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Effects of fat-emulsion-based early parenteral nutrition for patients after hemihepatectomy

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Abstract

This study investigates the effects of fat-emulsion-based early parenteral nutrition in patients following hemihepatectomy, addressing a critical gap in clinical knowledge regarding parenteral nutrition after hemihepatectomy. We retrospectively analyzed clinical data from 274 patients received non-fat-emulsion-based parenteral nutrition (non-fatty nutrition group) and 297 patients received fat-emulsion-based parenteral nutrition (fatty nutrition group) after hemihepatectomy. Fat-emulsion-based early parenteral nutrition significantly reduced levels of postoperative aspartate aminotransferase, total bilirubin, and direct bilirubin, while minor decreases in red blood cell and platelet counts were observed in the fatty nutrition group. Importantly, fat-emulsion-based early parenteral nutrition shortened lengths of postoperative hospital stay and fasting duration, but did not affect the incidence of short-term postoperative complications. Subgroup analyses revealed that the supplement of omega-3 fish oil emulsions was significantly associated with a reduced inflammatory response and risk of postoperative infections. These findings indicate that fat-emulsion-based early parenteral nutrition enhances short-term postoperative recovery in patients undergoing hemihepatectomy.

Keywords: Hemihepatectomy, Intravenous fat emulsions, Parenteral nutrition, Omega-3 fatty acids, Perioperative period

Abbreviations: alanine aminotransferase (ALT), aspartate aminotransferase (AST), body mass index (BMI), Hepatitis B virus surface antigen (HBsAg), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), interquartile range (IQR), long chain triglyceride (LCT), physically mixed medium and long chain triglyceride (MCT/LCT), structured triglyceride (STG), platelet count (PLT), postoperative day (POD), propensity score matching (PSM), red blood cell count (RBC), standard deviation (SD), white blood cell count (WBC), blood transfusion (BT), choleretic medication (CM), C-reactive Protein (CRP), One-way analysis of variance (ANOVA).

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Introduction

Parenteral nutrition, a widely adopted nutritional therapy, provided through intravenous administration of amino acids, glucose, lipids, electrolytes, vitamins and trace elements when patients cannot use the gastrointestinal tract or nutrition needs cannot be met through the gastrointestinal tract alone [(1)]. In response to major stress like abdominal surgery, the body shifts to a metabolic model of mixed energy supply based on glucose and lipids, particularly in the critical metabolic organs such as liver [(2)]. In clinical practice, patients undergoing abdominal surgery require fat-emulsion-based early parenteral nutrition to meet or replenish their nutritional needs, due to high nutritional risk, poor tolerance to enteral nutrition, and postoperative fasting [(3)]. Significant efforts are still being made to develop a more appropriate strategy in early parenteral nutrition to provide the necessary nutritional support for patients undergoing abdominal surgery.

Hemihepatectomy, a radical curative procedure, widely employed for treating hepatic malignancies and benign tumors [(4)]. Previous preclinical studies have shown that peripheral-derived lipids rapidly accumulate in liver after hepatectomy, and inhibiting this lipid accumulation delays hepatocyte proliferation and repair after hepatectomy [(5)], which provides a theoretical basis for the use of fat-emulsion-based early parenteral nutrition after hepatectomy. However, compared to partial hepatectomy, hemihepatectomy results in a smaller residual liver volume and the increased risk of small-for-size syndrome (SFSS), impeding the regeneration of residual liver and the recovery of liver function [(6, 7)]. Furthermore, patients following hemihepatectomy generally have chronic liver diseases such as viral hepatitis and cirrhosis, which placing their potential liver function in the vulnerable or decompensated states to exacerbate SFSS even liver dysfunction after hemihepatectomy [(6, 7)]. Importantly, the liver, as a key metabolic organ, is involved in the synthesis and metabolism of various substances, particularly lipids [(8)]. Post-hepatectomy liver dysfunction reduces the hepatic ability to consume and utilize lipids under stress conditions [(9)]. The excessive accumulation of lipids in the liver leads to the potential lipotoxicity, triggering inflammatory responses and metabolic disturbances, which further impairs liver function [(10)]. Notably, due to the difficulty in obtaining clinical samples regarding regenerative liver, it is

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little known about the impacts of fat-emulsion-based early parenteral nutrition on lipid metabolism in regenerative liver. Therefore, exploring the effects of fat-emulsion-based early parenteral nutrition on short-term recovery after hemihepatectomy could be a promising starting point.

Currently, clinical practice offers various formulations of fat emulsions, including long-chain triglyceride (LCT), physically mixed medium and long-chain triglyceride (MCT/LCT), structured triglyceride (STG), and omega-3 fish oil emulsions. Given the differences in carbon chain length and structure among triglycerides, emerging studies suggest that carbon chain length and structure might affects the metabolic processes of different fat emulsion types in the body [(11, 12)]. Although previous studies have reported the effects of different types of fat emulsions on perioperative outcomes in surgery[(13)], it is also unclear whether short-term postoperative recovery were influenced by the different types of fat emulsion in patients following hemihepatectomy. This necessitates an in-depth analysis involving in the effect of fat emulsions for patients undergoing hemihepatectomy.

In this study, we evaluated the effects of fat-emulsion-based early parenteral nutrition for patients undergoing hemihepatectomy. Furthermore, we investigated the differences in short-term postoperative recovery in early parenteral nutrition with different fat emulsion formulations.

Methods

Data Collection

Clinical data were retrospectively collected and analyzed from 571 patients who underwent hemihepatectomy at the Division of Hepatobiliopancreatic Surgery, Department of General Surgery, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong, China, between February 2010 and August 2020. The inclusion criteria for this study were as follows: (i) patients with indications for hemihepatectomy; (ii) patients who underwent either left or right hemihepatectomy; (iii) patients who received parenteral nutritional support from the day of surgery for at least five days postoperatively. Exclusion criteria included: (i) patients with

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incomplete clinical data; (ii) patients with immunodeficiency disorders, hyperthyroidism, hyperlipidemia, diabetes, severe jaundice, chronic renal disease, a history of acute myocardial infarction or stroke within the past six months, or contraindications to fat emulsion use (e.g., fat malabsorption, allergy to fat emulsion components, etc.); (iii) patients with preoperative malnutrition. The collected clinical data included demographic and perioperative variables such as age, gender, body mass index (BMI), surgical approach, Child-Pugh score, intraoperative blood loss, pathological findings, length of postoperative hospital stay, and postoperative complications (including liver dysfunction, lung infection, abdominal infection, pleural effusion, ascites and biliary leakage). Additionally, perioperative laboratory parameters were recorded, including red blood cell count (RBC), white blood cell count (WBC), platelet count (PLT), hemoglobin (HGB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), albumin (ALB) and C-reactive protein (CRP). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki (as revised in 2013) and was approved by the Medical Ethics Committee of Nanfang Hospital, Southern Medical University (NFEC-2017-119).

