

Nutritional Support of Patient with Inflammatory Bowel Disease



Stephanie C. Montgomery, MD^{a,*}, Cayla M. Williams, MD^b,
Pinkney J. Maxwell IV, MD^c

KEYWORDS

• Nutrition • Inflammatory bowel disease • Crohn's disease • Ulcerative colitis

KEY POINTS

- The overwhelming majority of patients with inflammatory bowel disease (IBD) have some degree of malnutrition.
- IBD can lead to specific nutrient deficiencies.
- There can be significant microbial alteration in intestinal flora in patients with IBD.
- Nutritional support is a critical aspect of the overall care of patients with IBD.
- Patients with IBD require special perioperative nutritional support.

INTRODUCTION

Ulcerative colitis (UC) and Crohn's disease (CD) are the 2 most prevalent chronic inflammatory disorders of the digestive tract and affect approximately 1 million Americans. They have common clinical and pathologic features, but each is a distinct condition requiring individual approaches to management. CD can occur at any part of the gastrointestinal tract and may cause transmural tissue damage, whereas UC affects only the superficial mucosal layer of the colon and rectum. In both of these conditions, there is an activation of the immune system that results in chronic inflammation and ulceration. The underlying cause of inflammatory bowel disease (IBD) has not been completely elucidated, but it is thought to be multifactorial, with both genetic and environmental factors playing a role.

The authors have nothing to disclose.

^a Department of Surgery, Saint Francis Hospital and Medical Center, 114 Woodland Street, Hartford, CT 06105, USA; ^b Department of Emergency Medicine Western Michigan University Homer Stryker M.D. School of Medicine, 1000 Oakland Drive Kalamazoo, MI 49008, USA;

^c Department of Surgery, Medical University of South Carolina, Ashley River Tower, 25 Courtenay Drive, Charleston, SC 29425, USA

* Corresponding author.

E-mail address: scmontgo@stfranciscare.org

Surg Clin N Am 95 (2015) 1271–1279

<http://dx.doi.org/10.1016/j.suc.2015.08.006>

surgical.theclinics.com

0039-6109/15/\$ – see front matter © 2015 Elsevier Inc. All rights reserved.

The incidence and prevalence of UC and CD continue to rise in the developing world.¹ The observed differences in the disease incidence across age, time, and geographic region suggest that environmental factors may significantly modify the expression of CD and UC.¹ This continuing increase in the number of patients diagnosed with IBD strongly suggests an environmental trigger that may be related to dietary patterns.²

EFFECT OF INFLAMMATORY BOWEL DISEASE ON DIET, NUTRITION, AND METABOLISM

Studies have shown that up to 92.1% of patients with IBD are considered malnourished and many factors can contribute to their overall nutritional state (Table 1).³ Recent evidence suggests that even patients who appear clinically to be well nourished may harbor baseline vitamin and mineral deficiencies, even during periods of disease remission.^{4,5} Patients with IBD frequently ask their physicians for recommendations regarding diet to improve or even cure their gastrointestinal symptoms while obtaining the appropriate quantities of both micronutrients and macronutrients. Despite data that suggest dietary factors may play a role in the onset and course of IBD, there is very limited information regarding specific foods to avoid or include in a patient's diet. Currently, the only recommendation most health care providers can offer is to adhere to a healthy and varied diet.⁶ To further confound the issue, important clinical trials on this topic have been limited by their inability to include a placebo control, contamination of study groups, and inclusion of patients receiving medical therapies.⁷

Dietary Intake in Patients with Inflammatory Bowel Disease

Studies have yet to reliably demonstrate an association between the Western diet rich in carbohydrates, starch, and sugar with worsening of IBD symptoms.⁸ However, observations of detailed dietary journals reveal most patients with IBD continue to self-restrict their diet.⁹ Pain and inflammatory mediators are known to induce anorexia and cachexia, thus a relationship between disease activity and nutrient intake exists in IBD. Patients admit to restricting certain foods to alleviate perceived symptoms or triggers for active disease. The most commonly avoided food groups among this patient population are dairy products and fiber-containing foods. Studies have shown that avoiding dairy is actually associated with an increase in severity of gastrointestinal symptoms, in addition to decreased levels of serum calcium and folate.¹⁰ Fiber has been shown to play a role in decreasing inflammation systemically; however, there is limited evidence supporting supplementation or restriction of fiber-containing foods in patients with IBD.¹¹ Also of concern, the fat intake of the average patients with IBD is above current recommended values.⁹

