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**Prehabilitation prior to intestinal resection in Crohn’s disease patients: An opinion review**

Bak MTJ *et al*. Prehabilitation in Crohn’s disease patients

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**Abstract**

Patients with Crohn’s disease (CD) are at a considerable risk for intestinal surgery. Approximately 25% of patients with CD will undergo an intestinal resection within 10 years of diagnosis. Postoperative complications after CD surgery have been reported in 20%-47% of the patients. Both general and CD-related risk factors are associated with postoperative complications, and comprise non-modifiable (*e.g.,* age) and potentially modifiable risk factors (*e.g.,* malnutrition). Prehabilitation focuses on the preoperative period with strategies designed to optimize modifiable risk factors concerning the physical and mental condition of the individual patient. The aim of prehabilitation is to enhance postoperative recovery and return to or even improve preoperative functional capacity. Preoperative improvement of nutritional status, physical fitness, cessation of smoking, psychological support, and critical revision of preoperative use of CD medication are important strategies. Studies of the effect on postoperative outcome in CD patients are scarce, and guidelines lack recommendations on tailored management. In this opinion review, we review the current evidence on the impact of screening and management of nutritional status, physical fitness, CD medication and laboratory valueson the postoperative course following an intestinal resection in CD patients. In addition, we aim to provide guidance for individualized multimodal prehabilitation in clinical practice concerning these modifiable factors.

**Key Words:** Crohn’s disease; Prehabilitation strategies; Nutrition; Physical fitness; Medication; Laboratory values

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**Core Tip:** Nutritional status, medication, and laboratory values are modifiable factors that influence the postoperative course of patients with Crohn’s disease. In addition, physical fitness is impaired in the perioperative course and therefore preoperative screening is warranted. Individualized multimodal prehabilitation programs aim to improve these modifiable risk factors before surgery, including smoking cessation and psychological screening and support, and should be integrated in the preoperative preparation period in order to reduce both postoperative complications and undesirable outcomes.

**INTRODUCTION**

Crohn’s disease (CD) is a chronic inflammatory bowel disease (IBD) characterized by segmental, transmural inflammation, which most commonly affects the ileum and/or colon[1]. Although the risk of intestinal resection and re-resection has declined considerably over the past decades, approximately 25% of patients will undergo an intestinal resection within 10 years of CD diagnosis[2,3].

An intestinal resection is potentially perceived as a major life event and has a significant psychological impact on CD patients, which can result in anxiety and depressive symptoms in the pre- and postoperative setting[4]. Despite the immediate relief of symptoms and a potential increase of quality of life after CD surgery[5], important concerns are the risk of potential (severe) complications and recurrence of CD[6]. Reports on the frequency of postoperative complications, following intestinal resection in CD patients, range from 20%-47%[7-12]. Several general and CD-specific risk factors for postoperative complications have been identified. Both non-modifiable risk factors (*i.e.,* comorbidity, older age) and modifiable risk factors (*i.e.,* malnutrition, preoperative medication use, abnormal preoperative laboratory values and smoking) have been associated with postoperative complications[8-10,12,13]. In addition, preoperative physical fitness, specifically aerobic fitness, seems impaired in patients with CD[14], which may increase the risk for adverse postoperative outcomes as has been observed in colorectal cancer (CRC) surgery[15,16].

Prehabilitation focuses on the preoperative period by suggesting strategies designed to optimize modifiable risk factors concerning the physical and mental condition of the individual patient. As such, prehabilitation aims to improve the postoperative course and promotes an earlier postoperative recovery and return to functional capacity[6]. A four-pillar multimodal prehabilitation program tailored to the individual patient involves improving: (1) Physical; (2) Nutritional; (3) Psychological status; and (4) Cessation of smoking, resulted in a significant earlier recovery to the baseline functional capacity in patients with CRC[17]. In addition, preoperative physical exercise training to improve aerobic fitness significantly reduced postoperative complications in high-risk patients, both in general[18] and those with CRC[19], undergoing abdominal surgery as compared to usual care. These programs may also benefit patients in other settings of abdominal surgery, including CD[20]. However, literature on prehabilitation in CD patients scheduled for intestinal resection is scarce and guidelines lack recommendations on tailored management[21,22].

In this opinion review, the available literature on the effect of potentially modifiable preoperative factors on the postoperative course following an intestinal resection in CD is critically appraised, with a focus on nutritional status, physical fitness, CD medication, and laboratory values. In addition, we aim to provide guidance for screening and specific interventions on these items during the preoperative course of patients with CD (Tables 1 and 2). Although psychological screening and support, as well as smoking cessation are considered essential during preoperative optimization in CD, these topics will not be addressed in this review. For these topics, management in accordance with general guidelines and integration into a multimodal prehabilitation program is recommended.

**METHODS**

A literature search of the EMBASE, Medline, Web of Science, Google Scholar and Cochrane Library databases was conducted, in collaboration with the Medical School Library of the Erasmus University Rotterdam. High-quality articles were cited in Reference Citation Analysis (*RCA*) (https://www.referencecitationanalysis.com). The following keywords, synonyms and their Medical Subject Headings terms were used for this search: ‘Crohn’s disease’, ‘intestinal surgery’, and ‘risk factors’ (Supplementary material).

Studies published in the English language up to July 2021 were considered according to their topical relevance for the impact of screening and management of nutritional status, physical fitness, CD medication and laboratory values in the preoperative period related to the postoperative course following an intestinal resection in CD patients. In the case that no relevant studies were present virtually for any of these topical contents, the literature was re-assessed in other settings of abdominal surgery (*e.g*., patients with CRC). Only randomized controlled trials, meta-analyses, systematic reviews, observational studies (case-control study and patient series without control) were selected. Study selection was independently performed by both two reviewers (Bak MTJ and Ruiterkamp MFE) based on title and abstract. The snowball method was then applied to all of the final selected studies.

**HOW TO SCREEN AND OPTIMIZE THE NUTRITIONAL STATUS AND PHYSICAL FITNESS OF PATIENTS WITH CD PRIOR TO INTESTINAL RESECTION?**

***Preoperative screening of nutritional status***

Malnutrition is an important risk factor for a dismal postoperative course after intestinal resection in CD[23]. Malnutrition encompasses undernutrition and overnutrition. CD patients are prone to undernutrition due to inadequate nutritional intake attributable to several causes (*e.g.,* anorexia, strictures), malabsorption (*e.g.,* active inflammation or after prior resection) and chronic inflammation. However, obesity in the CD population has increased over the years[24]. Recognition of nutritional status as the key issue in preoperative optimization for patients with CD is gaining ground, since a significant benefit from dietary intervention may not only be expected after optimization of the nutritional status but also from its potential immunomodulatory effect on CD.

A first screening for malnutrition is readily available to all caregivers treating patients with CD and is recommended in all preoperative CD patients according to current guidelines[21-23]. Since a survey among 146 gastroenterologists in 2016 revealed that one-third of respondents did not routinely screen for malnutrition, exploration of the reasons for non-adherence is required[25]. The initial nutritional assessment during preoperative screening requires a combination of: (1) Body mass index (BMI); (2) Evaluation of unintentional weight loss; and (3) Assessment of dietary intake. Assessment of muscle mass preferably complements these measures. Laboratory assessment of albumin and micronutrients is not a reliable marker of malnutrition, and will be addressed in a later paragraph[23].

BMI is a commonly used indicator for body fat and thus a proxy of nutritional status. Preoperative BMI value and the rate of postoperative complications are only moderately correlated, according to abundant reports[26-30]. Nevertheless, clearly underweight patients, defined with varying cut-off values in the literature (from BMI < 16.2 kg/m2 to BMI < 18.5 kg/m2), are at an increased risk of a dismal postoperative course after intestinal resection, including creation of an ileostomy[9], readmission[31], intra-abdominal septic complications (IASCs)[32], and overall postoperative complications[33,34]. Similarly, clearly overweight patients suffering from obesity, defined as a BMI cut-off > 30 kg/m2, also face an elevated risk of complications[9,28,34-36]. In addition, another study reported an increasing BMI by 1 unit (U) associated with an increased risk [odds ratio (OR) = 1.04; 95% confidence interval (CI): 1.0-1.1; *P* = 0.008] of postoperative complications[35].

Unintentional preoperative weight loss may occur in all CD patients independent of their baseline weight. Various studies assessing the effect of preoperative weight loss have confirmed the association with postoperative complications in CD patients. Unintentional weight loss of > 10%, as compared to baseline over the last 6 mo prior to surgery, is a commonly described cut-off[9,10,36-38]. This cut-off of significant weight loss has been observed in 23%-54% of CD patients scheduled for intestinal resection[23]. Various studies have reported a clear negative association between recent unintentional weight loss and postoperative complications in CD patients[9,10,36-38].

In addition, other measures of body composition may warrant evaluation during the preoperative assessment. The most important is sarcopenia, which is defined as low lean muscle mass in combination with either low muscle strength or low physical performance[39]. Sarcopenia can be present in both under- and overweight individuals[40]. Moreover, sarcopenia is common in CD patients, with a reported overall incidence of 52%, as determined by radiologic assessment of body mass composition (*e.g.,* skeletal mass index, total psoas index and/or Hounsfield U average calculations at the level of the third lumbar vertebral body)[40,41]. A recent meta-analysis identified sarcopenia as an independent predictor for both postoperative complications and/or undesirable outcomes (*i.e.,* poor quality of life, inadequate response to therapy) in the IBD population[42]. Especially in patients younger than 40 years, sarcopenia was a strong and independent risk factor for postoperative complications, and patients with a low or normal BMI were affected more often[43]. Handgrip strength is an accessible and reliable diagnostic method for sarcopenia applied in routine practice. When sarcopenia in CD patients is detected in the preoperative setting, a combined intervention to optimize the closely related nutritional status and improved physical fitness may enhance postoperative prognosis[44]. However, data on these specific interventions are lacking.