Patients and Treatment

According to whether fat-emulsion-based early parenteral nutrition was implemented during the patient's previous treatment, patients were categorized into the non-fat-emulsion-based early parenteral nutrition group (Non-fatty Nutrition Group, n = 274) and the fat-emulsion-based early parenteral nutrition group (Fatty Nutrition Group, n = 297) (Figure 1). Demographic and clinical characteristics are summarized in Table S1. From the day of surgery to postoperative day (POD) 5, all patients received continuous parenteral nutritional therapy, which included glucose, amino acids, electrolytes, trace elements, and vitamins. The nutritional regimens of both groups were isonitrogenous and isocaloric, with a nitrogen intake of 0.25 g/kg/day, a total caloric intake of 30 kcal/kg/day, and non-protein calories ranging from 15 to 20 kcal/kg/day. In the non-fat-emulsion-based nutrition group, non-protein calories were exclusively derived from glucose, whereas in the fat-emulsion-based nutrition group, non-protein calories were supplied by both glucose and fat emulsions, with an energy ratio of glucose to fat set at 6:4. Fat emulsions were administered at a dosage of 1.0–1.5 g lipid/kg/day to meet nutritional requirements. Based on the type of fat emulsion used, the fat-emulsion-based nutrition group was further stratified into the LCT subgroup (n = 97), the LCT/MCT subgroup (n = 97), and the STG subgroup (n = 103) (Figure 1). Additionally, using 1:1 propensity score matching (PSM), the fat-emulsion-based nutrition group was further divided into the conventional nutrition subgroup (n = 66) and the enhanced nutrition subgroup (n = 69) (Figure 1). In the enhanced nutrition subgroup, omega-3 fish oil fat emulsions (2 mL/kg/day) were continuously administered from the day of surgery to POD 5 in addition to the standard fat-emulsion-based nutrition regimen. In this study, the sources of fat emulsions were as follows: LCT was provided by a fat emulsion–amino acids (17AA)-glucose (11%) injection (1440 mL, Cavin, Fresenius Kabi AB, China); MCT/LCT was provided by Qiaoguang Kalu (Baxter, China); and STG was provided by a 250 mL Levin emulsion (Fresenius Kabi AB, China). Omega-3 fish oil emulsions were supplied as ω-3 Fish Oil Fat Emulsion Injection (Fresenius Kabi Austria GmbH, Austria). The nutritional solutions consisted of mixtures of glucose, amino acids, fat emulsions, electrolytes, and vitamins, all of which were infused via a central vein. All patients began oral intake following anal exhaust. In addition to nutritional support, comprehensive postoperative care was routinely provided.

Assessment

Venous blood samples were collected from all patients preoperatively and in the early morning on POD 1, POD 3, POD 5, and POD 7. The effects of fat emulsion administration were evaluated based on laboratory parameters related to routine blood tests, liver function tests, inflammatory response, and postoperative short-term outcome. These parameters included ALT, AST, TBIL, DBIL, IBIL, ALB, RBC, WBC, HGB, PLT and CRP. Additionally, postoperative short-term outcomes included liver dysfunction, lung infection, abdominal infection, pleural effusion, ascites, biliary leakage, lengths of postoperative hospital stay (LOPOHS), and fasting durations. Biliary leakage was defined as a bilirubin concentration in the drainage fluid at least three times higher than that in the serum on POD 3 [(14)]. Liver dysfunction following hepatectomy was defined as an international normalized ratio (INR) of prothrombin time (PT) > 1.5 or a total bilirubin level > 34.2 μmol/L on POD 5 [(15)]. Post-

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hepatectomy liver dysfunction was further classified into three grades: Grade A: No changes in the patient's clinical management were required. Grade B: The clinical course deviated from the standard postoperative trajectory but did not necessitate invasive intervention. Grade C: Invasive therapeutic interventions were required [15]. Lung infection was diagnosed based on positive postoperative sputum bacterial and/or fungal cultures or radiological evidence of pneumonia. Abdominal infection was confirmed by positive bacterial or fungal cultures from postoperative abdominal drainage fluid [16]. Pleural effusion was diagnosed via imaging findings of pulmonary effusion [17]. Ascites was identified using abdominal ultrasonography or computed tomography [18].

Statistical Analysis

All statistical analyses were performed using SPSS Statistics 23.0 software (IBM, Armonk, NY, USA). A p-value < 0.05 was considered statistically significant. Quantitative data with a normal distribution were presented as mean ± standard deviation (SD), while data with a skewed distribution were expressed as the median and interquartile range (IQR). Differences between two groups for normally distributed data were analyzed using the Student's t-test. One-way analysis of variance (ANOVA) was applied for comparisons among multiple groups of normally distributed data, with post hoc pairwise comparisons conducted using the least significant difference (t-test). The Mann-Whitney U test was used to compare skewed data between two groups, while the Kruskal-Wallis test was employed for comparisons among multiple groups of skewed data. Categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate. Propensity score matching (PSM) was applied to balance confounding factors between the conventional nutrition subgroup and the enhanced nutrition subgroup.

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Results

The effects of fat-emulsion-based early parenteral nutrition in liver function and routine blood tests in patients following hemihepatectomy

