Original Article

An observational study of the effects of ω-3 polyunsaturated fatty acid-supplemented parenteral nutrition on postoperative complications in patients with Crohn's disease

Yu Shen[1#], Huaying Liu[2#], Weilin Qi[3], Wei Liu[3], Lingna Ye[4], Qian Cao[4], Xiaolong Ge[3], Wei Zhou[3]

[1]Department of Nutrition and Food Safety, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, China; [2]Department of Medicine, Guangxi Medical College, Nanning, China; [3]Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China; [4]Department of Gastroenterology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China

Contributions: (I) Conception and design: X Ge, W Zhou; (II) Administrative support: X Ge; (III) Provision of study materials or patients: W Qi, W Liu; (IV) Collection and assembly of data: L Ye, Q Cao; (V) Data analysis and interpretation: Y Shen, H Liu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Wei Zhou. Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, 3 East Qingchun Road, Hangzhou 310016, China; Email: zhouweisrrs@zju.edu.cn; Xiaolong Ge. Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, 3 East Qingchun Road, Hangzhou 310016, China. Email: gxlmed@zju.edu.cn.

Background: Crohn's disease (CD) is a chronic inflammatory disease. Most patients with CD require surgery but exhibit an elevated incidence of postoperative complications. Omega-3 polyunsaturated fatty acids (ω-3 PUFAs) are considered beneficial for nutrition, anti-inflammation, immunity, and intestinal microflora balance in humans. This study assessed the effects of ω-3 PUFA-supplemented parenteral nutrition (PN) on postoperative complications in CD patients.

Methods: Overall, 186 CD patients undergoing bowel resection were recruited for this study. The patient data were collected from a prospectively maintained database. After surgery, 83 patients received ω-3 PUFA-supplemented PN, and 103 did not. The postoperative complications were compared between the groups. Complication risk factors were identified by univariate and multivariate analyses.

Results: Patients who received ω-3 PUFA-supplemented PN after surgery had lower C-reactive protein (CRP) levels on postoperative day 3 (57.2±5.3 *vs.* 43.5±3.9 mg/L, P=0.047) and shorter postoperative hospital stays (12.1±1.1 *vs.* 9.3±0.6 days, P=0.041) than those who did not. The ω-3 PUFA group exhibited significantly fewer overall complications (40.8% *vs.* 24.1%, P=0.016) and major complications (23.3% *vs.* 9.6%, P=0.014) than the control group. Postoperative complications were associated with infliximab, ω-3 PUFAs, CRP levels, operative time, and laparoscopic surgery. The multivariate regression revealed that preoperative infliximab use was a positive risk factor and postoperative ω-3 PUFA-supplemented PN was a negative risk factor for postoperative complications.

Conclusions: ω-3 PUFA-supplemented PN reduced post-surgery inflammatory response of CD patients, which in turn decreased the postoperative complications and accelerated recovery.

Keywords: Crohn's disease (CD); ω-3 polyunsaturated fatty acid (ω-3 PUFA); parenteral nutrition (PN); postoperative complications

Submitted Aug 11, 2022. Accepted for publication Nov 29, 2022. Published online Feb 02, 2023.
doi: 10.21037/apm-22-948
View this article at: https://dx.doi.org/10.21037/apm-22-948

Introduction

Crohn's disease (CD) is a chronic inflammatory disease that affects all segments of the gastrointestinal tract. The bowel damage and disability associated with CD occur due to the characteristic relapsing and remitting manner of the disease (1). It has been reported that almost 80% of CD patients require surgical therapy at least once during their lifetime, and that 10–37% of CD patients experience complications during recovery, especially infections (2-5). Thus, methods to improve postoperative outcomes in CD are urgently needed.

The postoperative negative nitrogen balance can cause incisions to heal poorly and increase the risk of postoperative infection. Thus, patient nutrition must be optimized after surgery (6,7). As a conventional treatment, total parenteral nutrition (TPN) can improve postoperative patient nutrition, assist in the healing of incisions, and relieve the suffering of CD patients (8-10). Additionally, omega-3 polyunsaturated fatty acids (ω-3 PUFAs) have been shown to be effective in improving the nutritional status and immunity of patients after gastrointestinal surgery (11).

