Preoperative Optimization of Crohn Disease

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Abstract

Crohn disease is a chronic disease that is treated with aminosalicylates, antibiotics, and immunosuppressant agents. Most patients ultimately require surgical intervention and many will require additional surgery for recurrent disease. Consequently, surgery is generally performed only when medical management fails; however, these patients are often malnourished and immunosuppressed. Preoperative optimization is necessary to minimize morbidity, including intra-abdominal septic complications and anastomotic leaks. In this article, the authors review some considerations to improve the surgical outcome in Crohn disease.

Keywords
- Crohn disease
- immunomodulators
- biologic therapy
- steroids
- nutrition

Objectives: Upon completion of this article, the reader should be able to identify factors that may contribute to improved surgical outcomes in Crohn disease.

Crohn disease (CD) continues to present both medical and surgical challenges. Throughout North America, the prevalence of CD varies regionally from 26.0 to 198.5 cases per 100,000 persons.[1] The five classes of drugs used to treat CD are aminosalicylates (5-ASA), antibiotics, steroids, immune modulators, and biologic therapy. Despite advances in medical management, 75 to 80% of patients require surgery for CD with up to 50% of these within the first 10 years after diagnosis.[2] The potential for multiple surgeries and short bowel syndrome exists with CD as more than 30% will require further surgery after their initial resection.[3] As a result, patients are generally maximized on nonoperative therapy and surgery is not recommended unless absolutely necessary. Consequently, at the time of surgical presentation, patients frequently are malnourished and immunosuppressed with some demonstrating intra-abdominal sepsis. These complicating factors of CD pose significant challenges for the surgeon. Preoperative optimization is critical to ensure the best possible surgical outcome and this review addresses some key issues.

Nutrition

Poor preoperative nutrition increases postoperative morbidity rates and intra-abdominal septic complications.[4–6] As most patients undergo surgery as a last option, many are malnourished due to chronic debilitation. However, there is no gold standard test to diagnose malnutrition as it involves a complex evaluation of multiple factors; it may be most simply defined as any nutritional imbalance.[7,8] The nutritional deficiencies encountered are a result of insufficient dietary intake (due to postprandial pain and diarrhea), malabsorption (from mucosal inflammation and diarrhea), systemic inflammation (that alters protein synthesis and increases protein catabolism), and the side effects of medications used to treat the CD.[9,10] Nutritional optimization should be performed to enhance the nonoperative management of CD and decrease postoperative morbidity.

Postoperative complications following anastomotic leaks may be devastating. There are numerous studies evaluating anastomotic leaks and hypo-albuminemia, with anastomotic dehiscence consistently associated with a serum albumin levels below 3.5 g/dL in elective colorectal resections.[11–15] Makela et al identified 44 anastomotic leaks and when compared with 44 controls matched for age, gender, and indication for surgery, hypoalbuminemia, and weight loss greater than 5 kg were significantly associated with leaks.[13] Suding et al demonstrated that a baseline albumin level of less than 3.5 g/dL was associated with leaks in both univariate and multivariate analysis.[14] Telem et al identified five risk factors in 90 anastomotic leaks in CD with an albumin level less than 3.5 g/dL being the only preoperative risk factor.[15]

As there are no prospective studies determining preoperative nutritional end points, optimization requires overall clinical considerations, including albumin levels. Attaining

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these levels and correcting other nutritional imbalances can be facilitated by either enteral or parenteral supplements. Total parenteral nutrition (TPN) used for at least 18 to 30 days prior to surgery may reestablish nutritional stores, lower postoperative complications, decrease the extent of resection required, or even result in clinical remission of moderate to severe CD.[16–18]

Enteral support when possible is preferred due to its more physiologic nature, diminished cost, and decreased potential for sepsis when compared with TPN. In addition to correcting nutritional imbalances, immunonutrition, or nutrition that enhances immune function, may also induce remission of CD or reduce the extent of resection needed by decreasing the inflammatory response. Elemental diets have been evaluated as a means of inducing disease remission by decreasing proinflammatory cytokines and serum inflammatory markers.[19] Many studies have shown that remission of disease can be obtained with an elemental diet, and in some studies, the elemental diet was found to be more efficacious than steroids in inducing remission.[20–23] Continuation of an elemental diet in the postoperative period has also been shown to reduce clinical and endoscopic recurrence of CD after resection.[24]

