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ECCO Topical Review: Roadmap to optimal peri-operative care in IBD

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Abstract

Background and aims:

Despite the advances in medical therapies, a significant proportion of patients with inflammatory bowel diseases (IBD) require surgical intervention. This Topical Review aims to offer expert consensus practice recommendations for peri-operative care to optimise outcomes of IBD patients who undergo surgery.

Methods:

A multidisciplinary panel of IBD health care providers systematically reviewed aspects relevant to peri-operative care in IBD. Consensus statements were developed using Delphi methodology.

Results:

A total of 20 current practice positions were developed following systematic review of the current literature covering use of medication in the peri-operative period, nutritional assessment and intervention, physical and psychological rehabilitation and prehabilitation and immediate postoperative care.

Conclusion:

Peri-operative planning and optimization of the patient are imperative to ensure favourable outcomes and reduced morbidity. This Topical Review provides practice recommendations applicable in the peri-operative period in IBD patients undergoing surgery.

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1. Introduction

Over the last two decades there has been a significant expansion in medical therapeutic options for patients with inflammatory bowel disease (IBD) and more are on the horizon. These newer therapeutic strategies have only modestly reduced the surgery rates in ulcerative colitis (UC) and Crohn's disease (CD) in the last 25 years (1,2). Thus, surgery remains an integral part of the multidisciplinary management in a significant proportion of patients with IBD.

Most patients with IBD undergoing surgery have concomitant treatment with medications such as steroids, immunomodulators, biologics or small molecules. There are understandable concerns for patients and healthcare professionals (3) regarding the risks associated with pre-operative therapy, such as potential increase in morbidity, infection risk and poorer wound healing, but these risks should be balanced against the risk of disease flare when the medications are withheld in the peri-operative period (4).

Pre-operative nutritional status is another important factor impacting postoperative morbidity and mortality (5,6). Focussed nutritional interventional strategies such as pre-operative nutrition, immunonutrition and correction of anaemia are emerging in elective gastrointestinal surgery (7,8,9).

In addition to physical health, there is a recognised negative impact of IBD on psychological health (10), which may be further exacerbated in the immediate peri-operative period (11). Furthermore, there is increasing interest in prehabilitation to enhance patients' functional

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capacity and nutritional status pre-operatively and in the implementation of enhanced recovery after surgery (ERAS) (12).

The purpose of this Topical Review is to evaluate the literature covering these different dimensions of peri-operative care in IBD and to develop practical suggestions for the multidisciplinary team (MDT) on the peri-operative management of patients with IBD.

2. Methods

European Colitis and Crohn's Organisation (ECCO) Topical Reviews are intended to develop expert opinion consensus and practice position statements, informed by literature reviews in clinical areas where there is insufficient scientific evidence to produce guidelines, and are endorsed by ECCO. Peri-operative care was identified by the Clinical Committee (ClinCom) and Surgical Committee (S-ECCO) of ECCO as an important area requiring practical recommendations and formulating consensus agreement from a large multidisciplinary panel of experts was agreed to be the optimal approach (13). This proposal was endorsed by the Guidelines Committee (GuiCom) and the Governing Board of ECCO.

The methodology used to reach the consensus involved several steps and followed the standard operating procedures for ECCO Topical Reviews. An open call for the Topical Review was made to all ECCO members and 13 participants were selected from 36 eligible applicants based on their content and methodological expertise, publication record, accomplishments and commitment to the project. Balance was ensured between medical and surgical gastroenterology specialists, as well as with respect to gender and geographical

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location. The entire consensus project was conducted between April and December 2021. The project was jointly led by one representative from ClinCom (SS) and one from S-ECCO (AS). The participants were divided into four working groups (WG) focussing on specific topics. Each WG member performed a systematic literature search of the assigned topic with the appropriate MeSH terms using Medline/PubMed/ISI/Scopus, the Cochrane database and conference abstracts. Each WG discussed the retrieved literature on their topic and formulated draft current practice positions and the supporting text for their practice position statements. The current practice positions were further developed using a Delphi methodology (14) incorporating two successive rounds. The first round was web based with anonymous voting, inviting feedback, exchange of available evidence and suggestions for inclusion in the iterative development of the statements. The second Delphi round was a dedicated web meeting involving all available participants on 16 December 2021, with discussion and completion of the consensus document. Current practice positions were accepted when ≥80% of participants agreed to the text of the statements. The final manuscript was prepared for consistency by the two project coordinators (SS, AS) before final review and approval by all WG participants.

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3. Current Practice Positions

3.A. Peri-operative use of drugs

Current Practice Position 3.A.1

In patients needing surgical intervention for inflammatory bowel disease, biological treatment can be continued during the peri-operative period.

There are conflicting results from studies and divergent opinions on the safety of peri-operative continuation of biologics. On the one hand, it may be argued that the diminished inflammatory activity may contribute to reduction of postoperative complications. Conversely, as biologics are potent immunosuppressants, there is an obvious concern regarding the risk of surgical and infectious complications in the postoperative period. Furthermore, there is controversy surrounding the effects of these agents at the tissue level, specifically in the healing of bowel anastomoses. The WG evaluated the emerging data on the currently used biologic and small molecule agents to propose the practice position.

Anti-TNF therapy

There are conflicting results from the multiple meta-analyses assessing the impact of peri-operative anti-TNF use on the risk of postoperative complications in patients with IBD undergoing surgery. Some early meta-analyses showed a positive association (15,16, 17) while others did not indicate increased risk (18,19,20,21,22). These studies varied in the

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methodologies used to address potential confounding factors, such as the type of medication, disease severity, time interval between medication and surgery, drug concentration, presence of antidrug antibodies and type of surgical intervention. In addition, studies reported different outcomes. Both of these factors may account for the divergent conclusions.

More recently, many prospective studies (23,24,25,26) have been reported and have shown no increased risk of postoperative infectious or non-infectious complications. The most recent of these is the PUCCINI study (26), which prospectively collected data from 955 abdominal operations in both UC and CD patients and confirmed that neither pre-operative exposure nor detectable drug levels before surgery were associated with increased risk of overall infectious complications or surgical site infections. A recent Cochrane review (27) as well as the most recent meta-analyses (28,29) showed no increased risk of postoperative complications in patients with IBD on biological treatment.