No significant differences were observed in the baseline characteristics between the non-fatty nutrition group and the fatty nutrition group, except for the pathological diagnosis of patients (Table S1). The fatty nutrition group showed the significantly reduced levels of AST on POD5 and POD 7 compared to the non-fatty nutrition group (POD 5, 42.00 IU/L vs. 37.00 IU/L, $p < 0.05$, POD 7, 37.00 IU/L vs. 31.00 IU/L, $p < 0.05$) (Table 1). Moreover, in the fatty nutrition group, the levels of TBIL and DBIL on POD 1 and POD 3 were significantly decreased compared with the non-fatty nutrition group (TBIL POD 1, 18.55 μmol/L vs. 15.40 μmol/L, $p < 0.05$, POD 3, 20.40 μmol/L vs. 18.50 μmol/L, $p < 0.05$, DBIL POD 1, 9.00 μmol/L vs 7.40 μmol/L, $p < 0.05$, POD 3, 11.80 μmol/L vs 9.20 μmol/L, $p < 0.05$) (Table 1). We also found no significant differences in the other liver function parameters, including ALT, IBIL, and ALB (Table 1). In the blood routine tests, from POD 3 to POD 7, RBC levels were significantly lower in the fatty nutrition group than those in the non-fatty nutrition group (POD 3, 3.88×10^{12}/L vs. 3.74×10^{12}/L, $p < 0.05$, POD 5, 3.85×10^{12}/L vs. 3.71×10^{12}/L, $p < 0.05$, POD 7, 3.92×10^{12}/L vs. 3.76×10^{12}/L, $p < 0.05$) (Table 2). Notably, anemia was not observed in either group, while the levels of HGB were significantly reduced in the fatty nutrition group on POD 7 (114.51×10^{9}/L vs. 111.34×10^{9}/L, $p < 0.05$) (Table 2). Additionally, PLT levels from POD 1 to POD 7 were also significantly decreased in the fatty nutrition group compared to the non-fatty nutrition group (POD1, 194.61×10^{9}/L vs. 181.59×10^{9}/L, $p < 0.05$, POD 3, 166.78×10^{9}/L vs. 147.73×10^{9}/L, $p < 0.05$, POD 5, 197.10×10^{9}/L vs. 172.09×10^{9}/L, $p < 0.05$, POD 7, 218.67×10^{9}/L vs. 191.39×10^{9}/L, $p < 0.05$) (Table 2). Interestingly, we observed the significant reduced WBC levels on POD 5 and POD 7 in the fatty nutrition group (POD 5, 8.86×10^{9}/L vs. 8.32×10^{9}/L, $p < 0.05$, POD 7, 8.48×10^{9}/L vs. 7.93×10^{9}/L, $p < 0.05$), with the significant decrease of CRP levels on POD 3 and POD 7 in the fatty nutrition group (POD 3, 92.52 mg/L vs. 78.36 mg/L, $p < 0.05$, POD 7, 27.73 mg/L vs. 24.65 mg/L, $p < 0.05$) (Table 2). These results collectively suggest that while the reduced trends of hemogram exist in the fat-emulsion-based early parenteral nutrition, fat-emulsion-based early parenteral nutrition improves liver function and reduces inflammatory response in patients following hemihepatectomy.

Fat-emulsion-based early parenteral nutrition accelerates postoperative recovery without affecting postoperative short-term complications in hemihepatectomy

Postoperative complications and short-term recovery outcomes were evaluated in the non-fatty nutrition and fatty nutrition groups. As shown in Table 3, no significant differences were

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observed in the incidence of different classified postoperative liver dysfunction between the non-fatty nutrition group and fatty nutrition group. Moreover, fat-emulsion-based early parenteral nutrition had no impact on the incidence of short-term complications including lung infection, abdominal infection, pleural effusion, ascites, and biliary leakage (Table 3). Notably, patients undergoing hemihepatectomy in the fatty nutrition group had significantly shorter LOPOHS and fasting durations compared to the non-fatty nutrition group (LOPOHS, 10.80 days vs. 9.95 days, $p < 0.05$, fasting duration, 3.45 days vs. 2.72 days, $p < 0.05$) (Table 3), suggesting that the fat-emulsion-based early parenteral nutrition promotes short-term recovery after hemihepatectomy.

Different fat emulsion formulations have no impact on liver function tests, routine blood tests, and postoperative short-term complications and recovery

Among the LCT, LCT/MCT, and STG subgroups, the baseline characteristics were comparable, including gender, age, BMI, HBsAg status, cirrhosis, Child-Pugh score, surgical approach, intraoperative blood transfusion (IBT), postoperative blood transfusion (PBT), and postoperative choleretic medication (PCM) (Table S2). No significant differences were found among these subgroups in liver function and routine blood tests, including ALT, AST, TBIL, DBIL, IBIL, ALB, RBC, WBC, PLT, HGB (Tables 4 and S3). Interestingly, we found that the levels of CRP were significantly different among these subgroups on POD 5 and POD 7 (POD 5, 52.46 mg/L vs. 57.63 mg/L vs. 37.77 mg/L, $p < 0.05$, POD 7, 23.11 mg/L vs. 31.37 mg/L vs. 19.49 mg/L, $p < 0.05$, respectively) (Table 4). In the STG subgroup, CRP levels were significantly reduced on POD 5 compared to the LCT subgroup or the LCT/MCT subgroup (Table 4). Similarly, the levels of CRP on POD 7 in the STG subgroup were significantly decreased compared to the LCT/MCT subgroup (Table 4). Additionally, there were no significant differences in the incidence of post-hepatectomy liver dysfunction, postoperative complications, LOPOHS, and fasting duration among the subgroups (Table S4). These findings collectively indicate that the early parenteral nutrition with different fat emulsion formulations has no marked effect on the short-term recovery in patients following hemihepatectomy.

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Additional administration of omega-3 fish oil emulsions reduces inflammation and the incidence of lung infections after hemihepatectomy

To explore the roles of additional administration of omega-3 fish oil emulsions, patients in the fatty nutrition group were further classified into the two groups: one receiving fat-emulsion-based early parenteral nutrition with omega-3 fish oil emulsions supplementation (Enhanced Nutrition Subgroup, n = 69), and the other receiving fat-emulsion-based early parenteral nutrition without omega-3 fish oil emulsions supplementation (Conventional Nutrition Subgroup, n = 228). We found that age, HBsAg status, surgical method, IBT, PBT, and PCM were significantly different in the baseline characteristics between the enhanced nutrition subgroup and conventional nutrition subgroup (Table S5). To minimize the biases of baseline characteristics, 1:1 PSM was performed using an allowable range of 0.10 and the predefined screening criteria including age, HBsAg status, surgical method, IBT, PBT, and PCM. No significant differences were found in the baseline characteristics between the enhanced nutrition subgroup (n = 69) and conventional nutrition subgroup (n = 66) after PSM (Table S6). Fat-emulsion-based early parenteral nutrition supplemented with omega-3 fish oil emulsions had no significant impact on liver function tests and routine blood tests (Tables 5 and S7). Similarly, no significant differences between these two subgroups were observed in post-hepatectomy liver dysfunction, pleural effusion, ascites, biliary leakage, LOPOHS, and fasting duration (Table 5). Notably, CRP levels were significantly reduced in the enhanced nutrition subgroup from POD 3 to POD 7 (POD 3, 81.18 mg/L vs. 66.20 mg/L, $p < 0.05$, POD 5, 59.03 mg/L vs. 32.49 mg/L, $p < 0.05$, POD 7, 26.62 mg/L vs. 16.69 mg/L, $p < 0.05$) (Table 5). Consistently, fat-emulsion-based early parenteral nutrition supplemented with omega-3 fish oil emulsions significantly reduced the incidence of lung infection, with a decreasing trend in the incidence of abdomen infection (Table 5), indicating that the fat-emulsion-based early parenteral nutrition with omega-3 fish oil emulsions has a positive effect on controlling inflammatory response in patients following hemihepatectomy.

