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Surgery for luminal Crohn's disease

Takayuki Yamamoto, Toshiaki Watanabe

Takayuki Yamamoto, Inflammatory Bowel Disease Center and Department of Surgery, Yokkaichi Social Insurance Hospital, Mie 510-0016, Japan

Toshiaki Watanabe, Department of Surgical Oncology, The University of Tokyo, Hongo, Tokyo 113-0033, Japan

Author contributions: Yamamoto T and Watanabe T contributed equally to this paper.

Correspondence to: Takayuki Yamamoto, MD, PhD, FACC, Inflammatory Bowel Disease Center and Department of Surgery, Yokkaichi Social Insurance Hospital, 10-8 Hazuyamacho, Yokkaichi, Mie 510-0016, Japan. nao-taka@sannet.ne.jp

Telephone: +81-59-3312000 Fax: +81-59-3310354

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Abstract

Many patients with Crohn's disease (CD) require surgery. Indications for surgery include failure of medical treatment, bowel obstruction, fistula or abscess formation. The most common surgical procedure is resection. In jejunoileal CD, strictureplasty is an accepted surgical technique that relieves the obstructive symptoms, while preserving intestinal length and avoiding the development of short bowel syndrome. However, the role of strictureplasty in duodenal and colonic diseases remains controversial. In extensive colitis, after total colectomy with ileorectal anastomosis (IRA), the recurrence rates and functional outcomes are reasonable. For patients with extensive colitis and rectal involvement, total colectomy and end-ileostomy is safe and effective; however, a few patients can have subsequent IRA, and half of the patients will require proctectomy later. Proctocolectomy is associated with a high incidence of delayed perineal wound healing, but it carries a low recurrence rate. Patients undergoing proctocolectomy with ileal pouch-anal anastomosis had poor functional outcomes and high failure rates. Laparoscopic surgery has been introduced as a minimal invasive procedure. Patients who undergo laparoscopic surgery have a more rapid recovery of bowel function and a shorter hospital stay.

The morbidity also is lower, and the rate of disease recurrence is similar compared with open procedures.

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Key words: Crohn's disease; Laparoscopic surgery; Resection; Strictureplasty; Surgery

Core tip: Strictureplasty is now an accepted procedure in the management of jejunoileal Crohn's disease (CD). However, the place for strictureplasty is less well defined in duodenal and colonic diseases. For patients with extensive colonic CD, the surgical choices include total colectomy with either an ileorectal anastomosis or end-ileostomy, or a total proctocolectomy with permanent end-ileostomy. Patients with CD undergoing ileal pouch-anal anastomosis are associated with poor functional outcomes and high failure rates. Laparoscopic surgery is safe and feasible. Patients who undergo laparoscopic surgery have a more rapid recovery of bowel function and a shorter hospital stay.

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INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disease of unknown cause that can involve any portion of the digestive tract. Inflammation can extend entirely through the intestinal wall, and most patients with CD will eventually develop stricturing or perforating complications^[1]. Accordingly, the majority of patients require surgery as part of the therapeutic management of their disease. Probability of surgical resection within 15 years after diagnosis was 70%^[2]. CD may be helped by surgery, but it

cannot be cured by surgery. The primary goals of surgery are to alleviate serious complications, achieve the best possible quality of life (QOL), and conserve as much bowel as possible.

INDICATIONS FOR SURGERY

Indications for surgery include failure of medical treatment, bowel obstruction, fistula or abscess formation, or combination of these indications. The majority of patients are treated with elective surgery. However, patients with intestinal perforation, peritonitis, excessive bleeding or toxic megacolon require urgent surgery. Improved medical treatment may lead to higher rates of elective operations^[3]. However, prolonged conservative treatment may also increase the number of serious complications before surgery. Therefore, a multidisciplinary approach with early involvement of the surgeon is important to avoid any delay in indication to surgery.

SURGICAL OPTIONS

In 1987 Alexander-Williams and Haynes^[4] formulated the 5 “Golden Rules” of surgical management of CD (Table 1). Surgical treatments for CD include bypass, resection, and stricturoplasty. The aim of surgery for CD has shifted from radical operation, achieving inflammation-free margins of resection, to minimal surgery, intended to remove just grossly inflamed tissue or performing stricturoplasty. The surgeon must assess which procedure is most suitable at each area of the disease.

Bypass

There are two types of bypass operations: exclusion bypass and simple (continuity) bypass. For certain types of ileocecal CD with associated with serious abscess or phlegmon densely adherent to the retroperitoneum, the proximal cut end of the transected ileum is anastomosed to the transverse colon in an end-to-side fashion with or without construction of a mucus fistula of the distal cut end of the ileum (exclusion bypass) or an ileotransverse colonic anastomosis is made in a side-to-side fashion (simple bypass). In the study by Homan and Dineen^[5], CD involving the ileum and cecum was treated with resection in 115 patients, exclusion bypass in 25, and simple bypass in 21. Overall recurrence rates were 25% for resection, 63% for exclusion bypass, and 75% for simple bypass. This difference was accounted for by early recurrence or by persistent disease in the two bypass groups: 21% for exclusion bypass and 45% for simple bypass as compared to 3% for resection. These results indicate that the recurrence rate following resection is significantly lower than bypass, and continuing disease in the bypassed loop accounts for a high percentage of reoperations in the bypass groups. Resection is the surgical treatment of choice for ileocecal CD. Furthermore, there is the risk of malignancy in the bypassed segment^[6]. At present, bypass surgery is rarely performed except for gastroduodenal

CD. The surgical management of gastroduodenal CD is discussed later.

Resection

Resection margin: The most commonly performed operation for patients undergoing surgical management of their CD is resection of the diseased segment. In small bowel disease, the involved segment is characterized by thickening of the mesenteric margin of the bowel, fat wrapping on the sides of the intestinal wall^[7]. The non-diseased bowel can be distinguished from diseased bowel by palpating the mesenteric border of the bowel wall. Several studies^[8,9] suggested that radical resection, the wide resection of normal bowel uninvolved microscopically, was associated with a lower recurrence rate as compared with non-radical resection. Other studies^[10,11] have shown no difference in the recurrence rates between patients treated with radical resection and non-radical resection. In a randomized controlled trial (RCT)^[12], 152 patients undergoing ileocolonic resection for CD were randomly assigned to two groups in which the proximal line of resection was 2 cm (limited resection) or 12 cm (extended resection) from the macroscopically involved area. With a median follow-up time of 56 mo, disease recurred in 25% of patients in the limited resection group and 18% of patients in the extended resection group (not significant). This study indicate that recurrence rate is unaffected by the width of the margin of resection from macroscopically involved bowel segment. Radical resection is not recommended because it does not reduce recurrence rates.

