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ORIGINAL PAPERS

Enteral nutrition is associated with a decreased risk of surgical intervention in Crohn's disease patients with spontaneous intra-abdominal abscess

Xiao-Bin Zheng[1,2], Xiang Peng[3], Xiao-Yu Xie[4], Lei Lian[1,2], Xian-Rui Wu[1,2], Jian-Cong Hu[1,2], Xiao-Wen He[1,2], Jia Ke[1,2], Yu-Feng Chen[1,2], Min Zhi[3], Xiao-Jian Wu[1,2], Xiao-Sheng He[1,2] and Ping Lan[1,2]

[1]Department of Colorectal Surgery. [2]Guangdong Provincial Key Laboratory of Colorectal and Pelvic Floor Diseases. [3]Department of Gastroenterology. [4]Department of Medical Oncology. The Sixth Affiliated Hospital of Sun Yat-sen University. Guangzhou, Guangdong. China

ABSTRACT

Background: The impact of enteral nutrition (EN) on surgical risk in Crohn's disease (CD) patients suffering from spontaneous intra-abdominal abscess (IAA) was evaluated.

Methods: CD patients diagnosed with spontaneous IAA from 2008 to 2015 were included in the study. The impact of EN on surgical risk was evaluated using both univariate and multivariate analyses.

Results: A total of 87 patients were enrolled, 66 (75.9%) were male. The mean age at the development of an abscess was 30.2 ± 10.1 years and the median duration of illness from CD diagnosis until the development of an abscess was three (2-6) years. After a median follow-up of 1.9 (1.1-2.9) years, surgical intervention was performed in 42 patients (48.3%). Patients treated with EN were less likely to require surgical intervention (26.1% *vs* 56.3%, p = 0.01). Multivariate analysis showed that EN was an independent protective factor for the risk of surgery with a hazard ratio of 0.27 (95% confidence interval: 0.11-0.65, p = 0.004) after adjusting for abdominal pain, history of abdominal surgery, concomitant intestinal stenosis and prior use of antibiotics within three months.

Conclusions: Surgical intervention is common for CD patients with IAA. Appropriate application of EN may help obviate the need for surgical treatment.

Key words: Crohn's disease. Intra-abdominal abscess. Enteral nutrition. Surgical intervention.

INTRODUCTION

Crohn's disease (CD) is a chronic disease characterized by inflammation that involves the full thickness of the bowel wall. Consequently, the occurrence of spontaneous intra-abdominal abscess (IAA) is common in CD patients. Approximately 10% to 30% of patients with CD will spontaneously develop IAA during the course of the illness (1,2). Management of CD patients with IAA is challenging and requires the expertise of multiple specialists working together. In a previous study (3), we showed that interventional procedures such as percutaneous drainage might be helpful in the treatment of CD-related IAA. However, surgery is often required due to the failure of non-operative management.

Risk factors and the timing of surgery in CD patients with IAA are controversial. It has been reported that nutritional status may influence the timing of surgical intervention (4). However, the impact of enteral nutrition (EN) on the risk of surgery in CD patients with spontaneous IAA is rarely studied. The current literature suggests that EN therapy is effective in patients with quiescent or severe CD (5-7) and may decrease the rate of intestinal surgery in pediatric CD (8). The aim of this study was to evaluate the influence of EN on surgical risk in CD patients with spontaneous IAA.

PATIENTS AND METHODS

Patients

The study was approved by the Institutional Review Board (IRB) of the Sixth Affiliated Hospital of Sun Yat-sen University. A historical cohort of eligible CD patients diagnosed with spontaneous IAA between October 2008 and December 2015 were evaluated. Both paper based and electronic medical records were carefully reviewed when necessary.

Inclusion and exclusion criteria

Patients who met the following inclusion criteria were included in the study: a) CD as an underlying diagnosis; b) regular follow-up

Author's contribution: Xiao-bin Zheng and Xiang Peng contributed equally to this study.

