

Efficacy of nutritional interventions in patients with hypopharyngeal-laryngeal and esophageal cancers treated with radiotherapy

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Abstract. The aim of the present study was to evaluate the effects of nutritional interventions in patients with hypopharyngeal-laryngeal and esophageal cancers treated with radiotherapy. Patients who received clinical intervention were compared with a control group. The intervention group received active nutritional support according to the regimen developed by the study team, while the control group followed a normal diet at the hospital or at home. After 1 month, in the intervention group, the patients' weight increased by 0.5 ± 1.7 kg, while in the control group, the patients weight decreased by 1.6 ± 1.9 kg. In addition, body mass index in the intervention group increased by 0.2 ± 0.6 kg/m², whereas this decreased by 0.6 ± 0.7 kg/m² in the control group. Significant differences between the groups were observed for both parameters ($P < 0.001$). As regards the quality of life, the general symptoms of the patients in the intervention group improved (a decrease of 3.4 ± 11.9 points), while those in the control group tended to worsen (an increase of 5.5 ± 12.6 points). Specifically, fatigue, and vomiting and nausea decreased by 2.4 ± 18.0 and 7.3 ± 23.9 points in the intervention group, respectively, whereas these increased by 8.0 ± 16.5 and 9.9 ± 26.4 points, respectively in the control group, with differences between groups being statistically significant for both parameters ($P < 0.05$). On the whole, the present study demonstrates that for patients with hypopharyngeal-laryngeal and esophageal cancers who are at a high risk of developing malnutrition, active nutritional interventions during radiotherapy improve the nutritional status and, ultimately, the quality of life of the patients.

Introduction

The incidence of hypopharyngeal-laryngeal and esophageal cancers has been increasing in recent decades, not only in developed countries, but also in developing countries, including Vietnam. As reported by the International Agency for Research on Cancer (IARC) (Globocan 2020), the number of new cases of esophageal and hypopharyngeal-laryngeal cancers was 604,100 and 367,281, respectively; the number of deaths from esophageal and hypopharyngeal-laryngeal cancers was 544,076 and 186,582, respectively. In Vietnam, in 2020, the number of new cases and deaths from esophageal cancers were 3,281 and 3,080, respectively; the number of new cases and deaths from hypopharyngeal-laryngeal cancers were 4,982 and 2,661, respectively (1).

Due to the effects of tumors and treatment, the majority of patients with hypopharyngeal-laryngeal and esophageal cancers are malnourished. The study by Bruzgielewicz *et al* (2) on 252 patients with hypopharyngeal-laryngeal cancer demonstrated a body mass index (BMI)-based malnutrition of 41%. The study by van Bokhorst-de van der Schuer *et al* (3) revealed that 30-50% of patients with head and neck cancers were malnourished. The survey by Pham Van *et al* (4) using the Patient-Generated Subjective Global Assessment (PG-SGA) revealed that up to 52.9 and 29.6% of patients with esophageal cancer had mild/moderate malnutrition and severe malnutrition, respectively. In their study, as assessed using BMI and mid-upper arm circumference, up to 47.6 and 50% of patients with esophageal cancer, respectively, were found to be malnourished. The percentages of patients with esophageal cancer suffering from malnutrition in terms of albumin, prealbumin and total lymphocyte counts were 10.7, 55.8 and 27.2%, respectively (4). Therefore, patients with hypopharyngeal-laryngeal and esophageal cancers will often receive nasogastric intubation or percutaneous endoscopic gastrostomy for better feeding and care (5).

A nasogastric tube is a thin, soft tube that is inserted through the nose, down the throat and into the stomach. These tubes are used to feed formulas to children who cannot receive nutrition by mouth. A gastrostomy tube, also commonly known as a G-tube, is a thin, flexible tube that is inserted through the

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abdomen directly into the stomach. It is a medical device used to provide nutrition to individuals who are unable to eat or drink safely or adequately by mouth for various reasons. Worldwide, the results of studies on the effectiveness of nutritional support for patients through a nasogastric tube or gastrostomy tube are inconsistent, including both positive (6,7) and unconvincing results (8). Active nutritional support has yet to be used in a widespread manner, partly due to concerns about increased costs and time for nutritional interventions, and a shortage of nutritional experts. In addition, for this reason, in Vietnam, only a limited number of studies on nutritional intervention for patients with tube feeding have been conducted to date (9). Therefore, the present study was conducted with the aim of evaluating the efficacy of nutritional interventions in patients with hypopharyngeal-laryngeal and esophageal cancers subject to ongoing radiotherapy at Vietnam National Cancer Hospital in 2022.

