurrence Trends and Surveillance

After an ileocolic resection with an anastomosis, recurrent Crohn's disease at the anastomotic site is noted in 70–90% of patients within 1 year on endoscopy [94], and 20–30% of these patients will require additional operations within 5 years [95]. Many factors have been cited as potential culprits in the recurrence of the disease at the anastomotic site, including fecal stasis, alteration in the microbiome, and local ischemia, just to mention a few [96, 97].

Over the years, a number of strategies to prevent postoperative recurrence have been proposed. On the medical side, postoperative biologic therapy has been shown to be effective [98, 99]. Regueiro [100] in a small prospective randomized trial comparing early administration of infliximab (5 mg/kg), for 1 year versus placebo, showed that the rate of endoscopic recurrence at 1 year was significantly lower in the infliximab group (1 of 11 patients, 9.1%) compared with the placebo group (11 of 13 patients, 84.6%) ($P = 0.0006$). In a larger multicenter follow-up study, the PREVENT trial [101], the primary endpoint of lower clinical recurrence was not met, but patients on infliximab had lower endoscopic scores and recurrence. The questions of optimal patient selection and timing of administration for prophylaxis remain unanswered.

Attempts at risk stratification based on clinical disease-specific factors and early colonoscopy findings have been proposed to guide postoperative medical management. De Cruz [102] randomized 174 high-risk patients to early colonoscopy vs standard clinical observation and noted that treatment based on clinical risk of recurrence, including early

colonoscopy and treatment step-up for recurrence, is better than conventional drug therapy alone for prevention of postoperative recurrence. Selective therapy, adjusted for risk of early recurrence rather than routine use, leads to disease control in most patients. The authors also noted that although clinical risk factors predicted recurrence, patients at low risk also should undergo monitoring and early remission did not preclude the need for ongoing surveillance.

Operative Considerations for Specific Locations

Gastroduodenal Disease

Clinically significant Crohn's disease of the foregut is rare, affecting 0.5–4% of patients [103]. Advances in digestive endoscopy have improved detection of this entity; 30–50% of patients with Crohn's disease have macroscopic UGI disease, and 40–70% have histologically visible UGI disease [104–106]. At least 2/3 of these patients are asymptomatic, and over 90% have coexisting Crohn's in the more distal GI tract [107, 108]. Patients may note insidious gastritis-like symptoms [109]. Early satiety, postprandial pain or emesis, and weight loss can indicate stricture, by far the most common pathology of gastroduodenal Crohn's disease. Fecal calprotectin is not a reliable indicator of gastroduodenal disease [105].

Aphthous erosions, longitudinal ulcers, and bamboo joint-like appearances in the cardia are characteristic of gastric Crohn's, while longitudinal and notch-like erosions of Kerckring folds characterize duodenal disease [106] (Fig. 48.6). Dynamic radiologic studies may reveal a rigid antrum or reduced duodenal peristalsis, while CT or MR enterography may demonstrate disease activity and stricturing (Fig. 48.7). Therapy for symptomatic gastroduodenal Crohn's mirrors that of more distal disease, with the addition of acid suppression [110].

Surgery for gastroduodenal Crohn's is uncommon and comprises <1% of surgery for Crohn's at tertiary centers [111]. Indications for surgery include obstruction and fistula. Almost all instances of gastroduodenal fistula result from penetration of the gastric or duodenal wall originating from another site, such as the terminal ileum or transverse colon. Fistula takedown requires thorough exposure, including Kocherization of the duodenum. The defect can be repaired primarily in one or two layers with low morbidity. A jejunal serosal patch is used for larger defects [112].

Strictures are the most common indication for intervention in gastroduodenal Crohn's disease. Successful endoscopic hydrostatic balloon dilation is feasible for short-segment strictures with a low rate of perforation. Patients are often able to avoid surgery, but multiple dilations are required, and

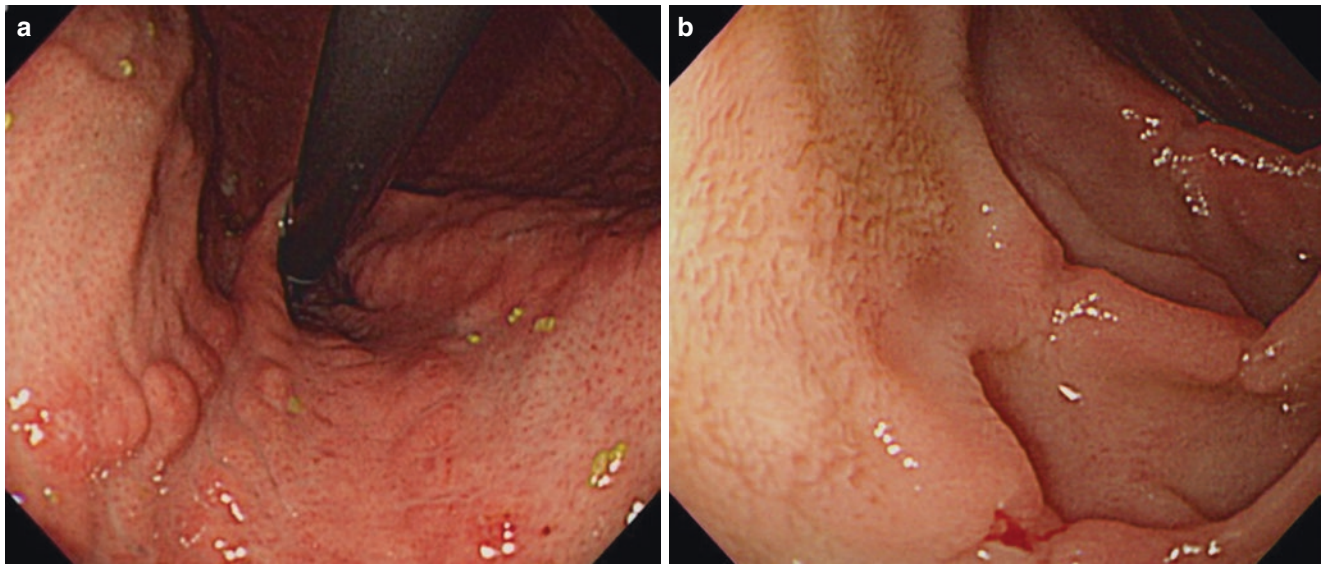


Fig. 48.6 Gastroduodenal disease. (a) Bamboo joint-like appearance in the gastric cardia. (b) Duodenal notching of Kerckring folds. (Courtesy of A. Sakuraba, MD)

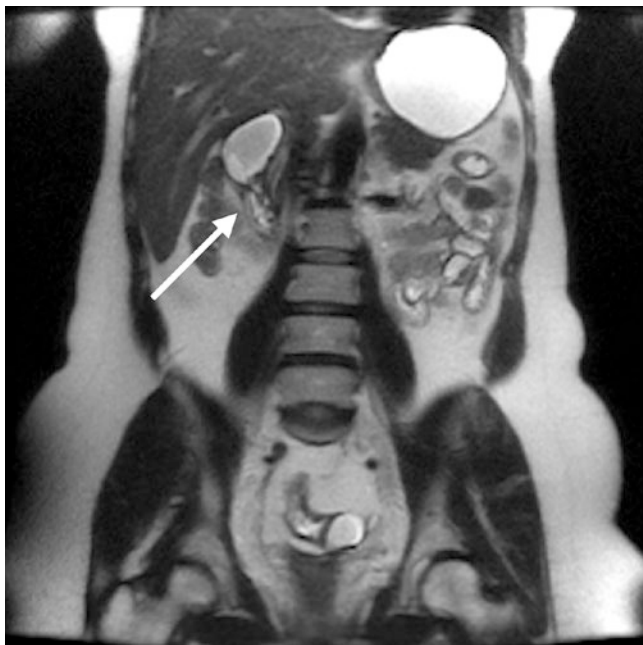


Fig. 48.7 T2-weighted MRI demonstrating a duodenal stricture (arrow). (Courtesy of A. Oto, MD)

recurrence is the rule. Surgical intervention for duodenal stricture includes strictureplasty and bypass. Both procedures are effective with low morbidity. Pancreaticoduodenectomy should be reserved only for instances of severe ampullary dysfunction and/or cholangitis.

