JBUON 2019; 24(4): 1673-1678
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
Email: editorial_office@jbuon.com

ORIGINAL ARTICLE

Effects of postoperative enteral nutrition combined with adjuvant radiotherapy on inflammatory response, nutrition, healing and prognosis in patients receiving radical surgery for esophageal carcinoma

Rong Yao[1], Tiecheng Zhang[1], Juan Zhang[2], Yuan Sun[1], Lijuan Xu[1], Dahong Zhang[1], Leilei Zhou[1]

[1]Department of Oncology and [2]Department of Gastroenterology, the Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University, Huai'an, China.

Summary

Purpose: *To explore the influence of postoperative enteral nutrition combined with adjuvant radiotherapy on inflammatory response, nutrition, healing and prognosis in patients undergoing radical surgery for esophageal carcinoma.*

Methods: *A total of 114 patients with esophageal carcinoma receiving radical surgery from January 2016 to July 2017 composed the observation group and randomly divided into control group (n=57) and study group (n=57). Patients in the control group were given routine nutritional support after surgery, while those in the study group received enteral nutrition after surgery. The changes in inflammatory response and nutritional level, healing and prognosis in the two groups of patients before and after treatment were compared and analyzed.*

Results: *After treatment, the levels of serum hypersensitive C-reactive protein (hs-CRP) and prostaglandin E (PGE) of patients were decreased in both the control group and study group, and they were lower in the study group than those in the control group, while the levels of serum pro-albumin (PA) and albumin (ALB) of patients in the study group were higher than those in the control group ($p<0.05$). The postoperative wound healing time, total length of hospital stay, postoperative first exhaust time and defecation time in the study group were shorter than those in the control group ($p<0.05$). The total incidence rate of postoperative complications of patients in the study group was lower than that in the control group ($p<0.05$).*

Conclusion: *The application of postoperative enteral nutrition combined with adjuvant radiotherapy in patients subjected to radical surgery for esophageal carcinoma can suppress systemic inflammatory response, improve the nutritional condition, promote postoperative wound healing and improve prognosis and therefore it is worthy of promotion in clinical practice.*

Key words: *radical surgery, esophageal carcinoma, enteral nutrition, radiotherapy, inflammatory response, prognosis*

Introduction

Esophageal carcinoma, a common and highly-prevalent malignant tumor of the digestive tract, is common in middle-aged and elderly populations and has high morbidity and mortality rates. Its clinical manifestations include typical and progressive dysphagia, seriously affecting the quality of daily life of patients [1]. Currently, radical surgery, radiotherapy and chemotherapy are mainly used for the treatment of esophageal carcinoma, which are able to effectively alleviate clinical symptoms.

Corresponding author: Leilei Zhou, MM. Department of Oncology, The Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University, No.6, Beijing West Rd, Huaiyin District, Huai'An, 223300 Jiangsu, China.
Tel: +86 015851726653, Email: bogy2004a@163.com
Received: 14/12/2018; Accepted: 09/01/2019

However, most patients often have malnutrition and weakened immune function after radiotherapy due to insufficient nutrient intake and increased metabolic burden caused by adverse reactions (including nausea and vomiting, esophageal mucositis and radiotherapy injuries) resulting from long-term dysphagia before surgery, trauma caused by surgery, preoperative preparation, postoperative recovery, and specific characteristics of radiotherapy and chemotherapy [2,3]. Therefore, to enhance the nutritional condition and immune function of the patients and improve their postoperative quality of life, providing nutritional support as early as possible is of great significance for patients receiving radiotherapy after radical surgery for esophageal carcinoma, which is the focus of clinical research [4]. With this in mind, the effects of postoperative enteral nutrition combined with adjuvant radiotherapy on the inflammatory response, nutrition, healing of postoperative wound and prognosis were analyzed in this study, providing information for clinical practice.

