Role of nutritional support for postoperative recovery of respiratory function in patients with primary lung cancer

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Abstract. This study explored the role of nutritional support for postoperative recovery of respiratory function in patients with primary lung cancer. Clinical data of 182 patients with primary lung cancer who were admitted to Weifang People's Hospital from January 2013 to December 2015 and underwent lung cancer surgery, were collected and retrospectively analyzed. According to the postoperative diet plan, patients were divided into two groups: General diet group (n=80) and nutrition therapy group (n=102). Patients in the general diet group were given a general diet without any nutritional instruction, whereas the patients in the nutrition therapy group were given an enteral nutritional supplement in addition to a general diet. The changes of nutritional indices, recovery status of respiratory function and incidence of adverse events for patients in the two groups were observed, and the data were analyzed statistically. At day 14 after the therapy started, the body mass index, mid-arm circumference and triceps skinfold of patients in the nutrition therapy group were significantly better than those in the general diet group ($P<0.05$). More significant improvements in levels of hemoglobin, serum albumin and prealbumin were observed in the nutrition therapy group, and the differences in comparison with levels in the general diet group were statistically significant ($P<0.05$). The respiratory function was more significantly improved for patients in the nutrition therapy group as well, compared to patients in the general diet group ($P<0.05$). At the end of 1-year follow-up, incidences of malnutrition, lung infection and mortality in the nutrition therapy group were lower than that of the general diet group ($P<0.05$). The positive impact of appropriate nutritional support on recovery of postoperative respiratory function improved overall outcomes of patients with lung cancer and reduced mortality as well. The nutrition therapy is worth further clinical study.

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Introduction

Lung cancer is one of the common cancers in China as well as in the world with a high incidence (1,2). According to statistical data published in 2016, the number of newly added patients with lung cancer in China was about 740,000 per year (3). Based on the 2015 version of Chinese guidelines on the diagnosis and treatment of primary lung cancer, the incidence of lung cancer was about 35/100,000, and the mortality rate was about 28/100,000. In the same time period, the number of deaths due to lung cancer was about 486,600, accounting for 24.87% of the total deaths caused by malignant tumors (4,5). The guidelines also clearly stated that surgery was a preferred treatment of early lung cancer, which can effectively improve patient outcomes following treatment (6). However, postoperative respiratory dysfunction often led to complications of respiratory infection and hypoxemia. In addition, declined nutritional indices and low immunity were observed following surgery, which may affect prognosis of the patients and subsequent quality of life, leading to higher mortality (7).

In recent years, increasing number of studies on nutritional support therapy were reported for cancer patients, which showed that good nutritional status was beneficial in reducing incidence of complications and improving survival. Nutritional support can maintain a stable respiratory muscle function (8). Currently a general diet is commonly provided in clinic to patients with early lung cancer following surgery. However, early nutritional support therapy can effectively protect the function of gastrointestinal mucosa and improve nutrient absorption, therefore overall improving the nutritional status and immunity of patients (9). Patients with lung cancer tended to experience malnutrition following treatment due to surgical trauma, resulting in respiratory dysfunction. In this study, roles of nutritional support therapy were explored for postoperative recovery of respiratory function in patients with primary lung cancer.

Patients and methods

Subjects. Clinical data of 182 patients with primary bronchogenic carcinoma admitted in Weifang People's Hospital (Weifang, China) from January 2013 to December 2015 were retrospectively analyzed. There were 104 males and 78 females, aged 42-72 years. According to the postoperative diet plan, patients were divided into two groups: General

Table I. General clinical data of patients in the two groups.

Items	Groups		t/x^2 value	P-value
	General diet	Nutrition therapy		
Cases (n)	80	102	0.218	0.828
Sex				
Male	52	67	0.506	0.614
Female	28	35		
Age (years)	60.32±5.13	61.08±4.45	0.004	1.000
Smoking status				
Yes	54	68	0.382	0.945
No	26	34		
Body weight (kg)	55.32±6.42	54.09±6.17	0.152	0.873
Disease course, month	5.92±2.12	6.09±2.37	0.252	0.871
Clinical stage				
II	15	21	0.635	0.713
III	37	46		
VI	28	35		

Table II. General nutritional indices of patients in the two groups.

