



## Original Research

# The role of exclusive enteral nutrition in the preoperative optimization of laparoscopic surgery for patients with Crohn's disease: A cohort study



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## ABSTRACT

**Background:** Growing evidence has shown that there are significant advantages associated with the use of laparoscopic surgery for Crohn's disease (CD). However, the impact of preoperative exclusive enteral nutrition (EEN) on postoperative complications and CD recurrence following laparoscopic surgery have not been investigated.

**Methods:** A total of 120 CD patients undergoing bowel resection with laparoscopic surgery were eligible for this study. Patient data were collected from a prospectively maintained database. Before laparoscopic surgery, 45 CD patients received EEN for at least 4 weeks, and 75 CD patients had no EEN. Postoperative complications, and endoscopic and clinical recurrence were subsequently measured and compared after laparoscopic surgery and during follow-up assessments.

**Results:** Patients who received EEN had significant improvements in their nutritional (albumin, prognostic nutritional index (PNI), and hemoglobin) and inflammatory (C-reactive protein) status after the EEN treatment prior to surgery ( $P < 0.05$ ). Patients who received EEN also experienced fewer postoperative complications, decreased surgical site infections, and a lower comprehensive complication index ( $P < 0.05$ ). The endoscopic recurrence rates 6 months after surgery were also decreased significantly in patients who received EEN ( $P < 0.05$ ). However, the incidence of clinical recurrence was similar in the 2 groups at 1-year follow-up. Endoscopic recurrence was correlated with ileocolonic disease, EEN before surgery, and PNI ( $P < 0.05$ ). PNI remained independently associated with endoscopic recurrence after surgery.

**Conclusions:** Preoperative EEN for at least 4 weeks improved CD patients' nutritional and inflammatory status, which in turn reduced postoperative complications following laparoscopic surgery and endoscopic recurrence on follow-up.

## 1. Introduction

Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD), is characterized as a chronic condition with periods of exacerbation and remission [1]. The incidence of CD is increasing steadily worldwide and the clinical pharmacology of various drug treatments for this condition has been explored extensively [2]. However, the disease course continues to result in surgery from complications mostly including stricturing or penetrating lesions. It is reported that approximately 80% of CD patients require surgical intervention during the course of the disease [3]. After the initial operation,

50% of CD patients will experience a second operation, and of these patients who accept a second surgery, 50% need a third operation due to complications [4].

As the step-up therapeutic strategy fails to change the course of the disease, a top-down approach including surgical treatment initially if necessary has been considered to minimize tissue damage [5]. In regard to the severely inflamed intestinal segment of CD patients with immunomodulator-refractory or steroid-refractory status, surgery is suggested as the first rescue therapy [5,6]. In gastrointestinal surgery, the laparoscopic approach has gained widespread acceptance in recent years. It has been demonstrated that laparoscopy leads to an earlier

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return to normal activity and diet, less postoperative pain, shorter hospital stays, lower rates of postoperative complications, improved quality of life, and better cosmesis [7]. Given the advantages of laparoscopy and the young age distribution of CD patients, laparoscopy seems to be particularly suitable in this cohort. Emerging studies have demonstrated that laparoscopic surgery is feasible and safe for ileocolic CD or even in complex cases [8]. The European Crohn's and Colitis Organisation (ECCO) guidelines also suggest that the laparoscopic approach is preferred for ileocolic resections in CD as it provides benefits associated with earlier recovery of normal intestinal function and lower postoperative morbidity [9]. Accumulated data indicate that laparoscopy is used increasingly in CD, but postoperative complications and recurrence are still topics requiring attention.

Due to decreased food intake and malabsorption of nutrients, increased intestinal loss, a hypermetabolic state, and drug interactions, malnutrition is common in CD patients [10]. Malnutrition is thought to be associated with postoperative complications in surgical patients [11]. Several studies also found that preoperative immunosuppressive therapy was a risk factor for postoperative complications in CD patients [12,13]. Thus, more studies have begun to focus on preoperative optimization. Exclusive enteral nutrition (EEN) is a liquid formula to meet all of the patient's nutritional requirements [14]. It is recommended that EEN be introduced in the management of CD to improve nutritional status and decrease inflammation before surgery [15].