Patients and methods

Ethics approval. The present study was approved by the Ethics Committee of Hanoi Medical University (Hanoi, Vietnam) under Decision No. 517/GCN-HDDNCYSH-DHYHN. It is understood that the study team provided the potential participants with study-related information on the contents and objectives of the study and sought their consent to participate by signing the consent form.

Location and time of study. The present study was carried out at the Head and Neck Radiation Department, General Radiation Department and Medical Oncology Department at Vietnam National Cancer Hospital (Hanoi, Vietnam) between January, 2021 and October, 2022.

Study methodology and participants. A controlled, one-group and two-group pre-test-post-test clinical interventional study was conducted on 64 patients with stage II, III or IV esophageal and hypopharyngeal-laryngeal cancers, from 18 years of age and older receiving the tubes, subject to the indications for radiotherapy and gastrointestinal nutrition at the Vietnam National Cancer Hospital. Patients with other concurrent chronic diseases, such as kidney failure, heart failure, liver failure, diabetes and patients received intravenous albumin or other forms of nutritional supplementation and patients with impaired consciousness were excluded from the study. All patients in the present study were male and ≥ 40 years of age. The patients participating in the study were divided into two groups based on age (40-59 years of age and >60 years), cancer type (hypopharyngeal-laryngeal and esophageal cancers), nutritional status (BMI from 16-16.99 kg/m², BMI from 17-18.49 kg/m², BMI from 18.5-24.99 kg/m²) and disease stage (II, III or IV); the intervention group received active nutritional support according to the regimen developed by the study team, while the control group followed the current normal diet at the hospital or the regular diet with meals prepared by their family. The efficacy of interventions at T0 (first week of radiotherapy) and T1 (week 5 of radiotherapy) were assessed according to biochemical indicators (albumin and prealbumin), anthropometric indicators (weight and height), and the PG-SGA tool for assessing the nutritional status of patients with cancer. The

PG-SGA assessment covers weight loss in 1 month prior and 6 months prior, servings per month, gastrointestinal symptoms, activities and functions in 1 month, and a physical examination (other comorbidities, metabolic demands, loss of subcutaneous fat, muscular atrophy and edema) and quality-of-life using the EORTC QLQ-C30 questionnaire [incorporating 30 questions with 5 scales: Functional scales (physical, role, cognitive, emotional and social), symptom scales (fatigue, pain, and nausea and vomiting), a global health status/QoL scale, and a number of other symptoms (dyspnea, insomnia, constipation, and diarrhea) and perceived financial impacts].

Content and plan of nutritional intervention. In the present study, patients in the intervention group were all subjected to 4-week nasogastric tube feeding with diets A and B. Each serving per patient was calculated to meet the energy demand of 30-35 kcal/kg of body weight/day, 12-20% protein per total energy and 2 g/day of eicosapentaenoic acid (EPA), as recommended by the Ministry of Health of Vietnam (10). The diets were as follows: Serving A: A 250 ml serving contains and provides 250 kcal, 9.5 g protein and 320 mg EPA. Serving B: A 200 ml serving contains and provides 300 kcal, 16.5 g protein, 750 mg EPA, 1,140 mg omega-3, 2 g arginine and 0.25 g RNA. Both servings A and B were in the form of soup, do not need to be mixed with water, are manufactured by the Orgalife Nutritional Science Co., Ltd., and have a shelf life of 8 months.