Items	Groups		t value	P-value
	General diet	Nutrition therapy		
Cases (n)	80	102		
Before surgery				
BMI (kg/m^2)	24.32±4.85	23.94±5.07	0.482	0.805
MAC (mm)	22.35±1.83	21.98±2.04	0.295	0.736
TSF (mm)	11.28±4.07	11.87±4.46	0.724	0.217
Day 14 after surgery				
BMI (kg/m^2)	21.32±4.85	22.63±4.87	2.653	0.010
MAC (mm)	20.32±4.85	20.42±1.87	3.292	0.002
TSF (mm)	10.02±3.95	11.06±4.23	3.041	0.012

BMI, body mass index; MAC, mid-arm circumference; TSF, triceps skinfold.

diet and nutrition therapy group. In the general diet group, there were 48 males and 32 females, with an average age of 60.32±5.13 years and a weight of 55.32±6.42 kg. In the nutrition therapy group, there were 56 males and 46 females, with an average age of 61.08±4.45 years and a weight of 54.09±6.17 kg. There was no statistical difference in any item of the basic clinical data between the two groups (P>0.05) (Table I).

Inclusion and exclusion criteria. Patients who met the following criteria were included in this study: i) Patients who were confirmed to have primary lung cancer and underwent surgical treatment; ii) patients who did not receive any lung cancer related radiotherapy, chemotherapy and surgery prior to current surgical treatment; and iii) patients who did not have serious gastrointestinal diseases, blood system diseases and metabolic diseases prior to current surgery. Patients who fell in the following criteria were excluded from this study: i) Patients who were younger than 14 years and older than 75 years; ii) patients who had other malignant tumors at the same time; iii) patients whose vital signs were not stable and patients who had other serious combined diseases of heart, lung, liver and kidney. This study was approved by the Ethics Committee of Weifang People's Hospital (Weifang, China), and all patients or their family signed the informed consent.

Treatment methods. Following surgery, patients in the general diet group were administered with conventional medicines and provided with a general diet. A general diet was routine meals that were prepared by the patient's family according to the patient's daily diet, including three meals a day without diet guidance. Patients in the nutrition therapy group were administered with the same conventional medicines and provided with not only a general diet but also an enteral nutritional supplement. Enteral nutritional suspensions manufactured by Danone Nutricia Early Life Nutrition (Schiphol, The Netherlands) were chosen as the enteral nutritional supplement. The enteral nutritional supplement was kept at 35-42˚C before being taken, and was given by mouth a few times at a daily dose of 25 kcal/kg. The entire nutrition therapy lasted for 14 days.

Observed indicators. Before surgery and at day 14 after surgery, patients' general nutritional indices including body mass index (BMI), mid-arm circumference (MAC) and triceps skinfold (TSF), as well as hematological indicators of nutritional status including hemoglobin (Hb), serum albumin (ALB) and prealbumin (PA), were measured. Variations of lung functional indicators in 14 days after surgery, including incidences of cough with or without sputum, lung infection and hypoxemia, were statistically analyzed. Patients were followed up for one year after surgery, and at the end of follow-up incidences of malnutrition, lung infection and mortality were obtained. Hypoxemia was defined as an arterial partial pressure of oxygen (PaO_2) of <60 mmHg or a blood oxygen saturation level (SpO_2) of <90%. Malnutrition was defined as a low serum ALB level of <35 g/l or total protein (TP) level of <60 g/l or Hb level of <110 g/l. Lung infection was defined as existence of clear lung infection lesions confirmed by lung imaging.

Statistical analysis. The SPSS 22.0 software (IBM Corp., Armonk, NY, USA) was used to analyze the experimental data. Measurement data were expressed as mean ± standard deviation (SD). The t-test was used in data comparison, and Chi-square analysis was applied in rate comparison. P<0.05 was considered to indicate a statistically significant difference.