Duodenal strictureplasty is a good option for short-segment strictures or if proximal jejunal inflammation prohibits consideration for gastrojejunostomy. After Kocherizing the duodenum, the stricture is assessed by visual inspection

and palpation. A Heineke-Mikulicz or Finney strictureplasty is then performed in two layers. These techniques are described in the next section. A 20-mm Foley balloon may be floated in to trawl for more distal strictures. In instances of dense scarring around the stricture, stricturing in the first or fourth portion of the duodenum, or more than two strictures, bypass is preferred [111, 113].

Bypass procedures include gastroduodenostomy, gastrojejunostomy, and duodenojejunostomy predicated on the site of stricture. These procedures are safe with low morbidity. One-quarter to one-third of patients require reoperation for marginal ulceration or disease recurrence [114, 115]. Vagotomy does not decrease the rate of marginal ulceration in this population and need not be performed.

Upper Small Bowel Disease

The jejunum and ileum, not including the terminal ileum, are affected by Crohn's disease in 3–10% of patients [116, 117]. The two most common indications for surgical treatment of patients with disease in these locations are obstruction and sepsis; massive hemorrhage and carcinoma are much less common. The approach to small bowel Crohn's disease has shifted from extensive resections, with the intent to achieve negative microscopic surgical margin, to the resection of only the macroscopically diseased bowel segment [36], and/or to perform bowel-sparing strictureplasty to preserve intestinal length [6, 118, 119]. In the last decade, attention has been directed to the type of anastomosis as an important variable from the standpoint of endoscopic and surgical recurrence [120].

In very general terms, resection of grossly involved bowel segments remains the most common approach when dealing with an inflammatory or penetrating phenotype. On the other hand, strictureplasty is often preferred for quiescent stricturing disease and in patients at risk of developing short bowel syndrome. Patients with jejunoileitis typically have disease recurrence and a need for a second operation in as many as 30% of patients; short bowel syndrome has been reported in 8.5% of cases 20 years after the index surgery [121].

A significant proportion of small bowel strictures are not identified on preoperative workup, and the entire small bowel should be examined at exploration. When dealing with multifocal small bowel disease, assessment of bowel lumen can be done by running a calibration sphere through the bowel or, more simply, by inserting a cuffed catheter. Fibrostenotic strictures with a luminal diameter less than 20 mm are clear indications for strictureplasty or resection, although these cutoffs may vary depending on patient size and normal bowel diameter. Less critical strictures, especially in patients with previous resections and extensive disease, may not mandate operative treatment in an era of effective medical therapy. Strictures may be marked with metal clips for future reference; measurements of remaining intestinal length and location of the strictures in the operative report are important for long-term management.

In an attempt to preserve bowel length and function, Lee and Papaioannou in 1982 and, subsequently, Alexander Williams and Haynes in 1985 described the use of strictureplasty techniques, which had been previously described in India to correct tuberculous stricture of the terminal ileum and cecum [95, 122]. Currently, the most commonly performed strictureplasty techniques are the Heineke-Mikulicz, Finney, Jaboulay, and the side-to-side isoperistaltic strictureplasties. Strictureplasty procedures were adopted from the experience of treating peptic ulcer disease of the duodenum and were initially thought to be risky procedures for Crohn's patients.

However, after Lee [123] published their report proving the safety of strictureplasties, the Heineke-Mikulicz has become the most commonly performed strictureplasty performed in Crohn's patients. It is particularly suited for short-segment (<10 cm) chronic intestinal strictures [124]. A single longitudinal incision is made over the antimesenteric side of the affected small bowel, extending 2 cm beyond both proximal and distal thickened portions, and is closed transversely to create a wide lumen (Fig. 48.8). Finney strictureplasty is used for strictures that are longer than 10 cm but shorter than 25 cm (Fig. 48.9) [124]. Strictures longer than 25 cm if treated with this technique would result in a functional large blind loop leading to bacterial overgrowth and blind loop

syndrome [124]. The segment of diseased is folded on itself, and a long, longitudinal enterotomy is made over the antimesenteric border. The anterior and posterior walls of the long enterotomy are sutured separately to create a wide lumen. The Jaboulay strictureplasty is also used for medium-sized (>10 and <25 cm) strictures. With this technique, bowel length is spared; however, there is the creation of a lateral diverticulum with resulting blind loop and potential for stasis in the strictured segment [124]. This short-segment "bypass" was also described in Lee's 1982 report [123], in which a shorter length of small bowel was involved. Both Jaboulay and Finney have the potential for stasis and bacterial overgrowth potentially resulting in a need for revision [125].

Michelassi proposed an isoperistaltic side-to-side strictureplasty for significantly long-segment strictures (>20 cm) or a long portion of bowel containing multiple short strictures in tandem, making the creation of multiple Heineke-Mikulicz strictureplasties unsafe [126]. The procedure involves dividing the bowel and its mesentery in the mid-point of the strictured bowel segment. The two loops are then approximated by a layer of interrupted seromuscular Lembert stitches, using nonabsorbable sutures. A longitudinal enterotomy is performed on both loops, with the intestinal ends tapered to avoid blind stumps. The outer suture line is reinforced with an internal row of running full-thickness 3–0 absorbable sutures, continued anteriorly as a running Connell suture; this layer is reinforced by an outer layer of interrupted seromuscular Lembert stitches using nonabsorbable 3–0 sutures (Fig. 48.10) [127]. This technique avoids sacrificing long segments of bowel and has achieved excellent long-term results [118, 119, 128]. With follow-up extending to 7.5 years in 20 patients, it has provided radiographic, endoscopic, and histopathologic evidence of regression of previously active Crohn's disease with restoration of intestinal function (Fig. 48.11) [129].

Several studies have confirmed the safety and efficacy of both short and longer strictureplasties [125, 128, 130–133]. Early postoperative complications, like bleeding and sepsis, have been reported in between 8% and 15% of cases [125]. Mucosal biopsies and marking the site with a metal clip should be considered, especially in long-standing disease, as cases of cancer at the strictureplasty site have been reported [125, 134, 135]. Reese [131] compared recurrence rates between patients undergoing strictureplasty or resection and found that surgical recurrence was more likely after strictureplasty ($p = 0.09$), and there was a significantly longer recurrence-free interval after resection ($p = 0.01$). Overall recurrence rates have been reported to be between 18% and 29% [130, 136, 137], but with only 4.6% of them at the previous strictureplasty site in one study [136].