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Correspondence: Xiao-Sheng He and Ping Lan. The Sixth Affiliated Hospital. Sun Yat-sen University. 26 Yuancun Erheng Road. 510655 Guangzhou, Guangdong. China
e-mail: sumslp@163.com

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at the hospital; and c) IAA identified by ultrasonography, computed tomography (CT) or magnetic resonance imaging (MRI). The study exclusion criteria included: a) perianal abscess without an intra-abdominal or pelvic abscess; b) abscess developed immediately after laparotomy (within three months of surgery) or caused by a silk suture; and c) < 3 months of follow-up after abscess resolution.

Patient groups

Patients were classified into the EN and non-EN group. The therapy option was determined by physicians according to their clinical experience. EN therapy was adopted mainly to improve the nutritional status of CD patients.

Definition of variables

In this study, EN therapy refers specifically to continuous feeding with elemental (Peptisorb Liquid, Nutricia, Wuxi) or polymeric formula (Fresubin, Sino-Swed Pharmaceutical Corp. Ltd, Wuxi) via a naso-intestinal tube (Flocare Bengmark Naso-Intestinal Tubes, Nutricia, Wuxi) for four weeks, during which no oral foods or fluids (except for water and weak tea) were allowed. Patients in the EN group were given a formula with 30 to 40 Kcal/kg body weight and 1.2 to 1.6 g protein/kg body weight. All patients enrolled in the EN group were fed as inpatients. Patients in the non-EN group were fed with an oral diet (liquid diet or semi-liquid diet without oral nutrition supplements) or parenteral nutrition including carbohydrates and electrolytes in order to maintain the water-electrolyte balance. Each patient was followed-up every day and the patient could contact their clinician whenever necessary.

Demographic and clinical variables were defined as follows: general information (sex, age), age at the time of CD diagnosis, age at development of an abscess, duration of CD until the development of an abscess (the time interval from the date of CD diagnosis to the date of IAA formation), Montreal classification L (including L1 [ileal], L2 [colonic], L3 [ileocolonic] and L4 [upper GI tract modifier]), body mass index (BMI) before treatment, fever, abdominal pain, simplified Crohn's disease activity index (simplified CDAI) before treatment, history of abdominal surgery, comorbidities (perianal abscess, intestinal fistula or intestinal stenosis), abscess location (peritoneal cavity, abdominal wall, pelvic cavity or multiple abscesses), maximum abscess diameter. Biologic variables before treatment included albumin (< 35 g/l *vs* ≥ 35 g/l), low hemoglobin (< 120 g/l for male, < 110 g/l for female), elevated platelet count (> 300*10^9/l), elevated white blood cell count (> 10*10^9/l), elevated erythrocyte sedimentation rate (ESR, > 15 mm/h for male, > 20 mm/h for female) and elevated C-reactive protein (CRP, > 10 mg/l).

Outcome measurement

The primary outcome was the need for surgical intervention to treat CD patients with IAA. Other outcomes including recurrence of an abscess and the time to recurrence were also examined. Patient follow-up started from the date of the first hospitalization due to IAA complicating CD until the date of the most recent contact.

Statistical analysis

Descriptive statistics were computed for all variables. Continuous data are expressed as mean ± standard deviation of the mean (mean ± SD) or medians (interquartile range, IQR) (M [Q25, Q75]), and categorical data are expressed as frequencies. Comparisons of the distribution of clinical characteristics between the EN and non-EN patients were performed using the 2-tail t-test (or Wilcoxon rank sum test as appropriate) for continuous variables and the Chi-squared test (or the Fisher's exact test as appropriate) for categorical variables. The impact of EN on surgical risk was depicted with Kaplan-Meier curves and the log-rank test. The multivariable Cox proportional hazards model using the enter method was used to identify risk factors associated with the requirement for surgery adjusting for confounding factors. A number of different combinations among the examined variables were tested for possible interactions, in particular among the independent factors related to the need for surgical intervention in the final multivariable model. A p value less than 0.05 was considered as statistically significant.