ω-3 PUFAs include α-linolenic acid (18:3 ω-3), stearidonic acid (18:4 ω-3), eicosapentaenoic acid (20:5 ω-3), docosapentaenoic acid (22:5 ω-3), and docosahexaenoic acid (22:6 ω-3). The beneficial effects of ω-3 PUFAs in patients with a myriad of health conditions and diseases, including cardiovascular diseases (atrial fibrillation, atherosclerosis, thrombosis, inflammation, and sudden cardiac death, among others), diabetes, cancer, depression and various other mental illnesses, age-related cognitive decline, periodontal disease, and rheumatoid arthritis, have been previously investigated (12,13). Many studies have confirmed that ω-3 PUFAs reduce the postoperative complications associated with gastrointestinal cancers, liver cancer and some other non-cancerous gastrointestinal diseases (14,15). In addition, ω-3 PUFA-supplemented parenteral nutrition (PN) has been proven to be safe, effective, and valuable for CD patients who do not undergo surgery (16-19). However, few studies have examined the effects of ω-3 PUFA-supplemented PN after surgery on the postoperative complications of patients with CD. This study sought to explore the effects of ω-3 PUFA-supplemented PN on postoperative complications in CD patients by comparing patients who did and did not receive ω-3 PUFA supplementations. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-948/rc).

Highlight box

Key findings

- Omega-3 polyunsaturated fatty acid (ω-3 PUFA supplemented parenteral nutrition (PN) improves the postoperative recovery of Crohn's disease (CD) patients.

What is known and what is new?

- ω-3 PUFAs reduce postoperative complications in cancer patients.
- ω-3 PUFAs have good clinical applications and clinical value for CD patients.
- ω-3 PUFAs reduce the postoperative inflammatory response and postoperative complications in CD patients.

What is the implication, and what should change now?

- The use of ω-3 PUFAs should be considered for patients who receive total PN after surgery.

Methods

Patients

A retrospective observational study was conducted. A series of consecutive clinical records of CD patients who underwent bowel resection at the Inflammatory Bowel Disease Center of our hospital from January 2017 to May 2019 were retrospectively reviewed. To be eligible for inclusion in this study, the patients had to meet the following inclusion criteria: (I) have a definitive diagnosis of CD based on the patient's history and imaging, endoscopy, and pathology results; (II) have undergone bowel resection for bowel disease; and (III) have received PN after surgery. To avoid any biases due to pre-existing factors, the exclusion criteria were as follows: (I) PN was administered <4 days after surgery; (II) the patient underwent emergency surgery; (III) the patient had another serious disease; and/or (IV) the patient had incomplete data for the 30-day follow-up period. Ultimately, 186 patients were enrolled in this retrospective analysis. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of Sir Run Run Shaw Hospital of Zhejiang University (No. 20210622-31). Written informed consent for the use of clinical records was obtained from each patient, as required by the Institutional Review Board.

Perioperative management

Case history analyses, normative physical examinations and routine preoperative laboratory measurements were

performed for all participants. All patients aged above 50 years were subjected to ultrasonic cardiography and pulmonary function tests to evaluate their cardiopulmonary condition before surgery. Based on their preoperative and intraoperative conditions, the patients were transferred to the intensive care unit for postoperative treatment as necessary. For all of the patients, reasonable perioperative management practices were implemented in line with the Enhanced Recovery After Surgery (ERAS) program, including preoperative patient education about the disease, preoperative fasting time minimization, preoperative carbohydrate loading 2 hours before surgery, the intraoperative use of minimally invasive techniques and opioid-sparing analgesia, the avoidance of mechanical bowel preparation or oral antibiotics, perioperative fluid restriction for the avoidance of overload, early postoperative drainage removal, off-bed mobilization and oral feeding until discharge.

Data collection

Patients' baseline characteristics, intraoperative data, postoperative treatment information, postoperative complication data for 30 days postoperatively, and laboratory data were collected from the database. The baseline characteristics included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) grade, comorbidities, and surgical indications. The intraoperative data included the operative time, type of surgery, surgical approach (open *vs.* laparoscopy), stoma creation information, intraoperative blood transfusion information, intraoperative fluid use, and estimated blood loss. The laboratory data included the hemoglobin (Hb), hematocrit, preoperative C-reactive protein (CRP), and albumin (ALB) levels. The postoperative blood results, including ALB, white blood cell (WBC), red blood cell (RBC), and Hb were collected on postoperative day (POD) 1, and CRP results, were collected on POD3.

