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Optimization of pre-, intra- and post-operative surgical management in patients affected by inflammatory bowel disease

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OPTIMIZATION OF PRE-, INTRA- AND POST-OPERATIVE SURGICAL MANAGEMENT IN PATIENTS AFFECTED BY INFLAMMATORY BOWEL DISEASE

TEXT

INTRODUCTION

Inflammatory bowel diseases (IBDs) are immune system disorders characterized by a chronic course with remissions and relapses. IBD includes two related but distinct disorders: Crohn's disease (CD) and ulcerative colitis (UC) (1, 2, 3). Utilizing immunomodulators and biological medications for maintaining remission in IBD is well established (4). However, adverse events of these medications, such as the increased risk of infection and malignancy, have always been concerning (5, 6).

Furthermore, despite advances in the medical management of CD, approximately 25% to 80% of the patients with Crohn's disease need surgery within 10 years of diagnosis (7, 8). In addition, 40-50% of patients that receive surgical treatment for Crohn's will require further surgery within the next 10-15 years (7). In UC about 40% of patients with severe disease require proctocolectomy (9). Furthermore, in UC, disease-specific causes of deaths include colorectal cancer (CRC), and surgical and postoperative complications (10, 11).

Malnutrition affects up to 70% of the IBD population (12,13) and is an independent risk factor for adverse postoperative outcomes. Protein-energy malnutrition in IBD was caused by low dietary intake, enhanced energy expenditure due to inflammation, impaired digestion and absorption, and protein leakage from ulcerative lesions. It leads to decreases in skeletal muscle and adipose tissue volumes. Altered body composition, such as reduced fat-free mass and decreased skeletal muscle volume has been reported in IBD patients (14).

The recent concept of Enhanced Recovery After Surgery (ERAS) underlines the necessity to adopt minimally invasive surgery and perioperative treatment to reduce postoperative complications and

length of stay. Laparoscopic resection has various benefits compared to conventional open resection, in selected patients (15, 16).

Considering their young age and the need for repeated operations, the benefits of improved cosmesis, less postoperative pain, shorter length of stay, earlier return to work, reduced adhesional formation and incidence of incisional hernias due to the conservation of abdominal wall are undeniably appealing (17, 18, 19).

Furthermore, the minimally invasive surgery associated with the concept of "fast-track" and ERAS protocol leads to faster recovery and further reduction of LOS (20, 21, 22).

The fast track protocol is an evidence-based care program including preoperative, intraoperative and postoperative items and it was introduced about 20 years ago by Kehlet et al. (23, 24) to reduce perioperative stress, improve patient outcomes, achieve faster recovery, shorten length of hospital stay (LOS), without compromising the safety of the patients (25). However, the application of ERAS pathway in IBD is not still diffuse.

The aim of this study was to implement the pre-, intra- and post-operative phases adopting nutritional prehabilitation, minimally invasive surgery and ERAS protocol and to evaluate the effect of these approaches on surgical outcome and length of hospital stay.

METHODS:

This study was prospectively carried out on consecutive adult patients (age 18) affected by CD or UC who referred to the Digestive Surgery Unit of Careggi University Hospital from December 2018 to June 2021.

Surgical indication for CD was the presence of a complicated disease (severe inflammation, strictures or fistulas/abscesses), while in UC was refractoriness illness to medical therapy, case of severe inflammation or presence of dysplasia.

All cases were discussed by a multidisciplinary IBD team, composed by dedicated surgeons, gastroenterologists, radiologists and dietitians.

Preoperative optimization included prehabilitation and nutritional evaluation with immunonutrition therapy before surgery. All patients were evaluated by a dedicated dietitian. Each patient was provided with a personalised nutrition care plan, protein supplementation and, in case of malnutrition, hypercaloric oral nutritional supplement (26, 27).

Intra-operative optimization included a minimally invasive surgical approach. All patients were treated by laparoscopic technique. Intra- and post-operative periods were optimized following ERAS protocol for oncological colorectal surgery (27).

Our intra- and post-operative protocol was based on the following items:

1. Antithrombotic prophylaxis starting the evening before surgery with LMWH and with elastic compressive stokes weared from the day of surgery until a complete mobilization
2. Intravenous antibiotic prophylaxis with I generation cephalosporin and metronidazole about 30 minutes prior to surgery
3. Balanced intravenous fluid therapy
4. Prevention of hypothermia with warming blankets and fluids

5. Intraoperatively prevention of postoperative nausea and vomiting is achieved with i.v. Dexamethasone and Ondansetron.

6. Drains only in selected cases.

7. Nasogastric tube removal at the end of surgery after the extubation

8. NSAIDs and paracetamol were used to control the pain. Intravenous somministration occurs until postoperative day (POD) I. These drugs are associated with proton-pump inhibitors.

