Clinical and Translational Oncology
https://doi.org/10.1007/s12094-024-03640-z

RESEARCH ARTICLE

Effects of different nutritional support methods on nutritional status and immune function in patients undergoing radiotherapy for head and neck cancer

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Received: 11 June 2024 / Accepted: 22 July 2024

Abstract

Objective This study aimed to analyze the effects of different nutritional support methods on nutritional status and immune function of patients undergoing radiotherapy for head and neck cancer (HNC).

Methods Patients with HNC were divided into the control (nutritional counseling and routine dietary guidance), parenteral nutrition (PN) (PN support on top of the control group), enteral nutrition (EN) (EN support on top of the control group), and EN + PN (EN combined with PN and routine dietary guidance) groups. After nutrition evaluation, the four groups were subjected to radiotherapy and nutritional support. Body mass index (BMI), serum albumin (ALB), prealbumin (PA), transferrin (TRF), hemoglobin (Hb), CD^{3+}, CD^{4+}, CD^{8+}, CD^{4+}/CD^{8+}, natural killer (NK) and quality of life were compared among the four groups before radiotherapy and after radiotherapy dose irradiation completion. The incidence of adverse reactions was assessed and recorded at 2 weeks, 4 weeks and the end of radiotherapy.

Results The four groups experienced some degree of malnutrition during radiotherapy and the EN + PN group possessed the lowest degree of malnutrition. After radiotherapy dose irradiation completion (T1), the PN, EN, and EN + PN groups possessed improved BMI (21.42 ± 1.62, 21.40 ± 1.68, 22.98 ± 1.87 vs. 20.18 ± 1.32), serum ALB (31.59 ± 3.49, 32.24 ± 4.23, 37.58 ± 3.23 vs. 26.67 ± 3.03), PA (182.63 ± 13.57, 183.43 ± 14.19, 201.59 ± 10.53 vs. 165.36 ± 20.13), TRF (162.46 ± 24.34, 157.36 ± 18.58, 182.36 ± 20.37 vs. 137.56 ± 23.19), and Hb (128.54 ± 9.21, 125.36 ± 10.23, 140.26 ± 7.23 vs. 103.24 ± 9.47) levels, higher $CD3^+$ (63.59 ± 2.88, 63.25 ± 3.17, 66.54 ± 1.32 vs. 59.36 ± 3.24), $CD4^+$ (39.92 ± 3.16, 39.87 ± 3.23, 43.36 ± 2.87 vs. 37.12 ± 4.29), $CD4^+/CD8^+$ (1.80 ± 0.06, 1.78 ± 0.06, 2.07 ± 0.03 vs. 1.54 ± 0.10) and NK-cells (33.87 ± 3.62, 33.26 ± 3.59, 36.82 ± 3.19 vs. 27.36 ± 4.21) levels, lower $CD8^+$ (22.18 ± 1.07, 22.36 ± 1.04, 20.46 ± 1.09 vs. 24.09 ± 1.21) levels, and improved quality of life (79.97 ± 7.96, 80.13 ± 7.98, 91.78 ± 7.38 vs. 71.53 ± 11.70) versus the control group, and the EN + PN group possessed the most pronounced effects (All $P < 0.05$). During radiotherapy, the incidence of radiotherapy adverse reactions was increased with time ($P < 0.05$).

Conclusion PN and EN, alone or in combination, can improve the nutritional status, immune function and quality of life of patients undergoing radiotherapy for HNC, and PN combined with EN has the best improvement effect.

Keywords Head and neck cancer · Radiotherapy · Parenteral nutrition · Enteral nutrition · Parenteral nutrition combined with enteral nutrition

Introduction

Head and neck cancer (HNC) belongs to typical epithelial cancers of upper aerodigestive tracts and might contain neoplasms of salivary glands, thyroid, and soft tissues [1]. HNC is a disfiguring and deadly disease [2], since it is consisted of a heterogeneous group of malignancies that are hard to treat successfully [3]. Radiation therapy performs an important role in curative-intent treatments for HNC [4]. During the postoperative period, patients with HNC possess a high

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Published online: 18 August 2024

rate of complications that can raise the morbidity rate [5]. Patients with HNC often confront various nutritional challenges prior to, during, and after treatment owing to close proximity of cancer to organs which are crucial for normal eating function [6].

Malnutrition is a main issue in HNC patients and is resulted from lack of food intake because of dysphagia, odynophagia, and lack of appetite led by tumors [7]. Malnutrition occurs at any stage of the treatment in HNC patients. The effects of disorder burden and treatment side effects result in compromised quantity and quality of saliva and damaged swallowing function, leading to deleterious impact on the nutritional status. Optimizing nutrition status is of great importance, since malnutrition is negatively involved in treatment tolerance and outcomes, quality of life and survival [8]. Resultant malnutrition and significant weight loss in patients undergoing radiotherapy for HNC are recognized and preventable clinical concerns [9]. In addition, HNC patients tend to develop muscle atrophy and muscular dystrophy. There are data that low skeletal muscle mass (sarcopenia) in HNC patients is associated with radiotherapy-related side effects such as mucositis, dysphagia and xerostomia. Moreover, cisplatin toxicity is more severe in HNC patients with low skeletal muscle mass, resulting in a higher risk of dose-limiting toxicity and treatment interruption [10]. Radiotherapy-related toxic reactions and platinum-related side effects are more frequent in patients with myasthenia gravis than in non-myasthenic patients. Thus, myasthenia gravis may be a potential biomarker for predicting prognosis and treatment toxicity in head and neck squamous cell carcinoma [11]. Nutritional support and intervention is an integral part of HNC management [12]. Nutritional care, such as enteral nutrition (EN), performs a key role in managing patients with HNC [13]. Early EN is essential for enhancing recovery after surgery [14]. EN is commonly implemented to provide critically ill patients with nutrients [15]. Parenteral nutrition (PN) is a treatment intravenously delivering basic nutrients to patients that cannot meet their nutrition requirements through standard enteral feeding [16]. Supplemental PN for perioperative esophageal cancer patients can sustain the optimal nutritional status, reduce inflammatory stress responses, and improve immune function [17]. EN can be applied alone or in combination with PN [18]. In our paper, the study was focused on the impact of different nutritional support methods on patients undergoing radiotherapy for HNC. Consequently, this research was aimed at investigating the effects of PN and EN, alone or in combination, on the nutritional status and immune function of patients undergoing radiotherapy for HNC.