RESULTS

Patient characteristics

A total of 87 eligible patients were identified from our registry, including 66 (75.9%) males and 19 (24.1%) females. The mean age at CD diagnosis and the development of an abscess was 28.3 ± 9.3 years and 30.2 ± 10.1 years, respectively. The median duration of illness from the diagnosis of CD until the development of an abscess was three (2-6) years. Among the 87 eligible patients, comorbidities included perianal abscess (n = 28, 32.2%), intestinal fistula (n = 67, 77.0%) and intestinal stenosis (n = 48, 55.2%). There were 27 patients (31.0%) who had a history of abdominal surgery (Table 1). After a median follow-up of 1.9 (1.1-2.9) years, surgical intervention was required in 42 patients (48.3%). Patients treated with EN were less likely to require surgical intervention (26.1% *vs* 56.3%, p = 0.01) (Table 1). There was no significant difference with regard to clinical characteristics between EN and non-EN patients such as prior medical therapy within three months, characteristics of IAA and laboratory values before treatment.

EN is associated with a lower risk for surgical intervention

Kaplan-Meier analysis was used to investigate the impact of EN on the risk of surgical intervention and showed that patients treated with EN had a lower surgical risk in comparison to patients without (log-rank test, p = 0.014) (Fig. 1). The univariate Cox proportional hazard regression model also showed that EN was significantly associated with a lower risk for surgical intervention, with a hazard ratio (HR) of 0.36 (95% confidence interval [CI]: 0.15-0.85, p = 0.019) (Table 2).

Table 1. Patient characteristics

Characteristic	*All cases*	*Non-EN*	*EN*	*p value*
Number of patients	87	64 (73.6%)	23 (26.4%)	
Male patients, n (%)	66	47 (73.4%)	19 (82.6%)	0.38
Age (years)	32.4 ± 10.1	31.8 ± 9.4	34.2 ± 11.9	0.34
Age at the time of CD diagnosis (years)	28.3 ± 9.3	27.6 ± 8.6	30.4 ± 11.0	0.21
Age at development of abscess (years)	30.2 ± 10.1	29.3 ± 9.3	32.8 ± 11.8	0.15
Duration of CD until development of abscess, years	3 (2-6)	3 (2-6)	2 (1-6)	0.07
Montreal classification L, n (%)				0.43
L1 (ileal)	4	3 (4.7%)	1 (4.3%)	
L2 (colonic)	11	6 (9.4%)	5 (21.7%)	
L3 (ileocolonic)	71	54 (84.4%)	17 (73.9%)	
L4 (upper GI tract modifier)	1	1 (1.6%)	0	
BMI before treatment, kg/m^2	17.6 ± 2.8	17.4 ± 2.8	17.8 ± 2.7	0.56
Fever, n (%)	33	22 (34.4%)	11 (47.8%)	0.25
Abdominal pain, n (%)	86	63 (98.4%)	23 (100%)	1.0
Simplified CDAI before treatment	5.8 ± 1.1	5.9 ± 1.1	5.5 ± 1.1	0.17
History of abdominal surgery, n (%)	27	18 (28.1%)	9 (39.1%)	0.33
Comorbidities, n (%)				
Perianal abscess	28	22 (34.4%)	6 (26.1%)	0.47
Intestinal fistula	67	48 (75.0%)	19 (82.6%)	0.46
Intestinal stenosis	48	34 (53.1%)	14 (60.9%)	0.52
Prior medical therapy within 3 months, n (%)				
Antibiotics	80	57 (91.9%)	23 (100%)	0.32
5-ASA	41	30 (48.4%)	11 (47.8%)	0.96
Immunosuppressor	30	21 (33.9%)	9 (39.1%)	0.65
Corticosteroid	24	19 (30.6%)	5 (21.7%)	0.42
Biologicals	9	6 (9.7%)	3 (13.0%)	0.70
Abscess location, n (%)				0.15
Peritoneal cavity	36	22 (34.4%)	14 (60.9%)	
Abdominal wall	14	11 (17.2%)	3 (13.0%)	
Pelvic cavity	18	16 (25.0%)	2 (8.7%)	
Multiple abscesses	19	15 (23.4%)	4 (17.4%)	
Maximum abscess diameter, mm	46.5 (27.3-72.0)	46.0 (21.0-71.0)	64.0 (30.0-75.0)	0.31
Biologic variables before treatment (yes vs *no)*				
Albumin < 35 g/l	27	20 (31.3%)	7 (30.4%)	0.94
Low hemoglobin	56	39 (60.9%)	17 (73.9%)	0.27
Elevated platelet count	59	41 (64.1%)	18 (78.3%)	0.21
Elevated white blood cell count	26	20 (31.3%)	6 (26.1%)	0.64
Elevated ESR	67	45 (76.3%)	22 (95.7%)	0.06
Elevated CRP	45	31 (62.0%)	14 (77.8%)	0.23
Need for surgery, n (%)	42	36 (56.3%)	6 (26.1%)	0.01