To date, several nutritional screening tools are available to assess the nutritional status in the IBD population. These tools combine such clinical features as BMI, weight loss, and symptoms (for instance diarrhea). Amongst these tools are the following: Nutrition Risk Screening (NRS-2002)[45]; Malnutrition Universal Screening Tool (MUST)[46]; Global Leadership Initiative on Malnutrition (GLIM) criteria[47]; and more IBD-specific tools, such as the Malnutrition Inflammatory Risk Tool (MIRT)[48] and Saskatchewan IBD Nutrition Risk Tool[49]. The GLIM has a higher rate of malnutrition detection in preoperative IBD patients as compared to several other screening tools (namely NRS-2002, MUST, MIRT, and Saskatchewan IBD Nutrition Risk Tool)[50]. Moreover, chronic inflammation is used as an indicator in this nutritional screening tool[47]. The Onodera’s prognostic nutritional index (OPNI) is a simple and useful index to merely reflect the preoperative immunological status using serum albumin level and total lymphocyte counts. OPNI predicts the risk of postoperative complications in various types of cancer[51]. Limited data of the prognostic value of the OPNI in CD suggests that OPNI < 40 is a predictor of infectious complications or postoperative abdominal bleeding[52-54]. Overall, more data on the association between malnutrition detected by these screening tools and the postoperative course are required to support their routine use.

***Future nutritional screening methods***

An altered body composition is a known risk factor for postoperative complications[23]. Current available imaging techniques provide the opportunity to screen the body composition and develop new nutritional predictors for postoperative outcome. Although cross-sectional imaging with the sole purpose of evaluating body composition is not indicated, and available scans may be used for objective evaluation. Visceral fat promotes both local and systemic inflammation, resulting in a chronic inflammatory status[55,56]. Increased[57] and decreased[58] subcutaneous fat as well as increased visceral fat[59] are associated with increased risk of early postoperative complications in CD patients. Moreover, an expanded visceral/subcutaneous fat ratio (VSR) was identified as a better predictor of the postoperative outcome compared to BMI[58]. However, another study reported no association between VSR and postoperative complications[60]. In addition, there seems to be different cut-off points of total subcutaneous fat for CD patients, compared to other patients[57]. Therefore, these promising markers warrant further investigation.

***Preoperative screening of physical fitness***

To date, there is no routine screening for physical fitness in patients with CD in the preoperative course. In general, the physical fitness of CD patients is impaired[14,61]. Two cross-sectional studies concluded that physical fitness, specifically aerobic fitness, is impaired in the perioperative course of patients with CD as compared to the general population[14] or other subgroups undergoing abdominal surgery[62]. This impairment is attributed to a lack of physical activity due to illness behavior and/or impaired nutritional status affecting muscle function[14,61,63,64]. More objective insights into the level of physical fitness in patients with CD are required, as well as into the association between physical fitness and patient-, disease-, and treatment-related outcomes. The specific subgroups of patients with impaired aerobic fitness may benefit most from a targeted and personalized physical exercise intervention. A validated self-reporting questionnaire (*e.g.,* Duke activity status index, veterans-specific activity questionnaire) may serve as a simple screening tool to identify patients with impaired aerobic fitness[65.66]. These patients may receive a comprehensive objective assessment by an exercise specialist (*e.g.,* physical therapist, clinical exercise physiologist) to evaluate the specific exercise intolerance and propose a personalized prescription for physical exercise training.

A cardiopulmonary exercise test is considered the gold standard for assessing aerobic fitness and also provides valuable information to determine physical exercise training safety (*e.g.,* contraindications) by assessing the body’s integrated physiological response to progressive exercise[67]. Moreover, cardiopulmonary exercise test results can be used to optimize and personalize training intensity. When performance of a cardiopulmonary exercise test is not possible, a more practical performance-based field test to evaluate a patient’s aerobic fitness can be used. The steep-ramp test is a short time maximal exercise test on a cycle ergometer, of which its primary outcome parameter (the achieved peak work rate) is highly correlated with aerobic fitness indicators obtained at the cardiopulmonary exercise test[68].

Low- to moderate-intensity physical exercise training interventions are feasible and safe in IBD patients in the non-perioperative setting, and have been associated with improved physical fitness as well as with a significant reduction of (severe) fatigue and stress, and a significant improvement of quality of life[69-71]. To date, no preoperative physical exercise training studies have been conducted in patients with CD. As aerobic and resistance training have been found to be effective for the reduction of postoperative complications and accelerates recovery of functional capacity in unfit patients undergoing abdominal surgery[18,19], patients with CD may benefit from these interventions as well in the preoperative course[72]. It seems that high-intensity physical exercise training should be avoided, as it may lead to an acute exacerbation of inflammation and CD symptoms[73]. Overall, future research for the effect of physical interventions on the preoperative course of CD patients is warranted.

***Preoperative optimization of nutritional status***

To reverse the negative impact of malnutrition on the postoperative course in CD patients, preoperative optimization of the nutritional status is indicated. The European Society of Clinical Nutrition and Metabolism (ESPEN) states that the preoperative optimization of the nutritional status by enteral nutrition (EN) for 7-10 d, in the case of mildly malnourished patients, or 7-14 d in the case of a severe nutritional risk, is appropriate[74]. Nutritional support is administered enterally, and only parenteral in case EN has failed or is contraindicated (*e.g*., due to an intestinal obstruction)[74].

A Cochrane review on preoperative nutritional support in patients scheduled for gastrointestinal surgery reported a significant reduction of anastomotic leakage and need for a temporary diverting stoma [overall risk ratio (RR) = 0.67; 95%CI: 0.53-0.85][75]. In line with these findings, a meta-analysis showed that preoperative nutritional therapy significantly reduces postoperative complications in patients with CD (OR = 0.26; 95%CI: 0.07-0.99)[76]. In particular, EN was superior to usual care (defined as no nutritional support) (OR = 0.09; 95%CI: 0.06-0.013)[76,77]. A trend towards superiority of total parenteral nutrition (TPN) as compared to standard care was observed, but statistical significance was not reached[76].

Exclusive EN (EEN) consists of complete liquid diet of various compositions and has been widely used as induction therapy in pediatric CD patients with a duration of 6 wk to 8 wk[78,79]. EEN is effective as preoperative therapy by inducing both clinical and histological remission in adult CD patients[80,81]. The anti-inflammatory effect of EEN can be attributed to the reduction of mucosal cytokines and composite alterations of the gut microbiome[81,82]. Cohort studies, which investigated the effect of EEN in the preoperative setting in the CD population, demonstrated a significant reduction in overall postoperative complications[83-85], IASCs[86,87], and postoperative abscesses and anastomotic leakage[80,86,88]. Moreover, EEN has proven to be beneficial in the reduction of C-reactive protein (CRP)[80,83-85] and the increase of albumin, OPNI, and hemoglobin level[83,84].

In case EN fails or is contraindicated, PN is suggested. PN can be divided into partial PN (PPN) and TPN. PN is administered into the venous system *via* a catheter into the superior vena cava or a peripherally-inserted central catheter. Patients treated with TPN only receive a completely intravenous (IV) nutritional liquid diet, while patients with PPN may receive nutrients from other sources alongside PN. The literature on the effect of PN on postoperative complications following intestinal resection in CD is scarce. Available studies reported a significant decrease in overall postoperative complications[89], non-infectious complications[90], anastomotic leakage[88], and the length of the resection specimen[91]. Benefits of TPN were observed in patients who were treated with TPN for ≥ 60 d[90] or for the duration of 18-90 d[89]. However, the benefit of PN as nutritional support needs to be weighed against the possible risk of catheter-related infections[92].

***Reviewers’ opinion***

In summary, since extremes in BMI (< 18.5 kg/m2 or > 30 kg/m2) and recent unintentional weight loss (> 10% within 6 mo prior to surgery) have been associated with a dismal postoperative course in CD patients, we recommend the assessment of both in the preoperative setting. The detection of significant unintentional weight loss is a red flag and postponement of the intestinal resection until after restoration of the catabolic status should be considered. Moreover, assessment of handgrip strength may be used to detect sarcopenia. We consider GLIM as an appropriate screening tool for malnutrition in CD patients as chronic inflammation is included as one of the indicators. Moreover, the GLIM had a higher detection rate of malnutrition as compared to other screening tools in preoperative IBD patients. In addition, the OPNI can be used as an immunological screening tool. However, the prognostic value of these tools on the postoperative course requires further research. In our opinion, nutritional support during preoperative optimization may be considered for all patients with either an impaired nutritional status and/or inadequate intake with regard to proteins and calories. After a diagnosis of malnutrition, an individualized window to surgery needs to be decided to optimize nutritional status. As physical fitness is impaired in CD and therefore may influence the postoperative course, preoperative screening is warranted with use of self-reporting questionnaires. In addition, patients at risk may benefit from an objective assessment to evaluate specific exercise intolerance and a personalized prescription for physical exercise training. When pre- and postoperative physical fitness is impaired in patients with CD, aerobic and resistance training are recommended. The optimization period as suggested by the ESPEN (7-14 d) may be considered a minimum and, after careful evaluation per individual case, be extended up to 6-8 wk in most cases to fully benefit from the dietary intervention. EEN seems a promising preoperative nutritional intervention to improve prognosis due to its immunomodulatory effect, especially in patients with penetrating CD complications. Nutritional support is administered enterally (oral or *via* a nasogastric tube) (*i.e*., EN), and only in exceptional situations parenterally (when enteral nutritional support fails). TPN seems a valid option only when EN is contraindicated, not effective, more tolerable.

