Original Article

Home enteral nutrition's effects on nutritional status and quality of life after esophagectomy

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Background and Objectives: We aimed to characterize the effect of home enteral nutrition (HEN) on the nutritional status and the quality of life (QOL) of esophageal cancer patients who underwent Ivor Lewis esophagectomy for cancer. **Methods and Study Design:** Sixty patients with esophageal cancer were assigned to receive either HEN (n=30) or standard care only (n=30) from 1 week to 24 weeks following surgery. Nutritional status was evaluated using The Mini Nutritional Assessment at 1 week preoperatively and at 12 and 24 weeks postoperatively. QOL-related parameters were analyzed in all patients using the QOL-core 30 questionnaire and the supplemental QOL-esophageal module 18 questionnaire for patients with esophageal cancer from 1-24 weeks after surgery. **Results:** At 12 weeks after surgery, the incidence of malnutrition or latent malnutrition in the HEN group was lower than that in the control group despite the absence of a significant difference between the two groups before surgery. Compared to the control group, the HEN group achieved higher Global QOL scores, and most of their functional index scores were better. Most of the symptomatic index scores were more reduced at 4 weeks and 12 weeks postoperatively in the HEN group. However, at 24 weeks after surgery, the incidence of malnutrition or latent malnutrition and most of the QOL indexes did not differ significantly between the two groups. **Conclusions:** HEN can reduce the incidence of malnutrition or latent malnutrition and help restore the QOL in the patients with esophageal cancer in the early period (24 weeks) after surgery.

Key Words: esophageal cancer, home enteral nutrition, quality of life, nutritional status, QOL

INTRODUCTION

Malnutrition is one of the main causes of the decline in quality of life (QOL) among patients with esophageal cancer.[1,2] Consequently, enteral nutrition is associated with an improved clinical outcome as it can efficiently ameliorate a poor post-operational nutritional status.[3] Thus, providing prolonged enteral nutrition to these patients is advocated in the field.[4] Nevertheless, although the benefits of enteral nutrition in the peri-operational setting during hospitalization are now fairly well-established,[5,6] the potential benefits of continuing enteral nutrition in addition to regular follow-up care following discharge from the hospital have not been intensively investigated. Home enteral nutrition (HEN) is a relatively novel nutritional intervention, introduced only 20 years ago, and provides enteral nutrition support through a jejunostomy tube or through a nasogastric feeding tube while the patient is at home.[7-10] The efficient delivery of nutrients to the body is presumed to provoke strong recovery of patient's nutritional status and, by inference, a substantial improvement in the QOL in this group. Evidence for the efficacy of HEN in patients with inoperable esophageal cancer is strong,[11] especially with respect to nutritional status and QOL, but this represents a fundamentally different terminal patient group compared with patients who undergo esophagectomy with curative intent. Hence, it is imperative that studies are carried out to investigate the effects of HEN in patients who are treated surgically. This is especially important in view of observations that improved nutritional status is not always associated with an improved QOL for cancer patients.[12] For post-operative esophageal cancer patients, however, the relationship between nutritional status and QOL has not been exhaustively explored and warrants further investigation. Prospective studies comparing HEN-supported care versus regular care are thus urgently needed in the field.[13]

METHODS

Patients

To avoid selection bias, we selected 60 patients (49 males, 11 females; age range, 38–76 years) who were treated by the same surgical team (directed by Dr Qixun Chen).

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patients were included if they underwent Ivor-Lewis surgery for esophageal cancer in Zhejiang Cancer Hospital between January and December 2013 and had a postoperative pathological diagnosis of squamous cell carcinoma. Patients with hypertension, diabetes mellitus, or psychiatric disorders were excluded. Before surgery, none of the patients were diagnosed with distant metastasis, and no patient had received chemotherapy or radiotherapy prior to surgery.

This clinical trial was registered on the Chinese Clinical Trial Registry website (No. ChiCTR-IOQ-15006476). The study was approved by the Ethics Committee of Zhejiang Cancer Hospital.