Materials and methods

Ethics statement

The written informed consent form was acquired from all patients and the study was under approval of the Ethic Committee of Northern Jiangsu People's Hospital Affiliated to Yangzhou University (approval number: 20211206).

Study subjects

A total of 128 HNC patients who received radiation therapy in the Oncology Department of Northern Jiangsu People's Hospital Affiliated to Yangzhou University from January 2022 to December 2022 were recruited for the investigation. Inclusion criteria: ① patients diagnosed with HNC by pathological examination and receiving radiation therapy for the first time; ② patients with normal mentality; ③ patients with certain literacy; ④ patients voluntarily participating in this study. Exclusion criteria: ① patients combined with cancer of other organs; ② patients with severe cardiac, hepatic and renal insufficiency; ③ patients with severe gastrointestinal diseases (severe intestinal obstruction, active bleeding, severe diarrhea, etc.); ④ patients allergic to enteral nutrients or other intolerable conditions; ⑤ patients with no high-risk factors for malnutrition (NRS-2002 score < 3) or with severe malnutrition intolerant of radiotherapy; ⑥ patients treated with immunotherapy that may affect the measurement of the immune function.

Grouping and general data

Combined with the patients' wishes and actual situation, the study subjects were grouped into the control group (nutritional counseling and routine dietary guidance), the PN group (PN support on top of the control group), the EN group (EN support on top of the control group), and the EN + PN group (EN combined with PN and routine dietary guidance), with 32 cases in each group. Gender, age, education, marriage, smoking, cancer site, clinical stage (TNM stage) and initial nutrition status of the respondents were asked, collected and recorded.

Treatment methods

The nutritional status of the four groups of the patients was assessed utilizing the Patient-Generated Subjective Global Assessment (SGA) [19] at the time of admission (0–3 for good nutrition, 4–5 for mild malnutrition, 6–8 for moderate malnutrition, and 9 or more for severe malnutrition). Dietary survey, laboratory examination, body composition analysis

and other means were conducted to clarify the type of malnutrition, and then the doctor formulated a radiotherapy program and started it in the corresponding parts. Nutritional support was given at the same time of radiotherapy. After completing the nutritional assessment, patients in the control group were given routine dietary guidance. According to the Dietary Guidelines for Chinese Residents Health Education Manual, the principles of diet and nutrition, dietary errors, dietary taboos, and examples of reference recipes were popularized, and patients were instructed to eat on their own. A dietary management file was established, and specific dietary instructions were provided according to the patients' dietary situation and tolerance level, including the amount of food to be eaten per day, the time of day, the number of times of day, and the choice of food types; patients in the PN and EN groups were referred to the nutritional treatment criteria in ESPEN [20], maintaining the target daily supply of energy at 30–40 kcal/kg (1kal = 4.186 kJ). Patients in the PN group were guided by conventional dietary instructions and were also given PN support, which mainly consisted of intravenous infusion of 1/5 forceps peptide, 1/5 compound amino acid injection, and 1/5 fat emulsion injection, plus potassium chloride, fat-soluble vitamins, 5% or 10% dextrose injection, saline, etc., for assistance; patients in the EN group: oral or tube feeding was the way of EN, i.e., EN (short peptide preparations, whole protein preparations) were given via the gastrointestinal route, and it could be formulated into liquid of a certain concentration in certain proportions, given in portions in a quantitative manner. Patients without feeding difficulties at the beginning of radiotherapy were selected to receive oral EN preparations, and if feeding difficulties appeared during the radiotherapy, they were changed to tube feeding [21]. PN and EN were given to patients in the EN + PN group at the same time, and the formulas of EN or PN were dynamically adjusted according to the patients' nutritional intake status.

Observation indicators

Nutritional status

Patients' body mass index (BMI) was assessed before radiotherapy (T0) and after radiotherapy dose irradiation (T1), and serum albumin (ALB), prealbumin (PA), transferrin (TRF), and hemoglobin (Hb) levels were measured after fasting venous blood collection. The nutritional status of each patient was assessed by SGA [19].

Immune function

Before radiotherapy and after radiotherapy dose irradiation, fasting venous blood specimens were collected from patients, and the contents of T-lymphocyte subpopulations CD^{3+}, CD^{4+}, CD^{8+}, and natural killer (NK) cells were measured by flow cytometry, and CD^{4+}/CD^{8+} values were counted.

Adverse reactions

The adverse reactions of patients after radiotherapy were measured and recorded in accordance with Common Terminology Criteria for Adverse Events [22]. The types of adverse reactions and the number of patients with adverse reactions in the four groups were observed and recorded at 2 weeks of radiotherapy, at 4 weeks of radiotherapy, and at the completion of radiotherapy dose irradiation.

Quality of life

The quality of life of the four groups of patients was assessed implementing the Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N) questionnaire [23] before and after radiotherapy, including emotional well-being (EWB, 0–24 points), functional well-being (FWB, 0–28 points), physical well-being (PWB, 0–28 points), social/family well-being (SFWB, 0–28 points), and additional concerns (HNS, 0–36 points), with a total score of 144 points [24, 25].

Statistics

SPSS 25.0 software was employed to analyze the data statistically. Numeration data were depicted as the number of cases (N) and statistical description was expressed by χ^2 test or Fishers exact probability method. Measurement data were presented as mean ± standard deviation. One-way analysis of variance (ANOVA) or two-way ANOVA was employed among multiple groups, with Tukey's test for post hoc test. $P < 0.05$ is an indicator of a statistically significant difference.

Results

General data

To explore the effects of different nutritional supports on the nutritional status and immune function of patients undergoing radiotherapy for HNC, we collected 128 cases of HNC patients undergoing radiotherapy in our hospital and grouped them according to their willingness and actual situation. The grouping and general data of the patients were displayed in Table 1. Comparison of the general data of patients in the four groups unearthed that no significant difference was found in the general data of the four groups of patients, which was comparable ($P > 0.05$).

