

# Association of malnutrition with postoperative complication risk after curative surgery for oral cancer

# **Observational study**

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# Abstract

Malnutrition is common among patients who have oral cavity squamous cell carcinoma (OSCC), but its effect on the incidence of postoperative complications remains uncertain. Validated nutrition and complication assessment tools were used to evaluate the effects of nutrition on the likelihood of postoperative complications after curative surgery for OSCC.

A retrospective study that spanned January 2014 to December 2018 enrolled 70 patients who received curative surgery for OSCC. Nutritional status before surgery was evaluated with the scored Patient-Generated Subjective Global Assessment (PG-SGA), and patients were classified as either well-nourished (rating A) or malnourished (ratings B and C). Complications 30 days after the operation were graded using Clavien-Dindo classification. The perioperative clinicopathological characteristics of the groups were compared, and risk factors for postoperative complications were identified through logistic regression.

A total of 44 (62.8%) patients formed the malnourished group, and they tended to be older (P = .03), weigh less (P = .001), have lower Body Mass Index (P = .003), higher PG-SGA scores (P < .001), higher neutrophil-to-lymphocyte ratio (P = .034), more postoperative complications (P < .001), and longer hospital stays (P = .021). Major complications (Clavien–Dindo classification  $\ge$  Illa) were experienced by 18.5% (n = 13) of patients and were more common in the malnourished group (P = .007). Multivariate logistic regression demonstrated that PG-SGA score  $\ge 4$  was an independent risk factor for postoperative complications (hazard ratio = 4.929, P = .008).

Malnutrition defined using the PG-SGA is an independent risk factor for postoperative complications of curative surgery in patients with OSCC. More prospective studies are warranted to confirm our findings.

**Abbreviations:** BMI = Body Mass Index, HNC = head and neck cancer, ICU = intensive care unit, IQR = interquartile range, NLR = neutrophil-to-lymphocyte ratio, OSCC = oral cavity squamous cell carcinoma, PG-SGA = Patient-Generated Subjective Global Assessment, TNM = tumor, node and metastasis.

Keywords: Clavien–Dindo classification, malnutrition, oral cavity squamous cell carcinoma, patient-generated subjective global assessment (PG-SGA), postoperative complication

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# 1. Introduction

A particularly high risk of developing malnutrition is associated with head and neck cancer (HNC). Nearly half of all patients are experiencing malnutrition at diagnosis, and such malnutrition may be because of excessive alcohol consumption or odynophagia and dysphagia resulting from HNC, which reduce dietary intake.<sup>[1]</sup> Neck lymph-node metastasis, impaired oral intake, concurrent chemoradiotherapy, diagnoses of oropharyngeal or hypopharyngeal cancer, weight loss, and low serum albumin levels are risk factors for malnutrition in patients with HNC,<sup>[2,3]</sup> and poor nutritional status is associated with a high likelihood of treatment toxicity, intolerance, morbidity, mortality, and adverse outcomes in quality of life.<sup>[4-6]</sup> Surgery remains the mainstay treatment for HNC, but certain postoperative complications are serious challenges for treatment and are difficult for early detection. The initial step in preventing postoperative complication is identifying high-risk factors, and few studies have analyzed the effect of preoperative nutritional status on complications after HNC surgery.<sup>[7,8]</sup> A Dutch study indicated a body weight reduction of >10% in the 6 months leading up to an operation as the greatest risk factor for major postoperative complications.<sup>[1]</sup> In a series of 515 patients with HNC who received free flap

reconstruction, Eskander et al determined that malnutrition, older age, and underlying diabetes were significant predictors of developing surgical site infections.<sup>[9]</sup> However, diverse nutritional assessment modalities, inconsistent surgical complication grading, and heterogeneity among patients enrolled in studies make the relationship between malnutrition and postoperative complications difficult to interpret in patients with oral cavity squamous cell carcinoma (OSCC).

