

# Nutritional status and body composition of patients with head and neck cancer treated with perioperative evidence-based nutritional management

Zhen Ding,<sup>1</sup> Lingmei Zhou,<sup>1</sup> Yan Zhou,<sup>2</sup> Kemei Jin,<sup>1</sup> Runjinxing Wu,<sup>1</sup> and Yihua Gui<sup>2,\*</sup>

<sup>1</sup>Clinical Nutrition Department and <sup>2</sup>Department of Otolaryngology, Head and Neck Surgery, Ningbo Medical Center Li Huili Hospital, Zhejiang Province, 315000, China

(Received 22 February, 2024; Accepted 4 May, 2024; Released online in J-STAGE as advance publication 21 May, 2024)

We aimed to describe nutritional status and body composition profiles perioperative head and neck cancer (HNC) patients managed with whole-course nutritional support. Scored Nutritional Risk Screening (NRS 2002), Patient-Generated Subjective Global Assessment (PG-SGA), and body composition were conducted. The factors related to weight loss and skeletal muscle mass (SMM) were identified. Lower weight and body composition levels in low skeletal muscle index ( $SMI \leq 9.90 \text{ kg/m}^2$ ) group were observed. Levels of albumin, prealbumin, prognostic nutritional index (PNI), and lymphocyte-to-monocyte ratio (LMR) were lower than pre-operative, but the values after 2 weeks were higher than 1 week post-operatively (all  $p < 0.01$ ). The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were increased at 1 and 2 weeks post-operative compared to pre-operative (both  $p < 0.01$ ). Post-operatively, NLR at 2 weeks was lower than 1 week ( $p = 0.02$ ). A negative correlation was observed between SMM loss and serum prealbumin ( $r = -0.255$ ,  $p = 0.029$ ). Pre-operative BMI ( $p < 0.01$ ), tumor differentiation ( $p = 0.003$ ), and nutritional risk ( $p = 0.049$ ) were risk factors for weight loss. In conclusions, for perioperative HNC patients, loss of adipose tissue occurred earlier than muscle. Prealbumin should be considered as an indicator for monitoring of recovery in clinical practice.

**Key Words:** head and neck cancer, nutrition status, perioperative period, body composition, weight loss

Head and neck cancers (HNCs) are tumors of the larynx, oral cavity, salivary glands, and nasal and paranasal sinuses.<sup>(1)</sup> Surgery and radiotherapy, sometimes combined with chemotherapy, are the primary treatment approaches.<sup>(2)</sup> Tumors consume many nutrients during development, resulting in metabolic disorders and reduced food intake,<sup>(3-5)</sup> leading to increased malnutrition and serious adverse conditions.<sup>(6)</sup> Notably, the effects of tumors are amplified by the side effects of treatments that compromise dietary intake resulting in unintentional weight loss accompanied by muscle wasting, leading to sarcopenia.<sup>(7)</sup> The high prevalence of skeletal muscle depletion (6.6–70.9%) and malnutrition (30–50%) in patients with HNC negatively impacts patient outcomes.<sup>(8-10)</sup> Sarcopenia has been recognized as an independent poor prognostic factor in patients with cancer, regardless of their weight or nutritional status.<sup>(11)</sup>

To date, in clinical practice, Patient-Generated Subjective Global Assessment (PG-SGA) has been widely used to identify and prioritize nutrition issues and to diagnose malnutrition for patients with cancer; it allows for quick identification and priori-

tization of malnutrition issues.<sup>(12)</sup> Weight loss and body mass index (BMI) are significant indicators of nutritional status. However, body composition assessment, particularly muscle and fat tissues in patients with HNC, is not routinely performed, and only few studies have focused this aspect. Therefore, a comprehensive assessment of weight and BMI combined with body composition features is necessary. According to 2019 Chinese Society of Clinical Oncology (CSCO) guidelines for nutrition in patients with cancer,<sup>(13)</sup> the evidence-based whole-course nutrition management system was built by our team. The algorithm was described in previous article.<sup>(14)</sup> In this present study, we aimed to examine the nutrition management along with the nutritional status and body composition profile of pre-and post-operative patients with HNC. Additionally, we sought to explore the effect factors affecting muscle mass and weight loss. This study could provide a reference for more precise nutritional interventions.

## Methods

**Participants.** The study population was selected from a cohort aimed at establishing a whole-nutrition management system for newly diagnosed patients with HNC who underwent surgery in the Head and Neck Surgery Department of our Hospital between January 2021 and December 2022. The algorithm of the system was referred in the supplementary material. All patients provided written informed consent and the study protocol was approved by the ethics committee of the hospital (KYSB2020YJ044-01). The inclusion criteria were as follows: patients  $\geq 18$  years old with a new diagnosis of squamous cell HNC, including laryngeal, hypopharynx, tongue and oropharyngeal cancer. Patients who received pre-operative chemoradiotherapy and had tumors at other sites, as well as those with an expected survival of less than 3 months were excluded.