Anastomotic technique: Stapled functional end-to-end anastomosis has become a popular procedure in colorectal surgery. Its potential benefits include a wide anastomotic lumen, minimal contamination, and a quick method. Fecal stasis and subsequent bacterial overgrowth are implicated in anastomotic recurrence in CD. A wider anastomosis is less likely to cause a functional obstruction, and may be associated with a lower risk of recurrence. Several studies^[13-15] reported that the stapled functional end-to-end anastomosis was associated with fewer postoperative complications and recurrences as compared with sutured end-to-end anastomosis (conventional anastomosis). In a meta-analysis, the outcomes were compared between end-to-end anastomosis and other anastomotic configurations after bowel resection for CD^[16]. Eight studies reported on 661 patients who underwent 712 anastomoses, of which 383 (53.8%) were sutured end-to-end anastomosis and 329 (46.2%) were other anastomotic configurations (259 stapled side-to-side, 59 end-to-side or side-to-end, 11 stapled circular end-to-end). End-to-end anastomosis was associated with increased anastomotic leak rates. Side-to-side anastomosis was associated with fewer anastomotic leaks and overall postoperative complications, and a shorter hospital stay. There was no significant difference between the groups in perianastomotic recurrence and reopera-

Table 1 Five "Golden Rules" of surgical management of Crohn's disease^[4]

Crohn's disease is a panintestinal disease, with intermittent activity and the potential of focal exacerbations throughout the patient's life
It is impossible to cure Crohn's disease by excision. The surgeon is required only to treat the complications
The essence of surgical treatment is to make the operation as safe as possible. If the operation becomes safe and patients survive, they will inevitably have recurrences and so repeated operations may be required. Therefore, it is important to conserve as much gut as possible
All diseased bowels need not be excised, only that part with complications
If only stenotic complications are being treated, perhaps the stenosis can be simply widened by strictureplasty or dilatation

tion needed because of perianastomotic recurrence. Five of the 8 studies included in this meta-analysis were non-randomized retrospective trials. In an RCT^[17], 139 patients who underwent an ileocolonic resection were randomized to side-to-side anastomosis (STSA group) or end-to-end anastomosis (ETEA group). There were no significant differences in overall complication rates (24% in the ETEA group *vs* 20% in the STSA group), anastomotic leak rates (7% in the ETEA group *vs* 7% in the STSA group) and reoperative rates for complications (7% in the ETEA *vs* 7% in the STSA group). After a mean follow-up of 11.9 mo, the symptomatic recurrence rate was 21.9% in the ETEA group, compared with 22.7% in the STSA group (not significant). The endoscopic recurrence rate was 42.5% in the ETEA group, compared with 37.9% in the STSA group. Based on these results^[16,17], CD recurrence after bowel resection is not affected by anastomotic type.

Kono *et al.*^[18] has recently introduced a new antimesenteric functional end-to-end handsewn anastomosis (Kono-S anastomosis) designed to minimize anastomotic restenosis in patients with CD. In their retrospective study, 69 patients with Kono-S anastomosis (group S) were compared with 73 historical patients with conventional anastomosis (group C) from 1993 to 2003. The frequency of endoscopic recurrence at anastomosis was comparable between the two groups (83% at 1 year and 100% at 5 years in group S *vs* 79% at 1 year and 100% at 5 years in group C). However, the median endoscopic recurrence score at the anastomosis was significantly lower in group S than in group C (2.6 *vs* 3.4). At 5 years after operation, surgical recurrence rate at the anastomosis was significantly lower in group S than in group C. The Kono-S anastomosis appears to be effective in preventing anastomotic surgical recurrence in CD. However, to rigorously evaluate the efficacy of the Kono-S anastomosis, large RCTs are necessary.

Strictureplasty

Indications: One of the risks of repeated or extensive resections for small bowel CD is the development of short bowel syndrome. The rationale for strictureplasty is to avoid resection and preserve intestinal length and

Table 2 Contraindications to strictureplasty

Excessive tension due to rigid and thickened bowel segments
Perforation of the intestine
Fistula or abscess formation at the intended strictureplasty site
Hemorrhagic strictures
Multiple strictures within a short segment
Malnutrition or hypoalbuminemia (< 2.0 g/dL)
Suspicion of cancer at the intended strictureplasty site

function of the small bowel^[19,20]. Strictureplasty is ideal for diffuse involvement of the small bowel with multiple strictures, and strictures in patients who have undergone extensive resections or multiple resections of the small bowel. Strictures of duodenum, and ileocolonic or ileorectal anastomosis can be treated with strictureplasty. In contrast, contraindications to strictureplasty are presented in Table 2.

At laparotomy, strictures are identified by careful palpation of the bowel. The Heineke-Mikulicz strictureplasty is used for short strictures of up to 10 cm in length. In contrast, the Finney strictureplasty is used for longer strictures of up to 25 cm. Heineke-Mikulicz strictureplasty rarely develops metabolic sequelae, which may suggest that absorptive capacity is preserved. Whether the bowel is similarly functionally preserved after Finney strictureplasty is open to question, and some would argue that the bacterial overgrowth and blind-loop syndrome may result from this type of strictureplasty. Very long strictures (> 30 cm) and multiple strictures within a short segment have traditionally been treated with resection. Several authors have introduced new types of strictureplasty for these conditions^[21-28]. We will discuss this in more detail towards the end of this section.

