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**Original Article** 

Nutritional counseling was insufficient to maintain dietary intake and nutritional status in head and neck cancer patients undergoing radiotherapy: A historical control study for future intervention in China



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# ABSTRACT

*Objective:* To determine whether nutritional counseling (NC) affects the dietary intake and nutritional status of head and neck cancer (HNC) patients undergoing radiotherapy (RT) in China. *Methods:* This historical control study enrolled 139 HNC patients in the NC group and 146 patients in the control group. Before RT, the latter received usual education about side effects. The former received three sessions (T<sub>1</sub>, before RT; T<sub>2</sub>, 3 weeks of RT; and T<sub>3</sub>, 6 to 7 weeks of RT) of individualized NC. Outcome measures were dietary intake, weight, body composition, and nutritional status. Generalized estimating equation (GEE) models were used to analyze intergroup differences. *Results:* The NC group had higher energy (P < 0.001) and protein intake (P = 0.003). However, some patients in the NC group still could not reach 60% of the recommended caloric goals (22.3% at T<sub>2</sub> and 32.4% at T<sub>3</sub>) or protein goals (23.0% at T<sub>2</sub> and 27.3% at T<sub>3</sub>). Although the NC group had a lower weight loss rate ( $\beta = -0.555$ , P = 0.037), they still lost  $6.15\% \pm 4.08\%$  of weight at T<sub>3</sub>. At T<sub>2</sub>, more patients in the control group lost  $\geq 5\%$  of weight (26.0% vs 15.8%, P = 0.049). More patients in the control group had malnutrition (P = 0.045), but 77% of the NC group had malnutrition at T<sub>3</sub>.

*Conclusions:* NC could effectively improve dietary intake, weight loss, and malnutrition in HNC patients receiving RT. Nevertheless, only NC was insufficient to maintain adequate intake and well-nourished status. We should adopt intensive nutritional intervention with a multidisciplinary team to enhance patients' nutritional status.

# Introduction

Head and neck cancer (HNC) is one of the most prevalent cancers in the world.<sup>1</sup> Radiotherapy (RT) is a mainstay of treatment for HNC patients,<sup>2</sup> which is based on lethal damage to single- and double-stranded DNA caused by the interaction of radiation with molecular oxygen, which produces superoxide, hydrogen peroxide, and hydroxyl radicals. Many patients experience treatment-related side effects, such as mucositis, pain, taste alteration, and loss of appetite, that can further damage their dietary intake and capability to absorb adequate amounts of required nutrients and energy.<sup>3</sup> Indeed, up to 74% of patients were malnourished at the end of RT.<sup>4</sup> The leading nutritional issue in cancer

patients is malnutrition with variant protein–energy lacking.<sup>5</sup> As such, outpatients are predisposed to a variety of caloric and protein deficits, which are serious and contribute to malnutrition. On the other hand, this undernourishment developed and deteriorated during RT, reflecting a decrease in food intake. During RT, diminished food intake resulted in the loss of body weight.<sup>6</sup> Weight loss has been shown to be a major predictor of poor cancer treatment response and survival, and patients with a lower body weight experienced more severe toxicity during RT.<sup>7</sup>

Nutritional counseling (NC) plays an important role in patients with chronic diseases, especially in cancer patients.<sup>8,9</sup> During disease development and anticancer treatments, patients can benefit from NC and dietary modification to ensure sufficient nutritional intake. A study of NC

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in HNC patients showed that replacing insoluble fiber with soluble fiber improves weight maintenance but not quality of life (QOL).<sup>10</sup> In another study, it was reported that during nutritional management, fewer patients lost more than 5% of their body weight compared to those in the control group.<sup>11</sup> Furthermore, it was shown that weight could be maintained with improved dietary compliance.<sup>12</sup> Several randomized controlled trials (RCTs) have found that nutritional intervention could improve the dietary intake of cancer patients.<sup>13,14</sup> A systematic review in patients with HNC showed that NC could improve energy intake but not reduce weight loss.<sup>17</sup> One study reported that nutritional advice plus oral nutritional supplementation (ONS) could help weight maintenance and protein-calorie intake.<sup>18</sup> Another report from southern China indicated that NC, combined with head and neck exercises, had beneficial effects on fatigue.<sup>19</sup> Therefore, improved nutritional status by NC is beneficial to maintain energy and physical strength and improve the quality of life that has been affected by therapies.

