Supportive Care in Cancer (2023) 31:723
https://doi.org/10.1007/s00520-023-08166-8

RESEARCH

Risk factors for malnutrition in patients with nasopharyngeal carcinoma

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Received: 29 December 2022 / Accepted: 7 November 2023 / Published online: 27 November 2023

Abstract

Background Malnutrition is a common complication in patients with nasopharyngeal carcinoma (NPC). However, there are few studies on risk factors for malnutrition in NPC patients. Our aims were to identify the risk factors for malnutrition in NPC patients.

Methods NPC patients were recruited in this cross-sectional study, and they were divided into well-nourished and malnourished groups according to the Global Leadership Initiative on Malnutrition (GLIM). Potential risk factors were initially screened using univariate analysis ($p < 0.1$), and the selected ones were analyzed by logistic regression analysis ($p < 0.05$) to identify the risk factors for malnutrition in NPC patients.

Results In total, 305 NPC patients meeting eligibility criteria were enrolled. Multivariate logistic regression analysis revealed that low body mass index (BMI) (OR = 0.596, 95% CI 0.520–0.683, $p < 0.001$), the high total radiation dose received (OR = 1.046, 95% CI 1.023–1.069, $p < 0.001$), appetite loss (OR = 2.839, 95% CI 1.269–6.353, $p = 0.011$), and low PA (OR = 0.993, 95% CI 0.988–0.998, $p = 0.008$) were risk factors for malnutrition in NPC patients.

Conclusions The low BMI, the high total radiation dose received, appetite loss, and low prealbumin were risk factors for malnutrition in NPC patients.

Keywords Nutrition · Malnutrition · Risk factors · Nasopharyngeal carcinoma · GLIM · Assessment

Introduction

As one of the most severe malignancies and a kind of epithelial carcinoma from the nasopharyngeal mucosal lining, NPC has a high incidence and mortality among all head and neck malignant tumors [1]. In a 2018 global report, NPC-related morbidity occupied about 0.7% of 36 cancers and 0.8% of all cancer-related mortality [2, 3]. NPC is dominantly prevalent in east and southeast Asia, with distinct geographical distribution [4].

Malnutrition is very common among NPC patients, with a prevalence of 5.3–94.8% [5–7], and it can lead to adverse outcomes [8–10]. Malnutrition could weaken the immune system, prolong hospital stays, and affect treatment efficacy [11–13]. It has been found that malnutrition or weight loss is significantly related to poorer quality of life and survival outcomes [14, 15]. Currently, there is no gold standard for the assessment of malnutrition [16]. The Global Leadership Initiative on Malnutrition (GLIM) is a global consensus that is built by four clinical nutrition societies (ESPEN, ASPEN, FELANPE, and PENSA) on the diagnosis of malnutrition [17]. However, there are few studies on risk factors for malnutrition and the application of GLIM in NPC patients. Our aim was to identify the risk factors for malnutrition in NPC patients according to the GLIM.

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Methods

Patient selection

All patients were prospectively recruited at the First Affiliated Hospital of Guangxi Medical University from September 2021 to November 2022. All patients were divided into well-nourished and malnourished groups according to GLIM.

Eligibility criteria

Inclusion criteria were as follows: (1) age ≥ 18 years old and (2) newly diagnosed NPC patients with no history of malignancy in other organs.

Exclusion criteria were as follows: NPC patients with severe endocrine, life-threatening, or psychiatric disorders.

Data collection

Baseline patient data, including gender, smoking, drinking, education level, tumor stage, age, BMI, the number of chemotherapy cycles completed, the total radiation dose received, biochemical markers, and adverse reactions in the past week, were collected. Malnutrition in NPC patients was assessed using GLIM during the same time period. We defined smoking as smoking more than 2 pack-years or current smoking. We defined drinking as drinking at least once a week for more than a year or currently drinking or quitting drinking for less than 3 years. The tumor stage was classified by the WHO classification criteria.

Statistical analysis

Means ± standard deviations (SD) or medians with interquartile ranges [P25, P75] were utilized to present quantitative data. The *t*-test for continuous variables, the chi-squared for categorical variables, and the Wilcoxon rank-sum tests for grade or skewed distribution variables were used in the univariable analysis. Multicollinearity was tested using the variance inflation factor (VIF) method, with VIF < 5 indicating no multicollinearity [18]. Variables with $p < 0.1$ were carried forward to the logistic regression model, where adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were obtained. A two-sided $p < 0.05$ was considered statistically significant.