Table 1 Etiologies of malnutrition in inflammatory bowel disease	
Drug Interactions	Abdominal Pain
Inflammation	Stricture formation
Fistula formation	Hypoalbuminemia
Short-gut syndrome	Diarrhea
Anorexia	Malabsorption
Altered bacterial flora	Disease chronicity
Nutrient losses from gut	Increased resting energy expenditure

Specific Nutrient Deficiencies in Inflammatory Bowel Disease

The pathophysiology of IBD predisposes patients to certain nutritional deficiencies (Table 2). To complicate matters further, the medications that are prescribed to treat these conditions can also negatively affect the nutritional state of this special patient population (Table 3).

Patients with IBD frequently exhibit calcium deficiencies due to the binding of calcium to unabsorbed fatty acids in the intestinal lumen, anatomically reduced absorptive surface area due to diseased tissue or secondary to intestinal resections, and patients' common practice of restricting dairy in their diets. The most common disease location in patients with CD is the terminal ileum, which causes distinct problems associated with bile acids, which are selectively reabsorbed in this region. As a result, these patients may experience fat-soluble vitamin deficiencies (vitamins A, D, E, and K) secondary to fat malabsorption. The use of medications such as sulfasalazine renders folate unavailable for absorption in the intestinal lumen. Therefore, folic acid supplementation is recommended if patients have low levels of serum folate. Zinc deficiency leads to increased apoptosis of intestinal cells and should be avoided in IBD.¹² Iron deficiency is common in patients with IBD and is a major concern for the development of anemia. The concurrent vitamin B12 deficiency that is observed in these patients can exacerbate this problem. Disease in the terminal ileum can further increase this prevalence as well as patients requiring resection of this important area of the bowel. Low circulating vitamin D levels have been reported as a risk factor for IBD and studies suggest that this associates with more severe disease.¹³ Studies also suggest that adequate intake of nutrients is important to prevent bone loss. Not surprisingly, an increase in prevalence of decreased bone mineral density has been reported in patients with IBD.¹⁴ Considering these circumstances, prescribing appropriate nutrient supplementation in early stages of disease is thought to decrease morbidity and mortality and should be considered.

Microbial Alterations in Inflammatory Bowel Disease

There is a symbiotic relationship between patients and their enteric community of microbes, referred to as the microbiota. This relationship provides nutritional optimization, protection against pathogenic organisms, and promotes immune homeostasis. Dysbiosis, or the imbalance of the normal enteric microbiota composition, along with altered mucosal immune response to luminal bacterial antigens, leads to the

Table 2
Nutrient deficiencies in inflammatory bowel disease

Nutrient Class	Specific Nutrient Deficiencies	Additional Considerations
Vitamins	Vitamins A, C, K, B12, D	International normalized ratio may be reduced due to low vitamin K levels
Electrolytes	Na, K, Cl	Most often occurs in patients with short bowel syndrome
Minerals	Magnesium, iron, zinc, calcium	Normal ferritin levels (acute phase reactant) do not exclude iron deficiency anemia Parathyroid hormone levels may be elevated due to low Ca levels
Protein	Serum albumin, total protein	50%–80% of patients with Crohn's disease and 25%–50% with ulcerative colitis have low levels

Table 3 Adverse effects of medications and their effect on nutrition		
Drug	Adverse Effect	Etiology of Malnutrition
Aminosalicylates	Abdominal pain and cramping	Decreased intake
Immunomodulators	Intestinal ulceration (mercaptopurine)	Malabsorption
Corticosteroids	Alterations in metabolism, binding interactions	Decreased absorption, increased losses
Biologic agents	Dyspepsia, pancreatitis, abscess formation, intestinal perforation (infliximab)	Decreased intake

All medications used in the treatment of inflammatory bowel disease can cause nausea, vomiting, and diarrhea.

chronic inflammation seen in IBD.¹⁵ Individual susceptibilities, genetic variants, and environmental factors, such as nutrition, medications, and smoking, can all modify one’s luminal environment and microbiome.^{16,17} Therapies targeted at restoration of enteric flora, including prebiotics, probiotics, and dietary polyphenols have been investigated with some encouraging results.¹⁵ When used in conjunction with a nutritionally diverse diet, these therapies favorably affect the overall microbial balance and possess anti-inflammatory properties. The result is a more appropriate immune response, enhanced gut barrier function, and increased absorptive capacity.^{18,19}