Our previous prospective observational research <sup>20,21</sup> has shown that Chinese HNC patients experienced prevalent nutritional problems during RT, but no reasonable intervention has yet been offered. NC is the first and basic step of stepwise nutritional interventions.<sup>22</sup> However, there is a lack of practical evidence that the NC is effective in HNC patients undergoing RT in China. Furthermore, these patients may not have easy access to specific dieticians for evaluation and treatment due to hospital system characteristics.<sup>23</sup> Moreover, current rational intervention measures and RCTs are limited in China. Therefore, this study aimed to provide preliminary evidence of practical outcomes in terms of energy consumption, weight and body composition in HNC patients with NC during RT.

### Methods

# Study design and participants

This was a historical control study evaluating NC on the outcome measures—weight loss and nutritional status as the primary outcome, while dietary intake and body composition change as the secondary outcome.

From November 2017 to July 2019, consecutive adult patients with HNC planning to accept intensity-modulated RT at one tertiary hospital were assessed for eligibility. Patients who accepted RT between November 2017 and July 2018 were in the control group, while those who accepted RT between October 2018 and July 2019 were in the NC group. Exclusion criteria were cognitive impairment or inability to communicate, distant metastasis, and receiving artificial nutrition support, including tube feeding or parenteral nutrition (PN). In the event of withdrawal, consultation, and measurements were stopped. Human Research Ethics Committees (No. IRB00001052-17002) of the authors' University approved the study. The STROBE guidelines were followed to report the research.

# Procedures

Patients in the control group were given education about side effects during regular doctor visits and had not received any other specific nutritional management. For these patients, data were obtained retrospectively from our previous longitudinal study. The NC group received NCs of three sessions during RT. The timing of the interventions was at  $T_1$  (baseline, 1 to 3 days before RT),  $T_2$  (in the middle of RT, 3 weeks after initiation), and  $T_3$  (the end of RT, 6 to 7 weeks after initiation).

## Nutritional counseling

Dietitians or oncology nurses who had been trained by nutritionists conducted the NC sessions in the NC group using a unified operation procedure. Rather than attempting to solve problems after they occurred,

the content of NC was designed to assist patients with potential side effects and food intake problems for adequate energy and protein intake before symptoms appeared. At the baseline session, (1) nutritional assessment was performed with dietary intake assessment, body weight measurement, and the Global Leadership Initiative on Malnutrition (GLIM) criteria<sup>24</sup> to evaluate patients' nutritional status and supervise the clarification of nutrition problems; (2) dietary advice pamphlets that contained beneficial nutritional information were included to help reduce RT-induced adverse effects that affect food intake behaviors, and (3) food selection and simple cooking methods were individually delivered according to their specific food reference, nutritional status, and environment.<sup>14,16</sup> At the follow-up sessions, (1) the nutritional condition was evaluated again with dietary intake assessment, body weight measurement, and GLIM criteria; (2) face-to-face nutrition advice and education were implemented by dietitians or trained nurses to reach targeted energy and protein goals of the European Society for Clinical Nutrition and Metabolism (ESPEN).<sup>25</sup> The average energy requirement was used to ensure energy intake, and the recommended energy requirement for patients was 25-30 kcal/kg/d and protein was 1.0-1.5 g/kg/d. (3) At the end of each NC session, NC executors would ask patients "Is there anything unclear or some other questions?" to verify patients' understanding of the content of NC. If patients had something unclear or questions, such as questions about food avoiding and how to prepare suitable food, we would clarify and give answers specifically. Hence, the pamphlet also provided recipes detailing specific antioxidant foods and traditional Chinese herbs to combat side effects. Each counseling session was implemented for 20-30 min.