EN: Enteral nutrition; CD: Crohn's disease; BMI: Body mass index; CDAI: Crohn's disease activity index; 5-ASA: 5-aminosalicylic acid; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

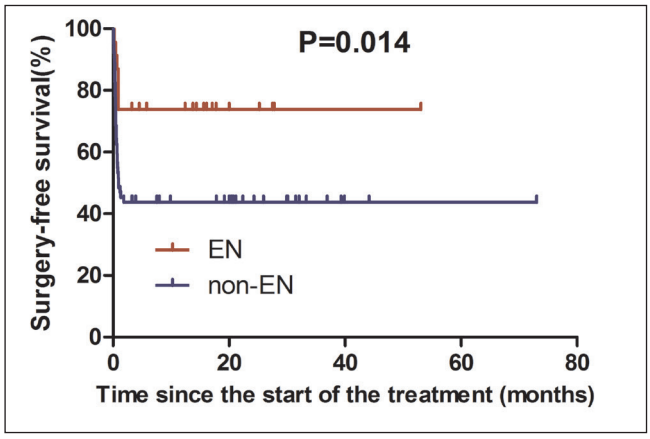

Fig. 1. Impact of EN on surgical risk: Kaplan–Meier survival analysis with the log-rank test. EN indicates enteral nutrition, $p < 0.05$ was considered as statistically significant.

Other potential risk factors for surgical intervention identified by univariate analysis included history of abdominal surgery ($p = 0.002$) and concomitant intestinal stenosis ($p = 0.025$). Abdominal pain ($p = 0.021$) and prior use of antibiotics within three months ($p = 0.043$) were both potential protective factors for surgical risk. Other variables such as simplified CDAI before treatment, concomitant perianal abscess or intestinal fistula, percutaneous drainage, characteristics of IAA and laboratory values had no relationship with the risk of requiring surgery (Table 2). A multivariate Cox proportional hazard regression model was constructed to identify the risk factors related to the need for surgical intervention in this patient population. EN was shown to be an independent protective factor for the risk of surgery with a HR of 0.27 (95% CI: 0.11-0.65, $p = 0.004$) after adjusting for abdominal pain, history of abdominal surgery, concomitant intestinal stenosis and prior use of antibiotics within three months (Table 3).

Table 2. Univariable Cox proportional hazard model for risk factors associated with the requirement for surgery in CD patients with IAA