Pediatric Patients with Inflammatory Bowel Disease: A Special Patient Population

Children with IBD, especially CD, represent a special challenge to clinicians. Vitamin and nutritional deficiencies as a result of IBD confer consequences unique to children and adolescents, such as growth stunting, slower pubertal development, and delayed weight gain.²⁰ Up to 85% of patients with a childhood diagnosis of CD exhibit linear growth deficiency and delayed puberty.²¹ The delay in growth observed in these children can be linked to malnutrition and the effects of the inflammatory process on the growth plate via the alterations in the growth hormone/insulinlike growth factor-1 axis.²² Thus, long-term control of active inflammation and adequate intake of nutrients are both fundamental in promoting normal growth and puberty.²¹ To further complicate the care of these patients, glucocorticoid therapy remains a mainstay for treatment for active disease, which clearly shows deleterious effects on growth in these children. Frequent and detailed nutritional assessments, including weight, height, and pubertal stage, should be considered critical in children and adolescents with any history of IBD.

DIAGNOSIS AND TREATMENT OF MALNUTRITION IN INFLAMMATORY BOWEL DISEASE
Nutritional Assessment

It is recognized that malnutrition is not readily diagnosable in early IBD, and even among experts there is no full agreement on the elements that define malnutrition.^{23,24} In the past only low body mass index (BMI) was associated with malnutrition, but we now know patients can lack vital nutrients while maintaining a normal to even obese-range BMI. In a large prospective cohort of US women, measures of obesity were associated with an increased risk of CD, and dietary logs reported less than ideal diet habits among these individuals.²⁵ Given the high percentage of patients with IBD at risk for malnutrition, self-screening may increase the detection of nutritional

deficiencies. Self-administered testing using the malnutrition universal screening tool has been shown to be reliable and easy to use and we should encourage patient involvement in self-screening.²⁶ Studies demonstrate that patient access to high-quality, written, IBD-specific information is variable, and nutritional software applications that are available for download onto electronic devices are an appropriate way to engage patients, especially those in the younger generations.^{27,28} At the very least, a detailed dietary history is necessary to get an appropriate estimate of food intake and is recommended. Obtaining BMI, serial weights, and laboratory studies, such as albumin and iron studies, are useful information to follow to provide a trend for your patient's nutritional status. Muscle mass depletion, as well as fat mass depletion, were observed in patients with IBD and should be monitored.²⁹

Nutritional Therapy

Although traditionally bowel rest was used in the treatment of IBD, it is no longer recommended.³⁰ Enteral nutrition is now considered a mainstay of treatment and should be considered. The exact mechanism by which enteral nutrition improves IBD remains unclear, but it is thought to decrease systemic inflammatory response and the subsequent hypermetabolic state during active disease.³¹ Specific enteral diet compositions have not shown to confer any advantage over standard polymeric diets among these patients.^{32,33} In addition to having the benefit of minimal adverse effects, enteral nutrition enhances mucosal healing, controls local inflammation, and confers benefits for growth and overall nutritional status.³²

There is robust evidence of the effectiveness of enteral nutrition in patients with CD.³⁴ Randomized controlled trials estimate an overall remission rate of 60% in patients with CD with enteral nutrition alone.³⁵ Enteral nutrition has been shown to decrease mesenteric adipose tissue hypertrophy and inflammation, a hallmark of active CD.³⁶ Stricture formation as a result of the inflammatory response to transmural intestinal edema is the most frequent complication of CD and a common indication for operative intervention in these patients. Exclusive enteral nutrition has been associated in studies with a 59% decrease in bowel wall thickness, as well as a 331% increase in luminal cross-sectional area.³⁷ Despite the usefulness of enteral nutrition, it is no panacea and corticosteroids continue to play a role in treating active CD with increased rates of remission.³³ Even with the robust evidence of the utility of exclusive enteral nutrition, there is a wide variability in its use. It is believed that monotony of the therapy would lead to poor patient compliance, but that has not been shown in studies and should be considered.³⁸

In IBD, the use of total parenteral nutrition (TPN) should be restricted to those patients in whom enteral nutrition is contraindicated or only during special circumstances, such as patients with short-gut syndrome, high-output fistulas, or intolerance of enteral nutrition.³⁹ In these instances, TPN should be used as a short-term solution and conversion to enteral nutrition should begin as soon as appropriate. In addition to the higher risk of complications, a lower quality of life was reported by patients who were subjected to parenteral nutrition.⁴⁰