Table 1 General data of subjects in the four groups

General data	Control ($n=32$)	EN ($n=32$)	PN ($n=32$)	EN + PN ($n=32$)	P
Gender					0.778
Male	17	19	16	15	
Female	15	13	16	17	
Age (years)	59.91 ± 9.47	61.19 ± 9.51	61.24 ± 9.08	61.19 ± 9.44	0.928
Education					0.921
Middle school and below	14	16	15	16	
High school	10	10	12	8	
University and above	8	6	5	8	
Marriage					0.762
Unmarried	1	0	2	1	
Married	26	24	22	25	
Divorced	5	8	8	6	
Smoking					0.526
Yes	21	18	22	17	
No	11	14	10	15	
Cancer sites					0.978
Oral cancer	10	8	10	11	
Nasopharyngeal carcinoma	12	13	9	11	
Laryngocarcinoma	4	6	5	3	
Esophageal cancer	3	3	6	4	
Hypopharyngeal carcinoma	3	2	2	3	
Clinical staging					0.932
Stage I	2	1	3	2	
Stage II	7	8	6	8	
Stage III	13	15	10	12	
Stage IV	10	8	13	10	
Nutritional status					0.943
Normal nutrition	19	17	17	16	
Mild malnutrition	9	12	10	13	
Moderate malnutrition	3	2	3	3	
Severe malnutrition	1	1	2	0	

Changes in nutritional indicators and the occurrence of malnutrition before and after radiotherapy

The patients were given nutritional support along with radiotherapy treatment. Patients' BMI was assessed before radiotherapy (T0) and after completion of radiotherapy dose irradiation (T1). Serum ALB, PA, TRF and Hb contents were measured after fasting venous blood collection. PG-SGA was utilized to measure the nutritional status of patients at the end of radiotherapy. The above data were recorded and compared, and it was found that at T0, no significant difference was found in BMI and serum ALB, PA, TRF, and Hb levels among the four groups ($P>0.05$); at T1, BMI and serum ALB, PA, TRF, and Hb contents of patients in the control, EN, and PN groups were lower versus those at T0, and the difference of BMI in the EN + PN group was not significant in comparison of T0 and T1 ($P<0.05$), with BMI and serum ALB, PA, TRF, and Hb contents in the EN, PN, and EN + PN groups higher versus those in the control group and those in the EN + PN group higher versus those in the EN and PN groups ($P<0.05$). No difference was found in BMI and serum ALB, PA, TRF, and Hb levels at T1 between the EN and PN groups ($P>0.05$) (Fig. 1; Table 2).

In terms of the incidence of malnutrition after radiotherapy, after radiotherapy, the comparisons revealed that patients in the EN, PN and EN + PN groups were all less malnourished versus those in the control group ($P<0.05$), and the incidence and degree of malnutrition in the EN + PN group were reduced in contrast with those in the EN and PN groups ($P<0.05$, Table 3).

Changes in immune function indicators before and after radiotherapy

Fasting venous blood specimen CD^{3+} (Fig. 2A), CD^{4+} (Fig. 2B), CD^{8+} (Fig. 2C), and NK (Fig. 2E) levels were

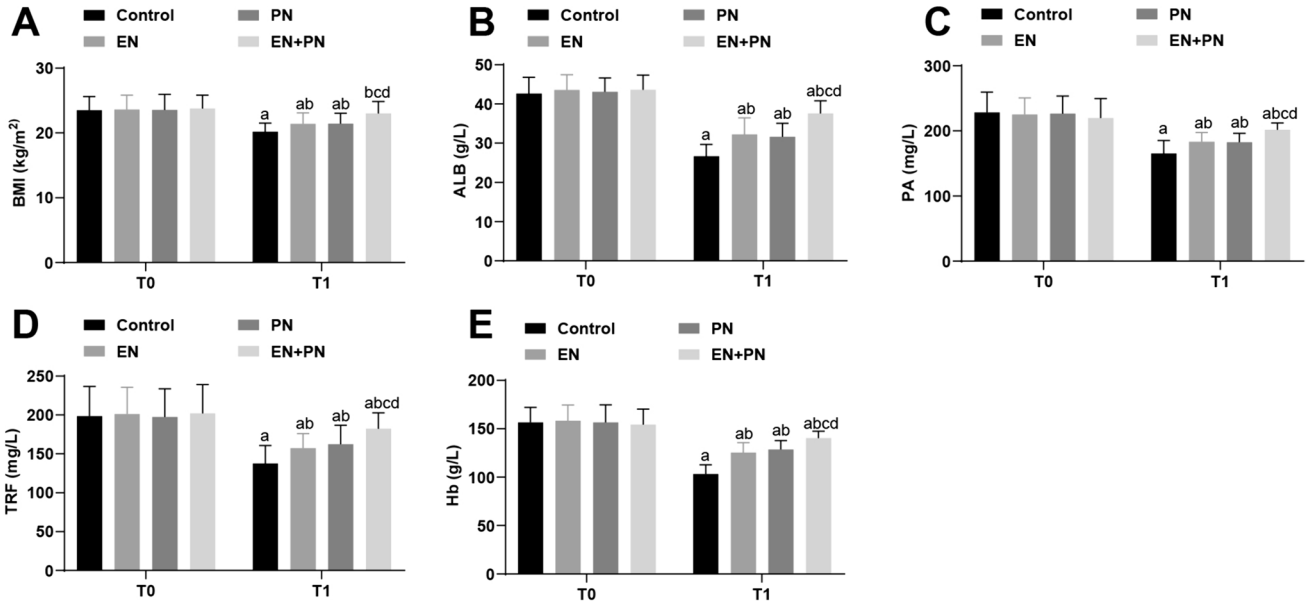

Fig. 1 Changes in nutritional indicators of patients before and after radiotherapy. **A** BMI in the four groups, **B** ALB levels in the four groups, **C** PA levels in the four groups, **D** TRF levels in the four groups, **E** Hb levels in the four groups. **a** Represented the comparison with the same group at T0; **b** Represented the comparison with the control group at T1; **c** Represented the comparison with the EN group at T1; and **d** Represented the comparison with the PN group at T1, $P < 0.05$