Characteristics	*HR (95% CI)*	*p value*
Gender (male *vs* female)	1.62 (0.75-3.50)	0.22
Age at the time of CD diagnosis, every 1 year increase	0.98 (0.94-1.01)	0.14
Duration of CD until development of abscess, every 1 year increase	1.03 (0.95-1.12)	0.5
Montreal classification L (L3/L4 *vs* L1/L2)	0.92 (0.43-2.00)	0.84
History of abdominal surgery (yes *vs* no)	2.63 (1.42-4.85)	0.002
BMI, every 1-kg/m^2 increase	0.93 (0.83-1.05)	0.25
Fever (yes *vs* no)	1.17 (0.63-2.17)	0.62
Abdominal pain (yes *vs* no)	0.084 (0.10-0.69)	0.021
Simplified CDAI before treatment, every 1-score increase	0.98 (0.74-1.29)	0.86
Concomitant perianal abscess (yes *vs* no)	0.87 (0.45-1.67)	0.67
Concomitant intestinal fistula (yes *vs* no)	1.96 (0.83-4.67)	0.13
Concomitant intestinal stenosis (yes *vs* no)	2.11 (1.096-4.074)	0.025
Prior medical therapy within 3 months (yes vs *no)*		
Antibiotics	0.34 (0.12-0.97)	0.043
5-ASA	1.00 (0.55-1.83)	1.0
Immunosuppressor	0.69 (0.35-1.34)	0.27
Corticosteroid	0.61 (0.29-1.27)	0.18
Biologicals	0.92 (0.33-2.59)	0.88
Percutaneous drainage (yes *vs* no)	0.70 (0.30-1.67)	0.43
EN (yes *vs* no)	0.36 (0.15-0.85)	0.019
Multiple abscesses (yes *vs* no)	0.92 (0.44-1.91)	0.81
Maximum abscess diameter, every 1-mm increase	1.004 (0.99-1.02)	0.61
Albumin < 35 g/l (yes *vs* no)	1.14 (0.59-2.20)	0.69
Low hemoglobin (yes *vs* no)	0.74 (0.40-1.37)	0.33
Elevated platelet count (yes *vs* no)	0.60 (0.32-1.12)	0.11
Elevated white blood cell count (yes *vs* no)	0.99 (0.51-1.94)	0.98
Elevated ESR (yes *vs* no)	0.52 (0.25-1.10)	0.087
Elevated CRP (yes *vs* no)	1.02 (0.49-2.11)	0.96

CD: Crohn's disease; IAA: Intra-abdominal abscess; BMI: Body mass index; CDAI: Crohn's disease activity index; 5-ASA: 5-aminosalicylic acid; EN: Enteral nutrition; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; HR: Hazard ratio; CI: Confidence interval.

Assessment of nutritional and inflammatory parameters in EN groups

A rising trend was observed when the BMI values before and after EN treatment of patients in the EN group were compared, although the difference did not reach statistical significance (before EN 17.8 ± 2.7 *vs* after EN 18.4 ± 2.6, p = 0.17). Other parameters of nutritional status such as albumin (p = 0.016) and hemoglobin (p = 0.002) significantly increased after four weeks of EN treatment (Table 4). Rapid declines were observed in the inflammatory index including ESR (p < 0.001), CRP (p = 0.002) and platelet count (p < 0.001). Simplified CDAI also decreased significantly after EN treatment (before EN 5.5 ± 1.1 *vs* after EN 2.3 ± 0.9, p < 0.001) (Table 4).

Outcomes after the first hospitalization due to IAA complicating CD

During the overall median follow-up of 1.9 (1.1-2.9) years, surgical intervention was performed in 42 patients (48.3%). The indications for surgery included medicine only failure (n = 1), percutaneous drainage failure (n = 7), intestinal fistula (n = 25) and intestinal obstruction (n = 9). The median surgery interval among these patients was 0.42 (0.27-0.79) months, while the median follow-up of the remaining 45 patients was 1.65 (0.73-2.37) years (Fig. 2). Abscesses recurred in 17.8% of the patients in