PN was started on the first day after enterotomy through the central vein and was stopped when oral or enteral nutrition was able to supply 60% of the energy needs of the patient. The non-protein energy was 20–25 kcal/kg/day, and the protein content of infusions was 1.2–1.5 g/kg/day. The glucose-to-lipid ratio was 6:4 to 1:1. A standardized PN protocol was used for the 2 groups. The patients were allocated to each group according to whether they received or did not receive theω-3 PUFA supplementation (Omegaven, Fresenius Kabi, Bad Homburg, Germany). The dosage of fish oil (Omegaven, Fresenius Kabi, Bad Homburg, Germany) was 0.2 g/kg/d. The medium- and long-chain fat emulsion (Structolipid, Fresenius Kabi, Bad Homburg, Germany) was supplemented at a dose of 1.0 g/kg/day with ω-3 PUFA supplementation and 1.2 g/kg/day without ω-3 PUFA supplementation, respectively.

The postoperative complications included abdominal infection, postoperative intestinal obstruction, wound infection, anastomotic leakage, abdominal bleeding, fever, blood transfusion, and a secondary operation. The complications were mainly classified using the Clavien-Dindo scheme, under which, a grade of I to II indicates a mild complication, a grade of III to IV indicates a major complication, and a grade of V indicates death (20). This study focused on the postoperative complications of wound infection and abdominal infection.

Statistical analysis

SPSS 20.0 (IBMCorp, Armonk, NY, USA) was used to analyze the data. Continuous variables are presented as the mean ± SE or median (range), whereas categorical variables are presented as the number (%). Normally distributed and continuous variables were analyzed by Student's *t*-test or the Mann-Whitney U test, and categorical variables were analyzed by Pearson's chi-squared test or Fisher's exact test. Variables with significant differences ($P<0.05$) in univariate analysis were analyzed by multivariate logistic regression analysis to identify the independent predictors for postoperative complications. P values <0.05 were considered to indicate statistical significance.

Results

Study population and baseline characteristics

In total, 186 CD patients were enrolled in this study (115 males, and 71 females). Of the patients, 51.6% had terminal ileal lesions and 4.8% had colonic lesions (*Table 1*). A total of 59.7% of patients were diagnosed with structuring CD, and 22.0% were diagnosed with penetrating CD. A total of 52 patients (28.0%) had perianal lesions.

A total of 62 patients (33.3%) had postoperative complications, of whom 30 (48.4%) had mild complications, 15 (24.2%) had major complications (Clavien-Dindo grade III to IV), and 17 patients (27.4%) had both mild and major complications. Additionally, 6 patients (3.2%) had abdominal abscesses, and 13 patients (7.0%) had

Table 1 Baseline characteristics of the study population

Clinical variables	Control group (n=103)	ω-3 PUFAs group (n=83)	P value
Preoperative RBC, 10^{12}/L	4.3±0.1	4.2±0.1	0.141
Preoperative WBC, 10^9/L	6.2±0.3	5.3±0.2	0.051
Preoperative Hb, g/L	12.0±0.2	11.8±0.2	0.584
Preoperative PLT, 10^9/L	255.5±9.2	253.1±9.4	0.860
Preoperative ESR, mm/hr	15.5±1.5	18.4±1.8	0.218
Preoperative ALB, g/L	36.7±0.5	36.2±0.6	0.511
Preoperative CRP, mg/L	17.3±3.6	14.1±3.6	0.525
Preoperative lymphocyte, 10^9/L	1.2±0.1	1.2±0.1	0.768
Preoperative Hct, %	36.5±0.5	36.0±0.6	0.583
Operative time, min	190.7±6.3	188.2±6.2	0.779
Laparoscopic surgery	61 (59.2)	60 (72.3)	0.063
ASA ≥3	11 (10.7)	7 (8.4)	0.607
CRP on POD3, mg/L	57.2±5.3	43.5±3.9	0.047
ALB on POD1, g/L	32.2±0.4	33.1±0.3	0.122
WBC on POD1, 10^9/L	6.5±0.2	6.1±0.2	0.242
RBC on POD1, 10^{12}/L	3.6±0.1	3.6±0.1	0.880
Hb on POD1, g/L	10.2±0.2	10.3±0.2	0.666

Values are expressed as the mean ± standard deviation or number (percentage). ω-3 PUFA, omega-3 polyunsaturated fatty acid; RBC, red blood cell; WBC, white blood cell; Hb, hemoglobin; PLT, platelets; ESR, erythrocyte sedimentation rate; ALB, albumin; CRP, C-reactive protein; Hct, hematocrit; ASA, American Society of Anesthesiologists; POD, postoperative day.

wound infections. All of the patients with postoperative complications ultimately recovered uneventfully.