PERIOPERATIVE CONSIDERATIONS

Surgery rates for patients with UC and CD have been declining recently, but remain very high compared with the general population. Recent population-based cohorts report surgery rates of 10% to 14% after 1 year and 18% to 35% after 5 years in patients with IBD.⁴¹ More notably, up to 75% of patients with CD will require an operation at some point during the course of their disease.⁴² Undergoing a surgical procedure

induces a stress response in these patients, which has a catabolic effect on the body's substrate stores. Nutrients that are believed to have immune-enhancing effects, such as glutamine, arginine, and taurine, become rapidly deficient under this surgical stress. Interestingly, studies have suggested that the supplementation of these nutrients may counteract the negative effects of surgical injury and improve clinical outcomes post-operatively.⁴³ Additionally, nutritional therapy should be considered in these patients to reverse their catabolic state and provide the support for healing of operative wounds.

Research continues to demonstrate that disease-related malnutrition in patients with IBD is a serious clinical problem in both hospitalized and nonhospitalized patients.⁴⁴ A malnourished state is associated with increased inpatient length of stay, increased mortality, increased infection rates, and higher resource utilization.²³ Surgical site infections continue to be an important perioperative complication that can significantly contribute to this reported increase in duration of hospital stay and post-operative morbidity. Studies reveal that having a low preoperative nutritional index correlates with an increased incidence of surgical site infections after bowel resection in CD. Also of concern, postoperative intra-abdominal septic complications were demonstrated in 9% to 12% of patients with CD after surgery.⁴⁵ Preoperative exclusive enteral nutrition (EEN) may reduce these risks, as research has shown that patients who receive EEN suffer a lower risk of septic complications.⁴⁶ Furthermore, the risk of anastomotic leak is significantly increased in patients whose preoperative albumin levels are lower than 3.5 g/dL and low albumin levels may be associated with higher rates of abdominal septic complications after surgery in patients with CD.^{47,48} Enterocutaneous fistulas (ECFs), highly morbid conditions that can lead to sepsis and death, remain a dreaded complication for surgeons. Aggressive nutritional support remains the most significant predictor of outcome with ECFs and cannot be overemphasized.⁴⁹ The elderly are a special population and are at an increased risk of hospital-related and therapy-related complications.⁵⁰ Despite this, some studies surprisingly demonstrate that they may have the same surgical complication rate as younger patients with IBD in the contemporary era.⁵¹ Enteral nutrition optimization before elective surgery is therefore essential for all patients. Also notable for surgeons, preoperative fasting has a negative effect on the patient's condition and recovery after surgery and should be discouraged, if possible.⁴³

SUMMARY

IBD remains a very complex issue that every surgeon will most likely encounter during his or her practice. The very nature of IBD lends itself to the development of nutritionally deficient states and the medications that are prescribed by physicians can further compound these nutritional problems. Surgeons must therefore be aware of the nutritional issues specific to this patient population and screen for underlying deficiencies that may be present, even in disease remission. Nutritional screening must be an integral part of the preoperative workup and postoperative plan, including supplementation where appropriate. Enteral nutrition should be encouraged and TPN should be used only in a small set of circumstances and only until enteral therapies can be instituted.

REFERENCES

1. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. *Gastroenterology* 2004;126(6):1504–17.