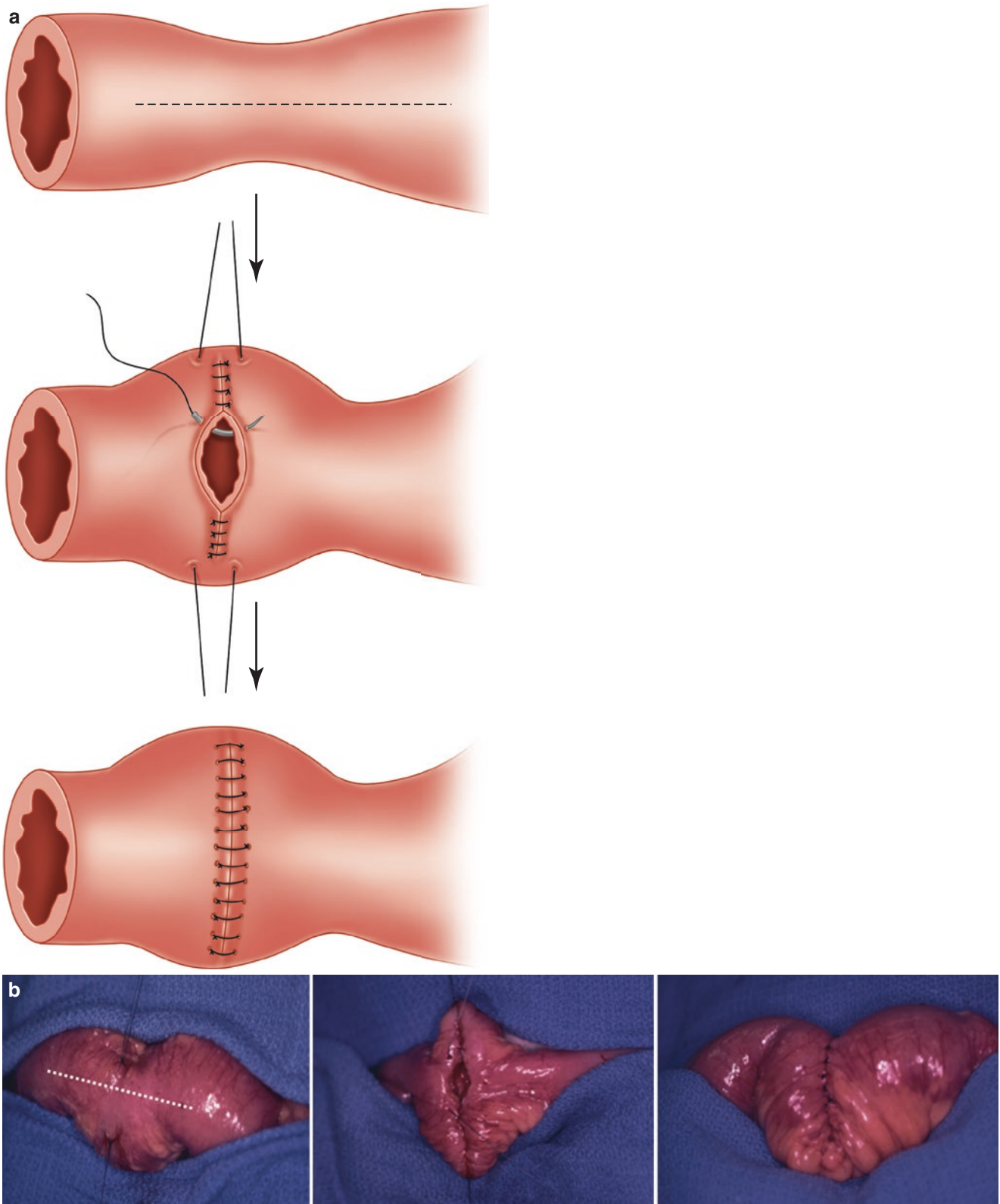


Fig. 48.8 (a) Heineke-Mikulicz strictureplasty. (b) The longitudinal incision (dashed line) is made over the antimesenteric border and closed transversely. (Courtesy of F. Michelassi, MD)

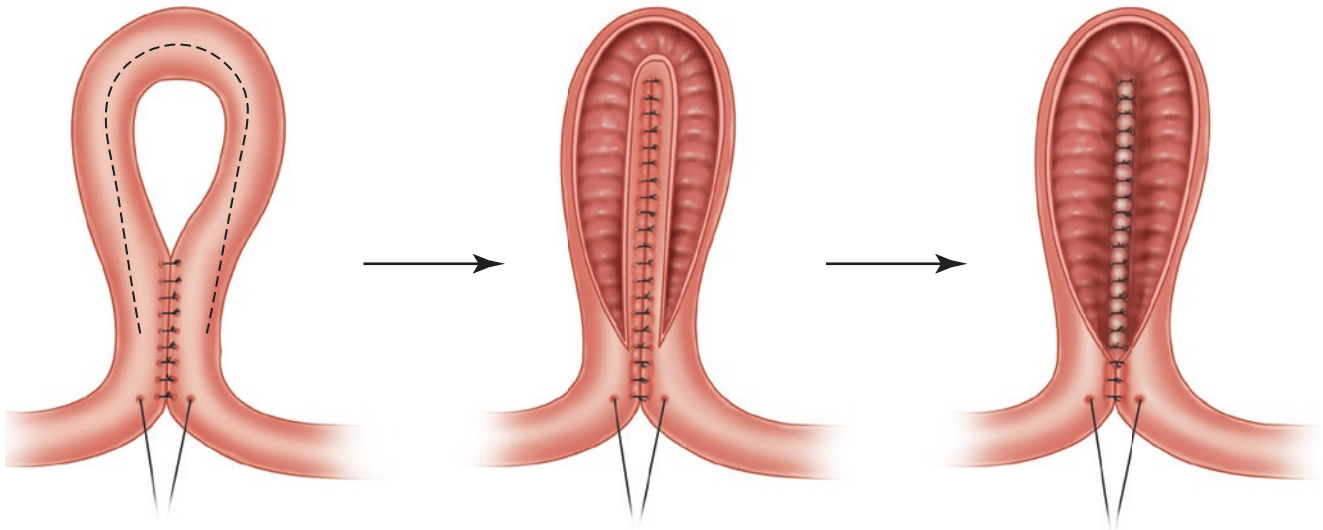


Fig. 48.9 Finney strictureplasty

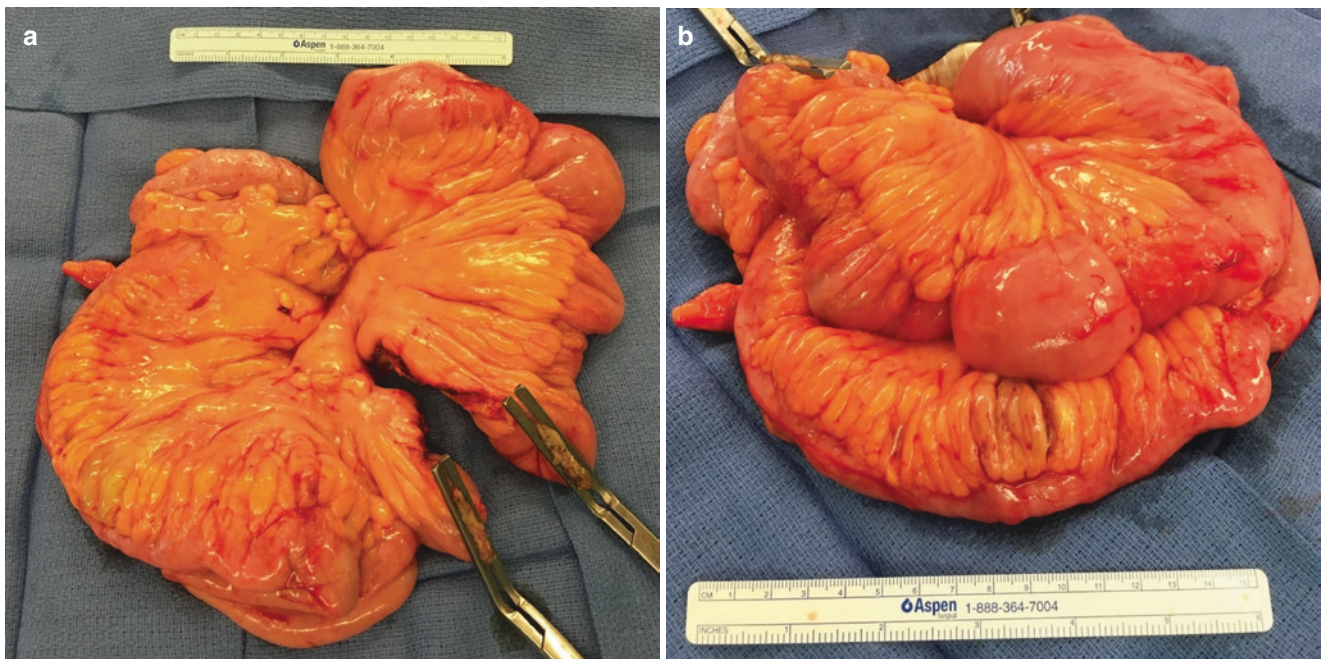


Fig. 48.10 Michelassi isoperistaltic side-to-side strictureplasty (a). The bowel is divided at the midpoint of the strictured segment. (b) The two loops are approximated. (c) A layer of interrupted seromuscular Lembert stitches is placed. (d) A longitudinal enterotomy is performed

on both loops. (e) The anastomosis is completed with the circumferential luminal layer of suture followed by an outer layer of interrupted seromuscular Lembert stitches. (Courtesy from F. Michelassi, MD)