#### Data collection

There were also three data collection points that were the same as the NC sessions: at baseline ( $T_1$ , 1 to 3 days before RT), at 3 weeks after RT initiation ( $T_2$ ), and at the end of RT ( $T_3$ , 6 to 7 weeks after RT initiation). At the first assessment point, sociodemographic information, dietary intake, body weight, body composition, and nutritional status were collected or assessed. At the following assessment points, dietary intake, body weight and body composition, and nutritional status were reassessed.

Sociodemographic including age, sex, marital status, etc., were assessed at baseline using a questionnaire-based interview. Clinical characteristics including RT type, tumor location, etc., were obtained from the patients' medical records.

Dietary intake was evaluated using a 24-h dietary recall via interviews by dietitians or trained nurses at  $T_1$ ,  $T_2$ , and  $T_3$  evaluations. They interviewed patients using 3-dimensional food models with portion size to help patients provide their food intake accurately and recorded food intake for each item during the last 24 h. Dietary recall records were entered into the Kang'ai system for the online dietary record, which incorporated the Chinese food nutrients table for the export amount of energy (kcal) and protein (g).

Bioelectrical impedance (BIA) (Inbody Co., LTD, Seoul, Korea) was used to determine body weight and body composition, including fat mass, fat mass index, fat-free mass, fat-free mass index (FFMI), appendicular skeletal muscle mass, and appendicular skeletal muscle mass index (ASMI). Briefly, patients were in the supine position, and foursurface standard electrodes were placed on the patient's hands and feet. The weight loss rate was calculated during treatment using the equation: weight loss rate = (baseline weight-present weight)/baseline weight  $\times$  100% and was categorized into 2 groups:  $\leq$  5%, > 5%.

Data about nutritional status have been prospectively collected before, including weight, body mass index (BMI), body composition, intake change, disease, and nutritional risk based on the Nutritional Risk Screening 2002 (NRS2002).<sup>20</sup> Then, we defined malnutrition using the GLIM criteria after it was published.<sup>24</sup> Its phenotypic criteria include low BMI (for age < 70 years, normal values were considered as BMI  $\geq$  20

kg/m<sup>2</sup>; for age  $\geq$  70, normal values were established as BMI  $\geq$  22 kg/m<sup>2</sup>), unintentional weight loss (in 6 months > 5%), and/or reduction of muscle mass based on FFMI and ASMI. The ESPEN cutoff values for FFMI were used, referring to reduced muscle mass for values < 17 kg/m<sup>2</sup> in men and < 15 kg/m<sup>2</sup> in women.<sup>24</sup> For ASMI, males with ASMI < 7.0 kg/m<sup>2</sup> and females with ASMI < 5.7 kg/m<sup>2</sup> were deemed to have muscle mass reduction according to the criteria of the Asian Working Group for Sarcopenia (AWGS).<sup>26</sup> The etiologic criteria include reduced intake and/or inflammatory response to the disease. To diagnose malnutrition, at least one phenotypic criterion and one etiologic criterion should be present in patients who already have nutritional risk.

# Data analysis

All statistical analyses were performed using the SPSS 24.0 program (SPSS Inc., Chicago, IL, USA). Mean  $\pm$  standard deviation (SD) was used to describe quantitative variables. With a skewed distribution, age, dietary intake, RT time and dosage were presented as the median and interquartile range (IQR). Categorical variables were expressed as a number and percentage. To compare the baseline characteristics of the two groups, a nonparametric Mann–Whitney test or Student's *t* test was used for quantitative variables, and for qualitative variables, a chi-square test was applied, as appropriate. We built generalized estimating equation (GEE) models with an exchangeable matrix to assess changes in repeated measures of dietary intake and nutritional status (weight, BMI, body composition, weight loss rate, GLIM) over time and their differences between groups. *P* < 0.05 was considered significant for two tails.

# Results

# Patient characteristics

A total of 520 patients were screened and 463 patients were enrolled, 234 of whom were in the NC group and 229 were in the control group. The questionnaires could not be obtained completely from three subjects in the control group. In terms of treatment discontinuation, 19 of the 234 (8.1%) patients in the control group discontinued treatment due to clinical adverse events versus 14 of the 229 (6.1%) patients in the NC group. With 131 (61 in the control group, 70 in the NC group) eligible

patients declining and 11 patients (5 in the control group, 6 in the NC group) changing the tube feeding/PN plan, ultimately 285 subjects were included for analysis (139 patients in the NC group and 146 patients in the control group; Figure 1).