Nutrition assessment tool

GLIM was utilized as the nutrition assessment tool in the study, which consists of three phenotypic and two etiological criteria. At least 1 phenotypic criterion and 1 etiologic criterion were required for the diagnosis of malnutrition based on the GLIM criteria (Table 1).

STROBE guidelines

This study is reported according to Strengthening The Reporting of Observational studies in Epidemiology (STROBE) guidelines [19].

Results

This study included 305 patients, including 162 in the well-nourished group and 143 in the malnourished group. Among them, the mean age was 46.02 ± 10.90 (range 18–75); the mean BMI was 22.85 ± 3.46 (range 15.59–39.89); 220 (72.1%) were male and 85 (27.9%) were female; 171 (56.1%) had no history of smoking, while 134 (43.9%) had a current or previous history of smoking; 189 (62.0%) had no history of drinking, while 116 (38.0%) had a current or previous history of drinking; 77 (25.2%) had an education level of primary school or below, 185 (60.7%) middle or high school, and 43 (14.1%) college and above college; 11 (3.6%) were stage II, 89 (29.2%) were stage III, and 205 (67.2%) were stage IV. Details are shown in Table 2A and B.

According to the results of univariate analysis, drinking ($p = 0.047$), oral mucositis ($p < 0.001$), dry mouth ($p < 0.001$), dysphagia ($p < 0.001$), difficulty in mouth opening ($p = 0.014$), sore throat ($p < 0.001$), appetite loss

Table 1 The GLIM criteria [17]

Phenotypic criteria		
Weight loss (%)	Low body mass index (kg/m^2)	Reduced muscle mass
> 5% within past 6 months or > 10% beyond 6 months	< 20 if < 70 years, or < 22 if > 70 years; Asia < 18.5 if < 70 years or < 20 if > 70 years	Reduced by validated body composition measuring techniques
Etiologic criteria		
Reduced food intake or assimilation		Inflammation
≤ 50% of ER > 1 week, or any reduction for > 2 weeks, or any chronic GI condition that adversely impacts food assimilation or absorption		Acute disease/injury or chronic disease-related

GI gastro-intestinal, *ER* energy requirements

Table 2 A The data of 305 NPC patients. (B) The data of 305 NPC patients

A		
Factors		NPC patients ($N=305$)
Gender	Female	85 (27.9%)
	Male	220 (72.1%)
Smoking	No	171 (56.1%)
	Yes	134 (43.9)
Drinking	No	189 (62.0%)
	Yes	116 (38.0%)
Education level	Primary school or below	77 (25.2%)
	Middle or high school	185 (60.7%)
	College and above college	43 (14.1%)
Tumor stage	II	11 (3.6%)
	III	89 (29.2%)
	IV	205 (67.2%)
Oral mucositis	No	262 (85.9%)
	Yes	43 (14.1%)
Dry mouth	No	179 (58.7%)
	Yes	126 (41.3%)
Dysphagia	No	269 (88.2%)
	Yes	36 (11.8%)
Difficulty in mouth opening	No	295 (96.7%)
	Yes	10 (3.3%)
Sore throat	No	234 (76.7%)
	Yes	71 (23.3%)
Facial numbness	No	282 (92.5%)
	Yes	23 (7.5%)
Appetite loss	No	225 (73.8%)
	Yes	80 (26.2)
Nausea	No	248 (81.3%)
	Yes	57 (18.7%)
Vomiting	No	278 (91.1%)
	Yes	27 (8.9%)
Diarrhea	No	298 (97.7%)
	Yes	7 (2.3%)
B		
Factors		NPC patients ($N=305$)
Age (year)	Mean ± SD	46.02 ± 10.90
	Range	18–75
BMI (kg/m^2)	Mean ± SD	22.85 ± 3.46
	Range	15.59–39.89
The number of chemotherapy cycles completed	(P25, P75)	(0, 3)
	Range	0–6
The total radiation dose received (Gy)	(P25, P75)	(0, 18.59)
	Range	0–72.27
TP (g/l)	Mean ± SD	71.88 ± 7.57
ALB (g/l)	Mean ± SD	40.23 ± 4.38
GLO (g/l)	Mean ± SD	31.97 ± 4.97
PA (mg/l)	Mean ± SD	250.79 ± 65.12