As a supplement, the use of omega-3 fatty acids found in fish oils may also decrease the production of proinflammatory leukotrienes and prostaglandins by competing with omega-6 fatty acids in the eicosanoid pathway.[25] This has been shown to reduce the steroid requirements in ulcerative colitis.[26] In CD where C-reactive protein and erythrocyte sedimentation rate are elevated, omega-3 fatty acids have been shown to lower production of proinflammatory interferon and prostaglandins; however, there has not been shown to be a significant effect on disease activity and further studies on this are warranted.[27]

Sepsis

Preoperative abdominal sepsis in the form of fistula or abscess is a common complication of Crohn disease. It may be seen in up to 10 to 30% cases and is an independent risk factor for postoperative complications.[4–6,28] Traditionally, abscesses were drained operatively with resection of bowel and stoma creation commonly performed. However, current practice is, when possible, to treat abscesses with antibiotics or percutaneous drainage and antibiotics to avoid surgery in an acute setting.

Xie et al showed that, compared with a percutaneous drainage group, those undergoing surgical drainage had more postoperative complications and a significantly higher rate of stoma creation.[29] During the interval between percutaneous drainage and surgery, coexisting metabolic imbalances can be corrected and the reduction of inflammation minimizes the length of bowel requiring resection and the potential need for a stoma. Rypens et al demonstrated that that an interval resection following percutaneous abscess drainage allows for easier operation with primary anastomosis.[30] In some situations, the initial nonoperative approach may delay the need for surgery or allow for its avoidance altogether. Gutierrez et al demonstrated that two-thirds of CD-associated abscesses treated with percutaneous drainage did not need any surgery for at least 1 year.[31] Lee et al reported on 24 patients admitted with CD abscesses, of whom 19 were treated nonoperatively, and five by percutaneous drainage.[32] During a median follow-up of 47.5 months, 12.5% developed recurrent abscesses within 7 months, but 67% required no further intervention.

Immunosuppressive Therapy

Crohn disease is a chronic inflammatory autoimmune condition thought to be the result of aberrant T-cell function, as well as environmental and/or microbial factors in genetically susceptible individuals.[33] Consequently, a large component of medical management involves suppression of the immune response using steroids/glucocorticoids, immunomodulators, and biologic agents. However, these agents contribute to the challenge in the surgical management of CD due to conflicting reports of postoperative intra-abdominal septic complications and anastomotic leaks. As a result, the potential for this increased risk should be considered intraoperatively when determining whether a stoma should be performed.

Glucocorticoids are mainly used for induction of remission by controlling acute inflammation in CD. There are conflicting reports on the overall risk and septic complications due to preoperative steroid use. Some studies demonstrated an increased risk of septic complications and anastomotic leaks due to preoperative steroid use,[5,6,28,34–37] while other studies have found no significant difference.[38–40] The lack of uniform results may represent different patient populations and comorbidities and well as the definition of steroid use. Some reports described steroid use as prednisone (or its equivalent) of 5 mg daily to greater than 40 mg daily, use within 14 to 60 days prior to surgery, use of 10 mg for at least 4 weeks prior to surgery or use for at least 3 months prior to surgery.[5,36,37,39,40]

In addition to the septic concerns related with steroids, their use can lead to the suppression of the hypothalamus–pituitary–axis (HPA) and subsequent adrenal insufficiency. For this reason, perioperative glucocorticoid replacement may be required. Although it has been traditionally believed that the degree of suppression was related to the dose and duration of therapy, poor data to support this exists.[41] Glucocorticoids equivalent to 5 mg of prednisone daily or less and glucocorticoids given for less than 3 weeks do not appear to cause clinically significant suppression of the HPA axis.[42–44] However, any patient who has received 15 mg of prednisolone daily or its equivalent for more than 3 weeks should be suspected of having suppression of the HPA.[45] Duration of the degree of HPA suppression once steroids are stopped is debatable, but may last up to 1 year and supplemental perioperative glucocorticoids may be required during this period.[46] More accurate evaluation for HPA suppression may be achieved through preoperative corticotropin testing; however, empiric coverage of a patient at risk may be more practical.[47]

Immunomodulators such as cyclosporine have been used to induce remission of CD, but more commonly, purine analogs such as 6-MP and azathioprine are used for their steroid-sparing effects to maintain remission. As with preoperative steroid use, there are conflicting experiences with the use of immunomodulators preoperatively. Myrelid et al found an increased risk of anastomotic complications in patients who were on purine analogues (16 vs. 6%) in 343 consecutive CD abdominal operations.[48] This risk increased significantly when combined with other established risk factors. If combined with colocolonic anastomosis and preoperative sepsis, the risk for anastomotic complications increased to 24%.