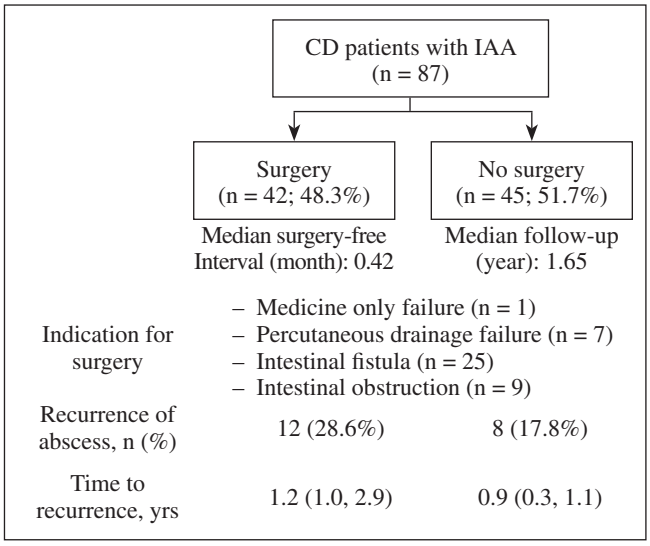

Fig. 2. Patient outcome in different treatment groups after the first hospitalization due to IAA complicating CD (CD: Crohn's disease; IAA: Intra-abdominal abscess).

Table 3. Multivariable Cox proportional hazard model for risk factors associated with the requirement for surgery in CD patients with IAA

Characteristics	*HR (95% CI)*	*p value*
Abdominal pain (yes *vs* no)	0.29 (0.04-2.49)	0.26
History of abdominal surgery (yes *vs* no)	3.41 (1.78-6.52)	< 0.001
Concomitant intestinal stenosis (yes *vs* no)	2.52 (1.30-4.88)	0.006
Prior use of antibiotics within 3 months (yes *vs* no)	0.32 (0.11-0.93)	0.036
EN (yes *vs* no)	0.27 (0.11-0.65)	0.004

CD: Crohn's disease; IAA: Intra-abdominal abscess; EN: Enteral nutrition; HR: Hazard ratio; CI: Confidence interval.

Table 4. Nutritional and inflammatory index before and after EN

Characteristic	*Before EN treatment*	*After EN treatment*	*p value*
Weight (kg)	51.3 ± 9.1	52.6 ± 9.3	0.2
Height (m)	1.7 ± 0.1	1.7 ± 0.1	0.34
BMI (kg/m^2)	17.8 ± 2.7	18.4 ± 2.6	0.17
Albumin (g/l)	37.2 ± 3.8	40.5 ± 4.9	0.016
Hemoglobin (g/l)	107.0 ± 16.1	120.1 ± 13.7	0.002
Platelet count (*10^9/l)	372.1 ± 124.9	228.6 ± 49.7	< 0.001
ESR (mm/h)	65.0 (36.0-71.0)	14.5 (11.5-29.3)	< 0.001
CRP (mg/l)	18.0 (10.9-45.1)	1.5 (0.7-3.6)	0.002
Simplified CDAI	5.5 ± 1.1	2.3 ± 0.9	< 0.001

EN: Enteral nutrition; BMI: Body mass index; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; CDAI: Crohn's disease activity index.

the conservative group and 28.6% of the surgical group, although this was not statistically significant (p = 0.23). There was a trend towards a longer interval to abscess recurrence in the surgical group than in the conservative group, although this did not reach statistical significance (1.2 [1.0-2.9] *vs* 0.9 [0.3-1.1] years, p = 0.053) (Fig. 2). No significant differences were observed with regard to nutritional or inflammatory parameters in patients with or without surgical intervention (Table 5).

DISCUSSION

CD is characterized by intestinal transmural inflammation, which always leads to deep ulceration, and this is sometimes followed by perforation of the bowel wall. As a result, spontaneous IAA is a common complication in CD patients with an incidence of about 10% to 30% (1). Management of these patients is a clinical challenge. Surgical intervention is integrant and frequently required for unresolved cases or those that are not amenable to or that have failed percutaneous drainage. Although surgery may treat the acute septic complication of CD, it is important to realize that surgical treatment usually does not cure CD, as recurrence after bowel resection is the rule rather than the exception. In addition, bowel resection for CD can be complicated by anastomotic septic complications and new fistula formation, which may hinder the recovery process. The advantage of surgical over nonsurgical management in reducing abscess recurrence rates and complications is controversial (9-15). As the concept of "bowel-sparing" is of paramount importance in the management of CD, factors