Table 2 Changes in nutritional indicators in patients before and after radiotherapy

Indicator	Time	Control	EN	PN	EN + PN
BMI (kg/m^2)	T0	23.49 ± 2.12	23.62 ± 2.20	23.54 ± 2.43	23.76 ± 2.05
	T1	20.18 ± 1.32^{a}	21.40 ± 1.68^{ab}	21.42 ± 1.62^{ab}	22.98 ± 1.87^{bcd}
ALB (g/L)	T0	42.63 ± 4.20	43.56 ± 3.87	43.06 ± 3.54	43.59 ± 3.77
	T1	26.67 ± 3.03^{a}	32.24 ± 4.23^{ab}	31.59 ± 3.49^{ab}	37.58 ± 3.23^{abcd}
PA (mg/L)	T0	228.25 ± 31.46	225.13 ± 25.58	226.32 ± 27.41	219.59 ± 30.12
	T1	165.36 ± 20.13^{a}	183.43 ± 14.19^{ab}	182.63 ± 13.57^{ab}	201.59 ± 10.53^{abcd}
TRF (mg/L)	T0	198.54 ± 38.23	201.23 ± 34.57	197.36 ± 36.25	202.01 ± 37.12
	T1	137.56 ± 23.19^{a}	157.36 ± 18.58^{ab}	162.46 ± 24.34^{ab}	182.36 ± 20.37^{abcd}
Hb (g/L)	T0	156.35 ± 15.76	158.21 ± 16.32	156.47 ± 18.32	154.23 ± 15.99
	T1	103.24 ± 9.47^{a}	125.36 ± 10.23^{ab}	128.54 ± 9.21^{ab}	140.26 ± 7.23^{abcd}

Note: $^{a}P < 0.05$ vs the same group at T0, $^{b}P < 0.05$ vs the Control group at T1, $^{c}P < 0.05$ the EN group at T1, and $^{d}P < 0.05$ the PN group at T1

Table 3 Malnutrition in patients after radiotherapy

Group	Normal nutrition	Mild malnutrition	Moderate malnutrition	Severe malnutrition
Control ($n = 32$)	4	6	9	13
EN ($n = 32$)^{a}	10	10	8	4
PN ($n = 32$)^{a}	11	8	7	6
EN + PN ($n = 32$)^{a,b,c}	17	10	4	1

Note: $^{a}P < 0.05$ vs the control group, $^{b}P < 0.05$ vs the EN group, and $^{c}P < 0.05$ the PN group

collected from the patients before radiotherapy (T0), and after completion of radiotherapy dose irradiation (T1), and CD^{4+}/CD^{8+} (Fig. 2D) values were calculated. The above data were recorded and compared, and we found that at T0, no significant difference presented in CD^{3+}, CD^{4+}, CD^{8+}, CD^{4+}/CD^{8+} and NK levels among the four groups ($P > 0.05$); serum CD^{3+}, CD^{4+}, and CD^{4+}/CD^{8+} contents were raised in the EN, PN, and EN + PN groups, while the contents of CD^{8+} was lower versus that at T0, and the contents of NK was higher in the EN + PN groups

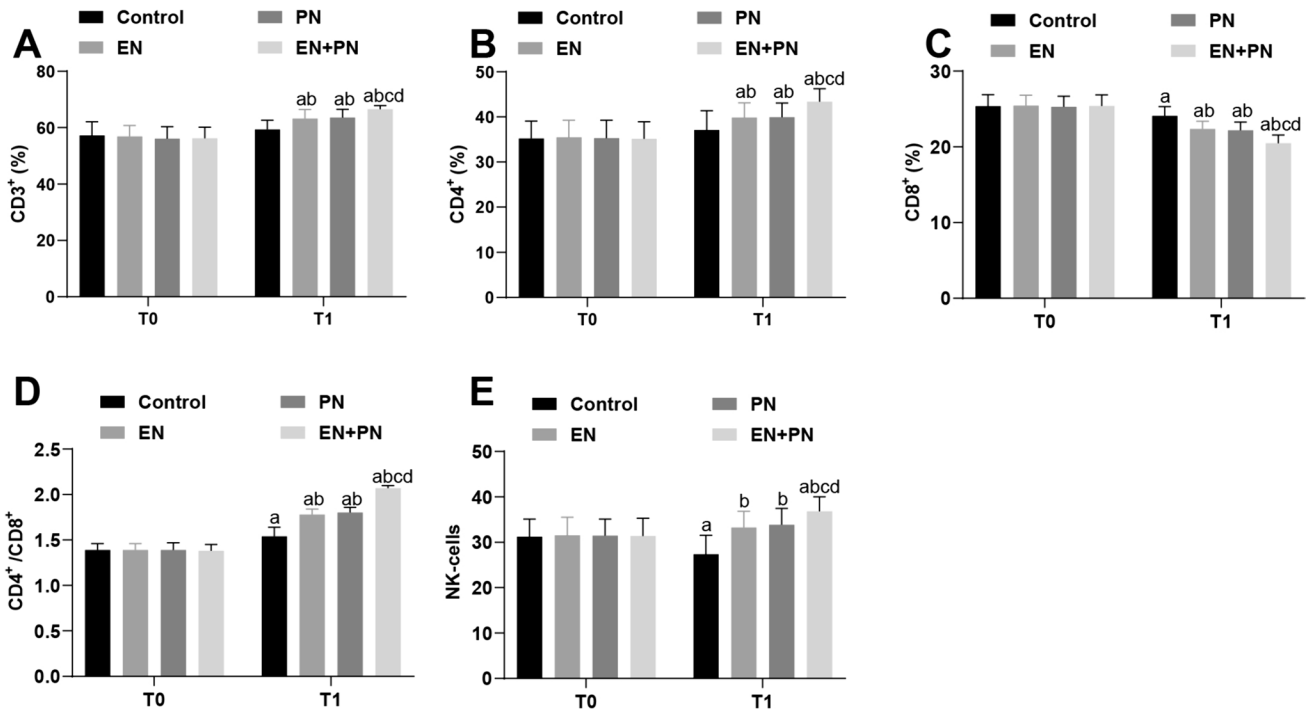

Fig. 2 Changes in immune function indicators of patients before and after radiotherapy. **A** CD^{3+} levels in the four groups; **B** CD^{4+} levels in the four groups; **C** CD^{8+} levels in the four groups; **D** CD^{4+}/CD^{8+} levels in the four groups; **E** NK levels in the four groups. **a** Represented the comparison with the same group at T0; **b** Represented the comparison with the control group at T1; **c** Represented the comparison with the EN group at T1; and **d** represented the comparison with the PN group at T1, $P < 0.05$