Monitoring, assessing and adjusting the intervention plan. For the patients subjected to the ongoing treatment at the hospital, their diets were monitored on a daily basis and recorded in the food intake monitoring chart at the hospital. During the outpatient times, the patients received servings, and detailed instructions on the number of required servings to meet the recommended energy and nutrient needs, and the method of caregiving. Phone calls were made to patients once a week to monitor and assess tolerance and adjust diets if necessary. The nutritional status and quality of life were re-assessed after 4 weeks of intervention.

Data collection techniques and methods of assessment and judgement of results. The present study employed the hospital-based data collection technique using questionnaires including general information about the participants, the classification of nutritional risks using PG-SGA, and assessment of the nutritional status by anthropometry together with certain biochemical indicators.

The criteria of the World Health Organization (WHO) for BMI were used to determine the nutritional status of the patients (11) as follows: Overweight and obesity, BMI ≥ 25 ; normal, BMI 18.5-24.9; grade-I chronic energy deficiency (CED), BMI 17-18.49 (mild thinness); grade-II CED, BMI 16-16.99 (moderate thinness); and grade-III CED, BMI <16.0 (severe thinness).

Nutritional risk assessment was performed using the PG-SGA (as a nutritional status assessment tool for patients with cancer) (12) and was graded as follows: Nourished (PG-SGA A), mildly or moderately malnourished (PG-SGA B), or severely malnourished (PG-SGA C).

The levels of serum albumin were assessed as follows (13): Malnutrition, serum albumin levels of <3.5 g/dl; mild and moderate malnutrition, serum albumin levels from 2.8 to

<3.5 g/dl; and severe malnutrition, serum albumin levels <2.8 g/dl.

The levels of prealbumin were also assessed as follows (14): Normal range for prealbumin levels, from 0.2 to 0.4 g/l; prealbumin concentration <0.1 g/l, severe protein-energy malnutrition; prealbumin concentration of 0.1 to <0.17 g/l, moderate malnutrition; and a prealbumin concentration of 0.17 to <0.2 g/l, mild malnutrition.

The quality of life of patients was assessed as follows (15): Using the EORTC QLQ-C30 questionnaire (incorporating 30 questions with 5 scales: Functional scales, symptom scales, a global health status/QoL scale, and other symptoms and perceived financial impacts). Patients answered 30 questions on a level of 0-1-2-3. RawScore (RS) of each index=RS=(I1+I2+ ... In)/n; normalization score: Functional area score: Score=[1-(RS-1)/3] x100; symptom and financial domain score: Score=S=[(RS-1)/3] x100; comprehensive health domain score: Score=S=[(RS-1)/6] x100.

Statistical analysis. The collected data were cleaned and entered into the computer using Epidata 3.1 software. The analysis was performed using SPSS 22 software (IBM Corp.). The Chi-squared test, Fisher's exact test or Cramér's V test were used to analyze nominal data, and the unpaired t-test was used to analyze continuous variables. A value of $P<0.05$ was considered to indicate a statistically significant difference.

Results

The present study was conducted on 64 patients with hypopharyngeal-laryngeal and esophageal cancers divided into the control and intervention groups, predominantly middle-aged (≥ 40 years of age) and male (100%). As regards ethnicity, education level, occupation, area of residence and economic classification, there were differences between the intervention group and the control group, although the differences were not statistically significant (Table I). In the present study, the number of patients with esophageal cancer accounted for 75%, the highest rate, while those with hypopharyngeal-laryngeal cancers accounted for 25% ($P=0.999$). The participants mainly had these diseases at stage III, accounting for 65.6%, while those with stage II and IV disease accounted for 12.5 and 21.9%, respectively ($P=0.809$) (Table I). The difference between the control and intervention groups was insignificant in terms of cancer type and stage (Table I).

There was no statistically significant difference between the intervention and control groups in terms of the nutritional status of the patients according to PG-SGA, BMI, prealbumin and albumin indicators (Table II).

