

Review

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Review

Preoperative Optimisation for Elective Surgery in Crohn's Disease

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Abstract: Crohn's disease is a chronic inflammatory bowel disease and despite an increase in the available drug treatments, many patients still require surgery at some point in their disease course. Stricturing and penetrating phenotypes of Crohn's disease are less likely to respond to our current medical treatment and therefore, surgical intervention may be required. This is most commonly elective, planned surgery, thereby affording the opportunity to optimise medications, nutritional and inflammatory status, steroid use. Poor nutritional status and previous surgery increase the risk of postoperative complications. Preoperative optimisation has three main goals: reduction of postoperative complications, reduction of reoperation rates and reduction of postoperative recurrence rates. In this narrative review, we examine the role of nutritional intervention, medical optimisation pre- and postoperatively and the role of personalised prehabilitation in the reduction of postoperative complications.

Keywords: Crohn's disease; inflammatory bowel disease; exclusive enteral nutrition; parenteral nutrition; prehabilitation; surgery; preoperative optimisation

1. Introduction

Crohn's disease (CD) is a chronic idiopathic inflammatory bowel condition characterised by skip lesions and transmural inflammation that can affect the entire gastrointestinal tract (GIT) from the mouth to the anus. It commonly presents with diarrhoea, abdominal pain, weight loss and fatigue [1]. Previous population-based cohort studies have shown that 30% of patients with CD have significant intestinal damage at diagnosis. Up to 50% of patients will require surgery within 20 years of diagnosis [2,3]. The cause of CD remains unclear but there are genetic, immunological and environmental factors that contribute to disease onset and progression [4]. Gut dysbiosis is a common feature of CD and a Western diet appears to play a role in its development. The host-gut microbiota relationship may have been altered by changes in the Western diet, with a shift from high-fibre, low-fat foods to processed foods that contain additives [5]. While genetics play a role in the distribution of GIT inflammation, the severity and phenotype of disease are influenced by other factors [6].

Stricturing CD may be present in up to 60% of patients and poses a particular therapeutic challenge [7]. Endoscopic balloon dilatation of short strictures, stricturoplasty or surgical resection of the affected segment remain the only therapeutic options available for the treatment of fibrostenosing disease. These treatments are however, associated with recurrence and requirement for repeated dilatation or successive resections. The most common surgical intervention in CD patients is ileocollectomy/ileocaecectomy [8]. Recurrence of fibrostenotic disease following resection is common with a wide range of reported frequencies as a consequence of differing durations of follow-up and varying definitions of recurrence including endoscopic recurrence, symptomatic recurrence or need for further surgery [9–11]. Multiple resections for recurrent disease can lead to a number of sequelae including malnutrition, short gut syndrome/intestinal failure, decreased quality of life and increased inpatient stay, with associated costs to the patient and the healthcare system [8]. Indications for surgery are expanding beyond management of complications from bowel wall damage i.e. strictures and fistulae.

The European Crohn's and Colitis Organisation (ECCO) and European Society of Coloproctology (ESCP) consensus guidelines suggest that surgery should be considered at an early stage in those with penetrating or fistulating disease and those with localised ileocaecal disease and obstructive symptoms but no significantly active inflammation [12]. The Laparoscopic Ileocaecal Resection Versus Infliximab for Terminal Ileitis in Crohn's Disease (LIR!C) study demonstrated that primary ileocaecal resection in patients with isolated ileocaecal disease had similar quality of life scores one year after surgery when compared to medical treatment [13].

2. Methods

This is a narrative review of the current literature on the pre-operative optimisation of patients with Crohn's disease. A search was completed using PubMed. The definition of surgery in this review is limited to bowel surgery in Crohn's disease and does not include perianal fistula surgery. We gathered high-quality papers including systematic reviews and meta-analyses, randomised controlled trials, observational data and the current European Crohn's and Colitis Organisation (ECCO) guidelines. The review focuses on the preoperative optimisation of Crohn's disease patients from a nutritional and pharmacotherapeutic perspective and the role of preoperative nutrition in preventing postoperative recurrence.

