**Original Article**

The effect of early enteral nutrition on the postoperative immune function and inflammatory indexes in patients with digestive tract cancers

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**Abstract:** Objective: To observe the effects of early enteral nutrition on the postoperative nutritional status, immune function, and inflammatory response in patients with digestive tract cancers. Methods: This prospective study recruited 108 patients with digestive tract cancer, and they were randomly divided into a control group and an observation group, with 54 cases in each group. The patients in the observation group underwent postoperative early enteral nutrition support, while the patients in the control group underwent routine enteral nutrition support. The nutritional indexes, immune function, intestinal function damage indexes, inflammatory indexes, and perioperative indexes between the two groups were compared. Results: The nutritional indexes in the two groups, including serum transferrin (TFN), albumin (Alb) and prealbumin (PA), were significantly elevated after the treatment (P<0.05). However, the nutritional indexes in the observation group were significantly higher compared with the indexes in the control group, and the food-intake start times and inpatient times in the observation group were shorter than they were in the control group (P<0.05). After treatment, the immune and inflammatory indexes in the two groups, including the CD4+/CD8+ ratios, plasma Diamine Oxidase (DAO), serum C-reactive protein (CRP), and interleukin-6 (IL-6), were lower than they were before treatment (P<0.05). But the improvement of the immune indexes and the decrease of the inflammatory indexes in the observation group were better than they were in the control group (P<0.05). There were no significant differences in the incidences of gastrointestinal complications between the two groups (P>0.05). Conclusion: Postoperative early enteral nutrition in patients with digestive tract cancers can significantly improve their nutritional status and immune function, reduce the inflammatory response and promote patient recovery. Meanwhile, it doesn’t increase the incidence of gastrointestinal adverse reactions.

**Keywords:** Early enteral nutrition, digestive tract cancers, nutritional status, immune function, inflammatory response, complication

**Introduction**

The digestive tract is a common cancer site. Studies have indicated that there are more than 2.8 million new cases of digestive tract cancer and up to 2 million deaths every year worldwide [1, 2]. Digestive tract cancers are diseases that occur in the digestive system, including the upper digestive tract (esophageal cancer and gastric cancer) and the lower digestive tract (colon cancer). The clinical features of digestive tract cancers mainly include a late diagnosis, a low opportunity for surgery, and poor overall healing [3]. Current research has confirmed that unhealthy lifestyles (high protein, high fat and carbohydrates, low dietary fiber), the lack of exercise and sedentariness, etc. are considered risk factors for digestive tract cancers. These risk factors are also common in contemporary society, resulting in an increased morbidity and a younger trend in the ages of patients with digestive tract cancers each year [4, 5].

At present, the chief treatment for digestive tract cancers is comprehensive therapy based on surgery. Previous postoperative treatment includes regular and adequate doses of chemoradiotherapy and targeted drug therapy [6-8]. Moreover, the nutrition intake methods are of great significance to patients due to the postoperative fasting requirement. Current nutrition
Early enteral nutrition in patients with digestive tract cancers

supply methods mainly include parenteral and enteral nutrition infusion via the central vein. Parenteral nutrition needs to be infused from the central vein, which has the risk of catheter infections, organ function damage and metabolic complications. However, enteral nutrition can be the first choice for intestinal nutrition due to the advantages of physiology, low cost, and the prevention of bacterial ectopia, etc. Moreover, with the further research on the immune system and the inflammatory response in the course of tumorigenesis and development, some scholars believe that early enteral nutrition can improve a patient’s immune function, reduce the inflammatory response, and thus improve the prognosis of patients with gastrointestinal cancer [9-12]. Therefore, this study explored the effects of early enteral nutrition on immune function and inflammatory factors in cancer patients. This study provided new theoretical foundations and interventional targets for the further improvement of the comprehensive diagnosis and treatment in gastrointestinal cancers.