Outcomes: In a meta-analysis^[19], a total of 1112 patients who underwent 3259 strictureplasties (Heineke-Mikulicz 81%, Finney 10%, side-to-side isoperistaltic 5%, others 4%) were identified. The sites of strictureplasty were jejunum and/or ileum (94%), previous ileocolonic or ileorectal anastomosis (IRA) (4%), duodenum (1%), and colon (1%). After jejunoleal strictureplasty, including ileocolonic anastomotic strictureplasty, septic complications (anastomotic leak, enteric fistula, intra-abdominal abscess) occurred in 4% of patients. Poor nutritional status, anemia, peritoneal contamination due to intra-abdominal sepsis, older age and emergency operation were risk factors for the complications after strictureplasty. In contrast, steroid use, synchronous bowel resection, and number, site or type of strictureplasties were not significant factors. Overall surgical recurrence was 23% (95%CI: 17%-30%). The 5-year recurrence rate after strictureplasty was 28%. In 90% of patients, recurrence occurred at non-strictureplasty sites, and the site-specific recurrence rate was 3%. Younger age was a risk factor for recurrence after strictureplasty. Few patients developed a short bowel syndrome. These results confirmed that strictureplasty may have largely replaced resection and minimized the

risk of the short bowel syndrome.

Strictureplasty vs resection: There was concern about a potential increase in septic complications and disease recurrence with strictureplasty, as this procedure preserves diseased bowel and as the suture line is fashioned through macroscopic disease. It is difficult to compare the outcomes of strictureplasty and resection, since resection is principally used for severely affected segments which are not suitable for strictureplasty. There have been no RCTs comparing the outcomes between strictureplasty and resection. In a recent meta-analysis^[29], seven studies comprising 688 patients (strictureplasty 45%, resection with/without strictureplasty 55%) were analyzed. Patients undergoing strictureplasty alone had a lower risk of developing postoperative complications than those who underwent resection (OR = 0.60, 95%CI: 0.31-1.16) although this was not statistically significant. Surgical recurrence after strictureplasty was more likely than after resection (OR = 1.36, 95%CI: 0.96-1.93). Patients who had a resection showed a significantly longer recurrence-free survival than those undergoing strictureplasty alone (HR = 1.08, 95%CI: 1.02-1.15). These results suggest that patients with small bowel CD undergoing strictureplasty alone may have fewer postoperative complications than those undergoing a concomitant bowel resection. However, surgical recurrence maybe higher following strictureplasty alone than with a concomitant small bowel resection. RCTs are necessary to rigorously compare the outcomes between strictureplasty and resection.

New types of strictureplasties: Multiple strictureplasties in a short segment may result in a bulky and unyielding segment of intestine, which leads to considerable tension on each suture line. In patients with long and rigid strictures, the Finney strictureplasty may not be technically feasible because the intestinal wall lacks the pliability to fold onto itself. Michelassi^[22] initially proposed a new technique, the side-to-side isoperistaltic strictureplasty in the management of long strictures or multiple strictures in a short segment. Other authors have also introduced their new types of strictureplasties^[24-28]. A prospective study^[30] reported on the results of 184 patients who underwent the side-to-side isoperistaltic strictureplasty in six centers. The average length of diseased bowel selected for the strictureplasty varied among centers, from 20.8 to 64.3 cm. The complication rate after surgery varied from 5.7% to 20.8%. The most commonly encountered complication was gastrointestinal hemorrhage (2%), followed by suture line dehiscence (1%), and bowel obstruction (1%). Forty-one of the 184 patients required surgery for recurrent disease, with an average time to recurrence of 35 mo. The cumulative reoperation-free rate at 5 years after surgery was 77% across all centers. This study suggests that the side-to-side isoperistaltic strictureplasty carries a low mortality and morbidity rate, with acceptable recurrence rates.

A recent systematic review compared short-term and

long-term results between conventional (Heineke-Mikulicz and Finney) and non-conventional (modified Finney, combined Heineke-Mikulicz and Finney, modified Heineke-Mikulicz, Michelassi, and modifications of it and others) strictureplasties^[31]. One thousand one hundred fifty-seven patients underwent conventional strictureplasties with an early complication rate of 15% vs 459 patients underwent non-conventional strictureplasties with an early complication rate of 8%. A late complication rate was 29% for the conventional strictureplasty group vs 17% for the non-conventional strictureplasty group. The early and late complication rates are comparable between the non-conventional and conventional strictureplasty procedures. However, bowel function is preserved after long strictureplasty is open to discussion because motility disturbances may occur after this type of strictureplasty. Michelassi *et al*^[23] found that in their enteroclysis study, flow of contrast was unimpeded, and no stasis or retention of contrast occurred in the strictureplasty site. Further investigation is necessary to evaluate the efficacy of the new types of strictureplasties.

SURGERY FOR SPECIFIC CONDITIONS

Duodenal CD

Gastroduodenal CD is an uncommon condition, occurring in about 1%-5% of all CD cases^[32,33]. The most common site of gastroduodenal CD was the duodenal bulb, and gastroduodenal CD was almost invariably present in association with disease elsewhere in the intestinal tract^[32,33]. Stricture was the most common pathology of gastroduodenal CD^[32,33]. Presence of symptoms of obstruction needs medical therapy with steroids and immunomodulatory drugs including infliximab. When these medications do not alleviate the symptoms, balloon dilation or surgery is the option to consider. In patients with gastroduodenal CD, the most common indication for surgery was obstruction.

