Safety analysis of early oral feeding after esophagectomy in patients complicated with diabetes

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Abstract

Objective To evaluate the safety of early oral feeding in patients with type II diabetes after radical resection of esophageal carcinoma.

Methods The clinical data of 121 patients with type II diabetes who underwent radical resection of esophageal carcinoma in the department of cardiothoracic surgery of Jinling Hospital from January 2016 to December 2018 were retrospectively analyzed. According to the median time of starting postoperative oral feeding, the patients were divided into early oral feeding group (EOF, 67 cases) and late oral feeding group (LOF, 54 cases). Postoperative blood glucose level, incidence of complications, nutritional index (ALB, PA, TRF, Hb), immune indexes (IgA, IgG, IgM), inflammatory indexes(CRP, IL-6), normalized T12-SMA, and QLQ-C30 (Quality Of Life Questionnaire) scores were recorded and compared in the two groups.

Results There was no statistical difference in preoperative nutritional index and postoperative complication rates between the two groups ($p>0.05$). The postoperative nutritional index (ALB, PA, TRF, Hb) and immune index (IgA, IgG, IgM) of the EOF group were higher than those of the LOF group ($p<0.05$), and the inflammatory indicators (CRP, IL-6) of the EOF group were significantly lower than those of the LOF group ($p<0.05$). Moreover, postoperative T12-SMA variation and QLQ-C30 scores of the EOF group were better than those in LOF group ($p<0.05$).

Conclusions Early oral feeding is safe and feasible for patients with type II diabetes after radical resection of esophageal cancer, and it can improve short-term nutritional status and postoperative life quality of the patients.

Introduction

Esophageal cancer is one of the most common digestive malignancies in the world, as its morbidity and mortality rank the 7th and 6th among all the malignant tumors, respectively. GLOBOCAN data shows that 572,000 new cases of esophageal cancer are reported and 509,000 deaths are expected in 2018 over the worldwide[1]. The number of new cases and deaths of esophageal cancer in China ranks the first in the world, accounting for about 50% of the cases and deaths globally[2]. Surgical resection is the main treatment method for patients with esophageal cancer at present. However, the surgical method of esophageal cancer is complex with many postoperative complications, and the 5-year survival rate is only 10%-30%[3].

It has been reported that diabetes may be an independent risk factor for the incidence of esophageal cancer[4]. As a metabolic disorder of glucose, protein and fat caused by defective insulin secretion or impaired biological function, diabetes is growing rapidly all over the world[5]. At present, about 10%~20% of surgical patients are accompanied with diabetes, mainly type II diabetes[6]. For patients of esophageal cancer accompanied with type II diabetes, postoperative complications such as difficult incision healing, pulmonary infection and anastomotic fistula are more likely to occur, which remarkably increases the risk

of esophageal cancer surgery[7–9]. It is of great significance to reduce the surgical risk of this group of patients.

Nutritional support for patients with esophagectomy is very important especially for patients with malnutrition, but the timing of oral intake after esophagectomy is still a bone of contention. Based on recent studies, more and more evidences prove that oral feeding is feasible and effective in the early postoperative period of digestive tract surgery[10, 11]. On the premise of not increasing postoperative complications and motility, early oral feeding may decrease stress response, quicken recovery of bowel function and improve short-term quality of life after esophagectomy[12, 13]. However, there are few studies on the safety of early oral feeding after esophagectomy in patients complicated with type II diabetes. In This study, we compared the incidence of postoperative complications and index of nutrition, immune and inflammation after esophagectomy between early oral feeding group and late oral feeding group in patients complicated with type II diabetes. We aim to investigate the safety and effectiveness of early oral feeding on this kind of patients.

Materials And Methods

Patients

Retrospective analysis was conducted on the clinical data of patients with esophageal cancer complicated with type II diabetes who underwent radical resection in the cardiothoracic surgery department of Jinling Hospital from January 2016 to December 2018. Inclusion criteria was: (1) all patients were 18 years old or older; (2) esophageal squamous cell carcinoma was diagnosed pathologically after surgery; (3) all patients were diagnosed with type II diabetes; (4) complete clinical data and follow-up information are available. Exclusion criteria was: (1) patients with severe heart disease and liver and kidney dysfunction; (2) severe coagulation dysfunction; (3) concurrent or previous history of other malignant tumors; (4) perioperative death. According to the median time of postoperative oral feeding, the patients were divided into early oral feeding group (EOF, 67 cases) and late oral feeding group (LOF, 54 cases). And the patients were staged using the 8th edition of the TNM staging standard for esophageal cancer issued by the Union for International Cancer Control (UICC). Written informed consent was obtained from all patients, and protocols for this study were approved by the Ethics Committee of Jinling Hospital.