**Multidisciplinary team management.** A multidisciplinary team (MDT) nutritional support group comprising physicians, nurses, nutritionists, and clinical pharmacists was established. Nutritional Risk Screening (NRS 2002) and Patient-Generated Subjective Global Assessment (PG-SGA) were conducted by nurses and nutritionists respectively. Body compositions were assessed using bioelectric impedance analysis (BIA, Inbody S10; InBody, Seoul, South Korea). In the first 24 h post-operative, enteral nutrition via nasogastric tube was initiated using 200 ml

\*To whom correspondence should be addressed.  
E-mail: 609719747@qq.com

of rice soup, which was almost no energy and taken only as a transition. Gradually, individualized nutritional interventions that targeted daily energy of 30–35 kcal/(kg/day) and 1.5 g of protein/(kg/day), were achieved within 24–48 h. Supplementary parenteral nutritional support was implemented, when enteral nutrition cannot be satisfied to the target. And pharmacist was responsible for the prescription of parenteral nutrition. Interventions were adjusted by nutritionists over time until discharge, according to the patients' enteral tolerance and nutritional needs.

**Data collection.** Basic patient information, baseline clinical characteristics and NRS2002 scores were collected upon admission. At 0 day after surgery, NRS 2002 was re-evaluated and PG-SGA was evaluated. Nutritional status including weight, serum albumin, prealbumin, prognostic nutritional index (PNI = serum albumin + 5 × total lymphocyte count), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to monocyte ratio (LMR) and body composition data were collected pre-operatively and reviewed at post-operative weeks 1 and 2. According to the mean skeletal muscle index [SMI = skeletal muscle mass/height (kg/m<sup>2</sup>)], all patients were categorized into either a high (SMI > 9.90 kg/m<sup>2</sup>) or low SMI group (SMI ≤ 9.90 kg/m<sup>2</sup>).

**Statistical analysis.** SPSS 20.0 statistical software was used to analyze the data. Continuous variables were expressed as mean ± SD and compared between groups using the two independent sample *t* tests. One-way analysis of variance was used for comparisons among multiple groups. Disordered classification data were expressed as numbers (percentages), and the chi-square test was used to compare the two groups. Serum indicators and body composition data were compared over time using analysis of variance for repeated measures, followed by the Bonferroni test for multiple comparisons. Pearson's correlation coefficient test was used to evaluate the correlation between quantitative variables. The significance level was set at 5% ( $p < 0.05$ ).

## Results

**Patient characteristics.** Within the study period, a total of 95 male patients with newly diagnosed HNC who underwent surgery were included. Preoperative data on body composition measurements for 10 patients were missing. According to the mean preoperative skeletal muscle index of the 85 patients, they were categorized into either high (SMI > 9.90 kg/m<sup>2</sup>) or low SMI groups (SMI ≤ 9.90 kg/m<sup>2</sup>). The baseline clinical characteristics and nutritional status of all patients ( $n = 95$ ) are summarized in Table 1A and B. Basic demographics and clinical characteristics did not significantly differ between the two groups ( $p > 0.05$ ). In terms of nutritional status, NRS 2002 and PG-SGA scores were significantly higher in the low SMI group, both pre-operatively (NRS 2002,  $p = 0.01$ ) and post-operatively on day 0 (NRS 2002,  $p = 0.008$ ; PG-SGA,  $p = 0.006$ ) and at 2 weeks (PG-SGA:  $p = 0.036$ ). In all patients, the nutritional scores increased post-operatively. NRS 2002 post-operative score was higher than that at admission ( $p < 0.01$ ), and the PG-SGA score was higher at 2 weeks than on day 0 post-operatively ( $p < 0.01$ ).

**Comparisons in body composition characteristics and serum nutritional indicators.** Changes in body composition and serum nutritional indicators during the pre- and post-operative periods are summarized in Table 2. We observed significantly lower weight and body composition including soft lean mass, skeletal muscle, body fat, body fat percentage and visceral fat area in low SMI (≤ 9.90 kg/m<sup>2</sup>) group (weight, soft lean mass, skeletal muscle, body fat:  $p < 0.01$ ; body fat percentage:  $p = 0.01$ ; visceral fat area:  $p = 0.007$ ); however, no significant differences were observed in serum albumin, serum prealbumin, PNI, NLR, PLR, or LMR between the two groups.