3. Timing of Surgery

Time is required to deliver good preoperative optimisation; therefore emergency surgery makes this impossible. The 2024 ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Management recommends against emergency surgery in Crohn's disease [14]. This is backed by a meta-analysis of cohort series including 75,971 Crohn's patients from 15 countries which reported a significantly lower mortality among patients who underwent elective [0.6%; 95% CI: 0.2%-1.7%] vs emergent surgery [3.6%; 95% CI: 1.8-6.9%] and highlights the importance of perioperative optimisation and avoidance, where possible, of emergent surgeries. The guidelines also recommend that preoperative optimisation should be initiated, followed by reassessment of the patient for surgical intervention. This was backed by a meta-analysis showing that emergency bowel resection is associated with a higher risk of overall postoperative complications and abdominal septic complications. Another multicentre, observational study highlighted that emergency intervention in patients with an abdominal abscess increased the risk of post-operative complications and abscess recurrence. In addition, patients undergoing emergency surgery have a higher risk of stoma formation and laparoscopic surgery in the emergency setting has a higher conversions rate and results in resection of longer segments of small bowel, a concern in CD due to the lifetime risk of short bowel [14]. Acute severe colitis and peritonitis are rare in Crohn's disease so avoidance of emergency surgery is possible in the majority of patients.

In 2024, recommendations from the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) "Making the Cut" study for patients undergoing Crohn's disease study was published. They recommended that surgery should be recognised as a necessary treatment option rather than a failure of medical management and should be undertaken sooner in Crohn's disease patients and once this decision has been made, it should be undertaken within four weeks. A final recommendation advised that continuous involvement of the IBD team would promote joined-up care postoperatively [15].

4. Preoperative Nutritional Assessment in Crohn's Disease

Patients with IBD frequently suffer from malnutrition and is more commonly seen, or to a greater extent in CD patients than UC [16]. The 2020 ECCO topical review examining perioperative dietary therapy in inflammatory bowel disease recommended that all patients should be screened for malnutrition and that a nutritional assessment should be performed if required, with a minimum of body mass index (BMI) and recommends the correction of over- or undernutrition despite a paucity of evidence currently available [17]. Nutritional optimisations prevent malnutrition, micronutrient

deficiencies and osteoporosis, promoting optimal growth and development in paediatric patients [18]. The current European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines also advise that all patients are screened for malnutrition at the time of diagnosis and then at regular intervals [19]. Malnourished patients with inflammatory bowel disease are more likely to suffer complications, require hospitalisation due to infection; and if hospitalised are more likely to have a prolonged admission and to require non-elective surgery and longer admissions [20], and have an increased mortality and postoperative complication rate [21].

A significant proportion of IBD patients will lose lean muscle mass over time and sarcopenic obesity is becoming more commonly recognised. Corticosteroids contribute to net protein loss in adult patients with Crohn's disease and therefore, enteral nutrition may be beneficial in slowing or preventing protein turnover in patients receiving steroids [17]. The current ESPEN guidelines advise that the daily intake of 1 g of protein per kilogram of body weight or 1.2 to 1.5 g/kg in patients with active inflammation in response to the proteolytic and catabolic state [19]. This is particularly true in patients who may have severe disease and requiring surgical intervention.

5. Role of Exclusive Enteral Nutrition and Other Diets in Preoperative Optimisation

Exclusive enteral nutrition (EEN) is when patients replace their habitual diet with an exclusively liquid diet. EEN can take the form of elemental or semi-elemental formulations, with elemental forms having poor palatability [22]. Polymeric (whole protein) and semi-elemental (peptide) formulas, are better tolerated. The most frequently used forms of EEN are polymeric feeds such as Fortisip™, Ensure™ or Modulen™ [23]. While the clinical use of EEN is limited in the adult population, it has been a mainstay of treatment in paediatric CD as first line therapy for induction of remission, thereby avoiding steroid use [24,25]. A Cochrane review showed that EEN was effective in an adult population but inferior to steroids, perhaps due to lack of compliance with EEN [26]. Evidence for EEN in reducing intraoperative complications is limited to retrospective cohort studies and case-control studies [27–29].

Heerasing et al demonstrated that those commenced on EEN when compared with matched controls had a shorter operating time and were nine times less likely to develop an abscess or anastomotic leak. This study also demonstrated that patients treated with pre-operative EEN had a lower CRP than matched controls at the time of surgery and a quarter of patients avoided surgery [28]. Li demonstrated that patients who were immunosuppressant-free pre-operatively and given EEN had a lower rate of stoma formation, reduced incidence of post-operative complications and a reduced need for an urgent operation [29].