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Discussion

This study presents the effects on fat-emulsion-based early parenteral nutrition for patients undergoing hemihepatectomy. We found that fat-emulsion-based early parenteral nutrition improves liver function and reduces LOPOHS and fasting duration in patients following hemihepatectomy, with a minor decrease in RBC and PLT. Moreover, the fat-emulsion-based early parenteral nutrition with omega-3 fish oil emulsions reduces inflammation after hemihepatectomy. These findings suggest that fat-emulsion-based parenteral nutrition is feasible during early recovery period of post- hemihepatectomy, serving as a conventional therapy of post-hemihepatectomy.

Appropriate therapies during post-hemihepatectomy are key to ensure the early postoperative recovery [(19)]. Early parenteral nutrition provides the adequate nutritional support to maintain physiological function under the hepatectomy-induced stress[(20)]. Given that peripheral-derived lipids rapidly accumulate in liver after hepatectomy, fat-emulsion-based early parenteral nutrition might further exacerbate lipid accumulation within the liver. Under the normal physiological conditions, the liver can metabolize such lipids accumulation [(8)]. However, due to the reduced number of functional hepatocytes, the hepatic ability to metabolize lipids is impaired after hemihepatectomy, leading to the excessive lipid accumulation [(5)]. These accumulated lipids damage hepatocytes by activating oxidative stress and inducing inflammatory responses, thereby exacerbating liver dysfunction [(10, 21)]. Therefore, it is crucial to assess the impact of fat-emulsion-based early parenteral nutrition on the short-term outcomes of hemihepatectomy.

Fat-emulsion-based early parenteral nutrition promotes the postoperative short-term recovery in surgical patients [(3)]. We found that fat-emulsion-based early parenteral nutrition significantly reduced the parameters of postoperative liver function tests, including AST, TBIL, and DBIL, indicating that the use of fat emulsions decreases transaminase leakage and improves bilirubin metabolism. Similarly, previous research revealed that polyunsaturated fatty acids in fat emulsions alleviate cholestasis and decrease the morbidity of parenteral-nutrition-related liver disease [(22)]. Additionally, our results showed that the early postoperative administration of parenteral nutrition with fat emulsions has no significant impact on the incidence of short-term postoperative complications after hemihepatectomy. Westvik TS et al. have reported that patients with chronic diseases are prone to occur postoperative malnutrition after major surgery, which is associated with a higher incidence of postoperative complications [23]. The European Society for Clinical Nutrition and Metabolism recommends the immediate nutritional intervention for malnourished patients following surgery, as it significantly adjusts their nutritional status to improve outcomes [24, 25]. Consistently, our findings showed that LOPOHS and fasting duration were markedly shortened in the fatty nutrition group, suggesting that the fat-emulsion-based early parenteral nutrition accelerates short-term recovery in patients following hemihepatectomy. However, we found the levels of RBC, HGB, and PLT were significantly reduced in the fatty nutrition group. Dahlan W et al. pointed out that the infusion of fat emulsions alters the lipid composition of cell membranes to affect membrane stability, leading to hemolysis or blood cells damage [26], which potentially contributes to the reduction in RBC and HGB levels. The decrease in PLT may be attributed to the activation of platelets by fatty acids contained in the fat emulsion, resulting in platelet consumption [27]. Moreover, the metabolism of intravenous fat emulsions primarily relies on the liver. In patients with chronic liver diseases, the reduced hepatic metabolic and synthetic functions may affect hematopoiesis [28], potentially resulting in a decrease in RBC, PLT, and HGB levels. Although RBC and PLT levels in the fatty nutrition group were significantly reduced compared to the non-fatty nutrition group, these values remained within the normal range and showed a trend of recovery. Given the major stress induced by hemihepatectomy, a more cautious approach is warranted. During the administration of fat-emulsion-based early parenteral nutrition after hemihepatectomy, monitoring vital signs and laboratory parameters, such as routine blood tests, liver function tests, and blood lipids, is essential to ensure safety and adjust therapeutic strategy.

The impacts on postoperative recovery are varied by using different types of fat emulsion [29]. Traditional long-chain triglyceride is rich in omega-6 polyunsaturated fatty acids, known to promote inflammation and suppress immune responses [30, 31]. The hydrolysis rate of medium-chain triglyceride and the production of ketone bodies are disturbed by the metabolism of the long-chain triglyceride, leading to metabolic dysregulation to increase the hepatic and renal burden [32]. In our study, we found no significant differences in the most laboratory parameters and clinical short-term outcomes among these three subgroups in patients undergoing hemihepatectomy. The relatively short duration of fat emulsion administration may contribute to the lack of significant differences among these three subgroups. Notably, we observed that CRP levels on POD 5 and POD 7 in the STG subgroup were significantly reduced compared to the LCT or LCT/MCT subgroups. STG, due to its faster clearance rate, is widely used in clinical practice [33]. Previous studies have confirmed that the parenteral nutrition containing STG after hepatectomy reduces inflammation and improves immune function [34]. Furthermore, we evaluated the effects of fat-emulsion-based early parenteral nutrition supplemented with omega-3 fish oil emulsions in patients following hemihepatectomy. Our results indicate that omega-3 fish oil emulsions supplementation significantly reduced CRP levels and the incidence of lung infections after hemihepatectomy. Similarly, a decreased trend of abdomen infections was observed in the enhanced nutrition subgroup. Omega-3 fatty acids, riched in eicosapentaenoic acid and docosahexaenoic acid, have been reported to regulate immune function in monocytes, macrophages, and endothelial cells [35, 36]. Previous studies have suggested that omega-3 fish oil emulsions are safe and effective in reducing postoperative inflammation [36-38]. Although our study explored the effects of fat-emulsion-based early parenteral nutrition in patients undergoing hemihepatectomy, due to the limited number of patients and single-center study, our results still need to be validated in larger and multi-center studies.

In conclusion, our findings indicate that fat-emulsion-based early parenteral nutrition promotes short-term postoperative recovery in patients following hemihepatectomy, with a slight decrease in hemogram. The additional administration of omega-3 fish oil emulsions in the fat-emulsion-based early parenteral nutrition is associated with reduced inflammatory response and risk of postoperative infections. These findings provide evidences for the clinical practice of fat-emulsion-based early parenteral nutrition after hemihepatectomy.