($P < 0.05$). Comparing between groups, the levels of CD^{3+}, CD^{4+}, CD^{4+} /CD^{8+} and NK at T1 in the EN, PN and EN + PN groups were significantly higher than those in the control group, while the levels of CD^{8+} were lower than those in the control group ($P < 0.05$); the levels of CD^{3+}, CD^{4+}, CD^{4+} /CD^{8+} and NK at T1 in the EN + PN group were higher than those in the EN and PN groups, while the levels of CD^{8+} were lower than those of EN and PN groups ($P < 0.05$); there was no significant difference in the comparison of CD^{3+}, CD^{4+}, CD^{4+} /CD^{8+} and NK levels between EN and PN groups ($P > 0.05$) (Table 4).

Adverse reactions

The types of adverse reactions and the number of patients with adverse reactions in the four groups at 2 weeks of radiotherapy, at 4 weeks of radiotherapy and at the completion of radiotherapy dose irradiation were observed and recorded.

Table 4 Changes in immune function indicators before and after radiotherapy

Indicator	Time	Control	EN	PN	EN + PN
$CD3^+$ (%)	T0	57.23 ± 4.87	56.89 ± 3.87	56.12 ± 4.23	56.21 ± 3.98
	T1	59.36 ± 3.24	63.25 ± 3.17^{ab}	63.59 ± 2.88^{ab}	66.54 ± 1.32^{abcd}
$CD4^+$ (%)	T0	35.23 ± 3.84	35.46 ± 3.79	35.26 ± 4.01	35.13 ± 3.79
	T1	37.12 ± 4.29	39.87 ± 3.23^{ab}	39.92 ± 3.16^{ab}	43.36 ± 2.87^{abcd}
$CD8^+$ (%)	T0	25.36 ± 1.52	25.43 ± 1.38	25.29 ± 1.40	25.40 ± 1.47
	T1	24.09 ± 1.21^{a}	22.36 ± 1.04^{ab}	22.18 ± 1.07^{ab}	20.46 ± 1.09^{abcd}
$CD4^+/CD8^+$	T0	1.39 ± 0.07	1.39 ± 0.07	1.39 ± 0.08	1.38 ± 0.07
	T1	1.54 ± 0.10^{a}	1.78 ± 0.06^{ab}	1.80 ± 0.06^{ab}	2.07 ± 0.03^{abcd}
NK-cells	T0	31.23 ± 3.87	31.50 ± 4.01	31.42 ± 3.67	31.39 ± 3.92
	T1	27.36 ± 4.21^{a}	33.26 ± 3.59^{b}	33.87 ± 3.62^{b}	36.82 ± 3.19^{abcd}

[a] represented the comparison with the same group at T0; [b] represented the comparison with the control group at T1; [c] represented the comparison with the EN group at T1; and [d] represented the comparison with the PN group at T1, P < 0.05

At 2 weeks of radiotherapy, the difference in the number of adverse reactions among the four groups was not significant ($P > 0.05$) (Table 5).

At 4 weeks of radiotherapy, the difference in the number of adverse reactions occurring between the Control, EN and PN groups was not significant ($P > 0.05$), and the total number of adverse reactions in the EN + PN group was lower than that in the Control group ($P < 0.05$) (Table 6).

At the completion of radiotherapy dose irradiation, the total number of adverse reactions in the EN, PN and EN + PN groups was significantly lower than that in the Control group ($P < 0.05$), and the total number of adverse reactions in the EN + PN group was lower than that in the PN group ($P < 0.05$), and the difference with the EN group was not significant ($P > 0.05$) (Table 7).

Quality of life scores before and after radiotherapy

The quality of life of the four groups of patients was assessed before radiotherapy (T0) and after the completion of radiotherapy dose irradiation (T1) utilizing the FACT-H&N, which included EWB, FWB, PWB, SFWB, and HNS, with a score of 0 to 144. At T0, no significant difference was found in the comparison of all scores of the FACT-H&N scale in the four groups ($P > 0.05$), and at T1, all scores and total scores of the FACT-H&N in the four groups were reduced in comparison with those at T0 ($P < 0.05$). Moreover, all FACT-H&N scores and total scores of the PN, EN and EN + PN groups were higher versus those of the control group ($P < 0.05$), and all FACT-H&N scores and total scores of the EN + PN group were higher versus those of the PN and EN groups ($P < 0.05$), and no significant difference was found between the PN and EN groups ($P > 0.05$) (Fig. 3A–F; Table 8).

Discussion

HNC is a common malignancy around the world and consists of a diverse group of tumors that affects the upper aerodigestive tract [26]. HNC patients are at a high risk for malnutrition because of dysphagia from the tumor and treatment

Table 5 Adverse reactions at 2 weeks of radiotherapy

Group	Radiation esophagitis	Radiation oral mucositis	Radiation dermatiti	Bone marrow suppression	Radiation pneumonitis	Gastrointestinal reactions	Total
Control ($n = 32$)	2	0	2	1	1	3	9
EN ($n = 32$)	2	1	1	1	1	2	8
PN ($n = 32$)	2	1	0	1	1	2	7
EN + PN ($n = 32$)	1	0	1	2	0	3	7

Table 6 Adverse reactions at 4 weeks of radiotherapy

Group	Radiation esophagitis	Radiation oral mucositis	Radiation dermatiti	Bone marrow suppression	Radiation pneumonitis	Gastrointestinal reactions	Total
Control ($n = 32$)	6	2	3	3	2	4	20
EN ($n = 32$)	3	2	3	1	1	4	14
PN ($n = 32$)	3	1	1	2	2	2	11
EN + PN ($n = 32$)[a]	2	0	1	2	1	2	8

