Current Status of Segmental Colectomy in Select Crohn's Disease Patients

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Abstract

Keywords

► Crohn's disease
► colitis
► surgical treatment
► inflammatory disorder
► anti-TNF

Crohn's disease is a complex disease with a varying clinical and anatomical spectrum. One-third of patients with Crohn's will have disease confined to the colon. In this article, the authors review the surgical treatment options for colonic Crohn's disease including the current status of performing segmental colectomy in colonic Crohn's, the pros and cons of segmental versus subtotal colectomy, and the influence of biologics on recurrence rates following segmental colectomy.

Crohn's disease (CD) is a chronic inflammatory disorder of the gastrointestinal tract with an increasing incidence[1] that is characterized by relapsing and remitting episodes, with progression over time to complications of stricture, fistulas, or abscesses.[2] In a U.S. population-based study, disease extent was colonic alone in 32% of cases and ileocolonic in a further 18%, representing a substantial burden of disease.[3] In addition, 40% of patients with colonic disease have coexistent perianal disease.[4] The rate of surgical intervention in this cohort is over 50% at 20-year follow-up, though the rate of surgery in isolated colonic disease was lowest based on the Montreal classification.[5] The Montreal classification (►Table 1) based on age at diagnosis, disease location, and behavior provides important prognostic information,[1] as it is known that the disease phenotype remains stable over time (i.e., ileal vs. colonic), but not disease behavior (i.e., penetrating vs. stricturing).[6]

Indications for surgery can be classified into acute disease complications such as fulminant colitis, toxic megacolon, uncontrolled bleeding, perforation, and nonperianal fistulae or chronic disease complications such as growth retardation, stricture, dysplasia or cancer, extra colonic complications that may respond to surgery such as pyoderma gangrenosum, polyarteritis nodosa, and uveitis, as well as failed medical therapy. The decision to perform colectomy in many instances can be relative and difficult owing to complications and high recurrence rates on the one hand versus evidence that surgery provides good long-term disease control on the other.[7] Deferral of surgery may result in more advanced disease leading to higher complication rates as well as more complex immunosuppressive medication regimes potentially raising complication rates even further.

Segmental versus Total Colectomy

In patients with colonic disease alone, there are few randomized studies guiding indications for surgery. Surgical options include segmental resection, subtotal colectomy (SC) with ileosigmoid or ileorectal anastomosis (IRA), and proctocolectomy with end ileostomy. Strictureplasty remains a good option for small bowel disease where short bowel can be an issue but is not recommended in colonic disease.[8] Proctocolectomy with ileoanal pouch anastomosis is not generally recommended,[9] though occurs inadvertently in cases where the preexisting diagnosis is thought to be ulcerative colitis. Despite advances in medical management of CD, the natural history of the disease has not changed and therefore the

Table 1 Montreal classification

	Montreal classification
Age at diagnosis	
< 16 y	A1
17–40 y	A2
> 40 y	A3
Disease location	
Ileal disease	L1
Colonic disease	L2
Ileocolonic	L3
Upper-isolated gastrointestinal disease	L4
Disease behavior	
Nonstricturing and nonpenetrating	B1
Stricturing	B2
Penetrating	B3
Perianal disease	p

subsequent need for surgery[7] and it is known that surgery will be required in up to 75% of patients with Crohn's after 10 years of disease.[10]

The optimal operation for segmental colonic CD has been long debated. Patients with colonic disease who come to surgery comprise approximately 25% of all patients with large bowel involvement requiring resection.[11] While segmental resection and strictureplasty are standard treatment for small bowel disease, treatment options for colonic disease are more contentious.[12] SC or abdominal colectomy and ileosigmoid or IRA are both valid options.[13] Both have a rate of recurrence and need for revisional surgery, but permanent stoma is avoided and thus quality of life is better.[14] The choice between the two operations will be influenced by the extent of colonic involvement, though decision making can be difficult where two colonic segments are involved or when short skip lesions are present.[15] Segmental resection may have a higher recurrence rate but all the benefits of colonic preservation.[7] The risk of recurrent disease necessitating further surgery and the morbidity of that surgery may be overstated in the era or anti-tumor necrosis factor (anti-TNF) agents, laparoscopic resections, and durable endoscopic dilatation, and such segmental colectomy should be recommended more often than was previously the case.