Despite early studies reporting that EEN reduces postoperative complications and improves nutritional status [14], there is a paucity of studies reporting the role of EEN in the preoperative optimization of laparoscopic surgery for CD. Thus, the aim of our study was to examine whether EEN therapy for at least 4 weeks before laparoscopic surgery could reduce postoperative complications and recurrence rates in CD patients.

## 2. Materials and methods

### 2.1. Patients

From January 2015 to December 2017, data from consecutive patients who had elective bowel resection for CD were retrospectively analyzed at the IBD center of our hospital. All data from CD patients undergoing laparoscopy were collected from the medical charts in our IBD database, including baseline characteristics, intraoperative, laboratory, and follow-up data. This study was approved by the ethics committee of our hospital and CD patients were screened for eligibility to participate. At our IBD center, patients are always recommended to have EEN for preoperative optimization; however, not all patients followed our suggestion. Thus, two CD patients groups exist based upon whether or not they received EEN. This study has been reported in line with the STROCSS criteria [16].

Inclusion criteria were as follows: (1) radiologic, endoscopic, and histologic diagnosis of CD according to European Crohn's and Colitis Organisation (ECCO) guidelines(1); (2) CD patients required a laparoscopic approach for bowel resection; (3) the score of Nutritional Risk Screening (NRS-2002) was more than 2; (4) patients received preoperative optimization, such as quitting smoking, stopping corticosteroid treatment, and nutritional therapy before surgery. For the EEN group, patients had EEN therapy for at least 4 weeks before surgery by nasogastric tube, and the daily calorie intake was 25–30 kcal/kg of body weight; For the non-EEN group, patients received a liquid diet, semiliquid diet, oral nutritional supplements (ONS), or intravenous solution to improve their nutrition status and maintain their nutrition status according to the suggestion from nutritionist, and they almost received equal calorie and protein compared to the EEN group. Patients with incomplete laboratory data, poor compliance with EEN therapy, or multivisceral resection were excluded. In our hospital, CD patients were always encouraged to receive nutrition treatment before surgery, but whether or not patients accepted a nasogastric tube were their

decisions.

The exclusive enteral nutrition used in this study was Peptison liquid (Nutricia, Amsterdam, Netherlands), which was composed of vitamins, minerals, hydrolyzed whey protein peptide, trace elements, very little fat, vegetable oil, and maltodextrin [17]. The content of major nutrients included carbohydrates (17.6 g), lipids (1.7 g), and protein (4 g) per 100 mL of liquid. The calorie density was 1 kcal/mL with an osmolality of 440 mosm/L.

### 2.2. Data collection

Baseline patient characteristics recorded included age, body mass index (BMI), comorbidities, sex, Montreal classification, preoperative medications and history of surgery. Intraoperative data included the duration of the operation, estimated blood loss, stoma creation, and conversion to open laparotomy. Laboratory data included hemoglobin, C-reactive protein (CRP), albumin (ALB), white blood cell (WBC) count, red blood cell (RBC) count, erythrocyte sedimentation rate (ESR), platelet (PLT) count, hematocrit, and total lymphocyte count (TLC) before enteral nutrition and before surgery. Follow-up data included clinical and endoscopic recurrence at 6 months and 12 months.

### 2.3. Definition of outcomes

The primary outcome of this study was overall postoperative complications based on the Clavien-Dindo classification [18]. Grades I to II were defined as mild complications, and Grades III to IV were defined as major complications. The comprehensive complication index (CCI), which was a score developed to include all complications after surgery and depends on the Clavien-Dindo classification [19], was calculated for each patient using the web site <http://www.assessurgery.com> [20]. Surgical site infections (SSIs) included incisional and organ/space SSIs. The definition of SSIs was described according to WHO guideline as: "Any infection of the superficial or deep tissues or the organ/space affected by surgery, and which occurs within 30 days of surgery when no prosthesis has been implanted". Other outcomes included clinical recurrence, endoscopic recurrence, and clinical effects of EEN which included CRP, WBC, ALB and so on. Clinical recurrence was defined as a Crohn's Disease Activity Index (CDAI) score of  $\geq 150$  or with an increase of more than 70 points, and endoscopic recurrence was defined according to Rutgeerts scores (i2, or higher)(1). The prognostic nutritional index (PNI) was used to evaluate the clinical effects of enteral nutrition. The following formula was used to calculate the PNI:  $10 \times \text{ALB (g/dL)} + 0.005 \times \text{TLC (per mL)}$  [21]. The cutoff value for the PNI was 40 as per original research by Onodera et al. [22].