Note: [a]$P < 0.05$ vs the control group

Table 7 Adverse reactions at completion of radiotherapy dose irradiation

Group	Radiation esophagitis	Radiation oral mucositis	Radiation dermatiti	Bone marrow suppression	Radiation pneumonitis	Gastrointestinal reactions	Total
Control ($n = 32$)	10	4	3	4	3	6	30
EN ($n = 32$)[a]	7	3	3	3	1	4	21
PN ($n = 32$)[a]	5	2	2	3	2	3	17
EN + PN ($n = 32$)[a,b]	3	1	2	2	1	1	10

Note: [a]$P < 0.05$ vs the control group, [b]$P < 0.05$ vs the PN group

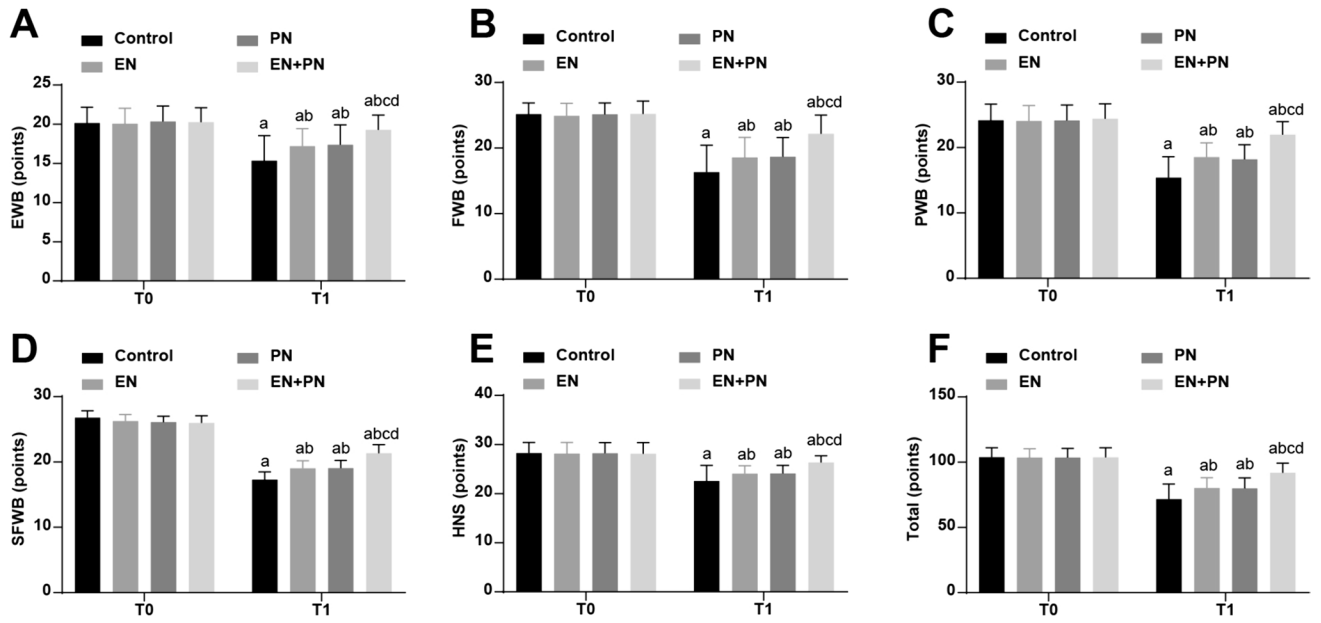

Fig. 3 Quality of life scores before and after radiotherapy. **A** EWB in the four groups; **B** FWB in the four groups; **C** PWB in the four groups; **D** SFWB in the four groups; **E** HNS in the four groups; **F** Total in the four groups. **a** Represented the comparison with the same group at T0; **b** Represented the comparison with the control group at T1; **c** Represented the comparison with the EN group at T1; and **d** Represented the comparison with the PN group at T1, $P < 0.05$

Table 8 Quality of life scores before and after radiotherapy

Indicator	Time	Control	EN	PN	EN + PN
EWB (points)	T0	20.16 ± 2.02	20.06 ± 1.97	20.34 ± 1.98	20.25 ± 1.87
	T1	15.34 ± 3.22[a]	17.19 ± 2.25[ab]	17.38 ± 2.54[ab]	19.28 ± 1.87[abcd]
FWB (points)	T0	25.16 ± 1.74	24.91 ± 1.92	25.13 ± 1.76	25.22 ± 1.95
	T1	16.31 ± 4.12[a]	18.56 ± 3.08[ab]	18.66 ± 2.94[ab]	22.16 ± 2.87[abcd]
PWB (points)	T0	24.16 ± 2.48	24.06 ± 2.38	24.13 ± 2.37	24.41 ± 2.27
	T1	15.38 ± 3.23[a]	18.53 ± 2.18[ab]	18.19 ± 2.25[ab]	21.97 ± 2.00[abcd]
SFWB (points)	T0	26.79 ± 1.06	26.25 ± 1.01	26.09 ± 0.93	25.97 ± 1.12
	T1	17.28 ± 1.20[a]	19.00 ± 1.19[ab]	19.03 ± 1.20[ab]	21.34 ± 1.31[abcd]
HNS (points)	T0	28.25 ± 2.18	28.16 ± 2.26	28.22 ± 2.17	28.13 ± 2.24
	T1	22.56 ± 3.19[a]	24.06 ± 1.62[ab]	24.09 ± 1.65[ab]	26.31 ± 1.42[abcd]
Total (points)	T0	103.75 ± 7.26	103.38 ± 6.90	103.56 ± 7.03	103.72 ± 7.38
	T1	71.53 ± 11.70[a]	80.13 ± 7.98[ab]	79.97 ± 7.96[ab]	91.78 ± 7.38[abcd]

[a] represented the comparison with the same group at T0; [b] represented the comparison with the control group at T1; [c] represented the comparison with the EN group at T1; and [d] represented the comparison with the PN group at T1, $P < 0.05$

[27]. This study focused on the effects of EN and PN on nutritional status and immune function of HNC patients undergoing radiotherapy.