Results

General nutritional indices of patients in the two groups. Before surgery, there were no significant differences in general nutritional indices between patients in the two groups (P>0.05). However, at day 14 after surgery, differences in BMI,

Table III. Hematological indicators of nutritional status of patients in the two groups.

Items	Groups		t value	P-value
	General diet	Nutrition therapy		
Cases (n)	80	102		
Before surgery				
Hb (g/l)	122.87±8.46	124.26±7.34	0.352	0.728
ALB (g/l)	36.4±2.72	35.3±2.84	1.691	0.925
PA (mg/l)	165.4±15.9	163.8±14.4	0.984	0.817
Day 14 after surgery				
Hb (g/l)	110.76±9.53	118.87±8.46	3.759	0.012
ALB (g/l)	31.6±3.06	33.7±2.65	2.472	0.024
PA (mg/l)	170.4±14.8	168.4±16.2	3.108	0.042

Hb, hemoglobin; ALB, albumin; PA, prealbumin.

Table IV. Respiratory functional indicators in 14 days after surgery.

Items	Groups		χ^2	P-value
	General diet	Nutrition therapy		
Cases (n)	80	102		
Incidence of adverse events, n (%)				
Cough with/without sputum	42 (52.50)	38 (37.25)	14.235	0.005
Lung infection	27 (33.75)	18 (17.64)	7.824	0.032
Hypoxemia	18 (22.50)	11 (10.78)	10.937	0.018

MAC and TSF were statistically significant. The BMI, MAC and TSF in the nutrition therapy group were all higher than those in the general diet group (P<0.05) (Table II).

Hematological indicators of nutritional status of patients in the two groups. Before surgery, there were no significant difference in hematological indicators of nutritional status between patients in the two groups (P>0.05). However, at day 14 after surgery, the nutrition therapy group got higher levels of Hb and ALB and lower level of PA compared with those in the general diet group (P<0.05) (Table III).

Respiratory functional indicators in 14 days after surgery. Incidence of cough with/without sputum, lung infection and hypoxemia in the general diet group were all higher than those in the nutrition therapy group. The differences were statistically significant (P<0.05) (Table IV).

Patient outcomes at the end of 1-year follow-up. At the end of 1-year follow-up, incidences of malnutrition, lung infection and mortality in the general diet group were significantly higher than those in the nutrition therapy group. The differences were statistically significant (P<0.05) (Table V).

Table V. Patient outcome at the end of 1-year follow-up.

Items	Groups		χ^2	P-value
	General diet	Nutrition therapy		
Cases (n)	80	102		
Incidence of lung infection, n (%)	19 (23.75)	12 (11.76)	12.136	0.014
Incidence of malnutrition, n (%)	12 (15.00)	8 (7.84)	8.625	0.037
Incidence of mortality, n (%)	3 (3.75)	2 (1.96)	9.912	0.024

Discussion

The incidence of primary bronchogenic carcinoma has gradually increased in recent years (10). Statistics show that malnutrition accompanies most cancer patients. For patients with lung cancer, the surgery can inflict severe harm to patient's normal physiological functions, making malnutrition even more serious (11). In clinical guidelines for nutrition support enacted by the American Society for Parenteral and Enteral Nutrition (ASPEN) or European Society for Parenteral and Enteral Nutrition (ESPEN), the importance of nutrition therapy for cancer patients, especially those after surgery, was highlighted (12). This was the rationale of current study to be focused on postoperative nutrition therapy in patients with lung cancer.

Nutritional support therapy includes enteral nutrition therapy and parenteral nutrition therapy (13). In the present study, the role of enteral nutrition therapy was explored for postoperative recovery and compared with the baseline of a general diet. This will not only reflect the value of nutritional support therapy in general, but also provide reliable data support for choosing appropriate nutritional support therapy in clinic. At the end of 1-year follow-up, the incidence of lung infection, malnutrition and mortality were selected as the observed indicators to reflect the outcomes. The outcomes at the end of 1-year follow-up can be used to evaluate the long-term effect of nutritional support therapy.