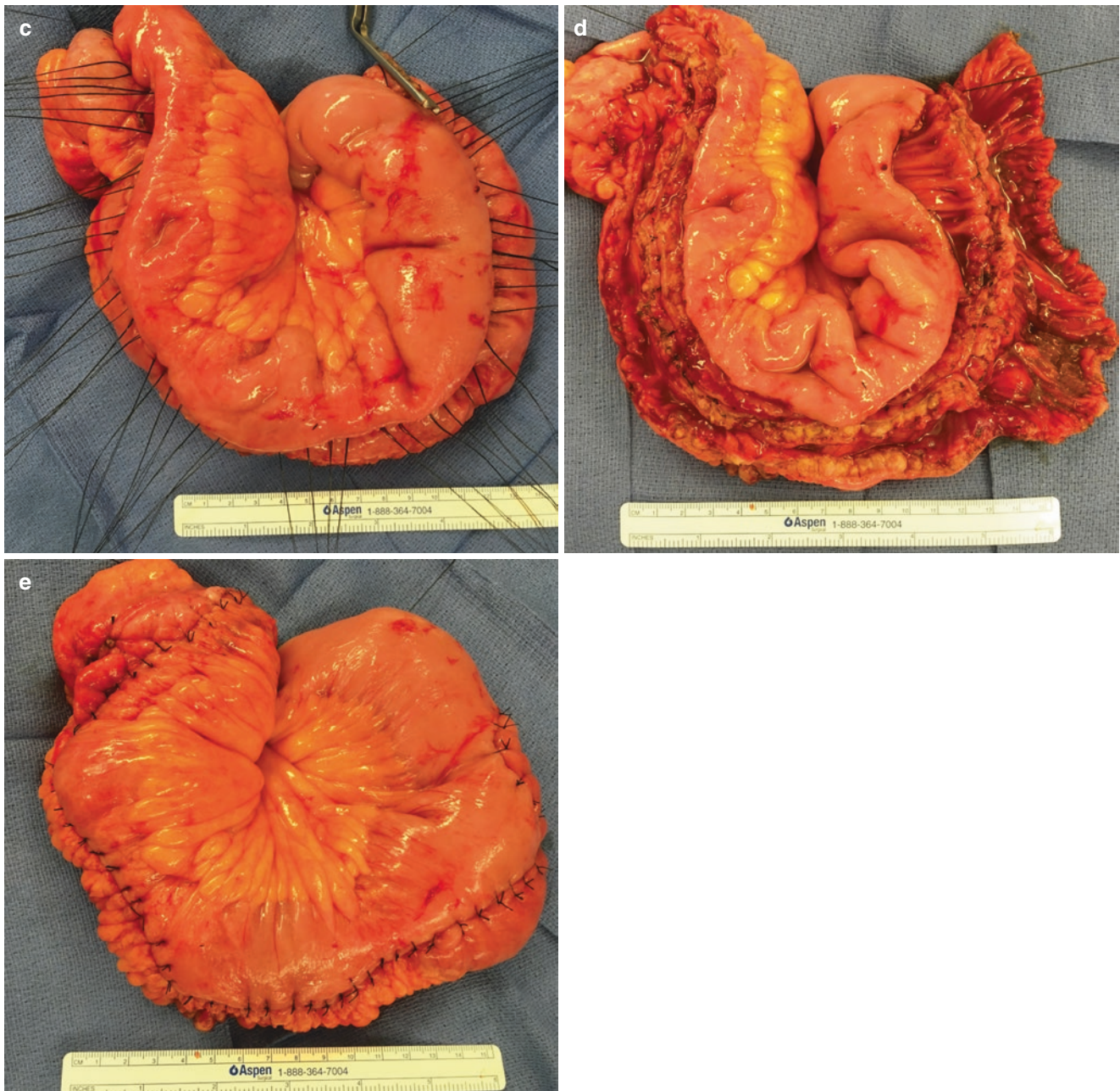


Fig. 48.10 (continued)

Colonic and Rectal Disease

The operations used to treat Crohn's disease of the colon and rectum include total proctocolectomy, total abdominal colectomy with ileostomy or ileorectal anastomosis, and segmental resection. Patients who present with toxic colitis typically require total abdominal colectomy with end ileostomy irrespective of rectal involvement. If the rectum has significant inflammation, there are several options to mitigate against rectal stump leak. If the stump is left intraperitoneally, a rectal

tube may be added for decompression. The rectal staple line can also be buried extraperitoneally in the left lower quadrant or fixed above the fascia in the lower midline; as such, the staple line leak will manifest as an abdominal wall, rather than pelvic abscess. The rectal stump may also be matured as a mucus fistula. A systematic review of rectal stump management, albeit in ulcerative colitis, reports that subcutaneous placement is associated with the lowest morbidity [138]. The decision to ultimately perform an ileorectal anastomosis or completion proctectomy can be determined at a later date.

The best operation to perform for a patient with medically refractory Crohn's colitis is less clear. Patients who present with rectal involvement in addition to their colitis are not good candidates for limited resection as there is no good distal target to establish an anastomosis; total proctocolectomy with end ileostomy is typically the indicated procedure. If the patient has poor nutritional status or is on high-dose steroids, a near-total proctocolectomy with an ultralow Hartmann pouch and end ileostomy may be performed to avoid the high risk of perineal wound sepsis. In this instance, the rectum is divided at the anorectal junction; a completion perineal proctectomy can be performed at a later date via perineal approach. Alternatively, a total abdominal colectomy with end ileostomy can be performed and the completion proctectomy accomplished at a later date.

For patients with short-segment Crohn's colitis and rectal-sparing, segmental resection is an option. Numerous retrospective studies have evaluated the outcomes of segmental resection for short-segment Crohn's colitis as compared to total colectomy or total proctocolectomy, reporting on recurrence rates, need for further surgery, and permanent stoma

formation. The perioperative complication rate is similar, with no approach emerging with clear benefit. The range of recurrence rate, reoperation rates, and permanent stoma formation are shown in Table 48.3.

Patients undergoing segmental resection or total abdominal colectomy with anastomosis experience relatively high rates of colon or rectal recurrence. Up to half of patients will ultimately require a permanent stoma in the long term.

The correct operation for Crohn's colitis remains intrinsically dependent on the distribution of disease. The initial surgical approach should usually be to resect colonic segments that are grossly involved with disease. Patients with two contiguous intestinal segments with disease involvement should undergo resection of these segments in continuity, not two separate segmental resections.

Smoking appears to be associated with the need for further intestinal surgery and need for eventual proctectomy [38]. Patients with isolated distal disease are significantly more likely to require a permanent stoma than patients with isolated proximal disease. Perianal disease, young age, and female sex are independent risk factors for disease recurrence and eventual permanent stoma, and these may inform the consent process [139, 140].

Though it is true that some patients require completion proctectomy after a more limited colonic resection, for many, this can be deferred for several years [38]. The only operation that minimizes risk of disease recurrence is total proctocolectomy with end ileostomy. However, even after total proctocolectomy with end ileostomy, there is an up to 39% rate of recurrence in the small bowel, with up to 32% of patients requiring surgical intervention at 10 years [38, 139, 141–143].

It is important to again note that these recommendations are for Crohn's colitis with rectal-sparing, and not applicable to patients with dysplasia.

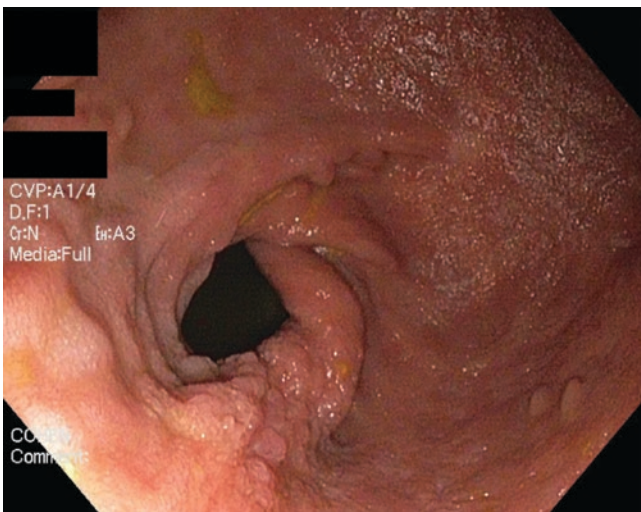


Fig. 48.11 Endoscopic evidence of regression of previously active Crohn's disease after Michelassi strictureplasty. (Courtesy of F. Michelassi, MD)

Ileal Pouch-Anal Anastomosis in Crohn's Disease

Because of the difficulty in distinguishing Crohn's disease from ulcerative colitis in various settings, some patients with

Table 48.3 Rates of disease recurrence, need for further intestinal surgery, and permanent stoma formation in patients with Crohn's colitis undergoing segmental resection, total abdominal colectomy, and total proctocolectomy

	Colon or rectal disease recurrence	Small bowel disease recurrence	Further intestinal surgery	Permanent stoma
Segmental resection [38, 156–160]	26–55%	4–14%	11–66%	5–44%
Total abdominal colectomy [38, 161–163]	24–66%	8–21%	30%	25–50%
Total proctocolectomy [38, 139, 141, 143]	n/a	Up to 39%	9–32%	Up to 100%

Crohn's disease inevitably undergo a restorative ileal pouch-anal anastomosis (IPAA). Older retrospective studies analyzing patients who were thought to have ulcerative colitis but were subsequently proven to have Crohn's disease demonstrated high complication and pouch failure rates; up to 56% required pouch excision, and a further proportion underwent indefinite diversion [144–146]. Patients with preoperative features suggestive of Crohn's, such as subtle perianal disease or discontinuous inflammation, do very poorly with no meaningful symptom-free intervals after ileal pouch formation. The authors of these studies did observe that a proportion of patients with Crohn's disease who underwent IPAA did well and enjoyed similar functional results as those patients with ulcerative colitis undergoing IPAA.

