Original Article

An Interdisciplinary Nutrition Support Team Improves Clinical and Hospitalized Outcomes of Esophageal Cancer Patients with Concurrent Chemoradiotherapy

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Abstract

Background: The prevalence of malnutrition is very high in patients with cancer. The purpose of this study was to investigate whether or not a nutrition support team (NST) could benefit esophageal cancer patients undergoing chemoradiotherapy (CRT).
Methods: Between June 2012 and April 2014, 50 esophageal cancer patients undergoing concurrent CRT were randomly assigned into two groups: The NST group and the control group. The nutritional statuses of 25 patients in the NST group were managed by the NST. The other 25 patients in the control group underwent the supervision of radiotherapy practitioners. At the end of the CRT, nutritional status, the incidence of complications, and completion rate of radiotherapy were evaluated. Besides, the length of hospital stay (LOS) and the in-patient cost were also compared between these two groups.
Results: At the completion of CRF, the nutritional status in the NST group were much better than those in the control group, as evidenced by prealbumin (ALB), transferrin, and ALB parameters ($P = 0.001$, 0.000, and 0.000, respectively). The complication incidences, including bone marrow suppression (20% vs. 48%, $P = 0.037$) and complications related infections (12% vs. 44%, $P = 0.012$), in the NST group were lower and significantly different from the control group. In addition, only one patient in the NST group did not complete the planned radiotherapy while 6 patients in the control group had interrupted or delayed radiotherapy (96% vs. 76%, $P = 0.103$). Furthermore, the average LOS was decreased by 4.5 days ($P = 0.001$) and in-patient cost was reduced to 1.26 ± 0.75 thousand US dollars person-times ($P > 0.05$) in the NST group.
Conclusions: A NST could provide positive effects in esophageal cancer patients during concurrent CRT on maintaining their nutrition status and improving the compliance of CRF. Moreover, the NST could be helpful on reducing LOS and in-patient costs.

Key words: Chemoradiotherapy; Complication; Esophageal Cancer; Nutrition Support Team; Prognosis

Introduction

Esophageal cancer is one of the most common cancers in the world, with diagnoses of more than 480,000 patients and 400,000 deaths annually.[1] The incidence and mortality rate of esophageal cancer rises continuously, especially in the mainland of China. Surgery and chemoradiotherapy (CRT) are the important strategies for the treatment of esophageal cancer.[2] It is reported that 79% of esophageal cancer patients experience malnutrition, which is caused mainly by anorexia and dysphagia, before the treatment starts.[3,4] The dysphagia-related nutrition deficiency could be even worse during the treatment and as a result, weight lost would occur. Furthermore, malnutrition is a sign of poor outcomes in cancer patients, which negatively affected the response to

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therapy, the length of hospital stay (LOS), the quality of life, complications, infections, and the survival rate.[5-7] Therefore, it is necessary to implement cancer patients' treatment on malnutrition.

Nutritional intervention could improve clinical outcomes of cancer patients, including esophageal cancer.[3] Besides, nutritional support was mainly given to patients by the routes of oral nutritional supplements (ONS), the enteral nutrition (EN), and the parenteral nutrition (PN). It has been shown clinical benefits of nutritional intervention via EN in esophageal cancer patients who are undergoing radiochemotherapy (RCT), which guiding clinicians using EN to enhance the nutritional status and functional capacity.[8] The rationale for nutritional support is to improve nutritional status, modulate inflammatory responses, decrease the risk of infection, and enhance the quality of life. In order to provide more reasonable and effective nutritional intervention, many countries have introduced nutrition support team (NST) in hospitals.[9] Besides, in order to provide nutrition supports, the European Society of Parenteral and Enteral Nutrition (ESPEN) recommends the contribution of multidisciplinary NST.

NST has been found to reduce the incidence of complications, in-patient costs, and mortality rates. Based on our knowledge, few randomized control trials have evaluated the effect of NST in esophageal cancer patients with concurrent CRT. NST was established in the Huanxing Hospital (Beijing, China) in April 2012. Team members includes: Physicians, registered dietitians, pharmacologists, nurses, and managers. The major goals of the NST were to normalize the medical nutrition therapy (MNT) and to emphasize on the nutrition care process during the MNT. The functional area includes the office, the metabolism laboratory, and configured rooms for dietary, EN, PN, etc. The purpose of this study was to investigate the clinical therapy effects of NST and to provide NST services to esophageal patients, who are treated with CRT.

Methods

Patients' eligibility

The patients were recruited in Department of Comprehensive Oncology, Chinese Academy of Medical Sciences Cancer Hospital (CAMSCH), including a total of 50 esophageal cancer in-patients, between June 2012 and April 2014. The study was designed and conducted in accordance with the *Declaration of Helsinki* and was approved by the Institutional Board and Ethics Committee of CAMSCH.