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Authors' contributions: Leyi Liao, and Yang Lei: Study conception and design, acquisition of data, drafting of the manuscript, analysis, and interpretation of data. Qinghua He, and Hanbiao Liang: Acquisition of data, Revision of the manuscript. Jie Zhou, Kai Wang, and Chuanjiang Li: Study conception and design, critical revision of the manuscript.

References

1. Baiu I, Spain DA. Parenteral Nutrition. Jama. 2019;321(21):2142.
2. Finnerty CC, Mabvuure NT, Ali A, Kozar RA, Herndon DN. The surgically induced stress response. JPEN J Parenter Enteral Nutr. 2013;37(5 Suppl):21s-9s.
3. Gao X, Liu Y, Zhang L, Zhou D, Tian F, Gao T, et al. Effect of Early vs Late Supplemental Parenteral Nutrition in Patients Undergoing Abdominal Surgery: A Randomized Clinical Trial. JAMA Surg. 2022;157(5):384-93.
4. Cai X. Laparoscopic liver resection: the current status and the future. Hepatobiliary Surg Nutr. 2018;7(2):98-104.
5. Shteyer E, Liao Y, Muglia LJ, Hruz PW, Rudnick DA. Disruption of hepatic adipogenesis is associated with impaired liver regeneration in mice. Hepatology. 2004;40(6):1322-32.

6. van den Broek MA, Olde Damink SW, Dejong CH, Lang H, Malagó M, Jalan R, et al. Liver failure after partial hepatic resection: definition, pathophysiology, risk factors and treatment. Liver Int. 2008;28(6):767-80.

7. Papamichail M, Pizanias M, Heaton ND. Minimizing the risk of small-for-size syndrome after liver surgery. Hepatobiliary Pancreat Dis Int. 2022;21(2):113-33.

8. Bechmann LP, Hannivoort RA, Gerken G, Hotamisligil GS, Trauner M, Canbay A. The interaction of hepatic lipid and glucose metabolism in liver diseases. J Hepatol. 2012;56(4):952-64.

9. Huang C, Gan J, Mo X, Li Q, Liao L, Wang B, et al. Accumulation of polyunsaturated lipids fuels ferroptosis to promote liver failure after extended hepatectomy in mice. Free Radic Res. 2024;58(11):733-47.

10. Neuschwander-Tetri BA. Hepatic lipotoxicity and the pathogenesis of nonalcoholic steatohepatitis: the central role of nontriglyceride fatty acid metabolites. Hepatology. 2010;52(2):774-88.

11. Hultin M, Müllertz A, Zundel MA, Olivecrona G, Hansen TT, Deckelbaum RJ, et al. Metabolism of emulsions containing medium- and long-chain triglycerides or interesterified triglycerides. J Lipid Res. 1994;35(10):1850-60.

12. Wanten GJ, Naber AH. Cellular and physiological effects of medium-chain triglycerides. Mini Rev Med Chem. 2004;4(8):847-57.

13. Calder PC, Jensen GL, Koletzko BV, Singer P, Wanten GJ. Lipid emulsions in parenteral nutrition of intensive care patients: current thinking and future directions. Intensive Care Med. 2010;36(5):735-49.

14. Koch M, Garden OJ, Padbury R, Rahbari NN, Adam R, Capussotti L, et al. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. Surgery. 2011;149(5):680-8.

15. Rahbari NN, Garden OJ, Padbury R, Brooke-Smith M, Crawford M, Adam R, et al. Posthepatectomy liver failure: a definition and grading by the International Study Group of Liver Surgery (ISGLS). Surgery. 2011;149(5):713-24.

16. Ljubicic N, Spajic D, Vrkljan MM, Altabas V, Doko M, Zovak M, et al. The value of ascitic fluid polymorphonuclear cell count determination during therapy of spontaneous

https://doi.org/10.1017/S0007114525000613 Published online by Cambridge University Press

bacterial peritonitis in patients with liver cirrhosis. Hepatogastroenterology. 2000;47(35):1360-3.

17. Ahmad Z, Krishnadas R, Froeschle P. Pleural effusion: diagnosis and management. J Perioper Pract. 2009;19(8):242-7.

18. Hou W, Sanyal AJ. Ascites: diagnosis and management. Med Clin North Am. 2009;93(4):801-17, vii.

19. Joliat GR, Kobayashi K, Hasegawa K, Thomson JE, Padbury R, Scott M, et al. Guidelines for Perioperative Care for Liver Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations 2022. World J Surg. 2023;47(1):11-34.

20. Gao LB, Tian H, Wang XG, Yu XF, Guan Y, Chen ML, et al. Early enteral and parenteral nutritional support after hepatectomy in patients with hepatic carcinoma: a systematic review and meta-analysis. Onco Targets Ther. 2015;8:623-31.

21. Ferro D, Baratta F, Pastori D, Cocomello N, Colantoni A, Angelico F, et al. New Insights into the Pathogenesis of Non-Alcoholic Fatty Liver Disease: Gut-Derived Lipopolysaccharides and Oxidative Stress. Nutrients. 2020;12(9).

22. Raman M, Almutairdi A, Mulesa L, Alberda C, Beattie C, Gramlich L. Parenteral Nutrition and Lipids. Nutrients. 2017;9(4).

23. Westvik TS, Krause LK, Pradhan S, Westvik HH, Maloney SP, Rutland R, et al. Malnutrition after vascular surgery: are patients with chronic renal failure at increased risk? Am J Surg. 2006;192(5):e22-7.

24. Wong CS, Praseedom R, Liau SS. Perioperative immunonutrition in hepatectomy: A systematic review and meta-analysis. Ann Hepatobiliary Pancreat Surg. 2020;24(4):396-414.

25. Braga M, Ljungqvist O, Soeters P, Fearon K, Weimann A, Bozzetti F. ESPEN Guidelines on Parenteral Nutrition: surgery. Clin Nutr. 2009;28(4):378-86.

26. Dahlan W, Richelle M, Kulapongse S, Rössle C, Deckelbaum RJ, Carpentier YA. Effects of essential fatty acid contents of lipid emulsions on erythrocyte polyunsaturated fatty acid composition in patients on long-term parenteral nutrition. Clin Nutr. 1992;11(5):262-8.

27. Barrachina MN, Pernes G, Becker IC, Allaeys I, Hirsch TI, Groeneveld DJ, et al. Efficient megakaryopoiesis and platelet production require phospholipid remodeling and PUFA uptake through CD36. Nat Cardiovasc Res. 2023;2(8):746-63.