The Patient-Generated Subjective Global Assessment (PG-SGA) is a widely used interdisciplinary nutritional evaluative tool that assists medical personnel in rapidly identifying malnutrition in patients with HNC.<sup>[3,10-12]</sup> The Clavien–Dindo classification system is a validated tool to accurately grade postoperative complications in numerous surgical procedures, including surgery for HNC.<sup>[13]</sup> This retrospective study focused on patients with OSCC who received curative surgery. The preoperative characteristics of patients who were well nourished or malnourished as categorized by PG-SGA rating were compared, and the risk factors for postoperative complications as categorized using the standardized 5-grade Clavien-Dindo system were analyzed. These analyses highlight the benefits of standardized methods of assessing nutritional status and surgical complications for ensuring record accuracy, communication efficiency, and comparison effectiveness in research and to early identify clinical practices requiring improvement.

# 2. Patients and methods

#### 2.1. Study population and data collection

For this single-center, retrospective, cohort study, we selected a sample population from our in-house retrospective OSCC cohort, which included 94 consecutive patients who received curative surgery and subsequent adjuvant therapy, if indicated, in accordance with institutional guidelines. Those patients whose medical histories included malignancy, synchronous second primary cancer, distant metastasis at diagnosis, infections or inflammatory conditions, or neoadjuvant therapy and those who were missing data excluded from this study. One patient who had received a liver transplantation was excluded from the analysis. In total, 70 patients with histologically diagnosed OSCC who received curative surgery between January 2014 and December 2018 at the Department of Otorhinolaryngology-Head and Neck Surgery at Chiayi Chang Gung Memorial Hospital were comprised the study population. All patients received a routine preoperative assessment that entailed a detailed medical history as well as a physical examination, laboratory tests, magnetic resonance imaging or computed tomography of the head and neck, chest radiography, abdominal echography, and nuclear bone scintigraphy. In the preoperative period, no additional nutritional support was provided. Patients' medical records describing baseline demographic and clinicopathological characteristics, body weight and height, pretreatment PG-SGA score, comorbidities defined using the Charlson Comorbidity Index,<sup>[14]</sup> preoperative biochemistry and hematology results, overall pathological tumor, node, and metastasis (TNM) classification (AJCC Cancer Staging Manual, Eighth Edition), adjuvant radiation dose, and administration of chemotherapy were documented. We collected body measurements and laboratory test results at most 1 week before surgery, and we calculated preoperative neutrophil-to-lymphocyte ratio (NLR) as peripheral blood neutrophil count/lymphocyte count.

Regarding surgical procedures, all patients received primary curative surgery for OSCC with unilateral (52 patients) or bilateral neck dissection (18 patients) and intraoperative frozen section analysis of margins. The primary curative surgery was performed by a head and neck surgeon (YT Tsai), and the primary closure of wounds after neck dissection and the reconstruction of surgical defects were performed immediately by plastic surgeon (HK Yeh) using primary closure (9 patients), myocutaneous flap reconstruction (5 patients), or free flap reconstruction (56 patients). All the operations were completed independently by the same surgeons, which may help to eliminate potential surgeon bias. This retrospective study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (No.202000032B0), and the requirement for informed consent was waived because of the retrospective nature of the study and use of anonymous information contained in medical records and charts.

# 2.2. Nutritional assessment

General nutritional assessment for patients was conducted by a dietician experienced with anthropometric parameters and the scored PG-SGA within 1 week before surgery. The scored PG-SGA provides both a qualitative classification to categorize nutritional status and a fine-tuned quantitative score to triage nutrition intervention and assess changes in the quality of life and nutrition of patients with HNC.<sup>[12]</sup> The assessment involves historical components provided by patients (body weight loss, nutrition impact symptoms, intake conditions, as well as functional capacity), professionally assessed components (age, diagnosis, physical examination, and metabolic stress), an overall nutrition assessment (A = well nourished, B = moderately malnourished, C = severely malnourished), a total score, and a nutritional triage recommendation. An A, B, or C PG-SGA rating summarizes a patient's overall status. We divided patients into well-nourished (A rating) and malnourished (B or C ratings) groups.<sup>[15,16]</sup> Total PG-SGA scores, which range from 0 to 35 and provide professionals with clear guidelines regarding the extent of required medical nutrition therapy, were calculated as described by Ottery et al.<sup>[11]</sup> In general, higher scores indicate a higher malnutrition risk, and PG-SGA scores of >4 suggest the need for a dietician's intervention.