Vedolizumab

Early reports raised concerns regarding the peri-operative use of vedolizumab (30,31,32), but the studies did not correct for disease severity or type of surgery, which may have impacted on the adverse outcomes. More recent literature adjusting for these confounders and meta-analyses (33,34,35,36) suggest a more favourable safety profile and in particular no increase in postoperative infections.

Ustekinumab

Data on peri-operative use of ustekinumab are scarce. In the multicentre study by Lightner *et al.* (37) there was no increased risk of surgical site infections or readmissions in

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ustekinumab-exposed patents compared with those exposed to anti-TNFs. Similar results were shown in a case-controlled study from Canada (38). A more recent retrospective single-centre study which included a cohort of patients with severely refractory CD, however, has suggested that pre-operative use of ustekinumab is an independent risk factor for intra-abdominal sepsis (39). A more recent large multicentre Spanish cohort (40) and a recent meta-analysis (41) indicate no increased risk of post-surgical complications in patients exposed to ustekinumab.

Tofacitinib

Very limited data are available on the peri-operative safety of tofacitinib in patients with IBD needing surgery. The single study available so far (42) reported an increase in the number of venous thromboembolic events and recommended prolonged use of thromboprophylaxis.

Current Practice Position 3.A.2.

In patients needing surgical intervention for inflammatory bowel disease, immunomodulators can be continued during the peri-operative period.

Evidence suggests that the use of purine analogues (azathioprine and mercaptopurine) does not adversely affect postoperative outcomes (43, 44). A systematic review by Subramanian et al (45) summarized data from 11 small retrospective studies and found no increase in risk of postoperative complications associated with use of thiopurines or cyclosporine. This finding is supported by a more recent review (46). It should be noted that thiopurines can take up to 3

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months to reach a therapeutic level and that a further 3 months may be required to fully wash out the system. Therefore, it is unlikely that stopping thiopurine immediately before surgery will have any measurable impact on the risk of complications (47). The elimination half-life of these agents is 1–2 hours and hence they can be safely restarted while recommencing oral intake in the immediate postoperative period.

Data specific to IBD relating to peri-operative use of other immunosuppressive drugs are limited. A meta-analysis on the use of pre-operative methotrexate (MTX) in patients with IBD or rheumatoid arthritis undergoing surgery suggested no increased risk of postoperative complications (48). Similarly, small retrospective studies (49,50) on pre-operative administration of cyclosporine did not indicate an increase in postoperative morbidity.

Current Practice Position 3.A.3

Steroid withdrawal is strongly recommended prior to surgical interventions in patients with IBD whenever possible. Where complete withdrawal is not achievable, progressive tapering to the lowest dose is recommended.

Steroids in the peri-operative period are considered a risk factor for development of postoperative complications, especially when high doses are administered for prolonged periods, namely above 20 mg prednisolone daily or equivalent for more than 6 weeks (51). This is supported by evidence from several narrative reviews, meta-analyses and retrospective and prospective studies (52,53,54,55). Indeed, a meta-analysis of observational

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studies (53) in patients with IBD found an increased risk of all postoperative complications (OR 1.41; 95% CI 1.07–1.87), as well as an increased risk of postoperative infectious complications (OR 1.68; 95% CI 1.24–2.28) among patients on steroids. A recent Cochrane review (54) found that the adjusted pooled OR for postoperative infectious complications in patients with IBD was 1.7 (95% CI 1.38–2.09). These unfavourable effects of corticosteroids are mediated by an increased susceptibility to infections, as well as by a negative impact on wound healing (56).

Regarding pre-operative steroid stress dose in patients on long-term corticosteroids, there is no evidence to support the practice of increasing the dose instead of continuing the pre-operative dose or converting to intravenous equivalents where necessary (57,58).

Current Practice Position 3.A.4

Longer use of pre-operative prophylactic antibiotics and antibiotic use as part of bowel preparation in IBD might be beneficial. More research is needed to explore the duration of prophylaxis, route of administration and type of antibiotics.

Prophylactic intravenous antibiotics have become a standard of care for patients undergoing colorectal surgery and represent an undisputed standard of pre-operative optimization (59). However, the use of oral antibiotics in addition to mechanical bowel preparation prior to elective colorectal surgery in IBD patients is still being debated. A recent study (60) concluded that the rate of septic intra-abdominal complications was significantly reduced by

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pre-operative mechanical bowel preparation combined with pre-operative oral antibiotics (paromomycin and metronidazole) on the day before surgery. Unger et al (61) carried out a study that included 255 patients with CD who underwent laparoscopic intestinal resection with or without mechanical bowel preparation and/or oral antibiotic prophylaxis and found that, while a single dose antibiotic alone without bowel preparation was associated with a low number of complications in patients undergoing small bowel resections, organ/space infections were more common if colorectal resections were performed without bowel preparation. These results suggest that combined bowel preparation and oral antibiotics might be beneficial when the colon is involved in the resection.

Data from an open label perspective study showed that combined oral and intravenous antibiotic prophylaxis prevented surgical site infection in patients with UC undergoing proctocolectomy with ileal pouch–anal anastomosis (62).

Prolonged prophylactic antibiotics could be an attractive approach in patients with penetrating CD and intra-abdominal abscesses (63). However, the effect of administration of prophylactic antibiotics for a period longer than that used for routine peri-operative administration is still unclear. Zerbib *et al.* (64) described 78 patients with CD who received 2 weeks of intravenous antibiotics, withdrawal from steroids and immunosuppressive therapy, abscess drainage and nutritional support and showed low rates of morbidity (18%) and no mortality. On the other hand, prolonged use of antibiotics raises the risk of *Clostridium difficile* infection or the development of antibiotic resistance (65). Overall, limited data are available to establish recommendations regarding the addition of prolonged oral antibiotic to intravenous antibiotic prophylaxis before surgery in patients with IBD.