As demonstrated in Table III, in the intervention group, there were no statistically significant differences in the pre-and-post-intervention weight, BMI and prealbumin indicators of the patients. The PG-SGA indicator decreased from 22.8 ± 4.8 to 19.6 ± 5.0 ; i.e., the difference was statistically significant ($P=0.014$). The serum albumin indicator decreased from 39.7 ± 3.3 to 36.8 ± 7.3 g/l; i.e., the difference was statistically significant ($P=0.012$). In the control group, the weight of the patients decreased from 52.3 ± 7.1 to 50.7 ± 7.1 kg; i.e., the difference was statistically significant ($P<0.001$). The BMI of the patients in the control group decreased from 19.4 ± 2.2 to

18.8 ± 2.1 kg/m²; i.e., the difference was statistically significant ($P<0.001$). In the control group, the PG-SGA, albumin and prealbumin indicators exhibited insignificant variations; i.e., the difference was not statistically significant ($P>0.05$).

As demonstrated in Table IV, in the intervention group, the patients' weight increased by 0.5 ± 1.7 kg, while in the control group, the patients' weight decreased by 1.6 ± 1.9 kg, i.e., the difference was statistically significant ($P<0.001$). BMI in the intervention group increased by 0.2 ± 0.6 kg/m², whereas it decreased by 0.6 ± 0.7 kg/m² in the control group, i.e., the difference was statistically significant ($P<0.001$). This finding suggested that nutritional intervention could improve the nutritional status of the patients. Furthermore, in the control group, the rate of weight loss and decrease in BMI was 84.4% and the rate of weight gain was 9.4%. In the intervention group, the rate of weight loss and decrease in BMI was 37.5%, the rate of weight gain and BMI was 59.4%, with the difference being statistically significant (Table V).

As demonstrated in Table VI, in the intervention group, the patients had a stable quality of life and experienced an insignificant change. However, there was a marked improvement in sleep disorders, with a decrease from 42.7 ± 29.6 to 2.7 ± 0.5 points, i.e., the difference was statistically significant ($P<0.001$). In the control group, the symptoms tended to worsen with an increase from 31.9 ± 10.5 to 37.3 ± 11.9 points, i.e., the difference was statistically significant ($P=0.02$). In the control group, while there was an improvement in sleep disorders (decreasing from 46.9 ± 29.2 to 2.8 ± 0.4 points; resulting in a statistically significant difference), the symptoms that tended to worsen included fatigue (with an increase from 51.0 ± 14.6 to 59.0 ± 12.8 points), and vomiting and nausea (with an increase from 9.4 ± 17.9 to 19.3 ± 27.5 points), loss of appetite (with an increase from 31.3 ± 35.9 to 51.0 ± 31.7 points), with the differences being statistically significant ($P<0.05$).

As regards the quality of life of patients, an improvement was observed in the general symptoms of the patients in the intervention group (a decrease of 3.4 ± 11.9 points), while those in the control group tended to worsen (an increase of 5.5 ± 12.6 points). Specifically, fatigue decreased by 2.4 ± 18.0 points in the intervention group, whereas it increased by 8.0 ± 16.5 points in the control group; vomiting and nausea decreased by 7.3 ± 23.9 points in the intervention group, but increased by 9.9 ± 26.4 points in the control group, with the differences being statistically significant ($P<0.05$; Table VII).

Discussion

The present study was conducted on 64 patients with hypopharyngeal-laryngeal and esophageal cancers, divided into the control and intervention groups. The present study demonstrated that the percentage of patients with BMI-based malnutrition in both groups was 43.8%. The finding was higher than that of the study conducted by Chien at the National ENT Hospital (31%) (16) and lower than that of the study conducted by Tien on patients with esophageal cancer (53.3%) (9). When comparing the findings of the present study with those of other studies on the assessment of the BMI-based nutritional status of patients with cancer worldwide, it was found that the findings presented herein were relatively similar to those of the study by Bruzgielewicz *et al* (2) on 252 patients with

Table I. General information of the patients in the present study.