#### 2.3. Postoperative complications

All patients were evaluated for postoperative complications over a 30-day period after surgery, and no patients were lost to followup after discharge. Postoperative complications were defined in accordance with the 5-grade Clavien–Dindo classification system, which is validated for grading complications from head and neck surgery with high validity, reliability, and acceptance.<sup>[13]</sup> Postoperative complications were categorized as none, minor (Clavien–Dindo classification I or II), or major (classifications III-V). The Enhanced Recovery After Surgery recommendations were used to define normal postoperative care and standardized management.<sup>[17]</sup>

#### 2.4. Outcome measurements

Primary outcomes were measured by comparing the baseline demographic and clinicopathological characteristics, PG-SGA scores, and postoperative parameters of the well-nourished and malnourished patients. Secondary outcome measurement was conducted by analyzing the risk factors for postoperative complication occurrence in patients with OSCC after curative surgery.

#### 2.5. Statistical analysis

Categorical data are presented as frequencies and percentages, and continuous data are presented as medians with interquartile ranges (IQRs). To compare the well-nourished and malnourished groups, the Chi-Square and Mann–Whitney U tests were used for the categorical and continuous variables, respectively. We used the univariate logistic regression analysis identify the potential risk factors for postoperative complications, and the multivariate logistic regression with stepwise selection was also performed to recognize which variables were significantly associated with the development of postoperative complications. Parameters included in the univariate logistic regression analysis included the TNM stage, underlying comorbidities, and median values of age, PG-SGA score, BMI, and NLR. A P value of <.05 was regarded as significant, and SPSS version 18.0 (SPSS Inc., Chicago, IL) was employed for all statistical analysis.

# 3. Results

The baseline characteristics of the 70 patients are presented in Table 1. The pretreatment medians were as follows: age was 72 years (IQR: 68-77 years), Body Mass Index (BMI) was 24.4 (IQR, 21.0-26.7), NLR was 2.5 (IQR: 1.8-3.5), and PG-SGA score was 4 (IQR: 2-6). In the nutritional assessment, 26 (37.1%) patients with a PG-SGA A rating were categorized into the wellnourished group, and 35 (50.0%) and 9 (12.9%) patients with PG-SGA ratings of B and C, respectively, were categorized into the malnourished group. OSCC occurred in 3 major regions: 23 (32.9%) cases were in the buccal mucosa, 16 (22.9%) were in the tongue, and 13 (18.6%) were in the gingiva. The study population was predominantly male (male to female ratio of 13:1); 38 (54.3%) patients were diagnosed as having early-stage cancer (stage I or II), whereas 32 (45.7%) patients had locally advanced OSCC (stage III or IV). In addition, 56 (80%) patients had underlying comorbidities, and the median hospital and ICU stay durations were 19 (IQR: 15-24) and 4 (IQR: 3-5) days, respectively.

Table 2 presents a comparison of the clinicopathological characteristics and outcomes of the well-nourished and malnourished groups. Compared with well-nourished patients, patients who were malnourished were significantly older (P = .03), weighed less (P = .001) and had lower BMIs (P = .003), scored higher on the PG-SGA (P < .001), had lower serum albumin (P = .01), had higher NLRs (P = 0.034), experienced more postoperative complications (P < .001), and stayed longer in the hospital (P = .021).

A total of 43 (61.4%) patients developed 1 or more postoperative complications, which were significantly more common among the malnourished patients (P < .001, Table 3). The complication rate was 74.3% (n=26) in patients with PG-SGA category B and 88.9% (n=8) in patients with PG-SGA category C. The incidence of major complications (Clavien-Dindo classification  $\geq$  IIIa) in the well-nourished and malnourished groups was 7.6% (n=2) and 25% (n=11), respectively (P=.013).

#### Table 1

Baseline characteristics of 70 patients with oral cavity cancer who underwent primary surgery.