Several authors reported the outcomes of surgery for gastroduodenal CD. In the Birmingham study^[34], 26 patients with obstructive duodenal CD were treated with strictureplasty ($n = 13$) or bypass surgery ($n = 13$). The median duration of follow-up was 159 mo. In the strictureplasty group, 2 patients developed an anastomotic breakdown leading to an enterocutaneous fistula. Obstructive symptoms were not improved in four patients, of whom 3 patients were managed with conservative treatments and the other patient required a gastrojejunostomy. In the long-term, 6 patients developed restructure at the previous strictureplasty site, of whom 5 required repeat strictureplasty and the other patient underwent duodenojejunostomy. Overall, 9 patients after strictureplasty required further surgical treatment due to 3 early postoperative complications (anastomotic leaks 2 and persistent obstructive symptoms 1) and 6 restructures at the previous strictureplasty site. In the bypass group, 3 patients had persistent obstructive symptoms and 1 developed intra-abdominal sepsis in the early postopera-

tive period. All settled on conservative treatments. In the long-term, 6 patients required further surgery for stomal ulceration ($n = 2$) and anastomotic obstruction ($n = 4$). In the Cleveland Clinic study^[35], 34 patients with duodenal CD were treated with strictureplasty ($n = 13$) or bypass ($n = 21$). Strictureplasty was associated with 2 postoperative complications, and 1 patient required reoperation for recurrence at a mean follow-up of 3.6 years. Bypass was associated with 2 postoperative complications, and 1 patient required reoperation for recurrence at a mean follow-up of 8 years. In the management of duodenal CD, strictureplasty has the advantage of avoiding a blind loop syndrome or stomal ulceration. In the Birmingham study, strictureplasty has no obvious advantages over bypass surgery. In contrast, the Cleveland Clinic study shows that strictureplasty is safe and effective, and has potential physiologic advantage over bypass. Thus, the results between these studies are very different probably because of differences in disease aggressiveness and follow-up duration. Most recently, the outcomes of surgery for duodenal CD in 10 patients were reported^[36]. Eight patients were treated with strictureplasty, and 2 patients were treated with resection: 1 with a gastroduodenal resection, and 1 with a duodenojejunal resection and an end to side duodenojejunal anastomosis. No recurrence of duodenal CD was observed in the 2 patients treated with resection, while 2 of the 8 patients treated with strictureplasty developed recurrence. The authors suggest that duodenal strictureplasty is indicated when less than 2 strictures are present in the second or third duodenal portion. In cases with multiple strictures localized in the first or the distal duodenal portion, resection is preferable. They also suggest that an accurate complete mobilization of the duodenum is an important step of the procedure, as it allows sutures without tension. In the previous studies, the number of patients is too small to conclude on the efficacy of duodenal strictureplasty. Further studies in larger cohorts of patients are necessary.

Diffuse jejunoileal CD

Diffuse jejunoileal disease (multiple segments of disease in the proximal ileum and jejunum) is relatively uncommon, the incidence being 3%-10% of entire CD population^[37]. Diffuse jejunoileal disease is one of the most difficult areas to treat in CD. Resectional surgery may lead to short bowel syndrome. A retrospective study^[38] reported on the long-term outcomes of surgical treatment for diffuse jejunoileal CD. Forty-six patients required surgery for diffuse jejunoileal CD. During an initial operation, strictureplasty was used on 63 strictures in 18 patients (39%). After a median follow-up of 15 years, 39 patients (85%) required 113 reoperations for jejunoileal recurrence. During 75 of the 113 reoperations (66%), strictureplasty was used on 315 strictures. Only two patients developed short bowel syndrome and required home parenteral nutrition. At the end of the study, 4 patients were symptomatic and required medical treatment. All other patients were asymptomatic and required neither medical

treatment nor nutritional support. Most patients with diffuse jejunoileal CD can be restored to good health with minimal symptoms by surgical treatment that includes strictureplasty.

The Cleveland Clinic reported their experience of strictureplasty for diffuse jejunoileal CD^[39]. One hundred twenty-three patients underwent strictureplasty for diffuse jejunoileitis. Total number of strictureplasties performed was 701 (median, 5 per patient). Seventy percent of patients underwent a synchronous bowel resection. The overall morbidity rate was 20%, with septic complications occurring in 6%. The surgical recurrence rate was 29% with a median follow-up period of 6.7 years. The recurrence rate in diffuse jejunoileitis patients did not differ from that seen in 219 patients with limited small bowel CD undergoing strictureplasty.

Extensive colorectal CD

For patients with extensive colonic CD, the surgical choices include total colectomy with either an IRA or end-ileostomy, or a total proctocolectomy with permanent end-ileostomy. Several authors^[40-52] reported on the outcomes of surgery for extensive Crohn's colitis. A retrospective study^[47] reviewed 144 patients who underwent a total colectomy for Crohn's colitis. IRA was performed in 118 patients, while 26 never had an IRA after colectomy because of severe anorectal lesions. The probability of clinical recurrence after IRA was 58% and 83% at 5 and 10 years respectively. The probability of rectal preservation at 5 and 10 years was 86% and 86% after IRA. Patients with extraintestinal manifestation had a higher risk of recurrence and of rectal preservation failure. In the literature review, the rate of functional IRA after total colectomy for extensive Crohn's colitis at 10 years was approximately 70% (Table 3). One study^[45] reviewed 69 patients who underwent a total colectomy and end-ileostomy with an oversewn rectal stump for extensive Crohn's colitis. Only 5 patients (7%) underwent IRA, of whom 2 required proctectomy later. Overall, 37 patients (54%) required proctectomy, with a median duration of 2 years. Sixteen patients (23%) developed small bowel recurrence requiring surgery, with a median duration of 6.8 years. In the literature review, the rate of secondary proctectomy for defunctioned rectum after a total colectomy with end-ileostomy is presented in Table 4. Half of the patients will subsequently require proctectomy after a total colectomy with end-ileostomy. In a retrospective study^[52], 103 patients who underwent single-stage proctocolectomy for extensive colorectal CD were reviewed. The commonest postoperative complication was delayed perineal wound healing (35%), followed by intra-abdominal sepsis (17%) and stomal complications (15%). In 23 patients the perineal wound healed between 3 and 6 mo after proctocolectomy, whereas in 13 patients the wound remained unhealed for more than 6 mo. There were 2 hospital deaths (2%) caused by sepsis. The 5-, 10-, and 15-year cumulative reoperation rates for small bowel recurrence were 13%, 17%, and 25%, respectively, after a

Table 3 Rate of functional ileorectal anastomosis after a total colectomy for extensive Crohn's colitis at 10 years

Ref.	n	Functioning ileorectal anastomosis
Buchmann <i>et al</i> ^[40]	105	70%
Ambrose <i>et al</i> ^[41]	63	71%
Longo <i>et al</i> ^[42]	118	48%
Chevallier <i>et al</i> ^[43]	83	63%
Pastore <i>et al</i> ^[44]	42	65%
Yamamoto <i>et al</i> ^[45]	65	78%
Bernell <i>et al</i> ^[46]	106	76%
Cattan <i>et al</i> ^[47]	118	86%

median follow-up of 18.6 years. Thus, proctocolectomy for CD is associated with a high incidence of complications, particularly delayed perineal wound healing. However, proctocolectomy carries a low recurrence rate in the long-term. A recent literature review confirms an approximately 30% risk of recurrence of CD after an end ileostomy^[53]. A penetrating phenotype and preexisting ileal disease are risk factors for disease recurrence. A thorough evaluation of the stoma/peristomal area and evaluation of the small bowel by ileoscopy and small bowel imaging are required to assess the extent of disease and extraluminal complications such as stomal retraction and fistulas that require further surgical intervention. While postoperative medical treatment with immunosuppression or biological therapy is often employed, these therapies are unproven to prevent postoperative recurrence in the setting of a stoma.