Characteristic	Intervention group (n=32), n (%)	Control group (n=32), n (%)	P-value
Sex			0.999 ^a
Male	32 (100)	32 (100)	
Age, years			0.999 ^a
40-59	14 (43.8)	14 (43.8)	
≥60	18 (56.2)	18 (56.2)	
Ethnicity			0.238 ^b
Kinh	29 (90.6)	32 (100)	
Other	3 (9.4)	0 (0)	
Educational level			0.301 ^c
Below high school	19 (59.4)	23 (71.9)	
High school	8 (25)	3 (9.4)	
Intermediate/college/university	5 (15.6)	5 (15.6)	
After university	0 (0)	1 (3.1)	
Occupation			0.305 ^c
Civil servant	2 (6.3)	2 (6.3)	
Farmer	19 (59.4)	20 (62.5)	
Worker	1 (3.1)	0 (0)	
Retired	9 (28.1)	5 (15.6)	
Other	1 (3.1)	5 (15.6)	
Area of residence			0.611 ^a
Countryside	18 (56.2)	20 (62.5)	
City	14 (43.8)	12 (37.5)	
Economic status			0.613 ^b
Poor or near poor	3 (9.4)	1 (3.1)	
Not classified	29 (90.6)	31 (96.9)	
	32 (100)	32 (100)	
Cancer type			0.999 ^a
Hypopharyngeal-laryngeal cancer	8 (25)	8 (25)	
Esophageal cancer	24 (75)	24 (75)	
Stage			0.809 ^c
II	4 (12.5)	4 (12.5)	
III	23 (71.9)	21 (65.6)	
IV	5 (15.6)	7 (21.9)	

Data were analyzed using the ^aChi-squared test, ^bFisher's exact test, or ^cCramér's V test.

hypopharyngeal-laryngeal cancers. Bruzgielewicz *et al* (2) demonstrated that patients with BMI-based malnutrition accounted for 41% (2). The reason for such a difference between studies was that the different types of cancer resulted in different rates of malnutrition, and the nutritional care conditions for patients are different but not similar territorially. The present study demonstrated that 100% of the patients participating in the study suffered from grade B and C nutritional risk, as assessed using PG-SGA. This finding was similar to that of the studies by Tien (9) and Pham Van *et al* (4), demonstrating that the rate of undernourished patients with esophageal cancer, as assessed using PG-SGA, reached 100% (9) and 81.5% (4), respectively. In the present study, the average albumin levels of patients at the baseline of

radiotherapy were 39.7 ± 3.3 and 40.7 ± 4.1 g/l, respectively and the rates of malnutrition were 6.3 and 9.4%, respectively, in the intervention and control groups, respectively, similar to that of the study of Tien (9), showing the average albumin of 40 g/l and the post-operative albumin malnutrition of 13.3% and the study of Hoa showing 10.4% of malnourished patients (17). This finding could be explained by the different timing of the studies and also consistent with the clinical features. Herein, the prealbumin levels of the patients at the baseline of radiotherapy were 23.3 ± 6.6 and 27.9 ± 9.0 mg/dl, respectively, and the proportion of prealbumin-based malnourished patients was 28.1 and 18.8%, respectively, in the intervention and control groups, respectively. According to the study by Hoa (17), the prealbumin levels of the patients after surgery on

Table II. Nutritional status of the patients at the pre-intervention phase.

Indicator	Nutritional status	Group		P-value
		Intervention group (n=32), n (%)	Control group (n=32), n (%)	
PG-SGA	PG-SGA B	14 (43.8)	19 (59.4)	0.211 ^a
	PG-SGA C	18 (56.3)	13 (40.6)	
BMI	Malnutrition (BMI <18.5)	14 (43.8)	14 (43.8)	0.999 ^a
	Normal (18.5 ≤ BMI <25)	18 (56.3)	18 (56.3)	
Prealbumin	Malnutrition (<0.2 g/l)	9 (28.1)	6 (18.8)	0.376 ^a
	Normal (≥0.2 g/l)	23 (71.9)	26 (81.3)	
Albumin	Malnutrition (<3.5 g/dl)	2 (6.3)	3 (9.4)	1 ^b
	Normal (≥3.5 g/dl)	30 (93.8)	29 (90.6)	

PG-SGA, Patient-Generated Subjective Global Assessment; BMI, body mass index. Data were analyzed using the ^aChi-squared test, or ^bFisher's exact test.

Table III. Effects of nutritional interventions on anthropometric indicators, PG-SGA and certain biochemical indicators.