Variable	Median (IQR)/n (%)
Sex	
Men	65 (92.9)
Women	5 (7.1)
Age (years)	72 (68–77)
BMI (kg/m <sup>2</sup> )	24.4 (21.0-26.7)
PG-SGA score	4 (2-6)
PG-SGA rating	
A	26 (37.1)
B+C	44 (62.9)
Primary tumor site	
Buccal mucosa	23 (32.9)
Tongue	16 (22.9)
Gingiva	13 (18.6)
Lip	10 (14.3)
Retromolar trigone	4 (5.7)
Mouth floor	3 (4.3)
Hard palate	1 (1.4)
pT classification	
T1	23 (32.9)
T2	19 (27.1)
T3	5 (7.1)
Τ4	23 (32.9)
Lymph node metastasis	
No	60 (85.7)
Yes	10 (14.3)
pTNM staging	
I—II	38 (54.3)
III—IV	32 (45.7)
WBC (x10 <sup>3</sup> cells/µl)	6.7 (5.7-8.6)
Hemoglobin (g/dl)	13.3 (12.0–14.7)
Albumin (g/dl)	4.4 (4.1-4.7)
NLR	2.5 (1.8-3.5)
Comorbidity	
No	14 (20.0)
Yes	56 (80.0)
ICU care (days)	4 (3-5)
Hospitalization (days)	19 (15-24)

Values are expressed as medians (interguartile range) or as number (%) of patients.

BMI = Body Mass Index, ICU = intensive care unit, IQR = interquartile range, NLR = neutrophil-tolymphocyte ratio, OSCC = oral cavity squamous cell carcinoma, PG-SGA = Patient-GeneratedSubjective Global Assessment, WBC = white blood cells.

Details of the postoperative complications based on Clavien-Dindo classification are listed in Table 4. Nearly 70% of the complications (n=30, 69.8%) were categorized as minor (Clavien-Dindo classifications I and II). Use of therapeutic antibiotics was the most common minor complication (n=7,16.3%, Clavien–Dindo classification II), followed by the frequent monitoring for pale free flap (n=5, 11.6%, Clavien-Dindo)classification I). For the major complications, the most severe complication was Clavien-Dindo classification IVa and was recorded in 1 patient who developed acute myocardial infarction with low cardiac output and was managed in the intensive care unit. Patients who underwent wound debridement, drainage tube placement, and hemostasis under endoscopic guidance were categorized as Clavien-Dindo classification IIIa, and those who underwent an intervention under general anesthesia, including flap revision surgery, tracheostomy surgery, and hemostasis in operating room, were categorized as Clavien-Dindo classification IIIb.

# Table 2

Clinicopathological characteristics in patients with different nutritional status (n = 70).

Variable	Well-nourished (n = 26)	Malnourished (n = 44)	P value
Sex, n (%)			
Men	24 (92.3)	41 (93.2)	.891
Women	2 (7.7)	3 (6.8)	
Age, median (IQR)	71 (67-73)	74 (69-80)	.03
BW, median (IQR)	68.3 (60.5-74.3)	59.4 (50.9-69.4)	.001
BMI, median (IQR)	26.2 (23.4-27.9)	22.1 (20.0-25.2)	.003
Cancer stage, n (%)			
I—II	16 (61.5)	22 (50.0)	.127
III—IV	10 (38.5)	22 (50.0)	
PG-SGA score, median (IQR)	2 (2-3)	5 (3-6)	<.001
WBC, median (IQR)	6.7 (5.8-9.9)	6.4 (5.6-8.5)	.854
Hemoglobin, median (IQR)	13.3 (12.3-15.0)	13.1 (11.6-14.5)	1.000
Albumin, median (IQR)	4.5 (4.1-4.7)	4.0 (3.6-4.3)	.01
NLR, median (IQR)	2.1 (1.6-2.7)	3.2 (1.9-4.5)	.034
Comorbidity, n(%)			
No	23 (88.5)	33 (75.0)	.174
Yes	3 (11.5)	11 (25.0)	
Complications, n(%)			
No	17 (65.4)	10 (22.7)	<.001
Yes	9 (34.6)	34 (77.3)	
ICU stay, median (IQR)	4 (3-5)	4 (3-6)	.416
Hospitalization (days) median (IQR)	15 (12-19)	22 (17-27)	.021

BMI = Body Mass Index, BW = body weight, ICU = intensive care unit, IQR = interquartile range, NLR = neutrophil-to-lymphocyte ratio, PG-SGA = Patient-Generated Subjective Global Assessment, WBC = white blood cells.