Data acquisition

By consulting the electronic medical record system, information of patients meeting the standard was collected, including preoperative clinical indicators (gender, age, body mass index, smoking and alcohol history, glycosylated hemoglobin (HbAlc), albumin, etc.), intraoperative indicators (operation mode, operation time, operative blood loss, etc.) and postoperative indicators (oral feeding time, oral food tolerance, blood glucose, complications, index of nutrition, immune and inflammation, TNM stage, differentiation degree and clinical outcome, etc.). Index of nutrition, immune and inflammation, weight change, quality of life score and T12-SMA were reviewed one month after discharge. Postoperative

complications were graded according to the severity grading system (2009, Clavien-Dindo) and quality of life scores were obtained by QLQ-C30 questionnaire.

Surgery methods

After admission, all patients underwent routine gastroscopy, chest and abdomen CT, electrocardiogram and pulmonary function examination to exclude contraindications. Surgical methods include open surgery and minimally invasive surgery (thoracoscopic radical esophagectomy and Da Vinci robot-assisted radical esophagectomy).

Glycemic management

Preoperative blood glucose monitoring was conducted, of which blood glucose was measured before meals and 2 hours after meals each day. The blood glucose value after meals was controlled below 7 ~ 11.1 mmol/L, and the blood glucose was kept stable for more than 3 days before the operation. After operation, blood glucose was monitored once a day at 6, 9, 11, 14, 17, 20 and 22 o 'clock. The blood glucose was regulated by subcutaneous injection of ordinary insulin as to control it smoothly at 7.0 ~ 11.1 mmol/L.

Postoperative nutritional support

Postoperative nutritional support was provided to patients in both groups according to the ESPEN (the guidelines of the European Society of Parenteral and Enteral Nutrition) and the guidelines of the American Nutrition Association. Patients in both groups received the same nutritional support after surgery. Supplementary Parenteral Nutrition (SPN) was given on the very day according to the principle of "allowable low-calorie calories" [20–25 kcal/kg].In addition, 500 ml 5% glucose and sodium chloride injection was pumped through the nasoenteral nutrition tube or jejunal stoma tube 12 h after the operation. According to the patient's tolerance, Enteral Nutrition (EN) and Perenteral Nutrition (PN) preparation were combined with intravenous infusion within 24 h after the operation, with a total daily calories of 30 kcal/kg. Patients began to drink water after anus exhaust defecation, and gradually shifted to liquid food.

Home nutrition

At discharge, the patients were given a follow-up table of home nutrition and required to record the patient's weight, diet and food intake, gastrointestinal reactions and other information every day. Patients received home enteral nutrition through oral nutrition solution or jejunostomy tube every day. On the basis of normal diet of patients, professional dietitians calculate the amount of extra nutrition needed, and conduct dietary guidance by telephone.

Statistical analysis

Statistical software SPSS 23.0 was used to analyze the data. Quantitative data were presented as Mean standard deviation (Mean ± SD). Independent sample t test was used for inter-group comparison. And chi-

square test was used for inter-group comparison. $P < 0.05$ indicated statistically significant difference (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$).

Results

General information

A total of 121 patients were included in this study. Patients were divided into EOF group (67 cases) and LOF group (54 cases) according to the postoperative oral feeding time (7 days). Among them, there were 50 males and 17 females in EOF group, with an average age of (63.37 ± 7.49) years. There were 41 males and 13 females in the LOF group, with an average age of (63.74 ± 7.22) years. The mean duration of diabetes was 4.96 ± 2.56 years in the EOF group and 5.27 ± 2.82 years in the LOF group. There were no statistically significant differences in gender, age and body mass index between the two groups ($p > 0.05$) (Table 1).

Blood glucose levels

Within 7 days after the operation, the blood glucose levels in EOF group and LOF group fluctuated from 6.86 to 11.47 mmol/L and 6.52 to 10.88 mmol/L, respectively. The blood glucose level varied greatly in the first 2 days after surgery, but both group showed similar blood glucose levels after surgery ($p > 0.05$) (Fig. 1A). It suggested that EOF did not affect the control of blood glucose.