Two more recent studies suggest lower rates of pouch loss or indefinite diversion. A large prospective series of pouch patients from the Cleveland Clinic published in 2013 reported a 13.3% rate of pouch failure in Crohn's patients, versus only 5.1% in those with ulcerative colitis [147]. Li evaluated intentional IPAA and ileorectal anastomosis for Crohn's, noting that these two patient populations have distinctly different disease characteristics. They reported a 15.5% rate of indefinite diversion in the IPAA group [148]. Taking the above data into consideration, highly selected patients with Crohn's colitis with no perianal disease and no small bowel disease may consider restorative IPAA, provided the risk tolerance and shared decision-making priorities of both the patient and surgeon are aligned.

Special Considerations

Ileosigmoid Fistula

Ileosigmoid fistula is a common complication of perforating Crohn's disease of the terminal ileum. Typically, the inflamed terminal ileum adheres to the sigmoid colon that is otherwise normal and free of primary involvement with Crohn's disease. Most ileosigmoid fistulas are small, may be asymptomatic, and do not in and of themselves require operative management. On the other hand, large ileosigmoid fistulas can result in bypass of the intestinal contents from the terminal ileum to the distal colon and thus give rise to debilitating diarrhea. Such symptomatic fistulas often fail to respond to medical therapy and should be managed surgically.

More than half of the ileosigmoid fistulas from Crohn's disease are not recognized prior to surgery despite imaging and endoscopic evaluation [149]. For this reason, the surgeon should be prepared to deal with this complication in any case of Crohn's disease that involves the terminal ileum. Ileosigmoid fistulas can be managed by simple division of the fistulous adhesion and standard resection of the ileal dis-

ease [150]. The defect in the sigmoid colon is then debrided, and simple closure is undertaken; 75% of ileosigmoid fistulas can be thusly managed [149, 151]. The remainder requires resection of the sigmoid colon. Sigmoid colon resection is necessary when primary closure of the fistula is at risk for poor healing. This is the case either when the sigmoid is also involved with Crohn's disease, when the fistulous opening is particularly large, or when there is extensive fibrosis extending along the sigmoid colon. Also, fistulous tracts that enter the sigmoid colon in proximity to the mesentery may be difficult to close and often require resection and primary anastomosis.

Complex Perineal Wounds

Perianal Crohn's disease is common and occurs in one-third of the patients who suffer from intestinal Crohn's disease; this is covered in the chapter on perianal Crohn's disease. Complicated and active rectal disease significantly increases the need for proctectomy [152]; aggressive medical management with antibiotics and biologics [153] is a mainstay along with drainage of local sepsis when required in the attempt to avoid proctectomy.

Conclusion

Management of Crohn's disease is complex and requires a multidisciplinary team approach. Surgical intervention is reserved for refractory disease or complications of the disease. While significant progress has been made over the past 30 years and new medications are changing the course of treatment, much more work remains to be done including understanding how these medications will shift surgical treatment and whether specific surgical techniques lower the risk of recurrent disease.

References

1. Regueiro M, et al. Reduced unplanned care and disease activity and increased quality of life after patient enrollment in an inflammatory bowel disease medical home. *Clin Gastroenterol Hepatol.* 2018;16(11):1777–85.
2. Bernell O, Lapidus A, Hellers G. Risk factors for surgery and postoperative recurrence in Crohn's disease. *Ann Surg.* 2000;231(1):38–45.
3. Vester-Andersen MK, et al. Disease course and surgery rates in inflammatory bowel disease: a population-based, 7-year follow-up study in the era of immunomodulating therapy. *Am J Gastroenterol.* 2014;109(5):705–14.
4. Ha FJ, Thong L, Khalil H. Quality of life after intestinal resection in patients with Crohn disease: a systematic review. *Dig Surg.* 2017;34(5):355–63.

5. Scott NA, Hughes LE. Timing of ileocolonic resection for symptomatic Crohn's disease – the patient's view. *Gut*. 1994;35(5):656–7.
6. Gionchetti P, et al. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 2: Surgical management and special situations. *J Crohns Colitis*. 2017;11(2):135–49.
7. Stenke E, Bourke B, Knaus U. Crohn's strictures—moving away from the knife. *Front Pediatr*. 2017;5:141.
8. Adler J, et al. Computed tomography enterography findings correlate with tissue inflammation, not fibrosis in resected small bowel Crohn's disease. *Inflamm Bowel Dis*. 2012;18(5):849–56.
9. Rimola J, et al. Characterization of inflammation and fibrosis in Crohn's disease lesions by magnetic resonance imaging. *Am J Gastroenterol*. 2015;110(3):432–40.
10. Kim NK, et al. Long-term outcome after ileocecal resection for Crohn's disease. *Am Surg*. 1997;63(7):627–33.
11. Bhattacharya A, Shen B, Regueiro M. Endoscopy in postoperative patients with Crohn's disease or ulcerative colitis. Does it translate to better outcomes? *Gastrointest Endosc Clin N Am*. 2019;29(3):487–514.
12. Klag T, Wehkamp J, Goetz M. Endoscopic balloon dilation for Crohn's disease-associated strictures. *Clin Endosc*. 2017;50(5):429–36.
13. Reutemann BA, et al. Endoscopic balloon dilation size and avoidance of surgery in stricturing Crohn's disease. *Inflamm Bowel Dis*. 2017;23(10):1803–9.
14. Nishida Y, et al. Analysis of the risk factors of surgery after endoscopic balloon dilation for small intestinal strictures in Crohn's disease using double-balloon endoscopy. *Intern Med*. 2017;56(17):2245–52.
15. Bettenworth D, et al. A pooled analysis of efficacy, safety, and long-term outcome of endoscopic balloon dilation therapy for patients with Strictureing Crohn's disease. *Inflamm Bowel Dis*. 2017;23(1):133–42.
16. Bossuyt P, et al. The operative risk and natural history after the diagnosis of ileal penetrating Crohn's disease. *Eur J Gastroenterol Hepatol*. 2018;30(5):539–45.
17. Hirten RP, et al. The management of intestinal penetrating Crohn's disease. *Inflamm Bowel Dis*. 2018;24(4):752–65.
18. Patil SA, Cross RK. Medical versus surgical management of penetrating Crohn's disease: the current situation and future perspectives. *Expert Rev Gastroenterol Hepatol*. 2017;11(9):843–8.
19. Feagins LA, et al. Current strategies in the management of intra-abdominal abscesses in Crohn's disease. *Clin Gastroenterol Hepatol*. 2011;9(10):842–50.
20. Felder JB, Adler DJ, Korelitz BI. The safety of corticosteroid therapy in Crohn's disease with an abdominal mass. *Am J Gastroenterol*. 1991;86(10):1450–5.
21. Bafford AC, et al. The clinical impact of preoperative percutaneous drainage of abdominopelvic abscesses in patients with Crohn's disease. *Int J Color Dis*. 2012;27(7):953–8.
22. Gervais DA, et al. Percutaneous abscess drainage in Crohn disease: technical success and short- and long-term outcomes during 14 years. *Radiology*. 2002;222(3):645–51.
23. Clancy C, et al. A meta-analysis of percutaneous drainage versus surgery as the initial treatment of Crohn's disease-related intra-abdominal abscess. *J Crohns Colitis*. 2016;10(2):202–8.
24. Muller-Wille R, et al. Influence of percutaneous abscess drainage on severe postoperative septic complications in patients with Crohn's disease. *Int J Color Dis*. 2011;26(6):769–74.
25. Zhang T, et al. Preoperative intra-abdominal sepsis, not penetrating behavior itself, is associated with worse postoperative outcome after bowel resection for Crohn disease: a retrospective cohort study. *Medicine (Baltimore)*. 2015;94(45):e1987.
26. Garg SK, Velayos FS, Kiesel JB. Intestinal and nonintestinal cancer risks for patients with Crohn's disease. *Gastroenterol Clin N Am*. 2017;46(3):515–29.
27. Hnatyszyn A, et al. Colorectal carcinoma in the course of inflammatory bowel diseases. *Hered Cancer Clin Pract*. 2019;17:18.
28. Laukoetter MG, et al. Intestinal cancer risk in Crohn's disease: a meta-analysis. *J Gastrointest Surg*. 2011;15(4):576–83.
29. Yamazaki Y, et al. Malignant colorectal strictures in Crohn's disease. *Am J Gastroenterol*. 1991;86(7):882–5.
30. Lovasz BD, et al. Risk of colorectal cancer in Crohn's disease patients with colonic involvement and stenosing disease in a population-based cohort from Hungary. *J Gastrointest Liver Dis*. 2013;22(3):265–8.
31. Belaiche J, et al. Acute lower gastrointestinal bleeding in Crohn's disease: characteristics of a unique series of 34 patients. Belgian IBD Research Group. *Am J Gastroenterol*. 1999;94(8):2177–81.
32. Pardi DS, et al. Acute major gastrointestinal hemorrhage in inflammatory bowel disease. *Gastrointest Endosc*. 1999;49(2):153–7.
33. Robert JR, Sachar DB, Greenstein AJ. Severe gastrointestinal hemorrhage in Crohn's disease. *Ann Surg*. 1991;213(3):207–11.
34. Goldstone RN, Steinhagen RM. Abdominal emergencies in inflammatory bowel disease. *Surg Clin North Am*. 2019;99(6):1141–50.
35. Remzi FH, et al. Combined use of preoperative provocative angiography and highly selective methylene blue injection to localize an occult small-bowel bleeding site in a patient with Crohn's disease: report of a case. *Dis Colon Rectum*. 2003;46(2):260–3.
36. Fazio VW, et al. Effect of resection margins on the recurrence of Crohn's disease in the small bowel. A randomized controlled trial. *Ann Surg*. 1996;224(4):563–71; discussion 571–3.
37. Angriman I, et al. A systematic review of segmental vs subtotal colectomy and subtotal colectomy vs total proctocolectomy for colonic Crohn's disease. *Color Dis*. 2017;19(8):e279–87.
38. Fichera A, et al. Long-term outcome of surgically treated Crohn's colitis: a prospective study. *Dis Colon Rectum*. 2005;48(5):963–9.
39. Fumery M, et al. Systematic review with meta-analysis: recurrence of Crohn's disease after total colectomy with permanent ileostomy. *Aliment Pharmacol Ther*. 2017;45(3):381–90.
40. Swaminath A, et al. Systematic review with meta-analysis: enteral nutrition therapy for the induction of remission in paediatric Crohn's disease. *Aliment Pharmacol Ther*. 2017;46(7):645–56.
41. Yamamoto T, Shiraki M. Efficacy of enteral nutrition during infliximab maintenance therapy in patients with Crohn's disease. *Dig Dis Sci*. 2013;58(6):1802–3.
42. Cao Q, et al. The prevalence and risk factors of psychological disorders, malnutrition and quality of life in IBD patients. *Scand J Gastroenterol*. 2019;54(12):1458–66.
43. Reindl W, et al. Reducing perioperative risks of surgery in Crohn's disease. *Visc Med*. 2019;35(6):348–54.
44. Gibbs J, et al. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. *Arch Surg*. 1999;134(1):36–42.
45. Gustafsson UO, et al. Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS(R)) society recommendations: 2018. *World J Surg*. 2019;43(3):659–95.
46. Waitzberg DL, et al. Postsurgical infections are reduced with specialized nutrition support. *World J Surg*. 2006;30(8):1592–604.
47. Maartense S, et al. Laparoscopic-assisted versus open ileocolic resection for Crohn's disease: a randomized trial. *Ann Surg*. 2006;243(2):143–9; discussion 150–3.
48. Milsom JW, et al. Prospective, randomized trial comparing laparoscopic vs. conventional surgery for refractory ileocolic Crohn's disease. *Dis Colon Rectum*. 2001;44(1):1–8; discussion 8–9.
49. Eshuis EJ, et al. Long-term outcomes following laparoscopically assisted versus open ileocolic resection for Crohn's disease. *Br J Surg*. 2010;97(4):563–8.

