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Accelerated rehabilitation combined with enteral nutrition in the management of lung cancer surgery patients

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Running title: The importance of nutrition in surgery rehabilitation

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ABSTRACT

Background and Objectives: To investigate the effect of accelerated rehabilitation combined with enteral nutrition on surgically treated lung cancer patients. **Methods and Study Design:** In total, 150 lung cancer patients treated in our hospital from January 2017 to January 2018 were retrospectively analysed. Sixty-six patients were randomly divided into a control group with conventional nutrition (Con group) and an accelerated rehabilitation combined with enteral nutrition group (EN group). Postoperative drainage; total hospitalization time; total hospitalization expenses; and albumin, haemoglobin and total lymphocyte counts (TLC) before and after treatment were compared. **Results:** The serum albumin, prealbumin and haemoglobin in both groups were decreased after operation and were significantly higher in the EN group ($p<0.05$) than in the Con group. The TLC decreased in both groups after operation and were significantly higher in the EN group than in the con group. The postoperative drainage volume, total hospitalization time and total hospitalization expenses were significantly lower in the EN group than in the Con group ($p<0.05$). **Conclusions:** The effect of accelerated rehabilitation combined with enteral nutrition in lung cancer surgery patients is clear. Surgery leads to stress, which enhances catabolism and reduces the synthesis of carbohydrates, protein, and fat, increasing patients' nutritional risk. Nutritional support combined with fast-track minimally invasive thoracic surgery for at-risk lung cancer patients who undergo preoperative nutritional screening and assessment can reduce postoperative complications and hospitalization time and improve nutritional indicators, immunity, respiratory function recovery and clinical outcomes, leading to socioeconomic benefits.

Key Words: enteral nutrition, rapid rehabilitation surgery, lung cancer, nutritional risk, social and economic benefits

INTRODUCTION

In recent years, the incidence and mortality of lung cancer have been increasing. According to the "Current Situation and Trends of Cancer in China" published by the National Cancer Centre in 2017, the incidence of lung cancer in China ranks first among males, whereas the incidence ranks second among women; however, the mortality due to lung cancer ranks first among all cancers in both men and women in China.¹ At present, the main treatment for lung cancer is surgery, and with the development of minimally invasive endoscopic treatment technology, thoracoscopic lobectomy is increasingly being used in the surgical treatment of early lung cancer and pulmonary nodules.² However, thoracotomy remains the main treatment

choice for pulmonary malignant tumours.³ Our previous study found that thoracotomy generates a large amount of trauma and can cause various complications, including a high nutritional risk after the operation, with a poor prognosis.⁴⁻⁶ Accelerated rehabilitation and enteral nutrition is a new perioperative multidisciplinary treatment developed on the basis of medical evidence that not only reduces the stress and trauma experienced by the patient but also ensures the nutritional supply needed to maintain the state of hypermetabolism during trauma, thus achieving the goal of rapid recovery.^{7,8} In this study, we retrospectively analysed the effect of accelerated rehabilitation combined with enteral nutrition in the treatment of lung cancer patients in our hospital from January 2017 to January 2018 to provide a basis for better clinical nutrition in the future.

MATERIALS AND METHODS

This study was based on the project "Single-hole sleeve and open chest sleeve pneumonectomy for the treatment of central lung cancer", with ethical approval number "K18-119".

Data collection

A total of 150 patients with lung cancer treated at Shanghai Pulmonary Hospital from January 2017 to January 2018 were included. After the application of strict inclusion and exclusion criteria, the patients were randomly divided into two groups by the double-blind method: the control group (Con group) with conventional nutrition and the accelerated rehabilitation combined with enteral nutrition group (EN group). Each group comprised 33 cases, and there were no significant differences in baseline sex, age, tumour stage or operation mode between the two groups ($p>0.05$). There was comparability between the two groups, as shown in Table 1.

Inclusion criteria

No patients underwent radiotherapy or chemotherapy before surgery. According to the 1998 International Anti-Cancer Alliance and American Cancer Federation lung cancer pathological staging criteria, all patients had stage I to III surgically resectable lung cancer.

Exclusion criteria

The exclusion criteria were as follows: age ≥ 65 years; severe metabolic and systemic diseases, such as diabetes, hypertension, or severe liver and kidney dysfunction; and preoperative Nutritional Risk Screening 2002 (NRS-2002) score >5 points.

