Colonic Crohn Disease

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Abstract

Colonic Crohn disease is a complicated disease entity that requires a multidisciplinary effort on the part of the surgeon, gastroenterologist, and pathologist. Crohn disease affects ~500,000 people in North America with nearly 300,000 people suffering from colonic manifestations. This represents a significant portion of the patient population in the typical colorectal surgeon's practice. As such, an intimate understanding of the disease process, presentation, and treatment options is imperative. In this article, the authors review the clinical manifestations, diagnosis, and medical and surgical treatment options with a focus on current strategies for surgical management.

Keywords
- Crohn disease
- colitis
- surgical management

Objectives: Upon completion of this article, the reader should be able to summarize the management of colon Crohn disease.

Clinical Presentation

Although Crohn disease (CD) can affect any portion of the gastrointestinal (GI) tract from the mouth to the anus, over 60% of patients have colonic involvement. Twenty percent of patients will have isolated colitis, while an additional 50% will have involvement of both the ileum and colon. Of those with colonic involvement, half will have rectal involvement.[1] As with other sites of disease, the clinical presentation of colonic CD is highly variable between patients.

Patients with colonic CD can present with a myriad of symptoms. Patients with colitis typically develop cramping abdominal pain and diarrhea. Although diarrhea is a very common presentation of patients with small bowel involvement, bloody diarrhea is more common in patients with Crohn colitis. Rarely, patients with CD develop severe life-threatening hemorrhage requiring emergent operation.[2,3]

A subset of patients also develops fulminant or toxic colitis as evident by bloody diarrhea in the setting of clinical signs of toxicity including fever, tachycardia, hypotension, metabolic acidosis, or oliguria and acute renal failure. Toxic colitis is more commonly seen in patients with ulcerative colitis, although it can occur in patients with CD and indeterminate colitis. It is important to note that the term "toxic megacolon" has fallen out of favor because the toxic inflammatory state often occurs in the absence of colonic dilation, which typically occurs late in the course of the disease. Delaying aggressive treatment until the patient has developed a megacolon will lead to unnecessary delays in treatment and poor outcomes.

The transmural inflammation that is associated with CD leads to the development of sinus tracts that can penetrate and develop into an abscess, a free perforation, or a fistula. Infrequently, patients with CD present with a free perforation. However, a subset of patients may perforate as the result of high-dose steroids in the setting of initial treatment for a complicated phlegmon. More commonly, patients with colonic CD develop an abscess, which may manifest in a variety of ways ranging from a low-grade fever to peritonitis.

A common site of colonic fistulas involves the redundant loop of the sigmoid colon and the terminal ileum. More often than not, the sigmoid colon is an "innocent bystander" in the patient with primary ileal CD. However, fistulas can arise between any segments of visceral inflammation. As such, patients may present with primary colonic fistulas that typically involve the vagina (posthysterectomy) or the bladder. Colonoscopy is important to distinguish the primary versus secondary colonic fistula. Primary colonic fistula will require resection of the entire diseased segment, whereas primary repair or a limited segmental resection may be possible for secondary fistula when the colonic mucosa appears normal. The presence of a colonic fistula is extremely important to recognize preoperatively. This is particularly true in the patient with primarily terminal ileal CD, who many surgeons will place in the supine position for surgery. An unrecognized distal sigmoid fistula requiring a sigmoid resection will prove difficult for a patient that is not in

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lithotomy and can lead to unnecessary mayhem in the operating room.

Finally, colonic CD may involve stricture formation similar to that seen in the small bowel. Given that there is up to a 7% incidence of colorectal cancer in patients with CD, it is imperative to rule out a malignancy when a colonic stricture is identified with endoscopic biopsy.[4]

Colorectal Cancer and Crohn Disease

The risk of colorectal cancer in CD has increased. However, the magnitude of that risk has been debated. A population-based study from Sweden demonstrated a relative risk of 5.6 in patients with colonic CD. Similar to ulcerative colitis, the risk seems to be increased in patients with pancolitis and long disease intervals.[5] Compared with sporadic cancers, the mean age for developing colorectal cancer is lower in the setting of CD (40–50 y vs. 60 y). As opposed to ulcerative colitis (UC), in which the associated cancers tend to be in the rectum or sigmoid colon, colorectal cancer associated with CD is evenly distributed. These tumors may appear ulcerated, nodular, plaque-like, or polypoid.