NPC nasopharyngeal carcinoma, *BMI* body mass index, *TP* total protein, *ALB* albumin, *GLO* globulin, *PA* prealbumin

($p < 0.001$), nausea ($p < 0.001$), vomiting ($p = 0.001$), BMI ($p < 0.001$), the number of chemotherapy cycles completed ($p < 0.001$), the total radiation dose received ($p < 0.001$), albumin (ALB) ($p = 0.007$), and prealbumin (PA) ($p < 0.001$) had statistically significant differences ($p < 0.1$), as shown in Table 3A and B. Variables with $p < 0.1$ were included in the logistic regression model. According to previous literature and clinical experience, the patients' age [20] and tumor stage [21] were also included in the logistic regression model. The results of the multicollinearity analysis are shown in Table 4. The VIF values of all variables were less than 5, so it could be considered that there was no multicollinearity between the variables, and all variables were included in the regression model. Multivariate logistic regression analysis proved that low BMI (OR = 0.596, 95%CI 0.520–0.683, $p < 0.001$), the high total radiation dose received (OR = 1.046, 95%CI 1.023–1.069, $p < 0.001$), appetite loss (OR = 2.839, 95%CI 1.269–6.353, $p = 0.011 < 0.05$), and low PA (OR = 0.993, 95%CI 0.988–0.998, $p = 0.008 < 0.05$) were risk factors for malnutrition in NPC patients. Details are shown in Table 5.

Discussion

NPC, an epithelial malignancy in the head and neck, is one of the most severe invasive and metastatic cancers in southern China as well as Southeast Asia [22, 23]. When most NPC patients are diagnosed, they are already in advanced stages [24]. Malnutrition is highly prevalent among NPC patients due to the disease and its treatment [5, 6]. Malnutrition delayed recovery, prolonged hospital stay, and increased the risks of morbidity and mortality, general practitioner visits, and probability of admission to tertiary care facilities [25]. In addition, poor nutrition is closely correlated with increased morbidity and mortality, hospitalization time, frequent readmissions, infectious and non-infectious clinical complications, and healthcare costs [26–28]. Nutrition assessment is the first step to supporting nutrition, but no diagnostic "gold standard" to assess malnutrition could be discovered [29–31]. GLIM was developed by ASPEN, ESPEN, FELANPE, and PENSA [17, 31]. However, there are few studies on risk factors for malnutrition and the application of GLIM in NPC patients. Our study identified the risk factors for malnutrition in NPC patients according to the GLIM.

BMI

Our results showed that low BMI affects malnutrition in NPC patients, which is consistent with other studies [32–35]. BMI is an indicator of malnutrition in most nutritional screening and assessment tools. BMI < 18.5 kg/m^2 is a phenotypic criterion for Asian patients younger than 70 years according to the GLIM [36]. Besides, BMI < 18.5 kg/m^2 and BMI < 19 kg/m^2 are indicators of malnutrition based on the Nutritional Risk Screening 2002 [37] and the Mini Nutritional Assessment [38], respectively. Furthermore, BMI < 18.5 kg/m^2 was defined as malnutrition based on the consensus statement of the European Society of Clinical Nutrition and Metabolism [39].

The total radiation dose received

Our results showed that the high total radiation dose received is a risk factor for malnutrition in NPC patients. Similarly, the results of other studies were in line with our results [24, 40]. Radiotherapy is the primary treatment modality for NPC patients [4], but it affects both tumor cells and normal tissue, thus leading to a lot of nutritional problems in patients. Radiation therapy could reduce nutritional status by interfering with ingestion, digestion, and absorption of nutrients [41]. Moreover, radiotherapy results in taste alteration, dysphagia, xerostomia, the loss of appetite, nausea, and vomiting that increase the risks of malnutrition [42–48]. What's more, during radiotherapy, inflammation, including radiation-induced mucositis, may occur [49–51] and increases energy expenditure and breaks down protein [52], with the loss of muscle mass [53]. According to Unsal et al. after radiotherapy, the malnutrition rate of patients with head and neck cancer is 88% [54].

Appetite loss

This study illustrated that appetite loss is a risk factor for malnutrition in NPC patients. Appetite loss has great impacts on the absorption of dietary energy and other nutrients, which cause weight loss and malnutrition progression [55]. Systemic inflammation responses by the tumor, chemoradiotherapy, anxiety, and depression can all lead to appetite loss [56]. Research has shown that loss of appetite and weight loss occur in more than 80% of advanced cancer patients [57]. Poor appetite causes poor nutritional status in elderly individuals [58, 59]. Nho et al. reported that malnutrition in gynecologic cancer was strongly correlated with appetite [60].