General information and methods

General information

There were 108 patients with digestive tract cancers who underwent treatment in Linyi People’s Hospital from January 2015 to December 2018 in this prospective, single-center, randomized and double-blind control study. According to each patient’s hospital identification number and with the application of numerical expressions, they were randomly divided into two groups by third-party data managers: the control group (24 patients with gastric cancer and 30 patients with colorectal cancer) and the observation group (28 patients with gastric cancer and 26 patients with colorectal cancer). The patients with gastric and colorectal cancer underwent radical gastrectomies and radical resections of their colorectal cancer (anuses retained), respectively. The patients in the control group received parenteral nutrition while the others in the observation group received early enteral nutrition. Inclusion criteria: patients who also had with cachexia, diabetes, or metabolic dysfunction preoperatively; patients who had cardio-cerebrovascular diseases or hepatorenal dysfunction; patients who received immunosuppression drugs or had preoperative infectious diseases; patients who had a surgical history of their ileocolon or sigmoid. All the patients in this study signed consent forms. This study was approved by the Linyi People’s Hospital medical ethics committee.

Methods

All the patients took oral magnesium sulfate (Zigong Honghe Pharmaceutical Co., Ltd., China) to cleanse their bowels. The postoperative daily energy, nitrogen, calories, and required fluid volume were calculated according to their weight.

Control group: The patients in the control group received parenteral nutrition via deep vein infusion postoperatively. The nutrient solution was composed proportionally of glucose, normal saline, lipid emulsion (Guangzhou Green Cross Pharmaceutical Co., Ltd., China), potassium, and insulin, etc. The administered dose was half of the total amount on the first day and the full amount beginning with the following day.

Observation group: Indwelling gastric tubes were inserted in the patients on the morning of their surgeries. The nasogastric tube was placed in the upper part of the jejunum during the surgery. Dextrose saline solution (5%) was infused intravenously at 10-20 mL per hour after 6-12 hours postoperatively. Enteral nutrition (RuiEnergy, Fresenius Kabir Huarui Pharmaceutical Co., Ltd., China) was infused intravenously via the nasogastric tube two days postoperatively. Starting with the third day, 1000 mL enteral nutrition was infused at the infusion rate of 50-70 mL per hour, while paying attention to the insulation.

Observation indexes

Monitoring of nutritional indexes: The serum nutritional indexes of TFN, Alb and PA in the two groups were recorded and compared before and one week after the treatment. These indexes were mainly monitored by the fully-automatic biochemical detector (Beckman Coulter, USA) in the clinical laboratory of Linyi People’s Hospital.
Immune function and intestinal function damage indexes: The CD4+/CD8+ ratio was used to evaluate the changes in immune function before and after treatment. Peripheral venous blood was collected, and the immune function was monitored with flow cytometry (Guangzhou Bianjin Biotechnology Co., Ltd., China). The serum diamine oxidase (DAO) activity was measured using modified spectrophotometry (the serum DAO kit was supplied by Sigma, USA).

Detection of inflammatory factors: Before treatment and on the seventh day after the surgery, approximately 6-8 mL fasting peripheral venous blood was collected into an anticoagulation tube. After the blood samples were centrifuged at 3000 r/min, the supernatant was harvested and stored at -80°C for further determination. The content of IL-6 was determined using an enzyme-linked immunosorbent assay (ELISA) kit, and the CRP was determined using an immunoturbidimetric assay kit according to the kits’ instructions (the enzyme-linked immunosorbent analyzer was purchased from Infinite F50, Tecan Inc., Switzerland; all the kits were purchased from Santa Inc., USA).

Statistical analysis

All the data were collected and analyzed by third-party data managers. The data were analyzed using SPSS 20.0 statistical analysis software. The measurement data were presented as the means ± standard deviations (\( \bar{x} \pm sd \)). Paired t-tests were used to analyze the indexes in the same group before and after the treatment and independent t-tests were used for the comparisons between groups. Chi-square tests were used for the count data comparisons. P<0.05 was considered statistically significant.

Results

Comparison of the baseline information between the two groups

This study showed that there were no significant statistical differences in disease type, age, gender, duration of disease, or clinical TNM staging between the two groups (P>0.05). The two groups were comparable. See Table 1.