Immune index

The immune index of the two groups showed a decreasing trend after the operation, with in POD 3 falling to the lowest and then slowly recovering. There was no significant difference in immune index between the two groups in the preoperative, POD 1 and POD 3 ($p > 0.05$). However, EOF group showed higher IgA (1.32 ± 0.53 VS 1.13 ± 0.41, $p = 0.032$) level in POD7 and higher IgA (1.91 ± 0.78 VS 1.56 ± 0.65, $p = 0.009$), IgG (12.64 ± 2.86 VS 11.36 ± 2.71, $p = 0.014$) and IgM (1.39 ± 0.42 VS 1.22 ± 0.37, $p = 0.021$) level in POD30 (Table 2) (Fig. 1B). These results indicated that EOF was conducive to the restoration of immunity.

Nutrition index

Similarly, nutrient level declined sharply after surgery and slowly rebounded in POD3. There was no significant difference in nutrition index between the two groups in the preoperative, POD 1 and POD 3 ($p > 0.05$). EOF group presented higher PA (208.62 ± 27.12 VS 195.37 ± 32.78, $p = 0.016$) level in POD 7 and higher ALB (39.67 ± 3.16 VS 38.14 ± 3.83, $p = 0.018$), PA (248.96 ± 47.85 VS 211.38 ± 55.23, $p = 0.004$), TRF (1.89 ± 0.42 VS 1.72 ± 0.35, $p = 0.019$) and Hb (119.95 ± 14.02 VS 112.06 ± 18.73, $p = 0.009$) level in POD 30 (Table 3) (Fig. 1C). This gives us a hint that EOF could improve the nutritional status of patients after surgery.

Inflammatory index

There was no significant difference in inflammatory index between the two groups in the preoperative, POD 1 and POD 3 ($p > 0.05$). Both CRP and IL-6 increased after surgery, of which CRP reached peak in POD 3 and IL-6 in POD 1. EOF group had lower CRP and IL-6 level in POD 7 (CRP, 47.58 ± 25.72 VS 60.87 ± 30.26, $p = 0.01$; IL-6, 19.34 ± 12.67 VS 26.19 ± 10.73, $p = 0.002$) and POD 30 (CRP, 6.13 ± 13.25 VS 13.57 ± 18.96, $p = 0.013$; IL-6, 5.86 ± 6.34 VS 10.35 ± 5.82, $p = 0.0001$) (Table 4) (Fig. 1D). It revealed that EOF could promote the recovery of inflammatory response.

Postoperative complications

Total complications in EOF group and LOF group were 25 cases (37.31%) and 21 cases (38.87%), respectively. The incidence of anastomotic fistula, incision infection and pulmonary infection complications in EOF group and LOF group were respectively (8.96% VS 9.26%), (7.46% VS 5.56%) and (7.46% VS 9.26%), and there was no statistically significant difference in the incidence of these three complications between the two groups ($p > 0.05$) (Table 5). This showed that EOF is safe and did not increase the incidence of complications.

Body weight loss and T12-SMA variation

The body weight loss of patients in EOF group was lower than that in LOF group in POD 30 (4.23 ± 2.06 VS 5.56 ± 2.86, $p = 0.004$) (Fig. 2A). Moreover, T12-SMA variation (the post/pre ratio) was greater in the EOF group (0.87 ± 0.25 VS 0.79 ± 0.16, $p = 0.043$) (Fig. 2B-C). These results suggested that EOF could inhibited the loss of body weight and skeletal muscle caused by surgery.

EORTC QLQ-C30 scores

As shown in TableS1, there was no statistical difference in preoperative QLQ-C30 scores between the two groups. However, 30 days after surgery, the overall health of patients in EOF group was better than that in LOF group (61.33 ± 10.18 VS 53.96 ± 14.87, $p = 0.001$).And in the functional rating scale, the EOF group was better than the LOF group in terms of physical function (59.12 ± 17.74 VS 50.35 ± 16.48, $p = 0.006$) and emotional function (61.17 ± 15.73 VS 54.98 ± 12.61, $p = 0.021$). Moreover, in the score of symptoms rating scale, fatigue (50.82 ± 19.47 VS 59.16 ± 18.04, $p = 0.017$), loss of appetite (27.67 ± 20.36 VS 38.62 ± 21.68, $p = 0.005$) and diarrhea (22.96 ± 16.08 VS 31.32 ± 17.79, $p = 0.008$) of the EOF group were lower than those of the LOF group (Table 6). These results showed that EOF might reduce the incidence of some certain symptoms and improve the quality life of patients.