A small prospective study by Wang et al included fifteen patients, with ten patients receiving preoperative EEN for a median duration of 41.5 days (15 – 70 days). During the EEN course, there was a significant reduction in mean HBI (8.7 ± 1.9 versus 4.1 ± 2.4 ; $p = 0.001$) and CRP (11.7 ± 10.3 versus 0.8 ± 0.8 mg/dl; $p = 0.008$) and an increase in serum albumin (3.1 ± 0.6 versus 4 ± 0.6 g/dl; $p = 0.022$). Two patients did not require surgery following EEN. The incidence of postoperative complications and hospital length of stay were similar in EEN and immediate surgery groups, as well as clinical and endoscopic recurrence rates six months postoperatively. Despite being malnourished, patients given EEN did not have increased postoperative complications compared with well-nourished patients [30].

A systematic review in 2021 by Gordon-Dixon et al, regarding the use of preoperative EEN in Crohn's disease found that the current data on the use of EEN in preoperative optimisation is of poor quality and underpowered to demonstrate significance [32]. Seven studies were included in the final analysis, including five retrospective cohort studies and two retrospective case-control studies. The review concluded that in patients treated with EEN preoperatively, there were fewer infectious complications and a trend towards fewer stoma formations but only one study included was powered enough to demonstrate significance [32]. Use of preoperative EEN was not associated with improvements in body mass index or haemoglobin but there was a trend towards improvement in C-reactive protein and albumin levels. This reduction in infectious complications was further supported by a meta-analysis by Krasnovsky et al, published in 2024, showing that preoperative EEN

is associated with reduced skin, soft tissue and intra-abdominal infections. There was no significant difference in recurrence rates of Crohn's disease at twelve months in any of the studies and the quality of the studies were either medium or poor [33].

EEN may have the potential to reduce the need for surgery. Hu et al have shown that twelve weeks of EEN can effectively relieve inflammatory strictures. In this prospective study, stricturing disease was suggested through patient-reported symptoms and confirmed radiologically and where possible, endoscopically. A preliminary differentiation between fibrous and inflammatory strictures was determined using serum markers of inflammation, radiological "string sign" and thickened bowel wall on CT. CT was performed at baseline and at week 12. A twelve-week course of EEN was administered as an outpatient with most patients receiving between 1500 to 2000 ml per day. 50 out of the 65 eligible patients completed the entire EN treatment, while nine required surgical intervention for progressive bowel obstruction. 48 (73.8%) of patients achieved symptomatic remission, with 35 (53.8%) achieving radiological remission and 42 (64.6%) achieved clinical remission. Overall, 50 patients (76.9%) achieved partial remission, while 30 patients (46.2%) achieved clinical remission and did not require surgery [34]. The aforementioned retrospective study by Heerasing et al showed that pre-operative EEN in patients with penetrating and stricturing CD resulted in 25% of patients avoiding surgery and in those who did proceed to surgery, there was a reduction postoperative complications [28]. Avoidance of surgery may however only be short term. Marafini et al looked at EEN in patients with small bowel stricturing CD and new subacute obstructive episodes and found that patients not randomised to EEN had a higher rate of intestinal resection within the first three months of follow-up, rather than evenly distributed over twelve months [35].

There is also interest in the use partial enteral nutrition (PEN) which is better tolerated by patients as it avoids the taste fatigue experienced by those on EEN. PEN can either be supplemental oral nutritional supplements (ONS), for example in malnourished patients, or replacement ONS whereby a proportion of daily nutritional intake is replaced by ONS. Supplemental ONS is recommended by ESPEN for all malnourished or at risk of malnutrition CD patient undergoing surgery but the role of replacement PEN in patients who are not underweight or at risk of malnutrition in the pre-operative setting is unclear [19].

Meade et al showed in their 2022 study that oral EN (≥ 600 kcal/day for ≥ 2 weeks duration) was reasonably well tolerated and associated with a reduction in 30-day postoperative complications although recommended that further randomised controlled trials are required to confirm their findings. In a cohort of 300 patients, 204 underwent nutritional optimisation with oral EN ($n = 173$) or PN ($n = 31$). The nutritionally optimised cohort had favourable outcomes on multivariate analysis: all complications [OR 0.29; 0.15-0.57, $p < 0.001$], surgical complications [OR 0.41; 95% CI 0.20-0.87, $p = 0.02$], non-surgical complications [OR 0.24 95% CI 0.11-0.52, $p < 0.001$], infective complications [OR 0.32; 95% CI 0.16-0.66, $p = 0.001$] [31].