The outcomes of the multivariate and univariate analyses of potential predictors of postoperative complications are presented in Table 5. Univariate analysis for postoperative complications revealed that age  $\geq$ 72 years (*P*=.014), PG-SGA score  $\geq$  4 (*P*=.002), and advanced cancer stage (*P*=.035) were found to be significantly associated with postoperative complications. In multivariate analysis, however, only PG-SGA score  $\geq$  4 (HR = 4.929, 95% CI: 1.516–16.031, *P*=.008) remained significant predictor for postoperative complications.

# Table 3

Postoperative complications based on the Clavien–Dindo classification.

CDC grade	Well-nourished	Malnourished	P value
Total	9	34	<.001
Minor, n (%)			
I	1 (11.1)	11 (32.4)	
II	6 (66.7)	12 (35.3)	
Major, n (%)			
Illa	1 (11.1)	4 (11.8)	.013
IIIb	1 (11.1)	6 (17.6)	
IVa	0 (0)	1 (2.9)	
IVb	0 (0)	0 (0)	
V	0 (0)	0 (0)	

 $\label{eq:CDC} \mathsf{CDC} = \mathsf{Clavien} - \mathsf{Dindo} \ \mathsf{classification}.$ 

# 4. Discussion

Among patients with HNC, 35% to 50% experience considerable malnutrition resulting from reduced food intake, mental stress, tumor-associated metabolic changes, or adverse effects related to cancer treatment; a relationship between malnutrition and postoperative events has been demonstrated in several studies.<sup>[1,9]</sup> According to our literature review, our study is the first to analyze nutritional status among individuals with OSCC before curative surgery by using the PG-SGA and to assess its association with postoperative complications defined using the Clavien-Dindo classification. Using the validated PG-SGA for nutritional assessment and the standardized Clavien-Dindo classification system to record surgical complications made our study results easily quantifiable and highly applicable in daily clinical practice for physicians treating OSCC. In the preset study, malnutrition was significantly associated with lower weight, lower BMI, older age, higher PG-SGA score, lower serum albumin level, higher systemic inflammatory index, more postoperative complications, and longer hospitalization period. The malnourished group experienced significantly more postoperative complications than did the well-nourished group, particularly major complications (Clavien-Dindo classification  $\geq$  IIIa). In addition, patients with severe malnourishment (PG-SGA category C) experienced a higher complication rate (88.9%)

Table 4

Complications stratified according to the Clavien-Dindo classification.			
CDC grade	Numbers	Detail	
Minor			
Ι	12	Wound was opened at the bedside for wet-to-dry dressing due to localized infection in 4 patients. Five patients required frequent pale free flap monitoring. Two developed postoperative wound oozing, which was controlled with gauze compression. One had a small amount of chylous leakage in the first 2 days after surgery.	
I	18	Seven patients received antibiotics for pneumonia. Four required blood transfusion. Two required total parenteral nutrition. Three developed acute delirium. One had alcohol withdrawal syndrome. One had a central line infection.	
Major			
Illa	5	Three patients underwent wound debridement. One underwent ultrasound-guided drainage placement due to seroma. One had repeated nose bleeding, requiring hemostasis under flexible nasopharyngoscopy guidance.	
IIIb	7	Four patients had flap revision surgery. Two underwent tracheostomy surgery. One developed neck hematoma, and hemostasis was achieved under general anesthesia.	
IVa	1	One patient was admitted to ICU due to acute myocardial infarction with low cardiac output.	
IVb	0		
V	0		

CDC = Clavien-Dindo classification, ICU = intensive care unit.

# Table 5

Univariate and multivariate analysis of predictive factors for the occurrence of postoperative complications in patients with oral cavity cancer.