50. Stocchi L, Milsom JW, Fazio VW. Long-term outcomes of laparoscopic versus open ileocolic resection for Crohn's disease: follow-up of a prospective randomized trial. *Surgery*. 2008;144(4):622–7; discussion 627–8.
51. Lowney JK, et al. Is there any difference in recurrence rates in laparoscopic ileocolic resection for Crohn's disease compared with conventional surgery? A long-term, follow-up study. *Dis Colon Rectum*. 2006;49(1):58–63.
52. Alves A, et al. Factors that predict conversion in 69 consecutive patients undergoing laparoscopic ileocecal resection for Crohn's disease: a prospective study. *Dis Colon Rectum*. 2005;48(12):2302–8.
53. Beyer-Berjot L, et al. Laparoscopic approach is feasible in Crohn's complex enterovisceral fistulas: a case-match review. *Dis Colon Rectum*. 2013;56(2):191–7.
54. Goyer P, et al. Impact of complex Crohn's disease on the outcome of laparoscopic ileocecal resection: a comparative clinical study in 124 patients. *Dis Colon Rectum*. 2009;52(2):205–10.
55. Wu JS, et al. Laparoscopic-assisted ileocolic resections in patients with Crohn's disease: are abscesses, phlegmons, or recurrent disease contraindications? *Surgery*. 1997;122(4):682–8; discussion 688–9.
56. Raskin ER, et al. Robotic-assisted ileocolic resection for Crohn's disease: outcomes from an early national experience. *J Robot Surg*. 2019;13(3):429–34.
57. Renshaw S, et al. Perioperative outcomes and adverse events of robotic colorectal resections for inflammatory bowel disease: a systematic literature review. *Tech Coloproctol*. 2018;22(3):161–77.
58. Moghadamyeghaneh Z, et al. Comparison of open, laparoscopic, and robotic approaches for total abdominal colectomy. *Surg Endosc*. 2016;30(7):2792–8.
59. Rencuzogullari A, et al. Case-matched comparison of robotic versus laparoscopic proctectomy for inflammatory bowel disease. *Surg Laparosc Endosc Percutan Tech*. 2016;26(3):e37–40.
60. Martinek L, et al. Does laparoscopic intracorporeal ileocolic anastomosis decrease surgical site infection rate? A propensity score-matched cohort study. *Int J Color Dis*. 2018;33(3):291–8.
61. Heimann TM, et al. Can laparoscopic surgery prevent incisional hernia in patients with Crohn's disease: a comparison study of 750 patients undergoing open and laparoscopic bowel resection. *Surg Endosc*. 2017;31(12):5201–8.
62. Scaringi S, et al. Totally robotic intracorporeal side-to-side isoperistaltic stricturoplasty for Crohn's disease. *J Minim Access Surg*. 2018;14(4):341–4.
63. Tou S, et al. Robotic-assisted stricturoplasty for Crohn's disease. *Tech Coloproctol*. 2015;19(4):253–4.
64. Maeda K, et al. A review of reports on single-incision laparoscopic surgery for Crohn's disease. *Surg Today*. 2019;49(5):361–8.
65. Schwartzberg DM, Remzi FH. The role of laparoscopic, robotic, and open surgery in uncomplicated and complicated inflammatory bowel disease. *Gastrointest Endosc Clin N Am*. 2019;29(3):563–76.
66. Cannon LM. The use of enhanced recovery pathways in patients undergoing surgery for inflammatory bowel disease. In: Flesher P, Hyman N, Strong S, editors. *Mastery of IBD surgery*. Springer Nature Switzerland AG Switzerland; 2019. p. 29–38.
67. de Campos Lobato LF, Ferreira P, Wick EC, Kiran RP, Remzi FH, Kalady MF, Vogel JD. Risk factors of prolonged length of stay after colorectal surgery. *J Coloproctol*. 2013;33(1):22–7.
68. Troung A, Zaghayan K. Perioperative steroid management in IBD patients undergoing colorectal surgery. In: Flesher P, Hyman N, Strong S, editors. *Mastery of IBD surgery*. Cham: Springer Nature Switzerland AG; 2019. p. 39–49.
69. Lamberts SW, Bruining HA, de Jong FH. Corticosteroid therapy in severe illness. *N Engl J Med*. 1997;337(18):1285–92.
70. Zaghayan KN, et al. High-dose perioperative corticosteroids in steroid-treated patients undergoing major colorectal surgery: necessary or overkill? *Am J Surg*. 2012;204(4):481–6.
71. Aytac E, et al. Impact of stress dose steroids on the outcomes of restorative proctocolectomy in patients with ulcerative colitis. *Dis Colon Rectum*. 2013;56(11):1253–8.
72. Zaghayan K, et al. A prospective, randomized, noninferiority trial of steroid dosing after major colorectal surgery. *Ann Surg*. 2014;259(1):32–7.
73. Abera FN, et al. Corticosteroids and immunomodulators: postoperative infectious complication risk in inflammatory bowel disease patients. *Gastroenterology*. 2003;125(2):320–7.
74. Subramanian V, et al. Preoperative steroid use and risk of postoperative complications in patients with inflammatory bowel disease undergoing abdominal surgery. *Am J Gastroenterol*. 2008;103(9):2373–81.
75. Zangenberg MS, et al. Preoperative optimization of patients with inflammatory bowel disease undergoing gastrointestinal surgery: a systematic review. *Int J Color Dis*. 2017;32(12):1663–76.
76. Rosen DR, Smith R. Managing immunomodulators perioperatively. In: Flesher P, Hyman N, Strong S, editors. *Mastery of IBD surgery*. Switzerland: Springer Nature Switzerland AG; 2019. p. 51–8.
77. Lau C, et al. The impact of preoperative serum anti-TNF α therapy levels on early postoperative outcomes in inflammatory bowel disease surgery. *Ann Surg*. 2015;261(3):487–96.
78. Fumery M, et al. Postoperative complications after ileocecal resection in Crohn's disease: a prospective study from the REMIND group. *Am J Gastroenterol*. 2017;112(2):337–45.
79. Lightner AL. Managing biologics perioperatively. In: Flesher P, Hyman N, Strong S, editors. *Mastery of IBD surgery*. Switzerland: Springer Nature Switzerland AG; 2019.
80. Lightner AL, et al. Postoperative outcomes in vedolizumab-treated Crohn's disease patients undergoing major abdominal operations. *Aliment Pharmacol Ther*. 2018;47(5):573–80.
81. Lightner AL, et al. Postoperative outcomes in Ustekinumab-treated patients undergoing abdominal operations for Crohn's disease. *J Crohns Colitis*. 2018;12(4):402–7.
82. Munoz-Juarez M, et al. Wide-lumen stapled anastomosis vs. conventional end-to-end anastomosis in the treatment of Crohn's disease. *Dis Colon Rectum*. 2001;44(1):20–5; discussion 25–6.
83. Simillis C, et al. A meta-analysis comparing conventional end-to-end anastomosis vs. other anastomotic configurations after resection in Crohn's disease. *Dis Colon Rectum*. 2007;50(10):1674–87.
84. Choy PY, et al. Stapled versus handsewn methods for ileocolic anastomoses. *Cochrane Database Syst Rev*. 2011;(9):CD004320.
85. Guo Z, et al. Comparing outcomes between side-to-side anastomosis and other anastomotic configurations after intestinal resection for patients with Crohn's disease: a meta-analysis. *World J Surg*. 2013;37(4):893–901.
86. Feng JS, et al. Stapled side-to-side anastomosis might be benefit in intestinal resection for Crohn's disease: a systematic review and network meta-analysis. *Medicine (Baltimore)*. 2018;97(15):e0315.
87. McLeod RS, et al. Recurrence of Crohn's disease after ileocolic resection is not affected by anastomotic type: results of a multicenter, randomized, controlled trial. *Dis Colon Rectum*. 2009;52(5):919–27.
88. Zurbuchen U, et al. Complications after end-to-end vs. side-to-side anastomosis in ileocecal Crohn's disease – early postoperative results from a randomized controlled multicenter trial (ISRCTN-45665492). *Langenbeck's Arch Surg*. 2013;398(3):467–74.
89. Kono T, et al. A new antimesenteric functional end-to-end handsewn anastomosis: surgical prevention of anastomotic recurrence in Crohn's disease. *Dis Colon Rectum*. 2011;54(5):586–92.