2. Hou JK, Lee D, Lewis J. Diet and inflammatory bowel disease: review of patient-targeted recommendations. *Clin Gastroenterol Hepatol* 2014;12(10):1592–600.
3. Sokulmez P, Demirbag AE, Arslan P, et al. Effects of enteral nutritional support on malnourished patients with inflammatory bowel disease by subjective global assessment. *Turk J Gastroenterol* 2014;25(5):493–507.
4. Vagianos K, Bector S, McConnell J, et al. Nutrition assessment of patients with inflammatory bowel disease. *JPEN J Parenter Enteral Nutr* 2007;31(4):311–9.
5. Filippi J, Al-Jaouni R, Wiroth JB, et al. Nutritional deficiencies in patients with Crohn's disease in remission. *Inflamm Bowel Dis* 2006;12(3):185–91.
6. Massironi S, Rossi RE, Cavalcoli FA, et al. Nutritional deficiencies in inflammatory bowel disease: therapeutic approaches. *Clin Nutr* 2013;32(6):904–10.
7. Lee D, Albenberg L, Compher C, et al. Diet in the pathogenesis and treatment of inflammatory bowel diseases. *Gastroenterology* 2015;148(6):1087–106.
8. Chan SS, Luben R, van Schaik F, et al. Carbohydrate intake in the etiology of Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis* 2014;20(11):2013–21.
9. Walton M, Alaunyte I. Do patients living with ulcerative colitis adhere to healthy eating guidelines? A cross-sectional study. *Br J Nutr* 2014;112(10):1628–35.
10. Brasil Lopes M, Rocha R, Castro Lyra A, et al. Restriction of dairy products: a reality in inflammatory bowel disease patients. *Nutr Hosp* 2014;29(3):575–81.
11. Wedlake L, Slack N, Andreyev HJ, et al. Fiber in the treatment and maintenance of inflammatory bowel disease: a systematic review of randomized controlled trials. *Inflamm Bowel Dis* 2014;20(3):576–86.
12. Ranaldi G, Ferruzza S, Canali R, et al. Intracellular zinc is required for intestinal cell survival signals triggered by the inflammatory cytokine TNFalpha. *J Nutr Biochem* 2013;24(6):967–76.
13. O'Sullivan M. Vitamin D as a novel therapy in inflammatory bowel disease: new hope or false dawn? *Proc Nutr Soc* 2015;74(1):5–12.
14. Lim H, Kim HJ, Hong SJ, et al. Nutrient intake and bone mineral density by nutritional status in patients with inflammatory bowel disease. *J Bone Metab* 2014;21(3):195–203.
15. Chen WX, Ren LH, Shi RH. Enteric microbiota leads to new therapeutic strategies for ulcerative colitis. *World J Gastroenterol* 2014;20(42):15657–63.
16. Bringiotti R, Ierardi E, Lovero R, et al. Intestinal microbiota: the explosive mixture at the origin of inflammatory bowel disease? *World J Gastrointest Pathophysiol* 2014;5(4):550–9.
17. Scharl M, Rogler G. Inflammatory bowel disease pathogenesis: what is new? *Curr Opin Gastroenterol* 2012;28(4):301–9.
18. Guandalini S. Are probiotics or prebiotics useful in pediatric irritable bowel syndrome or inflammatory bowel disease? *Front Med (Lausanne)* 2014;1:23.
19. Tilg H, Moschen AR. Food, immunity, and the microbiome. *Gastroenterology* 2015;148(6):1107–19.
20. dos Santos GM, Silva LR, Santana GO. Nutritional impact of inflammatory bowel diseases on children and adolescents. *Rev Paul Pediatr* 2014;32(4):403–11 [in Portuguese].
21. Gasparetto M, Guariso G. Crohn's disease and growth deficiency in children and adolescents. *World J Gastroenterol* 2014;20(37):13219–33.
22. Ezri J, Marques-Vidal P, Nydegger A. Impact of disease and treatments on growth and puberty of pediatric patients with inflammatory bowel disease. *Digestion* 2012;85(4):308–19.