The patients were assigned to two experimental groups of 30 patients each, based on their order of presentation at the clinic: the HEN group or control group (Table 1). Jejunostomy for intra-intestinal nutrition was applied in all 60 patients during the Ivor Lewis procedure. All the patients received enteral nutritional support within 2 days following surgery. The feeding tubes were maintained in the patients scheduled for allocation to the HEN group, whereas they were removed from patients in the control group before discharge. All enrolled patients accepted daily care and health education. Patients in the HEN group used oral food intake and enteral nutrition simultaneously, and the ratio between the two was decided by the patients themselves based on preference and appetite. Nutrient liquid "SUPPORTAN" produced by Sino-Swed Pharmaceutical Corp., Ltd. was chosen for enteral nutrition because its components have been shown to be useful for cancer patients.[14,15]

Evaluation of nutritional status

The Mini Nutritional Assessment (MNA) consists of 18 questions grouped into 4 parts: anthropometry (BMI, weight loss, mid upper arm and calf circumferences), clinical status (medications, mobility, pressure sores and skin ulcers, lifestyle, psychological stress or neuropsychological diseases), dietary assessment (autonomy on feeding, quality and number of meals, fluid intake) and self-perception of health status and nutrition. The total score ranges from 0 to 30 points. A MNA score of <17 points indicates malnutrition; a score ranging from 17 to 23.5 score is an indicator of being at risk of malnutrition and score ≥24 is an indicator of a good nutritional status.[14,15]

Many studies have shown that the MNA is a useful tool for assessing the nutritional status of hospitalized patients[14,15] or of nursing home residents.[14,15] In recent years, the MNA has been used to evaluate the nutritional status of cancer patients and has been shown to produce reliable results.[14,15]

Evaluation of QOL

The quality of life-core 30 questionnaire (QLQ-C30; ver. 3.0, in Chinese) and the supplemental quality of life-esophageal module 18 questionnaire (QLQ-ES18, in Chinese) for esophageal cancer patients, both of which were developed by the European Organization for Research and Treatment of Cancer (EORTC), were used to evaluate QOL in all patients. Each patient was visited 1 week after surgery during hospitalization and contacted by telephone at 4, 12, and 24 weeks after surgery. The questionnaires were completed by the patients themselves with the assistance of their relatives or physicians in cases of reading or writing difficulty. The index related to food intake was not evaluated at postoperative week 1, because the patients fasted during the first week after operation.

Numerous studies have shown that the QLQ-C30 (including the Chinese version) reflects QOL objectively in patients with all types of cancer.[16,17] This questionnaire included a total of 30 items in five functional scales (physical, role, emotional, cognitive, and social), three general symptom scales (fatigue, nausea and vomiting, and pain), one global QOL scale, and six single-item measures of general symptoms or problems (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). Responses to each item were structured on a four-point scale: "not at all" (scored as 1), "a little" (scored as 2), "quite a bit" (scored as 3), and "very much" (scored as 4). The global QOL scale ranged from "very poor" (scored as 1) to "excellent" (scored as 7). Higher functional and comprehensive QOL index scores indicated better functions and QOL, whereas higher symptomatic index scores indicated worse symptoms and lower QOL.[18]

The QLQ-E18 was applied specifically to patients with esophageal cancer and constitutes a supplement to the QLQ-C30. It addresses a total of 18 items symptoms such as reflux, coughing when swallowing, and dysphagia. Responses to each item were structured on the same four-point scale as used in the core questionnaire.[19] The combined use of the QLQ-C30 and QLQ-ES18 (including their Chinese versions) has been used in QOL studies of patients with esophageal cancer and has shown good reliability and validity.[19-21]

Statistical analysis

Each QOL questionnaire item score was converted linearly to a scale of 1-100 according to the EORTC scoring manual.[17,19,20] and means and standard deviations were calculated as appropriate. SPSS software (ver 13.0; SPSS Inc., Chicago, IL, USA) was used to process data, and the independent-sample t test, rank-sum test and the $\chi 2$ test were used to compare QOL indices and general patient information and incidence of malnutrition between the two groups. $p<0.05$ was considered statistically significant.

RESULTS

The two groups showed no significant differences with respect to basic characteristics, including sex, age, average tumor length, and clinical stage. In addition, the incidence of postoperative complications did not differ between the two groups (Table 1). All patients were alive at 24 weeks after operation, and no cases of tumor recurrence or metastases were observed during the 24-week follow-up period. Two patients had the tube removed before week 4; another patient's tube was blocked at week 5 and had to be removed then. We thus considered our cohort suitable for investigating the effects of HEN in esophagectomy patients.