Comparison of clinical data between CD patients in the ω-3 PUFA group and CD patients in the non-ω-3 PUFA group

A total of 103 enrolled CD patients (55.4%) did not receive ω-3 PUFA, while 83 (44.6%) received ω-3 PUFA. *Table 1* sets out the demographic information, intraoperative data, and laboratory data for each group. There were no significant differences between the 2 groups in terms of the preoperative laboratory data or the proportions of patients with postoperative mild complications. The postoperative serum CRP levels on POD3 were significantly higher in non-ω-3 PUFA-receiving patients than the ω-3 PUFA-receiving patients (57.2±5.3 *vs.* 43.5±3.9, P=0.047). Compared to the ω-3 PUFA-receiving patients, the non-ω-3 PUFA-receiving patients had higher postoperative complication rates (40.8% *vs.* 24.1%, P=0.016), higher major complication (Clavien-Dindo grade III to IV) rates (23.3% *vs.* 9.6%, P=0.014), and longer postoperative hospital stays (12.1±1.1 *vs.* 9.3±0.6 days, P=0.041; *Table 2*).

Analysis of the factors affecting postoperative complications

Based on the occurrence of postoperative complications, the patients were divided into a postoperative complications group and a non-postoperative complications group. Significant differences were found between the postoperative complications group and the non-postoperative complications group in relation to the preoperative biological medication use, postoperative ω-3 PUFA use, preoperative CRP level, operative time, and use of laparoscopic surgery (*Table 3*). The non-postoperative complications group had a lower incidence of preoperative biological medication use (12.9% *vs.* 27.4%, P=0.015), a higher incidence of postoperative ω-3 PUFA use (50.8% *vs.* 32.2%, P=0.016), lower preoperative CRP levels (10.2±2.0 *vs.* 27.3±6.3, P=0.001), shorter operative times (181.2±5.3 *vs.* 206.3±7.7, P=0.008), and a higher incidence of laparoscopic surgery (71.0% *vs.* 53.2%, P=0.017) than the

Table 2 Postoperative complications in CD patients with and without ω-3 PUFAs

Characteristics	Control group (n=103)	ω-3 PUFAs group (n=83)	P value
Postoperative complications	42 (40.8)	20 (24.1)	0.016
Mild complications (Grade I to II)	29 (28.2)	18 (21.7)	0.313
Wound infection	10 (9.7)	3 (3.6)	0.105
Fever >38.5 ℃ after surgery	8 (7.8)	5 (6.0)	0.643
Diarrhea	2 (1.9)	2 (2.4)	0.827
Early postoperative bowel obstruction	4 (3.9)	6 (7.2)	0.316
Postoperative blood transfusions >2 U	4 (3.9)	1 (1.2)	0.242
Line sepsis	1 (1.0)	1 (1.2)	0.695
Major complications (Grade III to IV)	24 (23.3)	8 (9.6)	0.014
Gastrointestinal bleeding	3 (2.9)	2 (2.4)	0.832
Intra-abdominal bleeding	2 (1.9)	0	0.305
Anastomotic leakage	5 (4.9)	2 (2.4)	0.374
Abdominopelvic collection	2 (1.9)	1 (1.2)	0.688
Intra-abdominal abscess	4 (3.9)	2 (2.4)	0.567
Stoma complications	3 (2.9)	0	0.058
Septic shock	4 (3.9)	1 (1.2)	0.242
Sepsis	1 (1.0)	0	0.554
Grade V	0	0	–
Postoperative stay, day	12.1±1.1	9.3±0.6	0.041

Values are expressed as the mean ± standard deviation or number (percentage). CD, Crohn's disease; ω-3 PUFA, omega-3 polyunsaturated fatty acid.

postoperative complications group.

Multivariate analysis of the risk factors associated with postoperative complications

The multivariate logistic regression analysis suggested that preoperative biological medication use was an independent risk factor for postoperative complications in CD patients [odds ratio (OR): 2.644, 95% confidence interval (CI): 1.137–6.152, P=0.024] and that ω-3 PUFA-supplemented PN after surgery was an independent protective factor against postoperative complications in CD patients (OR: 0.492, 95% CI: 0.249–0.974, P=0.042; *Table 4*).