As previously reported, PN is a life-sustaining treatment that provides nutrients for individuals with damaged intestinal tract function and enteral access challenges [28]. EN combined with PN improves nutrition intake at the acute phase of critical illness and is not inferior regarding the patients' results [29]. EN and/or total PN is administered for nutritional management at an early stage until resumption of oral intake after esophagectomy in accordance with the postoperative status of individual esophageal cancer patients [30]. PA refers to a small protein which has been widely evaluated as a nutritional and a prognostic marker [31]. Serum ALB and PA levels are associated with inflammatory and nutritional status [32]. It is also reported that BMI and Hb are useful biomarkers of malnutrition in older adults [33]. In our paper, we found that after completion of

radiotherapy dose irradiation, BMI and serum ALB, PA, TRF, and Hb contents of patients in the control, EN, and PN groups were lower. Patients in the EN, PN and EN + PN groups were all less malnourished than those in the control group, and the incidence and degree of malnutrition in the EN + PN group were lower in contrast with those in the EN and PN groups. Malnutrition and unintentional weight loss in HNC patients during and after the treatment are involved in poor treatment results, and elevated morbidity and mortality, even in overweight patients whose BMI is not suggestive of malnutrition [6]. The nutritional problems experienced by HNC patients need early nutritional evaluation and improved individually designed nutritional support [34]. In addition, previous studies performed on head and neck squamous cell carcinoma (HNSCC) report a reduction in the risk of death for both high CD^{4+} and high CD^{8+} tumor-infiltrating lymphocytes (TILs). High CD^{4+} TILs is related to better overall survival among oropharyngeal HNSCC [35]. In our study, it was found that after completion of radiotherapy dose irradiation, serum CD^{3+}, CD^{4+}, and CD^{4+}/CD^{8+} contents were raised in the EN, PN, and EN + PN groups, while the contents of CD^{8+} was lower, and the levels of NK was higher in the EN + PN groups.

Subsequently, we found HNC patients after radiotherapy had adverse reactions including radiation esophagitis, radiation oral mucositis, radiation dermatitis, bone marrow suppression, radiation pneumonia, and gastrointestinal reactions. During radiotherapy, the incidence of radiotherapy adverse reactions was increased with time. The total number of patients with adverse reactions in the EN, PN, and EN + PN groups was lower versus that in the control group. It is demonstrated that HNC treatment can substantially affect swallowing function, physical function, nutritional balance, and quality of life [36]. Usually, patients with HNC face functional changes because of the malignancy itself or the treatment [37]. It is revealed in a previous study that an 11-week structured workout program for HNC patients receiving chemo-radiotherapy helps in restoring their functional ability and quality of life [38]. In our paper, we found that all FACT-H&N scores and total scores of the PN, EN and EN + PN groups were higher versus those of the control group, and those of the EN + PN group were the highest.

In summary, this research demonstrates that PN and EN are effective in improving the nutritional status, immune function and quality of life of patients undergoing radiotherapy for HNC, and has the value of clinical promotion and application. This study lays a foundation to study the effects of PN and EN in HNC patients undergoing radiotherapy. Our study is based on limited clinical data, which is the main limitation of our research, and further exploration is necessary to further convince our findings.

Funding This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declarations

Conflict of interest statement The authors declare no conflicts of interest directly related to the contents of this article.

Ethical approval The written informed consent form was acquired from all patients and the study was under approval of the Ethic Committee of Northern Jiangsu People's Hospital Affiliated to Yangzhou University (approval number: 20211206).

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References

1. Georgopoulos R, Liu JC. Examination of the patient with head and neck cancer. Surg Oncol Clin N Am. 2015;24(3):409–21.
2. Horton JD, Knochelmann HM, Day TA, Paulos CM, Neskey DM. Immune evasion by head and neck cancer: foundations for combination therapy. Trends Cancer. 2019;5(4):208–32.
3. Spector ME, Farlow JL, Haring CT, Brenner JC, Birkeland AC. The potential for liquid biopsies in head and neck cancer. Discov Med. 2018;25(139):251–7.
4. Alterio D, Marvaso G, Ferrari A, Volpe S, Orecchia R, Jereczek-Fossa BA. Modern radiotherapy for head and neck cancer. Semin Oncol. 2019;46(3):233–45.
5. Barajas-Galindo DE, Vidal-Casariego A, Pintor-de la Maza B, Fernandez-Martinez P, Ramos-Martinez T, Garcia-Arias S et al. Postoperative enteral immunonutrition in head and neck cancer patients: impact on clinical outcomes. Endocrinol Diabetes Nutr (Engl Ed) 2020;67(1):13–19.
6. Ackerman D, Laszlo M, Provisor A, Yu A. Nutrition management for the head and neck cancer patient. Cancer Treat Res. 2018;174:187–208.
7. Brewczynski A, Jablonska B, Mrowiec S, Skladowski K. Rutkowski T Nutritional support in head and neck radiotherapy patients considering HPV status. Nutrients. 2020;13(1):57.
8. Cook F, Rodriguez JM, McCaul LK. Malnutrition, nutrition support and dietary intervention: the role of the dietitian supporting patients with head and neck cancer. Br Dent J. 2022;233(9):757–64.
9. Cady J. Nutritional support during radiotherapy for head and neck cancer: the role of prophylactic feeding tube placement. Clin J Oncol Nurs. 2007;11(6):875–80.
10. Erul E, Guven DC, Onur MR, Yazici G, Aksoy S. Role of sarcopenia on survival and treatment-related toxicity in head and neck cancer: a narrative review of current evidence and future perspectives. Eur Arch Otorhinolaryngol. 2023;280(8):3541–56.
11. Erul E, Guven DC, Ozbay Y, Altunbulak AY, Kahvecioglu A, Ercan F, et al. Evaluation of sarcopenia as a prognostic biomarker in locally advanced head and neck squamous cell carcinoma. Biomark Med. 2023;17(2):87–99.
12. Talwar B, Donnelly R, Skelly R, Donaldson M. Nutritional management in head and neck cancer: United