Discussion

Esophagectomy is the ideal treatment for patients with esophageal cancer at present. Due to the complexity, large trauma and long duration of the surgery, patients are at a state of stress and have a high incidence of postoperative complications, including anastomotic fistula, pulmonary infection, respiratory failure, etc[14]. Patients with esophageal cancer usually have malnutrition for its difficult swallowing and tumor consumption. And for patients complicated with type II diabetes, the blood glucose fluctuates widely and stress response is violent, thus increasing the inflammatory reaction, impairing the

immune system and decreasing tissue repair ability[15]. Therefore, esophageal cancer patients complicated with type II diabetes are more likely to suffer postoperative complications and tend to have a poorer life quality[16, 17]. It has important significance to reduce the surgical risk and improve the prognosis of these group of patients.

With the development of the concept of Enhanced Recovery After Surgery (ERAS) and its application in the field of surgery, patients can better endure surgical stress and recover more quickly. The core theory of ERAS is to allow patients to return to the physiological state, to relieve the body's stress state, and to accelerate the early recovery of patients as soon as possible after surgery[18, 19]. In the traditional surgical treatment scheme for esophageal cancer, clinicians often worry that the early postoperative oral feeding may increase the incidence of anastomotic leakage, so patients usually need to perform routine gastrointestinal decompression and fasting for 5–7 days after surgery[20]. For patients complicated with diabetes, anastomotic healing is often delayed, so postoperative fasting time of patients is usually prolonged in clinical practice[21]. However, in the treatment mode of ERAS, early oral feeding is the most physiological way of nutrition delivery, which has been regarded as one of the most crucial measures [22]. A great deal of studies have shown that early oral feeding after digestive tract surgery is safe and feasible, which does not increase the incidence of postoperative complications such as anastomotic fistula and pulmonary infection, and meanwhile benefits patients for their long-term quality of life[23–25]. At present, there are few reports on the safety and benefit of early oral feeding in patients of esophageal cancer complicated with type II diabetes.

Patients with esophageal cancer are often accompanied by malnutrition due to different degrees of eating obstruction and chronic consumption, and the high catabolism caused by surgical trauma and post-operative stress reaction will further aggravate malnutrition and immunosuppression[26]. In this study, we used ALB, PA, TRF, Hb to evaluate the nutrition status and IgA, IgG, IgM to present the immune status, and results revealed that postoperative nutritional and immune indexes of patients in EOF group were higher than those in LOF group, especially in POD 7 and POD 30. And inflammatory response is one of the main manifestations of postoperative. Changes in serum inflammatory cytokines can objectively reflect the state of postoperative inflammatory response of patients[27]. The CRP and IL-6 levels in EOF group are lower than LOF in POD7 and POD30, which suggested that early oral feeding led the inflammatory response subside faster. Furthermore, changes in digestive tract structure and dietary habits after surgery result in the loss of weight severe skeletal muscle[28]. The body weight loss and T12-SMA variation were less in EOF group. Lastly, QLQ-C30 scores of the EOF group were also better than those in LOF group. Previous studies have proved that early oral feeding can protect the intestinal mucosal barrier of patients undergoing gastrointestinal surgery, thus to improve nutrition, immunity, and promote the recovery of intestinal and organ functions[29]. And our results suggested that early oral feeding is a safe intervention for patients of esophageal cancer complicated with type II diabetes.

Conclusion

In summary, our study retrospectively analyzed the clinical data of 121 patients to explore the safety of early oral feeding in patients of esophageal cancer complicated with type II diabetes. And results showed that early oral feeding could speed up the recovery of nutritional and immune status, decrease the inflammatory response and weight loss of surgery, and meanwhile do not increase the incidence of complications.

Abbreviations

EOF, early oral feeding; LOF, late oral feeding; QLQ, Quality of Life Questionnaire; ALB, albumin; PA, prealbumin; TRF, transferrin; Hb, hemoglobin; CRP, C-Reactive Protein; IL-6, interleukin-6; HbAlc, glycosylated hemoglobin; EN, Enteral Nutrition; PN, Enteral Nutrition; POD, Postoperative Day; ERAS, Enhanced Recovery After Surgery

Declarations

Ethical Approval and Consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of supporting data

Not applicable.

Competing interests

Not applicable.