Trends in pre- and post-operative serum nutritional indicators

and body composition characteristics are presented (Table 3A and B). A statistically significant trend was observed in the serum albumin, prealbumin, PNI, NLR, PLR, and LMR. The levels of serum albumin, prealbumin, PNI and LMR decreased post-operatively, but their levels increased again after 2 weeks; these levels were increased in comparison to the levels at 1 week post-operatively (all  $p < 0.01$ ). Serum prealbumin level was an exception, and a difference between pre-operative and 2 weeks post-operative values was not found. The NLR and PLR were increased at 1 week and 2 weeks post-operative compared to pre-operative (both  $p < 0.01$ ). And post-operatively, NLR at 2 weeks was lower than 1 week ( $p = 0.02$ ). The difference of PLR between 1 week and 2 weeks post-operative was not found.

SLM and skeletal muscle mass (SMM) levels declined at 2 weeks post-operatively compared to pre-operative measurements and those at post-operative week 1, respectively. The fat level declined from post-operative week 1 to week 2. Reduced Body fat percentage (PBF) were found 1 week post-operatively compared with pre-operative assessment. No differences in the visceral fat area (VFA) were observed between the different time points.

**Influencing factors for SMM and weight loss.** The variables associated with skeletal muscle and weight loss are presented in Table 4. The evaluations of the independent variables are the same as those in Table 1A and B. A negative correlation was observed between SMM loss and serum prealbumin levels ( $r = -0.255$ ,  $p = 0.029$ ). Pre-operative BMI ( $p < 0.01$ ), tumor differentiation ( $p = 0.003$ ), and nutritional risk ( $p = 0.049$ ) were identified as risk factors for weight loss.

## Discussion

The incidence of nutritional risk and malnutrition in patients with cancer is as high as 40–80% and is associated with post-operative infections,<sup>(15)</sup> longer and more frequent hospital stays, and shorter survival time.<sup>(16)</sup> In a previous study, the 5-year overall survival rate of surgically treated patients was 68.5% in normal weight but only 55.9% in underweight patients.<sup>(17)</sup> Patients with HNC lose up to 20% of their body weight during the therapeutic and post-therapeutic phases.<sup>(18)</sup> The present study demonstrated that nutritional interventions using oral nutrition supplementation (ONS) or the initiation of tube feeding in patients with HNC improved body composition and nutritional status. This indicates that all patients with HNC should undergo nutritional screening, and appropriate steps should be taken to correct the nutritional deficiencies.<sup>(19)</sup> To ensure comprehensive and effective nutritional management, the study advocates for evidence-based whole-course nutritional management, involving a systematic, standardized, and individualized quantitative management method throughout the peri-operative treatment phase. Nutrition screening and assessment should be performed for each patient, and an individualized nutrition plan should be prepared by a nutritionist. Nutritional status and body composition should be assessed weekly post-surgery, and enteral nutritional schemes should be adjusted based on patient's specific circumstances to ensure sufficient nutritional support is provided.

Some measurement instruments for nutritional status include NRS2002, PG-SGA, Subjective Global Assessment, Malnutrition Universal Screening Tool. The PG-SGA was demonstrated to be the best sensitivity, specificity, and predictive value. It is a method more specific to patients with cancer as it considers more acute changes in weight and dietary intake as well as a greater variety of symptoms of nutritional impact that are possibly experienced by these patients.<sup>(20)</sup> It has been widely recommended by many organizations for nutritional screening of patients with cancer.<sup>(21,22)</sup> Our results showed that patients with HNC were found to be a well-nourished population at admission but were determined to be malnourished and at nutritional risk post-

**Table 1A.** Baseline clinical characteristics and nutritional status of all patients categorized based on skeletal muscle features

Characteristic	Overall	SMI		Statistical value	<i>p</i>
		High ( <i>n</i> = 43)	Low ( <i>n</i> = 42)		
Age (years)	64.21 ± 8.34	63.44 ± 7.62	65.21 ± 9.32	10.961 <sup>a</sup>	0.339
Degree of education					
Primary school and below	57 (60%)	26 (30.6%)	26 (30.6%)	1.931 <sup>b</sup>	0.381
Junior middle school	30 (31.6%)	13 (15.3%)	15 (17.6%)		
High school and above	8 (8.4%)	4 (4.7%)	1 (1.2%)		
Disease stage					
I–II	63 (66.3%)	23 (31.5%)	28 (38.4%)	1.204 <sup>c</sup>	0.273
III–IV	32 (33.7%)	13 (17.8%)	9 (12.3%)		
Tumor site					
Laryngocarcinoma	69 (72.6%)	31 (36.5%)	30 (35.3%)	0.005 <sup>b</sup>	0.998
Carcinoma of the mouth	21 (22.1%)	10 (11.8%)	10 (11.8%)		
Others	5 (5.3%)	2 (2.4%)	2 (2.4%)		
Tumor differentiation					
A (well)	22 (23.2%)	12 (14.1%)	9 (10.6%)	1.648 <sup>b</sup>	0.439
B (well-moderately and moderately)	45 (47.4%)	21 (24.7%)	18 (21.2%)		
C (moderately-poorly and poorly)	28 (29.5%)	10 (11.8%)	15 (17.6%)		
History of smoking					
No	23 (24.2%)	11 (12.9%)	12 (14.1%)	0.096 <sup>c</sup>	0.756
Yes	72 (75.8%)	32 (37.6%)	30 (35.3%)		
History of alcohol					
No	48 (50.5%)	18 (21.2%)	25 (29.4%)	2.652 <sup>c</sup>	0.103
Yes	47 (49.5%)	25 (29.4%)	17 (20.0%)		