Nutritional support

The Con group and EN group received accelerated rehabilitation measures, except for preoperative nutrition. References were made to the consensus of experts for the perioperative period of accelerated rehabilitation surgery according to the American Society for Parenteral and Enteral Nutrition (ASPEN) and European Society for Parenteral and Enteral Nutrition (ESPEN).^{4,5} In terms of the preoperative nutrition preparation, patients in the Con group were provided routine nutrition, including preoperative nutritional risk screening and assessment and preoperative nutrition education and dietary guidance, while patients in the EN group were provided additional enteral nutrition preparations combined with accelerated rehabilitation as in the control group. The main methods were (1) health education. After hospitalization, patients were given health education for diseases according to their educational level, and a risk assessment was made according to their physical condition, medical history and nutritional status to ensure that patients fully understood their own physical condition, thereby improving the success rate of surgery. (2) Preoperative preparation. The Con group was deprived of water six hours before surgery, while the EN group was given 1000 mL of 10% glucose solution (20:00) one night before the surgery and then 200 mL of 10% glucose solution 2 hours before surgery. (3) Postoperative nutritional intervention. The Con group sat up one day after the operation and were fed a semi-liquid diet, eventually transitioning to a normal diet three days after the operation. The patients were encouraged to eat and given dietary guidance. In the EN group, sitting up was encouraged, and 200 mL of 5% glucose solution was given in the evening the same day of the operation. One day after the operation, patients were instructed to eat normally and increase bed activity to assist with sputum expectoration. Those without cardiopulmonary insufficiency got out of bed. Three days after the operation, 400 mL of enteral nutrition was given orally based on a normal diet.

Statistical analysis

The total hospital stay, postoperative drainage, and total hospitalization expenses were compared between the two groups. The serum albumin, prealbumin, and haemoglobin and

total lymphocyte counts (TLCs) were measured before and after treatment. All results are expressed as the mean \pm SD. The statistical analysis was carried out using SPSS 21.0 (Chicago, USA). Two-way ANOVA, t-tests and Dunnett t-tests were used to determine whether differences were statistically significant among or between groups. A p value less than 0.05 was considered statistically significant.

RESULTS

Comparison of the changes in nutrition-related indicators before and after operation in the two groups

Compared to before surgical intervention (preoperative), we found that serum albumin, prealbumin and haemoglobin decreased significantly in both groups, and the difference was statistically significant ($p<0.05$), as shown in Figure 1.

Comparison of the changes in nutrition-related indicators between the two groups after operation

However, the serum albumin, prealbumin and haemoglobin in the EN group after surgical intervention (postoperative) were slightly better than those in the postoperative Con group, with statistically significant differences ($p<0.05$), as shown in Table 2.

Comparison of postoperative drainage, total hospitalization stay and expenses between the two groups

The postoperative drainage, total hospitalization stay and expenses in the EN group were lower than those in the Con group, and the differences were statistically significant ($p<0.05$), as shown in Figure 2.

DISCUSSION

In 2008, the incidences of malnutrition (insufficiency) and nutritional risk in first-class hospitals in the eastern, central and western cities of China were 12% and 35.2%, respectively.^{1,9} The incidences of malnutrition and nutritional risk in thoracic surgery patients were the highest in clinical departments.¹⁰ In thoracic surgery, the nutritional risk of patients after thoracotomy is mainly related to surgical stress. Changes in the body's internal environment induced by surgical stress can lead to glucose, protein, and fat metabolism disorders, especially due to the reverse regulation of hormones, which causes these three major nutrients to be in a state of high catabolism and reduced synthesis.⁷ The core of the