Changes in the nutritional indexes after treatment between the two groups

Before treatment, there were no statistical differences in the nutritional indexes between the two groups, including serum TFN, Alb, and PA. The nutritional indexes in both groups were significantly elevated after the treatment (P<0.05), but the indexes in the observation group were significantly higher compared with those in the control group (P<0.05), indicating that early enteral nutrition could improve the postoperative recovery of nutritional status in patients with digestive tract cancers. See Table 2.

Comparison of the immune function between the two groups before and after treatment

After the treatment, the immune index CD4+/CD8+ ratio in both groups was higher than it was before treatment, and the CD4+/CD8+ ratio in the observation group was higher than it was in the control group, indicating that enteral nutrition can improve the postoperative recovery of immune function in patients with digestive tract cancers. See Figure 1.

Comparison of the inflammatory indexes in the two groups before and after treatment

This study showed that there was no statistical difference in the inflammatory indexes, including CRP and IL-6, between the two groups.
Early enteral nutrition in patients with digestive tract cancers

Table 2. Comparison of the nutritional indexes in the two groups before and after treatment

<table>
<thead>
<tr>
<th>Group</th>
<th>Observation group</th>
<th>Control group</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>1.19±0.33</td>
<td>1.24±0.27</td>
<td>0.862</td>
<td>0.391</td>
</tr>
<tr>
<td>After treatment</td>
<td>1.70±0.65</td>
<td>2.01±0.61</td>
<td>2.556</td>
<td>0.012</td>
</tr>
<tr>
<td>Alb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>25.96±2.64</td>
<td>26.11±2.71</td>
<td>0.291</td>
<td>0.771</td>
</tr>
<tr>
<td>After treatment</td>
<td>31.45±3.01</td>
<td>38.23±4.18</td>
<td>9.672</td>
<td>0.000</td>
</tr>
<tr>
<td>PA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>0.15±0.03</td>
<td>0.16±0.04</td>
<td>1.470</td>
<td>0.145</td>
</tr>
<tr>
<td>After treatment</td>
<td>0.18±0.07</td>
<td>0.22±0.05</td>
<td>3.417</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, *P<0.05. TFN for Transferrin; Alb for Albumin; PA for Prealbumin.

Comparison of intestinal food-intake time, inpatient time, and the incidence of gastrointestinal complications in the two groups

The intestinal food-intake times and hospital stays in the observation group were less than those in the control group, indicating that enteral nutrition can promote postoperative recovery. In addition, there was no statistical difference in the incidence of gastrointestinal complications (nausea, vomiting, abdominal distension, constipation, etc.) between the two groups (4/54 vs 7/54, χ²=0.405, P=0.525), indicating that early enteral nutrition didn’t increase the patients’ gastrointestinal side effects, which was relatively safe and reliable. See Table 4.

Discussion

Digestive tract cancers are major diseases that jeopardize public health with a high incidence (40.75%) and mortality (9.29%) in China [13]. Surgical resection of digestive tract cancer is the main and effective treatment currently. Therefore, it is of importance to improve the perioperative recovery effect of the patients with digestive tract cancers. The patients are prone to malnutrition postoperatively due to various factors. Hence, nutritional support is also a necessary postoperative treatment measure for patients [14]. Moreover, postoperative nutrition has a great acceleration effect on patient recovery [15].

At present, the indexes used to evaluate postoperative nutritional status mainly include serum TFN, Alb and PA. A decrease in the above indexes indicates that the patient’s nutritional status is poor. Therefore, the nutritional indexes can serve as an indicator to reflect the postoperative recovery of nutritional status. Enteral nutrition containing essential fatty acids cannot only provide nutrients for the patients, but it also can improve their immune status. Ultimately, the nutritional status is comprehensive-ly improved. Our study found that the nutritional indexes in the observation group were better than those in the control group. Previous studies also showed that in the first week postoperatively, enteral nutrition increased the serum

Figure 1. Changes in the CD4+/CD8+ ratios in the two groups before and after treatment. Compared with the CD4+/CD8+ ratio before treatment, ***P<0.001. Compared with the control group, #P<0.05.
Early enteral nutrition in patients with digestive tract cancers

TFN, Alb and PA at different degrees in patients with digestive tract cancers [16, 17], which is consistent with our results.

