

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Diseases

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Prevention of Postoperative Crohn's Disease Recurrence

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G&H What is the current rate of surgical resection and disease recurrence among Crohn's disease patients?

GD Primary surgery is required in up to 70% of Crohn's disease (CD) cases at some point in the course of disease. However, these are not always classic ileocolonic resections. They could be partial small bowel or colonic resections. Following the first procedure, the incidence of endoscopic recurrence is over 80%, but recurrence does not necessarily indicate a second surgery. Of the group of patients with postsurgical recurrence, only 20–30% require a second resection. Most other recurrences can be controlled with the current armamentarium of medical therapies.

G&H Are there challenges involved in establishing the extent of CD before surgery in order to ensure the complete resection of affected tissue?

GD In the surgical therapy of CD, it is, of course, important to remove all of the macroscopically diseased bowel. This is easily evaluable through signs of chronic inflammation (creeping fat and fibrosis) visible to the surgeon on the outside of the bowel. Studies have shown that removal of microscopically inflamed mucosa is not necessary, only the grossly diseased segment is. Further assessment can be made with radiologic or computed tomography scans, but in most instances the tissue that requires resection can be determined by the surgeon.

G&H What part do medical therapies play in the development of perioperative complications in CD surgery?

GD Our group performed a study examining the effect of infliximab (Remicade, Centocor) therapy on peri- and immediately postoperative complications, and we did not detect an increase in the proportion or incidence of complications in patients who had recently received infliximab. It now seems quite clear that infliximab can be administered up to 2 weeks before surgery. Although there are few data on the use of the immunosuppressives azathioprine (AZA) or 6-mercaptopurine (6-MP) in this regard, no increase in complications has been noted with them either.

However, other studies have shown that the use of corticosteroids is related to a higher incidence of complications at the time of surgery. Therefore, the use of corticosteroids must be reduced as much as is clinically possible in prospective surgical patients. Even patients requiring continuous intravenous steroids up to the time of surgery should have their dose lowered to the absolute minimum before undergoing resection.

G&H What risk factors are associated with post-surgical recurrence of CD?

GD Study results in this regard are somewhat conflicting. The single factor that has been unequivocally linked to recurrence is smoking, which has been associated with more rapid and severe recurrence, particularly in female patients. Other factors with some evidence of an association with recurrence include early age of disease onset and perforating disease. If a patient presents with an abscess

or fistula, the likelihood of recurrence is higher. Beyond these characteristics, patients who have had numerous resections in the past have the highest likelihood of more rapid recurrence.

Another widely held belief is that the type of surgery and width of the anastomosis plays a part in the likelihood of recurrence, as recurrence is thought to be related to the reflux of colonic fluids into the ileum. However, Dr. Robin McLeod of the University of Toronto coordinated a trial in which different types of surgery and widths of anastomosis were compared, and her group found no difference in terms of recurrence rates. Therefore, the type of surgery is not relevant.

G&H Is there a standard treatment algorithm for preventing recurrence of CD after surgery?

GD There are numerous strategies proposed by clinicians. In patients with a high-risk profile, I believe that immediate postoperative therapy is indicated. The most effective therapy in this scenario has been shown to be AZA or 6-MP. In patients with severe and destructive disease, my proposal would be to start one of those treatments immediately or to continue in patients already receiving them.

Furthermore, recent data have shown that the addition of an antibiotic, such as metronidazole or ornidazole, during the 3 months following surgery can further reduce the incidence of endoscopic recurrence. These antibiotics work as a preventive treatment directed against anaerobic bacteria, which are believed to play a role in inciting recurrence. They can be given immediately after surgery in patients who are free of symptoms, for several months.

In patients with less severe disease behavior, who are less prone to developing early recurrence, my practice is to give no treatment for a period of 3–6 months after surgery, then to encourage the patient to undergo a colonoscopy. Colonoscopic findings in the terminal ileum determine the ensuing course of treatment. This protocol is attractive in that patients have a period of time during which they are not required to take any therapy. Further, if they

show no signs of recurrence at the time of colonoscopic examination, treatment need not be instituted. It should be noted that manifestation of symptoms lags behind the endoscopic appearance of recurrence, and therefore a lack of recurrence must be established endoscopically.

G&H Is there a role for other CD therapies in the prevention of recurrence?

GD A number of trials have been performed with probiotics, including *Lactobacillus*, that are believed to support proper bowel function. These trials have been negative and have not shown any benefit in postsurgical patients.

5-aminosalicylate (5-ASA) therapies, which many clinicians give to their patients immediately following surgery, have been effective in a certain subset of patients with milder disease, specifically in the ileal or small bowel. Trials have been performed with timed-release and delayed-release formulations and all seem to work equally, though none has proven as consistently effective as immunomodulators.

There is currently no research into a role for any of the biologic therapies as a postoperative prophylactic measure. However, if a severe recurrence manifests endoscopically or clinically, there may be a role for biologic therapy in curbing the inflammatory process.

Suggested Reading

- Rutgeerts P, Van Assche G, Vermeire S, D'Haens G, Baert F, et al. Ornidazole for prophylaxis of postoperative Crohn's disease recurrence: a randomized, double-blind, placebo-controlled trial. *Gastroenterology*. 2005;128:856-861.
- Marchal L, D'Haens G, Van Assche G, Vermeire S, Noman M, et al. The risk of post-operative complications associated with infliximab therapy for Crohn's disease: a controlled cohort study. *Aliment Pharmacol Ther*. 2004;19:749-754.
- D'Haens G. Prevention of postoperative recurrence in Crohn's disease. *Curr Gastroenterol Rep*. 1999;1:476-481.
- McLeod RS. Is it possible to prevent recurrent Crohn's disease with medical or surgical interventions? *Neth J Med*. 1996;48:68-70.
- McLeod RS, Wolff BG, Steinhart AH, Carryer PW, O'Rourke K, et al. Prophylactic mesalamine treatment decreases postoperative recurrence of Crohn's disease. *Gastroenterology*. 1995;109:404-413.