SMI, skeletal muscle index; NRS 2002, Nutritional Risk Screening 2002; PG-SGA, Patient-Generated Subjective Global Assessment. \*The comparison of NRS 2002 score and PG-SGA score assessed over time, *p*<0.05. <sup>a</sup>*t* value; <sup>b</sup>*F* value; <sup>c</sup> $\chi^2$  value.

**Table 1B.** Baseline clinical characteristics and nutritional status of all patients categorized based on skeletal muscle features

Characteristic	Overall	SMI		Statistical value	<i>p</i>
		High ( <i>n</i> = 43)	Low ( <i>n</i> = 42)		
History of diabetes					
No	84 (88.4%)	40 (47.1%)	36 (42.4%)	1.218 <sup>c</sup>	0.27
Yes	11 (11.6%)	3 (3.5%)	6 (7.1%)		
History of hypertension					
No	58 (61.1%)	24 (28.2%)	26 (30.6%)	0.325 <sup>c</sup>	0.568
Yes	37 (38.9%)	19 (22.4%)	16 (18.8%)		
Post-operative stay (day)	19.01 ± 4.76	18.93 ± 4.55	19.81 ± 5.08	0.841 <sup>a</sup>	0.403
NRS2002 score					
At discharge	1.67 ± 1.15	1.19 ± 0.39	2.17 ± 1.48	—	0.01
After surgery, day 0	3.51 ± 0.73*	3.30 ± 0.56	3.74 ± 0.86	—	0.008
PG-SGA score					
After surgery, day 0	5.27 ± 3.12	4.14 ± 2.25	6.00 ± 3.44	—	0.006
After surgery, 2 weeks	7.51 ± 2.38*	6.93 ± 2.11	8.05 ± 2.69	2.136 <sup>a</sup>	0.036

SMI, skeletal muscle index; NRS 2002, Nutritional Risk Screening 2002; PG-SGA, Patient-Generated Subjective Global Assessment. \*The comparison of NRS 2002 score and PG-SGA score assessed over time, *p*<0.05. <sup>a</sup>*t* value; <sup>b</sup>*F* value; <sup>c</sup> $\chi^2$  value.

operatively. A comparison of the preoperative and post-operative scores for NRS and PG-SGA, which are widely used methods for diagnosing nutritional risk and malnutrition, showed an increase in scores after surgery. Higher NRS and PG-SGA scores were

observed in patients with low SMM. Additionally, for patients with different carcinomas, prognostic nutritional index (PNI), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) are good

**Table 2.** Comparisons of serum indicators and body composition characteristics of all patients categorized based on skeletal muscle features

Characteristic	SMI		Statistical value	p
	High	LOW		
Serum albumin (g/L)	38.64 ± 5.18	39.09 ± 3.01	0.473	0.638
Serum prealbumin (g/L)	0.28 ± 0.09	0.27 ± 0.07	-0.342	0.733
CRP (mg/L)	14.62 ± 15.58	9.63 ± 15.09	-1.482	0.142
PNI	45.87 ± 6.02	46.12 ± 4.13	0.213	0.832
NLR	4.62 ± 3.26	4.12 ± 2.57	-0.76	0.449
PLR	299.96 ± 175.09	295.53 ± 125.68	-0.129	0.898
LMR	2.46 ± 1.11	2.67 ± 1.29	0.796	0.428
Weight (kg)	66.35 ± 7.79	55.71 ± 6.92	-6.561	<0.01
Weight loss percent				
≤-5%	16	10	1.436	0.248
>-5%	27	30		
Serum albumin (g/L)	38.64 ± 5.18	39.09 ± 3.01	0.473	0.638
Serum prealbumin (g/L)	0.28 ± 0.09	0.27 ± 0.07	-0.342	0.733
Soft lean mass (SLM, kg)	50.37 ± 4.15	43.36 ± 8.21	-4.749	<0.01
Skeletal muscle mass (SMM, kg)	29.75 ± 2.72	25.71 ± 2.45	-6.864	<0.01
Body fat (FAT, kg)	12.91 ± 5.24	8.75 ± 4.28	-3.813	<0.01
Body fat percentage (PBF, %)	18.81 ± 5.99	15.12 ± 6.25	-2.629	0.01
Visceral fat area (VFA, cm <sup>2</sup> )	46.38 ± 18.06	35.79 ± 15.09	-2.752	0.007