Methods

General data

A total of 114 patients with esophageal carcinoma who underwent radical surgery in our hospital from January 2016 to July 2017 were enrolled as observation subjects and divided into the control group (n=57) and the study group (n=57) using a random number table. In the control group, there were 33 males and 24 females aged 48-80 years, with a mean of 65.6±4.2 years. As for the histology of esophageal carcinoma, 41 patients had squamous cell carcinoma and 16 had adenocarcinoma. Based on clinical TNM staging, there were 5 cases of stage I carcinoma, 37 cases of stage II and 15 cases of stage III.

In the study group, there were 35 males and 22 females aged 45-78 years, with an average of 64.9±4.5 years. In terms of histology, 44 cases were squamous cell carcinoma and 13 adenocarcinoma. According to clinical TNM staging, 7 cases were stage I carcinoma, 38 stage II and 12 stage III.

Inclusion and exclusion criteria

All enrolled patients should have definite diagnosis of esophageal carcinoma via clinical imaging and operative-pathological examinations [5], and should have no contraindications for radiotherapy, severe cardiac insufficiency and abnormal liver and kidney function. Patients who were unconscious or had mental disorders, hematological disorders, systemic infectious diseases, communicable diseases, autoimmune diseases or other malignant tumors were excluded. The basic clinical data of patients in the two groups were balanced, showed no statistically significant differences ($p>0.05$) and were comparable.

The content of this study was consistent with relevant requirements of hospital ethics, and all patients and their families signed informed consent before study entry.

Radiotherapy

Patients in both groups received adjuvant radiotherapy after surgery, including three-field radiation therapy for thoracic lesions and two-front oblique-field or T-shaped-field radiation therapy for cervical lesions according to the treatment system plan. The radiation exposure range was as follows: from 3 cm above the esophageal lesion to 3 cm below the lesion and surrounding 0.8 cm outward the esophageal lesion. Routine radiotherapy was performed with a single dose of 2 Gy, 5 times/week, and the total radiation dose was 60-66Gy in 30-33 fractions.

Enteral nutrition intervention

(1): Patients in the control group were given routine nutrition support, that is, semi-liquid and fluid diet supplemented with a certain amount of vitamins, amino acids, electrolytes and glucose, during postoperative radiotherapy based on their condition, taste and preference. (2): Patients in the study group were given early enteral nutrition in addition to routine nutrition intervention in the control group: a nasogastric tube was placed after surgery for gastrointestinal decompression, Nutrison Fibre was infused via the nasogastric tube at the initial dose of 20 mL/h continuously for 24 h, and nasal feeding of 5 mg mosapride (3 times/day) through the nasointestinal tube was carried out to enhance gastrointestinal motility. At the same time, the infusion rate was gradually increased to the full dose of 30 kcal/(kg•d), according to the tolerance of patients.

Observation indicators

The changes in inflammatory response and nutritional level, healing of postoperative wound and prognosis of patients in the two groups were observed and compared before and after treatment. 1): Inflammatory response: It included indexes like hypersensitive C-reactive protein (hs-CRP) and prostaglandin E (PGE). Fasting venous blood (3 mL) was taken from all patients in the morning before and after postoperative nutrition support and radiotherapy, followed by centrifugation at 3000 r/min for 10 min. Then, the serum was collected, and serum inflammatory indexes were detected through enzyme-linked immunosorbent assay (ELISA) according to the instructions of the manufacturer (Elab Science Biotechnology Co.Ltd., China) [6]. 2): Nutritional level: It included serum pro-albumin (PA), albumin (ALB). Fasting venous blood (2 mL) was taken from all patients in the morning before and after treatment, centrifuged at 3000 r/min for 10 min, and the serum was collected. Next, immunity transmission turbidity was employed to measure serum PA, and colorimetry was used to determine serum ALB. All assays were conducted in accordance with the instructions [7]. 3): Postoperative wound healing and the total length of hospital stay of

patients [8]. 4): Prognosis: It was evaluated based on the postoperative gastrointestinal function recovery and the incidence rate of postoperative complications. Gastrointestinal recovery included the postoperative first exhaust and defecation time, while postoperative complications included incision infection, gastrointestinal adverse reactions, anastomoti c leakage and aspiration [9,10].