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3.B. Peri-operative nutritional management

Current Practice Position 3.B.1

The prevalence of malnutrition is higher in patients with active disease and in CD compared with UC. Malnutrition in surgical patients with IBD worsens clinical outcomes and therefore it is recommended that nutritional status is optimized before elective surgery whenever possible.

The prevalence of malnutrition in IBD ranges between up to 38% in patients in remission and up to 70% in patients with active disease (66, 67). Malnutrition can occur in both UC and CD but is more frequent in CD, where small bowel involvement can lead to malabsorption (68, 69). The onset of malnutrition in patients with CD can be insidious, whilst patients with UC generally develop acute problems during disease flare (70). Malnutrition can be caused by reduced oral intake, malabsorption, increased nutrient losses in the gastrointestinal tract and increased nutrient requirements or drug–nutrient interactions (68). The severity of malnutrition depends on the duration, activity, phenotype and extent of disease, and particularly on the inflammatory burden, which drives catabolism and causes anorexia and nausea (68, 70). There is no consensus on the best way to define malnutrition and its criteria and definitions have changed over time. For an overview of available criteria (71,72,73,74,75), see **Table 1.**

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Although hypoalbuminaemia is clearly a surgical risk factor (76), inflammation may reduce serum albumin concentrations independently of malnutrition (77). Historically, patients with IBD were frequently malnourished and underweight. However, due to the obesity epidemic, 15%–40% of patients with IBD are now overweight or obese (78). Over time, IBD patients develop a relative reduction in lean mass and an increase in adiposity. This may occur due to deficits in dietary intake, higher protein turnover and loss of nutrients during active luminal disease or as a consequence of disease treatments. Corticosteroids increase net loss of protein in children (79) and adults (80) with CD. A raised BMI may mask malnutrition as weight and BMI do not always reflect body composition, which may be more relevant. These covert deficits in lean mass may be unmasked by tools such as skin-fold thickness measurement (81). Loss of muscle mass and reduced muscle function have now been integrated into the consensus definitions of malnutrition (82,73,75). In patients with IBD, sarcopenia and malnutrition have been associated with increased hospitalizations, disease flares, need for surgery and postoperative complications (83,84,85). In hospitalized patients, malnutrition is an independent risk factor for venous thromboembolism (86), non-elective surgery, longer admission, and increased mortality (87).

In patients undergoing surgery, nutritional support should be initiated in the presence of malnutrition, in those at nutritional risk at the time of surgery and in patients who are either unable to eat within 5 days postoperatively or cannot achieve an oral intake of >50% of the recommended intake within 7 days postoperatively (72,74,88). Where possible, delaying surgery by up to 8 weeks to address modifiable risk factors can reduce postoperative complications and morbidity and may also reduce the postoperative length of stay or the need

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for a diverting stoma (72, 74, 89-93). The aims of pre-operative nutritional therapy include downgrading of inflammation, enabling withdrawal of steroids and improvement of malnutrition in terms of both calorie intake and the replacement of nutritional deficits such as calcium, vitamin D, folate, vitamin B_{12} and zinc (68, 94). Nutritional imbalance should be treated with either oral or enteral nutritional (EN) support. Parenteral nutrition (PN) should be reserved for cases where enteral nutrition is not feasible or not successful (95, 96). In the case of an emergency where surgery cannot be postponed, EN or PN should be commenced postoperatively (95).

Nutritional screening and assessment

Current Practice Position 3.B.2.

In the pre-operative period, all patients should be routinely screened for malnutrition (including BMI and unintentional weight loss as a minimum). In those identified to be at risk, full nutritional assessment should be performed.

Early nutritional screening for malnutrition and subsequent assessment enables earlier intervention (95,96,) and may improve clinical outcomes (97,98,99,100). Sarcopenic patients with CD undergoing bowel resection who received pre-operative nutritional support showed fewer major complications than those who did not (6.5% *vs* 28.6%, p=0.045) (84). Sarcopenia is a predictor of surgical morbidity in IBD, despite normal or elevated BMI (10, 102). The nutritional state of patients impacts on the length of hospital stay (103,104). In line

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with these results, the European Society of Clinician Nutrition and Metabolism (ESPEN) recommends nutritional support in malnourished presurgical patients with IBD (74).

A survey among 146 gastroenterologists in 2016 showed that 33% of the practicing gastroenterologists did not routinely screen for malnutrition in patients with IBD (105).
A recent systematic review by Li *et al.* identified five nutritional screening tools that were used in IBD studies that were associated with nutritional and or clinical outcomes (106). These are summarized in **Table 2**.
Nutrition Risk Screening 2002 (NRS-2002) (98) has shown promise in hospitalized patients as have the Malnutrition Inflammation Risk Tool (MIRT) (107), Nutritional Risk Index (NRI) (108,109) and the Malnutrition Universal Screening Tool (MUST) (102) in outpatients. Recently, a Dutch study using the Short Nutritional Assessment Questionnaire (SNAQ) (110) SNAQ, an additional screening tool, demonstrated an OR for flares of 2.61 (95% CI 1.02–6.69) among those with impaired nutritional compared with those with 'normal' nutritional status (111). Subjective global assessment (SGA) (112), comprehensive registered dietitian and gastroenterologist (RD/GI) assessment (113), bioelectrical impedance analyses (BIA) (114,115,116) and computed tomography (CT) scan with various measurements have been used as nutritional assessment tools. In line with a previous systematic review by Ryan *et al.* (117), the review of Li *et al. (*106) concluded that CT measures of sarcopenia were associated with clinical outcomes. Although many patients with IBD undergo abdominal CT scan, these are costly and there is risk of radiation and contrast exposure. Therefore, research into more practical methods such as handgrip strength, ultrasound or bio-impedance analysis is required (115,118,119).

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Crohn's disease

Enteral nutrition

Current practice position 3.B.3

Pre-operative exclusive enteral nutrition in patients with stricturing or penetrating CD improves nutritional status and may reduce postoperative complications. The multidisciplinary team should determine the most appropriate treatment duration and route of administration.