28. van Dievoet MA, Eeckhoudt S, Stephenne X. Primary Hemostasis in Chronic Liver Disease and Cirrhosis: What Did We Learn over the Past Decade? Int J Mol Sci. 2020;21(9).

29. Chambrier C, Lauverjat M, Bouletreau P. Structured triglyceride emulsions in parenteral nutrition. Nutr Clin Pract. 2006;21(4):342-50.

30. Larbi A, Grenier A, Frisch F, Douziech N, Fortin C, Carpentier AC, et al. Acute in vivo elevation of intravascular triacylglycerol lipolysis impairs peripheral T cell activation in humans. Am J Clin Nutr. 2005;82(5):949-56.

31. Wu MH, Wang MY, Yang CY, Kuo ML, Lin MT. Randomized clinical trial of new intravenous lipid (SMOFlipid 20%) versus medium-chain triglycerides/long-chain triglycerides in adult patients undergoing gastrointestinal surgery. JPEN J Parenter Enteral Nutr. 2014;38(7):800-8.

32. Cotter R, Johnson RC, Young SK, Lin LI, Rowe WB. Competitive effects of long-chain-triglyceride emulsion on the metabolism of medium-chain-triglyceride emulsions. Am J Clin Nutr. 1989;50(4):794-800.

33. Nordenström J, Thörne A, Aberg W, Carneheim C, Olivecrona T. The hypertriglyceridemic clamp technique. Studies using long-chain and structured triglyceride emulsions in healthy subjects. Metabolism. 2006;55(11):1443-50.

34. Zhao Y, Wang C. Meta-Analysis of Structured Triglyceride versus Physical Mixture Medium- and Long-Chain Triglycerides for PN in Liver Resection Patients. Biomed Res Int. 2017;2017:4920134.

35. Calder PC. Polyunsaturated fatty acids and inflammatory processes: New twists in an old tale. Biochimie. 2009;91(6):791-5.

36. Gong Y, Liu Z, Liao Y, Mai C, Chen T, Tang H, et al. Effectiveness of omega-3 Polyunsaturated Fatty Acids Based Lipid Emulsions for Treatment of Patients after Hepatectomy: A Prospective Clinical Trial. Nutrients. 2016;8(6).

37. Gura KM, Puder M. Rapid infusion of fish oil-based emulsion in infants does not appear to be associated with fat overload syndrome. Nutr Clin Pract. 2010;25(4):399-402.

38. Zhu X, Wu Y, Qiu Y, Jiang C, Ding Y. Effects of omega-3 fish oil lipid emulsion combined with parenteral nutrition on patients undergoing liver transplantation. JPEN J Parenter Enteral Nutr. 2013;37(1):68-74.

https://doi.org/10.1017/S0007114525000613 Published online by Cambridge University Press

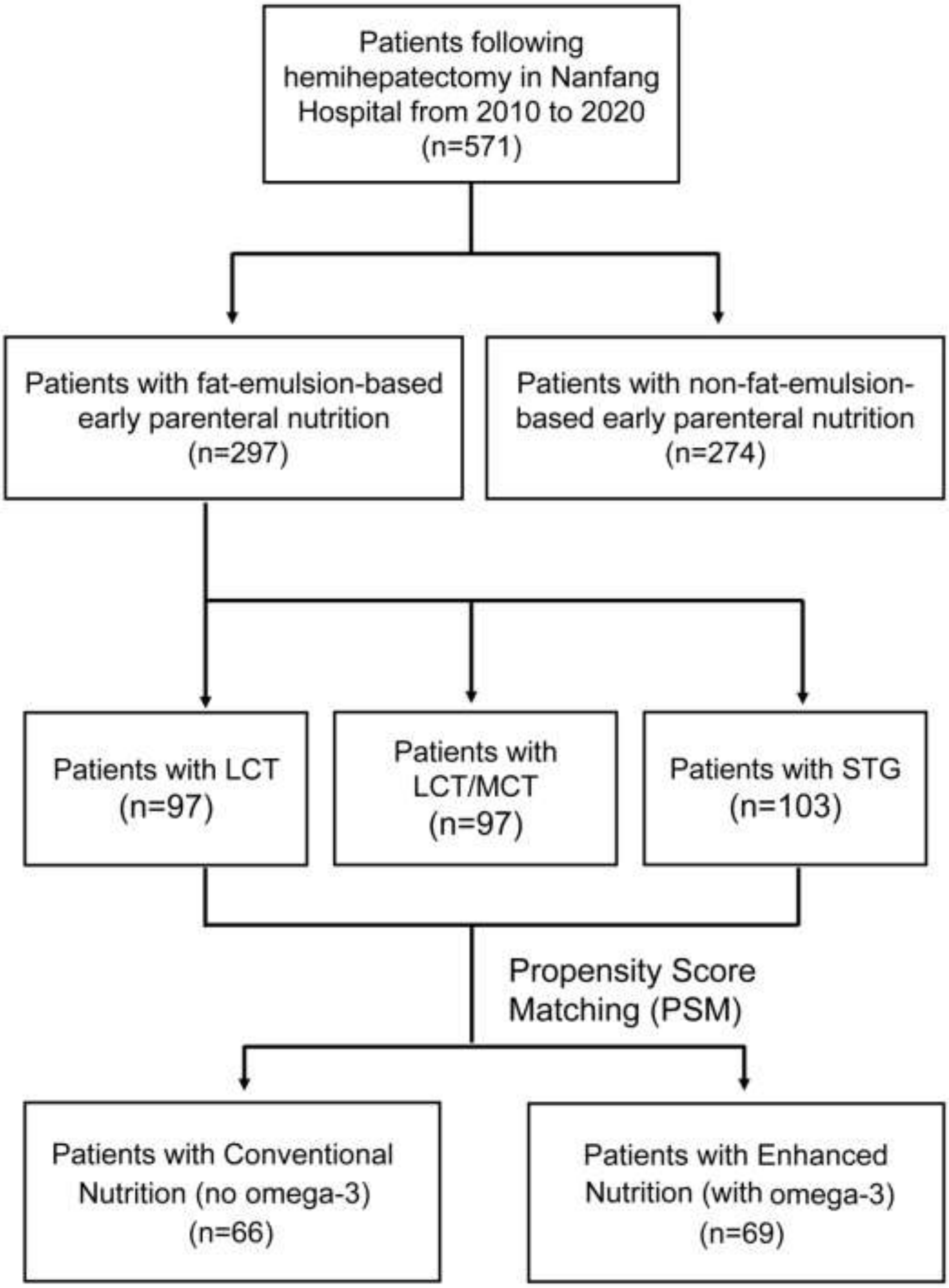

Figure 1. The flow chart of the study. LCT Subgroup, long chain subgroup; LCT/MCT Subgroup, physically mixed medium and long chain; STG Subgroup, structured triglyceride.