Overall, 396 questionnaires were collected from 60 patients; 18 questionnaires were not finished because of a

Table 1. Clinical data of 60 patients who underwent esophagectomy and jejunostomy

Clinical data	HEN group	Control group	$Z/X^2/t$	p
Patient (n)	30	30		
Gender, n (%)			0.373	0.542
Men	24 (80)	22 (73.3)		
Women	6 (20)	8 (26.7)		
Mean age(years), mean±SD	61.7±8.4	59.3±10.4	0.983	0.330
Average tumor length (cm), mean±SD	4.9±2.7	5.3±3.9	0.462	0.646
Levelof anastomosis, n (%)			0.693	0.405
Intrathoracic anastomosis	22 (73.3)	19 (63.3)		
Left cervical anastomosis	8 (26.7)	11 (36.7)		
Clinical staging, n (%)			0.127	0.899
I	1 (3.3)	0		
II	13 (43.3)	15 (50)		
III	16 (53.3)	15 (50)		
IV	0	0		

SD: standard deviation; HEN: home enteral nutrition.

Table 2. The number and proportion of malnutrition or latent malnutrition in patients treated with a HEN or standard post-operative nutritional protocols

Time point with respect to day of surgery	HEN, n (%)	Control, n (%)	X^2	p
1 week before	8 (26.7)	6 (20.0)	0.373	0.542
12 weeks after	15 (50.0)	25 (83.3)	7.500	0.006
24 weeks after	13 (43.3)	19 (63.3)	2.411	0.121

HEN: home enteral nutrition.

failure to reach these patients for follow-up visits. Another 6 questionnaires were not completed because one patient refused consent for the last three interviews. The results of nutritional status assessment are listed in Table 2. Both groups displayed some incidence of malnutrition or latent malnutrition before operation, but no statistically significant difference between the groups was detected. Between the two groups, no significant differences in the QOL indices were found at 1 week after surgery.

Most of the patients were assessed as being malnourished or having a latent malnutrition state at 12 weeks after surgery, but more so in the control group compared with the HEN group (p<0.01). At 24 weeks after surgery, the nutrition status in both groups was improved. The incidence of malnutrition or latent malnutrition in HEN group was lower than that in control group, but the difference between two groups was not statistically significant (p>0.05).

All patients showed rather poor QOL at 1 week after surgery. Many functional index scores such as those for physical and social items were low, whereas symptomatic index scores such as pain and fatigue were relatively high (Figure 1, Table 3).

Subsequently, however, the QOL improved gradually in both groups. Compared with the control group, the QOL in the HEN group improved more quickly. Global QOL scores were higher in the HEN group than in the control group at postoperative weeks 4 and 12 (p<0.05, p<0.01; Figure 1). Concomitantly, the HEN group showed higher scores with respect to physical function, social function, and role function (Table 3), had lower fatigue scores, and did better with respect to weakness, reflux, and appetite than the control group (Figure 2A, 2B, Table 3). From this time point onwards, however, the QOL in the two groups gradually converged, and the Global QOL scores in the two groups showed no significant differences at 24 weeks after surgery (p=0.517; Figure 1).

Postoperative diarrhea occurred more frequently after esophagectomy in the HEN group with 57.2% and 40.1% of patients in the HEN group complaining of varying degrees of diarrhea at 4 and 12 weeks after surgery, respectively, compared with 27.1% and 12.6% of patients, respectively, in the control group. At the same time, the HEN group showed a worse emotional status. Emotional function scores in the HEN group were lower than those in the control group at 4 weeks after surgery (p<0.05).

Postoperative pain occurred frequently following Ivor Lewis esophagectomy, and the pain scores showed no significant differences between the two groups during the complete follow-up period. In the HEN group, 48.4% of patients complained of varying degrees of pain, and this percentage was similar in the control group.

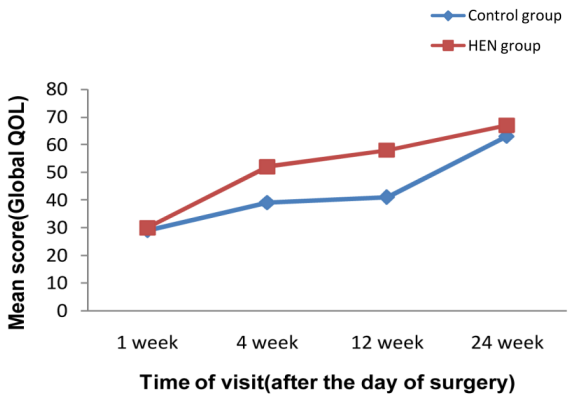

Figure 1. Global scores, as determined by quality of life-core 30 questionnaire scores at 1, 4, 12, and 24 weeks after surgery with or without HEN support, in patients with esophageal cancer. HEN: home enteral nutrition; QOL: quality of life.