Regarding baseline characteristics, there was no significant difference between the two groups (Table 1).

#### Primary outcomes

#### Weight loss

Compared to the baseline, the body weight and BMI in both control and NC groups decreased significantly during follow-up (Table 2). The weight and BMI in the two groups did not have significant differences during RT. Compared to the control group, patients in the NC group had a significant improvement in the weight loss rate from baseline to T<sub>3</sub>. However, they still lost an average of  $6.15\% \pm 4.08\%$  of baseline weight at the end of RT. At T<sub>2</sub>, more patients in the control group lost  $\geq 5\%$  of baseline weight (38/146, 26.0% vs 22/139, 15.8%;  $\chi^2 = 3.865$ , P =0.049). At T3, there was no significant difference between the proportions of patients who lost  $\geq 5\%$  of baseline weight in the two groups (103/146, 70.5% vs 84/139, 60.4%;  $\chi^2 = 2.797$ , P = 0.094).

#### Nutritional status by GLIM criteria

Table 3 presents the change in nutritional status during RT. More patients in the control group had malnutrition during RT (P = 0.045), but 77% of patients in the NC group were malnourished at T<sub>3</sub>.

# Secondary outcomes

# Dietary intake

Participants in the NC group had significantly higher daily standard energy and protein intake than participants in the control group during their RT, and more of the NC group patients reached the recommended caloric goals and protein goals (Table 4). Based on the ESPEN's guideline on gradual and step-by-step treatment, if patients' food taken cannot reach the 60% standard during the continuous first and second weeks, it is suggested to move to the next stage for nutritional support.<sup>25</sup> However, a considerable number of patients in the NC group during RT still could not reach 60% of the recommended caloric goals (22.3% at T<sub>2</sub> and 32.4%

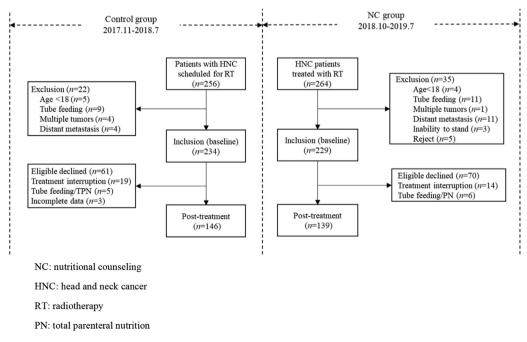


Figure 1. Patient eligibility of the control and NC group.

#### Table 1

Demographic and Clinical Characteristics.