PA

Our study shows that low PA is a risk factor for malnutrition in NPC patients. Because serum concentrations of PA are closely related to early changes in nutritional status, it is often used as a marker for monitoring malnutrition [61–65]. PA has a small body pool, a short half-life of 48 h, and a rapid rate of synthesis that responds to protein intake [65, 66]. It has been shown that PA decreased significantly after only 3 days of inadequate nutrient intake [63] and increased by 1 mg/day when nutrient requirements were met [64].

Table 3 (A) The results of univariate analysis. (B) The results of univariate analysis

A					
Variable		Well-nourished group ($n=162$)	Malnourished group ($n=143$)	X^2/Z	p
Gender	Female	39	46	2.475	0.116
	Male	123	97		
Smoking	No	84	87	2.491	0.115
	Yes	78	56		
Drinking	No	92	97	3.929	0.047
	Yes	70	46		
Oral mucositis	No	155	107	27.274	< 0.001
	Yes	7	36		
Dry mouth	No	115	64	21.558	< 0.001
	Yes	47	79		
Dysphagia	No	154	115	15.642	< 0.001
	Yes	8	28		
Difficulty in mouth opening	No	161	134	6.031	0.014
Yes	1	9			
Sore throat	No	140	94	18.197	< 0.001
	Yes	22	49		
Facial numbness	No	153	129	1.953	0.162
	Yes	9	14		
Appetite loss	No	140	85	28.572	< 0.001
	Yes	22	58		
Nausea	No	146	102	17.656	< 0.001
	Yes	16	41		
Vomiting	No	156	122	11.352	0.001
	Yes	6	21		
Diarrhea	No	159	139	0.303	0.582
	Yes	3	4		
Education level*	Primary school or below	41	36	− 0.689	0.491
	Middle or high school	94	91		
	College and above college	27	16		
Tumor grade*	I	0	0	− 0.840	0.401
	II	5	6		
	III	52	37		
	IV	105	100		

B				
Variable	Well-nourished group ($n=162$)	Malnourished group ($n=143$)	t/Z	p
Age (year)	45.87 ± 10.26	46.2 ± 11.62	− 0.260	0.795
BMI (kg/m^2)	24.65 ± 2.95	20.82 ± 2.83	11.501	< 0.001
The number of chemotherapy cycles completed*	(0, 2)	(1, 4)	− 5.255	< 0.001
The total radiation dose received (Gy)*	(0, 2.14)	(0, 38.52)	− 7.073	< 0.001
TP (g/l)	72.35 ± 8.63	71.35 ± 6.12	1.153	0.250
ALB (g/l)	40.87 ± 4.49	39.52 ± 4.16	2.718	0.007
GLO (g/l)	32.03 ± 4.58	31.90 ± 5.39	0.229	0.819
PA (mg/l)	269.57 ± 62.59	229.51 ± 61.47	5.625	< 0.001

*The Wilcoxon rank-sum test was used to compare the two groups

BMI body mass index, *TP* total protein, *ALB* albumin, *GLO* globulin, *PA* prealbuminF

Table 4 Multicollinearity evaluation results

Covariates	Tolerance	VIF
Age	0.873	1.146
Tumor stage	0.880	1.136
BMI (kg/m^2)	0.862	1.160
Drinking	0.942	1.062
The number of chemotherapy cycles completed	0.584	1.711
The total radiation dose received (Gy)	0.347	2.886
Oral mucositis	0.401	2.494
Dry mouth	0.561	1.783
Dysphagia	0.599	1.669
Difficulty in mouth opening	0.735	1.361
Sore throat	0.557	1.795
Appetite loss	0.523	1.910
Nausea	0.476	2.100
Vomiting	0.569	1.758
ALB (g/l)	0.762	1.312
PA (mg/l)	0.748	1.336

BMI body mass index, *ALB* albumin, *PA* prealbumin, *VIF* variance inflation factor

Practical implications

This study has several practical implications. Our study showed that low BMI, high total radiation dose received, appetite loss, and low prealbumin are risk factors for malnutrition in NPC patients. Although low BMI and appetite loss are well-recognized risk factors for malnutrition, radiation dose and prealbumin do not serve as indicators in commonly used nutritional assessment tools, such as Patient-Generated Subjective Global Assessment (PG-SGA), Mini Nutritional Assessment (MNA), and GLIM. This limitation suggests that these tools may not adequately capture the specific nutritional risks associated with NPC. To overcome this gap, future studies should focus on enhancing the existing nutritional assessment tools or developing a novel nutritional assessment tool specifically designed for NPC patients, integrating these risk factors.