Table 3. Scores (95% CIs) of QOL, as determined by QLQ-C30 at 1, 4, 12, and 24 weeks after surgery with or without HEN support, in patients with esophageal cancer

	HEN group (postoperative)				Control group (postoperative)			
	1 week	4 weeks	12 weeks	24 weeks	1 week	4 weeks	12 weeks	24 weeks
Functioning scores								
Physical function	54.4 (48.6, 60.2)	75.2 (69.8, 80.6)*	82.4 (77.4, 87.4)*	90.8 (86.6, 95.0)	59.2 (52.7, 65.7)	67.3 (62.7, 71.9)	73.2 (66.8, 79.6)	88.1 (84.5, 91.7)
Social function	3.4 (2.8, 4.0)	51.3 (46.0, 56.6)**	67.6 (60.8, 74.4)*	71.0 (68.3, 73.7)	4.2 (3.3, 5.1)	37.7 (35.3, 40.1)	56.9 (51.0, 62.8)	69.2 (65.4, 73.0)
Role function	3.4 (2.7, 4.1)	45.9 (40.2, 51.6)**	57.9 (52.9, 62.9)**	62.5 (56.6, 68.4)	4.3 (3.5, 5.1)	23.1 (20.2, 26.0)	48.4 (44.6, 52.2)	59.3 (52.5, 66.1)
Emotional function	47.3 (39.9, 54.7)	55.0 (51.2, 58.8)*	56.9 (50.9, 62.9)	67.1 (63.3, 70.9)	49.2 (44.6, 53.8)	60.1 (57.8, 62.4)	61.2 (57.9, 64.6)	65.2 (59.8, 70.6)
Symptom scores								
Weakness	95.1 (91.7, 98.5)	64.7 (60.1, 69.3)**	42.0 (34.6, 49.4)*	39.3 (32.6, 46.0)	97.2 (95.9, 98.5)	88.1 (82.4, 93.8)	53.3 (46.5, 60.1)	42.9 (35.7, 50.1)
Diarrhea	67.4 (62.0, 72.8)	58.2 (50.5, 65.9)**	42.7 (35.6, 49.8)**	19.1 (13.1, 25.1)	68.1 (64.7, 71.5)	23.2 (15.9, 30.5)	14.9 (11.5, 18.3)	14.0 (10.2, 17.8)
Fatigue	97.0 (95.1, 98.9)	68.0 (60.3, 75.7)**	52.8 (45.2, 60.4)*	41.0 (34.7, 47.3)	94.3 (90.1, 98.5)	85.2 (78.8, 91.6)	64.9 (57.9, 71.9)	43.1 (38.2, 48.0)
Pain	5.2 (4.5, 5.9)	75.6 (63.2, 88.0)	32.5 (29.6, 35.4)	29.6 (26.5, 32.7)	4.4 (3.5, 5.3)	79.6 (71.0, 88.2)	29.0 (25.6, 32.4)	26.2 (24.0, 28.4)

QOL: quality of life; QLQ-C30: the quality of life-core 30 questionnaire.
*p<0.05; **p<0.01.