SMI, skeletal muscle index; CRP, C-reactive protein; PNI, prognostic nutritional index (PNI = serum albumin + 5 × total lymphocyte count); NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to monocyte ratio.

inflammatory response follow-up markers and predictive survival markers.<sup>(23,24)</sup> Research has shown that tumors have the ability to alter their host's systemic inflammation and immune response.<sup>(25)</sup> PNI, NLR, PLR, and LMR are all based on peripheral lymphocyte, the key component of the human immune system counts. It can be seen from our results that these inflammation markers in HNC patients changed after surgery. The increased NLR and PLR, the decreased LMR at 1 week and 2 weeks post-operative than preoperative. And compared with 1 week post-operative, the decreased NLR and the increased LMR were found at 2 weeks post-operative. Here, the levels of serum albumin and prealbumin, initially decreased followed by an increase. Moreover, prealbumin, an indicator with a short half-life, returned to the pre-operative level. The above results suggesting a positive value in the nutritional supporting and monitoring of recovery.

Approximately 80% of patients with HNC experience significant unintentional weight loss accompanied by muscle wasting.<sup>(26,27)</sup> Although sufficient nutrition was provided in this study, patients with HNC still had 2.4 kg of weight loss and 0.84 kg/m<sup>2</sup> of BMI decline. Muscle and fat tissue mass both decreased. Low skeletal muscle mass is a phenotypic Global Leadership Initiative on Malnutrition (GLIM) criterion for the diagnosis of malnutrition; it may also arise from involuntary weight loss or a low BMI.<sup>(28)</sup> The progressive and systemic loss of skeletal muscle mass and strength, known as sarcopenia, is associated with unplanned hospital admission and longer length of stay; these can lead to adverse outcomes, such as reduced quality of life and mortality.<sup>(29)</sup> In this study, a loss of adipose tissue was observed 1 week post-operatively, and a decline was still observed when comparing 2 weeks post-operative and pre-operative values. Soft lean mass and skeletal muscle mass declined at 2 weeks post-operative. These results indicated that during the process of weight loss, adipose tissue plays a protective role in the muscles. Recent evidence has suggested

that factors secreted by the tumor cell, such as IL-1 and TNF- $\alpha$ , lead to a systemic inflammatory response which could induce fat degradation and a reduction in fat generation.<sup>(30,31)</sup> Subsequently, protein synthesis decreases and hydrolysis increases, inducing a late loss of muscle tissue.<sup>(32)</sup> Overall, the loss of adipose tissue is preceded by muscle loss; however, higher weight and BMI loss are observed in the high SMI group, suggesting that the loss of muscle mass accounts for a significant proportion of weight loss.<sup>(33)</sup> Analysis of the factors influencing SMM and weight loss showed that lower serum prealbumin levels were negatively correlated with SMM loss, and that pre-operative BMI, tumor differentiation, and nutritional risk were risk factors for weight loss. BMI and weight loss are currently used as consensual indicators of nutritional assessment in clinical practice. The findings of this study suggested that body composition should be determined to assess the patient's muscle and fat tissues. In addition, prealbumin levels should be considered as sensitive indicators for monitoring of recovery.

The present study had some limitations. Although some significant results were observed, the sample size was too small to allow detailed group stratification for sarcopenia and myosteatosis, though we recently demonstrated that both sarcopenia and myosteatosis have prognostic value in patients with HNC.<sup>(34)</sup> In addition, the shorter follow-up time was another limitation, which limited the ability to fully capture the changes in muscle and fat tissues. Moreover, the predictive value of inflammatory biomarkers (PNI, NLR, PLR, and LMR) for overall survival was not available. A large-scale and long-term sample cohort should be built to capture the nature of nutritional status, muscle, and fat status interrelationships as well as changes over time. Future prospective studies exploring the relationship between sarcopenia and myosteatosis, types of malnutrition, long-term quality of life, and survival time using validated methods are recommended. Moreover, recent literature clarified