Discussion

CD is a chronic inflammatory disease that can involve the whole digestive tract but mostly involves the terminal ileum and right colon. The etiology of CD remains unknown, and there is still no specific radical treatment for CD. Amino salicylic acid preparations, glucocorticoids, and thiopurine drugs can be used for maintenance therapy during the active period and after drug-induced remission; however, surgical treatment is often needed. Indeed, it has been reported that approximately 78% of patients who have CD for >20 years require surgical treatment (1,21-23). Surgical treatment can only address complications such as obstructions, bleeding, perforations, abscesses, inflammatory masses, and internal and external intestinal fistulas; it cannot cure the primary disease. In addition, postoperative complications are still major problems after colorectal surgery that prolong in-hospital stays, increase treatment costs, and worsen the long-term survival of patients. Malnutrition, preoperative drug use, preoperative intestinal fistulas, and abdominal abscesses can all increase the risk of postoperative complications (24-26). Thus, reliable treatments are needed

Table 3 Univariate analysis of risk factors associated with postoperative complications

Characteristics	Without complications (n=124)	With complications (n=62)	P value
Male/female	80/44	35/27	0.286
Age, y	39.3±1.2	37.8±1.7	0.482
BMI, kg/m^2	19.2±0.3	19.2±0.4	0.877
Previous surgery	54 (43.5)	24 (38.7)	0.528
Montreal classification			
Age (years)			
A1 (≤16)	2 (1.6)	1 (1.6)	0.742
A2 (17–40)	68 (54.8)	39 (62.9)	0.294
A3 (>40)	54 (43.5)	22 (35.5)	0.292
Location			
L1 (ileal)	62 (50.0)	34 (54.8)	0.534
L2 (colonic)	7 (5.6)	2 (3.2)	0.717
L3 (ileocolonic)	46 (37.1)	24 (38.7)	0.831
L4 (upper gastrointestinal)	9 (7.3)	2 (3.2)	0.442
Behavior			
B1 (inflammatory/failure of medical therapy)	6 (4.8)	2 (3.2)	0.898
B2 (structuring)	93 (75.0)	44 (71.0)	0.556
B3 (penetrating)	43 (34.7)	24 (38.7)	0.589
P (perianal disease)	38 (30.6)	14 (22.6)	0.248
Preoperative medications			
5-ASA	29 (23.4)	17 (27.4)	0.548
Corticosteroids	9 (7.3)	5 (8.1)	0.845
Thiopurine	49 (39.5)	19 (30.6)	0.236
Infliximab	16 (12.9)	17 (27.4)	0.015
Others	21 (16.9)	4 (6.5)	0.080
Preoperative TPN	28 (22.6)	12 (19.4)	0.614
Postoperative TPN with ω-3 PUFAs	63 (50.8)	20 (32.2)	0.016
Preoperative RBC, 10^{12}/L	4.3±0.1	4.2±0.1	0.807
Preoperative WBC, 10^9/L	5.6±0.2	6.1±0.4	0.261
Preoperative Hb, g/L	12.0±0.2	11.8±0.3	0.520
Preoperative PLT, 10^9/L	249.3±7.9	264.6±11.9	0.273
Preoperative ESR, mm/hr	15.8±1.3	18.7±2.2	0.253
Preoperative ALB, g/L	36.9±0.5	35.7±0.7	0.131
Preoperative CRP, mg/L	10.2±2.0	27.3±6.3	0.001
Preoperative lymphocyte, 10^9/L	1.18±0.04	1.11±0.08	0.347

Table 3 (*continued*)

Table 3 (*continued*)

Characteristics	Without complications (n=124)	With complications (n=62)	P value
Preoperative Hct, %	36.5±0.5	35.9±0.7	0.502
Operative time, min	181.2±5.3	206.3±7.7	0.008
Laparoscopic surgery	88 (71.0)	33 (53.2)	0.017
ASA ≥3	11 (8.9)	7 (11.3)	0.599

Values are expressed as the mean ± standard deviation or number (percentage). BMI, body mass index; 5-ASA, 5-aminosalicylic acid; TPN, total parenteral nutrition; ω-3 PUFA, omega-3 polyunsaturated fatty acid; RBC, red blood cell; WBC, white blood cell; Hb, hemoglobin; PLT, platelets; ESR, erythrocyte sedimentation rate; ALB, albumin; CRP, C-reactive protein; Hct, hematocrit; ASA, American Society of Anesthesiologists.

Table 4 Multivariate analysis of risk factors associated with postoperative complications

Characteristics	OR	95% CI	P value
Preoperative medications with infliximab	2.644	1.137–6.152	0.024
Postoperative TPN with ω-3 PUFAs	0.492	0.249–0.974	0.042
Preoperative CRP	1.885	0.927–3.833	0.080
Operative time	1.780	0.897–3.531	0.099
Laparoscopic surgery	0.894	0.413–1.934	0.776

OR, odds ratio; TPN, total parenteral nutrition; ω-3 PUFA, omega-3 polyunsaturated fatty acid; CRP, C-reactive protein.

to reduce postoperative complications to enable early and safe patient discharge, especially under the ERAS program.