concept of accelerated rehabilitation surgery combined with enteral nutrition is to reduce the surgical stress response by strengthening psychological counselling before and after surgery, improving anaesthesia, administering unconventional bowel preparation, paying attention to intraoperative heat preservation, reducing water and sodium retention, implementing early extubation and promoting early out-of-bed activities.¹¹ Mechanical bowel preparation is not only a stressor but also leads to dehydration and electrolyte imbalance, especially in elderly patients. Studies have found that bowel preparation has no benefit to patients undergoing colon surgery and may increase the risk of postoperative anastomotic leakage.⁸ Therefore, in the concept of accelerated rehabilitation surgery, preoperative fasting is no longer required, and patients are encouraged to consume oral sugar-containing liquids before surgery.¹² In this study, the patients in the EN group were allowed to ingest clear fluids 2 hours before the start of anaesthesia, drinking 800 mL of 12.5% carbohydrate liquid one day before surgery and 400 mL 2 to 3 hours before surgery. The results showed that although the serum albumin, haemoglobin and prealbumin in the EN group with unconventional bowel preparation also decreased to some extent after surgery, the decrease was significantly lower than that in the Con group. Clinically, serum albumin, prealbumin and haemoglobin are commonly used as indicators for evaluating the nutritional status of humans with regard to protein. Prealbumin is a plasma transport protein located in front of albumin during plasma protein electrophoresis and has dual functions in transporting thyroxine and vitamin A. It is synthesized in the liver and has a short half-life (1.9 days). Its renewal rate is fast, with its *in vivo* conversion rate reaching up to 36.6% per day. It can be rapidly reduced in the case of reduced protein intake and protein-energy deficiency. It was found that serum prealbumin changes prior to body mass, subcutaneous fat and other anthropometric indicator changes, reflecting early and subclinical nutritional deficiencies in the body.¹³ In this study, the concentrations of albumin, prealbumin and haemoglobin in the EN group were higher than those in the Con group, indicating that accelerated rehabilitation combined with enteral nutrition could improve the nutritional status of postoperative patients. The reason may be that the combination of the two can quickly restore the patient's physical strength and intestinal peristalsis, ensuring the absorption of food and promoting improvements in patient nutrition. TLC can be used to monitor the patient's immune function status, with elevated trends indicating that the patient's immune function has improved.¹⁴ In this study, the immune function of patients in the EN group was improved. In addition, the postoperative drainage, hospitalization time, and total hospitalization cost were significantly lower in the EN group than in the Con group. The difference was statistically significant, indicating that accelerated rehabilitation combined

with enteral nutrition can reduce the surgical stress state of postoperative patients, prevent and correct malnutrition in patients and enhance their tolerance to surgical trauma. In addition, it can shorten the length of hospital stay and the total cost of hospitalization and promote the early recovery of patients. This may be related to the fact that accelerated rehabilitation combined with enteral nutrition can enhance the immune function of patients.

Nutritional support therapy refers to supplementation through the enteral or parenteral route in cases of insufficient or inadequate diet, providing patients with a comprehensive set and sufficient amount of nutrients needed by the body to prevent and correct malnutrition, thereby enhancing the patient's tolerance to surgical trauma and promoting the patient's early recovery.^{8,15-17} The concept of accelerating rehabilitation is to promote using a carbohydrate-rich isotonic solution preoperatively, early out-of-bed activities for patients if the condition allowed after surgery and early starting up enteral nutrition. The underlying mechanism of this action are maintaining nitrogen balance, reducing insulin resistance and promoting intestinal peristalsis and maintaining the integrity of intestinal mucosal structure and function, which is beneficial to the recovery of gastrointestinal function thereby.

Immunosuppression is common in tumor patients. The immune function of lung cancer patients will also be restrained due to the dysfunction of nutritional absorption and other issues. The stress response caused by surgery will further exacerbate the suppression of immune function in patients, which will be susceptible to the occurrence of infection and affect the patient's clinical outcomes. Early enteral nutrition can promote the recovery of gastrointestinal function of patients faster, maintain the immune function of the body meanwhile, and improve the nutritional status of the body quicker and more effectively, which can provide the basis for systematic anti-tumor treatment.¹⁴ It is a safer and more effective nutrition support method.

In conclusion, the implementation of accelerating rehabilitation programs using a set of perioperative measures combined with enteral nutrition which are effective produces a synergistic action to reduce postoperative morbidity and length of hospital stay. The application of nutritional management is simple and should be audited to improve the adherence and effectiveness of the programs. Proper nutritional support should be based on a complete understanding of the metabolic changes that occur under various conditions the body is subjected to, the correct evaluation of the nutritional status, the selection of a reasonable nutritional support route, the provision of appropriate nutritional substrates, and the prevention of or reduction in complications as much as possible.^{18,19}

AUTHOR DISCLOSURE

The authors declare they have no conflicts of interest. This study received no external funding.