Statistics

SPSS 19.0 software (SPSS Inc., Chicago, IL, USA) was used for data processing. Quantitative data were assessed with t-test and expressed as mean ± standard deviation (x±s). Numerical data were evaluated with x^2 test and expressed as percents. P<0.05 suggested that the difference was statistically significant.

Results

Hs-CRP level

Compared with that before treatment, the serum hs-CRP expression level of patients was decreased in the two groups after treatment, and it was significantly lower in the study group than in the control group (p<0.05; Table 1).

PGE level

After treatment, both the control and study groups had declined serum PGE expression level compared with that before treatment, and the serum PGE expression level in the study group was significantly lower than that in the control group (p<0.05; Table 2).

PA level

Before treatment, there was no statistically significant difference in PA level between the two groups of patients (p>0.05). After treatment, the PA level of patients declined in both groups compared with that before treatment, and it was significantly lower in the study group than in the control group (p<0.05; Table 3).

ALB level

No statistically significant difference existed in ALB level between the two groups of patients before treatment (p>0.05). The ALB level was lowered in both groups after treatment, while it was higher in the study group compared to the control group (p<0.05; Table 4).

Table 1. Comparison of hs-CRP level of patients before and after treatment between the two groups (x±s)

Group	*Hs-CRP (mg/L)*			
	Before treatment	*After treatment*	*t*	*p*
Control group (n=57)	13.3±1.8	10.5±1.3	9.521	0.000
Study group (n=57)	13.2±1.7	7.4±0.9	22.765	0.000
t	0.305	14.802		
p	0.761	0.000		

Table 2. Comparison of PGE level of patients before and after treatment between the two groups (x±s)

Group	*PGE (ng/mL)*			
	Before treatment	*After treatment*	*t*	*p*
Control group (n=57)	20.8±2.9	17.7±1.4	7.268	0.000
Study group (n=57)	21.0±2.7	11.2±1.6	23.575	0.000
t	0.381	23.082		
p	0.704	0.000		

Table 3. Comparison of PA level before and after treatment between the two groups (x±s)

Group	*PA (mg/L)*			
	Before treatment	*After treatment*	*t*	*p*
Control group (n=57)	1.8±1.1	1.2±0.4	3.870	0.000
Study group (n=57)	1.7±0.9	1.6±0.7	0.662	0.509
t	0.531	3.746		
p	0.596	0.000		

Wound healing

In comparison with the control group, the study group had significantly shorter postoperative wound healing time and total length of hospital stay (p<0.05; Table 5).

Prognosis

The first exhaust and defecation time of patients in the study group were shorter than those in the control group, showing statistically significant difference (p<0.05; Table 6).

Complications

The total incidence rate of postoperative complications in the study group (4/57; 7%) was lower than that in the control group (12/57; 21.1%), and the difference was statistically significant (p<0.05; Table 7).

Discussion

As a highly-prevalent malignant tumor threatening the life and health of people, esophageal carcinoma occurs in middle-aged and elderly people. There are no typical symptoms at its early stage, but with its progression, patients tend to have symptoms such as progressive dysphagia and difficulty to swallow liquids including water and saliva [11]. Studies have shown that surgery and radiotherapy, as common clinical treatment methods for esophageal cancer, can relieve the clinical symptoms to a certain extent and improve the quality of life of patients, but patients are in

Table 4. Comparison of ALB level before and after treatment between the two groups (x±s)

Group	*ALB (g/L)*			
	Before treatment	*After treatment*	*t*	*p*
Control group (n=57)	269.5±20.4	195.7±19.6	19.695	0.000
Study group (n=57)	268.3±20.8	263.2±20.9	1.306	0.194
t	0.311	17.786		
p	0.756	0.000		

Table 5. Comparisons of postoperative wound healing time and total length of hospital stay between the two groups of patients [(x±s) d]