**WHAT IS THE OPTIMAL TIMING TO DISCONTINUE CD MEDICATION PREOPERATIVELY?**

CD-related medication has an immunomodulatory effect and may increase the risk of infections. This may also result in postoperative surgical site infections (SSIs) and/or IASCs. The European Crohn & Colitis Organization(ECCO) guideline recommends to wean off corticosteroids 6 wk before surgery[21], while the guideline of the British Society for Gastroenterology(BSG) recommends to stop corticosteroids or minimize the dose, without specifying a window to surgery[22]. Moreover, the BSG recommends cessation of infliximab and adalimumab 6-8 wk and 4 wk prior to surgery, respectively[22], whereas the ECCO guideline states that cessation of anti-tumor necrosis factor-alpha (TNF)-α therapy prior to surgery is not mandatory[21].

A recent Cochrane review studied the potential impact of perioperative IBD medication on the risk of postoperative (infectious) complications within 30 d in IBD patients[93]. The pooled data of this meta-analysis reported a significant association of corticosteroids with the risk of overall infectious postoperative complications (OR = 1.70; 95%CI: 1.38-2.09) and intra-abdominal infections (OR = 5.95; 95%CI: 1.04-34.1) in CD patients[93]. Furthermore, a significant increased risk of overall infectious complications (OR = 1.60; 95%CI: 1.20-2.13) was observed in patients treated with an anti-TNF-α agent[93]. No significant association was reported for patients who received the last dose of anti-TNF-α more than 8 wk before surgery[93]. However, these results should be interpreted with caution since the evidence for all outcomes was of low or very low quality, mostly due to the observational design, heterogeneity, and risk of bias of the included studies[93].

Pooled data of that meta-analysis demonstrated no significantly increased risk of overall postoperative infectious complications in CD patients treated with immunomodulatory, anti-interleukin and anti-integrin therapy[93]. Nevertheless, two retrospective studies have found a significant association of thiopurines, in combination with anti-TNF-α or corticosteroids, with IASC and overall infectious complications in the postoperative course[94,95].The relation between vedolizumab, an anti-integrin agent, and postoperative complications has been studied in nine observational cohort studies including a total number of 799 patients and predominantly evaluating patients who underwent abdominal surgery with overall postoperative (infectious) complications as the primary endpoint[29,96-102]. Two studies found a significant increased risk of SSIs in patients treated with vedolizumab in the preoperative course[29,96]. Another study reported a significant decreased risk of postoperative ileus in CD patients with detectable vedolizumab levels as compared to non-detectable vedolizumab levels[99]. Four observational studies found the outcomes of preoperative ustekinumab use on postoperative complications and infectious complications, and found no significantly increased risk[96-98,103].

***Reviewers’ opinion***

In accordance to the current literature and guidelines, we would recommend to wean off corticosteroids to a minimal dose, preferably < 20 mg, 6 wk prior to surgery. Moreover, cessation of anti-TNF-α agents may be considered, especially in non-responders and/or therapy refractory CD. When cessation is considered, a time interval of 4-8 wk (depending on type of anti-TNF-α agent) prior to surgery seems appropriate. Although the evidence on an association with increased risk of infections is unclear for other CD-medication, critical revision of the benefit of continuation until the date of surgery is indicated in all patients on an individual basis. In addition, since the biologic effect may last longer and vary per agent from 1 mo (prednisolone < 10 mg) to 3 mo (immunomodulators, anti-TNF-α) or longer (vedolizumab and ustekinumab), data on the effect of intervention are required to prove the beneficial effect of timely cessation[104].

**WHICH LABORATORY VALUES ARE ASSOCIATED WITH THE POSTOPERATIVE COURSE AND NEED TO BE ASSESSED PRIOR TO INTESTINAL RESECTION IN PATIENTS WITH CD?**

Specific recommendations concerning the preoperative assessment of laboratory values in CD patients are lacking in the BSG and ECCO guidelines[21,22]. Nevertheless, abnormal laboratory values in the preoperative setting have been associated with a dismal postoperative course in CD. Hypoalbuminemia (defined as serum albumin < 30 g/L) is one of the criteria for the diagnosis of (severe) malnutrition in general[74]. However, albumin is an acute-phase reactant protein and serum levels may decrease due to active inflammation[23]. Probably due to the chronic inflammatory state, serum albumin levels are lower in CD patients, as compared to the general population, and are reversely correlated to the disease activity[105]. Therefore, serum albumin is not a reliable marker for malnutrition in CD. Nevertheless, low serum albumin (ranging from < 29 g/L to 35 g/L) is associated with an increased risk of postoperative complications in CD patients[10,102,106-108]. These complications comprised overall early postoperative complications (< 30 d)[60,102,109-111], IASCs[10,106,112,113], SSIs[107,114], anastomotic leakage[88], and infectious complications[33,108,115].

Assessment of a full blood count, including hemoglobin and leucocyte and platelet counts, is advised in patients undergoing elective abdominal surgery[116]. The most important test seems to be that for hemoglobin, as anemia is present in up to 78% of patients requiring a surgical intervention[117]. Both a preoperative anemia (defined as < 10 g/dL)[9,37,106,108,118] and a lowered hemoglobin level (defined as lower than the reference value)[27,38,102,119] are associated with postoperative complications in CD patients. Iron deficiency anemia is the most common cause of anemia in the preoperative setting of CD. Preoperative IV iron therapy is highly effective to rapidly increase hemoglobin levels, and should be considered the first choice. Blood transfusion is a common practice to treat anemia when treatment for the underlying cause has been unsuccessful. Both intra- and perioperative blood transfusions have been associated with infectious- and/or non-infectious postoperative complications in CD patients, whereas a preoperative blood transfusion was not associated with postoperative complications[120-123].

Elevated levels of the inflammatory markers (*i.e.,* leucocyte count) are risk factors for postoperative complications[30,120,121,124]. Furthermore, a preoperative elevated CRP level has been associated significantly with overall postoperative complications[52,125-127], infectious complications[33,57,125-127], and SSIs[57]. It is known that the malabsorption of vitamins and other trace elements is prevalent in CD patients. Plasma concentrations are influenced by active disease or result from earlier intestinal resections. These micronutrient deficiencies comprise several vitamins (most often B6, B12, D, and K), iron, folic acid, selenium, and zinc. Micronutrient deficiencies are associated with a complicated course of disease[128]. For reliable assessment of body micronutrient status, the patient needs to be in biochemical remission. However, in cases of high suspicion due to deficiency-related complaints or malnutrition, assessment of these values is indicated[23,128].

***Reviewers’ opinion***

Although preoperative anemia, hypoalbuminemia, elevated CRP and elevated leucocyte count are associated with postoperative complications, CD-specific recommendations concerning the preoperative assessment of laboratory values and subsequent management cannot be derived from the current literature. Laboratory findings for vitamins and other trace elements are often disturbed in CD and may not reflect the actual nutritional status. These assessments only reflect the patient’s nutritional status when a patient is in remission. We recommend to assess full blood count, CRP and serum albumin preoperatively as predictive markers of a complicated postoperative course and to preoperatively correct iron deficiency anemia, in accordance with the ECCO guideline[21].

**CONCLUSION**

Nutritional status, medication and laboratory values are modifiable factors that influence the postoperative course of patients with CD. In addition, physical fitness is impaired in CD patients and may impact postoperative outcomes. As a lower preoperative physical fitness is associated with a higher risk for postoperative complications in other populations undergoing intestinal resection, further research into interventions in CD patients is warranted. Individualized multimodal prehabilitation programs aim to improve these modifiable risk factors before surgery, including smoking cessation and psychological screening and support, and should be integrated in the preoperative preparation period in order to reduce both postoperative complications and undesirable outcomes.

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**REFERENCES**

1 **Abraham C**, Cho JH. Inflammatory bowel disease. *N Engl J Med* 2009; **361**: 2066-2078 [PMID: 19923578 DOI: 10.1056/NEJMra0804647]

2 **Tsai L**, Ma C, Dulai PS, Prokop LJ, Eisenstein S, Ramamoorthy SL, Feagan BG, Jairath V, Sandborn WJ, Singh S. Contemporary Risk of Surgery in Patients With Ulcerative Colitis and Crohn's Disease: A Meta-Analysis of Population-Based Cohorts. *Clin Gastroenterol Hepatol* 2021; **19**: 2031-2045.e11 [PMID: 33127595 DOI: 10.1016/j.cgh.2020.10.039]

3 **Beelen EMJ**, van der Woude CJ, Pierik MJ, Hoentjen F, de Boer NK, Oldenburg B, van der Meulen AE, Ponsioen CIJ, Dijkstra G, Bruggink AH, Erler NS, Schouten WR, de Vries AC; Dutch Initiative on Crohn's and Colitis (ICC). Decreasing Trends in Intestinal Resection and Re-Resection in Crohn's Disease: A Nationwide Cohort Study. *Ann Surg* 2021; **273**: 557-563 [PMID: 31188225 DOI: 10.1097/SLA.0000000000003395]

4 **Menichetti J**, Fiorino G, Vegni E. Personalizing Psychological Treatment Along the IBD Journey: From Diagnosis to Surgery. *Curr Drug Targets* 2018; **19**: 722-728 [PMID: 28464774 DOI: 10.2174/1389450118666170502142939]

5 **de Groof EJ**, Stevens TW, Eshuis EJ, Gardenbroek TJ, Bosmans JE, van Dongen JM, Mol B, Buskens CJ, Stokkers PCF, Hart A, D'Haens GR, Bemelman WA, Ponsioen CY; LIR!C study group. Cost-effectiveness of laparoscopic ileocaecal resection versus infliximab treatment of terminal ileitis in Crohn's disease: the LIR!C Trial. *Gut* 2019; **68**: 1774-1780 [PMID: 31233395 DOI: 10.1136/gutjnl-2018-317539]

6 **Zangenberg MS**, Horesh N, Kopylov U, El-Hussuna A. Preoperative optimization of patients with inflammatory bowel disease undergoing gastrointestinal surgery: a systematic review. *Int J Colorectal Dis* 2017; **32**: 1663-1676 [PMID: 29051981 DOI: 10.1007/s00384-017-2915-4]