In the current study, we analyzed the protective effects of ω-3 PUFA-supplemented PN after surgery on postoperative complications for patients with CD. The results revealed that CD patients who did not receive ω-3 PUFA after surgery were at higher risk of postoperative complications, exhibited higher postoperative serum CRP levels, and experienced longer postoperative hospital stays after enterotomy than those who received ω-3 PUFAs. These findings indicate that ω-3 PUFA-supplemented PN after surgery reduces the postoperative inflammatory response and reduces the incidence of postoperative complications, especially major complications, thus accelerating the recovery of CD patients. This study was the first to focus on the relationship between ω-3 PUFA-supplemented PN and postoperative rehabilitation in CD patients.

ω-3 PUFAs have been shown to be effective at enhancing the nutritional status and immune function of gastrointestinal patients who have undergone surgery. ω-3 PUFA-supplemented PN has been proven to be successful, safe, and effective and has good clinical applications and clinical value for CD patients who have not undergone surgery (27,28). However, little is known about the relationship between the use of ω-3 PUFAs after surgery and clinical outcomes.

The effects of ω-3 PUFAs in surgical patients are still controversial. One prospective randomized controlled study showed that ω-3 PUFAs significantly ameliorated the postoperative inflammatory response in 48 patients with gastric cancer (29). Zhang *et al.* (30) found that ω-3 PUFA-supplemented PN improved postoperative recovery, reduced postoperative complications, and shortened hospital stays after hepatectomy in patients with liver cirrhosis or liver cancer. A meta-analysis by Zhao *et al.* (31) revealed that the early application of ω-3 PUFAs in patients with gastrointestinal cancer improved immunity, reduced the postoperative stress response, and attenuated metastasis or recurrence. However, other studies have found no significant correlations between ω-3 PUFAs and postoperative complications in colorectal or esophageal cancer patients (12,32,33).

Our findings suggest that ω-3 PUFA-supplemented PN reduces the postoperative inflammatory response, promotes the recovery of intestinal function, reduces the incidence of anastomotic leakage, and reduces the incidence of abdominal abscesses and other major postoperative

complications in CD patients after enterotomy. However, the incidence of postoperative incision infection was not significantly reduced in our study. CD is characterized by the abnormal activation of the intestinal immune system and a major inflammatory response; however, the application of ω-3 PUFAs after surgery has been shown to reduce the inflammatory response caused by surgical trauma stress, and further control the inflammatory response caused by CD itself (34).

ω-3 PUFAs may mediate the improvement of postoperative rehabilitation in a number of ways. It may be that ω-3 PUFAs regulate the arachidonic acid pathway and control the release of prostaglandins, thromboxanes, leukotrienes, and other molecules, which reduce the levels of inflammatory molecules, such as interleukin (IL)-6, IL-8, and tumor necrosis factor alpha (35-37). It may also be that ω-3 PUFAs regulate sterol regulatory element binding protein, protein acylation reactions, and calcium ion release, which maintain cell membrane integrity, stability, and fluidity, thus reducing the production and release of cytokines and ameliorating the postoperative inflammatory response (38). Alternately, ω-3 PUFAs may alter the phospholipid composition and function of T-cell membranes, which enhances the function of antigen-presenting cells and the cytotoxicity of natural killer cells and regulates the function of dendritic cells to affect immune function (39). Finally, it may that ω-3 PUFAs regulate the intestinal flora and their metabolites, such as short chain fatty acids (40).

The current study had several limitations. First, as a retrospective observational analysis, the effects of residual confounding factors cannot be fully excluded. Second, as a single-center study, the perioperative management strategies were dependent on our local experience, which may have affected the outcomes (41). Large multicenter prospective studies must be performed to verify the findings of the current study.

Conclusions

The current study confirmed that ω-3 PUFA-supplemented PN after surgery can reduce the postoperative inflammatory response and the incidence of postoperative complications, especially major complications, in CD patients. To optimize perioperative treatment measures, surgeons should be aware of the benefits of ω-3 PUFA-supplemented PN after surgery. The use of ω-3 PUFAs should be considered for patients who receive TPN after surgery, which is conducive to reducing postoperative complications and ultimately accelerating rehabilitation.