Tay et al described 100 consecutive patients undergoing resection with primary anastomosis or strictureplasty. Seventy patients were treated with azathioprine, 6-MP, or methotrexate within 8 weeks of surgery, with 20 receiving concomitant biologic therapy.[3] Fewer episodes of abdominal septic complications were found with immunomodulator therapy (5.6%) compared with those not receiving immunomodulation (25%). It was hypothesized that the prior immunomodulator and biologic therapy was more effective at controlling inflammation than 5-ASA agents, glucocorticoids, or antibiotics and this provided a protective effect postoperatively. Also, additional reports by Colombel et al of 207 patients and Canedo et al of 225 patients undergoing surgery identified no increase in complications with immunosuppressive therapy.[39,49]

Biologic therapy utilizing monoclonal antibodies directed at tumor necrosis factor has evolved as a highly effective treatment for CD.[50] Infliximab as maintenance therapy improves the quality of life, facilitates cessation of steroids and other immunosuppressive drugs, and helps to avoid surgery.[51] Preoperative use of biologic therapy has raised concerns due to potential sepsis with its general use, and data regarding postoperative complications and sepsis shows conflicting results.

Appau et al showed that the use of biologic agents within 3 months before surgery in CD increases postoperative sepsis, anastomotic leaks, and readmission rates.[52] Other studies, however, have demonstrated no increase in postoperative complications associated with biologic use.[39,40,49,53,54] Kunitake et al evaluated 413 consecutive patients with inflammatory bowel disease (IBD; 188 with CD, 156 with indeterminate colitis, and 69 with ulcerative colitis) and 101 received infliximab within 12 weeks of surgery.[54] There was no evidence of any differences in rates of infections, anastomotic leaks, or other complications. Similarly, Canedo et al demonstrated no increase in complications in 65 of 225 patients undergoing surgery for CD who had received infliximab within 90 days of surgery.[39]

White et al evaluated 338 consecutive patients who received steroids, immunomodulators, or biologic therapy within 3 months preoperatively and examined unplanned hospital readmission within 30 days of discharge as an end point.[55] The most common cause for readmission was intra-abdominal abscess. The incidence of unplanned readmission was similar among patients treated with steroids (11%), immunomodulators (9%), and biologics (12%). Steroid use within 3 months prior to surgery was associated with an increased rate of unplanned readmission. The use of immunomodulators or biologics alone did not increase readmission; however, combination therapy did. The incidence of unplanned readmissions was 3, 7, 11, and 16% when 0, 1, 2, or 3 agents used. The increasingly greater need for preoperative immunosuppression may result in greater overall immunosuppression that increases the risk for postoperative morbidity and readmission and this should be part of the surgical consideration.

Smoking

CD is more common in smokers than in nonsmokers, and its effects are dose-dependent and related to the nicotine within the tobacco smoke.[56–58] However, preoperative smoking does not appear to increase the incidence of anastomotic leaks.[3,5] Yamamoto and Keighley did find that smokers have a twofold increase in postoperative CD recurrence compared with nonsmokers, with recurrences being dose dependent.[59] The recurrence rate was also greater in those with a longer smoking history and in women compared with men. Former smokers have a similar recurrence rate as nonsmokers; hence, smoking cessation should be part of the preoperative optimization.

Venous Thromboembolism Prophylaxis

As with all abdominal and pelvic surgery, VTE prophylaxis, as suggested by the American College of Chest Physicians Evidence–Based Clinical Practice Guidelines (9th edition), should be considered.[60] In population-based studies, the risk for deep vein thrombosis and pulmonary embolism in IBD patients was two- to threefold greater than the general population and pharmacologic prophylaxis may not be sufficient.[61–63] Consequently, patients with CD requiring surgery may be at high risk for VTE, and the combination of mechanical and pharmacologic prophylaxis should be considered unless contraindicated.

Conclusion

CD is a chronic condition that is treated with antibiotics, anti-inflammatory agents, and immunosuppressant therapy. Most patients will ultimately require surgery; many may require multiple surgeries. As a result, surgery is deferred until absolutely necessary and the patient has exhausted nonoperative management. For this reason, patients may not be in optimal preoperative condition due to malnutrition, sepsis, or immunosuppression. If the clinical situation permits, surgery should be delayed until achievement of a good functional status, by correction of nutritional imbalances with either enteral or parenteral support, and by treating intra-abdominal sepsis with radiographically guided drainage and antibiotics. Postoperative infection and/or anastomotic leak with the prior use of immunosuppressive therapy should be considered, and the need for diversion should be

individualized based upon the patient's overall condition and presence of additional risk factors. Unique concerns related to adrenal insufficiency, tobacco use, and increased risk for VTE should be considered as well.

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