**Table 3A.** Comparisons of serum indicators assessed over time

Characteristic	Pre-operative	1 week after surgery	2 weeks after surgery	p1	p2	p3
Serum albumin (g/L)	44.09 ± 3.56	33.51 ± 3.22	38.84 ± 4.15	<0.01	<0.01	<0.01
		<i>p</i> <0.01				
Serum prealbumin (g/L)	0.30 ± 0.09	0.19 ± 0.07	0.27 ± 0.08	<0.01	0.284	<0.01
		<i>p</i> <0.01				
PNI	52.47 ± 5.43	38.10 ± 4.60	46.00 ± 5.18	<0.01	<0.01	<0.01
		<i>p</i> <0.01				
NLR	3.18 ± 2.82	5.52 ± 4.47	4.44 ± 3.35	<0.01	<0.01	0.02
		<i>p</i> <0.01				
PLR	165.68 ± 109.27	274.99 ± 194.08	293.59 ± 153.07	<0.01	<0.01	0.12
		<i>p</i> <0.01				
LMR	3.37 ± 1.56	1.84 ± 0.87	2.59 ± 1.23	<0.01	<0.01	0.01
		<i>p</i> <0.01				

PNI, prognostic nutritional index (PNI = serum albumin + 5 × total lymphocyte count); NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio. *p*: The comparison among three groups. *p*1: The comparison between pre-operative and 1 week after surgery. *p*2: The comparison between pre-operative and 2 weeks after surgery. *p*3: The comparison between 1 and 2 weeks after surgery.

**Table 3B.** Comparisons of body composition characteristics assessed over time

Characteristic	Pre-operative	1 week after surgery	2 weeks after surgery	p1	p2	p3
Soft lean mass (SLM, kg)	48.01 ± 5.12	48.34 ± 5.47	47.03 ± 7.19	0.933	0.03	0.038
		<i>p</i> = 0.013				
Skeletal muscle (SMM, kg)	28.08 ± 3.30	28.22 ± 3.57	27.87 ± 3.29	0.996	0.024	0.021
		<i>p</i> = 0.007				
Body fat (FAT, kg)	11.54 ± 5.49	10.86 ± 4.97	11.13 ± 5.34	<0.01	0.002	0.74
		<i>p</i> <0.01				
Body fat percentage (PBF, %)	17.58 ± 6.62	16.89 ± 6.01	17.25 ± 6.41	0.003	0.266	0.346
		<i>p</i> = 0.004				
Visceral fat area (VFA, cm <sup>2</sup> )	42.61 ± 19.23	41.50 ± 18.21	42.06 ± 17.92	—	—	—
		<i>p</i> = 0.405				

*p*: The comparison among three groups. *p*1: The comparison between pre-operative and 1 week after surgery. *p*2: The comparison between pre-operative and 2 weeks after surgery. *p*3: The comparison between 1 and 2 weeks after surgery.

that serum albumin, transferrin, serum transthyretin, and prealbumin characterized inflammation rather than describe nutrition status or protein-energy malnutrition. The inflammation and hepatic reprioritization of protein synthesis occurs, resulting in lower serum concentrations of albumin and prealbumin. These proteins correlate well with patients' risk for adverse outcomes rather than with protein-energy malnutrition. Their normalization may indicate the resolution of inflammation, the reduction of nutrition risk, a transition to anabolism, or potentially lower calorie and protein requirements.<sup>(35)</sup> In conclusion, this study indicates that whole-course nutritional management pre- and post-operatively is beneficial for maintaining and improving the nutritional status of patients with HNC. In addition to traditional BMI and weight loss, consideration of muscle and fat tissues, sensitive serum prealbumin levels and readily available biomarkers (PNI, NLR, PLR, and LMR) should be feasible, complete, and integrated.

### Author Contributions

ZD, conceived the study question, and contributed to the study design, supervision of data collection, and writing the manuscript; LZ, data curation, writing – original draft preparation; YZ, data curation, writing – review & editing; KJ, validation and supervision; RW, contributed to data interpretation; YG, contributed to the study design and writing – review & editing.

### Acknowledgments

We want to thank all medical workers, especially the frontline medical doctor and nurse, for their cooperation and support. Funding was provided by the Medical Health Science and Technology Project of Zhejiang Provincial Health Commission (2021KY309).