9. Urinary catheter removal on POD I.

10. Early mobilization from POD I. Physiotherapist aid in case of older enticed patients.

11. The postoperative nutritional protocol included a clear fluids diet from POD 1 and three progressive low residue diets according to patients tolerance from POD 2 (Table 1). In malnourished patients, additional oral nutritional supplements were administered starting from POD 1 in order to reach energy and protein requirements.

Postoperative day (POD)	Type of diet	Energy	Protein
POD 1	Clear fluids		
POD 2	Low residue semi-solid	600 kcal	14 g
POD 3	Low residue solid 1	1350 kcal	62 g
POD 4 and later	Low residue solid 2	2100 kcal	96 g

Table 1

Data were prospectively recorded for each patient of both groups (CD and UC). The data recorded were age, gender, smoke, weight, body mass index (BMI), Duke Activity Status Index (DASI),

duration of disease, recurrence, preoperative presence of ileostomy, disease localization and behaviour.

Body composition parameters were recorded using bioelectrical impedance vector analysis (BIVA) calibrated devices (Nutrilab-Monitor, AKERN, Florence, Italy). The BIVA parameters analysed in each phase were: Free Fat Mass (FFM), Fat Mass (FM), Free Fat Mass Index (FFMI) and Phase Angle.

Nutritional risk was detected according to the NRS 2002 screening tool (28).

The impact of the adherence to our protocol on postsurgical recovery was analysed, in particular first flatus and stool passage, surgical or medical complications and length of hospital stay.

Discharging criteria included full mobilization with the ability to perform activities of daily living, recovery of bowel function patients, adequate oral feeding and pain control with oral analgesia. Patients received the phone numbers to contact the hospital in case of need and they were visited as outpatients within 5 days from discharge.

Statistical analysis was performed with IBM SPSS Statistics for Mac, Version 20.0. Armonk, NY: IBM Corp. Descriptive statistics of nominal data were described with raw numbers and percentages, while continuous variables were reported with mean and standard deviation (SD). Changes in body composition parameters throughout all stages of the study (baseline, hospital admission, hospital discharge, follow-up after surgery) were assessed with paired-samples T test. Independent samples T test was utilized to assess differences in body composition among patients at high and low nutritional risk in the period between baseline assessment and hospital admission evaluation (preoperative phase). Pearson's X2 test was performed to identify associations between pre-existing muscle wasting and other relevant categorical variables, including presence of ileostomy or previous IBD surgical procedures.

Associations between continuous variables (refeeding timing vs length of hospital stay/first flatus/first stool passage) were explored with Pearson's correlation. Significance was set at $p < 0.05$.

RESULTS:

A total of 61 patients were included in the study, 45 pts with CD and 16 pts with UC.

CD GROUP

In the group with CD the median age was 53 years (range 26-79), 25 (56%) male and 20 (44%) female, 12 pts (27%) were smokers. The mean weight was 63,7, with a mean value of BMI of 22.8 kg/m2. The mean values of FFM and FM were 49.3 (SD 8.4) and 13.4 (SD 6.9), respectively. All patients were screened using NRS-2002: 35 pts (76%) had NRS < 3, while 10 pts (24%) had NRS ≥ 3.

The mean disease duration was 12.7 years. The disease pattern was inflammatory in 3 pts (7%), stricturing in 30 pts (68%) and fistulizing in 11 pts (25%). The localization of the disease was ileal in 34 pts (79%), colonic in 5 pts (12%) and ileocolonic in 4 pts (9%). The surgical recurrence was present in 18 patients (40%) and only one patient (2%) had a preoperative ileostomy. The mean DASI score was 44.3.

In these pts, 26 (77%) ileo-colic resections, 5 (14%) colic resections and 3 (9%) ileal resections were performed. Ileostomy was performed in 1 pts (3%). The mortality rate was 0%. No major complications and no anastomotic dehiscence occurred. Minor postoperative complications affected 4 pts (11%), in particular two wound infections, one venous thrombosis, one pneumonia. Postoperative nausea or vomiting (PONV) occurred in 3 pts (9%). The mean time of passage of the first flatus and stool was 3 and 3.9 days. Mean days of refeeding were 1,6 for clear liquid diet, 2,4 for semi-solid diet and 3,6 for solid diet. The mean length of hospital stay was 4,8 days.