Table 5. The nutritional and inflammatory index of patients with or without surgical intervention

Characteristic	*All cases*	*Patients with surgical intervention*	*Patients without surgical intervention*	*p value*
Weight (kg)				
Before treatment	49.3 ± 9.5	48.2 ± 10.1	50.3 ± 8.8	0.33
After treatment	50.8 ± 8.9	50.1 ± 9.0	51.5 ± 8.7	0.45
Height (m)				
Before treatment	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	0.79
After treatment	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	0.54
BMI (kg/m^2)				
Before treatment	17.6 ± 2.8	17.1 ± 2.7	18.0 ± 2.8	0.16
After treatment	18.1 ± 2.4	17.7 ± 2.1	18.5 ± 2.6	0.14
Albumin (g/l)				
Before treatment	37.6 ± 6.8	38.4 ± 8.2	36.7 ± 4.9	0.26
After treatment	40.9 ± 6.8	40.9 ± 6.0	40.9 ± 7.6	1.0
Hemoglobin (g/l)				
Before treatment	109.8 ± 20.0	112.6 ± 20.9	107.2 ± 18.9	0.21
After treatment	116.8 ± 17.1	118.1 ± 18.5	115.5 ± 15.8	0.49
*Platelet count (*10^9/l)*				
Before treatment	354.0 ± 117.1	337.5 ± 116.5	369.5 ± 116.8	0.2
After treatment	254.1 ± 84.2	247.6 ± 99.8	260.5 ± 66.1	0.48
ESR (mm/h)				
Before treatment	47.5 (24.0-68.8)	38.0 (18.3-63.5)	54.5 (36.0-72.5)	0.1
After treatment	19.0 (9.8-34.3)	16.0 (7.5-33.5)	19.0 (12.5-41.5)	0.32
CRP (mg/l)				
Before treatment	14.3 (7.6-55.2)	14.1 (5.2-74.5)	19.2 (9.2-46.0)	0.66
After treatment	2.9 (1.4-8.8)	2.0 (0.9-8.2)	3.6 (1.5-8.9)	0.28
Simplified CDAI				
Before treatment	5.8 ± 1.1	5.7 ± 1.1	5.8 ± 1.2	0.59
After treatment	2.7 ± 1.1	2.7 ± 0.9	2.7 ± 1.2	0.85

BMI: Body mass index; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; CDAI: Crohn's disease activity index.

involved in the need for surgery should be further studied. This may help to avoid unnecessary and invasive surgery.

EN serves as an adjunctive therapy and has been widely used in a variety of diseases including abdominal sepsis (16), pancreatitis (17,18) and inflammatory bowel diseases (IBD) (5,19-22). A large body of evidence (5,8,21,23-30) suggests a beneficial role of EN in the management of CD. It is well known that malnutrition is common in CD patients. The Malnutrition Universal Screening Tool was proposed to be combined with body composition to detect more CD patients at risk of malnutrition and sarcopenia in order to start EN therapy immediately (31). EN is now recommended by the pediatric committee of the European Crohn's and Colitis Organization and the European Society for Paediatric Gastroenterology Hepatology and Nutrition as a first-choice agent to induce remission in pediatric CD. The remission rates in pediatric studies are consistently > 75% (32). In addition, EN has also been reported to be effective in reducing postoperative complications (33,34) and recurrence (35) in CD patients, which may be linked with the improvement of nutritional and inflammatory status. However, the impact of EN on surgical risk in CD patients with spontaneous IAA has rarely been studied.