7 **SICCR Current status of Crohn’s disease surgery collaborative**. Surgical treatment of colonic Crohn's disease: a national snapshot study. *Langenbecks Arch Surg* 2021; **406**: 1165-1172 [PMID: 33263140 DOI: 10.1007/s00423-020-02038-z]

8 **Galata C**, Hodapp J, Weiß C, Karampinis I, Vassilev G, Reißfelder C, Otto M. Skeletal Muscle Mass Index Predicts Postoperative Complications in Intestinal Surgery for Crohn's Disease. *JPEN J Parenter Enteral Nutr* 2020; **44**: 714-721 [PMID: 31444789 DOI: 10.1002/jpen.1696]

9 **Brouquet A**, Maggiori L, Zerbib P, Lefevre JH, Denost Q, Germain A, Cotte E, Beyer-Berjot L, Munoz-Bongrand N, Desfourneaux V, Rahili A, Duffas JP, Pautrat K, Denet C, Bridoux V, Meurette G, Faucheron JL, Loriau J, Guillon F, Vicaut E, Benoist S, Panis Y; GETAID chirurgie group. Anti-TNF Therapy Is Associated With an Increased Risk of Postoperative Morbidity After Surgery for Ileocolonic Crohn Disease: Results of a Prospective Nationwide Cohort. *Ann Surg* 2018; **267**: 221-228 [PMID: 29300710 DOI: 10.1097/SLA.0000000000002017]

10 **Alves A**, Panis Y, Bouhnik Y, Pocard M, Vicaut E, Valleur P. Risk factors for intra-abdominal septic complications after a first ileocecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Dis Colon Rectum* 2007; **50**: 331-336 [PMID: 17252288 DOI: 10.1007/s10350-006-0782-0]

11 **Yamamoto T**, Spinelli A, Suzuki Y, Saad-Hossne R, Teixeira FV, de Albuquerque IC, da Silva RN, de Barcelos IF, Takeuchi K, Yamada A, Shimoyama T, da Silva Kotze LM, Sacchi M, Danese S, Kotze PG. Risk factors for complications after ileocolonic resection for Crohn's disease with a major focus on the impact of preoperative immunosuppressive and biologic therapy: A retrospective international multicentre study. *United European Gastroenterol J* 2016; **4**: 784-793 [PMID: 28408996 DOI: 10.1177/2050640615600116]

12 **Fumery M**, Seksik P, Auzolle C, Munoz-Bongrand N, Gornet JM, Boschetti G, Cotte E, Buisson A, Dubois A, Pariente B, Zerbib P, Chafai N, Stefanescu C, Panis Y, Marteau P, Pautrat K, Sabbagh C, Filippi J, Chevrier M, Houze P, Jouven X, Treton X, Allez M; REMIND study group investigators. Postoperative Complications after Ileocecal Resection in Crohn's Disease: A Prospective Study From the REMIND Group. *Am J Gastroenterol* 2017; **112**: 337-345 [PMID: 27958285 DOI: 10.1038/ajg.2016.541]

13 **Spinelli A**, Allocca M, Jovani M, Danese S. Review article: optimal preparation for surgery in Crohn's disease. *Aliment Pharmacol Ther* 2014; **40**: 1009-1022 [PMID: 25209947 DOI: 10.1111/apt.12947]

14 **Otto JM**, O'Doherty AF, Hennis PJ, Mitchell K, Pate JS, Cooper JA, Grocott MP, Montgomery HE. Preoperative exercise capacity in adult inflammatory bowel disease sufferers, determined by cardiopulmonary exercise testing. *Int J Colorectal Dis* 2012; **27**: 1485-1491 [PMID: 22842663 DOI: 10.1007/s00384-012-1533-4]

15 **West MA**, Asher R, Browning M, Minto G, Swart M, Richardson K, McGarrity L, Jack S, Grocott MP; Perioperative Exercise Testing and Training Society. Validation of preoperative cardiopulmonary exercise testing-derived variables to predict in-hospital morbidity after major colorectal surgery. *Br J Surg* 2016; **103**: 744-752 [PMID: 26914526 DOI: 10.1002/bjs.10112]

16 **Cuijpers ACM**, Heldens AFJM, Bours MJL, van Meeteren NLU, Stassen LPS, Lubbers T, Bongers BC. Relation between preoperative aerobic fitness estimated by steep ramp test performance and postoperative morbidity in colorectal cancer surgery: prospective observational study. *Br J Surg* 2022; **109**: 155-159 [PMID: 34536001 DOI: 10.1093/bjs/znab292]

17 **van Rooijen SJ**, Molenaar CJL, Schep G, van Lieshout RHMA, Beijer S, Dubbers R, Rademakers N, Papen-Botterhuis NE, van Kempen S, Carli F, Roumen RMH, Slooter GD. Making Patients Fit for Surgery: Introducing a Four Pillar Multimodal Prehabilitation Program in Colorectal Cancer. *Am J Phys Med Rehabil* 2019; **98**: 888-896 [PMID: 31090551 DOI: 10.1097/PHM.0000000000001221]

18 **Barberan-Garcia A**, Ubré M, Roca J, Lacy AM, Burgos F, Risco R, Momblán D, Balust J, Blanco I, Martínez-Pallí G. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. *Ann Surg* 2018; **267**: 50-56 [PMID: 28489682 DOI: 10.1097/SLA.0000000000002293]

19 **Berkel AEM**, Bongers BC, Kotte H, Weltevreden P, de Jongh FHC, Eijsvogel MMM, Wymenga M, Bigirwamungu-Bargeman M, van der Palen J, van Det MJ, van Meeteren NLU, Klaase JM. Effects of Community-based Exercise Prehabilitation for Patients Scheduled for Colorectal Surgery With High Risk for Postoperative Complications: Results of a Randomized Clinical Trial. *Ann Surg* 2022; **275**: e299-e306 [PMID: 33443905 DOI: 10.1097/SLA.0000000000004702]

20 **Bongers BC**, Dejong CHC, den Dulk M. Enhanced recovery after surgery programmes in older patients undergoing hepatopancreatobiliary surgery: what benefits might prehabilitation have? *Eur J Surg Oncol* 2021; **47**: 551-559 [PMID: 32253075 DOI: 10.1016/j.ejso.2020.03.211]

21 **Adamina M**, Bonovas S, Raine T, Spinelli A, Warusavitarne J, Armuzzi A, Bachmann O, Bager P, Biancone L, Bokemeyer B, Bossuyt P, Burisch J, Collins P, Doherty G, El-Hussuna A, Ellul P, Fiorino G, Frei-Lanter C, Furfaro F, Gingert C, Gionchetti P, Gisbert JP, Gomollon F, González Lorenzo M, Gordon H, Hlavaty T, Juillerat P, Katsanos K, Kopylov U, Krustins E, Kucharzik T, Lytras T, Maaser C, Magro F, Marshall JK, Myrelid P, Pellino G, Rosa I, Sabino J, Savarino E, Stassen L, Torres J, Uzzan M, Vavricka S, Verstockt B, Zmora O. ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Treatment. *J Crohns Colitis* 2020; **14**: 155-168 [PMID: 31742338 DOI: 10.1093/ecco-jcc/jjz187]

22 **Lamb CA**, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, Hayee B, Lomer MCE, Parkes GC, Selinger C, Barrett KJ, Davies RJ, Bennett C, Gittens S, Dunlop MG, Faiz O, Fraser A, Garrick V, Johnston PD, Parkes M, Sanderson J, Terry H; IBD guidelines eDelphi consensus group, Gaya DR, Iqbal TH, Taylor SA, Smith M, Brookes M, Hansen R, Hawthorne AB. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019; **68**: s1-s106 [PMID: 31562236 DOI: 10.1136/gutjnl-2019-318484]

23 **Adamina M**, Gerasimidis K, Sigall-Boneh R, Zmora O, de Buck van Overstraeten A, Campmans-Kuijpers M, Ellul P, Katsanos K, Kotze PG, Noor N, Schäfli-Thurnherr J, Vavricka S, Wall C, Wierdsma N, Yassin N, Lomer M. Perioperative Dietary Therapy in Inflammatory Bowel Disease. *J Crohns Colitis* 2020; **14**: 431-444 [PMID: 31550347 DOI: 10.1093/ecco-jcc/jjz160]

24 **Steed H**, Walsh S, Reynolds N. A brief report of the epidemiology of obesity in the inflammatory bowel disease population of Tayside, Scotland. *Obes Facts* 2009; **2**: 370-372 [PMID: 20090388 DOI: 10.1159/000262276]

25 **Tinsley A**, Ehrlich OG, Hwang C, Issokson K, Zapala S, Weaver A, Siegel CA, Melmed GY. Knowledge, Attitudes, and Beliefs Regarding the Role of Nutrition in IBD Among Patients and Providers. *Inflamm Bowel Dis* 2016; **22**: 2474-2481 [PMID: 27598738 DOI: 10.1097/MIB.0000000000000901]

26 **Grass F**, Ansell J, Petersen M, Mathis KL, Lightner AL. Risk factors for 90-day readmission and return to the operating room following abdominal operations for Crohn's disease. *Surgery* 2019; **166**: 1068-1075 [PMID: 31548096 DOI: 10.1016/j.surg.2019.08.006]

27 **Uchino M**, Ikeuchi H, Bando T, Chohno T, Sasaki H, Horio Y, Nakajima K, Takesue Y. Efficacy of Preoperative Oral Antibiotic Prophylaxis for the Prevention of Surgical Site Infections in Patients With Crohn Disease: A Randomized Controlled Trial. *Ann Surg* 2019; **269**: 420-426 [PMID: 29064884 DOI: 10.1097/SLA.0000000000002567]

28 **Krane MK**, Allaix ME, Zoccali M, Umanskiy K, Rubin MA, Villa A, Hurst RD, Fichera A. Does morbid obesity change outcomes after laparoscopic surgery for inflammatory bowel disease? Review of 626 consecutive cases. *J Am Coll Surg* 2013; **216**: 986-996 [PMID: 23523148 DOI: 10.1016/j.jamcollsurg.2013.01.053]