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Authors' contributions

Yi Shen designed and supervised the study. Zhisheng Jiang and JingLuo collected the data and wrote the manuscript. Mengqing Xu and Zhuangzhuang Cong was responsible for statistical analysis. Saiguang Ji, Yifei Diao and Yang Xu provided technical support and helped to refine the manuscript. All authors read and approved the final manuscript.

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The authors declare that there are no conflicts of interest.

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Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section.

Figures

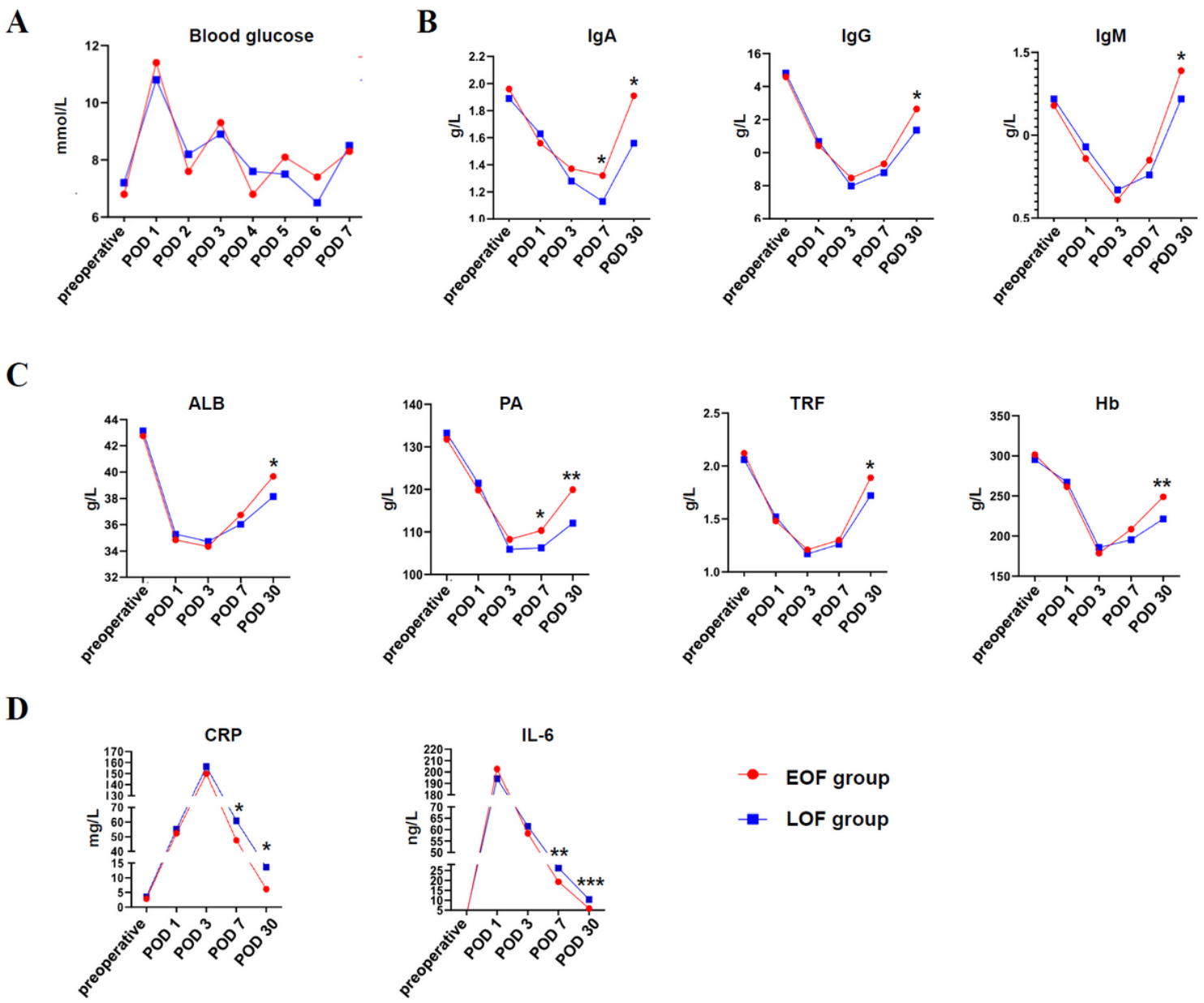

Figure 1

A. EOF group and LOF group showed similar blood glucose levels after surgery. B. EOF group showed higher IgA level in POD7 and higher IgA, IgG and IgM level in POD30. C.EOF group presented higher PA level in POD 7 and higher ALB, PA, TRF and Hb level in POD 30. D. EOF group had lower CRP and IL-6 level in POD 7 and POD 30.