The patients were eligible to participate in the study if they had confirmed pathological result of primarily phase III esophageal cancer (squamous cell carcinomas) with a planned treatment by radiotherapy combined chemotherapy, weight loss <10% and diet decrease (but >60% targeted feeding volume), the patient-generated subjective global assessment (PG-SGA) score ≥4 points, and accepted written informed consent.

Exclusion criteria were being severe malnutrition (weight loss >10%, blood albumin [ALB] <30 g/L, or body mass index [BMI] <18.5 kg/m^2), having serious heart, lung or brain disease, with chronic hepatitis, cirrhosis, chronic nephritis or renal insufficiency, complicated with infectious fever, and EN or PN intolerance.

Protocol design

Based on the different nutrition intervention methods, 50 eligible patients were randomly assigned into the NST group and the control group, all of whom received the same CRT treatment for two cycles of chemotherapy followed by the radiotherapy. The study was stopped at the end of radiotherapy. The standard anti-cancer therapy included concurrent CRT with cisplatin/carboplatin with paclitaxel and radiotherapy according to the center's current practice 50–60 Gy/2 Gy/25–30 f. Nutritional support included diet counseling, ONS, EN, and PN.

The patients in the NST group met with a member of the NST, which consisted of board-certified dietitians and advanced-practice nurses. Specific attention was paid to nutrition risk screening, nutrition assessment, nutrition intervention, nutrition monitoring, and evaluation via standardized clinical nutrition process. The energy intake goal was 30–35 kcal·kg^{-1}·d^{-1} and the macronutrient intakes were protein: 1.5 g/kg (20%), fat: 1.3 g/kg (40%), and carbohydrates: 3 g/kg (40%). Micronutrients' intakes were based on the conventional proportional. On the other hand, the patients in the control group were conducted by chief physicians and were not scheduled to meet with the NST service. The nutrition therapy for the control group mainly included ONS and PN without intake goals.

Data collection

All the following parameters were measured in the beginning and the end of the study.

Nutritional and blood determinations

Height (m) and weight (kg) were measured and BMI were calculated as BMI = kg/m^2. The quantity of prealbumin (PALB), transferrin, and ALB were tested from the peripheral blood.

Incidence of complications

The number of hemoglobin (Hgb), leukocyte, platelet (PLT) were counted automatically. Infections related to complications were identified and recorded, including catheter related infection, pulmonary infection, local skin infection, and mucosal inflammation infection. Bone marrow depression were observed and graded according to the National Cancer Institute-Common Toxicity Criteria version 3.0.[10]

Clinical outcomes

The completion rates of therapy, the LOS, and the in-patient cost were recorded during the study.

Statistical analysis

All statistical analysis was performed with SPSS, version 20.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were described by percentages and compared using Chi-square test. Continuous variables were described by mean ± standard deviation (SD) and compared using two-sample Student's *t*-test or analysis of variance (ANOVA), when appropriate. A two-tailed $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics of the patients

A total of 50 patients with esophageal cancer were selected randomly in the study. Baseline characteristics of patients were shown in Table 1. There were 25 patients in the NST group (18 males, 7 females) and 25 patients in the control group (17 males, 8 females). Homogeneity analyses for baseline characteristics were performed for all the patients' data sets [Table 1]. Baseline characteristics (age, gender, weight, BMI, PG-SGA value, cancer diagnosis, treatment protocols, and hematological parameters) were well-balanced between the two groups. However, comparing with the control group, during the CRT treatment course, more patients in the NST group used tube feedings (68% vs. 32%, $P = 0.023$).

Table 1: Baseline characteristics of the esophageal cancer patients undergoing concurrent CRT in both NST and control groups

Variables	NST group ($n = 25$)	Control group ($n = 25$)	*t* or X^2	*P*
Age (years)	51.36 ± 11.02	50.88 ± 8.80	0.170	0.866
Gender (*n*)			0.095*	1.000
Male	18	17		
Female	7	8		
Number of squamous esophageal carcinoma cases (*n*)	25	25		
Stage (*n*)			0.402	0.818
IIIa	2	3		
IIIb	17	15		
IIIc	6	7		
Anti-cancer therapy				
Chemotherapy (*n*)			0.080	0.777
Paclitaxel + cisplatin	12	11		
Paclitaxel + carboplatin	13	14		
Radiation dose (Gy)	58.2 ± 3.4	57.5 ± 3.9	−0.688	0.495
PG-SGA	6.64 ± 1.77	6.84 ± 1.18	−0.469	0.641
Weight (kg)	57.84 ± 8.50	56.12 ± 8.17	0.729	0.469
BMI (kg/m^2)	20.52 ± 2.12	20.84 ± 2.19	−0.524	0.603
WBC (g/L)	5.54 ± 1.26	5.99 ± 1.47	−1.180	0.244
Hgb (g/L)	10.77 ± 1.89	10.26 ± 1.33	1.102	0.276
PLT (g/L)	260.72 ± 45.93	262.23 ± 53.51	−0.107	0.915
PALB (mg/L)	155.74 ± 28.15	157.47 ± 43.40	−0.168	0.867
Transferrin (g/L)	2.41 ± 0.33	2.33 ± 0.47	0.683	0.498
ALB (g/L)	35.36 ± 2.55	35.80 ± 3.72	−0.488	0.628
Nutritional support (*n*)				
Tube feeding	17	8	6.480*	0.023
Diet ± ONS ± SPN	8	17		