	Number of patients	Univariate analysis		Multivariate analysis	
Variable		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age (years)					
<72	34	Reference		Reference	
≥72	36	2.021 (1.106-5.372)	.014	1.233 (0.377-4.037)	.629
PG-SGA score					
<4	37	Reference		Reference	
≥4	33	5.906 (1.970-17.707)	.002	4.929 (1.516-16.031)	.008
BMI					
< 24.4	35	Reference		Reference	
≥ 24.4	35	0.544 (0.205-1.444)	.221	1.084 (0.299-3.938)	.902
TNM stage					
Early (I—II)	38	Reference		Reference	
Advanced (III-IV)	32	3.081 (1.080-8.337)	.035	2.435 (0.701-8.464)	.161
NLR					
<2.5	33	Reference		Reference	
≥2.5	37	2.225 (0.834-5.935)	.110	1.208 (0.356-4.095)	.762
Comorbidity					
Absence	14	Reference		Reference	
Presence	56	1.804 (0.552-5.868)	.331	1.703 (0.409–7.085)	.464

CI = confidence interval, ICU = intensive care unit, NLR = neutrophil-lymphocyte ratio, OSCC = oral cavity squamous cell carcinoma, PG-SGA = Patient-Generated Subjective Global Assessment.

than did those with moderate malnutrition (PG-SGA category B; 74.3%). Multivariate analyses revealed a PG-SGA score of  $\geq$ 4 to be an independent predictor of postoperative complications among those receiving curative surgery for OSCC. According to the original PG-SGA recommendations for nutritional triage, patients with scores of  $\geq$ 4 require a dietician's intervention,<sup>[10]</sup> and our results suggest that pretreatment malnutrition that requires intervention is a risk factor for postoperative complication. Findings of the present study not only highlight the association between the need of dietician intervention and postoperative complications but also suggest the feasibility of using the PG-SGA nutritional triage recommendations for preventing postoperative complications in patients with OSCC.

The incidence of malnutrition we observed is consistent with that of patients with HNC, among whom the incidence has varied between 43% and 67% depending on the nutritional assessment tool used.[3,5,12,18] Moreover, we observed that patients with malnutrition exhibited significantly higher PG-SGA scores, lower serum albumin levels, more postoperative complications, and longer hospitalization periods than the well-nourished patients did, a result consistent with other studies that have used the PG-SGA to evaluate patients with gastroesophageal and gynecologic cancers.<sup>[19,20]</sup> Although we may have underestimated the exact effect of malnutrition, the literature has demonstrated that malnutrition determined using the PG-SGA is an independent predictor of survival in advanced cancer.<sup>[21]</sup> Clavien-Dindo classification is a highly valid, reliable, and comprehensive grading system for events occurring after surgery of the head and neck.<sup>[13]</sup> Here, the incidence of postoperative complications graded using Clavien-Dindo classification in patients with OSCC was 61.4%, consistent with previous studies on patients with HNC.<sup>[1,22]</sup> Postoperative complications are an independent risk factor for prolonged hospitalization and reduced quality of life in patients receiving surgery. This is particularly relevant for patients with HNC, for whom complications such as pharyngocutaneous fistula formation and free flap necrosis can

significantly extend hospital stays and reduce quality of life.<sup>[23]</sup> Little research has investigated the relationship of malnutrition with postoperative complications in HNC. A study in the Netherlands reviewed 64 patients who received major surgeries for advanced HNC and revealed that >10% body weight loss within 6 months before an operation is risk factor for major postoperative complications.<sup>[1]</sup> Robbins et al prospectively studied 400 patients with HNC and revealed malnutrition to predictive of surgical wound infection.<sup>[7]</sup> However, the authors did not distinctly define malnutrition, and both minor and extensive surgical procedures were included. Linn et al demonstrated a significant relationship of malnutrition with postoperative complications and survival in older patients with HNC, but this result does not accord with our findings because preoperative nutritional support was provided to many of the malnourished patients in their study population.<sup>[8]</sup> By contrast, Matthews et al did not identify an association of nutritional status with surgical complication incidence, independent of tumor stage.<sup>[24]</sup> In our study, only pretreatment malnutrition indicated by a PG-SGA score of  $\geq 4$  was an independent risk factor for complications, and other conventional risk factors, such as older age, high BMI, advanced cancer stage, high NLR, and presence of comorbidities, exhibited non-statistically significant correlations. Given our small sample, comparatively old average age of participants, and retrospective study design, future large, prospective studies are warranted to confirm our findings.