A widely referenced meta-analysis examining the issue of segmental versus total colectomy was published by Tekkis et al in 2005.[12] Six studies published between 1997 and 2002 reporting outcomes in 488 patients comparing need for reoperation, overall recurrence, time to surgical recurrence, postoperative complications and the need for permanent stoma were examined. All studies, but one, were nonrandomized retrospective observational studies with follow-up ranging from 4.6 to 14.2 years. Study periods were not contemporary and ranged from 1955 to 1998, illustrating

some of the difficulty interpreting findings due to selection and publication bias, methodologic heterogeneity, as well as subsequent improvements in medical and endoscopic management.[1,7,16]

Despite these caveats, no significant difference in surgical recurrence rates between SC and IRA was found. It should be noted that more patients in the IRA group had multisegment disease. Overall recurrence was not different, but the time to recurrence was 4.43 years earlier in the SC group. The rate of postoperative complications was similar. It can therefore be concluded that no level I evidence exists and that recommendations are largely confined to expert opinion.

Prabhakar and colleagues identified 49 patients who had undergone either segmental colectomy or abdominal colectomy with ileosigmoid or IRA.[17] Patients with primary anorectal or primary ileal disease or who had undergone a total proctocolectomy were excluded. Thirty-nine patients had a segmental colectomy and 10 underwent an abdominal colectomy. Following surgery, 22 patients (45%) required no further treatment during the follow-up period of 14 years. Of the 27 patients who experienced a recurrence, 11 (23%) were treated medically and 16 (33%) required further surgery. For patients requiring further surgery, 10 patients had another segmental resection and 6 required completion proctocolectomy. A third procedure for recurrence was required in six patients, of which only one underwent completion proctocolectomy and ileostomy for control of disease. Thus, 86% of the patients in this study remained stoma free. In those six patients requiring a stoma, the mean stoma-free interval was 23 months. Factors such as extent of resection, margins of resection, disease location, and extent of disease did not predict recurrence. Segmental colectomy did have a greater recurrence rate than abdominal colectomy and ileosigmoid or IRA, but the rate of stoma formation did not differ between the two groups. It was concluded that although there is a clear and definite risk of recurrent colorectal disease, segmental and abdominal colectomy are both viable options for patients with limited colonic CD.

Holubar et al reported a series of 69 double segmental resections of which 20% were for colonic CD and reported no anastomotic leakage providing evidence that double segmental resection is safe.[18]

Segmental versus Total Colectomy: Guideline Recommendations

In the absence of high-quality contemporary evidence, it is useful to examine consensus guidelines. British Society of Gastroenterology Guidelines[7] published in 2010 provide limited recommendations only and emphasize the importance of multidisciplinary discussion. Recommendations are for SC in left-side disease or where more than two segments are involved, and segmental resection for isolated right colonic disease. NICE guidelines for surgery in CD do not address colonic disease at all.[19] European Guidelines also published in 2010[8] suggest that if less than one-third of the colon is affected then segmental resection should be performed. For cases where macroscopic disease affects both ends of the colon, segmental resections can be considered; however, a

lack of consensus is noted with the final decision to perform SC/IRA left to patient preference and surgeon discretion.American Society Guidelines published in 2015 reference the Tekkis meta-analysis and recommend SC/IRA for "more extensive disease" defined as more than one segment involved.[20] This option is recommended on the basis that the subgroup of patients with more than two segments involved "has a higher recurrence rate when segmental resections are performed"; however, this was not what the Tekkis study reported.[12] A metaregression technique was used to examine patients with more than two colonic segments and found that SC/IRA was associated with lower reoperation rates, but this finding was not statistically significant. As noted earlier, however, the data informing this meta-analysis are retrospective observational data and not contemporary. Advances in medical and endoscopic therapies such as durable pneumatic dilatation of strictures[16] and the introduction of biologics[1] may have reduced the surgical recurrence rate significantly for patients having segmental colectomy.