In the management of extensive colitis, after a total colectomy with IRA, the recurrence rates and functional outcomes are reasonable if the rectum is not severely affected and sphincter function is not compromised. For patients with rectal involvement, total colectomy and end-ileostomy is safe and effective; however, a few patients can have subsequent IRA, and half of the patients will require proctectomy later. Proctocolectomy is associated with a high incidence of complications, particularly delayed perineal wound healing, but it carries a low recurrence rate. Algorithm for surgical treatment of extensive colitis is presented in Figure 1.

Ileal pouch surgery for CD

Ileal pouch-anal anastomosis (IPAA) is the surgical treatment of choice for most patients with ulcerative colitis (UC)^[54,55]. In contrast, CD is considered a contraindication to IPAA. The unexpected diagnosis of CD after IPAA operation is a relatively frequent occurrence. Several authors^[56-58] reported the outcomes of IPAA for patients with CD. Hartley *et al*^[56] reviewed 60 patients who underwent IPAA for UC subsequently had that diagnosis revised to CD. With a median follow-up of 46 mo, pouch loss rate was 12%. Median daily bowel movement in those with IPAA *in situ* was seven (range 3-20), with 50% of patients rarely or never experiencing urgency and 59% reporting perfect or near perfect continence. In 1985, Panis *et al*^[57] decided to investigate an alternative to total proctocolectomy with definitive end-ileostomy by a

Table 4 Rate of secondary proctectomy for defunctioned rectum after a total colectomy with end-ileostomy for extensive Crohn's colitis

Ref.	n	Follow-up (yr)	Secondary proctectomy
Harling <i>et al</i> ^[48]	59	7.7	50%
Guillem <i>et al</i> ^[49]	47	6	51%
Sher <i>et al</i> ^[50]	25	6	40%
Yamamoto <i>et al</i> ^[51]	65	10	54%

prospective study of IPAA for selected patients with CD. Between 1985 and 1992, 31 patients with CD, but with no evidence of anoperineal or small bowel disease, were recruited to their study. All patients underwent IPAA. The short-term and long-term functional results of this procedure were compared with those of 71 UC patients who also underwent IPAA during the same period in their unit. With a mean follow-up of 59 mo, no significant differences were observed between patients with CD and UC in the postoperative complication rate. Of the 31 patients with CD, 6 (19%) experienced specific complications nine mo to 6 years after surgery: 3 had pouch-perineal fistulas, which required pouch excision in 2 cases, 1 had a pouch-vaginal fistula that was treated by gracilis muscle interposition, and 1 had an extrasphincteric abscess, which was treated surgically. Two patients (6%), 1 of whom was treated for an extrasphincteric abscess, experienced CD recurrence on the reservoir, and were treated successfully with azathioprine. At 5-year follow-up, there were no significant differences between patients with CD and UC in stool frequency (5.0 *vs* 4.7 per day), continence, gas/stool discrimination, leak or need for protective pads, and sexual activity. Their results show that in selected cases of CD without anoperineal or small bowel manifestations, IPAA can be recommended as an alternative to proctocolectomy with definitive end-ileostomy. In 2001, the same research group reported 10-year results of IPAA in selected patients with colorectal CD^[58]. Forty-one patients underwent IPAA for colorectal CD between 1985 and 1998. None had past or present history of anal manifestations or evidence of small bowel involvement. Follow-up was 113 mo, 20 patients having been followed for more than 10 years. Eleven (27%) patients experienced CD-related complications, 47 mo after IPAA: 2 had persistent anal ulcerations with pouchitis and granulomas on pouch biopsy and were treated medically, 2 experienced extrasphincteric abscesses and 7 presented pouch-perineal fistulas which were treated surgically. Among them, 3 patients with persistent perineal fistula despite surgery required definitive end-ileostomy. Of the 20 patients followed for more than 10 years, 7 (35%) experienced CD-related complications which required pouch excision in 2 (10%). These good long-term results justify for surgeons to propose IPAA in selected patients with colorectal CD.

Melton *et al*^[59] reviewed 204 CD patients (108 female, median age 33 years, and median follow-up 7.4 years) with primary IPAA. CD diagnosis was before IPAA (in-

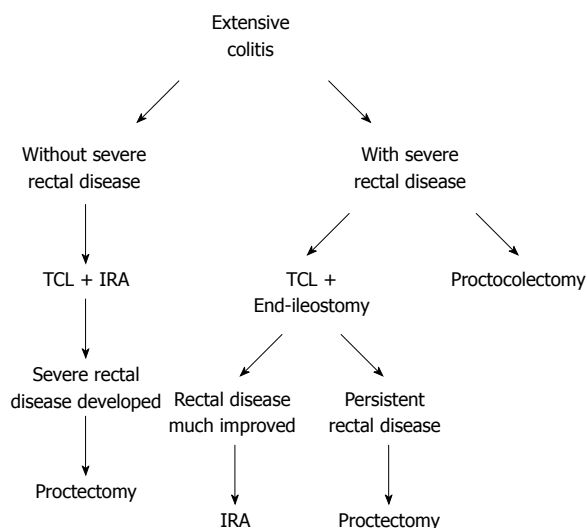


Figure 1 Algorithm for surgical treatment of extensive colitis. TCL: Total colectomy; IRA: ileorectal anastomosis.