Alteration of dietary texture in patients with stenotic disease and obstructive symptoms seems logical. Robust data in patients with CD are lacking but low-residue or soft/liquid diets have been associated with symptomatic relief (120) and therefore likely reduce the risk of worsening obstruction necessitating more emergent surgery (121,122,123). No randomized data exist comparing the frequently described 'step-up' nutritional algorithm including oral nutritional supplements, EN and PN, but it appears logical to initiate the least invasive and most tolerable method that enables achievement of nutritional goals. The potential benefits of exclusive EN (EEN) include improved nutritional status (124), induction of mucosal healing (125), changes to the microbiome and to cytokine pathways (126,127,128) and reduction in post-operative complications mainly due to ability to achieve corticosteroid withdrawal (129,130).

Three systematic reviews investigating the effect of pre-operative EN in patients with CD suggest a reduction in postoperative morbidity (97,120,131), with one reporting a number

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needed to treat of 2 (97). There are a number of monocentric retrospective observational studies with heterogeneity of data, potential selection bias and poor group matching (89,132,133,134,). The largest retrospective cohorts suggest that patients proceeding straight to surgery are five times more likely to develop intra-abdominal septic complications than those receiving EEN ($p<0.001$) (130) and that it is associated with an extended immunosuppressant-free interval ($p<0.001$), reduced stoma formation ($p<0.05$) and reduced postoperative complications ($p=0.001$) (126). The only RCT investigating EN in CD randomized patients to nutritional endpoints with similar outcomes in each group (135). Improvement in CRP and albumin has been demonstrated in other studies where EEN has been associated with reduced complications (89,129,136,137).

In a prospective propensity-matched cohort study, EEN was associated with deferment of surgery in 25% cases and a ninefold reduction in postoperative complications when compared with proceeding straight to surgery (137). In the subgroup analysis of the GETAID multicentre study there was a trend towards reduction in intra-abdominal septic complications and stoma formation (138). EEN regimens across studies vary between 1 and 12 weeks. Two out of three studies in which the minimum duration of EEN was $\leq$2 weeks demonstrated non-significant results (138, 139,140). The outcome of an ongoing study in the United Kingdom is eagerly awaited to assess the optimum duration of treatment (141).

In surgical emergencies, where the optimum duration of nutritional optimization cannot be achieved, nutritional optimization should be considered postoperatively (73,95, 142).

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Parenteral nutrition

Current Practice Position 3.B.4.

In malnourished patients with CD administration of parenteral nutrition pre-operatively may reduce overall postoperative complications. Therefore, parenteral nutrition can be used to optimize nutritional status before surgery as a supplement to enteral nutrition, or as an alternative if enteral nutrition is not possible or is contraindicated.

Parenteral nutrition (PN) is usually recommended for patients who are unable to tolerate EN or do not meet their nutritional requirements via the enteral route. PN may also be considered in cases of bowel obstruction when placement of a feeding tube distal to the obstruction is not possible. Additionally, PN may be indicated in ileus, high-output fistulae, bowel ischaemia, severe haemorrhage, anastomotic leak or short bowel or gut dysfunction due to active disease (95,142). Decisions around pre-operative nutrition should take into account any planned postoperative fasting period.

One meta-analysis (97) examined the association between pre-operative administration of nutritional support and postoperative outcomes. Five observational studies were included, three of which focussed on the use of total parenteral nutrition (TPN) (a total of 280 patients). Patients with CD who received preoperative TPN had a non-significant trend towards reduced rates of postoperative complications (15%) compared with the group that received standard care without specific nutritional support (24%) (OR= 0.65, 95% CI 0.23–1.88, p= 0.43) (97). An earlier systematic review comparing various outcomes in PN-treated and non-

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PN-treated patients, reported that those who received PN treatment had improvements in infectious complications, serious early (30-day) postoperative complications, IgM levels, BMI and rate of recommencement of work at 6-month follow-up (131). More recent retrospective studies have not reported EN- and PN-treated patients separately (143,144). Ayoub *et al.* reported a retrospective cohort of 55 TPN-treated CD patients compared with 89 CD patients without TPN, all of whom underwent major abdominal surgery and found that 30-day non-infectious postoperative complications were lower in the TPN group (OR 0.07, 95% CI 0.01–0.80, p=0.03) (145). TPN was not associated with a reduction in the rate of infectious complications.

Ulcerative colitis

Current Practice Position 3.B.5.

The role of enteral or parenteral nutrition in improving the surgical outcomes of patients with UC requires further studies.

Data supporting nutritional optimization in UC are scarce. The first unblinded RCT (146) investigating 7 days of pre-operative EEN versus standard of care in acute severe colitis (n=62) demonstrated reduced corticosteroid failure in patients who tolerated EEN (19% vs 43%, p=0.04) Rates of rescue therapy and colectomy at acute admission were similar, whilst patients on pre-operative EEN had a lower composite endpoint of colectomy and re-admission at 6 months (16% vs 39%, p=0.045) (though no significant difference was observed with regard to the colectomy rate alone).

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A retrospective study comparing surgical outcomes in patients with UC demonstrated no significant difference in surgical complications between patients who received ≥7 days preoperative TPN (n=56) and those who received no TPN (n=179) (OR 1.42; 95% CI 0.64–3.13, p=0.39) (147). In a study of 42 patients with active UC (148) that compared preoperative EEN and TPN (for a median duration of 16 days), a significantly greater increase in albumin was demonstrated in the EEN group (p=0.02) but postoperative infectious complications were more frequent amongst those receiving TPN (p=0.03) (148); it is to be noted, however, that there was potential for selection bias in those receiving TPN at the outset.

There is a need for large prospective controlled studies of pre-operative nutrition in UC. Until such data are available, it is recommended that nutritional assessment is carried out on all patients with UC in whom surgery is planned and nutritional deficiencies are corrected.

Peri-operative immunonutrition

Current Practice Position 3.B.6

The use of immunonutrition in improving postoperative outcomes in adult IBD patients requires further studies.