Dysplasia clearly precedes cancer in the setting of inflammatory bowel disease. Therefore, frequent surveillance is imperative in patients with longstanding disease. Unfortunately, it can be difficult to recognize dysplasia both endoscopically and histologically. The endoscopic appearance of dysplasia ranges from flat to plaque-like lesions, polyps, or masses. Histologically, dysplasia may be uniform, affecting all parts of the crypt and surface epithelium in contrast to regenerative changes, which are most prominent at the crypt base. It is important that an experienced GI pathologist confirm the presence of dysplasia in inflammatory bowel disease.

The natural history of dysplasia has been much more widely studied in UC than in CD. However, the association with dysplasia seems to be similar in CD.[3,6,7] There is little argument that a finding of high-grade dysplasia warrants colectomy given the high incidence of associated cancer (up to 40%).[8] The finding of low-grade dysplasia is more debated. Bernstein et al[8] found a 19% rate of malignancy in colectomy specimens performed for low-grade dysplasia in inflammatory bowel disease while Gorfine et al[9] found that that 34% of patients with low-grade dysplasia on colonoscopy had a malignancy at the time of surgery. Conversely, Lim et al demonstrated that only 10% of patients progressed to high-grade dysplasia or cancer at 10 years.[10] Much of this variability is likely the result of the difficulty in recognizing and grading dysplasia histologically, further emphasizing the need for review by a specialized GI pathologist before subjecting any patient to colectomy.

Dysplasia associated with nonadenoma-like lesions or mass (DALM) can be associated with an underlying malignancy in up to 60% of patients and is an immediate indication for colectomy.[11] On the other hand, sporadic adenomas may occur in an area of colitis and are not necessarily associated with an increased risk of malignancy. Therefore, it is critical to make the distinction between a nonadenoma-like DALM and a sporadic adenoma. In general, patients with nonadenoma-like DALMs tend to have more severe colitis, larger lesions, longer duration of disease, and are younger than those with sporadic adenomas.[12] Additionally, if the polyp appears endoscopically like a typical adenoma, it has a favorable prognosis.[13] Finally, sporadic adenomas tend to stain positive for β catenin and negative to P53 as opposed to DALM.[14,15]

Surveillance

Most major societies recommend that patients with longstanding Crohn colitis be surveyed similar to patients with ulcerative colitis. The British Society of Gastroenterology has published the most updated recommendations:[15]

- Colonoscopic surveillance should be initiated after 10 years from the onset of symptoms.
- The interval for continued surveillance ranges from 1 to 5 years depending on the patients risk of malignancy including family history, extent of disease, and active inflammation (►**Fig. 1**).
- Chromoendoscopy (topical application of stains or pigments) with targeted biopsies of abnormal areas or two to four random biopsies every 10 cm should be obtained
- If a dysplastic polyp is detected within an area of inflammation and can be removed in its entirety, colectomy can be avoided.

Diagnosis

Colonoscopy with intubation of the terminal ileum is the gold standard for obtaining the diagnosis of colonic CD. Diagnosis is based on the findings of aphthous ulcers, focal ulcerations interspersed with normal mucosa, and polypoid mucosal changes that give a cobblestone appearance in a discontinuous distribution. Histologically, Crohn colitis is characterized by focal ulcerations and inflammation with granulomas demonstrated in up to 30% of patients. Contrast enemas can be helpful in identification of fistula tracts. Colonoscopy is also helpful in distinguishing primary from secondary colonic fistulas. The presence of active inflammation in the surrounding mucosa of the fistula tract is usually demonstrated in the case of a primary colonic fistula, whereas the surrounding mucosa is typically normal in a secondary fistula that typically originates in the small bowel.

It can often be difficult to distinguish Crohn colitis from ulcerative colitis in the setting of pancolitis. Antibody tests have shown some promise in assisting with this distinction in some reports. Antineutrophil cytoplasmic antibodies (pANCAs) are more strongly associated with UC, while anti-*Saccharomyces cerevisiae* antibiodies (ASCAs) are associated with CD. Unfortunately, however, the accuracy of antibody testing is uncertain in patients with indeterminate colitis who often do not express either antibody.[16]

Medical Management

Medical therapy is the mainstay of treatment for patients with CD. The use of 5- aminosalicylic acid (ASA) is controversial in patients with colonic CD, given the uncertainty of