UC GROUP

In the group of UC, the median age was 49 years (range 20-69); 11 (69%) were men and 5 (31%) were women. The mean weight was 65,4 with a mean value of BMI of 22.7 kg/m2. The mean

values of FFM and FM were 48.5 (SD 9.4) and 15.7 (SD 10.1), respectively. All patients were screened using NRS-2002: 11 pts (69%) had NRS < 3 and 5 pts (31%) had NRS ≥ 3.

The mean duration of disease was 12.8 years.

The pattern of the disease was proctitis in 8 pts (50%), left side colitis in 1 pts (6%) and extensive colitis in 7 pts (44%). The secondary surgery was present in 11 pts (69%), while 10 pts (62,5%) had a preoperative ileostomy. The mean DASI score was 45.5.

In these pts, 5 (33%) underwent total colectomy with ileostomy and rectal stump abandoning (first surgical step for acute severe UC), 8 (53%) underwent proctectomy with ileal pouch-anal anastomosis and loop ileostomy (second surgical step in acute severe UC) and 2 (13%) had total proctocolectomy with ileal-pouch anal anastomosis (IPAA) and loop ileostomy. Ileostomy was performed 14 pts (93%). The mortality rate was 0%. No major complications and no anastomotic dehiscence occurred. Minor postoperative complications affected 2 pts (12%), in particular wound infection and prerenal kidney failure due to dehydration related to the ileostomy. Postoperative nausea or vomiting (PONV) did not occur. The great majority of UC patients had a temporary ileostomy, so we evaluated the mean time to first stool passage that was 1.6 days. Mean days of refeeding were 1,5 for clear liquid diet, 2,3 for semi-solid diet and 3,5 for solid diet. The mean length of hospital stay was 7,9 days.

Post-operative outcomes were reported in Table 2.

CD		**UC**	
Type of resection, n (%) - ileal - ileocolic - colic	 3 (9%) 26 (77%) 5 (14%)	Type of resection, n (%) - total colectomy with ileostomy and rectal stump abandoning -proctectomy with ileal pouch-anal anastomosis and loop ileostomy -total proctocolectomy with ileal-pouch anal anastomosis and loop ileostomy	 5 (33%) 8 (53%) 2 (14%)
Ileostomy, n (%)	1 (3%)	Ileostomy, n (%)	14 (93%)
Postoperative minor complication, n (%)	4 (11%)	Postoperative minor complication, n (%)	2 (12%)
Clear liquid diet (days, mean ± SD)	1,6 (+/- 1,2)	Clear liquid diet (days, mean ± SD)	1,6 (+/- 0,8)
Low residue semi-solid diet (days, mean ± SD)	2,4 (+/- 1,6)	Low residue semi-solid diet (days, mean ± SD)	2,3 (+/-1,0)
Low residue solid diet (days, mean ± SD)	3,6 (+/- 1,6)	Low residue solid diet (days, mean ± SD)	3,5 (+/- 1,2)
PONV	3 (9%)	PONV	0
Time to first flatus (days, mean ± SD)	3 (+/- 1,1)		
Time to first stool (days, mean ± SD)	3,9 (+/- 1,2)	Time to first stool (days, mean ± SD)	1,6 (+/- 0,8)
Length of hospital stay (days, mean ± SD)	4,8 (+/- 3,1)	Length of hospital stay (days, mean ± SD)	7,9 (+/-6,8)

Table 2

GLOBAL REFEEDING RESULTS

The mean time of prehabilitation and consequently the necessary nutritional support was 103 days before surgery (period between baseline observation and hospital admission assessment). The patients were evaluated by a dedicated dietitian in order to maximise the compliance and to obtain a considerable nutritional intervention. The analysis of the IBD patients with low FFMI (10 CD and 7 UC) showed that muscle wasting was associated with the presence of ileostomy ($p < 0.011$) and with second surgery ($p < 0.011$). While the duration of the disease was not associated with reduced muscle mass. The screening using NRS-2002 showed a total of 46 pts (75%) with NRS < 3, while 15 pts (25%) with NRS $\geq$ 3. At hospital admission, an increase of body weight (in particular FFM) from baseline was reported in all cases. The overall evaluation of data obtained at hospital discharge reported a decrease of all body composition parameters during the hospital stay (not statistically significant). Comparing baseline and follow-up assessments data, we found no significant changes in body composition. In particular, the improvement in body composition during the preoperative phase was more evident in patients at higher nutritional risk (NRS 3 according to NRS 2002).