Values are expressed as *n* or mean ± SD. *Chi-square test was used; others were used *t*-test. CRT: Chemoradiotherapy; PG-SGA: Patient-generated subjective global assessment; BMI: Body mass index; WBC: White blood cell; Hgb: Hemoglobin; PLT: Platelets; PALB: Prealbumin; ALB: Albumin; ONS: Oral nutritional supplements; SPN: Supplementary parenteral nutrition; NST: Nutrition support team; SD: Standard deviation.

Nutritional status

The results showed that the NST group had better weight maintenance data compared to the control group (NST group: 0.36 ± 2.16, $P = 0.412$; and control group: −2.44 ± 2.60, $P = 0.000$). Besides, changes of weight between the two groups had a significant difference [$P = 0.000$; Table 2].

After treatment, PALB in both groups increased. However, a significant increase in PALB was observed in NST group (79.98 ± 57.54, $P = 0.000$) while no significant difference (17.43 ± 66.52, $P = 0.203$) was found in the control group. In addition, changes of PALB between the two groups had a significant difference [$P = 0.001$; Table 2].

Compared with baseline, the transferrin of the NST group increased significantly (0.36 ± 0.67, $P = 0.013$), whereas transferrin in the control group decreased significantly (−0.43 ± 0.61, $P = 0.002$). The changes of transferrin between the two groups had a significant difference [$P = 0.000$; Table 2].

ALB in NST group remained almost the same (0.00 ± 4.57, $P = 1.000$). In contrast, ALB in the control group decreased significantly (−5.80 ± 4.79, $P = 0.000$). The changes in ALB had a significant difference between both groups [$P = 0.000$; Table 2].

In the NST group, white blood cell (WBC), Hgb, and PLT did not decline significantly ($P = 0.238$, 0.145, and 0.178, respectively). On the contrary, all these three levels in the control group had a significant decrease ($P = 0.000$, 0.000, and 0.001, respectively). Furthermore, the changes of WBC and PLT had a significant difference between these two groups (WBC: −0.56 ± 2.30 vs. −2.69 ± 3.13, $P = 0.008$; PLT: −19.21 ± 69.24 vs. −76.44 ± 98.09, $P = 0.021$), and the NST group tended to have a greater Hgb than control group after the treatment (−0.59 ± 1.96 vs. −1.15 ± 0.99, $P = 0.205$) [Table 2].

The incidences of bone marrow suppression (Grade II and above) and complications related infection were both lower in the NST group than in the control group. There were significant differences in the percentage of patients experienced bone marrow suppression (20% vs. 48%, $P = 0.037$) and complications related infection (12% vs. 44%, $P = 0.012$) [Table 3].

Completion rates of therapy

There was only one patient in the NST group who did not

Table 2: Changes in the characteristics of patients before and after the treatments

Variables	Baseline	End	Change
Weight (kg)			
NST group	57.84 ± 8.50	58.20 ± 8.05	0.36 ± 2.16†
Control group	56.12 ± 8.17	53.68 ± 8.06*	−2.44 ± 2.60
ALB (g/L)			
NST group	35.36 ± 2.55	35.36 ± 3.95	0.00 ± 4.57†
Control group	35.80 ± 3.72	30.00 ± 3.82*	−5.80 ± 4.79
PALB (mg/L)			
NST group	155.74 ± 28.15	235.71 ± 48.02*	79.98 ± 57.54†
Control group	157.47 ± 43.40	174.90 ± 42.07	17.43 ± 66.52
Transferrin (g/L)			
NST group	2.41 ± 0.33	2.77 ± 0.67*	0.36 ± 0.67†
Control group	2.33 ± 0.47	1.91 ± 0.44*	−0.43 ± 0.61
WBC (g/L)			
NST group	5.54 ± 1.26	4.98 ± 2.18	−0.56 ± 2.30†
Control group	5.99 ± 1.47	3.30 ± 2.23*	−2.69 ± 3.13
Hgb (g/L)			
NST group	10.77 ± 1.89	10.18 ± 1.62	−0.59 ± 1.96
Control group	10.26 ± 1.33	9.11 ± 1.20*	−1.15 ± 0.99
PLT (g/L)			
NST group	260.72 ± 45.93	241.51 ± 59.66	−19.21 ± 69.24†
Control group	262.23 ± 53.51	185.80 ± 95.73*	−76.44 ± 98.09

Values are expressed as mean ± SD. *P<0.05 when compared with baseline values in each group; †P<0.05 when compared with control group. PALB: Prealbumin; ALB: Albumin; WBC: White blood cell; Hgb: Hemoglobin; PLT: Platelets; SD: Standard deviation; NST: Nutrition support team.