Table 1. Liver function of groups with or without early fatty nutrition.

characteristic	Non-fatty Nutrition Group (n=274)	Fatty Nutrition Group (n=297)	*p*-value
ALT, IU/L, $\overline{M}$ (IQR)			
POD 1	236.00 (136.00 -396.00)	241.00 (145.00 -368.00)	0.694
POD 3	152.00 (92.75 -246.00)	149.00 (89.00 -224.00)	0.575
POD 5	76.00 (50.00 -128.00)	73.00 (52.00 -105.00)	0.376
POD 7	52.00 (37.00 -84.00)	54.00 (36.00 -75.00)	0.720
AST, IU/L, $\overline{M}$ (IQR)			
POD 1	275.00 (156.00 -459.25)	250.00 (162.00 -380.00)	0.101
POD 3	84.00 (56.00 -147.75)	83.00 (56.00 -124.00)	0.283
POD 5	42.00 (31.00 -60.00)	37.00 (27.00 -53.00)	**0.002** [a]
POD 7	37.00 (28.00 -48.00)	31.00 (25.00 -42.00)	**<0.001** [a]
TBIL, μmol/L, $\overline{M}$ (IQR)			
POD 1	18.55 (11.70 -26.30)	15.40 (10.25 -23.50)	**0.002** [a]
POD 3	20.40 (14.80 -30.63)	18.50 (12.80 -28.35)	**0.040** [a]
POD 5	20.10 (13.60 -28.73)	19.20 (13.10 -30.10)	0.455
POD 7	16.35 (11.28 -23.75)	17.60 (11.90 -26.30)	0.191
DBIL, μmol/L, $\overline{M}$ (IQR)			
POD 1	9.00 (6.10 -13.93)	7.40 (5.00 -11.20)	**<0.001** [a]
POD 3	11.80 (8.00 -16.80)	9.20 (6.70 -15.00)	**0.001** [a]
POD 5	10.70 (6.90 -15.73)	9.80 (6.50 -15.60)	0.434
POD 7	8.10 (5.80 -13.00)	8.80 (5.80 -14.00)	0.276
IBIL, μmol/L, $\overline{M}$ (IQR)			
POD 1	8.35 (5.00 -13.80)	7.30 (4.60 -11.30)	0.080
POD 3	8.60 (4.90 -13.73)	8.50 (5.50 -12.30)	0.999
POD 5	9.30 (6.10 -13.20)	8.70 (5.60 -12.60)	0.111
POD 7	7.60 (5.10 -12.00)	8.30 (5.30 -12.60)	0.452
ALB, g/L, $\overline{X}$ ± SD			
POD 1	31.48 ± 4.35	31.36 ± 4.34	0.726
POD 3	33.45 ± 3.51	33.27 ± 3.47	0.550
POD 5	35.56 ± 4.42	35.31 ± 4.44	0.490
POD 7	37.86 ± 4.78	37.66 ± 5.42	0.631

[a] Indicates statistical significance, $p<0.05$.

POD, postoperative day; ALT, alanine aminotransferase; ALB, albumin; AST, aspartate aminotransferase; DBIL, direct bilirubin; IBIL, indirect bilirubin; TBIL, total bilirubin

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Table 2. Blood routine tests and CRP test of groups with or without early fatty nutrition.

characteristic	Non-fatty Nutrition Group (n=274)	Fatty Nutrition Group (n=297)	*p*-value
RBC, ×10^{12}/L, $\overline{X}$ ±			
POD 1	4.24 ± 0.77	4.15 ± 0.77	0.163
POD 3	3.88 ± 0.76	3.74 ± 0.70	**0.029** [a]
POD 5	3.85 ± 0.70	3.71 ± 0.67	**0.018** [a]
POD 7	3.92 ± 0.72	3.76 ± 0.69	**0.008** [a]
WBC, ×10^{9}/L, $\overline{X}$ ±			
POD 1	15.23 ± 5.22	14.67 ± 4.84	0.179
POD 3	11.10 ± 3.83	10.47 ± 3.83	0.051
POD 5	8.86 ± 3.14	8.32 ± 3.27	**0.046** [a]
POD 7	8.48 ± 3.46	7.93 ± 3.06	**0.045** [a]
PLT, ×10^{9}/L, $\overline{X}$ ± SD			
POD 1	194.61 ± 72.99	181.59 ± 69.65	**0.030** [a]
POD 3	166.78 ± 72.44	147.73 ± 68.01	**0.001** [a]
POD 5	197.10 ± 86.19	172.09 ± 74.48	**<0.001** [a]
POD 7	218.67 ± 92.06	191.39 ± 79.77	**<0.001** [a]
HGB, ×10^{9}/L, $\overline{X}$ ±			
POD 1	124.69 ± 19.16	122.50 ± 20.79	0.193
POD 3	112.53 ± 18.75	109.85 ± 19.83	0.099
POD 5	111.80 ± 17.09	109.49 ± 18.74	0.126
POD 7	114.51 ± 17.43	111.34 ± 18.01	**0.034** [a]
CRP, mg/L, $\overline{M}$			
POD 1	28.59 (16.67 -48.52)	29.15 (16.42 -45.24)	0.433
POD 3	92.52 (62.02 -123.20)	78.36 (47.93 -116.34)	**0.006** [a]
POD 5	53.61 (27.27 -79.58)	51.39 (28.92 -78.42)	0.908
POD 7	27.73 (18.56 -49.95)	24.65 (13.34 -42.92)	**0.010** [a]

[a] Indicates statistical significance, $p<0.05$.

POD, postoperative day; HGB, hemoglobin; PLT, platelet count; RBC, red blood cell count; WBC, white blood cell count; CRP, C-reactive Protein.

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Table 3. Postoperative recovery situations and complications in groups with or without early fatty nutrition.

characteristic	Non-fatty Nutrition Group (n=274)	Fatty Nutrition Group (n=297)	*p*-value
Lung Infection, %	5.80	6.42	0.773
Abdomen Infection,%	8.00	5.41	0.210
Pleural effusion, %	4.40	3.70	0.688
Biliary leakage, %	4.40	4.40	0.994
Ascites, %	9.90	8.10	0.466
LOPOHS, d, $\bar{X}$ ± SD	10.80 ± 5.15	9.95 ± 4.26	**0.032** [a]
Fasting days, d, $\bar{X}$ ±	3.45 ± 1.45	2.72 ± 1.50	**<0.001** [a]
Liver dysfunction, %			
Grade A	10.20	11.50	0.532
Grade B	8.80	6.40	

[a] Indicates statistical significance, $p<0.05$.