tentional) in 20 (10%), from postoperative histopathology (incidental) in 97 (47%) or made in a delayed fashion at median 36 mo after IPAA in 87(43%). Overall 10-year pouch retention was 71%. On multivariate analysis, pouch loss was associated with delayed diagnosis (HR = 2.6, 95%CI: 1.1-6.5), pouch-vaginal fistula (HR = 2.8, 95%CI: 1.3-6.4), and pelvic sepsis (HR = 9.7, 95%CI: 3.4-27.3). Patients with retained IPAA at follow-up had near-perfect/perfect continence (72%), rare/no urgency (68%) with median daily bowel movements 7 (range 2-20). Median overall QOL, quality of health, level of energy, and happiness with surgery were 9, 9, 8, and 10 of 10, respectively. For CD patients with IPAA, when the diagnosis is established preoperatively or immediately following surgery, pouch loss rates are low and functional results are favorable. Outcomes in patients with delayed diagnosis are worse but half retain their pouch at 10 years with good functional outcomes. Most recently, Le *et al*⁶⁰ reported the surgical outcomes of IPAA when used intentionally for well-defined CD. Seventeen patients with preoperative CD were identified, whereas the preoperative diagnosis was UC in 261 patients. Seven of the 17 patients (41%) in the preoperative CD group developed postoperative CD (recurrence in the afferent limb 3, pouch fistulizing disease 4) *vs* 27 of the 261 patients (11%) in the UC group (afferent limb inflammation 23, perianal disease 4) ($P = 0.002$). Of the seven CD patients with recurrent inflammation, three patients were maintained on immunosuppressive therapy and another three patients were controlled with antibiotics alone. Only one patient (6%) of the preoperative CD patient cohort with severe pouch inflammation and perianal disease required pouch excision and permanent ileostomy after failing aggressive medical therapy. The incidence of pouch failure was not statistically significant between patient groups.

A meta-analysis compared postoperative complications and functional outcomes after IPAA between

patients with CD and those with non-CD diagnoses⁶¹. Ten clinical trials comprising 3103 patients (CD 225, UC 2711, indeterminate colitis 167) were included. Patients with CD developed more anastomotic strictures than non-CD diagnoses (OR = 2.12, $P = 0.05$) and experienced pouch failure more frequently than patients with UC (CD *vs* UC: 32% *vs* 4.8%, $P < 0.001$; CD *vs* indeterminate colitis: 38% *vs* 5%, $P < 0.001$). Urgency was more common in CD compared with non-CD: 19% *vs* 11% ($P = 0.02$). Incontinence occurred more frequently in CD compared with non-CD patients: 19% *vs* 10% (OR = 2.4, $P = 0.01$). Twenty-four-hour stool frequency did not differ significantly between CD, UC, or indeterminate colitis. Patients with isolated colonic CD were not significantly at increased risk of postoperative complications or pouch failure ($P = 0.06$). If surgeons were to undertake IPAA in the presence of CD, then the patient would require careful counseling to outline the risk of poorer functional outcomes and higher failure compared with non-CD patients. If patients are prepared to accept these risks and meet the selection criteria, such as isolated colonic CD without any evidence of terminal ileal or perianal involvement, there may be a role for IPAA in this select group of patients.

LAPAROSCOPIC SURGERY

Laparoscopic surgery is “minimally invasive” procedure commonly used to treat diseases of the gastrointestinal tract. Unlike traditional gastrointestinal surgery where a long incision down the center of the abdomen is required, laparoscopic surgery requires only small incisions in the abdomen. As a result, patients undergoing the procedure may experience less pain and scarring after surgery and a more rapid recovery. Several clinical studies have reported the outcomes of laparoscopic surgery for CD. These studies have reported conflicting results. Most of the studies have been limited by a small sample size and a short follow-up duration.

Several meta-analyses on efficacy of laparoscopic surgery for CD were conducted^{62,63}. Rosman *et al*⁶² found that laparoscopic surgery required more operative time than open surgery (26.8 min; 95%CI: 6.4-47.2), but resulted in a shorter duration of ileus and a decreased hospital stay (-2.62 d; 95%CI: -3.62--1.62). Laparoscopic surgery also was associated with a decreased rate for postoperative bowel obstruction and surgical recurrences. Tan and Tjandra⁶³ found that the rate of conversion from laparoscopic to open surgery was 11.2%. Laparoscopic procedures took longer to perform compared with open procedures, with a weighted mean difference of 25.54 min ($P = 0.03$). Patients who underwent laparoscopic surgery had a more rapid recovery of bowel function, with a weighted mean difference of 0.75 d ($P = 0.02$) and were able to tolerate oral intake earlier, with a weighted mean difference of 1.43 d ($P = 0.0008$). The duration of hospitalization was shorter, with a weighted mean difference of 1.82 d ($P = 0.02$). Morbidity was lower for

laparoscopic procedures compared with open procedures (OR = 0.57, 95%CI: 0.37-0.87, $P = 0.01$). The rate of disease recurrence was similar for both laparoscopic and open surgery. From these results in the 2 meta-analyses, although laparoscopic procedures take longer to perform, patients who undergo laparoscopic surgery have a more rapid recovery of bowel function and a shorter hospital stay. The morbidity also is lower, and the rate of disease recurrence is similar compared with open procedures. Thus, laparoscopic surgery for CD is safe and feasible.