Table 3: Complication incidence and completion rates of therapy

Variables	NST group	Control group	χ^2	P
Bone marrow suppression (Grade II and above)	5 (20)	12 (48)	4.367	0.037
Complications	3 (12)	11 (44)	6.349	0.012
Completion rates	24 (96)	19 (76)	2.658	0.103

Values are expressed as n (%). P values were calculated using the Chi-square test. NST: Nutrition support team.

complete the treatment plan while 6 patients in control group experienced treatment interruptions (dose reductions or delays). Although there was no significantly difference between the two groups, the completion rates of therapy was higher in the NST group than control group (96% vs. 76%, $P = 0.103$) [Table 3].

Length of hospital stay and hospitalization cost

At last, the average LOS and the in-patient cost were compared between the two groups. By comparing to the control group, the average LOS of patients in the NST group decreased by 4.5 days (45.68 ± 3.87 vs. 50.16 ± 5.38 days, $t = -3.382$, $P = 0.001$) and the in-patient cost reduced 1.3 thousand dollars person-times (16.95 ± 2.50 vs. 18.22 ± 2.80 thousand dollars, $t = -1.683$, $P = 0.099$) (Student's t-test).

Discussion

The prevalence of malnutrition, caused by dysphagia and anorexia, is high in patients with esophageal cancer.[11] During the CRT, some patients experienced malnutrition/cachexia-related complications, which affected the therapy outcomes negatively.[12] In our study, a significant difference between the two groups on nutritional status and blood parameters after CRT for about 45 days was occurred. Normalized nutritional support through the NST has showed more effective roles on improving treatment compliances and nutritional status than through the control group.

In-patients' nutritional status in the NST group were improved or maintained, yet the status decreased significantly in the control group during CRT. As we known, PALB was associated with dietary intake when synthetic functions were normal in the liver. Moreover, PALB is suggested as a sensitive nutritional biomarker for evaluating the nutritional status of esophageal cancer patients undergoing concurrent CRT.[13] The patients in both groups had a low level of PALB and transferrin with normal liver function before treatment, which was caused by inadequate intake. After treatment, PALB and transferrin increased significantly in the patients of NST group while decreased or did not change in control group, suggesting NST has benefits on dietary intake and nutritional status.

Bone marrow suppression was one of the most common complications during CRT due to the decreasing production of blood cells. In the control group, WBC, Hgb, and PLT decreased significantly, associated with the high incidence of bone marrow suppression. In stark contrast, these three parameters corresponded to low incidence in the NST group. The results suggested that the incidence of bone marrow suppression decreased significantly in patients with better nutritional status, although simple nutrition support could not improve bone marrow suppression during CRT.

Several studies demonstrated that malnutrition was associated with high occurrence of complications related infection.[14] Our results also showed clearly that less patients in NST group experienced complications related infection compared with the control group. Furthermore, the LOS and the in-patient cost were both increased because of the complications related infection in the control group.

The outcomes of locally advanced esophageal cancer patients by concurrent RCT were related to the nutritional status and the dosage of RCT. However, chemotherapy or radiotherapy for cancer patients were often delayed or terminated due to complications, significantly affecting the outcomes.[4] Besides, the prolonged treatment caused by interrupting radiotherapy was also associated with a poor prognosis. Compared with 76% patients in the control group, 96% patients in NST group completed the RCT plan, suggesting that normalized nutritional support through NST provided better RCT compliance.

More patients in NST group used tube feeding than in the control group. EN via tube feeding was recommended by ESPEN for esophageal cancer patients, who could not eat regular food, were likely to have mucositis in the course of radiotherapy, which was benefit to nutritional status and to improve prognosis.[15] However, this recommendation was not widely used in clinical practice.

In conclusion, our results indicated that nutrition management via NST was conducive to maintain nutritional status, improve RCT compliance and tolerability, and reduce the LOS and the in-patient cost for esophageal cancer patients concurrent RCT. In future, we will pay more attention to the comparison of prognosis between the two groups. Our study suggests that the NST is necessary for the proper administration of nutrition intervention for the hospitalized esophageal cancer patients with RCT to achieve the best therapeutic effect.

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Conflicts of interest

There are no conflicts of interest.

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