**Table 4.** Univariate analysis of skeletal muscle loss and weight loss

Characteristic	SMM loss		5% weight loss	
	Statistical value	<i>p</i>	Statistical value	<i>p</i>
Age (years)	<i>r</i> = 0.056	0.625	<i>t</i> = 0.132	0.895
Pre-operative BMI <sup>a</sup>	<i>F</i> = 0.666	0.517	$\chi^2$ = 42.468	<0.01
Degree of education	<i>F</i> = 0.665	0.517	$\chi^2$ = 3.866	0.145
Disease stage	<i>t</i> = -1.266	0.21	$\chi^2$ = 0.011	0.915
Tumor differentiation	<i>F</i> = 1.752	0.181	$\chi^2$ = 11.414	0.003
Tumor site	<i>F</i> = 0.165	0.848	$\chi^2$ = 2.057	0.358
Smoking	<i>t</i> = 0.720	0.474	$\chi^2$ = 0.37	0.543
Drinking	<i>t</i> = -0.499	0.619	$\chi^2$ = 0.086	0.769
History of diabetes	<i>t</i> = -0.595	0.554	$\chi^2$ = 1.849	0.174
History of hypertension	<i>t</i> = -0.451	0.654	$\chi^2$ = 2.033	0.154
Post-operative stay	<i>r</i> = 0.089	0.446	<i>t</i> = -0.175	0.862
NRS2002 stage <sup>b</sup>	<i>F</i> = -1.892	0.059	$\chi^2$ = 3.886	0.049
PG-SGA stage <sup>c</sup>	<i>F</i> = 0.053	0.948	$\chi^2$ = 0.455	0.796
Albumin fluctuations(g/L)	<i>r</i> = 0.060	0.613	<i>t</i> = -0.579	0.564
Serum prealbumin (g/L)	<i>r</i> = -0.255	0.029	<i>t</i> = -0.043	0.966
NLR	<i>r</i> = 0.037	0.751	<i>t</i> = -0.234	0.816
PLR	<i>r</i> = 0.202	0.085	<i>t</i> = -0.939	0.351
LMR	<i>r</i> = -0.019	0.874	<i>t</i> = -0.778	0.439

SMM, skeletal muscle mass; BMI, body mass index; NRS 2002, Nutritional Risk Screening 2002; PG-SGA, Patient-Generated Subjective Global Assessment; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to monocyte ratio. <sup>a</sup>BMI was defined as (1): <18.5 kg/m<sup>2</sup>, (2): 18.5–23.9 kg/m<sup>2</sup>, (3): ≥24 kg/m<sup>2</sup>. <sup>b</sup>NRS 2002 stage was defined as (1): <3, no nutritional risk; (2): ≥3, nutritional risk. <sup>c</sup>The PG-SGA stage was defined as (1): ≤3, suspected malnutrition; (2): 3–8, moderate malnutrition; and (3): ≥9, severe malnutrition.

## Conflict of Interest

No potential conflicts of interest were disclosed.

## References

- Bye A, Sandmael JA, Stene GB, *et al.* Exercise and nutrition interventions in patients with head and neck cancer during curative treatment: a systematic review and meta-analysis. *Nutrients* 2020; **12**: 3233.
- Forouzanfar MH, Foreman KJ, Delossantos AM, *et al.* Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *Lancet* 2011; **378**: 1461–1484.
- Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KCH. Cancer-associated cachexia. *Nat Rev Dis Primers* 2018; **4**: 17105.
- Fearon K, Strasser F, Anker SD, *et al.* Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011; **12**: 489–495.
- Fearon K, Arends J, Baracos V. Understanding the mechanisms and treatment options in cancer cachexia. *Nat Rev Clin Oncol* 2013; **10**: 90–99.
- Correia MI, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clin Nutr* 2003; **22**: 235–239.
- Kubrak C, Olson K, Jha N, *et al.* Nutrition impact symptoms: key determinants of reduced dietary intake, weight loss, and reduced functional capacity of patients with head and neck cancer before treatment. *Head Neck* 2010; **32**: 290–300.
- Findlay M, White K, Lai M, Luo D, Bauer JD. The association between computed tomography-defined sarcopenia and outcomes in adult patients undergoing radiotherapy of curative intent for head and neck cancer: a systematic review. *J Acad Nutr Diet* 2020; **120**: 1330–1347.
- van Bokhorst-de van der Schueren MA, van Leeuwen PA, Kuik DJ, *et al.* The impact of nutritional status on the prognoses of patients with advanced head and neck cancer. *Cancer* 1999; **86**: 519–527.
- Marshall KM, Loeliger J, Nolte L, Kelaart A, Kiss NK. Prevalence of malnutrition and impact on clinical outcomes in cancer services: a comparison of two time points. *Clin Nutr* 2019; **38**: 644–651.
- Ryan AM, Power DG, Daly L, Cushen SJ, Ní Bhuachalla É, Prado CM. Cancer-associated malnutrition, cachexia and sarcopenia: the skeleton in the hospital closet 40 years later. *Proc Nutr Soc* 2016; **75**: 199–211.
- Enzinger PC, Kulke MH, Clark JW, *et al.* A phase II trial of irinotecan in patients with previously untreated advanced esophageal and gastric adenocarcinoma. *Dig Dis Sci* 2005; **50**: 2218–2223.
- Guidelines Working Committee of Chinese Society of clinical oncology. Guidelines for nutritional treatment of patients with malignant tumors [M]. *People's Medical Publishing House*; 2019. (in Chinese)
- Ding Z, Gui Y, Zhou L, *et al.* Whole-course nutritional support therapy and indicators in head and neck cancer surgery. *Asia Pac J Clin Nutr* 2022; **31**: 348–354.
- Bozzetti F, Mariani L, Lo Vullo S, *et al.* The nutritional risk in oncology: a study of 1,453 cancer outpatients. *Support Care Cancer* 2012; **20**: 1919–1928.
- Bozzetti F, Arends J, Lundholm K, *et al.* ESPEN Guidelines on Parenteral Nutrition: non-surgical oncology. *Clin Nutr* 2009; **28**: 445–454.
- Takenaka Y, Takemoto N, Nakahara S, *et al.* Prognostic significance of body mass index before treatment for head and neck cancer. *Head Neck* 2015; **37**: 1518–1523.
- Ehrsson YT, Langius-Eklöf A, Laurell G. Nutritional surveillance and weight loss in head and neck cancer patients. *Support Care Cancer* 2012; **20**: 757–765.
- Alshadwi A, Nadershah M, Carlson ER, Young LS, Burke PA, Daley BJ. Nutritional considerations for head and neck cancer patients: a review of the literature. *J Oral Maxillofac Surg* 2013; **71**: 1853–1860.
- Mendes NP, Barros TA, Rosa COB, Franceschini SDCC. Nutritional