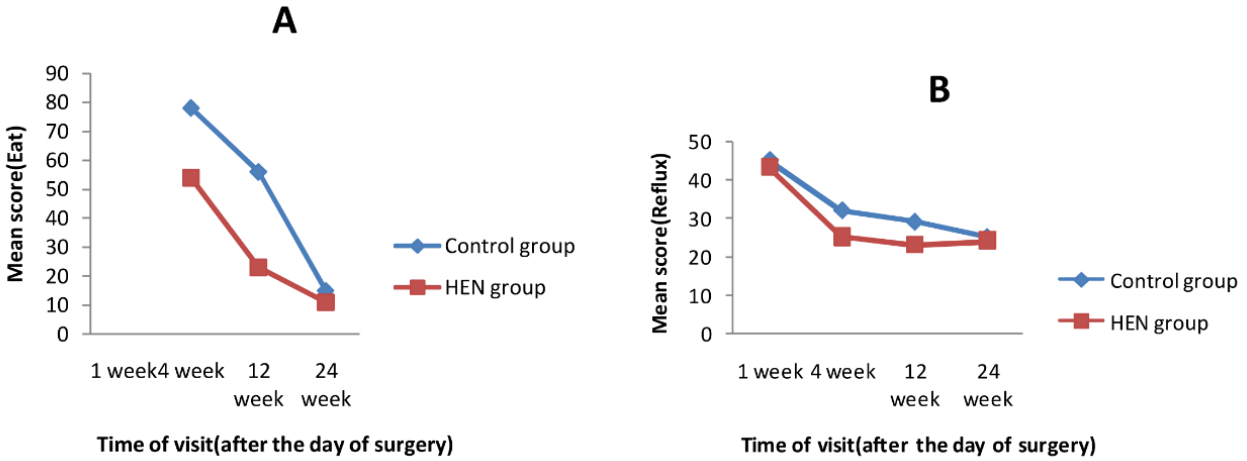

Figure 2. Severity of symptoms associated with esophageal cancer, as determined by quality of life-esophageal module 18 questionnaire scores at 1, 4, 12, and 24 weeks after surgery with or without HEN support, in patients with esophageal cancer. A: Eating discomfort; B: reflux. HEN: home enteral nutrition.

DISCUSSION

Esophageal cancer is one of the most common gastrointestinal cancers and is often characterized by progressive dysphagia, putting patients at substantial risk of malnutrition. Indeed, the present study displayed substantial preoperative malnutrition in both experimental groups, highlighting the seriousness of this issue and thus the need for improved protocols in this respect. The fact that both experimental groups were similar in this respect suggested that altered baseline characteristics did not account for the effects observed. Digestive tract reconstruction after esophagectomy impacts heavily on the capacity of patients to maintain nutritional status, both because of ingestion problems as well as of the induction of a hyper catabolic state caused by stress. With respect to QOL, surgery for esophageal cancer creates a large amount of trauma and substantially affects patients both physically and mentally. We observed that at 1 week following surgery, the QOL of all the patients in both groups was poor, with surgery-related pain, weakness, and psychological problems mainly impacting QOL. A reduction in surgical trauma is an important goal in the field, and toward this goal, developments like endoscopically guided esophagectomy have been developed that may reduce surgical trauma and enable a higher postoperative QOL.[22] Concomitantly, however, improvements in post-procedural patient management may help as well. The poor QOL scores observed in the present study highlight the importance of such developments.

Following surgery, patients gradually recovered, both in terms of physical and psychological aspects. The direct influence caused by surgical trauma diminishes gradually, while simultaneously, malnutrition and other symptoms caused by the reconstruction of the digestive tract become the principal factors negatively impacting patients' QOL. Numerous studies have shown that malnutrition after esophagectomy is common and the main cause of low postoperative QOL. Doningtonet al[23] found that it was common for patients with esophageal cancer to lose up to 15%of their body weight from the time of diagnosis through the first 6 months following surgery due to a multitude of factors including dumping syndrome, delayed gastric emptying, reflux, and dysphagia, which all contribute to nutritional deficiency and thus a poor QOL. Martin et al[24] reported that weight loss can be long lasting after esophagectomy and that overweight patients are at a particularly increased risk of malnutrition. It is thus important to investigate strategies aimed at improving postsurgical nutrition status. Our study found that at 12 weeks after surgery, the levels of malnutrition or latent malnutrition in both groups rose substantially, which highlights the universality and severity of malnutrition after esophagectomy.

After esophagectomy, the normal physiological structure is grossly altered, and the observed nausea, reflux, chest congestion, and belching are not unexpected. Most patients experience a correlation between these symptoms and *per os* food intake as the more and the faster they eat, the more obvious these symptoms become. Consequently, the patients' appetite is affected and patients refrain from eating as they are afraid of experiencing the symptoms involved. A considerable percentage of patients complained of varying degrees of fatigue and weakness. Two of the patients in the control group even were so weak that it was difficult for them to assume long-standing or sedentary positions, and they had to rest in bed most of the time. During follow-up, we found that such patients could not always adapt to full oral food intake, which caused malnutrition. Simultaneously, such patients complained of many symptoms associated with oral food intake, especially of reflux, belching, and chest congestion after eating. At 4 weeks after surgery, 13 patients in the control group had varying degrees of reflux, and 7 patients complained of belching following eating. This observation was objectified by relatively high symptom indexes in our questionnaires. Therefore, our study has highlighted further the need to improve the postoperative nutrition status of patients with esophageal cancer and to reduce the symptoms associated with food ingestion.