### 2.4. Statistical analysis

Statistical Product and Service Solutions (SPSS) version 21.0 (Armonk, NY: IBM Corp) was used to analyze the data. Continuous data were presented as the mean  $\pm$  standard error (SE) or median (range), while categorical data were presented as n (%). The continuous variables were analyzed by the Student's *t*-test or Mann-Whitney *U* test depending on the normality of the data distribution, and the categorical variables were analyzed by the Pearson's  $\chi^2$  test or the Fisher's exact test, as appropriate. Significant associations ( $p < 0.05$ ) from univariate analysis were used in multivariate logistic regression analyses to verify independent predictors of endoscopic recurrence in CD patients undergoing laparoscopic surgery. Values of  $p < 0.05$  were considered statistically significant.

## 3. Results

### 3.1. Study population and baseline characteristics

During the study period, 36 patients were excluded, and 120

**Table 1**  
Characteristics of the study population.

Clinical variable	EEN (n = 45)	Non-EEN (n = 75)	P value
Male/female	32/13	53/22	0.959
Age (years)*	31.5 ± 1.5	35.7 ± 1.3	0.036
BMI (kg/m <sup>2</sup> )*	18.3 ± 0.4	19.2 ± 0.3	0.102
Previous abdominal surgery, n (%)	10 (22.2)	21 (28.0)	0.484
Appendectomy, n (%)	7 (15.6)	9 (12.0)	0.579
Comorbidities, n (%)	4 (8.9)	7 (9.3)	0.935
Diabetes mellitus	0	1 (1.3)	–
Hypertension	1 (2.2)	1 (1.3)	–
Hepatitis B	3 (6.7)	5 (6.7)	–
Motreal classification			
Age (years)			
A1 (≤16)	0	1 (1.3)	0.625
A2 (17–40)	36 (80.0)	50 (66.7)	0.117
A3 (> 40)	9 (20.0)	24 (32.0)	0.154
Location			
L1 (ileal)	11 (24.4)	19 (25.3)	0.913
L2 (colonic)	4 (8.9)	8 (10.7)	0.752
L3 (ileocolonic)	28 (62.2)	43 (57.3)	0.598
L4 (upper gastrointestinal)	2 (4.4)	5 (6.7)	0.609
Behavior			
B1 (inflammatory/failure of medical therapy)	2 (4.4)	5 (6.7)	0.609
B2 (stricturing)	32 (71.1)	53 (70.7)	0.959
B3 (penetrating)	15 (33.3)	27 (36.0)	0.767
P (perianal disease)	14 (31.1)	21 (28.0)	0.717
Preoperative medications			
5-ASA	16 (35.6)	25 (33.3)	0.804
Corticosteroids	3 (6.7)	3 (4.0)	0.523
Thiopurine	12 (26.7)	31 (41.3)	0.105
Infliximab	8 (17.8)	7 (9.3)	0.176
Others	6 (13.3)	9 (12.0)	0.831
Duration of operation*	178.4 ± 6.7	193.9 ± 6.1	0.104
Estimated blood loss*	68.3 ± 10.7	68.9 ± 6.4	0.959
Stoma	9 (20.0)	24 (32.0)	0.154
Conversion to open laparotomy	11 (24.4)	23 (30.7)	0.464

Values in parentheses are percentages unless indicated otherwise; \*values are mean ± SE.EEN, exclusive enteral nutrition.

patients undergoing laparoscopic surgery for CD were enrolled (men:women = 85:35). Among the 120 patients included, 45 (37.5%) had EEN therapy before laparoscopic surgery, and 75 (62.5%) did not. In the EEN group, the mean age was 31.5 ± 1.5 years, and 10 patients had a history of previous abdominal surgery. In the non-EEN group, the mean age was 35.7 ± 1.3 years, and 21 patients had a history of previous abdominal surgery. There were no significant differences in comorbidities, Montreal classification, preoperative medications, and emergency surgery between the EEN group and the non-EEN group. In addition, no significant differences were observed between patient groups with regard to the duration of operation, estimated blood loss, stoma creation, or conversion to open laparotomy. The clinical characteristic details for each group are shown in Table 1.