Characteristic	Intervention group (mean ± SD)			Control group (mean ± SD)		
	T0	T1	P-value ^a	T0	T1	P-value ^a
Weight (kg)	52.4±5.3	52.9±5.4	0.109	52.3±7.1	50.7±7.1	<0.001
BMI (kg/m ²)	19.0±1.7	19.2±1.9	0.096	19.4±2.2	18.8±2.1	<0.001
PG-SGA	22.8±4.8	19.6±5.0	0.014	21.2±5.7	21.7±5.8	0.733
Albumin (g/l)	39.7±3.3	36.8±7.3	0.012	40.7±4.1	39.8±3.0	0.262
Prealbumin (mg/dl)	23.3±6.6	22.8±7.9	0.654	27.9±9.0	24.4±6.3	0.056

PG-SGA, Patient-Generated Subjective Global Assessment; BMI, body mass index; T0, pre-intervention; T1, post-intervention. ^aData were analyzed using the t-test. Values in bold font indicate statistically significant differences (P<0.05).

Table IV. Change of post-intervention anthropometric indicators and PG-SGA.

Characteristic	Intervention group (mean ± SD), T1-T0	Control group (mean ± SD), T1-T0	P-value ^a
Weight (kg)	0.5±1.7	-1.6±1.9	<0.001
BMI (kg/m ²)	0.2±0.6	-0.6±0.7	<0.001
PG-SGA	-2.5±5.6	0.4±7.2	0.065

PG-SGA, Patient-Generated Subjective Global Assessment; BMI, body mass index; T0, pre-intervention; T1, post-intervention. ^aData were analyzed using the t-test. Values in bold font indicate statistically significant differences (P<0.05).

day 7 were 18.5 mg/dl, while the rate of malnourished patients was 55.9%. According to the studies by Khan *et al* (18) in 2010 and Wu *et al* (19) in 2013, the mean prealbumin concentration was 22 and 21.7 mg/dl, respectively. The present study demonstrated a prealbumin concentration quite similar to that

Table V. Weight/BMI change rate before and after intervention.

Characteristic	Intervention group (%)	Control group (%)	P-value ^a
Weight/BMI gain	59.4	15.6	0.001
Maintain weight/BMI	3.1	6.3	
Weight/BMI loss	37.5	78.1	

^aData were analyzed using Cramér's V test.

in the studies by Khan *et al* (18) and Jang Wu Wu *et al* (19); however, the malnutrition rate was lower than that found by the study of Hoa (17), as our study was conducted at the baseline of radiotherapy, while the study of Hoa (17) was conducted on the patients who just had surgery.

The patients participating in the present study received nutritional interventions according to the Vietnamese Ministry of Health guidelines on nutritional care for cancer patients who are required to receive tube feeding. During active feeding and patient monitoring throughout our study, it was found that the patients can digest and absorb the nutritional regimens well.

Table VI. Characteristics and quality of life of the patients at pre- and post-intervention.

Aspect	Intervention group, (mean \pm SD)			Control group, (mean \pm SD)		
	T0	T1	P-value ^a	T0	T1	P-value ^a
General function	59.4 \pm 15.6	58 \pm 16.6	0.3	58.6 \pm 13.3	56.1 \pm 9.1	0.275
Symptom	37.5 \pm 14.5	34.1 \pm 12	0.117	31.9 \pm 10.5	37.3 \pm 11.9	0.020
Fatigue	58 \pm 17.6	55.6 \pm 15.5	0.451	51.0 \pm 14.6	59.0 \pm 12.8	0.010
Nausea and vomiting	20.3 \pm 24.2	13.0 \pm 18.3	0.095	9.4 \pm 17.9	19.3 \pm 27.5	0.042
Pain	45.8 \pm 16.4	43.8 \pm 19.7	0.458	43.2 \pm 20.2	40.6 \pm 24.3	0.556
Shortness of breath	29.2 \pm 23.6	24.0 \pm 25.7	0.169	27.1 \pm 27.4	30.2 \pm 24.5	0.557
Sleep disorders	42.7 \pm 29.6	2.7 \pm 0.5	<0.001	46.9 \pm 29.2	2.8 \pm 0.4	<0.001
Loss of appetite	45.8 \pm 43.0	44.8 \pm 34.5	0.908	31.3 \pm 35.9	51.0 \pm 31.7	0.022
Constipation	21.9 \pm 27.6	17.7 \pm 26.8	0.354	12.5 \pm 25.0	20.8 \pm 27.8	0.088
Diarrhea	4.2 \pm 14.0	2.1 \pm 11.8	0.161	6.3 \pm 15.7	2.1 \pm 11.8	0.255
Global health status/QoL	40.6 \pm 15.8	43.8 \pm 14.2	0.296	37.5 \pm 18	34.6 \pm 14.5	0.376
Financial impact	69.8 \pm 17.7	67.7 \pm 10.3	0.572	64.6 \pm 26.7	61.5 \pm 20.9	0.447