The CDED (Crohn's disease exclusion diet) diet is also being looked at in the preoperative setting. Phase 1 of the CDED diet involves 50% of nutritional intake coming from ONS [36,37]. Wall et al have published a New Zealand feasibility study looking at RCT of CDED vs EEN vs standard care for patients who are not malnourished. They have shown this study is feasible and the diets tolerated and their final results are awaited [38].

6. Role of Parenteral Nutrition

In cases where the use of enteral nutrition is not possible, the use of parenteral nutrition (PN) is recommended for five days or more and has previously been shown to reduce postoperative complication rates to 15% when compared to 24.4% in those who did not receive nutritional support, but did not reach statistical significance [39]. An historic study by Lashner et al demonstrated that patients receiving PN required a reduced length of small bowel resection of 20 cm when compared to the non-PN group [40]. Additionally, Ayoub has shown that sixty days of PN when compared with placebo significantly reduces rates of non-infectious complications when controlled for disease severity and malnutrition preoperatively, in addition to preoperative weight loss $>10\%$ in six months

being an independent risk factor and predictor of postoperative complications [41]. The ECCO consensus paper does not however recommend deferring emergency surgery and nutritional status should only be optimised in patients in which surgery can be delayed.

7. Steroids and Perioperative Complications

Steroids may be used to control symptoms prior to elective surgery but are a risk factor for intra-abdominal septic complications (OR 1.99, CI: 1.54 – 2.57) [12,42]. They have also been shown to delay wound healing, increase the risk of superficial and deep surgical site infection, pneumonia, myocardial infarction, adrenal insufficiency and prolonged intubation [43–45]. Steroids also increase the risk of re-admission within thirty days by 58%, risk of reoperation by 21%, hospital stay over thirty days by 31% and risk of mortality by 32% [46]. Two single centre prospective studies showed the use of EEN preoperatively allowed up to 62.5% of steroid-dependent patients to successfully wean off steroids in the preoperative period [27,47]. A single-centre prospective study noted that perioperative EEN prolongs the immunosuppressant-free, including steroids, interval, reduces the risk for urgent surgery and re-operation and reduced postoperative complications [29,48,49].

While systemic corticosteroids are indicated for attaining remission in IBD, they are not recommended for maintenance therapy [50]. A study by Stuck et al pooled the data from 71 controlled trials and showed that the risk of infection was not increased in patients on less than 10 mg of prednisolone. For patients receiving 10 mg daily, the overall rate of infectious complications was 12.7% when compared to 8% in controls (2111 patients vs 2087 controls; RR: 1.6; 95% CI: 1.3-1.9; $p < 0.001$) [51]. Two further studies by Huang et al and Subramanian et al showed that corticosteroid use was associated with a high risk of intra-abdominal septic complications (OR 1.99; 95% CI: 1.54-2.57) and all postoperative complications (OR 1.41, 95% CI: 1.07-1.87) and an increased risk for postoperative infectious complications (OR 1.68, 95% CI: 1.24-2.28), respectively [52,53]. The 2018 ECCO-ESCP Consensus on Surgery for Crohn's Disease advise that prednisolone at a daily dose of 20 mg or equivalent for six weeks or more is a risk factor for postoperative complications and should be weaned if possible [12].

8. Preoperative Pharmacotherapy

The PUCCINI (Prospective Cohort of Ulcerative Colitis and Crohn's Disease Patients Undergoing Surgery to Identify Risk Factors for Post-Operative Infection) trial was the largest multicentre prospective surgical cohort study to examine the safety of anti-tumour necrosis factor (anti-TNF) agents in the perioperative setting in IBD [54]. This study was designed in response to the French GETAID and REMIND prospective cohort studies [55,56]. The GETAID study showed a correlation with anti-TNF use less than three months prior to surgery and increased postoperative morbidity and mortality as well as intra-abdominal septic complications. It did not however assess preoperative serum drug concentrations [55]. The aim of the PUCCINI study was to determine if preoperative anti-TNF exposure is an independent risk factor for infectious complications in patients with IBD undergoing abdominal surgery, with a secondary aim of examining the effects of serum drug concentration on post-operative infectious complications [54]. 947 patients were enrolled in the trial, with 387 (40.9%) of patients using systemic corticosteroids within two weeks of surgery. 235 patients (24.8%) were using thiopurines. 382 patients (40.3%) had used anti-TNF within twelve weeks, with 136 (14.4%) on vedolizumab and 21 (2.2%) on ustekinumab. 208 patients had detectable anti-TNF serum levels at the time of surgery. Anti-TNF exposure within twelve weeks of surgery was not associated with increased risk of any infection or surgical site infection. Additionally, thiopurine exposure was not associated with postoperative complications. Smoking preoperatively was found to be a significant risk factor for both any infection and surgical site infection in the cohort and represents one of the most significant modifiable risk factors for postoperative complications [54]. A 2023 retrospective analysis by Schnitzler et al. examined postoperative complications in 447 patients undergoing surgery for IBD between 2012 and 2022. 275 (61.3%) patients were exposed to biologics within twelve weeks of surgery, with 68.7% of patients receiving a biologic dose within four weeks