Long-term results of laparoscopic surgery *vs* conventional surgery for CD were evaluated in 2 RCTs^[64,65]. In the first RCT^[64], recurrence and complication rates were compared between laparoscopic (LC) and open ileocollectomy (OC) for ileocolonic CD. Mean follow-up for 56 patients (27 LC *vs* 29 OC) was 10.5 years and comparable between LC and OC (10.0 *vs* 11.0, respectively; $P = 0.64$). One patient died 8 years after OC of causes unrelated to CD. Eight patients for each group underwent initial reoperative (LC 26% *vs* OC 28%, $P = 0.89$). One patient underwent incisional hernia repair after LC (4%) *vs* 4 patients (14%) after OC ($P = 0.61$). Two patients in the LC group underwent adhesiolysis *vs* none after OC ($P = 0.23$). Incidences of anorectal disease, anorectal surgery, endoscopic or radiologic recurrence, and medication use were also similar between LC and OC. OC patients requiring operation during follow-up were significantly more likely than LC to require multiple operations ($P = 0.006$). This study confirms that LC is at least comparable to OC in the treatment of ileocolonic CD. In the second RCT^[65], 60 patients who underwent ileocolonic resection between 1999 and 2003 were studied. Five patients were lost to follow-up. Median follow-up was 6.7 years. Sixteen of 29 and 16 of 26 patients remained relapse free after ileocolonic resection in the laparoscopic and open groups respectively (risk difference 6, 95%CI: -20-32). Resection of recurrent CD was necessary in 2 of 29 *vs* 3 of 26 patients (risk difference 5, 95%CI: -11-20). Overall reoperation rates for recurrent CD, incisional hernia and adhesion-related problems were 2 of 29 *vs* 6 of 26 (risk difference 16, 95%CI: -3-35). QOL was similar, whereas body image and cosmesis scores were significantly higher after laparoscopy ($P = 0.029$ and $P < 0.001$, respectively). This study confirms that laparoscopically assisted ileocolonic resection results in better body image and cosmesis, whereas open surgery is more likely to produce incisional hernia and obstruction. These 2 RCTs indicate that laparoscopic surgery for small bowel CD is as safe as the open operation. There is no significant difference in the perioperative outcomes and the long term reoperation rates for disease-related or non-disease related complications of CD^[66].

PREOPERATIVE CONDITIONS AND RISK OF POSTOPERATIVE COMPLICATINS

Nutritional status and septic conditions

Currently, the use of biological agents constitutes one

way to diminish local, and alleviate mucosal inflammation, thereby allowing surgery to be performed at complicated disease sites. However, evidence to date would suggest that there has been little change in the natural history of the disease and hence surgical therapies. Surgery provides good long-term disease control in many patients, and that delay in operating may result in more advanced disease and hence more postoperative complications^[67]. Yamamoto *et al*^[67] reviewed 343 patients who underwent 1008 intestinal anastomoses during 566 operations for primary or recurrent CD between 1980 and 1997. Intra-abdominal septic complications, defined as anastomotic leak, intra-abdominal abscess, or enterocutaneous fistula, developed after 76 operations (13%). Intra-abdominal septic complications were significantly associated with preoperative low albumin level (< 30 g/L), preoperative steroids use, abscess at the time of laparotomy, and fistula at the time of laparotomy. The intra-abdominal septic complication rate was 50% (8/16 operations) in patients with all of these 4 risk factors, 29% (10/35 operations) in patients with 3 risk factors, 14% (14/98 operations) in patients with 2 risk factors, 16% (33/209 operations) in patients with 1 risk factor, and 5% (11/208 operations) in patients with none of these risk factors ($P < 0.0001$). The following factors did not affect the incidence of septic complications; age, duration of symptoms, number of previous bowel resections, site of disease, type of operation (resection, strictureplasty, or bypass), covering stoma, and number, site, or method (sutured or stapled) of anastomoses. Preoperative low albumin level, steroid use, and the presence of abscess or fistula at the time of laparotomy significantly increased the risk of septic complications after surgery in CD. A surgical decision about avoiding an anastomosis must take into account many issues, especially age, degree of malnutrition, severity of coexisting sepsis and the dose of steroids or immunosuppressants. However, we must conclude from our data that an anastomosis is much more likely to break down if three or four of the four risk factors are present in a particular patient. It is not clear that preoperative nutritional intervention can reduce the risk of postoperative complications. Preoperative management of septic conditions may be associated with a lower incidence of complications after surgery. However, there has been no striking evidence that management of malnutrition and sepsis before surgery improves the surgical outcomes in CD. Delay in operation may be associated with an increased risk of serious complications. Further studies are necessary on these practical issues.

Impact of biologic therapy on postoperative complications

The immunosuppressive effects of preoperative anti-tumor necrosis factor (TNF)- α therapy may increase the risk for postoperative complications among CD patients undergoing abdominal surgery. A number of meta-analyses^[68-70] were conducted to compare the rates of postoperative complications among CD patients treated

with anti-TNF- α therapy *vs* alternative therapies. A total of eight studies including 1,641 patients were included in the meta-analysis by Kopylov *et al*^[68]. Preoperative infliximab therapy in CD patients undergoing abdominal surgery was associated with a trend toward an increased rate of total complications (OR = 1.72, 95%CI: 0.93-3.19). Anti-TNF- α treatments were associated with a modestly increased risk of infectious complications (OR = 1.50, 95%CI: 1.08-2.08), mostly remote from the surgical site (OR = 2.07, 95%CI: 1.30-3.30) and with a trend toward a higher rate of noninfectious complications (OR = 2.00, 95%CI: 0.89-4.46). Preoperative infliximab treatment was associated with an increased risk of postoperative infectious complications, mostly nonlocal. A trend toward an increased risk of noninfectious and overall complications was also observed. In the meta-analysis by Billioud *et al*^[69], the prevalence of infectious postoperative complications was increased in CD patients who underwent preoperative anti-TNF- α therapy (OR = 1.45, 95%CI: 1.03-2.05). In the meta-analysis by Rosenfeld *et al*^[70], data were extracted from 6 studies including 1159 patients among whom 413 complications were identified. The most common complications were wound infections, anastomotic leak and sepsis. There was no significant difference in the major complication rate (OR = 1.59, 95%CI: 0.89-2.86), minor complication rate (OR = 1.80, 95%CI: 0.87-3.71), reoperation rate (OR = 1.33, 95%CI: 0.55-3.20) or 30 day mortality rate (OR = 3.74, 95%CI: 0.56-25.16) between the infliximab and control groups. Thus, the impact of anti-TNF- α therapy on postoperative complications remains unclear.

POSTOPERATIVE MANAGEMENT FOR THE PREVENTION OF RECURRENCE

Risk factors for postoperative recurrence

In the surgical management of CD, postoperative recurrence is common, and many patients require repeat operation for recurrence. The reoperation rates for recurrence have been reported to be 10%-30% at 5 years, 20%-40% at 10 years and 40%-60% at 20 years after surgery^[71]. The reoperation rate tends to steadily increase with time, reaching approximately 50% at 20 years after surgery. The most significant factor affecting postoperative CD recurrence was found to be smoking^[71,72]. Smokers had an increased risk of recurrence compared to non-smokers. Similarly, perforating CD appeared to be associated with a higher recurrence rate compared with non-perforating CD^[71,72].