- screening tools used and validated for cancer patients: a systematic review. *Nutr Cancer* 2019; **71**: 898–907.
- 21 Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PGSGA) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr* 2002; **56**: 779–785.
- 22 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**: S32–S40.
- 23 Duan F, Ma RC, Liao L, *et al.* Analysis of the effect of prognostic nutrition index in predicting the prognosis of patients with oral squamous cell carcinoma. *Oncol Clin Rehabil Chin* 2021; **28**: 1165–1168.
- 24 Harada M, Hato T, Horio H. Intratumoral lymphatic vessel involvement is an invasive indicator of completely resected pathologic stage I non-small cell lung cancer. *J Thorac Oncol* 2011; **6**: 48–54.
- 25 Ulich TR, del Castillo J, Keys M, Granger GA, Ni RX. Kinetics and mechanisms of recombinant human interleukin 1 and tumor necrosis factor-alpha-induced changes in circulating numbers of neutrophils and lymphocytes. *J Immunol* 1987; **139**: 3406–3415.
- 26 Orell-Kotikangas H, Österlund P, Mäkitie O, *et al.* Cachexia at diagnosis is associated with poor survival in head and neck cancer patients. *Acta Otolaryngol* 2017; **137**: 778–785.
- 27 Gorenc M, Kozjek NR, Strojjan P. Malnutrition and cachexia in patients with head and neck cancer treated with (chemo)radiotherapy. *Rep Pract Oncol Radiother* 2015; **20**: 249–258.
- 28 Cederholm T, Jensen GL, Correia MITD, *et al.* GLIM criteria for the diagnosis of malnutrition—A consensus report from the global clinical nutrition community. *Clin Nutr* 2019; **38**: 1–9.
- 29 Cruz-Jentoft AJ, Baeyens JP, Bauer JM, *et al.*; European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010; **39**: 412–423.
- 30 Fouladiun M, Körner U, Bosaeus I, Daneryd P, Hylander A, Lundholm KG. Body composition and time course changes in regional distribution of fat and lean tissue in unselected cancer patients on palliative care—correlations with food intake, metabolism, exercise capacity, and hormones. *Cancer* 2005; **103**: 2189–2198.
- 31 Tijerina AJ. The biochemical basis of metabolism in cancer cachexia. *Dimens Crit Care Nurs* 2004; **23**: 237–243.
- 32 Glass DJ. Signaling pathways perturbing muscle mass. *Curr Opin Clin Nutr Metab Care* 2010; **13**: 225–229.
- 33 Aoyama T. Perioperative body composition changes in the multimodal treatment of gastrointestinal cancer. *Surg Today* 2020; **50**: 217–222.
- 34 Findlay M, Brown C, De Abreu Lourenço R, White K, Bauer J. Sarcopenia and myosteatosis in patients undergoing curative radiotherapy for head and neck cancer: impact on survival, treatment completion hospital admission and cost. *J Hum Nutr Diet* 2020; **33**: 811–821.
- 35 Evans DC, Corkins MR, Malone A, *et al.* The use of visceral proteins as nutrition markers: an ASPEN position paper. *Nutr Clin Pract* 2021; **36**: 22–28.



This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).