Kingdom National Multidisciplinary Guidelines. J Laryngol Otol. 2016;130(S2):S32–40.
13. Przekop Z, Milewska M, Szostak-Wegierek D, Panczyk M, Sobocki J. GLIM-defined malnutrition in patients with head and neck cancer during the qualification visit for home enteral nutrition. Nutrients. 2022;14(3):502.
14. Imai T, Saijo S, Fujii K, Nakazato A, Nakamura K, Miyakura Y, et al. Early enteral nutrition after head and neck surgery with free tissue transfer reconstruction. Auris Nasus Larynx. 2022;49(1):141–6.
15. Kim H, Stotts NA, Froelicher ES, Engler MM, Porter C. Why patients in critical care do not receive adequate enteral nutrition? A review of the literature. J Crit Care. 2012;27(6):702–13.
16. Wichman BE, Nilson J, Govindan S, Chen A, Jain A, Arun V, et al. Beyond lipids: novel mechanisms for parenteral nutrition-associated liver disease. Nutr Clin Pract. 2022;37(2):265–73.
17. Xu B, Chen H, Zhang Q, Chen P. Supplemental parenteral nutrition improves patient outcomes after esophageal cancer surgery: a single-center randomized controlled study. Medicine (Baltimore). 2022;101(47): e31893.
18. Stamenekovic D, Basic M, Palibrk I, Jankovic Z. Enteral nutrition and surgical patient. Acta Chir Iugosl. 2003;50(4):109–13.
19. Bauer J, Capra S, Ferguson M. Use of the scored patient-generated subjective global assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr. 2002;56(8):779–85.
20. Arends J, Bodoky G, Bozzetti F, Fearon K, Muscaritoli M, Selga G, et al. ESPEN guidelines on enteral nutrition: non-surgical oncology. Clin Nutr. 2006;25(2):245–59.
21. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z, E.W.G. Ad Hoc. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003;22(3):321–36.
22. Freites-Martinez A, Santana N, Arias-Santiago S, Viera A. Using the Common Terminology Criteria for Adverse Events (CTCAE - Version 50) to evaluate the severity of adverse events of anticancer therapies. Actas Dermosifiliogr (Engl Ed). 2021;112(1):90–2.
23. Campos JA, Spexoto MC, Serrano SV, Maroco J. Psychometric characteristics of the functional assessment of cancer therapy-general when applied to Brazilian cancer patients: a cross-cultural adaptation and validation. Health Qual Life Outcomes. 2016;14:8.
24. Amano K, Maeda I, Ishiki H, Miura T, Hatano Y, Tsukuura H, et al. Effects of enteral nutrition and parenteral nutrition on survival in patients with advanced cancer cachexia: analysis of a multicenter prospective cohort study. Clin Nutr. 2021;40(3):1168–75.
25. Furuta M, Yokota T, Tsushima T, Todaka A, Machida N, Hamauchi S, et al. Comparison of enteral nutrition with total parenteral nutrition for patients with locally advanced unresectable esophageal cancer harboring dysphagia in definitive chemoradiotherapy. Jpn J Clin Oncol. 2019;49(10):910–8.
26. Mody MD, Rocco JW, Yom SS, Haddad RI, Saba NF. Head and neck cancer. Lancet. 2021;398(10318):2289–99.
27. Raykher A, Russo L, Schattner M, Schwartz L, Scott B, Shike M. Enteral nutrition support of head and neck cancer patients. Nutr Clin Pract. 2007;22(1):68–73.
28. Derenski K, Catlin J, Allen L. Parenteral nutrition basics for the clinician caring for the adult patient. Nutr Clin Pract. 2016;31(5):578–95.
29. Hill A, Heyland DK, Ortiz Reyes LA, Laaf E, Wendt S, Elke G, et al. Combination of enteral and parenteral nutrition in the acute phase of critical illness: an updated systematic review and meta-analysis. JPEN J Parenter Enteral Nutr. 2022;46(2):395–410.
30. Hamai Y, Hihara J, Emi M, Ibuki Y, Kurokawa T, Yoshikawa T, et al. Prospective randomized trial of early postoperative enteral and total parenteral nutrition for treating esophageal cancer. Anticancer Res. 2021;41(12):6237–46.
31. Ranasinghe RN, Biswas M, Vincent RP. Prealbumin: The clinical utility and analytical methodologies. Ann Clin Biochem. 2022;59(1):7–14.
32. Li L, Li Z, Bi J, Li H, Wang S, Shao C, et al. The association between serum albumin/prealbumin level and disease severity in non-CF bronchiectasis. Clin Exp Pharmacol Physiol. 2020;47(9):1537–44.
33. Zhang Z, Pereira SL, Luo M, Matheson EM. Evaluation of blood biomarkers associated with risk of malnutrition in older adults: a systematic review and meta-analysis. Nutrients. 2017;9(8):829.
34. Sandmael JA, Sand K, Bye A, Solheim TS, Oldervoll L, Helvik AS. Nutritional experiences in head and neck cancer patients. Eur J Cancer Care (Engl). 2019;28(6): e13168.
35. Borsetto D, Tomasoni M, Payne K, Polesel J, Deganello A, Bossi P, et al. Prognostic significance of CD4+ and CD8+ tumor-infiltrating lymphocytes in head and neck squamous cell carcinoma: a meta-analysis. Cancers (Basel). 2021;13(4):781.
36. Hajdu SF, Wessel I, Dalton SO, Eskildsen SJ, Johansen C. Swallowing exercise during head and neck cancer treatment: results of a randomized trial. Dysphagia. 2022;37(4):749–62.
37. Makitie AA, Alabi RO, Orell H, Youssef O, Almangush A, Homma A, et al. Managing cachexia in head and neck cancer: a systematic scoping review. Adv Ther. 2022;39(4):1502–23.
38. Samuel SR, Maiya AG, Fernandes DJ, Guddattu V, Saxena PUP, Kurian JR, et al. Effectiveness of exercise-based rehabilitation on functional capacity and quality of life in head and neck cancer patients receiving chemo-radiotherapy. Support Care Cancer. 2019;27(10):3913–20.