Immunonutrition involves the use of oral, enteral or parenteral nutritional formulations enriched with various pharmaconutrients [arginine, glutamine, omega-3 fatty acids, growth factors, nucleotides and antioxidants (copper, selenium, zinc and vitamins B, C and E)] to improve immune responses and modulate inflammatory responses and have been

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recommended in cancer patients prior to surgery (72,149,150,151). High-quality data on immunonutrition in surgical patients with IBD is lacking, but inference from the colorectal cancer literature may help. Several meta-analyses have concluded that immunonutrition reduces morbidity by 20%–40% and length of stay by 1–1.8 days with no effect on mortality (151,152,153,154,155,156,157). The most recent French nationwide analysis of patients who underwent colorectal cancer surgery showed no difference in morbidity/mortality when immunonutrition was offered, yet a reduction in length of stay of 1.3 days was reported (158). A benefit of immunonutrition in the induction and maintenance of remission in CD has been shown in the paediatric literature (159,160). Unfortunately, the literature is scarce when it comes to adults, particularly in the peri-operative setting. Recent meta-analyses (161,162) could not find clear superiority of immunonutrition in adult patients over conventional steroid therapy and nutritional support, irrespective of the formula composition and administration. On the other hand, a small prospective trial (163) showed an effect of immunonutrition on the clinical course of complex CD, including induction of clinical remission, promotion of fistula healing and mucosal healing. Furthermore, three studies suggested a positive effect of immunonutrition on disease recurrence after ileocolonic resection for CD (16,164,165,166). Considering all the available evidence, immunonutrition may have a role to play in induction and maintenance of CD remission in patients with a luminal or ileocolonic phenotype (167, 168) and may help prevent surgical recurrence.

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3.C. Peri-operative psychological and physical rehabilitation

Psychological rehabilitation

Current Practice Position 3.C.1.

The need for peri-operative psychological care for patients with IBD who undergo surgery should be considered. Specific psychological assessment tools and interventions for patients with IBD undergoing surgery remain largely unexplored.

Intestinal resection is a major life event for patients with IBD and may have a significant and long-lasting psychological impact (169,170). The pre-operative period is associated with a lower quality of life (QoL), contributed to by concerns regarding surgery. Patient counselling regarding the benefits, expected outcome, time to functional recovery, complication risks and potential alternatives to the proposed surgery are of paramount importance to increase the patient's feeling of control (171).

A range of psychological disturbances may be seen postoperatively, including body image disturbance, sexual impairment, sleep disturbance, fatigue, and psychiatric disorders (172). It has been suggested that the psychological and psychosocial impact of IBD surgery is higher in women (173). Anxiety and depression have been described in patients with IBD who are undergoing surgery (174,175). The risk of depression after IBD surgery in CD patients is 6% after 1 year and increases to 16% after 5 years, while the corresponding figures for UC patients are 5% and 11% respectively. The risk of generalized anxiety is 7% after 1 year and 14% after 5 years in CD, and 7% and 12% respectively in UC patients. Data on whether the

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risk of depression is significantly higher in patients requiring surgery as compared with patients who have never had surgery are conflicting (176,177). Predictors of depression and/ or anxiety after IBD surgery include female gender, younger age at surgery, co-morbidity, surgery within 3 years of diagnosis, use of immunomodulators, perianal disease and re-resection. Stoma surgery and ileoanal pouch surgery have not been consistently associated with a psychological disturbance or reduced QoL (176,178,179,180,181,182).

While the association between IBD activity and psychological stress is well documented (183), the consequence of postoperative psychological disturbance on the disease course of IBD is unknown. Anxiety and depression have been associated with the risk of readmission, including after surgery (184). Therefore, timely referral for psychological support is indicated to reduce the impact of pre- and postoperative psychological disturbances. This is particularly important in patients needing surgery shortly after diagnosis and those with significant medical and/or psychiatric comorbidities or a complicated disease course. The nature of the psychological intervention should probably follow general strategies since specific data are lacking in the pre- and postoperative setting in patients with IBD (173).

Burden of physical disturbances

Current Practice Position 3.C.2.

Patients with IBD experience variable degrees of limitation in activity after surgery. The speed and extent of recovery are influenced by many factors and should be included in pre-operative counselling.

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A study on the physical health status after colectomy in young patients with UC found that around half of patients (14/30) were engaging with athletic activities after colectomy, whereas the rest had factors which prevented active physical exercise, such as soiling and leakage, urgency and joint pain (185).

Looking at the impact of bowel surgery on exercise capacity in patients with CD, Brevinge *et al.* (186) enrolled 29 consecutive patients with an ileostomy, who were classified into: (I) those who underwent <10 cm resection, (II) those with 15%–30% small bowel resection and (III) those with >50% small bowel resection. Resections were performed at least one year before the observation, and none of the patients had signs of active CD. They found that maximal exercise load reduced by 9%, 22% and 40% in groups I, II and III respectively; these figures were greater than predicted when considering muscle mass loss.

In a study in 227 patients with IBD (CD=140, UC=87), almost half of the patients reported that their disease impacted their ability to exercise, mainly due to fatigue (81%), joint pain (37%) or embarrassment (23%). Similar findings were reported by others (187), with a correlation between disease activity and physical activity levels.

Such factors would need to be considered when designing peri-operative pathways to optimise patient physical status (188).

Sarcopenia

Current Practice Position 3.C.3.

Sarcopenia in patients with IBD is associated with a more aggressive disease course and higher short- and long-term postoperative complication rates.

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Sarcopenia is the most frequently reported and objectively measurable marker of reduced physical capacity. Sarcopenia is not directly related to BMI, as it can also be seen in overweight patients with IBD (189). Of the 99 patients included in one study, 41 (45%) were sarcopenic, of whom 42% had a normal BMI and 20% were overweight or obese. Sarcopenia was associated with higher CRP and lower albumin and was the only significant predictor of need for surgery in overweight and obese patients. A combination of sarcopenia and high visceral fat has been confirmed to predict worse outcomes in CD (190,191). Bamba *et al.* (192) identified sarcopenia as an independent predictor of the need for bowel resection.