In all patients a bivariate analysis was performed to explore associations between refeeding time and post-surgical outcomes. Patients with earlier resumption of oral feeding had a shorter hospital stay (Table 3).

ORAL FEEDING	**LOS (p value)**
CD	
Re-feeding time with clear fluids diet	$p < 0,001$
Re-feeding time with semi-solid low residue diet	$p < 0,001$
Re-feeding time with solid low residue diet	$p < 0,001$
UC	
Re-feeding time with clear fluids diet	$p = 0,039$
Re-feeding time with semi-solid low residue diet	$p = 0,038$
Re-feeding time with solid low residue diet	$p = 0,043$

Table 3

DISCUSSION:

Up to 70% of patients with CD require abdominal surgery during their lifetime (29, 30). In UC about 40% of patients with severe disease require proctocolectomy (9). Postoperative complications are seen more frequently in patients with IBD than in patients requiring surgery for other conditions (31, 32).

This observation relates to the associated unfavourable clinical settings in which surgery is often performed (poor nutritional status, acute infection and use of immunosuppressive medications), as well as factors that make surgery more challenging (for example, peritonitis, perforation and obstruction) (33).

Therefore, it is crucial to enhance the recovery by optimising perioperative management. Patients with IBD often undergo surgery with impaired nutritional status due to the chronic inflammatory state and the frequent presence of complications related to the disease (34).

Our pre-operative optimization showed that muscle wasting was present at baseline assessment in 10 CD and 7 UC, and it was significantly associated with the presence of ileostomy ($p < 0.011$) and of a previous surgical operation for IBD ($p < 0.011$). While the duration of the disease was not associated with reduced muscle mass. We observed a similar prevalence of malnutrition in CD and UC, probably due to the more frequent presence of ileostomy in UC patients, while CD patients malnutrition was associated with the operation for surgical recurrence.

The good practice in oncological surgery is to adopt a preoperative nutritional support in patients who cannot maintain an acceptable nutritional intake (above 50% of recommended) for more than seven consecutive days or are severely malnourished as defined by ESPEN clinical nutrition in surgery guidelines (35).

In our program, prehabilitation was adopted in all patients undergoing surgery for IBD, as a routine practice to be implemented not only in case of severe malnutrition. Our study has demonstrated a significant improvement in weight, BMI and lean mass during the preoperative phase both in CD

and UC patients (p=0.035; p=0.017). Consequently, the FFMI (CD ns; UC p=0.011) was also improved.

However, our IBD patients showed a weight loss and FFM decrease during the late postoperative phase. Nevertheless, both CD and UC patients did not have significant changes in terms of body composition, when the perioperative period is globally evaluated. We believe that this is a positive result considering the catabolic effect induced by surgery, which indicates that prehabilitation attenuated the loss of surgically induced catabolism in the IBD population.

In our study, regarding the intra- and postoperative phase, the principles of ERAS should be applied whenever possible to the surgical management of IBD patients.

Enhanced recovery after surgery pathways have been implemented across a variety of surgical procedures in adults. These have demonstrated decreased length of stay without increasing complication rates (36, 37, 25).

In our experience, the ERAS postoperative nutritional protocol had good compliance both in CD and UC patients with a similar mean time of resumption of oral intake in the two groups. Our data are comparable to those few already published in literature that apply ERAS to IBD surgery [24,25]. Patients with earlier resumption of feeding had a significant shorter hospital stay and a faster recovery of bowel function. No significant relationship with early postoperative complications was found, whereas in literature early postoperative nutrition is reported to be associated with significant reductions in overall complications after colorectal oncological surgery [26-28]. Limitations of our study were the relatively small sample size and the absence of a control group dictated by ethical reasons.

CONCLUSION:

In conclusion, preoperative patient optimization for IBD surgery is complex and requires a multidisciplinary approach.

Nutritional prehabilitation positively modulated the body composition of IBD patients scheduled for elective surgery and may be a beneficial strategy to attenuate the impact of surgical stress response.

Early postoperative oral feeding in an ERAS setting seems feasible and well tolerated and it positively influences the restoration of bowel function and the duration of hospital stay.

Optimization of the pre-, intra- and postoperative management has a substantial beneficial effect on postoperative outcome and should therefore always be attempted.

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