Variable	Category	Control group $(n = 146)$	NC group ( <i>n</i> = 139)	$Z/t/\chi^2$	Р
Age (years) <sup>a</sup>		54.00 [24.00]	54.00 [20.00]	-0.385	0.700
Times of RT <sup>a</sup>		30.00 [3.00]	30.00 [3.00]	-1.441	0.150
RT dose (Gy) <sup>a</sup>		63.00 [7.00]	66.00 [7.00]	-1.494	0.135
T <sub>2</sub> Cumulative RT dose (Gy) <sup>a</sup>		31.50 [3.10]	29.70 [4.82]	-1.330	0.184
T <sub>3</sub> Cumulative RT dose (Gy) <sup>a</sup>		60.90 [7.84]	59.73 [6.94]	-1.713	0.087
Gender <sup>b</sup>	Male Female	96 (65.8) 50 (34.2)	87 (62.6) 52 (37.4)	0.188	0.665
Marital status <sup>b</sup>	Married	136 (93.2)	125 (89.9)	0.587	0.444
Tumor site <sup>b,d</sup>	Other Pharynx Oral cavity	10 (6.8) 59 (40.4) 55 (37.7)	14 (10.1) 62 (44.6) 49 (35.3)	0.516	0.773
Tumor stage <sup>b</sup>	Other I II III IV	32 (21.9) 8 (5.5) 16 (11.0) 30 (20.5) 83 (56.8)	28 (20.1) 10 (7.2) 15 (10.8) 24 (17.3) 77 (55.4)	1.703	0.790
Surgery <sup>b</sup>	Unsure Yes No	9 (6.2) 83 (56.8) 63 (43.2)	13 (9.4) 83 (59.7) 56 (40.3)	0.137	0.712
Inducive chemotherapy <sup>b</sup>	Yes No	35 (24.0) 111 (76.0)	26 (18.7) 113 (81.3)	0.882	0.348
Concurrent chemotherapy <sup>b</sup>	Yes No	61 (41.8) 85 (58.2)	67 (48.2) 72 (51.8)	0.941	0.332
Baseline DEI (kcal/kg/d) <sup>a</sup>		20.46 [9.22]	21.95 [11.16]	1.625	0.104
Baseline DPI (g/ kg/d) <sup>a</sup>		0.80 [0.46]	0.87 [0.52]	1.743	0.081
Baseline weight (kg) <sup>c</sup>		$65.01 \pm 12.38$	$65.47 \pm 11.93$	-0.316	0.752
Baseline BMI (kg/ m <sup>2</sup> ) <sup>c</sup>		$\begin{array}{c}\textbf{23.19} \pm \\\textbf{3.71}\end{array}$	$23.59 \pm 3.57$	-0.910	0.364
Baseline nutritional status	Well- nourished	110 (75.3)	115 (82.7)	1.917	0.166
According to GLIM <sup>b</sup>	Malnutrition	36 (24.7)	24 (17.3)		

BMI, body mass index; DEI, daily energy intake; DPI, daily protein intake; GLIM, Global Leadership Initiative on Malnutrition; RT, radiotherapy.

<sup>a</sup> Median [interquartile range], nonparametric Mann-Whitney test

<sup>b</sup> n (%), chi-square test

<sup>c</sup> Mean  $\pm$  standard deviation, Student's *t* test

<sup>d</sup> The tumor sites were divided into three categories: a) pharynx including nasopharyngeal cancer, oropharyngeal carcinoma, hypopharyngeal carcinoma and laryngeal cancer; b) oral cavity including oral cancer and salivary gland carcinoma; and c) all the others.

at  $T_3$ ) and 60% of the recommended protein goals (23.0% at  $T_2$  and 27.3% at  $T_3$ ), and these patients should be treated by superior nutritional intervention.

Table 2	
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Body Weight Change by GEE, *Mean*  $\pm$  *SD*.

## Body composition

Changes in body composition did not differ significantly between the two groups, and the body composition of patients in both the NC group and the control group lost significantly over time (Table 5).

# Discussion

In this study, compared with the control group, NC enhanced daily energy and protein intake and improved the weight loss rate and nutritional status during RT to a certain degree. Nevertheless, NC was insufficient to maintain adequate intake, weight, body composition, and nutritional status.

Various results of this study are significant to address. First, to our knowledge, this is the first study assessing weight change and the benefit of nutritional management among HNC patients treated with RT in Northern China. The prevalence of HNC has significant regional differences. For instance, as an important type of HNC, nasopharyngeal carcinoma has much higher incidence in the Southeast Asia according to the data published by International Agency for Research on Cancer (IARC) in 2020.<sup>27</sup> While in China, the Southern China has higher incidence because of gene and living habits,<sup>28</sup> so there are more studies conducted in that region but limited evidence in Northern China. Our findings provide a preliminary positive effect of NC in this population. Adequate food intake is a prerequisite for the maintenance of weight and nutritional status. The NC group consumed more food, and the number of patients who achieved the calorie and protein goals increased significantly after the intervention. The oral intake benefit of NC found in the intervention group was consistent with the finding of a meta-analysis that NC could significantly improve energy intake in malnourished or at risk of malnutrition cancer patients.<sup>17</sup> The study of Poulsen<sup>9</sup> also indicated that individual NC could improve protein and energy intake in cancer patients.