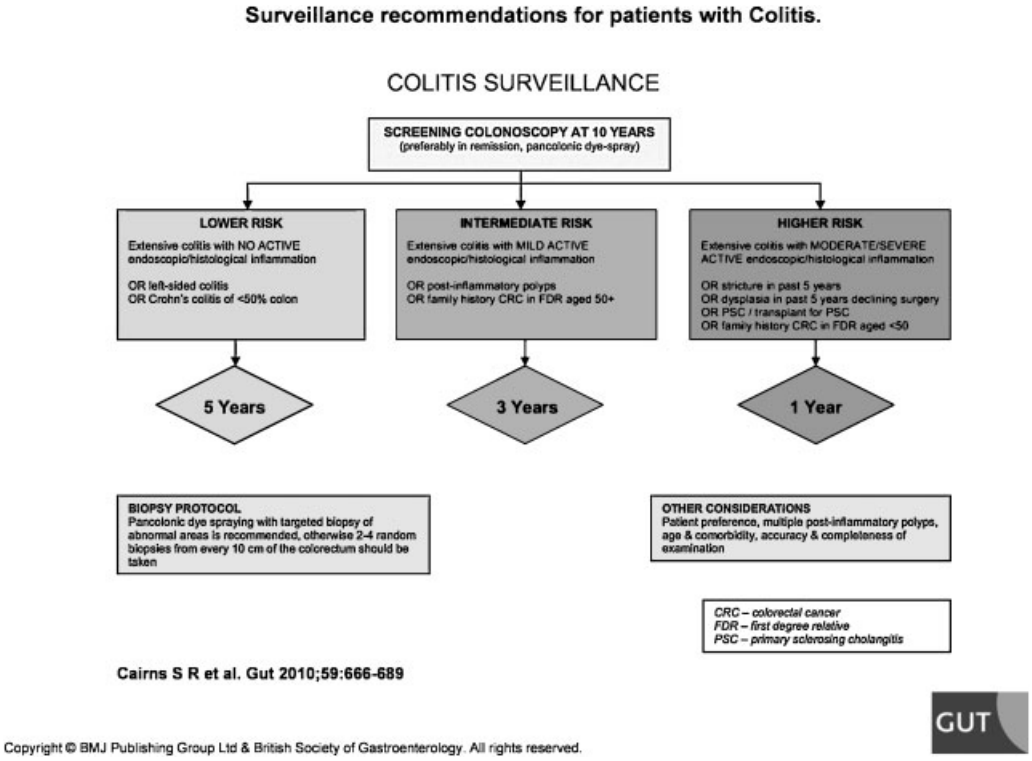

Fig. 1 Depicted are the surveillance recommendations for patients with inflammatory bowel disease. (Reproduced from Cairns SR, Scholefield JH, Steele RJ, et al. Gut 2010;59(5):666–689. © 2010 with permission from BMJ Publishing Group Ltd.)

benefit in several studies of 5-ASA drugs in patients with CD. Sulfasalazine or one of the mesalamine drugs can be used for the patient with mild to moderate symptoms. More commonly, antibiotics are used to treat colonic CD. Most literature suggests a benefit from oral metronidazole (10 or 20 mg/kg/d) alone or in combination with ciprofloxacin for the induction of or maintenance of remission in active colonic CD.[17] Patients who fail to respond to 5-ASA or antibiotics are placed on glucocorticoids, generally prednisone at 40 to 60 mg/daily. Within 14 days, 60 to 80% of patients with CD will respond to this dose. Budesonide, a glucocorticoid with a high first-pass hepatic metabolism and fewer systemic side effects, may be used as an alternative for patients with right-sided colitis.

Patients with more severe or refractory disease are treated with azathioprine or 6-mercaptopurine, which usually takes 3 to 6 months to take effect and is associated with significant toxicities, including bone marrow suppression and malignancy. Biologic therapies are generally reserved for patients with refractory disease or in patients who are steroid dependent. The three antitumor necrosis factor (anti-TNF) therapies include infliximab, adalimumab, and certolizumab pegol. Infliximab is given intravenously while adalimumab and certolizumab are given subcutaneously at every 2 and 4 weeks, respectively. Infliximab was a breakthrough for patients with CD, offering patients a medical alternative to surgery with moderate to severe CD or fistulizing CD. However, there are significant toxicities including infusion reactions, infections, and malignancy. The medical treatment of CD is beyond the scope of this article, but is an obviously complex algorithm that must be individualized to each patient.