Acknowledgments

The authors gratefully acknowledge all of the investigators for their contributions to the study.
Funding: This study was supported by grants from National Natural Science Foundation of China (No. 81800474).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-948/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-948/dss

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-948/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-948/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of Sir Run Run Shaw Hospital of Zhejiang University (No. 20210622-31). Written informed consent for the use of clinical records was obtained from each patient, as required by the Institutional Review Board.

References

1. Torres J, Mehandru S, Colombel JF, et al. Crohn's disease. Lancet 2017;389:1741-55.
2. Fumery M, Seksik P, Auzolle C, et al. Postoperative Complications after Ileocecal Resection in Crohn's Disease: A Prospective Study From the REMIND Group. Am J Gastroenterol 2017;112:337-45.
3. Feuerstein JD, Cheifetz AS. Crohn Disease: Epidemiology, Diagnosis, and Management. Mayo Clin Proc 2017;92:1088-103.
4. Fuglestad MA, Thompson JS. Inflammatory Bowel Disease and Short Bowel Syndrome. Surg Clin North Am 2019;99:1209-21.
5. Liu S, Miao J, Wang G, et al. Risk factors for postoperative surgical site infections in patients with Crohn's disease receiving definitive bowel resection. Sci Rep 2017;7:9828.
6. Torgersen Z, Balters M. Perioperative nutrition. Surg Clin North Am 2015;95:255-67.
7. Ali Abdelhamid Y, Chapman MJ, Deane AM. Perioperative nutrition. Anaesthesia 2016;71 Suppl 1:9-18.
8. Brennan GT, Ha I, Hogan C, et al. Does preoperative enteral or parenteral nutrition reduce postoperative complications in Crohn's disease patients: a meta-analysis. Eur J Gastroenterol Hepatol 2018;30:997-1002.
9. Triantafillidis JK, Papalois AE. The role of total parenteral nutrition in inflammatory bowel disease: current aspects. Scand J Gastroenterol 2014;49:3-14.
10. Gouma DJ, von Meyenfeldt MF, Rouflart M, et al. Preoperative total parenteral nutrition (TPN) in severe Crohn's disease. Surgery 1988;103:648-52.
11. Yu J, Liu L, Zhang Y, et al. Effects of omega-3 fatty acids on patients undergoing surgery for gastrointestinal malignancy: a systematic review and meta-analysis. BMC Cancer 2017;17:271.
12. Sorensen LS, Thorlacius-Ussing O, Schmidt EB, et al. Randomized clinical trial of perioperative omega-3 fatty acid supplements in elective colorectal cancer surgery. Br J Surg 2014;101:33-42.
13. Freitas RDS, Campos MM. Protective Effects of Omega-3 Fatty Acids in Cancer-Related Complications. Nutrients 2019;11:945.
14. Ma YJ, Liu L, Xiao J, et al. Perioperative omega-3 Polyunsaturated Fatty Acid Nutritional Support in Gastrointestinal Cancer Surgical Patients: A Systematic Evaluation. Nutr Cancer 2016;68:568-76.
15. Lee HJ, Han YM, An JM, et al. Role of omega-3 polyunsaturated fatty acids in preventing gastrointestinal cancers: current status and future perspectives. Expert Rev Anticancer Ther 2018;18:1189-203.
16. Zhu X, Wu Y, Qiu Y, et al. Effect of parenteral fish oil lipid emulsion in parenteral nutrition supplementation combined with enteral nutrition support in patients undergoing pancreaticoduodenectomy. JPEN J Parenter Enteral Nutr 2013;37:236-42.
17. Tevar R, Jho DH, Babcock T, et al. Omega-3 fatty acid supplementation reduces tumor growth and vascular endothelial growth factor expression in a model of progressive non-metastasizing malignancy. JPEN J Parenter Enteral Nutr 2002;26:285-9.
18. Gong Y, Liu Z, Liao Y, et al. Effectiveness of ω-3 Polyunsaturated Fatty Acids Based Lipid Emulsions for Treatment of Patients after Hepatectomy: A Prospective Clinical Trial. Nutrients 2016;8:357.
19. Zhu X, Wu Y, Qiu Y, et al. Effects of omega-3 fish oil lipid emulsion combined with parenteral nutrition on patients undergoing liver transplantation. JPEN J Parenter Enteral Nutr 2013;37:68-74.
20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
21. Hemperly A, Sandborn WJ, Vande Casteele N. Clinical Pharmacology in Adult and Pediatric Inflammatory Bowel Disease. Inflamm Bowel Dis 2018;24:2527-42.
22. Heerasing N, Thompson B, Hendy P, et al. Exclusive enteral nutrition provides an effective bridge to safer interval elective surgery for adults with Crohn's disease. Aliment Pharmacol Ther 2017;45:660-9.
23. Liu W, Zhou W, Xiang J, et al. Lemann Index at Diagnosis Predicts the Risk of Early Surgery in Crohn's Disease. Dis Colon Rectum 2018;61:207-13.
24. Jouvin I, Lefevre JH, Creavin B, et al. Postoperative Morbidity Risks Following Ileocolic Resection for Crohn's Disease Treated With Anti-TNF Alpha Therapy: A Retrospective Study of 360 Patients. Inflamm Bowel Dis 2018;24:422-32.
25. Ding Z, Wu XR, Remer EM, et al. Association between high visceral fat area and postoperative complications in patients with Crohn's disease following primary surgery. Colorectal Dis 2016;18:163-72.
26. Frischer JS, Rymeski B. Complications in colorectal surgery. Semin Pediatr Surg 2016;25:380-7.
27. Calder PC. Intravenous Lipid Emulsions to Deliver Bioactive Omega-3 Fatty Acids for Improved Patient Outcomes. Mar Drugs 2019;17:274.