The systemic inflammatory marker NLR can significantly predict survival outcomes in patients with HNC, and it may be associated with malnutrition in patients with advanced cancers.<sup>[21]</sup> NLR also predicts postoperative complications in various cancers, such as colorectal cancer, cholangiocarcinoma, and pancreatic cancer.<sup>[25–27]</sup> However, its role in assessing postoperative complications in patients with OSCC has not yet been thoroughly examined. Maruyama et al reviewed 103 patients who received head and neck tumor resection and microsurgical reconstruction, and they discovered NLR to be a

predictor of poor wound healing.<sup>[28]</sup> In the present study, the malnourished group had a significantly higher baseline NLR than did the well-nourished group, and preoperative NLR  $\geq 2.5$  is associated with the increased risk of postoperative complication but did not reach the statistical significance. These results suggest that pretreatment NLR is an informative biomarker of nutrition among patients with OSCC, and comprehensive prospective research is required to confirm its role in predicting postoperative complications for such patients.

Peters et al retrospectively analyzed the outcomes of 1201 patients with HNC after surgical intervention, and indicated that age and cancer stage were strong predictors of medical and surgical complications, respectively.<sup>[29]</sup> Similarly, Cramer et al indicated that elderly patients, particularly those  $\geq$ 75 years old, who received surgery for both benign and malignant neoplasms in the head and neck were prone to cardiopulmonary and urologic complications but not to local surgical complications, such as wound disruption or infections at the surgical site.<sup>[30]</sup> However, Boruk et al discovered no significant relationship between age >70 years and complications after major surgery in the head or neck in a population of 157 relatively young patients with few comorbidities.<sup>[31]</sup> Linn et al evaluated the influence of nutritional status and age on surgical outcomes among older and younger malnourished and well-nourished patients with HNC. They found that older patients with malnutrition had a significantly higher morbidity rate and significantly more complications than the other groups did, and the outcomes of the older well-nourished patients were the same as those of younger patients.<sup>[8]</sup> Genther et al retrospectively analyzed 61 740 elderly patients with HNC from the National Inpatient Sample and determined that perioperative morbidity and mortality, longer hospital stays, and higher costs after receiving surgery for HNC are more common among those with comorbidities.<sup>[32]</sup> These results suggest that age is not a contraindication for patients with HNC to receive major surgery, and underlying comorbidity and malnutrition play critical roles in the development of surgical complications. By expanding on these studies, we observed that patients older than 72 years and those with comorbidities tended to develop postoperative complications, but this results did not reach significance. This may be explained by the old average age and small size of our sample. However, aging may complicate the OSCC treatment course because of reduced organ-system functional reserve and a high incidence of underlying comorbidities. For older patients with cancer who are malnourished or at nutritional risk, nutritional intervention and regular dietary counseling during treatment for HNC could help them maintain their body weight, minimize muscle atrophy, and prevent severe malnutrition, thereby improving quality of life.<sup>[33,34]</sup> These benefits of nutritional supplementation and dietary counseling may reduce PG-SGA scores and the postoperative complication risk in patients with OSCC and should be confirmed by future large-scale prospective study.

Our study had several limitations. First, our single-institute and few enrolled participants might contribute some selection bias. Second, the Clavien–Dindo classification system is used to collect data on all types of surgical complications rather than data on complications of head and neck surgery specifically. Therefore, we could not investigate the association between malnutrition and specific complications, such as specific cranial nerve injuries or orocutaneous fistula. Assessing complications of head and neck surgery by using an adapted grading scale may improve patients' future quality of life and care. In addition, this study did not assess nutritional intervention effects. Future studies should investigate the use of nutritional support for preventing, treating, and reducing complications in malnourished patients with OSCC.

#### 5. Conclusions

In patients with OSCC who received curative surgery, malnutrition as defined by the PG-SGA was associated with an increased risk of postoperative complications as defined by the Clavien– Dindo classification system. A PG-SGA score of  $\geq 4$  was an independent predictor of postoperative complications, suggesting the value of preoperative nutritional support through dietitian intervention for minimizing surgical complications. The validated nutritional assessment and complication grading used in our study make the results applicable in daily practice and clinical research for physicians treating OSCC. Prospective, multiinstitutional studies are warranted in the future to confirm our findings, since the present study was a retrospective analysis that only included a small number of patients.

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