QoL, quality of life; T0, pre-intervention; T1, post-intervention. ^aData were analyzed using the t-test. Values in bold font indicate statistically significant differences ($P < 0.05$).

Table VII. Post-intervention changes in quality-of-life scores in terms of symptoms.

Characteristic	Intervention group, (mean \pm SD), T1-T0	Control group, (mean \pm SD), T1-T0	P-value ^a
General symptoms	-3.4 \pm 11.9	5.5 \pm 12.6	0.005
Fatigue	-2.4 \pm 18.0	8.0 \pm 16.5	0.019
Nausea and vomiting	-7.3 \pm 23.9	9.9 \pm 26.4	0.008
Pain	-2.1 \pm 15.7	-2.6 \pm 24.7	0.920
Shortness of breath	-5.2 \pm 20.9	3.1 \pm 29.8	0.200
Sleep disorder	-40.0 \pm 29.5	-44.1 \pm 29.0	0.576
Loss of appetite	-1.0 \pm 50.4	19.8 \pm 46.3	0.090
Constipation	-4.2 \pm 25.0	8.3 \pm 26.8	0.058
Diarrhea	-2.1 \pm 8.2	-4.2 \pm 20.3	0.592

T0, pre-intervention; T1, post-intervention. ^aData were analyzed using the t-test. Values in bold font indicate statistically significant differences ($P < 0.05$).

After 4 weeks of intensive nutritional intervention, in the intervention group, the patients' weight increased by 0.5 \pm 1.7 kg, while in the control group, the indicator decreased by 1.6 \pm 1.9 kg (with the difference being statistically significant; $P < 0.001$). BMI increased by 0.2 \pm 0.6 kg/m² in the intervention group, but decreased by 0.6 \pm 0.7 kg/m² in the control group (with the difference being statistically significant; $P < 0.001$). Radiotherapy in the head and neck areas and esophagus leads to marked adverse conditions, such as aphthous ulcer, bleeding and difficulty in the patients' eating ability, degrading eating ability, and increasing the need for tube feeding. The conventional nutritional care regimens with inadequate control over quantity and quality hinder the satisfaction of the nutritional needs of patients. The active nutritional interventions with the use of specialized nutritional products for tube feeding and in strict compliance with the nutritional recommendations of the Ministry of Health of Vietnam enabled the provision of

healthy diets with adequate energy and nutrients. As regards the PG-SGA score, that of the patients in the intervention group decreased from 22.8 \pm 4.8 to 19.6 \pm 5.0 points, indicating that their nutritional status had improved, compared with the score which increased from 21.2 \pm 5.7 to 21.7 \pm 5.8 points in the control group. These findings were similar to those of the study by Tien (9) on nutritional interventions for patients with esophageal cancer, demonstrating that there was a difference in the pre- and post-intervention PG-SGA scores. The findings in the present study were similar to those of the study of Yang *et al* (20) on oral nutritional intervention in patients with esophageal cancer undergoing radiotherapy in China. A survey of the intervention for patients with advanced-stage nasopharyngeal cancer also demonstrated that following nutritional intervention, patients in the intervention group had a higher weight than those in the control group (59.11 vs. 58.14 kg), with difference being statistically significant ($P = 0.036$) (21). The