Weight loss is a crucial feature of malnutrition. In our study, both groups lost weight significantly during RT, but the weight loss rate was significantly improved in our NC group compared to the control group, which is consistent with the findings of an Italian RCT in HNC patients receiving (chemo) radiotherapy.<sup>29</sup> Furthermore, in terms of nutritional status identified by the newly developed GLIM, more patients in the control group had malnutrition during RT. From the clinical point of view, it is worth paying attention to the tendency that fewer patients interrupted their treatment plan (6.1% vs 8.1%), which is in line with other studies.<sup>29,30</sup> Thus, we can draw the preliminary conclusion that NC could exert a certain positive effect on patients' intake and nutritional status, which was in accordance with recent evidence that emphasized the multiple benefit of NC in cancer patients.<sup>31,32</sup>

Although NC was effective, participants in the NC group were unable to obtain sufficient dietary intake to maintain a stable weight and good nutritional status. First, more than half of participants were unable to meet the nutritional standard during RT, and a considerable proportion of patients in the NC group were unable to reach 60% of the recommended caloric goals (22.3% at  $T_2$  and 32.4% at  $T_3$ ) and 60% of the recommended protein goals (23.0% at  $T_2$  and 27.3% at  $T_3$ ). Second, even patients who received NC still lost a considerable proportion (6.15%  $\pm$  4.08%) of baseline weight at the end of RT. A retrospective observational study

Items	Time point	Control group ( $n = 146$ )	NC group ( <i>n</i> = 139)	Time Wald $\chi^2$	Р	Group Wald $\chi^2$	Р
Weight (kg)	T <sub>1</sub>	$65.01 \pm 12.38$	65.47 ± 11.93	595.794	< 0.001*	0.322	0.571
	$T_2$	$63.01\pm12.00$	$63.96 \pm 11.33$				
	T <sub>3</sub>	$60.40 \pm 11.33$	$61.30\pm10.77$				
BMI (kg/m <sup>2</sup> )	$T_1$	$23.19\pm3.71$	$23.59 \pm 3.57$	595.996	< 0.001*	1.349	0.245
	$T_2$	$\textbf{22.48} \pm \textbf{3.61}$	$23.01\pm3.42$				
	T <sub>3</sub>	$21.56 \pm 3.49$	$22.07 \pm 3.29$				
Weight loss rate (%)	$T_1$	0	0	708.052	< 0.001*	4.349	0.037*
	$T_2$	$3.04 \pm 3.38$	$2.18\pm2.62$				
	T <sub>3</sub>	$6.95\pm4.44$	$6.15\pm4.08$				

BMI, body mass index; GEE, generalized estimating equation; SD, standard deviation. \* Significant (P < 0.05).

#### Table 3

Nutritional Status Change by GEE, n (%).

Items	Time point	Category	Control group ( $n = 146$ )	NC group ( <i>n</i> = 139)	Time Wald $\chi^2$	Р	Group Wald $\chi^2$	Р
Nutritional status according to GLIM	T <sub>1</sub> T <sub>2</sub> T <sub>3</sub>	Well-nourished Malnutrition Well-nourished Malnutrition Well-nourished Malnutrition	110 (75.3) 36 (24.7) 65 (44.5) 81 (55.5) 26 (17.8) 120 (82.2)	115 (82.7) 24 (17.3) 75 (54.0) 64 (46.0) 32 (23.0) 107 (77.0)	186.288	< 0.001*	4.030	0.045*

GEE, generalized estimating equation; GLIM, Global Leadership Initiative on Malnutrition; WLR, weight loss rate.

\* Significant (P < 0.05).

# Table 4

Twenty four-hour Energy and Protein Intake by GEE.