90. Kono T, et al. Kono-S anastomosis for surgical prophylaxis of anastomotic recurrence in Crohn's disease: an international multicenter study. *J Gastrointest Surg.* 2016;20(4):783–90.
91. Shimada N, et al. Surgical recurrence at anastomotic site after bowel resection in Crohn's disease: comparison of Kono-S and end-to-end anastomosis. *J Gastrointest Surg.* 2019;23(2):312–9.
92. Luglio G, et al. Surgical prevention of anastomotic recurrence by excluding mesentery in Crohn's disease: the SuPREMe-CD study - a randomized clinical trial. *Ann Surg.* 2020;272(2):210–7.
93. Coffey CJ, et al. Inclusion of the mesentery in ileocolic resection for Crohn's disease is associated with reduced surgical recurrence. *J Crohns Colitis.* 2018;12(10):1139–50.
94. Rutgeerts P, et al. Predictability of the postoperative course of Crohn's disease. *Gastroenterology.* 1990;99(4):956–63.
95. Fichera A, Michelassi F. Surgical treatment of Crohn's disease. *J Gastrointest Surg.* 2007;11(6):791–803.
96. Cameron JL, et al. Patterns of ileal recurrence in Crohn's disease. A prospective randomized study. *Ann Surg.* 1992;215(5):546–51; discussion 551–2.
97. D'Haens GR, et al. Early lesions of recurrent Crohn's disease caused by infusion of intestinal contents in excluded ileum. *Gastroenterology.* 1998;114(2):262–7.
98. De Cruz P, et al. Efficacy of thiopurines and adalimumab in preventing Crohn's disease recurrence in high-risk patients - a POCER study analysis. *Aliment Pharmacol Ther.* 2015;42(7):867–79.
99. Regueiro M, et al. Postoperative therapy with infliximab prevents long-term Crohn's disease recurrence. *Clin Gastroenterol Hepatol.* 2014;12(9):1494–502.e1.
100. Regueiro M, et al. Infliximab prevents Crohn's disease recurrence after ileal resection. *Gastroenterology.* 2009;136(2):441–50 e1; quiz 716.
101. Regueiro M, et al. Infliximab reduces endoscopic, but not clinical, recurrence of Crohn's disease after ileocolonic resection. *Gastroenterology.* 2016;150(7):1568–78.
102. De Cruz P, et al. Crohn's disease management after intestinal resection: a randomised trial. *Lancet.* 2015;385(9976):1406–17.
103. Reynolds HL Jr, Stellato TA. Crohn's disease of the foregut. *Surg Clin North Am.* 2001;81(1):117–35, viii.
104. Fujiya M, et al. A bamboo joint-like appearance is a characteristic finding in the upper gastrointestinal tract of Crohn's disease patients: a case-control study. *Medicine (Baltimore).* 2015;94(37):e1500.
105. Laube R, et al. Oral and upper gastrointestinal Crohn's disease. *J Gastroenterol Hepatol.* 2018;33(2):355–64.
106. Sakuraba A, et al. Endoscopic and pathologic changes of the upper gastrointestinal tract in Crohn's disease. *Biomed Res Int.* 2014;2014:610767.
107. Annunziata ML, et al. Upper gastrointestinal involvement of Crohn's disease: a prospective study on the role of upper endoscopy in the diagnostic work-up. *Dig Dis Sci.* 2012;57(6):1618–23.
108. Yamamoto T, Allan RN, Keighley MR. An audit of gastroduodenal Crohn disease: clinicopathologic features and management. *Scand J Gastroenterol.* 1999;34(10):1019–24.
109. Pimentel AM, Rocha R, Santana GO. Crohn's disease of esophagus, stomach and duodenum. *World J Gastrointest Pharmacol Ther.* 2019;10(2):35–49.
110. Lightner AL. Duodenal Crohn's disease. *Inflamm Bowel Dis.* 2018;24(3):546–51.
111. Tonelli F, et al. Symptomatic duodenal Crohn's disease: is strictureplasty the right choice? *J Crohns Colitis.* 2013;7(10):791–6.
112. Schwartzberg DM, Brandstetter S, Grucela AL. Crohn's disease of the esophagus, duodenum, and stomach. *Clin Colon Rectal Surg.* 2019;32(4):231–42.
113. Worsey MJ, et al. Strictureplasty is an effective option in the operative management of duodenal Crohn's disease. *Dis Colon Rectum.* 1999;42(5):596–600.
114. Murray JJ, et al. Surgical management of Crohn's disease involving the duodenum. *Am J Surg.* 1984;147(1):58–65.
115. Nugent FW, Roy MA. Duodenal Crohn's disease: an analysis of 89 cases. *Am J Gastroenterol.* 1989;84(3):249–54.
116. Michelassi F, et al. Primary and recurrent Crohn's disease. Experience with 1379 patients. *Ann Surg.* 1991;214(3):230–8; discussion 238–40.
117. Tan WC, Allan RN. Diffuse jejunoileitis of Crohn's disease. *Gut.* 1993;34(10):1374–8.
118. Dietz DW, et al. Strictureplasty in diffuse Crohn's jejunoileitis: safe and durable. *Dis Colon Rectum.* 2002;45(6):764–70.
119. Dietz DW, et al. Safety and long-term efficacy of strictureplasty in 314 patients with obstructing small bowel Crohn's disease. *J Am Coll Surg.* 2001;192(3):330–7; discussion 337–8.
120. Molloy JW, Kim E, Mahadevan U. Do side-by-side anastomoses decrease the risk of recurrence in Crohn's disease? *Gastroenterology.* 2010;138(5):2010–2.
121. Watanabe K, et al. Long-term incidence and characteristics of intestinal failure in Crohn's disease: a multicenter study. *J Gastroenterol.* 2014;49(2):231–8.
122. Katariya RN, et al. Stricture-plasty for tubercular strictures of the gastro-intestinal tract. *Br J Surg.* 1977;64(7):496–8.
123. Lee EC, Papaioannou N. Minimal surgery for chronic obstruction in patients with extensive or universal Crohn's disease. *Ann R Coll Surg Engl.* 1982;64(4):229–33.
124. Ambe R, Campbell L, Cagir B. A comprehensive review of strictureplasty techniques in Crohn's disease: types, indications, comparisons, and safety. *J Gastrointest Surg.* 2012;16(1):209–17.
125. Campbell L, et al. Comparison of conventional and nonconventional strictureplasties in Crohn's disease: a systematic review and meta-analysis. *Dis Colon Rectum.* 2012;55(6):714–26.
126. Michelassi F. Side-to-side isoperistaltic strictureplasty for multiple Crohn's strictures. *Dis Colon Rectum.* 1996;39(3):345–9.
127. Maggiori L, Michelassi F. How I do it: side-to-side isoperistaltic strictureplasty for extensive Crohn's disease. *J Gastrointest Surg.* 2012;16(10):1976–80.
128. Fazi M, et al. Long-term results and recurrence-related risk factors for Crohn disease in patients undergoing side-to-side isoperistaltic strictureplasty. *JAMA Surg.* 2016;151(5):452–60.
129. Michelassi F, et al. Side-to-side isoperistaltic strictureplasty in extensive Crohn's disease: a prospective longitudinal study. *Ann Surg.* 2000;232(3):401–8.
130. Michelassi F, et al. Long-term results of the side-to-side isoperistaltic strictureplasty in Crohn disease: 25-year follow-up and outcomes. *Ann Surg.* 2020;272(1):130–7.
131. Reese GE, et al. Strictureplasty vs resection in small bowel Crohn's disease: an evaluation of short-term outcomes and recurrence. *Color Dis.* 2007;9(8):686–94.
132. Rottoli M, et al. Predictors of early recurrence after strictureplasty for Crohn's disease of the small bowel during the years of biologics. *Dig Liver Dis.* 2019;51(5):663–8.
133. Stebbing JF, et al. Recurrence and reoperation after strictureplasty for obstructive Crohn's disease: long-term results [corrected]. *Br J Surg.* 1995;82(11):1471–4.
134. Jaskowiak NT, Michelassi F. Adenocarcinoma at a strictureplasty site in Crohn's disease: report of a case. *Dis Colon Rectum.* 2001;44(2):284–7.
135. Marchetti F, Fazio VW, Ozuner G. Adenocarcinoma arising from a strictureplasty site in Crohn's disease. Report of a case. *Dis Colon Rectum.* 1996;39(11):1315–21.
136. Tichansky D, et al. Strictureplasty for Crohn's disease: meta-analysis. *Dis Colon Rectum.* 2000;43(7):911–9.
137. Yamamoto and Keighley. Follow up of more than 10 years after strictureplasty for jejunoileal Crohn's disease: long-term results and predictive factors for outcome. *Color Dis.* 1999;1(2):101–6.