28. Limketkai BN, Wolf A, Parian AM. Nutritional Interventions in the Patient with Inflammatory Bowel Disease. Gastroenterol Clin North Am 2018;47:155-77.
29. Wei Z, Wang W, Chen J, et al. A prospective, randomized, controlled study of omega-3 fish oil fat emulsion-based parenteral nutrition for patients following surgical resection of gastric tumors. Nutr J 2014;13:25.
30. Zhang B, Wei G, Li R, et al. n-3 fatty acid-based parenteral nutrition improves postoperative recovery for cirrhotic patients with liver cancer: A randomized controlled clinical trial. Clin Nutr 2017;36:1239-44.
31. Zhao Y, Wang C. Effect of ω-3 polyunsaturated fatty acid-supplemented parenteral nutrition on inflammatory and immune function in postoperative patients with gastrointestinal malignancy: A meta-analysis of randomized control trials in China. Medicine (Baltimore) 2018;97:e0472.
32. Sultan J, Griffin SM, Di Franco F, et al. Randomized clinical trial of omega-3 fatty acid-supplemented enteral nutrition versus standard enteral nutrition in patients undergoing oesophagogastric cancer surgery. Br J Surg 2012;99:346-55.
33. Massironi S, Rossi RE, Cavalcoli FA, et al. Nutritional deficiencies in inflammatory bowel disease: therapeutic approaches. Clin Nutr 2013;32:904-10.
34. Zhang W, Wang ZM, Zhu WM, et al. The effects of induction remission of omega-3 polyunsaturated fatty acid in combination with TPN for active Crohn's disease with bowel obstruction. Parenter Enteral Nutr 2014;21:65-8.
35. Innes JK, Calder PC. Omega-6 fatty acids and inflammation. Prostaglandins Leukot Essent Fatty Acids 2018;132:41-8.
36. Calder PC. Omega-3 fatty acids and inflammatory processes. Nutrients 2010;2:355-74.
37. Linecker M, Limani P, Kambakamba P, et al. Omega-3 Fatty Acids Protect Fatty and Lean Mouse Livers After Major Hepatectomy. Ann Surg 2017;266:324-32.
38. Sekiya M, Yahagi N, Matsuzaka T, et al. Polyunsaturated fatty acids ameliorate hepatic steatosis in obese mice by SREBP-1 suppression. Hepatology 2003;38:1529-39.
39. Chen J, Zuo LT, Zhang HR. The research development of oil fat emulsion in severe acute pancreatitis. Parenter Enteral Nutr 2017;24:181-8.
40. Watson H, Mitra S, Croden FC, et al. A randomised trial of the effect of omega-3 polyunsaturated fatty acid supplements on the human intestinal microbiota. Gut 2018;67:1974-83.
41. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. Stat Med 1998;17:2265-81.

Cite this article as: Shen Y, Liu H, Qi W, Liu W, Ye L, Cao Q, Ge X, Zhou W. An observational study of the effects of ω-3 polyunsaturated fatty acid-supplemented parenteral nutrition on postoperative complications in patients with Crohn's disease. Ann Palliat Med 2023;12(2):336-345. doi: 10.21037/apm-22-948