Items	Time point	Control group ( $n = 146$ )	NC group ( <i>n</i> = 139)	Time Wald $\chi^2$	Р	Group Wald $\chi^2$	Р
DEI (kcal/kg/d) <sup>a</sup>	T1	20.46 [9.22]	21.95 [11.16]	28.032	< 0.001*	14.036	< 0.001*
	$T_2$	17.43 [9.13]	21.12 [11.50]				
	T <sub>3</sub>	16.39 [10.16]	19.64 [14.27]				
DPI (g/kg/d) <sup>a</sup>	$T_1$	0.80 [0.46]	0.87 [0.52]	2.169	0.338	8.634	0.003*
	T <sub>2</sub>	0.75 [0.46]	0.88 [0.65]				
	T <sub>3</sub>	0.70 [0.60]	0.87 [0.65]				
DEI reach goal <sup>b</sup>	$T_1$	40 (27.4)	42 (30.2)	1.579	0.454	8.296	0.004*
	T <sub>2</sub>	27 (18.5)	44 (31.7)				
	T <sub>3</sub>	26 (17.8)	47 (33.8)				
DPI reach goal <sup>b</sup>	$T_1$	43 (29.5)	53 (38.1)	1.935	0.380	10.868	0.001*
	T <sub>2</sub>	36 (24.7)	58 (41.7)				
	T <sub>3</sub>	43 (29.5)	63 (45.3)				
DEI reach 60% <sup>b,c</sup>	$T_1$	126 (86.3)	120 (86.3)	38.910	< 0.001*	7.669	0.006*
	T <sub>2</sub>	87 (59.6)	108 (77.7)				
	T <sub>3</sub>	85 (58.2)	94 (67.6)				
DPI reach 60% <sup>b,c</sup>	$T_1$	110 (75.3)	116 (83.5)	12.287	0.002*	6.789	0.009*
	$T_2$	98 (67.1)	107 (77.0)				
	T <sub>3</sub>	91 (62.3)	101 (72.7)				

DEI, daily energy intake; DPI, daily protein intake; GEE, generalized estimating equation.

\* Significant (*P* < 0.05).

<sup>a</sup> Median [Interquartile range]

<sup>b</sup> n (%).

<sup>c</sup> Intake goals: set according to the European Society for Clinical Nutrition and Metabolism (ESPEN) recommendation, energy was 25 kcal/kg/d and protein was 1.0 g/kg/d.

# Table 5

Body C	Composition	Change	by	GEE,	Mean $\pm$ SD.
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Items	Time point	Control group ( $n = 145$ )	NC group ( <i>n</i> = 136)	Time Wald $\chi^2$	Р	Group Wald $\chi^2$	Р
Fat mass (kg)	T <sub>1</sub>	$16.91 \pm 7.25$	17.77 ± 6.64	147.613	< 0.001*	2.035	0.154
	T <sub>2</sub>	$16.28\pm7.14$	$17.74 \pm 6.42$				
	T <sub>3</sub>	$15.46\pm 6.89$	$16.41 \pm 6.36$				
Fat mass index (kg/m <sup>2</sup> )	T <sub>1</sub>	$6.08 \pm 2.69$	$6.46 \pm 2.47$	148.262	< 0.001*	2.451	0.117
	T <sub>2</sub>	$5.85 \pm 2.66$	$6.44 \pm 2.41$				
	T <sub>3</sub>	$5.57 \pm 2.56$	$5.95 \pm 2.39$				
Fat free mass (kg)	$T_1$	$\textbf{48.25} \pm \textbf{8.52}$	$47.55\pm8.38$	292.911	< 0.001*	0.247	0.619
	T <sub>2</sub>	$\textbf{46.87} \pm \textbf{8.27}$	$46.21 \pm 7.95$				
	T <sub>3</sub>	$45.02\pm7.92$	$\textbf{45.00} \pm \textbf{7.62}$				
Fat free mass index (kg/m <sup>2</sup> )	$T_1$	$17.14 \pm 2.04$	$17.04 \pm 2.03$	303.973	< 0.001*	0.010	0.919
	T <sub>2</sub>	$16.63\pm2.01$	$16.56 \pm 1.95$				
	T <sub>3</sub>	$16.00 \pm 1.98$	$16.11 \pm 1.88$				
Skeletal muscle mass (kg)	$T_1$	$26.58 \pm 5.18$	$26.15 \pm 5.08$	286.736	< 0.001*	0.229	0.632
	T <sub>2</sub>	$25.81 \pm 5.00$	$25.42 \pm 4.81$				
	T <sub>3</sub>	$24.67 \pm 4.78$	$24.67 \pm 4.63$				
Skeletal muscle mass index (kg/m <sup>2</sup> )	$T_1$	$9.43 \pm 1.30$	$9.36 \pm 1.28$	298.704	< 0.001*	0.016	0.900
	T <sub>2</sub>	$9.15 \pm 1.26$	$9.10 \pm 1.23$				
	T <sub>3</sub>	$8.75 \pm 1.23$	$\textbf{8.82} \pm \textbf{1.19}$				