HEN is a continuation of hospital enteral nutrition support and constitutes enteral nutrition support at home while the patients' condition is stable. HEN is the preferred form of home nutritional support with advantages of being convenient and safe.[11] Consequently, HEN to support conventional care is gaining interest and attention for post-operative cancer patients, including those suffering from esophagogastriccancer.[25] In Europe and the United States in particular, the use of HEN is widespread,[8,10] but in China, HEN remains uncommon although it is gaining in popularity, prompting the need for a study addressing the potential benefits of HEN in the Chinese clinical situation. The current study demonstrated that HEN indeed can be an excellent option for patients who cannot meet their nutrition requirements by oral intake, in line with the results of earlier research.[9,26] Importantly, our study is the first prospective study of HEN following esophageal cancer surgery, whereas previous studies focused on patients with upper gastrointestinal obstruction or those treated with radiotherapy or chemotherapy.[7,27] Thus, we feel the current study has made an important contribution to the field.

We hold the opinion that after surgery, a period of time is required for the newly reconstructed digestive tract to adapt to total oral intake, and HEN can facilitate the transition process from fasting to total oral intake by maintaining nutrition status. In our study, the patients in the HEN group supplemented oral intake with enteral nutrition at libitum. If patients adapted quickly to oral food intake, they usually elected to reduce the quantity of HEN support; if the patients had symptoms related to eating, then increasing the quantity of HEN while reducing oral intake helped to relieve symptoms. We feel that in general our results supported self-determination by patients in this respect.

At 4 and 12 weeks after surgery, the patients in the HEN group had better nutrition status because of enteral nutrition support. Most of the patients were satisfied with their general performance and could cope with the needs of daily life and social activities such as visiting friends and community activities. Meanwhile, the patients had fewer symptoms such reflux and nausea because of the lower requirement for oral food intake and were liberated from the negative association with eating, which contributed to appetite. As the patients gradually adapted to the

newly reconstructed digestive track, the quantity of oral food intake concomitantly increased until full oral intake was eventually achieved. The amount of enteral nutrient liquid consumed was less than 250 mL daily in 93.9% of the patients and patients had adapted fully to total oral intake at 24 weeks after surgery. Hence, HEN offered substantial benefits for this patient group.

Nevertheless, there were also substantial disadvantages associated with HEN. Compared with the control group, the HEN group had a higher incidence of diarrhea. About 56.7% patients in the HEN group complained of varying degrees of diarrhea, which might be due to improper dropping speed and nutrient liquid temperature upon ingestion. Importantly, the jejunostomy tube provoked an adverse psychological effect in the patients, which caused lower emotional function scores. Some of the patients expressed care about their confrontational change in appearance, and others appeared worried about possible tube loss or infection at the stoma. For two patients, the perceived disfiguration was so severe that had the tubes had to be removed at 3 weeks after surgery. One patient reported her disturbed sleep caused by the jejunostomy tube. These findings are similar to those reported by a previous study.[26,28] Appropriate counseling for psychological intervention may be needed to reduce these negative psychological impacts.

Post-thoracotomy pain syndrome (PTPS) consists of chronic pain complaints following thoracic surgery and represents a significant clinical problem in 25%-60% of patients, with inter costal nerve injury seeming to be to be the most important pathogenic factor.[29] As an important QOL index, PTPS is a very common symptom that severely affects patients' satisfaction with life. In our study, a high incidence of PTPS was observed in all of our patients during the 24-week follow-up period. Although minimally invasive surgical techniques for esophageal cancer have been used to reduce the risk of PTPS,[30] it is a problem that warrants further attention and study.

At 24 weeks after surgery, the incidence of malnutrition or latent malnutrition in HEN group was lower than that in control group, but the difference between two groups did not reach statistical significance, and the QOL of patients in the two groups tended to be similar, with the global QOL and most of the other QOL indexes showing no significant differences between the two groups. At this point, most of the patients had basically adapted to total oral intake physically and mentally, and thus, the jejunostomy tubes could be removed. Therefore, our study results indicated that considered from the perspectiveof the improvement of nutrition status and the quality of life, HEN may offer advantages in the early months after esophagectomy. At that time, there was also a certain percentage of patients with malnutrition or latent malnutrition detected in the HEN group, and thus, further studies are needed to determine how to improve long-term nutritional status after esophagectomy.

This study has intrinsic limitations, some of which are related to the impossibility of conducting such a study in a blinded fashion and some of which are related to randomization. We explicitly acknowledge these limitations. The assignment of patients to the two groups was not strictly randomized but was based on their order of presentation. The 24-week follow-up period was also relatively short, and the sample size was small. To evaluate long-term QOL and survival rates, a larger sample size and further observations are needed.

AUTHOR DISCLOSURES

No authors report any conflict of interest.

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