of surgery. The study found that biologic exposure in the pre-operative setting did not increase the risk of postoperative infectious complications [57].

The 2024 ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Management, as mentioned previously recommend against cessation of biologics prior to surgery as the current evidence suggests that pre-operative treatment with anti-TNF therapy, vedolizumab and ustekinumab does not increase the risk of post-operative complications in CD patients undergoing abdominal surgery [14]. Data on the Janus kinase inhibitor and sphingosine 1 phosphate receptor modulators is lacking.

Communication between the medical and surgical team as well as involvement of the patient is key to ensure appropriate management of patients in the pre and post operative periods. This is highlighted in the 2024 NCEPOD 'Making the cut' paper. Involvement of the wider multidisciplinary team including pharmacist and IBD nurses to ensure there is clarity required timing of surgery and post operative plans regarding medication is essential for safe patient care [15]. They emphasised that all patients with Crohn's disease should have access to holistic care and require careful medication management prior to, during and post-operatively.

9. Surgical Prehabilitation

The American College of Surgeons (ACS) defines surgical prehabilitation as "a process of improving the functional capability of a patient prior to a surgical procedure so the patient can withstand any postoperative inactivity and associated decline" [58]. Currently the evidence for prehabilitation in Crohn's disease is lacking, with most studies focusing on nutritional intervention and optimisation in the perioperative period. The term "prehabilitation" encompasses a wide range of interventions that aim to improve the preoperative medical, physical, nutritional and psychological status of the patient [59]. A systematic review by Jain et al, demonstrated that a trimodal prehabilitation programme, including exercise and inspiratory muscle training, nutritional and psychological support improves a patient's preoperative functional capacity and reduces postoperative complications following abdominal surgery [60]. The majority of patients included in this study were undergoing cancer surgery and may not be directly applicable to the IBD cohort but did emphasise the importance of exercise for building muscle, improving cardiopulmonary fitness and reducing the debilitating effects of reduced mobility in the perioperative period [61].

A 2022 study by Ferrandis et al, showed that personalised prehabilitation reduces anastomotic complications compared to up front surgery before ileocolic resection in high-risk patients with Crohn's disease [62]. This was a single-centre retrospective study involving 90 patients and examined all high-risk patients undergoing ileocaecal resection with primary anastomosis over a ten year period. Patients were classified as high-risk if they had one of the following risk factors; hypoalbuminaemia <30 g/l or weight loss $>10\%$ of total body weight in the preceding six months, treatment with corticosteroids within four weeks of surgery or the presence of preoperative intra-abdominal sepsis. Personalised prehabilitation included nutritional support, corticosteroid adjustment and management of intra-abdominal sepsis for at least seven days preoperatively. 71% of patients received personalised prehabilitation for a median duration of 37 days, with the number of preoperative risk factors improved (1.21 vs 1.06; $p = 0.001$). The 90-day anastomotic complication and re-operation rates were lower in patients that received prehabilitation; 6.25 vs 23.1%; $p = 0.031$ and 3.1 vs 19.2%; $p = 0.019$, respectively [62].

Overall, the evidence for prehabilitation in Crohn's disease surgery is lacking and requires prospective studies to support its role as used in other surgical interventions in populations such as cancer or elderly patients.

10. Conclusions

Preoperative optimisation of patients undergoing surgery for Crohn's disease is an example of collaborative multidisciplinary care. Corticosteroid dose should be reduced and stopped where possible. Nutritional screening and optimisation is key and how best to deliver this is an area of ongoing research. Emergent surgery should be avoided where possible. Biologic medications should

not be stopped in the perioperative period, as backed by international guidelines. Further research regarding newer advanced oral therapies is needed. Close communication between the IBD MDT with a patient centred approach is key for successful surgical outcomes.

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