### 3.2. Postoperative complications in patients after laparoscopic surgery

85 (70.8%) patients recovered uneventfully, and 35 (29.2%) patients had postoperative complications, with 33 mild complications and 21 major complications. As shown in Table 2, the rate of postoperative complications in the EEN group was 17.8%, which was significantly lower (p = 0.033) than that in the non-EEN group (36.0%). The median CCIs in patients with postoperative complications in the EEN group and non-EEN group was 0 (interquartile range, 0–0) and 0 (interquartile range, 0–20.9), respectively, and there was a significant difference between these two groups. In addition, patients in the non-EEN group had more SSIs (24.0% vs 8.9%, p = 0.038) and longer postoperative hospital stays (10.3 ± 0.7 vs 9.4 ± 0.6, p = 0.444). In this study, there were patients suffering more than one complication after surgery.

**Table 2**  
Postoperative complications, endoscopic recurrence and clinical recurrence in Crohn's disease.

Clinical variable	EEN (n = 45)	Non-EEN (n = 75)	P value
Postoperative complications	8 (17.8)	27 (36.0)	0.033
Mild complications (Grade I to II)	8 (17.8)	25 (33.3)	0.065
Wound infection	3 (6.7)	9 (12.0)	–
Fever > 38.5 °C after surgery	2 (4.4)	4 (5.3)	–
Diarrhea	1 (2.2)	2 (2.7)	–
Early postoperative bowel obstruction	2 (4.4)	6 (8.0)	–
Postoperative blood transfusions > 2U	0	2 (2.7)	–
Line sepsis	0	2 (2.7)	–
Major complications (Grade III to IV)	5 (11.1)	16 (21.3)	0.154
Gastrointestinal bleeding	2 (4.4)	3 (4.0)	–
Anastomotic leakage	1 (2.2)	5 (6.7)	–
Abdominopelvic collection	2 (4.4)	2 (2.7)	–
Intra-abdominal bleeding	0	1 (1.3)	–
Stoma complications	0	2 (2.7)	–
Intra-abdominal abscess	0	2 (2.7)	–
Septic shock	0	1 (1.3)	–
CCI patients with complications	0 (0–0)	0 (0–20.9)	0.049
Surgical site infection	4 (8.9)	18 (24.0)	0.038
Incisional SSIs	3 (6.7)	11 (14.7)	0.186
Organ/Space SSIs	1 (2.2)	7 (9.3)	0.103
Postoperative stay*	9.4 ± 0.6	10.3 ± 0.7	0.444
Endoscopic recurrence			
Postoperative 6 months	5/42 (11.9)	19/67 (28.4)	0.044
Postoperative 12 months	11/42 (26.2)	25/67 (37.3)	0.059
Clinical recurrence			
Postoperative 6 months	3 (6.7)	6 (8.0)	0.683
Postoperative 12 months	4 (8.9)	9 (12.0)	0.820

Values in parentheses are percentages unless indicated otherwise; \*values are mean ± SE; # value are median (interquartile range); EEN, exclusive enteral nutrition.; CCI, comprehensive complication index; SSI, surgical site infection.

**Table 3**  
Clinical assessment in EEN group.

Laboratory indices	Before EEN	After EEN	P value
White blood cell	6.7 ± 0.4	6.1 ± 0.5	0.344
Red blood cell	4.3 ± 0.1	4.4 ± 0.1	0.203
Albumin	35.3 ± 0.6	37.7 ± 0.6	0.015
Hemoglobin	11.9 ± 0.2	12.7 ± 0.2	0.013
Hematocrit	36.0 ± 0.6	38.1 ± 0.6	0.021
Erythrocyte sedimentation rate	17.5 ± 1.7	12.7 ± 1.6	0.059
C-reactive protein	24.3 ± 5.7	8.2 ± 1.7	0.032
Platelet	254.4 ± 9.6	234.0 ± 10.6	0.172
Lymphocyte	1.0 ± 0.1	1.3 ± 0.1	0.006
PNI	40.3 ± 0.8	44.2 ± 0.9	0.002

Values in parentheses are mean ± SE unless indicated otherwise. EEN, exclusive enteral nutrition.; PNI, prognostic nutritional index.

For example, one patient suffered from a wound infection and anastomotic leakage simultaneously.