23. Nguyen GC, Munsell M, Harris ML. Nationwide prevalence and prognostic significance of clinically diagnosable protein-calorie malnutrition in hospitalized inflammatory bowel disease patients. *Inflamm Bowel Dis* 2008;14(8):1105–11.
24. Meijers JM, van Bokhorst-de van der Schueren MA, Schols JM, et al. Defining malnutrition: mission or mission impossible? *Nutrition* 2010;26(4):432–40.
25. Khalili H, Ananthakrishnan AN, Konijeti GG, et al. Measures of obesity and risk of Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis* 2015;21(2):361–8.
26. Sandhu A, Mosli M, Yan B, et al. Self-screening for malnutrition risk in outpatient inflammatory bowel disease patients using the Malnutrition Universal Screening Tool (MUST). *JPEN J Parenter enteral Nutr* 2015. [Epub ahead of print].
27. Prince AC, Moosa A, Lomer MC, et al. Variable access to quality nutrition information regarding inflammatory bowel disease: a survey of patients and health professionals and objective examination of written information. *Health Expect* 2014. [Epub ahead of print].
28. Boyce B. Nutrition apps: opportunities to guide patients and grow your career. *J Acad Nutr Diet* 2014;114(1):13–5.
29. Rocha R, Santana GO, Almeida N, et al. Analysis of fat and muscle mass in patients with inflammatory bowel disease during remission and active phase. *Br J Nutr* 2009;101(5):676–9.
30. Wiese DM, Rivera R, Seidner DL. Is there a role for bowel rest in nutrition management of Crohn's disease? *Nutr Clin Pract* 2008;23(3):309–17.
31. Zhao J, Dong JN, Gong JF, et al. Impact of enteral nutrition on energy metabolism in patients with Crohn's disease. *World J Gastroenterol* 2015;21(4):1299–304.
32. Hartman C, Eliakim R, Shamir R. Nutritional status and nutritional therapy in inflammatory bowel diseases. *World J Gastroenterol* 2009;15(21):2570–8.
33. Zachos M, Tondeur M, Griffiths AM. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst Rev* 2007;(1):CD000542.
34. Yamamoto T, Nakahigashi M, Saniabadi AR. Review article: diet and inflammatory bowel disease—epidemiology and treatment. *Aliment Pharmacol Ther* 2009;30(2):99–112.
35. Wahed M, Geoghegan M, Powell-Tuck J. Novel substrates. *Eur J Gastroenterol Hepatol* 2007;19(5):365–70.
36. Feng Y, Li Y, Mei S, et al. Exclusive enteral nutrition ameliorates mesenteric adipose tissue alterations in patients with active Crohn's disease. *Clin Nutr* 2014;33(5):850–8.
37. Hu D, Ren J, Wang G, et al. Exclusive enteral nutritional therapy can relieve inflammatory bowel stricture in Crohn's disease. *J Clin Gastroenterol* 2014;48(9):790–5.
38. Kansal S, Wagner J, Kirkwood CD, et al. Enteral nutrition in Crohn's disease: an underused therapy. *Gastroenterol Res Pract* 2013;2013:482108.
39. Goh J, O'Morain CA. Review article: nutrition and adult inflammatory bowel disease. *Aliment Pharmacol Ther* 2003;17(3):307–20.
40. Raczowska A, Lawinski M, Gradowska A, et al. Quality of life considering patients with chronic inflammatory bowel diseases—natural and parenteral nutrition. *Pol Przegl Chir* 2014;86(9):410–7.
41. Burisch J, Munkholm P. The epidemiology of inflammatory bowel disease. *Scand J Gastroenterol* 2015;50(8):1–10.
42. Latella G, Papi C. Crucial steps in the natural history of inflammatory bowel disease. *World J Gastroenterol* 2012;18(29):3790–9.
43. Buijs N, Worner EA, Brinkmann SJ, et al. Novel nutritional substrates in surgery. *Proc Nutr Soc* 2013;72(3):277–87.

44. Elia M, Stratton RJ. How much undernutrition is there in hospitals? *Br J Nutr* 2000; 84(3):257–9.
45. Morar P, Hodgkinson J, Thalayasingam S, et al. Determining predictors for intra-abdominal septic complications following ileocolonic resection for Crohn's disease—considerations in pre-operative and peri-operative optimisation techniques to improve outcome. *J Crohns Colitis* 2015;9(6):483–91.
46. Li G, Ren J, Wang G, et al. Preoperative exclusive enteral nutrition reduces the postoperative septic complications of fistulizing Crohn's disease. *Eur J Clin Nutr* 2014;68(4):441–6.
47. Telem DA, Chin EH, Nguyen SQ, et al. Risk factors for anastomotic leak following colorectal surgery: a case-control study. *Arch Surg* 2010;145(4):371–6 [discussion: 376].
48. Huang W, Tang Y, Nong L, et al. Risk factors for postoperative intra-abdominal septic complications after surgery in Crohn's disease: a meta-analysis of observational studies. *J Crohns Colitis* 2015;9(3):293–301.
49. Polk TM, Schwab CW. Metabolic and nutritional support of the enterocutaneous fistula patient: a three-phase approach. *World J Surg* 2012;36(3):524–33.
50. Shung DL, Abraham B, Sellin J, et al. Medical and surgical complications of inflammatory bowel disease in the elderly: a systematic review. *Dig Dis Sci* 2015;60(5):1132–40.
51. Bautista MC, Otterson MF, Zadvornova Y, et al. Surgical outcomes in the elderly with inflammatory bowel disease are similar to those in the younger population. *Dig Dis Sci* 2013;58(10):2955–62.