138. Bedrikovetski S, et al. Systematic review of rectal stump management during and after emergency total colectomy for acute severe ulcerative colitis. *ANZ J Surg.* 2019;89(12):1556–60.
139. Bernell O, Lapidus A, Hellers G. Recurrence after colectomy in Crohn's colitis. *Dis Colon Rectum.* 2001;44(5):647–54. discussion 654
140. Stocchi L. The role of segmental resection in Crohn's colitis. In: Flesher P, Hyman N, Strong S, editors. *Mastery in IBD surgery.* Switzerland: Springer Nature Switzerland AG; 2019. p. 161–5.
141. Amiot A, et al. Crohn's disease recurrence after total proctocolectomy with definitive ileostomy. *Dig Liver Dis.* 2011;43(9):698–702.
142. Lightner AL. Segmental resection versus total proctocolectomy for Crohn's colitis: what is the best operation in the setting of medically refractory disease or dysplasia? *Inflamm Bowel Dis.* 2018;24(3):532–8.
143. Lopez J, et al. Natural history of Crohn's disease following total colectomy and end ileostomy. *Inflamm Bowel Dis.* 2014;20(7):1236–41.
144. Brown CJ, et al. Crohn's disease and indeterminate colitis and the ileal pouch-anal anastomosis: outcomes and patterns of failure. *Dis Colon Rectum.* 2005;48(8):1542–9.
145. Hyman NH, et al. Consequences of ileal pouch-anal anastomosis for Crohn's colitis. *Dis Colon Rectum.* 1991;34(8):653–7.
146. Mylonakis E, Allan RN, Keighley MR. How does pouch construction for a final diagnosis of Crohn's disease compare with ileoproctostomy for established Crohn's proctocolitis? *Dis Colon Rectum.* 2001;44(8):1137–42; discussion 1142–3.
147. Fazio VW, et al. Ileal pouch anal anastomosis: analysis of outcome and quality of life in 3707 patients. *Ann Surg.* 2013;257(4):679–85.
148. Li Y, et al. Long-term outcomes of sphincter-saving procedures for diffuse Crohn's disease of the large bowel. *Dis Colon Rectum.* 2016;59(12):1183–90.
149. Block GE, Schraut WH. The operative treatment of Crohn's enteritis complicated by ileosigmoid fistula. *Ann Surg.* 1982;196(3):356–60.
150. Fennern E, et al. Surgical techniques and differences in postoperative outcomes for patients with Crohn's disease with ileosigmoid fistulas: a single-institution experience, 2010–2016. *Dis Colon Rectum.* 2019;62(10):1222–30.
151. Schraut WH, Chapman C, Abraham VS. Operative treatment of Crohn's ileocolitis complicated by ileosigmoid and ileovesical fistulae. *Ann Surg.* 1988;207(1):48–51.
152. Michelassi F, et al. Surgical treatment of anorectal complications in Crohn's disease. *Surgery.* 2000;128(4):597–603.
153. Present DH, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. *N Engl J Med.* 1999;340(18):1398–405.
154. Alves A, et al. Risk factors for intra-abdominal septic complications after a first ileocecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Dis Colon Rectum.* 2007;50(3):331–6.
155. Yamamoto T, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Dis Colon Rectum.* 2000;43(8):1141–5.
156. Andersson P, et al. Segmental resection or subtotal colectomy in Crohn's colitis? *Dis Colon Rectum.* 2002;45(1):47–53.
157. Longo WE, Ballantyne GH, Cahow CE. Treatment of Crohn's colitis. Segmental or total colectomy? *Arch Surg.* 1988;123(5):588–90.
158. Makowiec F, et al. Long-term follow-up after resectional surgery in patients with Crohn's disease involving the colon. *Z Gastroenterol.* 1998;36(8):619–24.
159. Polle SW, et al. Recurrence after segmental resection for colonic Crohn's disease. *Br J Surg.* 2005;92(9):1143–9.
160. Martel P, et al. Crohn's colitis: experience with segmental resections; results in a series of 84 patients. *J Am Coll Surg.* 2002;194(4):448–53.
161. Longo WE, et al. Outcome of ileorectal anastomosis for Crohn's colitis. *Dis Colon Rectum.* 1992;35(11):1066–71.
162. O'Riordan JM, et al. Long-term outcome of colectomy and ileorectal anastomosis for Crohn's colitis. *Dis Colon Rectum.* 2011;54(11):1347–54.
163. Pastore RL, Wolff BG, Hodge D. Total abdominal colectomy and ileorectal anastomosis for inflammatory bowel disease. *Dis Colon Rectum.* 1997;40(12):1455–64.