### 3.3. Clinical effects of enteral nutrition before laparoscopic surgery

As shown in Table 3, after EEN therapy, patients' nutritional statuses were obviously improved, and the inflammatory indices were decreased. The level of albumin, total lymphocyte count, hemoglobin, and PNI value were significantly higher compared to those before enteral nutrition (p < 0.05), while the CRP level decreased significantly (24.3 ± 5.7 vs 8.2 ± 1.7, p = 0.032). The ESR also decreased after EEN (17.5 ± 1.7 vs 12.7 ± 1.6), but there was no significant difference (p = 0.059).

**Table 4**  
Factors associated with endoscopic recurrence in Crohn's disease.

Clinical variable	Endoscopic recurrence (n = 24)	No Endoscopic recurrence (n = 85)	P value
Male	18 (75.0)	56 (65.9)	0.398
Age (years)	37.5 ± 2.3	32.9 ± 1.1	0.063
BMI (kg/m <sup>2</sup> )	18.6 ± 0.6	18.9 ± 0.3	0.601
Previous abdominal surgery, n (%)	7 (29.2)	22 (25.9)	0.748
Appendectomy, n (%)	2 (8.3)	13 (15.3)	0.359
Stoma	8 (33.3)	23 (27.1)	0.547
Motreal classification			
Age (years)			
A1 (≤16)	0	1 (1.2)	0.780
A2 (17–40)	16 (66.7)	63 (74.1)	0.470
A3 (> 40)	8 (33.3)	21 (24.7)	0.398
Location			
L1 (ileal)	3 (12.5)	27 (31.8)	0.062
L2 (colonic)	3 (12.5)	9 (10.6)	0.794
L3 (ileocolonic)	18 (75.0)	44 (51.8)	0.042
L4 (upper gastrointestinal)	0	5 (5.9)	0.110
Behavior			
B1 (inflammatory/failure of medical therapy)	2 (8.3)	4 (4.7)	0.512
B2 (stricturing)	18 (75.0)	59 (69.4)	0.596
B3 (penetrating)	6 (25.0)	34 (40.0)	0.178
P (perianal disease)	8 (33.3)	26 (30.6)	0.798
Preoperative medications			
5-ASA	8 (33.3)	31 (36.5)	0.777
Corticosteroids	0	6 (7.1)	0.079
Thiopurine	9 (37.5)	28 (32.9)	0.677
Infliximab	3 (12.5)	11 (12.9)	0.954
Others	4 (16.7)	9 (10.6)	0.433
EEN before surgery	5 (20.8)	37 (43.5)	0.044
Preoperative Laboratory indices			
ALB	34.6 ± 1.3	36.6 ± 0.5	0.093
HB	11.6 ± 0.4	12.3 ± 0.2	0.070
ESR	19.0 ± 2.3	15.4 ± 1.5	0.262
CRP	25.2 ± 7.5	18.1 ± 4.7	0.464
L	0.9 ± 0.1	1.2 ± 0.1	0.111
PNI	39.3 ± 1.6	42.4 ± 0.7	0.047
Postoperative medications			
5-ASA	2 (8.3)	2 (2.4)	0.210
Thiopurine	11 (45.8)	23 (27.1)	0.080
Infliximab	3 (12.5)	30 (35.3)	0.032
Thiopurine + Infliximab	2 (8.3)	15 (17.6)	0.428
Others	6 (25.0)	15 (17.6)	0.881

BMI, body mass index; EEN, exclusive enteral nutrition.; ALB, albumin; HB, hemoglobin; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; L, lymphocyte; PNI, prognostic nutritional index.

### 3.4. Postoperative recurrence in patients with laparoscopic surgery

As shown in Table 2, a total of 42 (93.3%) patients in the EEN group and 67 (89.3%) patients in the non-EEN group completed an ileocolonoscopy. At 6 months after laparoscopic surgery, the rate of endoscopic recurrence in the EEN group was significantly lower than that in the non-EEN group (11.9% vs 28.4%,  $p = 0.044$ ). At 12 months after laparoscopic surgery, 11 (26.2%) patients in the EEN group and 25 (37.3%) patients in the non-EEN group developed endoscopic recurrence ( $p = 0.059$ ). No significant difference was found during follow-up, at 6 months, 3 (6.7%) patients in the EEN group and 6 (8.0%) patients in the non-EEN group developed clinical recurrence ( $p = 0.683$ ); at the 12-month follow-up, there were 4 (8.9%) patients in the EEN group and 9 (12.0%) patients in the non-EEN group that developed clinical recurrence ( $p = 0.820$ ).