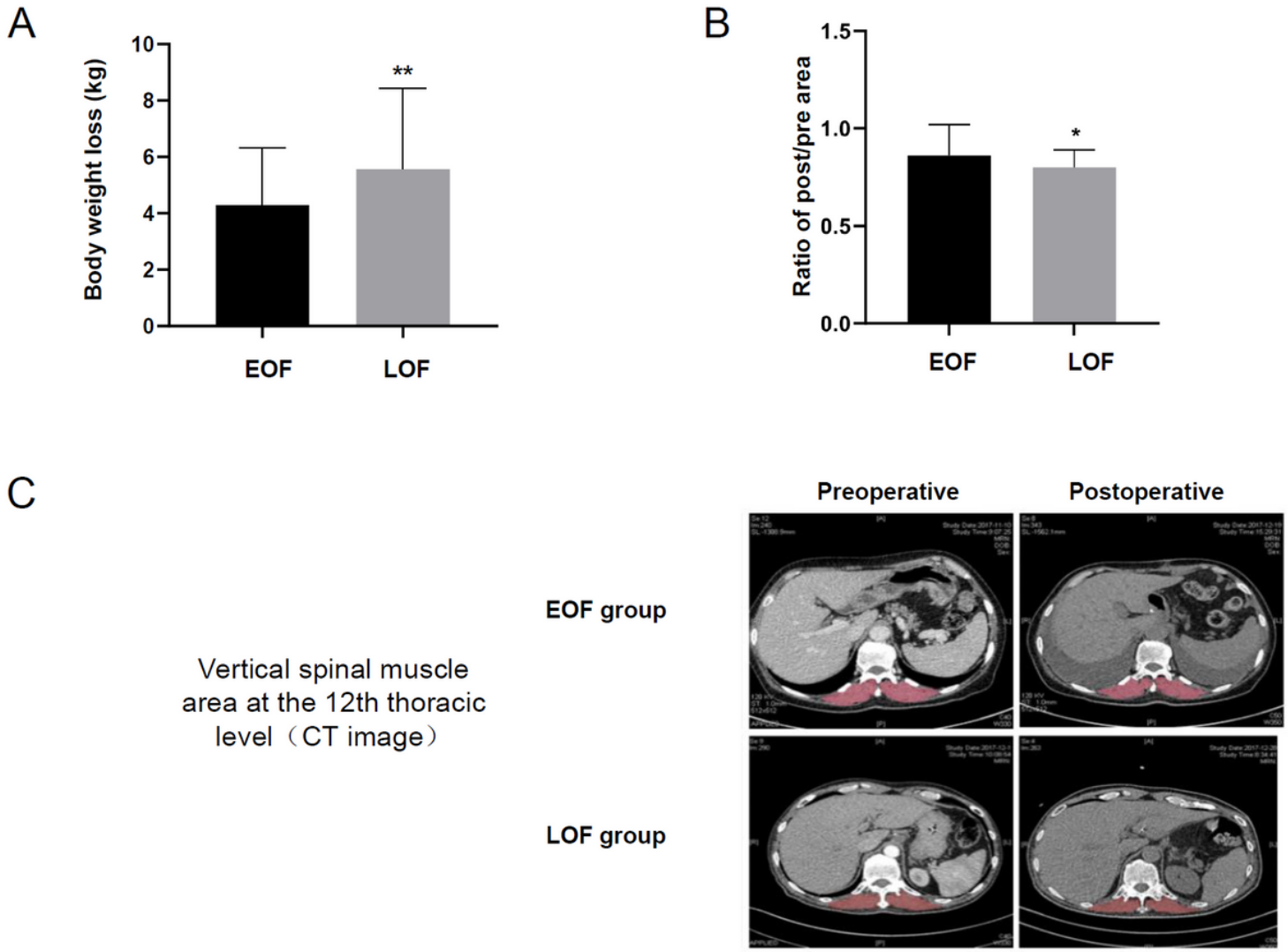

Figure 2

A. The body weight loss of patients in EOF group was lower than that in LOF group in POD 30. B. T12-SMA variation was greater in the EOF group. C. CT images of calculating T12-SMA were shown.

Supplementary Files

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- Table1.xlsx
- Table3.xlsx
- Table6.xlsx
- Table5.xlsx
- Table4.xlsx
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