29 **Lightner AL**, Raffals LE, Mathis KL, Cima RR, Tse CS, Pemberton JH, Dozois EJ, Loftus EV. Postoperative Outcomes in Vedolizumab-Treated Patients Undergoing Abdominal Operations for Inflammatory Bowel Disease. *J Crohns Colitis* 2017; **11**: 185-190 [PMID: 27543504 DOI: 10.1093/ecco-jcc/jjw147]

30 **O'Brien SJ**, Chen RC, Stephen VT, Jorden J, Farmer R, Manek S, Schmidt M, Pan J, Rai SN, Galandiuk S. Preoperative Opioid Prescription Is Associated With Major Complications in Patients With Crohn's Disease Undergoing Elective Ileocolic Resection. *Dis Colon Rectum* 2020; **63**: 1090-1101 [PMID: 32015287 DOI: 10.1097/DCR.0000000000001571]

31 **Kulaylat AN**, Hollenbeak CS, Sangster W, Stewart DB Sr. Impact of smoking on the surgical outcome of Crohn's disease: a propensity-score matched National Surgical Quality Improvement Program analysis. *Colorectal Dis* 2015; **17**: 891-902 [PMID: 25808234 DOI: 10.1111/codi.12958]

32 **Zhang M**, Gao X, Chen Y, Zhi M, Chen H, Tang J, Su M, Yao J, Yang Q, Chen J, Hu P, Liu H, Min L. Body Mass Index Is a Marker of Nutrition Preparation Sufficiency Before Surgery for Crohn's Disease From the Perspective of Intra-Abdominal Septic Complications: A Retrospective Cohort Study. *Medicine (Baltimore)* 2015; **94**: 1 [PMID: 26334908 DOI: 10.1097/MD.0000000000001455]

33 **Zhu Y**, Zhou W, Qi W, Liu W, Chen M, Zhu H, Xiang J, Xie Q, Chen P. Body mass index is a practical preoperative nutritional index for postoperative infectious complications after intestinal resection in patients with Crohn's disease. *Medicine (Baltimore)* 2017; **96**: e7113 [PMID: 28591060 DOI: 10.1097/MD.0000000000007113]

34 **Hossne RS**, Sassaki LY, Baima JP, Meira Júnior JD, Campos LM. ANALYSIS OF RISK FACTORS AND POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH CROHN'S DISEASE. *Arq Gastroenterol* 2018; **55**: 252-257 [PMID: 30540087 DOI: 10.1590/S0004-2803.201800000-63]

35 **Nguyen GC**, Elnahas A, Jackson TD. The impact of preoperative steroid use on short-term outcomes following surgery for inflammatory bowel disease. *J Crohns Colitis* 2014; **8**: 1661-1667 [PMID: 25107847 DOI: 10.1016/j.crohns.2014.07.007]

36 **Alavi K**, Sturrock PR, Sweeney WB, Maykel JA, Cervera-Servin JA, Tseng J, Cook EF. A simple risk score for predicting surgical site infections in inflammatory bowel disease. *Dis Colon Rectum* 2010; **53**: 1480-1486 [PMID: 20940595 DOI: 10.1007/DCR.0b013e3181f1f0fd]

37 **Aydinli HH**, Aytac E, Remzi FH, Bernstein M, Grucela AL. Factors Associated with Short-Term Morbidity in Patients Undergoing Colon Resection for Crohn's Disease. *J Gastrointest Surg* 2018; **22**: 1434-1441 [PMID: 29663305 DOI: 10.1007/s11605-018-3763-4]

38 **Iesalnieks I**, Hoene M, Bittermann T, Schlitt HJ, Hackl C. Mechanical Bowel Preparation (MBP) Prior to Elective Colorectal Resections in Crohn's Disease Patients. *Inflamm Bowel Dis* 2018; **24**: 908-915 [PMID: 29529206 DOI: 10.1093/ibd/izx088]

39 **Cruz-Jentoft AJ**, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M; European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010; **39**: 412-423 [PMID: 20392703 DOI: 10.1093/ageing/afq034]

40 **Adams DW**, Gurwara S, Silver HJ, Horst SN, Beaulieu DB, Schwartz DA, Seidner DL. Sarcopenia Is Common in Overweight Patients with Inflammatory Bowel Disease and May Predict Need for Surgery. *Inflamm Bowel Dis* 2017; **23**: 1182-1186 [PMID: 28410342 DOI: 10.1097/MIB.0000000000001128]

41 **Ryan E**, McNicholas D, Creavin B, Kelly ME, Walsh T, Beddy D. Sarcopenia and Inflammatory Bowel Disease: A Systematic Review. *Inflamm Bowel Dis* 2019; **25**: 67-73 [PMID: 29889230 DOI: 10.1093/ibd/izy212]

42 **Erős A**, Soós A, Hegyi P, Szakács Z, Benke M, Szűcs Á, Hartmann P, Erőss B, Sarlós P. Sarcopenia as an independent predictor of the surgical outcomes of patients with inflammatory bowel disease: a meta-analysis. *Surg Today* 2020; **50**: 1138-1150 [PMID: 31617016 DOI: 10.1007/s00595-019-01893-8]

43 **Pedersen M**, Cromwell J, Nau P. Sarcopenia is a Predictor of Surgical Morbidity in Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2017; **23**: 1867-1872 [PMID: 28604415 DOI: 10.1097/MIB.0000000000001166]

44 **Sayer AA**, Robinson SM, Patel HP, Shavlakadze T, Cooper C, Grounds MD. New horizons in the pathogenesis, diagnosis and management of sarcopenia. *Age Ageing* 2013; **42**: 145-150 [PMID: 23315797 DOI: 10.1093/ageing/afs191]

45 **Kondrup J**, Allison SP, Elia M, Vellas B, Plauth M; Educational and Clinical Practice Committee, European Society of Parenteral and Enteral Nutrition (ESPEN). ESPEN guidelines for nutrition screening 2002. *Clin Nutr* 2003; **22**: 415-421 [PMID: 12880610 DOI: 10.1016/s0261-5614(03)00098-0]

46 **Elia M**. Screening for malnutrition: A multidisciplinary responsibility. Development and Use of the Malnutrition Universal Screening Tool (MUST) for Adults. Redditch: BAPEN**,** 2003

47 **Jensen GL**, Cederholm T, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, de Baptista GA, Barazzoni R, Blaauw R, Coats AJS, Crivelli A, Evans DC, Gramlich L, Fuchs-Tarlovsky V, Keller H, Llido L, Malone A, Mogensen KM, Morley JE, Muscaritoli M, Nyulasi I, Pirlich M, Pisprasert V, de van der Schueren M, Siltharm S, Singer P, Tappenden KA, Velasco N, Waitzberg DL, Yamwong P, Yu J, Compher C, Van Gossum A. GLIM Criteria for the Diagnosis of Malnutrition: A Consensus Report From the Global Clinical Nutrition Community. *JPEN J Parenter Enteral Nutr* 2019; **43**: 32-40 [PMID: 30175461 DOI: 10.1002/jpen.1440]

48 **Jansen I**, Prager M, Valentini L, Büning C. Inflammation-driven malnutrition: a new screening tool predicts outcome in Crohn's disease. *Br J Nutr* 2016; **116**: 1061-1067 [PMID: 27546478 DOI: 10.1017/S0007114516003044]

49 **Haskey N**, Peña-Sánchez JN, Jones JL, Fowler SA. Development of a screening tool to detect nutrition risk in patients with inflammatory bowel disease. *Asia Pac J Clin Nutr* 2018; **27**: 756-762 [PMID: 30045418 DOI: 10.6133/apjcn.112017.01]

50 **Fiorindi C**, Luceri C, Dragoni G, Piemonte G, Scaringi S, Staderini F, Nannoni A, Ficari F, Giudici F. GLIM Criteria for Malnutrition in Surgical IBD Patients: A Pilot Study. *Nutrients* 2020; **12** [PMID: 32722435 DOI: 10.3390/nu12082222]

51 **Jian-Hui C**, Iskandar EA, Cai ShI, Chen CQ, Wu H, Xu JB, He YL. Significance of Onodera's prognostic nutritional index in patients with colorectal cancer: a large cohort study in a single Chinese institution. *Tumour Biol* 2016; **37**: 3277-3283 [PMID: 26438061 DOI: 10.1007/s13277-015-4008-8]

52 **Zhou W**, Cao Q, Qi W, Xu Y, Liu W, Xiang J, Xia B. Prognostic Nutritional Index Predicts Short-Term Postoperative Outcomes After Bowel Resection for Crohn's Disease. *Nutr Clin Pract* 2017; **32**: 92-97 [PMID: 27566600 DOI: 10.1177/0884533616661844]

53 **Maeda K**, Nagahara H, Shibutani M, Otani H, Sakurai K, Toyokawa T, Tanaka H, Kubo N, Muguruma K, Kamata N, Yamagami H, Hirakawa K. A preoperative low nutritional prognostic index correlates with the incidence of incisional surgical site infections after bowel resection in patients with Crohn's disease. *Surg Today* 2015; **45**: 1366-1372 [PMID: 25319215 DOI: 10.1007/s00595-014-1044-8]

54 **Kang WM**, Zhu CZ, Yang XX, Yu JC, Ma ZQ, Ye X, Li K, Liu D. Application of the Onodera prognostic nutrition index and neutrophil-to-lymphocyte ratio in risk evaluation of postoperative complications in Crohn's disease. *Sci Rep* 2017; **7**: 8481 [PMID: 28814767 DOI: 10.1038/s41598-017-09265-3]

55 **Bertin B**, Desreumaux P, Dubuquoy L. Obesity, visceral fat and Crohn's disease. *Curr Opin Clin Nutr Metab Care* 2010; **13**: 574-580 [PMID: 20625283 DOI: 10.1097/MCO.0b013e32833cf0f4]