Sarcopenia has been reported to occur in up to 69% of patients hospitalised with acute severe UC, while the lowest prevalence has been reported in newly diagnosed patients aged under 13 years. In CD the prevalence of sarcopenia ranges between 31% and 61% (193).

Interestingly, surgery itself can have a beneficial effect on active IBD-associated skeletal muscle depletion. Zhang *et al.* (194) studied body composition in 204 patients with IBD (CD n=105, UC n=99) and 60 controls using skeletal muscle area, visceral fat area and subcutaneous fat area calculated at CT scan. Sarcopenia was more frequent in CD (59%) and UC (27%) compared with controls (8%). Following medical or surgical treatment, the extent of sarcopenia was remarkably reduced in patients with UC.

A recent systematic review and meta-analysis (195) found that sarcopenia was a risk factor for surgery (OR=2.66) and postoperative complications (OR=6.1). Fujikawa *et al.* (196) found that sarcopenia was associated with increased risk of surgical site infection following restorative proctocolectomy for UC. Major complications are more likely to occur in sarcopenic patients with CD (197).

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Peri-operative physical rehabilitation in IBD

Current Practice Position 3.C.4.

Peri-operative physical rehabilitation may be beneficial to optimise postoperative recovery in IBD. Rehabilitation programmes should be multidimensional and the modality and intensity need to be adapted to patients' baseline characteristics.

A recent ECCO Topical Review (198) on complementary medicine and psychotherapy in IBD suggested that exercise can have beneficial effects on overall health, physical well-being, perceived stress and QoL in patients with IBD, whereas its role in disease management needs to be clarified. Some caution is necessary when considering exercise in patients scheduled for surgery, as most studies have reported on the effects of physical activity to reduce inflammation in patients whose IBD is in remission. In fact, even if regular exercise exerts anti-inflammatory effects, it has been suggested that intense/strenuous exercise can induce transient mild systemic inflammation, increasing circulating cytokines, which might exacerbate IBD (199). Of note, exercise has been reported to make 72% of patients with IBD feel better, but 80% had to stop exercising temporarily or permanently due to severity of symptoms (199,200).

It is important that consistent measures are used to assess physical fitness and body composition in order to plan pre-operative rehabilitation adequately (201). There is evidence that pre-operative exercise therapy can improve physical fitness in patients who need surgery for gastrointestinal malignancies, facilitating recovery to baseline function postoperatively (202). Cronin *et al.* (203) randomised 20 physically active patients with quiescent IBD into

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two groups: moderate-intensity aerobic and resistance exercise and control. The former experienced improved physical fitness and had a favourable effect on body composition, with a median decrease of 2.1% body fat vs 0.1% in controls (p=0.022) after 8 weeks of therapy. In the experimental group, lean tissue mass increased by a median of 1.59 kg and fat mass decreased by 1.52 kg. In another RCT, Tew *et al.* (204) proposed that high-intensity interval training (HIIT) and moderate-intensity continuous training are feasible and acceptable in patients with CD, the former achieving greater mean increase in oxygen uptake. Of note, 8.3% of patients experienced non-serious exercise-related adverse events, and 5.5% had a recurrence. HIIT and moderate-intensity exercise may be difficult to perform in those patients who need surgery, and safety is yet to be demonstrated when disease is active.

A 2020 multidisciplinary consensus from the UK on the management of IBD suggested that optimisation of physical condition is recommended prior to elective surgery (205). Enriquez-Navascués *et al.* (206) suggested that patients with CD have distinct features that can impact the effectiveness of the enhanced recovery after surgery (ERAS) pathway, in which physical conditioning has a relevant role; in a cohort of patients with CD they identified several factors that can slow the restoration of function and hospital discharge.

Exercise and physical rehabilitation after surgery may be effective in reducing recurrence and maintaining remission, but at present this can be hypothesized only, by translating evidence from non-surgical IBD patients (208,209).

ERAS protocols can be particularly beneficial in expediting recovery, with a particular focus on early mobilisation (210). Evidence from non-IBD patients has suggested that multicomponent exercise intervention can reverse frailty, as proven in a recent RCT (211); similar approaches are increasingly being proposed (212) to optimise fitness and are likely to

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be important especially in frail patients with IBD, particularly when surgery is needed. Pathways need to be adapted to each specific patient and their baseline condition/health status.

Furthermore, yoga has been associated with reduced levels of fatigue and depression in IBD, improving QoL, suggesting that it can have a synergistic role peri-operatively, at least in selected patients with IBD (198, 213).

How and where peri-operative physical rehabilitation should be delivered

Current Practice Position 3.C.5.

Physical rehabilitation should be delivered in a setting that facilitates patient participation.

Peri-operative physical rehabilitation, or prehabilitation, aims to optimise the condition of the patient prior to surgery by means of exercise, nutrition and psychosocial interventions that enable the patient to combat the stresses induced by surgery and to potentially recover more quickly, thus spending less time in hospital and having a lower risk of complication(s). This is generally not possible to any significant extent in the emergency surgery setting and is more applicable to planned, elective surgery, with evidence supporting its role in reducing length of hospital stay in patients undergoing surgery for colorectal, upper gastrointestinal and hepatobiliary cancers (209,214).

Increasing exercise may have many challenges for patients, and data suggest that while those with IBD often appreciate the importance of exercise, the relapsing and remitting nature of

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the disease means that some experience limitations such as fatigue, muscle weakness and abdominal pain (197,215,216). In addition, exercise may decrease the risk of future active disease in those patients with IBD who are in remission (208) and may also modulate the intestinal microbiome composition (217). There are no data to support either supervised or unsupervised exercise programmes prior to IBD surgery, but after some in-person or virtual instruction, such programmes could be implemented in an appropriate environment inside or outside of the hospital.

Data are scant, but it is logical that the duration of physical prehabilitation should be such as to achieve a positive impact on outcome: a minimum of 4 weeks prior to surgery is probably necessary though a longer period seems appropriate if feasible. Appropriately skilled members of a wider IBD multidisciplinary team should deliver the elements of pre-operative rehabilitation for which they have expertise in an in-person or virtual environment.