study by Chitapanarux (22) examined nutritional intervention in 40 patients with head and neck cancer with chemo-radiotherapy. The patients were randomly divided into two groups, including group A (n=20 patients) receiving regular diets and regimen-based diets under counseling by a dietitian and group B (n=20 patients) with a regular diet supplemented with immune-enhancing nutrients and receiving dietary counseling by the same dietitian. The total body weight in patients in group A ($P<0.001$) exhibited a significant decrease, while the reduction in body weight was no significant in the patients in group B ($P=0.109$) (22). Cereda *et al* (23) conducted a study in Italy on clinical intervention for 159 patients with head and neck cancer receiving radiotherapy. The patients were randomly divided into two groups, including those receiving nutrition counseling combined with oral feeding (n=78) and receiving nutrition counseling alone without oral feeding (n=81) from the baseline of radiotherapy and continuing until 3 months after the end of radiotherapy. The results of that study revealed that body weight loss in the group with nutritional counseling combined with oral feeding was less than that in the group with nutritional counseling alone (mean difference of 1.6 kg; 95% CI, 0.5-2.7; $P=0.006$) (23).

In the present study, the findings after 4 weeks demonstrated that the patients in the intervention group had a stable quality of life and experienced insignificant changes, while there was an improvement in sleep disorders (with a statistically significant difference, $P<0.001$). In the control group, the symptoms tended to worsen (with a statistically significant difference; $P=0.02$). In the control group, whereas there was an improvement in sleep disorders was improved, the symptoms that tended to worsen included fatigue, vomiting and nausea, and loss of appetite (the differences were statistically significant; $P<0.05$). When comparing the two groups, the quality of life in terms of symptoms (including general symptoms, fatigue, and vomiting and nausea) of the patients in the intervention group improved. By contrast, that of the control group tended to worsen. The results of the present study were similar in many aspects to those of other domestic and foreign studies. Compared with various studies worldwide, the results of the present study were also similar to those of the study by Cereda *et al* (23) on patients receiving radiotherapy for head and neck cancers, also demonstrating that the group of patients receiving intervention nutrition exhibited an improvement in their quality of life ($P<0.001$). Ravasco *et al* (24) conducted a study on 75 patients with head and neck cancer receiving radiotherapy. The patients were randomly divided into three groups (25 patients per group), including patients in group 1 who followed the counseled diets with common food, patients in group 2 who followed normal diets in combination with supplements, and patients in group 3 who followed free dietary intake. Their study demonstrated that following radiotherapy, the score of the patients' quality of life had improved ($P<0.003$) proportional to the nutritional intake; specifically, the condition improved in groups 1 and 2 ($P<0.05$) and worsened in group 3 ($P<0.05$). Following 3 months of radiotherapy, patients in group 1 had an improved overall quality of life, while in those in groups 2 and 3, the overall quality of life worsened (24). Studies performed worldwide have also demonstrated that an association exists between nutritional status and the quality of life of adults, and that the nutritional status plays a crucial role and significantly influences the quality of life

of patients. Quality of life is one of the factors that could be improved and targeted by interventions (25-27).

In conclusion, the present study demonstrates that for patients with hypopharyngeal-laryngeal and esophageal cancers who are at a high risk of developing malnutrition, the active nutritional interventions during radiotherapy improve the nutritional status and improve sleep conditions of the patients.

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Availability of data and materials

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

Authors' contributions

All authors (BVH, HTTN, DDN, THN, LTTN and HTL) were involved in the conception and design of the study. BVH, HTTN and DDN performed the statistical analysis of the data. BVH, HTTN, DDN, THN and LTTN were involved in the investigative aspects of the study. BVH and HTN were involved in the interpretation of the data. BVH and HTTN were involved in the writing of the original draft of the manuscript. BVH, HTTN and HTL were involved in the writing, reviewing and editing of the manuscript. All authors have read and agreed to the published version of the manuscript. BVH and HTTN confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Hanoi Medical University (Hanoi, Vietnam) under Decision No. 517/GCN-HDDNCYSH-DHYHN, dated February 2, 2022. It is understood that the study team provided the potential participants with study-related information on the contents and objectives of the study and sought their consent to participate by signing the consent form.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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