The role of EN in reducing surgical risk in CD patients with spontaneous IAA was investigated in the present study. No difference was observed before treatment between patients in the EN and non-EN groups with regard to patient demography, duration of CD, BMI, history of abdominal surgery, co-morbidities, prior medical therapy within three months, characteristics of IAA and laboratory values. About 48.3% of patients in this study underwent a surgical intervention after a median follow-up of 1.9 (1.1-2.9) years, which was lower than the rate of 80% reported in the study by Yamaguchi (1) in 2004. This might be due to the increasing use of interventional procedures such as percutaneous drainage over the past decade (36). Due to the benefits of EN in the management of CD patients as mentioned above, we expect that EN will serve as a protective factor for the risk of surgery after adjusting for the other factors. The results in this study support our hypothesis that EN exerts beneficial effects with regard to the avoidance of surgical intervention in CD patients with IAA.

The underlying mechanisms that constitute the association between EN and surgical risk in IAA complicating CD are not clear. Defects in intestinal epithelial tight junction barrier function have been shown to lead to increased intestinal permeation to toxic luminal substances (e.g., bacteria, bacterial by-products, antigens and enzymes). Altered permeability has been reported in those suffering from CD (37-38). It has been reported that EN was able to maintain normal transepithelial electrical resistance, short circuit current, paracellular permeability and the morphological distribution of tight junction proteins (39), and therefore maintain a normal permeability and gut barrier function. This restoration of gut barrier morphology and function is closely related with a mechanism involving the inhibition of long myosin light chain kinase (MLCK) (39). Moreover, previous studies (23,25,29,40,41) have indicated that EN modulates the gut microbiota which is linked with CD disease activity and thus exerts a beneficial effect on the recovery of bowel function. Interestingly, it was suggested that ileal enterocytes might experience nutrient stress during EN treatment as the amino acid requirements of enterocytes were primarily provided by first pass catabolism of a lumen-supplied dietary amino acids and enterocytes were limited in their ability to utilize arterial supplied amino acids (42). Amino acid limitation and other nutrient stress might inhibit the serine/threonine protein kinase, which are mammalian targets of rapamycin (mTOR), resulting in the activation of autophagy (43,44). Thus, EN might further support mucosal healing by limiting the growth and functional activity of potentially antagonistic microbes while simultaneously inducing autophagy to repair damaged host cells. In addition, Hu et al. (45) have reported that EN therapy was effective to relieve inflammatory bowel stricture. Interestingly, they also observed a dramatic decrease in the inflammatory index including CRP, ESR and CDAI after EN treatment. This is consistent with the finding of this study. Given that mural inflammation could cause bowel wall edema and thus lead to stricture in CD patients, we assumed that EN might reduce the thickness of the bowel wall and relieve inflammatory bowel stricture by effectively reversing the inflammatory component and alleviating mural inflammation. This could also help to eliminate the need for surgical treatment.

Our study also indicated that a history of abdominal surgery and concomitant intestinal stenosis were both potential risk factors for surgical intervention, which was consistent with previous studies (11,36). Therefore, it is also important that surgical history and concomitant diseases are considered when determining whether surgery is indicated for an IAA case. In line with several previous studies (10-12,15), we found no significant differences in the rate of abscess recurrence between the conservative group and the surgical group. These data suggest that it would be advantageous to use EN therapy in CD patients with IAA in order to avoid invasive operations according to the concept of damage control (46).

The findings of this study have several clinical implications. To the best of our knowledge, our study is the first to show that EN was associated with a decreased risk of surgical intervention in CD patients with spontaneous IAA. This information is valuable to patients as well as clinicians as it may help to evaluate the risk of surgical intervention and determine the individual treatment schedule. Moreover, efforts could be made in the future to decrease the surgery rate by the appropriate use of EN therapy in patients.

There are several limitations in our study, particularly relating to its retrospective design. For example, the heterogeneity with regard to patient characteristics is inevita-

ble. In particular, the clinical decision making with regard to surgery was subjective and dependent on a variety of specific clinical circumstances. Given that this research was conducted in one single center with a relatively small sample size, a careful interpretation of our data and further studies including more examples are definitely required to overcome this limitation.

In conclusion, our findings imply that EN was an independent protective factor for the risk of surgical intervention in CD patients with spontaneous IAA. Appropriate application of EN should be encouraged to help patients recover from the disease and obviate the need for surgical intervention.

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