In terms of the impact of exercise, studies have demonstrated that improving fitness before cancer surgery can result in improvements in physiological parameters (e.g., $VO2_{max}$, anaerobic threshold and functional capacity) (218,219).

Correction of Iron deficiency

Current Practice Position 3.C.6.

Screening for anaemia is recommended prior to IBD surgery. Intravenous iron is likely to correct iron deficiency anaemia more quickly than oral supplementation.

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Correcting anaemia is critical to optimize the outcomes of surgery, allowing appropriate postoperative physical rehabilitation. Pre-operative anaemia is associated with a poor outcome of surgery, including overall postoperative morbidity, intra-abdominal septic complications and prolonged hospital stay (220,221,222,223,224). The associations described in these studies may be confounding, since anaemia may be a marker of severe IBD. Although the prognostic effect of optimization of iron deficiency anaemia has not been studied in the setting of IBD surgery, anaemia is a modifiable risk factor and correction should be considered pre-operatively. Since most patients scheduled for surgery have active IBD and prompt pre-operative correction is warranted, intravenous iron supplementation is indicated in most cases. Recurrent anaemia should not be overlooked, and adequate safety nets and strategies should be in place to monitor and treat this. It has been suggested that patients should be monitored every 3 months after correction for a year, and every 6-12 month thereafter (225).

Stoma and pouch information

Current Practice Position 3.C.7

Pre-operative stoma counselling and marking should be carried out by appropriately trained specialists including stoma therapists or specialist nurses.

Patients can benefit from pre-operative contact with patients living with a stoma or ileo-anal pouch.

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A correctly placed and adequately fashioned stoma is an important determinant of QoL after surgery for IBD. It is therefore of utmost importance that the stoma site is appropriately marked ahead of surgery, after a thorough discussion with the patient and a physical examination.

The IBD specialist nurses and stoma nurses have the skills and knowledge to support and educate patients who are scheduled to undergo surgery that includes stoma and/or ileoanal pouch formation (226). Contact with other patients who have undergone the same procedure can also help with decision making about stoma and pouch surgery. Psychologists, sexual therapists and patient organizations can assist in the provision of information and psychological support to patients considering this surgery (226).

3.D. Immediate postoperative period

Current Practice Position 3.D.1.

The use of enhanced recovery principles in colorectal surgery is recommended to improve immediate postoperative recovery. These protocols should be tailored to the specific needs of patients with IBD.

Enhanced recovery pathways (ERP) have been shown to improve the short- and long-term results of patients undergoing colorectal surgery (227,228,229). The ECCO-ESCP consensus for the surgical management of CD described a specific statement which recommends the use of ERP protocols after elective abdominal surgery for CD (230).

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Components of ERP usually include pre-operative counselling (including on the possibility of stoma formation and demarcation), pre-operative smoking and alcohol cessation and optimized treatment of prior comorbidities such as anaemia or diabetes. In addition, ERP recommend limited pre-operative fasting, regional anaesthesia use, laparoscopy whenever feasible, multimodal pain control, early urinary catheter removal, postoperative venous thromboembolism prophylaxis, and early mobilization and feeding. There is still controversy over the use of mechanical bowel preparation and oral antibiotics (227,228,229), and some studies have demonstrated improved postoperative outcomes with full adherence to the protocol (229).

Current evidence suggests that ERP can improve short-term clinical outcomes immediately after abdominal surgery in patients with IBD (231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246), and only two studies have mentioned multidisciplinary evaluation and planning prior to discharge (237,242). These protocols decrease length of stay and in most studies show similar complication and readmission rates. ERP protocols are heterogeneous among publications. Half of the studies included only patients with CD (231,233,236,238,239,243,244,245). No study focussed exclusively on UC, and several publications included a mixed population of IBD and patients with cancer (232,239,240,246).

Pre-operative visits and counselling are key factors for a successful ERAS protocol (227,228,229). In patients with IBD, who are mostly young and motivated, these visits should be used for discussion of detailed information on all peri-operative interventions. Optimization of malnutrition and anaemia, especially important in patients with IBD, has

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been described in a few studies on ERP in IBD patients. Steroid and biological therapy optimization was not included in ERP protocols in any of the previously published studies (231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246), and only two mentioned multidisciplinary evaluation and planning prior to discharge (237,242). Further research is needed to define the importance of these interventions for the success of enhanced recovery pathways in IBD.

Current Practice Position 3.D.2.

Re-introduction or initiation of biological and/or immunomodulatory therapy after abdominal surgery in CD depends on multiple factors such as the type of agent, the presence of residual disease, risk stratification for recurrence and postoperative complications.

There is a lack of evidence on the optimal timing of re-introduction of previous biological therapies or initiation of new agents in CD patients who have undergone abdominal operations. In patients with no residual disease after surgery, one dosing interval can be missed, mostly in biologics with short intervals of administration. In patients with residual disease (e.g. perianal CD after ileocolonic resection), re-introduction of therapy is indicated as soon as safely possible with the aim of reducing the risk of flares (247). Depending on the urgency of the need for therapy and the presence of residual disease, treatment can be started within 2–4 weeks.

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Current Practice Position 3.D.3.

Patients with IBD have an increased risk of thromboembolic events. Thromboprophylaxis is recommended for all surgical patients and should be extended after discharge in patients with relevant risk factors.

Thromboprophylaxis is recommended for all admitted IBD patients, especially in the peri-operative period, as disease activity and surgery (248,249,250,251) significantly increase the risk of venous thromboembolic events (VTE). A recent international consensus on prevention of venous and arterial thromboembolic events in IBD reported that the risk of VTE is twofold higher in patients with CD or UC (252). Prophylaxis is recommended with low molecular weight heparin and needs to be maintained during hospital admission. Extension of prophylaxis after discharge is recommended in patients with strong risk factors for VTE, such as previous VTE history, age greater than 65 years and obesity. The extension is recommended for at least 8 weeks, as 91% of readmissions for thromboembolic events after discharge tend to occur within 60 days after discharge (253).