In addition, early enteral nutrition can also improve a patient’s immune function and reduce inflammation. The main clinical manifestation for immunodeficiency is T-cell dysfunction, which mainly means that the CD4+/CD8+ ratio decreases. The increased inflammatory factor levels indicate the status of the inflammatory response. These two indicators have been confirmed to be involved in the occurrence and development of cancer. Therefore, postoperative intervention in the recovery of immune function and a reduction of the inflammation response will have a positive effect on a patient’s prognosis. Early enteral nutrition provides adequate nutrition to patients, it actively improves the function of B lymphocyte, and increases the CD4+/CD8+ ratio to improve a patient’s immune function. Our study also proved that the immune function in the observation group was better than it was in the control group, which corroborated the previous theory that immunity can be improved by early enteral nutrition [18].

The inflammatory response promotes tumor regeneration or metastasis by stimulating the growth of the tumor and changing the local microenvironment of the body. Enteral nutrition containing proteins can antagonize the metabolism of arachidonic acid and effectively control the activity of phospholipase, so as to reduce the release of any inflammatory factors. In this study, our results also indicated that the inflammatory factors can be reduced by early enteral nutrition. Previous studies have also confirmed that postoperative digestive tract enteral nutrition can reduce the inflammatory response as well as the secretion of inflammatory factors to some extent [19, 20].

DAO keeps low activity in a natural state and mainly expresses on the upper villus of the small intestine mucosa. Once the intestinal mucosa is injured, its activity increases. Therefore, the changes in DAO activity can accurately reflect the changes of the intestinal mucosal function [21, 22]. The results of our study showed that there was no difference in the serum DAO activity between the two groups before treatment. The intestinal function in both groups partially recovered after treatment, but the DAO activity in the observation group was lower, indicating that enteral nutrition can further promote the recovery of intestinal function. Moreover, in our study, the food-intake and hospital stays in the observation group were less than those of the control group, which further confirms that enteral nutrition can promote the recovery of intestinal function after intestinal surgery. Previous studies have also showed the same findings that enteral nutrition can reduce DAO activity and promote patient recovery [23].

Currently, the main potential controversy for the implementation of enteral nutrition is its effect on gastrointestinal function. The results in our study indicated that early enteral nutrition didn’t affect gastrointestinal function; conversely, enteral nutrition can protect the gastro-

### Table 3. Comparison of the serum DAO activity in two groups before and after treatment

<table>
<thead>
<tr>
<th>Group</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>3.68±0.51</td>
<td>2.01±0.43*</td>
</tr>
<tr>
<td>Control group</td>
<td>3.57±0.49</td>
<td>2.72±0.38*</td>
</tr>
<tr>
<td>t</td>
<td>1.143</td>
<td>9.092</td>
</tr>
<tr>
<td>P</td>
<td>0.256</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Note: compared with the DAO activity before treatment, *P<0.05. DAO for Diamine oxidase.

### Figure 2. Comparison of the C-reactive protein and IL-6 in the two groups before and after treatment. (A) for C-reactive protein; (B) for interleukin-6. Compared with before treatment, *P<0.05. Compared with the control group, #P<0.05.
intestinal mucosa and prevent the ectopic implantation of intestinal bacterial by stimulating intestinal peristalsis. Other scholars have reached the same conclusion [24]. However, this study was a single-center study which recruited a limited number of participants, so the results need to be further confirmed by a multi-center joint study with a larger cohort. In addition, patients’ long-term prognoses and comparisons of more perioperative indexes should also be further studied.

In conclusion, providing early enteral nutrition for patients with digestive tract cancers post-operatively can positively improve their nutritional status, promote the recovery of immune function, and reduce the inflammatory response without affecting gastrointestinal function.

Disclosure of conflict of interest

None.

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Early enteral nutrition in patients with digestive tract cancers