Practical Surgical Decision Making

As surgery is highly individualized due to widely variable patient, disease, and anatomic factors, it is worth considering in detail factors for the surgeon to consider. Scott Strong has written extensively[21,22] on surgery for CD colitis. Recommendations are for patients with disease limited to the ascending colon to have a resection with and an anastomosis to the midtransverse colon, so that the anastomosis does not lie over the duodenum and pancreas, potentially resulting in a complex fistula in this area upon disease recurrence in this bowel segment. Omentum or residual mesentery should be placed if possible between the anastomosis and retroperitoneum. Transverse colon disease with or without ascending colon involvement is best managed by extended right hemicolectomy. The mesenteric defect can be minimized by rotating the small bowel anticlockwise so that the whole of the small bowel resides in the right side of the abdomen. Descending colon or sigmoid disease is treated by anterior resection and/or left hemicolectomy. If the disease affects the distal transverse colon as well, the proximal colon can be brought through a retroileal window between the ileocolic and superior mesenteric vessels. Alternatively, the ascending colon can be rotated anticlockwise following mobilization of the hepatic flexure with anastomosis onto the rectum (►**Table 2**).

Where colonic involvement is extensive, colectomy with IRA is recommended provided the rectum is spared and continence is reasonable with good rectal compliance and minimal perianal disease. Rectal compliance can be judged at endoscopy or during anorectal physiology testing. When maximum tolerated volume on anal physiology is less than 150 mL, continence is expected to be poor following IRA.[23] If severe anorectal CD is present in conjunction with colitis, proctocolectomy with end ileostomy is the procedure of choice. If a patient has severe lower colonic and anorectal disease, something short of a proctocolectomy may be performed, with a descending or sigmoid colostomy.

The major postoperative complications that can occur are anastomotic leak and fistula, so obviously grossly normal-appearing or histologically normal tissue is preferable for anastomosis. If left-side colonic CD extends all the way to the transverse colon, most of the absorptive capacity of the colon resides in the resected specimen. The right hemicolon should be resected as well and an end ileostomy constructed if the rectum is not suitable for IRA as a well-made ileostomy is preferable to a wet transverse colostomy.[13]

Proctocolectomy offers the lowest risk of recurrence for any surgical procedure performed for CD of the colon and anorectum. The recurrence rate of 10 to 25% compares favorably with the usual 50% recurrence rate quoted for CD elsewhere in the bowel. A significant problem is that only half of the perineal wounds heal promptly. Thirty percent may exhibit delayed healing for up to 1 year, and 15 to 20% may still have persistent perineal sinus after 1 year.[13]

Table 2 Surgical decision making

Disease involvement	Surgery
Ascending colon alone	Right hemicolectomy. Resect to mid transverse colon to avoid anastomosis over duodenum
Transverse colon +/− ascending colon involvement	Extended right hemicolectomy
Descending colon/sigmoid	Anterior resection/left hemicolectomy
Distal transverse, descending colon, sigmoid	Anterior resection, left hemicolectomy, resect distal transverse with retro ileal window between ileocolic and superior mesenteric vessels for length
Entire transverse, descending colon, sigmoid colon	Anterior resection, left hemicolectomy, resect transverse colon, counter-clockwise rotation ascending colon with coloproctostomy
Extensive colonic involvement, rectal sparing	Proctocolectomy/IRA if reasonable rectal compliance, minimal perianal disease
Skip lesions right and left colon	Double resection, e.g., right hemicolectomy, anterior resection, or total colectomy/IRA
Proctosigmoiditis alone	Proctosigmoidectomy, end colostomy descending colon

Abbreviation: IRA, ileorectal anastomosis.

Medical Therapy and the Impact of Biologics

Mild to moderate CD is treated with mesalazine, budesonide, or systemic corticosteroids, though these medications are limited by long-term side effects and are not effective for maintenance therapy.[24] Azathioprine, 6-mercaptopurine, and methotrexate are prescribed in patients for whom first-line therapies fail, or as steroid sparing agents.[8] Metronidazole, mesalazine, azathioprine, 6-mercaptopurine, and infliximab are superior to placebo in the prevention of postoperative CD recurrence.[25] The introduction of anti-TNF) agents in 1998 has greatly changed the treatment paradigm of patients with CD.[26] Prior to the introduction of anti-TNFs, patients usually received symptom-based therapy, which did not change the long-term course, leading to stricturing or penetrating complications.[2] Anti-TNFs are effective in inducing and maintaining clinical remission of active IBD with complete mucosal healing in half of patients treated and remission rates of 40 to 50% in patients with moderate to severe disease.[27–29] This has changed the focus of treatment from symptom based to preventing structural damage and improving disease course by achieving mucosal healing.[30] In the SONIC trial, remission rate of 60% was seen in patients treated with infliximab and azathioprine combination.[24]

Top Down or Bottom Up?