56 **Erhayiem B**, Dhingsa R, Hawkey CJ, Subramanian V. Ratio of visceral to subcutaneous fat area is a biomarker of complicated Crohn's disease. *Clin Gastroenterol Hepatol* 2011; **9**: 684-687.e1 [PMID: 21642015 DOI: 10.1016/j.cgh.2011.05.005]

57 **Cai X**, Shen W, Guo Z, Li Y, Cao L, Gong J, Zhu W. Thickness of Subcutaneous Fat Is a Predictive Factor of Incisional Surgical Site Infection in Crohn's Disease Surgery: A Retrospective Study. *Gastroenterol Res Pract* 2018; **2018**: 1546075 [PMID: 30140279 DOI: 10.1155/2018/1546075]

58 **Connelly TM**, Juza RM, Sangster W, Sehgal R, Tappouni RF, Messaris E. Volumetric fat ratio and not body mass index is predictive of ileocolectomy outcomes in Crohn's disease patients. *Dig Surg* 2014; **31**: 219-224 [PMID: 25277149 DOI: 10.1159/000365359]

59 **Ding Z**, Wu XR, Remer EM, Lian L, Stocchi L, Li Y, McCullough A, Remzi FH, Shen B. Association between high visceral fat area and postoperative complications in patients with Crohn's disease following primary surgery. *Colorectal Dis* 2016; **18**: 163-172 [PMID: 26391914 DOI: 10.1111/codi.13128]

60 **Zhang T**, Cao L, Cao T, Yang J, Gong J, Zhu W, Li N, Li J. Prevalence of Sarcopenia and Its Impact on Postoperative Outcome in Patients With Crohn's Disease Undergoing Bowel Resection. *JPEN J Parenter Enteral Nutr* 2017; **41**: 592-600 [PMID: 26471990 DOI: 10.1177/0148607115612054]

61 **Wiroth JB**, Filippi J, Schneider SM, Al-Jaouni R, Horvais N, Gavarry O, Bermon S, Hébuterne X. Muscle performance in patients with Crohn's disease in clinical remission. *Inflamm Bowel Dis* 2005; **11**: 296-303 [PMID: 15735436 DOI: 10.1097/01.mib.0000160810.76729.9c]

62 **Brevinge H**, Berglund B, Bosaeus I, Tölli J, Nordgren S, Lundholm K. Exercise capacity in patients undergoing proctocolectomy and small bowel resection for Crohn's disease. *Br J Surg* 1995; **82**: 1040-1045 [PMID: 7648147 DOI: 10.1002/bjs.1800820813]

63 **van Langenberg DR**, Papandony MC, Gibson PR. Sleep and physical activity measured by accelerometry in Crohn's disease. *Aliment Pharmacol Ther* 2015; **41**: 991-1004 [PMID: 25783784 DOI: 10.1111/apt.13160]

64 **Mack DE**, Wilson PM, Gilmore JC, Gunnell KE. Leisure-time physical activity in Canadians living with Crohn disease and ulcerative colitis: population-based estimates. *Gastroenterol Nurs* 2011; **34**: 288-294 [PMID: 21814062 DOI: 10.1097/SGA.0b013e3182248732]

65 **Hlatky MA**, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, Cobb FR, Pryor DB. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 1989; **64**: 651-654 [PMID: 2782256 DOI: 10.1016/0002-9149(89)90496-7]

66 **McAuley P**, Myers J, Abella J, Froelicher V. Evaluation of a specific activity questionnaire to predict mortality in men referred for exercise testing. *Am Heart J* 2006; **151**: 890.e1-890.e7 [PMID: 16569555 DOI: 10.1016/j.ahj.2005.09.017]

67 **Tran D**. Cardiopulmonary Exercise Testing. *Methods Mol Biol* 2018; **1735**: 285-295 [PMID: 29380321 DOI: 10.1007/978-1-4939-7614-0\_18]

68 **Weemaes ATR**, Beelen M, Bongers BC, Weijenberg MP, Lenssen AF. Criterion Validity and Responsiveness of the Steep Ramp Test to Evaluate Aerobic Capacity in Survivors of Cancer Participating in a Supervised Exercise Rehabilitation Program. *Arch Phys Med Rehabil* 2021; **102**: 2150-2156 [PMID: 34023324 DOI: 10.1016/j.apmr.2021.04.016]

69 **van Erp LW**, Roosenboom B, Komdeur P, Dijkstra-Heida W, Wisse J, Horjus Talabur Horje CS, Liem CS, van Cingel REH, Wahab PJ, Groenen MJM. Improvement of Fatigue and Quality of Life in Patients with Quiescent Inflammatory Bowel Disease Following a Personalized Exercise Program. *Dig Dis Sci* 2021; **66**: 597-604 [PMID: 32239380 DOI: 10.1007/s10620-020-06222-5]

70 **Ng V**, Millard W, Lebrun C, Howard J. Low-intensity exercise improves quality of life in patients with Crohn's disease. *Clin J Sport Med* 2007; **17**: 384-388 [PMID: 17873551 DOI: 10.1097/JSM.0b013e31802b4fda]

71 **Loudon CP**, Corroll V, Butcher J, Rawsthorne P, Bernstein CN. The effects of physical exercise on patients with Crohn's disease. *Am J Gastroenterol* 1999; **94**: 697-703 [PMID: 10086654 DOI: 10.1111/j.1572-0241.1999.00939.x]

72 **Pérez CA**. Prescription of physical exercise in Crohn's disease. *J Crohns Colitis* 2009; **3**: 225-231 [PMID: 21172280 DOI: 10.1016/j.crohns.2009.08.006]

73 **Bilski J**, Brzozowski B, Mazur-Bialy A, Sliwowski Z, Brzozowski T. The role of physical exercise in inflammatory bowel disease. *Biomed Res Int* 2014; **2014**: 429031 [PMID: 24877092 DOI: 10.1155/2014/429031]

74 **Weimann A**, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, Laviano A, Ljungqvist O, Lobo DN, Martindale R, Waitzberg DL, Bischoff SC, Singer P. ESPEN guideline: Clinical nutrition in surgery. *Clin Nutr* 2017; **36**: 623-650 [PMID: 28385477 DOI: 10.1016/j.clnu.2017.02.013]

75 **Burden S**, Todd C, Hill J, Lal S. Pre-operative nutrition support in patients undergoing gastrointestinal surgery. *Cochrane Database Syst Rev* 2012; **11**: CD008879 [PMID: 23152265 DOI: 10.1002/14651858.CD008879.pub2]

76 **Brennan GT**, Ha I, Hogan C, Nguyen E, Jamal MM, Bechtold ML, Nguyen DL. Does preoperative enteral or parenteral nutrition reduce postoperative complications in Crohn's disease patients: a meta-analysis. *Eur J Gastroenterol Hepatol* 2018; **30**: 997-1002 [PMID: 29738326 DOI: 10.1097/MEG.0000000000001162]

77 **Grass F**, Pache B, Martin D, Hahnloser D, Demartines N, Hübner M. Preoperative Nutritional Conditioning of Crohn's Patients-Systematic Review of Current Evidence and Practice. *Nutrients* 2017; **9** [PMID: 28587182 DOI: 10.3390/nu9060562]

78 **Ruemmele FM**, Veres G, Kolho KL, Griffiths A, Levine A, Escher JC, Amil Dias J, Barabino A, Braegger CP, Bronsky J, Buderus S, Martín-de-Carpi J, De Ridder L, Fagerberg UL, Hugot JP, Kierkus J, Kolacek S, Koletzko S, Lionetti P, Miele E, Navas López VM, Paerregaard A, Russell RK, Serban DE, Shaoul R, Van Rheenen P, Veereman G, Weiss B, Wilson D, Dignass A, Eliakim A, Winter H, Turner D; European Crohn's and Colitis Organisation; European Society of Pediatric Gastroenterology, Hepatology and Nutrition. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. *J Crohns Colitis* 2014; **8**: 1179-1207 [PMID: 24909831 DOI: 10.1016/j.crohns.2014.04.005]

79 **Logan M**, Gkikas K, Svolos V, Nichols B, Milling S, Gaya DR, Seenan JP, Macdonald J, Hansen R, Ijaz UZ, Russell RK, Gerasimidis K. Analysis of 61 exclusive enteral nutrition formulas used in the management of active Crohn's disease-new insights into dietary disease triggers. *Aliment Pharmacol Ther* 2020; **51**: 935-947 [PMID: 32249975 DOI: 10.1111/apt.15695]

80 **Heerasing N**, Thompson B, Hendy P, Heap GA, Walker G, Bethune R, Mansfield S, Calvert C, Kennedy NA, Ahmad T, Goodhand JR. Exclusive enteral nutrition provides an effective bridge to safer interval elective surgery for adults with Crohn's disease. *Aliment Pharmacol Ther* 2017; **45**: 660-669 [PMID: 28105752 DOI: 10.1111/apt.13934]

81 **Yamamoto T**, Nakahigashi M, Umegae S, Kitagawa T, Matsumoto K. Impact of elemental diet on mucosal inflammation in patients with active Crohn's disease: cytokine production and endoscopic and histological findings. *Inflamm Bowel Dis* 2005; **11**: 580-588 [PMID: 15905706 DOI: 10.1097/01.mib.0000161307.58327.96]

82 **Horwat P**, Kopeć S, Garczyk A, Kaliciak I, Staręga Z, Drogowski K, Mardas M, Stelmach-Mardas M. Influence of Enteral Nutrition on Gut Microbiota Composition in Patients with Crohn's Disease: A Systematic Review. *Nutrients* 2020; **12** [PMID: 32842543 DOI: 10.3390/nu12092551]

83 **Ge X**, Tang S, Yang X, Liu W, Ye L, Yu W, Xu H, Cao Q, Zhou W, Cai X. The role of exclusive enteral nutrition in the preoperative optimization of laparoscopic surgery for patients with Crohn's disease: A cohort study. *Int J Surg* 2019; **65**: 39-44 [PMID: 30905758 DOI: 10.1016/j.ijsu.2019.03.012]