Analysis of possible risk factors for early endoscopic recurrence in patients with Crohn's disease undergoing laparoscopic surgery.

As shown in Table 4, factors evaluated to be significantly associated with early endoscopic recurrence in CD patients undergoing laparoscopic surgery included EEN before surgery, PNI and ileocolonic resection based upon univariate analysis. These factors were then further

**Table 5**  
Multivariate analysis of factors associated with endoscopic recurrence.

Risk factor	OR	95% CI	P value
L3 (ileocolonic)	3.305	1.105–9.879	0.032
EEN before surgery	0.328	0.113–0.949	0.040
PNI	0.487	0.151–1.571	0.229
Infliximab	0.243	0.062–0.958	0.043

EEN, exclusive enteral nutrition.; PNI, prognostic nutritional index.

analyzed using a multivariate analysis model to find the independent risk factors associated with early endoscopic recurrence in this study. Thus, enteral nutrition before laparoscopic surgery was determined to be an independent risk factor for early endoscopic recurrence (Table 5).

## 4. Discussion

In the current study, we focused on exclusive enteral nutrition in the preoperative optimization of laparoscopic surgery for CD. This study revealed that EEN before laparoscopic surgery was associated with a reduction in systemic inflammation, fewer postoperative complications, and less endoscopic recurrence in CD patients. In addition, EEN could also improve the nutritional status of patients before surgery. Preoperative EEN was demonstrated to be an independent risk factor to predict early endoscopic recurrence in CD patients undergoing laparoscopic surgery.

It is reported that EEN could be used to induce clinical remission in active Crohn's disease, especially in children [10]. Shamir et al. [23] reported that proinflammatory cytokines including TNF- $\alpha$  and IL-6 were decreased and growth hormones including IGF-1 and IGFBP-3 were increased after EEN in pediatric CD patients. EEN could be an effective bridge for CD patients with stricturing or penetrating complications, providing a safer gateway to elective surgery, thereby avoiding the need for urgent surgery [14]. Even in patients with percutaneously undrainable abdominal abscesses, EEN was considered feasible, resulting in a decreased need for surgery [24,25]. Thus, surgery became technically easier as a result of EEN because the inflammatory burden was reduced.

Approximately 10%–37% of CD patients experience postoperative complications after surgery [26]. Emerging evidence suggests that laparoscopic resection could provide substantial benefits with regard to postoperative morbidity(1). Nutritional therapy is a necessary component of treatment in gastrointestinal surgery, especially for patients with malnutrition and underfeeding which are considered risk factors for postoperative complications [10]. With the advantages of EEN, more patients could undergo laparoscopic surgery and experience less postoperative complications. A meta-analysis revealed that preoperative nutrition supplementation reduced postoperative complications in CD patients compared to the standard of care without nutritional support [27,28]. Recently, researchers reported that preoperative anti-TNF $\alpha$  therapy was a risk factor for postoperative morbidity and septic complications(2). Corticosteroid treatment for CD patients in 4 weeks before surgery was also suggested to be associated with an elevated postoperative complication rate [26]. To avoid the adverse effects of corticosteroids and anti-TNF $\alpha$ , alternative treatment with EEN can act as a bridge to surgery, resulting in fewer postoperative complications. There is limited information concerning the effectiveness of EEN prior to laparoscopic surgery on complication rates. In the present study, we found that a lower incidence of complications was observed in patients that received EEN compared to those that did not. The SSIs were also decreased in the EEN group. All the findings may be a result of improved nutritional status, modification of inflammation, and optimization of preoperative medical therapy.

Surgery is still a fundamental part of disease management in a significant proportion of CD patients. Historically, approximately 70%

of patients undergoing a bowel resection will develop a postoperative endoscopic recurrence within 1 year [29]. It is common knowledge that postoperative recurrence always starts with a minimal aphthous ulceration, proceeding to larger and more ulcerations, which can result in complications including stricturing and fistulization [30]. To avoid postoperative endoscopic recurrence, several studies have investigated potential risk factors. Barcelos et al. [31] reported that preoperative steroid use was associated with a significant risk for endoscopic recurrence after ileocolonic resection in CD patients. Other studies also suggested that history of smoking, postoperative perianal disease and undergoing an emergency operation were risk factors. In our study, we found that EEN before surgery, PNI and ileocolonic resection were risk factors, and enteral nutrition before laparoscopic surgery was an independent protective factor for early postoperative endoscopic recurrence. In addition, in the EEN group, endoscopic recurrence was 11.9% which was lower than that in the non-EEN group. Thus, our study indicated that there was room for improvement in endoscopic recurrence rates after laparoscopic surgery, and enteral nutrition may play an important role.