Summary

The modern peri-operative management of patients with IBD requires the consideration and optimization of numerous patient- and disease-oriented factors in order to reduce

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complications, enhance recovery and limit any adverse psychological impact. Proper peri-operative management of drugs, correction of nutritional deficits, implementation of psychological support and improvement of physical condition can all contribute to a successful pathway through the challenges posed by surgery. The present Topical Review provides a set of expert consensus practice recommendations on the peri-operative care required in order to optimise outcomes of IBD patients who undergo surgery. We acknowledge that joint planning by a multidisciplinary team is paramount in order to optimize surgical outcomes and reduce long-term morbidity. The consensus process highlighted that further high-quality prospective studies are required in many areas of peri-operative care. Nevertheless, the consensus statements produced by the multidisciplinary working group have provided balanced and clinically applicable recommendations that may contribute in promoting effective communication between the different specialties involved in the care of patients with IBD in a range of healthcare settings.

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Conflict of Interest

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Table 1. Definitions of malnutrition

European Society for Clinical Nutrition and Metabolism (ESPEN) 2015 [71]	1. Unintentional weight loss >10%–15% within 6 months or 2. BMI <18.5 kg/m^2
European Society for Clinical Nutrition and Metabolism 2021 (ESPEN)[72]	Addition of third criterion: 3. Serum albumin <30 g/L (with no evidence of hepatic or renal dysfunction) "Severe" nutritional risk was defined as the presence of at least one of these three criteria
American Society for Parenteral and Enteral Nutrition (ASPEN)[73], ESPEN[74] and the Global Leadership Initiative on Malnutrition (GLIM)[75]	Addition of loss of muscle mass and reduced muscle function
Global Leadership Initiative on Malnutrition (GLIM)[75]	Two-step procedure: 1. Screening on malnutrition 2. Confirmation of diagnosis: • three phenotypic criteria (weight loss, reduced BMI, and reduced muscle mass) • two aetiological criteria (malabsorption, high disease burden/inflammation).

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	A combination of at least one phenotypic criterion with at least one aetiological criterion would fulfil the diagnosis of malnutrition

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Table 2. Nutritional screening tools

Screening tool	Nutrition screening item	Score	Total score	Association with nutritional assessment/ clinical outcomes
Nutrition Risk Screening 2002 (NRS-2002)[98]	1. Is BMI <20.5 kg/m^2? 2. Has the patient lost weight within the last 3 months? 3. Has the patient had a reduced dietary intake in the last week? 4. Is the patient severely ill?	If "Yes" to any question, a final screening should be performed. If the answer is "No" to all questions, the patients is rescreened at weekly intervals. If the patient is, for example, scheduled for a major	In the final screening a nutritional assessment is performed	Nutritional assessment tool: Skeletal Muscle Index (SMI) Clinical outcome: Length of stay

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		surgery, a preventive nutritional care plan is considered to avoid the associated risk status.		
Malnutrition Universal Screening tool (MUST)[102]	Step 1: BMI score BMI=kg/m^2 Step 2: Weight loss score: Unplanned weight loss in past 3–6 months (% Score) Step 3: Acute disease effect score Patient is acutely ill and there has been or is likely to be no nutritional intake for >5 days	1. >20=0, 18.5–20=1, <18.5=2 2. <5=0, 5–10=1, >10=2 3. "No" = 0, "Yes" =2	Total score: 0=low risk, 1=medium risk, ≥2=high risk	Nutritional assessment tools: Fat Free Mass Index (FFMI) SMI registered dietitian/gastroenterologist (RD/GI) Assessment

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Nutritional Risk Index (NRI) [109,110]	NRI = 1.519 × serum albumin level (g/L) + 41.7 × (current weight/ usual weight)	NRI <83.5: risk of advanced malnutrition. NRI between 83.5 and 97.4: risk of moderate malnutrition. NRI >97.5: no risk of malnutrition.		Clinical outcomes: Response to infliximab
Malnutrition Inflammation Risk Tool (MIRT)[108]	• BMI >20 (kg/m^2) • Weight loss over past 3 months (%) • CRP (mg/l)	• BMI >20=0; 18.5–20.0=1; <18.5=2 • <5=0; 5–<10=2; >10=3 • <5=0; 5–50=2;	Total score between 0 and 8; no cut-off values for malnutrition in other articles.	Nutritional assessment tools: Subjective Global Asessment (SGA) Clinical outcomes: Hospitalization, disease flares, disease complications, need for surgery

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		>50=3		
SaskIBD-NR-tool[111]	1. Have you experienced nausea, vomiting, diarrhoea or poor appetite for greater than 2 weeks? 2. Have you lost weight in the last month without trying? If 'yes', how much weight have you lost? 3. Have you been eating poorly because of a decreased appetite? 4. Have you been restricting any foods or food groups?	1."No symptoms"=0, "1–2 symptoms"=1, "≥3 symptoms"=2 2."No"=0, "unsure"=1, "yes"=see below "<5 lbs"=0, "5-10 lbs"=1, "10-15 lbs"=2, ">15 lbs"=3 3. "No"=0, "yes"=2	SaskIBD-NR Tool: Total score: 0–2=low risk, 3–4=medium risk, ≥5=high risk	Nutritional assessment tools: RD/GI Assessment

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		4.“No”=0, “yes”=2		
Short Nutritional Assessment Questionnaire (SNAQ)[110]	• Unintentional weight loss: o >6 kg in the last 6 months o >3 kg in the last month • Decreased appetite during the last month • Use of supplemental drinks or tube feeding during the last month	If yes: 3 points If yes: 2 points If yes: 1 point If yes: 1 point	Total score: ≥2 points: moderately malnourished ≥3 points: severely malnourished	Clinical outcomes: disease flares

Abbreviations: SMI: Skeletal Muscle Index; FFMI: Fat Free Mass Index; SGA: Subjective Global Assessment; RD/GI: registered dietitian/gastroenterologist