Monitoring for postoperative recurrence

Rutgeerts *et al*^[73] reported that recurrent lesions were observed endoscopically in the neo-terminal ileum (the proximal site of the ileocolonic anastomosis) within 1 year of resection in 73% of patients, although only 20% of the patients had symptoms. Three years after surgery, the endoscopic recurrence rate increased to 85% and symptomatic recurrence occurred in 34%. Patients with

severe endoscopic lesions within 1 year after resection developed early clinical recurrence. In contrast, patients with no or mild endoscopic lesions had a low frequency of subsequent clinical recurrence. The severity of the endoscopic inflammation in the neo-terminal ileum during the first year after resection was found to be a reliable predictive risk factor for future clinical recurrence. Ileocolonoscopy is the gold standard in the diagnosis of postoperative recurrence by defining the presence and severity of morphologic recurrence and predicting the clinical course. Ileocolonoscopy is recommended within the first year after surgery where treatment decisions may be affected.

Prophylactic medications

Prophylactic treatment is recommended after small intestinal resection^[74,75]. High dose mesalazine is an option for patients with an isolated ileal resection^[74,75]. Thiopurines are more effective than mesalazine or imidazole antibiotics alone for preventing both clinical and endoscopic recurrence^[74,75]. In patients with a risk factor for early postoperative recurrence the drug of choice is azathioprine/mercaptopurine^[74,75]. Imidazole antibiotics have been shown to be effective after ileocolonic resection but are less well tolerated. Probiotics have failed to show efficacy in postoperative CD recurrence, but should merit further investigations^[72,75]. There has been no RCT evaluating the efficacy of enteral nutrition in the prevention of postoperative CD recurrence^[72,75]. Several RCTs^[76-78] investigated the efficacy of biologic agents for the prevention of recurrence after resection for CD. Regueiro *et al*^[76] randomly assigned 24 patients who had undergone ileocolonic resection to receive intravenous infliximab (5 mg/kg), administered within 4 wk of surgery and continued for 1 year, or placebo. The primary end point was the proportion of patients with endoscopic recurrence at 1 year. Secondary end points were clinical recurrence and remission and histologic recurrence. The rate of endoscopic recurrence at 1 year was significantly lower in the infliximab group (1/11 patients; 9.1%) compared with the placebo group (11/13 patients; 84.6%). There was a nonsignificant higher proportion of patients in clinical remission in the infliximab group (8/10 patients; 80.0%) compared with the placebo group (7/13 patients; 53.8%). The histologic recurrence rate at 1 year was significantly lower in the infliximab group (3/11 patients; 27.3%) compared with the placebo group (11/13 patients; 84.6%). Administration of infliximab after intestinal resection was effective at preventing endoscopic and histologic recurrence of CD. In the study by Yoshida *et al*^[77], 31 patients who had ileocolonic resection within the past 4 wk were randomly assigned to scheduled infliximab at 5 mg/kg intravenously every 8 wk for 36 mo ($n = 15$) or without infliximab (control, $n = 16$). At 12 and 36 mo, 100% and 93.3% of patients in the infliximab group were in remission, respectively *vs* 68.8% and 56.3% in the control arm ($P < 0.03$). Further, the infliximab group achieved higher endoscopic remission at 12 mo (78.6%

vs 18.8%, $P = 0.004$). Savarino *et al*^[78] randomly assigned 51 patients who had undergone ileocolonic resection to receive after 2 wk from surgery adalimumab at the dose of 160/80/40 mg every 2 wk, azathioprine at 2 mg/kg per day, or mesalamine at 3 g/d, and they were followed up for 2 years. The primary end point was the proportion of patients with endoscopic and clinical recurrence. The rate of endoscopic recurrence was significantly lower in adalimumab (6.3%) compared with the azathioprine (64.7%; OR = 0.036, 95%CI: 0.004-0.347) and mesalamine groups (83.3%; OR = 0.013, 95%CI: 0.001-0.143). There was a significantly lower proportion of patients in clinical recurrence in the adalimumab group (12.5%) compared with the AZA (64.7%; OR = 0.078, 95%CI: 0.013-0.464) and mesalamine groups (50%; OR = 0.143, 95%CI: 0.025-0.819). The administration of adalimumab after intestinal resection was effective in preventing endoscopic and clinical recurrence of CD. Further larger studies are necessary to confirm the therapeutic advantage and to show the economic implications of biologic therapy in this field. Antibiotics, immunomodulatory medications and anti-TNF- α agents have been shown to be efficacious in preventing postoperative recurrence of CD, although the potential risks and benefits of therapy need to be balanced in individual patients.

CONCLUSION

In the management of jejunoileal CD, stricturoplasty is an accepted surgical technique that relieves the obstructive symptoms, while preserving intestinal length and avoiding the development of short bowel syndrome. However, the role of stricturoplasty in duodenal and colonic diseases remains controversial. In extensive colitis, after total colectomy with IRA, the recurrence rates and functional outcomes are reasonable. For patients with rectal involvement, total colectomy and end-ileostomy is safe and effective; however, a few patients can have subsequent IRA, and half of the patients will require proctectomy later. Proctocolectomy is associated with a high incidence of delayed perineal wound healing, but it carries a low recurrence rate. Patients undergoing proctocolectomy with IPAA had poor functional outcomes and high failure rates. However, if patients accept these risks and meet the selection criteria, such as isolated colonic CD without any evidence of terminal ileal or perianal involvement, there may be a role for IPAA.

Laparoscopic surgery has been introduced as a minimal invasive procedure. As compared with conventional surgery, laparoscopic procedures take longer to perform; however, patients who undergo laparoscopic surgery have a more rapid recovery of bowel function and a shorter hospital stay. There is no significant difference in the perioperative outcomes and the long-term reoperation rates between laparoscopic and conventional surgeries.

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