Surgical Management

Unlike ulcerative colitis, Crohn colitis may not be isolated to the colon, and surgery is never considered curative. The objective of surgery, therefore, is to provide palliation for the complications of Crohn colitis. The most common chronic complications are stricture, fistula, and debilitating diarrhea despite aggressive medical management. Emergent or urgent complications include perforation, toxic colitis, and bleeding. Because recurrence is common following surgery for CD, the objective of surgery is to provide immediate palliation for the dominant symptoms, while preserving bowel function.

For many patients with Crohn colitis, this often involves a discussion surrounding stoma formation and strategies to avoid permanent stomas. In patients with pancolitis or severe perianal disease, avoidance of a stoma may not be possible. However, in situations when the disease seems isolated to segments of the colon, a segmental resection with restoration of intestinal continuity may be feasible. A thorough assessment of disease extent is therefore critical for surgical planning. In particular, if the rectum and anus are free of disease, options for restoring intestinal continuity are greatly enhanced.

Unfortunately, compared with total proctocolectomy and permanent ileostomy, recurrence rates for segmental resections are higher. Therefore, the final decision about the best

surgical approach includes an understanding of the patient's current symptoms, the bowel function following surgery, and recurrence of CD, which may result in more symptoms and additional surgical interventions. Clearly, patient preference will impact these decisions and communication with the patient is critical to optimize the success of any surgical intervention.

Total Proctocolectomy with End Ileostomy

Total proctocolectomy with an end ileostomy remains the gold standard for patients with Crohn colitis. For patients with pancolitis, severe perianal disease, or anal incontinence, this procedure provides excellent palliation with the lowest recurrence rates. It also eliminates the risk of future colorectal cancer and the need for ongoing surveillance. Recurrence rates have been reported to be less than 10% with this procedure, but other series with longer follow-up periods report surgical recurrence rates as high as 30%.[18,19]

In addition to a permanent ileostomy, the disadvantages of this operation are the need for a pelvic dissection and the perineal wound. Pelvic dissection can have an impact on sexual function, including impotence and retrograde ejaculation in men and dyspareunia in women.[20] Furthermore, although there is little data on the effects of total proctocolectomy with ileostomy on fertility, there is data demonstrating decreased fertility for women who have a total proctocolectomy with restorative proctocolectomy. Because it is proposed that pelvic scarring of the fallopian tubes may contribute to infertility, it certainly is feasible that the pelvic dissection associated with total proctocolectomy with an ileostomy may have a similar effect on fertility.[20]

Lastly, a proctectomy also includes a perineal wound. These wounds can present healing difficulties, especially in the presence of perianal fistulous disease, malnutrition, and immunosuppression. In a review of 144 patients with a total proctocolectomy, it was reported that two-thirds of the patients had excellent healing, while one-third had problems with healing, including 10% that were very difficult.[21] Despite these difficulties, in properly selected patients, a total proctocolectomy with an end ileostomy is an excellent option, which provides the best chance at long-term control of the disease.[21]

Subtotal Colectomy with Ileostomy

A subtotal colectomy with an ileostomy will remove the majority of the disease and frequently restore the health of debilitated patients. It is the procedure of choice in the emergency setting and in patients who are severely debilitated.[22] The operation can be performed quickly and safely, with the avoidance of a difficult pelvic dissection. It can also be done when the diagnosis is in question, allowing the pathologist to examine the entire colon to better establish a definitive diagnosis. In a review by Hyman et al of 74 patients undergoing a subtotal colectomy for severe colitis, just over one-third had a change in diagnosis following the colectomy.[22] This may give an opportunity for some patients to have attempts at intestinal restoration, either with an ileorectal anastomosis or a restorative J pouch, while others, satisfied with the function of an ileostomy, may choose to forego further surgery.[22]

The question of what to do with the rectal stump following a successful subtotal colectomy remains a dilemma. In patients with minimal rectal disease, attempt at an ileorectal anastomosis may be reasonable. However, in patients with a diseased rectum, creation of an anastomosis is ill advised. Some patients will have persistent symptoms from the diseased rectum, including persistent drainage or perianal fistulous disease. In these patients, a delayed proctectomy once the patient is fully recovered makes the most sense. Even in patients with very few rectal symptoms, the rectal stump should not be left indefinitely due to the risk of developing a rectal cancer over time. Certainly, if the rectum is not removed, then rectal surveillance with biopsies is necessary.[23]