84 **Li Y**, Zuo L, Zhu W, Gong J, Zhang W, Gu L, Guo Z, Cao L, Li N, Li J. Role of exclusive enteral nutrition in the preoperative optimization of patients with Crohn's disease following immunosuppressive therapy. *Medicine (Baltimore)* 2015; **94**: e478 [PMID: 25654387 DOI: 10.1097/MD.0000000000000478]

85 **Wang H**, Zuo L, Zhao J, Dong J, Li Y, Gu L, Gong J, Liu Q, Zhu W. Impact of Preoperative Exclusive Enteral Nutrition on Postoperative Complications and Recurrence After Bowel Resection in Patients with Active Crohn's Disease. *World J Surg* 2016; **40**: 1993-2000 [PMID: 26940580 DOI: 10.1007/s00268-016-3488-z]

86 **Li G**, Ren J, Wang G, Hu D, Gu G, Liu S, Ren H, Wu X, Li J. Preoperative exclusive enteral nutrition reduces the postoperative septic complications of fistulizing Crohn's disease. *Eur J Clin Nutr* 2014; **68**: 441-446 [PMID: 24549026 DOI: 10.1038/ejcn.2014.16]

87 **Zhu F**, Li Y, Guo Z, Cao L, Feng D, Zhang T, Zhu W, Gong J. Nomogram to Predict Postoperative Intra-abdominal Septic Complications After Bowel Resection and Primary Anastomosis for Crohn's Disease. *Dis Colon Rectum* 2020; **63**: 629-638 [PMID: 32032204 DOI: 10.1097/DCR.0000000000001602]

88 **Guo Z**, Guo D, Gong J, Zhu W, Zuo L, Sun J, Li N, Li J. Preoperative Nutritional Therapy Reduces the Risk of Anastomotic Leakage in Patients with Crohn's Disease Requiring Resections. *Gastroenterol Res Pract* 2016; **2016**: 5017856 [PMID: 26858749 DOI: 10.1155/2016/5017856]

89 **Jacobson S**. Early postoperative complications in patients with Crohn's disease given and not given preoperative total parenteral nutrition. *Scand J Gastroenterol* 2012; **47**: 170-177 [PMID: 22242614 DOI: 10.3109/00365521.2011.648954]

90 **Ayoub F**, Kamel AY, Ouni A, Chaudhry N, Ader Y, Tan S, Iqbal A, Zimmermann EM, Glover SC. Pre-operative total parenteral nutrition improves post-operative outcomes in a subset of Crohn's disease patients undergoing major abdominal surgery. *Gastroenterol Rep (Oxf)* 2019; **7**: 107-114 [PMID: 30976423 DOI: 10.1093/gastro/goy033]

91 **Lashner BA**, Evans AA, Hanauer SB. Preoperative total parenteral nutrition for bowel resection in Crohn's disease. *Dig Dis Sci* 1989; **34**: 741-746 [PMID: 2496960 DOI: 10.1007/BF01540346]

92 **Attar A**, Messing B. Evidence-based prevention of catheter infection during parenteral nutrition. *Curr Opin Clin Nutr Metab Care* 2001; **4**: 211-218 [PMID: 11517355 DOI: 10.1097/00075197-200105000-00008]

93 **Law CC**, Bell C, Koh D, Bao Y, Jairath V, Narula N. Risk of postoperative infectious complications from medical therapies in inflammatory bowel disease. *Cochrane Database Syst Rev* 2020; **10**: CD013256 [PMID: 33098570 DOI: 10.1002/14651858.CD013256.pub2]

94 **Myrelid P**, Olaison G, Sjödahl R, Nyström PO, Almer S, Andersson P. Thiopurine therapy is associated with postoperative intra-abdominal septic complications in abdominal surgery for Crohn's disease. *Dis Colon Rectum* 2009; **52**: 1387-1394 [PMID: 19617749 DOI: 10.1007/DCR.0b013e3181a7ba96]

95 **Yu CS**, Jung SW, Lee JL, Lim SB, Park IJ, Yoon YS, Kim CW, Yang SK, Ye BD, Park SH, Han M, Kim JC. The Influence of Preoperative Medications on Postoperative Complications in Patients After Intestinal Surgery for Crohn's Disease. *Inflamm Bowel Dis* 2019; **25**: 1559-1568 [PMID: 30753560 DOI: 10.1093/ibd/izz010]

96 **Lightner AL**, Mathis KL, Tse CS, Pemberton JH, Shen B, Kochhar G, Singh A, Dulai PS, Eisenstein S, Sandborn WJ, Parry L, Stringfield S, Hudesman D, Remzi F, Loftus EV Jr. Postoperative Outcomes in Vedolizumab-Treated Patients Undergoing Major Abdominal Operations for Inflammatory Bowel Disease: Retrospective Multicenter Cohort Study. *Inflamm Bowel Dis* 2018; **24**: 871-876 [PMID: 29509927 DOI: 10.1093/ibd/izx076]

97 **Lightner AL**, McKenna NP, Alsughayer A, Harmsen WS, Taparra K, Parker ME, Raffals LE, Loftus EV Jr. Biologics and 30-Day Postoperative Complications After Abdominal Operations for Crohn's Disease: Are There Differences in the Safety Profiles? *Dis Colon Rectum* 2019; **62**: 1352-1362 [PMID: 31567927 DOI: 10.1097/DCR.0000000000001482]

98 **Novello M**, Stocchi L, Holubar S, Shawki S, Lipman J, Gorgun E, Hull T, Steele SR. Surgical outcomes of patients treated with ustekinumab vs. vedolizumab in inflammatory bowel disease: a matched case analysis. *Int J Colorectal Dis* 2019; **34**: 451-457 [PMID: 30535559 DOI: 10.1007/s00384-018-3212-6]

99 **Parrish AB**, Lopez NE, Truong A, Zaghiyan K, Melmed GY, McGovern DPB, Ha C, Syal G, Bonthala N, Jain A, Landers CJ, Targan SR, Fleshner P. Preoperative Serum Vedolizumab Levels Do Not Impact Postoperative Outcomes in Inflammatory Bowel Disease. *Dis Colon Rectum* 2021; **64**: 1259-1266 [PMID: 34516445 DOI: 10.1097/DCR.0000000000001920]

100 **Kotze PG**, Ma C, Mckenna N, Almutairdi A, Kaplan GG, Raffals LE, Loftus EV Jr, Panaccione R, Lightner AL. Vedolizumab and early postoperative complications in nonintestinal surgery: a case-matched analysis. *Therap Adv Gastroenterol* 2018; **11**: 1756284818783614 [PMID: 29977340 DOI: 10.1177/1756284818783614]

101 **Park KT**, Sceats L, Dehghan M, Trickey AW, Wren A, Wong JJ, Bensen R, Limketkai BN, Keyashian K, Kin C. Risk of post-operative surgical site infections after vedolizumab vs anti-tumour necrosis factor therapy: a propensity score matching analysis in inflammatory bowel disease. *Aliment Pharmacol Ther* 2018; **48**: 340-346 [PMID: 29876995 DOI: 10.1111/apt.14842]

102 **Yamada A**, Komaki Y, Patel N, Komaki F, Aelvoet AS, Tran AL, Pekow J, Dalal S, Cohen RD, Cannon L, Umanskiy K, Smith R, Hurst R, Hyman N, Rubin DT, Sakuraba A. Risk of Postoperative Complications Among Inflammatory Bowel Disease Patients Treated Preoperatively With Vedolizumab. *Am J Gastroenterol* 2017; **112**: 1423-1429 [PMID: 28719595 DOI: 10.1038/ajg.2017.201]

103 **Shim HH**, Ma C, Kotze PG, Seow CH, Al-Farhan H, Al-Darmaki AK, Pang JXQ, Fedorak RN, Devlin SM, Dieleman LA, Kaplan GG, Novak KL, Kroeker KI, Halloran BP, Panaccione R. Preoperative Ustekinumab Treatment Is Not Associated With Increased Postoperative Complications in Crohn's Disease: A Canadian Multi-Centre Observational Cohort Study. *J Can Assoc Gastroenterol* 2018; **1**: 115-123 [PMID: 31294352 DOI: 10.1093/jcag/gwy013]

104 **Dutch National Institute for Public Health and the Environment**. National guidelines for vaccination in chronic inflammatory diseases. 2019. [cited 11 December 2021]. Available from: https://lci.rivm.nl/richtlijnen/vaccinatie-bij-chronisch-inflammatoire-aandoeningen

105 **Su Q**, Li X, Mo W, Yang Z. Low serum bilirubin, albumin, and uric acid levels in patients with Crohn's disease. *Medicine (Baltimore)* 2019; **98**: e15664 [PMID: 31083269 DOI: 10.1097/MD.0000000000015664]

106 **Morar PS**, Hodgkinson JD, Thalayasingam S, Koysombat K, Purcell M, Hart AL, Warusavitarne J, Faiz O. 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**: 483-491 [PMID: 25796553 DOI: 10.1093/ecco-jcc/jjv051]

107 **Uchino M**, Ikeuchi H, Matsuoka H, Bando T, Ichiki K, Nakajima K, Tomita N, Takesue Y. Risk factors for surgical site infection and association with infliximab administration during surgery for Crohn's disease. *Dis Colon Rectum* 2013; **56**: 1156-1165 [PMID: 24022533 DOI: 10.1097/DCR.0b013e31829f682c]

108 **Nguyen GC**, Du L, Chong RY, Jackson TD. Hypoalbuminaemia and Postoperative Outcomes in Inflammatory Bowel Disease: the NSQIP Surgical Cohort. *J Crohns Colitis* 2019; **13**: 1433-1438 [PMID: 31253985 DOI: 10.1093/ecco-jcc/jjz083]