The preoperative data showed that there were no significant differences in the general nutritional indices (BMI, MAC and TSP) and hematological indicators of nutritional status (Hb, ALB and PA) for all enrolled patients. However, at day 14 after surgery, all the observed general nutritional indices and hematological indicators of nutritional status were lower in the general diet group than those in the nutrition therapy group. In the same time period, incidence of cough with/without sputum, lung infection and hypoxemia were higher in the general diet group. Aufaure and Grigoroiu reported that early enteral nutritional support therapy can significantly reduce incidence of lung infection (14). Wang *et al* found that cancer surgery can inflict

serious trauma to the body of a cancer patient. Postoperative stress response triggered by the surgery can lead to gastrointestinal dysfunction. This included poor appetite resulted from postoperative pain and discomfort. Therefore, patients may experience postoperative nutritional imbalance and a calorie deficit if a general diet was provided without nutritional guidance (15). For patients undergoing lung cancer surgery, a general diet cannot provide enough nutrients and, moreover, it may lead to malnutrition. In addition, patients may experience discomfort such as gastric retention, abdominal distention and constipation (16). In the present study, at the end of 1-year follow-up, the incidence of malnutrition, lung infection and mortality in the general diet group were obviously higher than those in the nutrition therapy group. Aoyama *et al* showed that when a patient was malnourished for a long period of time, the body increased protein consumption from the storage, resulting in reduced protein storage, weakened immunity and increased incidence of complications. Therefore, malnutrition had a negative impact on patient's prognosis and, moreover, increased the risk of death (17). Nutritional support therapy can effectively improve the patient's nutritional status. Early enteral nutritional support therapy can promote the recovery of gastrointestinal absorption and protect the intestinal mucosal cells by maintaining their barrier function. This was directly beneficial to protein absorption and metabolism during the long-term recovery, and overall beneficial to improving the patient's nutritional status (12,16-18).

This is a retrospective study using existing data that were recorded a few years ago. Accurate control of the general diet in both groups was not available back then. Differences in daily diet among patients may lead to biased data. In addition, respiratory function was evaluated using only incidence of lung infection and hypoxemia due to constraints of subject availability, time and area. Lack of a thorough evaluation of respiratory function provided limited data, not allowing for a more accurate statistical analysis.

In recent years, there has been a rising trend in adoption of nutritional support therapy in cancer patient care. In the clinical guidelines for nutrition support enacted in 2009 by ASPEN, it was clearly pointed out that active nutrition therapy can effectively improve the immunity of cancer patients (19,20). Studies have shown that early enteral nutrition support therapy can promote the recovery of digestive system function, allowing sufficient consumption of nutrients that were actively absorbed by gastrointestinal mucosal epithelium (21). In the past, nutrition therapy was often a combination of a general diet and parenteral nutrition. Recent clinical studies on enteral nutrition therapy indicated that early enteral nutrition therapy was more beneficial to patient in overall recovery than parenteral nutrition therapy (22). In our future study plan, more patients will be enrolled, and more nutritional indicators will be observed to monitor the status of respiratory function, aiming to obtain more clinical data to support the adoption of nutrition therapy in the recovery of respiratory function.

In conclusion, the results of this study can be used as a reference to guide clinical practice. Early nutritional support therapy can be beneficial to patients with lung cancer in respiratory function recovery and, moreover, reduce the incidence of related complications by effectively improving the patient's nutritional status. In addition to promoting overall postoperative recovery, nutrition therapy can significantly reduce the cost of postoperative care and improve quality of life.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

JY wrote the manuscript and helped with treatment. QZ and XW analyzed and interpreted patients' general nutritional indices and PaO_2. All authors read and approved the final study.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Weifang People's Hospital (Weifang, China). Patients who participated in this research, signed an informed consent and had complete clinical data. Signed informed consents were obtained from the patients or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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