\* Significant (*P* < 0.05).

showed that patients who received early or late NC lost 4.8% and 5.6% of weight, respectively.<sup>33</sup> Third, at T<sub>3</sub>, 60.4% of the NC group lost  $\geq$  5% of baseline weight, and 77% of them were diagnosed with malnutrition using the GLIM, which was lower than other studies.<sup>29,34</sup> Critical weight loss and malnutrition have been associated with impaired survival.<sup>35,36</sup> Consistent with other recommendations,<sup>11,37,38</sup> NC should be given before radiation and during every follow-up between baseline and end of RT when RT-related side effects usually appear; weight and nutritional

status should be assessed by healthcare professionals on a regular basis once weight loss begins in order to maximum the benefits of NC.

In addition, there were no significant changes in other nutritional measures, including weight, BMI, and body composition, between the NC group and the control group. The results of one meta-analysis also suggested that dietary advice has no effect on body weight in cancer patients who are malnourished.<sup>17</sup> A RCT performed in patients with metastatic colorectal cancer undergoing chemotherapy showed that NC had a

positive impact on weight but could not improve the change in muscle mass.<sup>39</sup> This was partially a result of difficulties the patients faced in achieving the intake goals. On the one hand, cancer patients may experience a variety of treatment-related side effects that can impede the intake, digestion, or absorption of food.<sup>16</sup> On the other hand, patients could consume much more energy during treatment. Therefore, even though the NC group had a relatively higher dietary intake, they still could not obtain adequate intake and could encounter serious nutritional problems.

Therefore, NC had a limited benefit in terms of helping HNC patients in maintaining a good nutritional level during RT. According to the current nutritional management research, there is a lack of practical nutritional management in China (such as the low level and low acceptance of tube feeding).<sup>40</sup> Only 20 patients in our study received tube feeding among all of these patients scheduled for RT. In the future, we should focus more on step-by-step nutritional treatment, form a multidisciplinary team and develop more comprehensive nutritional intervention plans that includes the artificial nutrition applications to help maintain patients' intake, weight, body composition, and nutritional status.

There are several limitations in out study. First, set in a historical control design with not many samples, the benefits of NC among patients with HNC undergoing RT should be tested by large RCTs in China in the future. Second, other factors such as side effects (e.g., appetite loss, pain, etc.) that could affect intake or nutritional status should be considered when investigating the relationship between NC and patient outcomes in future research. Additionally, in future intervention plans, healthcare professionals can integrate symptom management with nutritional management. Third, many participants did not complete the study, so data for some outcome variables were missing. Finally, we did not follow patients for a longer period of time after their treatments, and the results cannot be extended to stages after RT.

#### Conclusions

In conclusion, based on the clinical practice setting, this study indicated that NC could effectively improve energy intake and further mitigate the weight loss rate and malnutrition in HNC patients receiving RT. Nevertheless, only NC was insufficient to maintain adequate dietary intake, stable weight and body composition, and nutritional status. To improve the nutritional status of HNC patients during radiation therapy, healthcare professionals in China should implement a stepwise, intensive, and more comprehensive nutritional management strategy through a multidisciplinary team in the future.

## Author contributions

Yujie Wang: data analysis, interpretation of data. Dan Zhao: patients' enrollment and acquisition of data. Lichuan Zhang, Tong Zhang, Yan Sun, Shaowen Xiao, Yaru Zhang, Liqing Gong: acquisition of data. Qian Lu: editing and proofreading. Qian Lu, Weihu Wang: supervision.

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# Conflict of interest statement

None declared.

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