109 **Ge X**, Liu H, Tang S, Wu Y, Pan Y, Liu W, Qi W, Ye L, Cao Q, Zhou W. Preoperative hypoalbuminemia is an independent risk factor for postoperative complications in Crohn's disease patients with normal BMI: A cohort study. *Int J Surg* 2020; **79**: 294-299 [PMID: 32505647 DOI: 10.1016/j.ijsu.2020.05.064]

110 **Galata C**, Kienle P, Weiss C, Seyfried S, Reißfelder C, Hardt J. Risk factors for early postoperative complications in patients with Crohn's disease after colorectal surgery other than ileocecal resection or right hemicolectomy. *Int J Colorectal Dis* 2019; **34**: 293-300 [PMID: 30460473 DOI: 10.1007/s00384-018-3196-2]

111 **Li Y**, Zuo L, Zhu W, Gong J, Zhang W, Gu L, Guo Z, Li N, Li J. The impact of bacterial DNA translocation on early postoperative outcomes in Crohn's patients undergoing abdominal surgery. *J Crohns Colitis* 2015; **9**: 259-265 [PMID: 25555386 DOI: 10.1093/ecco-jcc/jju029]

112 **Liu X**, Wu X, Zhou C, Hu T, Ke J, Chen Y, He X, Zheng X, He X, Hu J, Zhi M, Gao X, Hu P, Wu X, Lan P. Preoperative hypoalbuminemia is associated with an increased risk for intra-abdominal septic complications after primary anastomosis for Crohn's disease. *Gastroenterol Rep (Oxf)* 2017; **5**: 298-304 [PMID: 29230300 DOI: 10.1093/gastro/gox002]

113 **Kotze PG**, Saab MP, Saab B, da Silva Kotze LM, Olandoski M, Pinheiro LV, Martinez CA, Ayrizono ML, Magro DO, Coy CS. Tumor Necrosis Factor Alpha Inhibitors Did Not Influence Postoperative Morbidity After Elective Surgical Resections in Crohn's Disease. *Dig Dis Sci* 2017; **62**: 456-464 [PMID: 27933472 DOI: 10.1007/s10620-016-4400-2]

114 **Liu S**, Miao J, Wang G, Wang M, Wu X, Guo K, Feng M, Guan W, Ren J. Risk factors for postoperative surgical site infections in patients with Crohn's disease receiving definitive bowel resection. *Sci Rep* 2017; **7**: 9828 [PMID: 28852175 DOI: 10.1038/s41598-017-10603-8]

115 **Higgens C**, Allan RN, Keighley MR, Arabi Y, Alexander-Williams J. Sepsis following operation for inflammatory intestinal disease. *Dis Colon Rectum* 1980; **23**: 102-105 [PMID: 7379654 DOI: 10.1007/BF02587605]

116 Routine preoperative tests for elective surgery: © NICE (2016) Routine preoperative tests for elective surgery. *BJU Int* 2018; **121**: 12-16 [PMID: 29314537 DOI: 10.1111/bju.14079]

117 **Hans GA,** Jones N. Preoperative anaemia. *BJA Education* 2013; **13**: 71-74 [DOI: 10.1093/bjaceaccp/mks064]

118 **Novello M**, Stocchi L, Steele SR, Holubar SD, Duraes LC, Kessler H, Shawki S, Hull LT. Case-matched Comparison of Postoperative Outcomes Following Surgery for Inflammatory Bowel Disease After Exposure to Vedolizumab vs Other Biologics. *J Crohns Colitis* 2020; **14**: 185-191 [PMID: 31328222 DOI: 10.1093/ecco-jcc/jjz129]

119 **Michailidou M**, Nfonsam VN. Preoperative anemia and outcomes in patients undergoing surgery for inflammatory bowel disease. *Am J Surg* 2018; **215**: 78-81 [PMID: 28359559 DOI: 10.1016/j.amjsurg.2017.02.016]

120 **Rahal MA**, Karaoui WR, Mailhac A, Tamim H, Shaib Y. Surgical outcomes among inflammatory bowel disease patients undergoing colectomy : results from a national database. *Acta Gastroenterol Belg* 2018; **81**: 387-392 [PMID: 30350526 DOI: 10.1016/S0016-5085(17)31469-5]

121 **Li Y**, Stocchi L, Rui Y, Liu G, Gorgun E, Remzi FH, Shen B. Perioperative Blood Transfusion and Postoperative Outcome in Patients with Crohn's Disease Undergoing Primary Ileocolonic Resection in the "Biological Era". *J Gastrointest Surg* 2015; **19**: 1842-1851 [PMID: 26286365 DOI: 10.1007/s11605-015-2893-1]

122 **Moon T**, Smith A, Pak T, Park BH, Beutler SS, Brown T, Kaye AD, Urman RD. Preoperative Anemia Treatment with Intravenous Iron Therapy in Patients Undergoing Abdominal Surgery: A Systematic Review. *Adv Ther* 2021; **38**: 1447-1469 [PMID: 33580485 DOI: 10.1007/s12325-021-01628-7]

123 **Miller JL**. Iron deficiency anemia: a common and curable disease. *Cold Spring Harb Perspect Med* 2013; **3** [PMID: 23613366 DOI: 10.1101/cshperspect.a011866]

124 **Galata C**, Weiss C, Hardt J, Seyfried S, Post S, Kienle P, Horisberger K. Risk factors for early postoperative complications and length of hospital stay in ileocecal resection and right hemicolectomy for Crohn's disease: a single-center experience. *Int J Colorectal Dis* 2018; **33**: 937-945 [PMID: 29736773 DOI: 10.1007/s00384-018-3072-0]

125 **Riss S**, Bittermann C, Schwameis K, Kristo I, Mittlböck M, Herbst F, Stift A. Determinants for postoperative complications after laparoscopic intestinal resection for Crohn's disease. *Surg Endosc* 2012; **26**: 933-938 [PMID: 22002203 DOI: 10.1007/s00464-011-1970-0]

126 **Zhang W**, Zhu W, Ren J, Zuo L, Wu X, Li J. Skeletal muscle percentage: a protective factor for postoperative morbidity in Crohn's disease patients with severe malnutrition. *J Gastrointest Surg* 2015; **19**: 715-721 [PMID: 25666099 DOI: 10.1007/s11605-015-2763-x]

127 **Tang S**, Dong X, Liu W, Qi W, Ye L, Yang X, Cao Q, Ge X, Zhou W. Compare risk factors associated with postoperative infectious complication in Crohn's disease with and without preoperative infliximab therapy: a cohort study. *Int J Colorectal Dis* 2020; **35**: 727-737 [PMID: 32060607 DOI: 10.1007/s00384-019-03481-1]

128 **Weisshof R**, Chermesh I. Micronutrient deficiencies in inflammatory bowel disease. *Curr Opin Clin Nutr Metab Care* 2015; **18**: 576-581 [PMID: 26418823 DOI: 10.1097/MCO.0000000000000226]

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**Table 1 Recommendations on screening for prehabilitation prior to intestinal surgery in Crohn’s disease**

|  |  |
| --- | --- |
| **Screening** | |
| Nutritional status | Screening in all patients: Body mass index, evaluation of unintentional weight loss and assessment of dietary intake with nutritional or immunological screening tools (*e.g.,* GLIM and OPNI). Preferably assess the muscle mass (*e.g.,* with handgrip strength or consider available imaging techniques) to complement the measures of nutritional status |
| Physical fitness | Screening in all patients to estimate aerobic fitness with validated self-reporting questionnaire (*e.g.,* Duke activity status index, veterans-specific activity questionnaire). Consider referral of patients at risk for impaired physical fitness for comprehensive objective assessment by an exercise specialist |
| CD medication | Critically revise all current CD medication on a case-by-case basis |
| Laboratory assessment | Preoperative assessment of full blood count, CRP, and serum albumin. Assessment of vitamins and other trace elements may only be indicative in patients with biochemical remission |
| Smoking psychological status | Screen all patients on active smoking |
| Discussion of expectations and potential fears for the perioperative course by treating physicians IBD team members |

CD: Crohn’s disease; CRP: C-reactive protein; GLIM: Global Leadership Initiative on Malnutrition; IBD: Inflammatory bowel disease; OPNI: Onodera’s prognostic nutritional index.

**Table 2 Recommendations for prehabilitation interventions prior to intestinal surgery in Crohn’s disease**

|  |  |
| --- | --- |
| **Intervention** |  |
| Nutritional | Nutritional support may be considered in case of impaired nutritional status and/or inadequate intake with regard to proteins and calories. Minimum duration of nutritional support is 1-2 wk and may be extended to 6-8 wk to fully benefit from the dietary intervention. EEN may be considered as nutritional support for immunomodulatory effect and reduction of postoperative complications. TPN seems a valid option only when enteral nutrition is contraindicated, not effective or tolerated |
| Physical fitness | Physical exercise (aerobic activity and muscular resistance training may be considered to improve physical fitness in the preoperative course. High-intensity physical exercise should be avoided due to risk of exacerbation of inflammation and symptoms |
| CD medication | Wean off corticosteroids to a minimal dose (preferably < 20 mg) 6 wk prior to surgery. Consider cessation of anti-TNF-α agents (especially in case of therapy-refractory disease). If considered, a time-interval of 4 wk (ADA) or 6-8 wk (IFX) seems appropriate |
| Laboratory assessment | Preoperative intravenous iron therapy is recommended in case of iron deficiency anemia in the preoperative course. In case of hypoalbuminemia and an impaired nutritional status, nutritional support is advised (see nutritional and physical status) |
| Smoking | Preoperative cessation is recommended (*e.g.,* within smoking cessation program) |
| Psychological status | Provide individualized psychosocial support or refer to psychologist |

CD: Crohn’s disease; ADA: Adalimumab; EEN: Exclusive enteral nutrition; IFX: Infliximab; TNF-α: Tumor necrosis factor-alpha; TPN: Total parenteral nutrition.