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Table 1. Comparison of preoperative general data between the two groups

	Control (N:33)	EN (N:33)	t/ χ^2	<i>p</i>
Sex (N)				
Man	27	26		
Woman	6	7	0	0.99
Age				
Mean	56.5	55.4		
SD	6.54	8.56	0.60	0.54
Staging (N)				
I	10	8		
II	13	12	0.65	0.72
III	10	13		
Operation methods (N)				
One Lobe	12	10		
Double Lobe	11	12	0.27	0.87
Whole Lobe	10	11		
Serum albumin (g/L)				
Mean	39.4	41.3		
SD	3.54	3.27	1.92	0.06
Serum prealbumin (g/L)				
Mean	237	270		
SD	72.6	45.5	1.88	0.06
Hemoglobin (g/L)				
Mean	133	136		
SD	16.5	16.5	0.58	0.56
TLC (10 ⁹ /L)				
Mean	1.76	1.93		
SD	0.50	0.54	1.01	0.31

Table 2. Comparison of indicators after surgery between the two groups

	Control (N:33)	EN (N:33)	t	<i>p</i>
Serum albumin (g/L)	32.3	37.1*		
Mean				
SD	2.22	1.79	9.30	<0.001
Serum prealbumin (g/L)				
Mean	163	204*		
SD	70.6	52.7	2.60	0.01
Hemoglobin (g/L)				
Mean	111	121*		
SD	17.4	13.5	2.50	0.01
TLC (10 ⁹ /L)				
Mean	1.20	1.49*		
SD	0.52	0.46	2.37	0.02

*Represents that the difference is statistical significance compared to the Con group, $p < 0.05$.