Total Colectomy with Ileorectal Anastomosis

In patients with minimal rectal disease, a total colectomy with an ileorectal anastomosis is possible. This can either be done at the initial operation or to restore continuity after an urgent total colectomy with an ileostomy. Functionally, patients can expect approximately five loose bowel movements per day.[24] Incontinence can be an issue when patients have poor anal sphincter control. Therefore, preoperative assessment of anal continence is critical to properly select patients. Although functional outcomes are imperfect, some patients still prefer these imperfections compared with the alternative, which is a permanent ileostomy. Unfortunately, recurrent colitis requiring subsequent proctectomy and ileostomy occur in nearly one-third to one-half of patients.[21,24] Furthermore, even in patients with a functional anastomosis, many have symptomatic disease requiring ongoing medical management. Despite the high rate of subsequent proctectomy, however, patients may still be stoma free for many years, which, especially in younger patients, may be an acceptable compromise.

Segmental Colectomy

When operating for CD with small bowel involvement, limited resections are important to prevent significant loss of small bowel, which can have subsequent nutritional consequences. However, in patients with Crohn colitis, the role of a limited colonic resection has often been debated. Once again, the balance between bowel function and the likelihood of recurrence requiring further intervention is at the center of this discussion. Although unusual, some patients will have CD isolated to a segment of the colon. Under these circumstances, a segmental resection is a reasonable option.

The major advantage is the avoidance of a stoma and preservation of the absorptive properties of the colon, improving functional outcome. Even in patients with pure rectal involvement, an abdominal perineal resection with a permanent colostomy may be easier to maintain than a total proctocolectomy with an ileostomy. The clear disadvantage is the relatively frequent recurrence, which requires further surgeries and interventions. Fichera et al reported a 40% surgical recurrence in 55 patients undergoing a segmental

resection.[18] Martel et al reported a similar surgical recurrence rate over a 10-year period in their series of 84 patients. Despite the high surgical recurrence, only 13 patients had a permanent stoma at the completion of this study.[25] Prabhakar et al reported similar findings in 49 patients with a segmental resection, with 33% of the cohort requiring further surgery, but 86% remaining stoma free over a 14-year period.[26] Andersson et al compared segmental resection with subtotal resections with an ileorectal anastomosis. In this series, recurrence rates were similar between the two groups, but patients with segmental resections had improved bowel function and a higher quality of life.[27] In contrast, Sanfey et al found that only three of 13 patients with an ileorectal anastomosis maintained intestinal continuity long term, compared with 14 of 16 with a segmental resection, despite the high recurrence rates and the need for several procedures.[28]

In summary, in properly selected patients, a segmental resection seems to be an excellent option. Patients need to be counseled that recurrence is very common and may involve the need for subsequent surgical procedures. However, many patients can avoid stomas for years, and in some situations, permanently.[29]

Ileal Pouch Anal Anastomosis

Due to the high recurrence rates in patients with CD, it has generally been accepted that an ileal pouch anal anastomosis is contraindicated. The major concern is the significant loss of small bowel if a pouch needs to be excised due to recurrent disease. However, there are now reports of successful pouch creations in highly selected patients with CD. Most of the data come from series when patients were identified as having CD after the pouch had been created for suspected UC. In a report of 204 patients from the Cleveland Clinic, 20 patients had a pouch created with a known diagnosis of CD, while 97 were diagnosed immediately following surgery from the final pathology of the excised colon and 87 were diagnosed when CD developed years following the pouch creation. At 10 years, 70% of the patients still had a functional J pouch. For patients who had a known diagnosis or an early diagnosis, pouch retention was quite high with excellent functional outcomes. Even in patients with a delayed diagnosis, ~50% of the patients were able to salvage the pouch and maintain intestinal continuity.[30] Regimbeau et al[31] also reported on 41 patients with Crohn colitis who had an ileal pouch anal anastomosis. All of the patients had longstanding colitis without any anal or small bowel involvement. At 10 years, 35% had some CD-related complications, but only 10% had the pouch excised.[31]

Therefore, in highly selected situations an ileal pouch anal anastomosis can be considered for patients with CD. These patients must not have any evidence of perianal or small bowel disease; they should have evidence of prolonged disease activity confined only to the colon. Finally, a patient needs to be highly motivated and understand that pouch failure rates are high and that further medical management may be necessary. Under these highly selected conditions, a pouch may be attempted, but only after prolonged counseling with the patient. As a general rule, however, most patients with Crohn colitis are not a candidate for an ileal pouch anal anastomosis.

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