LOPOHS, lengths of postoperative hospital stay.

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Table 4. Blood routine tests and CRP test of LCT, LCT/MCT and STG subgroups.

characteristic	LCT Subgroup (n=97)	LCT/MCT Subgroup (n=97)	STG Subgroup (n=103)	*p*-value
RBC, $\times10^{12}$/L, $\bar{X}$ ±				
POD 1	4.14 ± 0.84	4.12 ± 0.77	4.17 ± 0.72	0.914
POD 3	3.75 ± 0.73	3.68 ± 0.72	3.78 ± 0.65	0.602
POD 5	3.75 ± 0.70	3.69 ± 0.65	3.69 ± 0.65	0.786
POD 7	3.74 ± 0.71	3.78 ± 0.67	3.78 ± 0.68	0.904
WBC, $\times10^{9}$/L, $\bar{X}$ ±				
POD 1	15.21 ± 4.96	14.34 ± 4.85	14.42 ± 4.71	0.965
POD 3	10.16 ± 4.20	10.67 ± 3.26	10.52 ± 4.00	0.444
POD 5	8.06 ± 3.47	8.51 ± 2.95	8.34 ± 3.38	0.455
POD 7	8.07 ± 3.46	8.04 ± 2.96	7.67 ± 2.73	0.524
HGB, $\times10^{9}$/L, $\bar{X}$ ±				
POD 1	122.04 ± 20.52	125.03 ± 20.81	120.31 ± 20.99	0.271
POD 3	109.20 ± 20.29	111.11 ± 21.21	109.11 ± 18.07	0.727
POD 5	110.82 ± 18.31	110.40 ± 18.88	107.26 ± 18.93	0.337
POD 7	111.57 ± 18.26	113.09 ± 18.18	109.39 ± 17.54	0.343
PLT, $\times10^{9}$/L, $\bar{X}$ ± SD				
POD 1	186.80 ± 70.95	175.38 ± 71.14	182.35 ± 66.85	0.664
POD 3	149.74 ± 70.87	141.78 ± 67.52	151.02 ± 65.84	0.532
POD 5	175.47 ± 84.37	168.95 ± 72.51	171.43 ± 66.29	0.189
POD 7	196.41 ± 90.38	190.15 ± 72.23	187.23 ± 76.13	0.342
CRP, mg/L, $\bar{M}$				
POD 1	26.19 (14.89 -45.65)	28.83 (17.01 -47.27)	31.33 (15.59 -44.70)	0.824
POD 3	69.41 (39.69 -98.13)	84.63 (52.92 -	77.84 (40.97 -	0.137
POD 5	52.46 (31.25 -83.58)	57.63 (41.55 -84.40)	37.77 (21.49 -64.29)	**0.003** [a, b]
POD 7	23.11 (12.55 -37.65)	31.37 (19.10 -44.22)	19.49 (11.11 -44.75)	**0.016** [a]

[a] STG subgroup is significantly different from LCT/MCT subgroup (p＜0.05).

[b] STG subgroup is significantly different from LCT subgroup (p＜0.05).

LCT Subgroup, long chain subgroup; LCT/MCT Subgroup, physically mixed medium and long chain; STG Subgroup, structured triglyceride. POD, postoperative day; HGB, hemoglobin; PLT, platelet count; RBC, red blood cell count; WBC, white blood cell count; CRP, C-reactive Protein.

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Table 5. Blood routine tests ,CRP test and postoperative recovery situations and complications between Conventional Nutrition Subgroup and Enhanced Nutrition Subgroup after PSM.

characteristic	Conventional Nutrition Subgroup (n=66)	Enhanced Nutrition Subgroup (n=69)	*p*-value
RBC, $\times 10^{12}$/L, $\bar{X} \pm SD$			
POD 1	4.28 ± 0.89	4.11 ± 0.77	0.247
POD 3	3.89 ± 0.79	3.66 ± 0.64	0.058
POD 5	3.83 ± 0.77	3.66 ± 0.57	0.142
POD 7	3.85 ± 0.75	3.68 ± 0.57	0.136
WBC, $\times 10^{9}$/L, $\bar{X} \pm SD$			
POD 1	14.21 ± 4.52	14.58 ± 5.38	0.670
POD 3	10.02 ± 3.98	10.40 ± 3.44	0.560
POD 5	8.11 ± 3.06	7.92 ± 2.96	0.715
POD 7	7.82 ± 2.81	7.79 ± 2.75	0.964
PLT, $\times 10^{9}$/L, $\bar{X} \pm SD$			
POD 1	184.36 ± 79.21	179.90 ± 68.36	0.726
POD 3	154.12 ± 75.74	139.22 ± 59.45	0.206
POD 5	178.59 ± 84.18	167.90 ± 71.65	0.428
POD 7	201.03 ± 96.37	186.80 ± 75.17	0.339
CRP, mg/L, $\bar{M}$ (IQR)			
POD 1	31.41 (15.18 -47.63)	25.98 (13.35 -42.50)	0.076
POD 3	81.18 (49.44 -122.08)	66.20 (28.45 -93.12)	**0.050** [a]
POD 5	59.03 (42.06 -88.95)	32.49 (22.07 -62.00)	**0.001** [a]
POD 7	26.62 (18.50 -41.38)	16.69 (10.28 -31.37)	**0.004** [a]
Liver dysfunction, %			
Grade A	10.60	8.70	0.262
Grade B	1.50	7.20	
Lung Infection, %	9.10	1.40	**0.045** [a]
Abdomen Infection, %	6.10	4.30	0.054
Pleural effusion, %	3.00	1.40	0.533
Biliary leakage, %	3.00	7.20	0.269
Ascites, %	3.03	10.14	0.098
LOPOHS, d, $\bar{X} \pm SD$	9.32 ± 3.30	10.52 ± 5.46	0.126
Fasting days, d, $\bar{X} \pm$	2.06 ± 1.23	2.48 ± 1.37	0.064

[a] Indicates statistical significance, $p<0.05$.

POD, postoperative day; HGB, hemoglobin; PLT, platelet count; RBC, red blood cell count; WBC, white blood cell count; CRP, C-reactive Protein; LOPOHS, lengths of postoperative hospital stay.