Group	*Wound healing time*	*Total length of hospital stay*
Control group (n=57)	18.4±6.0	11.5±3.1
Study group (n=57)	15.3±5.6	9.7±3.2
t	2.852	3.050
p	0.005	0.003

Table 6. Comparisons of first exhaust and defecation time of patients between the two groups [(x±s) h]

Group	*First exhaust time*	*First defecation time*
Control group (n=57)	59.7±9.5	62.4±13.0
Study group (n=57)	49.8±8.3	54.6±9.9
t	5.925	13.604
p	0.000	0.001

Table 7. Comparison of incidence rate of postoperative complications between two groups of patients

Group	*Incision infection* *n (%)*	*Gastrointestinal reaction* *n (%)*	*Anastomotic leakage* *n (%)*	*Aspiration** *n (%)*	*Total incidence rate* *n (%)*
Control group (n=57)	3 (5.3)	4 (7.0)	3 (5.3)	2 (3.5)	12 (21.1)
Study group (n=57)	1 (1.8)	2 (3.5)	1 (1.8)	0 (0.0)	4 (7.0)
x^2					4.653
p					0.031

a state, with increased metabolism of water, protein and energy due to the specific impact of radical surgery and radiotherapy [12,13]. Meanwhile, radiotherapy can lead to adverse symptoms such as nausea and vomiting, abdominal distension and esophageal mucositis, reduced appetite of patients and increased difficulty of food intake, resulting in decreased body mass, malnutrition and weakened immune function together with generally older age and weak physical performance of patients, thus decreasing the tolerance of patients to relevant subsequent treatment, which is not conducive to good prognosis [14]. Therefore, patients receiving postoperative radiotherapy after radical surgery for esophageal carcinoma should be given reasonable nutrition intervention.

Studies have suggested the surgical nutrition support interventions in clinical medicine since the concept of intravenous hyperalimentation has been proposed, and relevant interventional ways have been gradually developed and improved [15]. It has been considered that implementation of surgical nutritional intervention can regulate the systemic immune function, relieve the oxidative stress response, thus improving the prognosis of patients [16,17]. Enteral nutrition support is common in clinical practice [18]. However, traditional medical philosophy believes that patients undergoing surgical treatment should receive enteral nutrition support after the gastrointestinal function recovers to normal level. With the development of clinical medicine, the emerging rapid rehabilitation surgical research considers that early implementation of enteral nutrition interventions promotes the recovery of gastrointestinal motility [19]. The results of this study showed that after treatment, the inflammatory response, improvement of nutritional level, postoperative wound healing and prognosis of patients in the study group were superior compared to the control group, indicating that the application of postoperative enteral nutrition support combined with adjuvant radiotherapy in patients with esophageal carcinoma undergoing radical surgery can relieve the damage caused by radiotherapy, regulate or eliminate the inflammatory response, maintain the nutritional level, promote wound healing and improve prognosis, thus improving the overall surgical effect. The reason could be that early nutrition support performed can better protect the structure and function of the intestine of patients, promote the growth of the repair mechanisms related to gastrointestinal mucosal epithelial cells, and inhibit the alteration of intestinal flora, thereby protecting the intestinal barrier function. Furthermore, enteral nutrition can regulate portal circulation, facilitating protein synthesis and liver metabolism and thereby indirectly improving the nutritional condition of the patients [20].

Conclusions

In conclusion, the postoperative enteral nutrition combined with adjuvant radiotherapy applied in patients undergoing radical surgery for esophageal carcinoma achieves clear therapeutic effects: suppression of systemic inflammatory response, improvement of the nutritional level, acceleration of postoperative wound healing, promotion of patient recovery and improvement of prognosis, and is worthy of clinical popularization.

Conflict of interests

The authors declare no conflict of interests.