Moreover, by paying attention to NPC patients with these risk factors, healthcare providers can closely monitor the nutritional status of NPC patients during treatment and implement personalized nutritional support strategies to prevent malnutrition. For example, personalized nutrition supplementation plans can be developed for patients with low BMI to ensure an adequate intake of nutrients. For patients experiencing appetite loss, strategies such as increasing meal frequency, providing oral supplements, or exploring other methods of assisted feeding can be considered.

Finally, healthcare policies can be formulated based on these risk factors. Government health departments could develop or update specific nutritional assessment criteria for NPC patients. These departments could utilize the research findings to establish guidelines that guide nutritional intervention measures for NPC patients. Moreover, healthcare institutions could develop targeted nutritional care standards for NPC patients based on the study's conclusions.

Strengths and limitations

While numerous studies have investigated the risk factors for malnutrition in cancer patients [67–69], the research specifically focused on NPC patients is limited [24, 70, 71]. The limited research on utilizing GLIM in NPC patients can be attributed to multiple factors: the novelty of GLIM as a nutritional assessment tool [17], the relatively lower prevalence of NPC compared to other cancers, and the significant geographical imbalance in its global distribution [4]. Additionally, there exists a gap in the literature as no studies have utilized the GLIM to identify risk factors for malnutrition in NPC patients. Therefore, our study aimed to address this gap and contribute to the field. Furthermore, our study was conducted in a high-incidence area of NPC. In comparison to previous studies [24, 70, 71], our study featured a larger sample size, thereby increasing the reliability of our results. Additionally, we conducted a comprehensive analysis of various potential variables, including demographic factors, clinical characteristics, biochemical markers, and adverse reactions. Lastly, in contrast to previous studies that assessed radiotherapy (yes or no) [67] or focused on radiotherapy side effects [72] as risk factors for malnutrition, our study analyzed the relationship between radiotherapy dose and malnutrition, providing more precise results.

Table 5 The results of the multivariable logistic regression model

Variable	*B*	S.E	Wald	Sig	Exp(*B*)	95% C.I. for EXP(*B*)	
						Lower	Upper
BMI (kg/m^2)	−0.517	0.069	55.309	<0.001	0.596	0.520	0.683
Appetite loss	1.044	0.411	6.451	0.011	2.839	1.269	6.353
PA (mg/l)	−0.007	0.003	6.966	0.008	0.993	0.988	0.998
The total radiation dose received (Gy)	0.045	0.011	15.690	<0.001	1.046	1.023	1.069

BMI body mass index, *PA* prealbumin

Despite these strengths, our study also has many limitations. Although GLIM has been validated in other patients [73], its diagnostic efficacy was not validated in our study. On the other hand, although our study has a larger sample size compared with previous studies, more large sample sizes and high-quality studies are needed to identify risk factors for malnutrition in NPC patients. Finally, while our study analyzed the association between the number of chemotherapy cycles completed and malnutrition in NPC patients, the relationship between chemotherapy dose and malnutrition was not analyzed in our study. Therefore, further studies need to be carried out to fully elucidate the impact of chemotherapy dosages on malnutrition in the NPC population.

Conclusions

The low BMI, the high total radiation dose received, appetite loss, and low prealbumin are risk factors for malnutrition in NPC patients.

Author contribution Pengpeng Wang, Kim Lam Soh, Yanping Ying, and Jinlian Liao designed the study. Xueling Huang, Huihan Zhao, Xiao Pan, and Lan Deng collected and analysed the data. Pengpeng Wang, Kim Lam Soh, Yanping Ying, Jinlian Liao, and Xiaoxia Yu prepared, drafted, and revised the manuscript. All authors reviewed the manuscript.

Data Availability Data is available on reasonable request from the corresponding author.

Declarations

Ethics approval and consent to participate The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the institutional review Board of the First Affiliated Hospital of Guangxi Medical University (No. 2022-KT-Gui Wei-005). All the data collected were anonymous. Participation was voluntary and all participants provided informed consent.

Consent for publication Obtained.

Competing interests The authors declare no competing interests.

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