Generally, surgical trauma is common and results in surgical stress, which could even happen in laparoscopic surgery cases with minor intervention [32]. The inflammatory response caused by surgical trauma could lead to a reduction in albumin levels, and hypoalbuminemia is considered to be a risk factor for postoperative complications [33]. As CD patients are always malnourished with lower albumin, they are at high risk for complications. Fortunately, EEN before surgery was found to improve albumin level in CD patients in this study. Therefore, nutritional therapy is necessary for CD patients undergoing laparoscopic surgery.

There were some limitations that must be considered in the analysis of these results. First, this was a retrospective observational analysis, and some residual confounding factors remain. Second, this was a single-center study, and the outcome might be influenced by our local experience in perioperative management strategies. Therefore, a large, multicenter, randomized controlled trial should be performed to assess the results of the current study. Third, our sample of patients was limited as we only analyzed CD patients undergoing laparoscopic surgery in a single center.

## 5. Conclusion

The current study confirmed that preoperative EEN treatment for at least 4 weeks could improve the nutritional and inflammatory status of patients, which in turn reduced postoperative complications after laparoscopic surgery. In addition, early postoperative endoscopic recurrence was decreased by EEN. Therefore, nutritional therapy before surgery is necessary for CD patients.

## Ethical approval

This study was approved by the Committee of Ethics of Sir Run Run Shaw Hospital of Zhejiang University, Hangzhou, China.

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## Author's contributions

Xiaolong Ge and Wei Zhou contributed to study conception and design, Xiaolong Ge, Wei Liu, Xiaoyan Yang and Shasha Tang contributed to acquisition of data, Wei Liu, Linna Ye, Haili Xu and Weihua Yu contributed to analysis and interpretation of data, Xiaolong Ge and Shasha Tang contributed to drafting of manuscript, Qian Cao, Xiujun

Cai and Wei Zhou contributed to critical revision.

## Conflicts of interest

There is no conflicts of interest.

## Research registration number

Chinese Clinical Trial Registry (Number: ChiCTR1900020628).

## Guarantor

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## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Disclosure

Xiaolong Ge, Shasha Tang, Xiaoyan Yang, Wei Liu, Linna Ye, Weihua Yu, Haili Xu, Qian Cao, and Wei Zhou have no conflicts of interest or financial ties to disclose.

## Data statement

We retrospective studied 120 CD patients undergoing bowel resection with laparoscopic surgery from January 2015 to December 2017 at the IBD center of Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China. Before laparoscopic surgery, 45 CD patients received EEN for at least 4 weeks, and 75 CD patients had no EEN. The continuous variables were analyzed by the Student's t test or Mann-Whitney U test depending on the normality of the data distribution, and the categorical variables were analyzed by the Pearson's  $\chi^2$  test or the Fisher's exact test, as appropriate. Significant associations ( $p < 0.05$ ) from univariate analysis were used in multivariate logistic regression analyses to verify independent predictors of endoscopic recurrence in CD patients undergoing laparoscopic surgery. Values of  $p < 0.05$  were considered statistically significant. Patients receiving EEN had a significant improvement in their nutritional (albumin, prognostic nutritional index (PNI), and hemoglobin) and inflammatory (C-reactive protein) status after the EEN treatment prior to surgery ( $P < 0.05$ ). Patients having EEN also experienced fewer postoperative complications, decreased surgical site infections, and a lower comprehensive complication index ( $P < 0.05$ ). Endoscopic recurrence rates 6 months after surgery were also reduced significantly in patients that received EEN ( $P < 0.05$ ); however, the incidence of clinical recurrence was similar in both groups at the 1-year follow-up. Endoscopic recurrence was correlated with ileocolonic disease location, EEN before surgery, and PNI ( $P < 0.05$ ). PNI remained independently associated with endoscopic recurrence after surgery.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijssu.2019.03.012>.

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