References

1. Aadam AA, Abe S. Endoscopic submucosal dissection for superficial esophageal cancer. Dis Esophagus 2018;31:7.
2. Natsugoe S, Matsumoto M, Okumura H et al. Initial metastatic, including micrometastatic, sites of lymph nodes in esophageal squamous cell carcinoma. J Surg Oncol 2005;89:6-11.
3. Zhang Z, Zong L, Xu B et al. Observation of clinical efficacy of application of enhanced recovery after surgery in perioperative period on esophageal carcinoma patients. JBUON 2018;23:150-6.
4. van der Sluis PC, Ruurda JP, Verhage RJ et al. Oncologic Long-Term Results of Robot-Assisted Minimally Invasive Thoraco-Laparoscopic Esophagectomy with Two-Field Lymphadenectomy for Esophageal Cancer. Ann Surg Oncol 2015;22 (Suppl 3):S1350-6.
5. Teodori L, Gohde W, Persiani M et al. DNA/protein flow cytometry as a predictive marker of malignancy in dysplasia-free Barrett's esophagus: thirteen-year follow-up study on a cohort of patients. Cytometry 1998;34:257-63.
6. Maghsudlu M, Farashahi YE. Heat-induced inflammation and its role in esophageal cancer. J Dig Dis 2017;18:431-44.
7. Hirahara N, Matsubara T, Mizota Y, Ishibashi S, Tajima Y. Prognostic value of preoperative inflammatory re-

sponse biomarkers in patients with esophageal cancer who undergo a curative thoracoscopic esophagectomy. BMC Surg 2016;16:66.

8. Song JH, Han YM, Kim WH et al. Oxidative stress from reflux esophagitis to esophageal cancer: the alleviation with antioxidants. Free Radic Res 2016;50:1071-9.
9. Miyazaki T, Sakai M, Sohda M et al. Prognostic Significance of Inflammatory and Nutritional Parameters in Patients with Esophageal Cancer. Anticancer Res 2016;36:6557-62.
10. Li S, Liu H, Diao C et al. Prognosis of surgery combined with different adjuvant therapies in esophageal cancer treatment: a network meta-analysis. Oncotarget 2017;8:36339-53.
11. Xu W, Liu Z, Bao Q, Qian Z. Viruses, Other Pathogenic Microorganisms and Esophageal Cancer. Gastrointest Tumors 2015;2:2-13.
12. Markar SR, Mackenzie H, Lagergren P, Lagergren J. Surgeon Age in Relation to Prognosis After Esophageal Cancer Resection. Ann Surg 2018;268:100-5.
13. Markar SR, Wahlin K, Lagergren P, Lagergren J. University hospital status and prognosis following surgery for esophageal cancer. Eur J Surg Oncol 2016;42:1191-5.
14. Taniyama Y, Nakamura T, Mitamura A et al. A strategy for supraclavicular lymph node dissection using recurrent laryngeal nerve lymph node status in thoracic esophageal squamous cell carcinoma. Ann Thorac Surg 2013;95:1930-7.
15. Yu HM, Tang CW, Feng WM, Chen QQ, Xu YQ, Bao Y. Early Enteral Nutrition Versus Parenteral Nutrition After Resection of Esophageal Cancer: a Retrospective Analysis. Indian J Surg 2017;79:13-8.
16. Modi RM, Mikhail S, Ciombor K et al. Outcomes of nutritional interventions to treat dysphagia in esophageal cancer: a population-based study. Dis Esophagus 2017;30:1-8.
17. Zeng J, Hu J, Chen Q, Feng J. Home enteral nutrition's effects on nutritional status and quality of life after esophagectomy. Asian Pac J Clin Nutr 2017;26:804-10.
18. Matsuda S, Niihara M, Tsubosa Y et al. Clinical significance of postoperative recovery of serum albumin levels in patients with esophageal cancer who underwent transthoracic esophagectomy. Surg Today 2016;46:1138-45.
19. Heber D, Li Z. Nutrition Intervention in Cancer. Med Clin North Am 2016;100:1329-40.
20. Gangadharan A, Choi SE, Hassan A et al. Protein calorie malnutrition, nutritional intervention and personalized cancer care. Oncotarget 2017;8:24009-30.