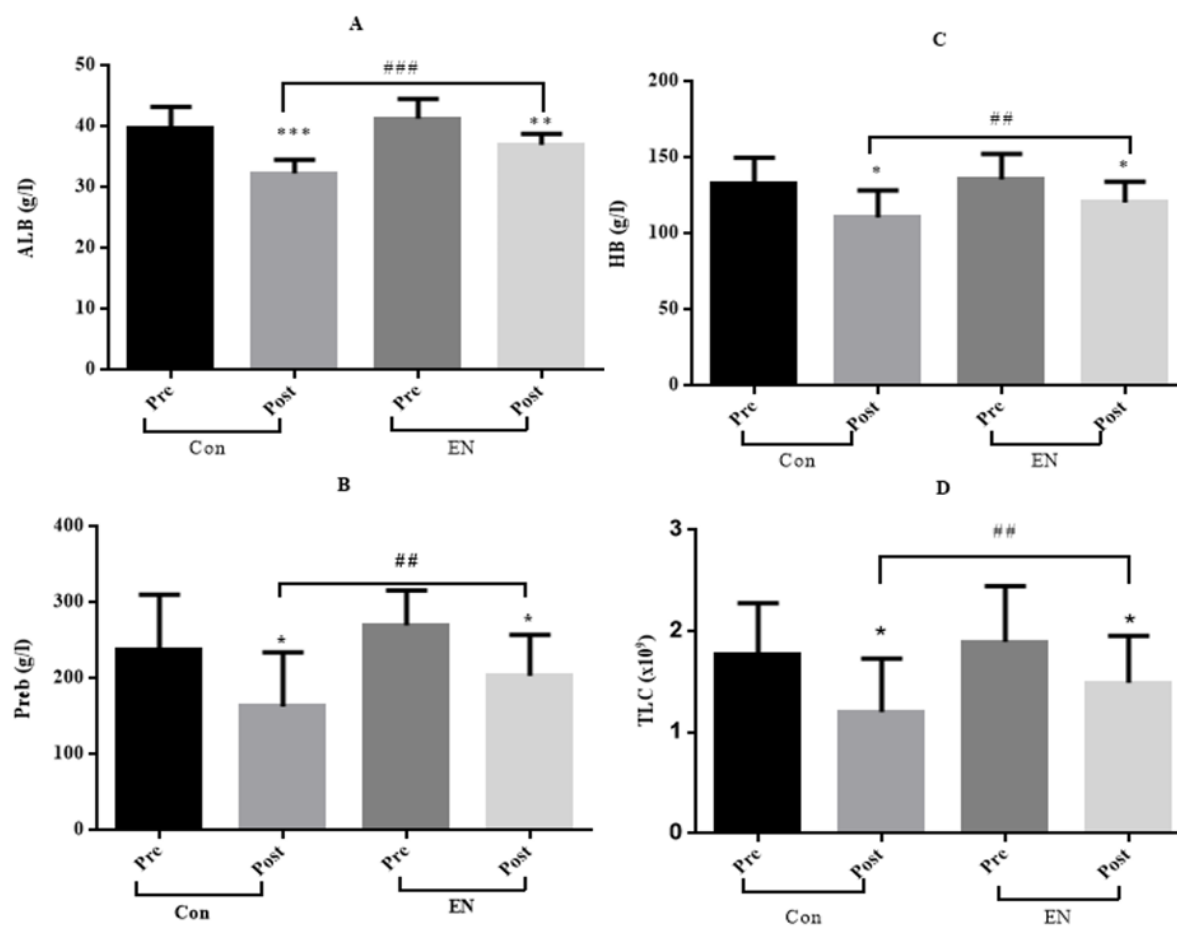


Figure 1. Comparison of serum albumin, prealbumin, haemoglobin and TLC between preoperative and postoperative patients in the Con and EN groups. Values are represented as the mean \pm SD (n=33 per group). *** represents $p < 0.001$ vs pre control, * represents $p < 0.05$; ### represents $p < 0.001$ vs post control, ## represents $p < 0.01$, # represents $p < 0.05$.

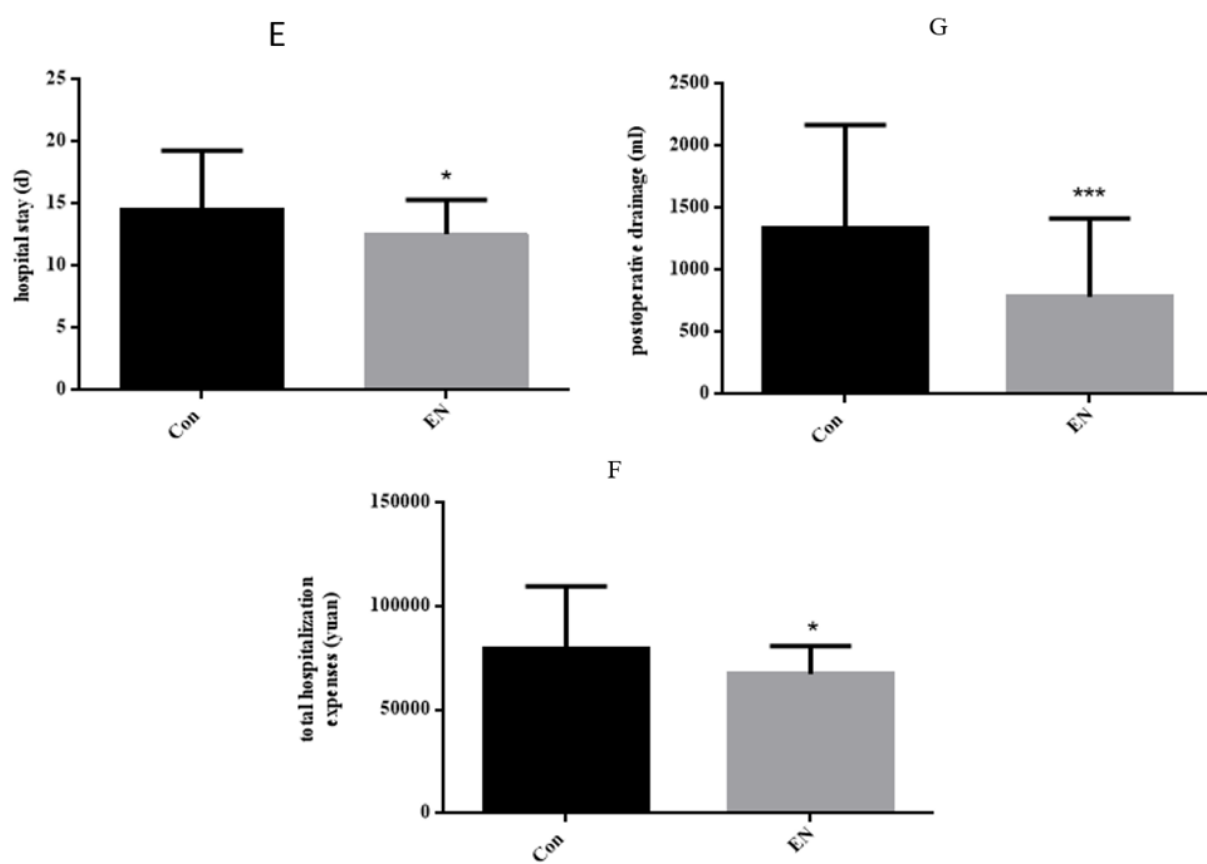


Figure 2. Comparison of the hospital stay (d), total hospitalization expenses (yuan) and postoperative drainage (mL) between the Con and EN groups. *** represents $p < 0.001$, * represents $p < 0.05$.