Previously patients were started on aminosalicylates, steroids, or thiopurines with escalation to more effective treatments only after these treatments had failed (step-up therapy).[1] This failed to change the disease course as reflected by high rates of surgery. Endoscopic healing became a therapeutic focus because it correlates with reduced relapse rates and need for surgery.[31] Many studies of anti-TNF therapy in CD have shown that initiation of therapy earlier in the disease process predicts higher remission rates.[32,33] Concerns regarding increased risk of opportunistic infections and T cell lymphoma, especially with combined immunomodulator and anti-TNF therapy, have tempered enthusiastic use.[34,35] This effect is increased even further with concurrent use of steroids.[36] To date there are no prospective disease modification trials confirming "deep remission" (i.e., clinical and endoscopic remission) as changing the disease course and reducing rates of surgery. In this light, "top-down" or early anti-TNF therapy should be considered for CD patients with poor prognostic factors, severe or complicated disease.[37] This approach is supported by evidence showing early combined immunosuppression had slower progression to surgery and lower rates of hospital admissions than patients treated conventionally.[38]

Do Biologics Reduce Rates of Surgery?

Bowel preservation is an achievable goal and is a rationale for using anti-TNF medications in CD.[39] However, the change in the rate of surgical intervention for CD since the introduction of biologic medications such as infliximab is equivocal, some authors reporting a reduction[40,41] and some reporting no change.[42–45] None of these studies report data later than 2005.

An Irish population-based study examining admissions from 2000 to 2010 reported no change in small bowel, right colon, or proctectomy rates, but reduced left colon procedures and increased numbers of total colectomy.[46] The authors speculated an increase in total colectomy and the reduction in left-side colectomy may reflect the impact of infliximab on left-side colitis as opposed to fibrostenotic right-side disease as well as a recognition by surgeons that segmental resection is associated with shorter time to reoperation by referencing the Tekkis meta-analysis. The authors noted the rate of proctectomy did not change significantly and questioned the long-term efficacy of infliximab in treating perianal disease. This study did not take into account either changes in the incidence of CD over the study period or aging of the population during that time. The heterogeneous results must therefore be interpreted with caution. Detailed prospective registry data are needed.

Effect on Surgical Complications

Numerous studies, including retrospective papers as well as several meta-analyses, have examined the risk of increased infectious and noninfectious postoperative complications among patients on anti-TNF therapies, with varying results.[47] Some studies have found an increased risk of postoperative complications in all IBD patients; however, when the cohorts were divided by disease type, only the CD patients were noted to have an increased risk.[48,49]

In other studies including only CD patients, some found an increased risk of complications,[50–52] another reported an increased risk only in those with an anti-TNF drug level above a certain cut off,[53] and another showed a protective effect of anti-TNF therapy in CD patients with penetrating disease.[54] In contrast, other studies reported no increased risk for postoperative complications associated with anti-TNF use in CD patients.[55] One small retrospective study found no association between timing of infliximab before surgery and the rate of postoperative complications.[47]

The disconnect between CD activity and clinical symptoms may explain why conventional medical strategies have failed to alter the course of the disease.[56] Persistent and under treated subclinical inflammation that occurs during clinical remission may lead to complications such as stricture, fistula or abscess, and progressive bowel damage.[1,57] On this basis, tighter medical control may lead to lower long-term complications and less need for surgery, thus justifying segmental colectomy. If the clinical goal of deep remission is widely achieved, we may see a greater justification for minimalist resection,[58] in addition to the wider use of laparoscopic re-resection obviating the arguments for one-step surgery. Evidence for this comes from the REACT study published in 2015.[38] Despite follow-up of only 2 years, patients randomized to intensive medical therapy with anti-TNF and immunomodulator had lower rates of major adverse events such as hospital admission, surgery, and major disease-related complications. Further long-term studies are required to determine whether this effect is sustained.

Conclusion

Surgical decision making in CD is complex, and must be individualized according to both patient factors and disease phenotype. Segmental colectomy is increasingly appropriate in selected patients managed within a multidisciplinary team and in association with aggressive medical management focused on deep remission.

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