Received: 7 December 2022 | Revised: 10 July 2023 | Accepted: 18 July 2023

DOI: 10.1002/hed.27479

ORIGINAL ARTICLE

WILEY

Computed tomography-defined sarcopenia as a risk factor for short-term postoperative complications in oral cancer patients with free flap reconstruction: A retrospective population-based cohort study

Bo Lin D.D.S, Ph.D[1,2,3] | **Jianlin Lin M.D**[2,3] | **Feng Wang M.D**[1,2,3] | **Yufan Wang D.D.S, Ph.D**[1,2,3] | **Shiyue Shen D.D.S, Ph.D**[1,2,3] | **Xia Hong D.D.S, Ph.D**[1,2,3] | **HuiJun Yang M.D**[1,2,3] | **Shunji Wang D.D.S, Ph.D**[1,2,3] | **Hongyu Yang D.D.S, Ph.D**[1,2,3]

[1]Department of Oral and Maxillofacial Surgery, Stomatological Center, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China

[2]Department of Oral and Maxillofacial Surgery, Guangdong Provincial High-Level Clinical Key Specialty, Shenzhen, Guangdong, China

[3]Department of Oral and Maxillofacial Surgery, Guangdong Province Engineering Research Center of Oral Disease Diagnosis and Treatment, Shenzhen, Guangdong, China

Correspondence
Hongyu Yang, Department of Oral and Maxillofacial Surgery, Stomatological Center, Peking University Shenzhen Hospital, 1120 Lianhua Road, Futian, Shenzhen, Guangdong, 518036, China.
Email: hyyang192@hotmail.com

Funding information
Basic Research Program of Shenzhen Innovation Council, Grant/Award Number: JCYJ20210324110014037; Shenzhen Clinical Research Center for Oral Diseases, Grant/Award Number: 20210617170745001-SCRC202201001

Section Editor: Patrick Ha

Abstract

Background: Postoperative complications after free flap reconstruction for oral cancer can increase cost and prolong hospitalization. This study explored risk factors for complications, focusing on sarcopenia.

Methods: The study explored the associations between computed tomography-defined sarcopenia and the occurrence of postoperative complications, adjusted for age, gender, smoking, alcohol, ASA scoring, clinical stage of tumor, tumor site, type of free flap used, presence of tracheotomy, and blood test parameters.

Results: Of 253 patients, 17.39% (44/253) of oral cancer patients had comorbid sarcopenia. Univariate analysis showed an overall postoperative complication rate of 65.90% in the sarcopenia group and 51.67% in the non-sarcopenia group. Multivariate modeling showed sarcopenia and smoking were major risk factors for total and respiratory complications, increasing the risks by over two-fold. No factors significantly impacted surgery-specific complications.

Conclusions: This study identified sarcopenia as a risk factor for postoperative complications in oral cancer patients undergoing flap reconstruction.

KEYWORDS

complications, cohort study, oral cancer, sarcopenia

1 | INTRODUCTION

Oral squamous cell carcinoma is the most common malignancy of the head and neck. Radical oral cancer surgery with concurrent reconstruction is a profoundly

Bo lin and Jianlin Lin contributed equally to this work and should be considered co-first authors.

complex procedure with a high incidence of postoperative complications, including dysphagia, pneumonic pneumonia, flap crisis, and wound infection.[1] Therefore, preoperative screening of high-risk groups and targeted adaptation of perioperative care and support are important steps to prevent postoperative complications and mortality.

Sarcopenia is a progressive, widespread loss of skeletal muscle mass and function that clinically manifests as reduced skeletal muscle mass, decreased muscle strength, and decreased motor function.[2] It has been identified as a poor prognostic factor for postoperative complications and prognosis in various malignancies. The classical diagnosis of sarcopenia relies on imaging measurements of the abdominal muscles.[3] However, there are not many studies available on sarcopenia in oral cancer patients because CT or MRI of the abdomen is not routinely performed in oral cancer cases. Recently, some studies have used CT data at the level of the third transverse cervical vertebra (C3) in oral cancer patients to assess sarcopenia, which has been shown to be a valid alternative.[4,5] Compared with other malignant tumors, oral cancer patients mostly experience eating and swallowing disorders and have a higher risk of malnutrition and sarcopenia. Furthermore, research has shown that sarcopenia can lead to treatment interruption, delayed dosing, or increased chemotherapy toxicity in patients undergoing radiotherapy for head and neck cancer.[6] However, its specific impact on short-term postoperative complications in oral cancer patients with free flap reconstruction is still poorly understood. Malignant tumors cause a systemic inflammatory response in the patient's body, and the inflammatory state also plays a key role in the development and progression of cancer. The systemic inflammatory state is also an important etiology of sarcopenia, combined with abnormalities in lipid and protein metabolism.[7] Merging inflammatory markers, including platelet-lymphocyte ratio, have gained attention as potential tools to diagnose the inflammatory state of patients and predict treatment outcomes.[8,9] However, their impact on postoperative complications in oral cancer patients remains unclear. Therefore, this study utilized population-based data to investigate the effects of sarcopenia and inflammatory markers on short-term postoperative complications in patients undergoing free flap reconstruction for oral cancer.

2 | METHODS

2.1 | Patients

This is a retrospective cross-sectional cohort study of patients undergoing concurrent flap surgery for oral cancer, approved by the Institutional ethics committee and individual patient consent was waived. Data were obtained from a database of single-center oral and maxillofacial surgery for the period 2018–2021. Inclusion criteria: (1) Inclusion of patients undergoing their first surgical treatment for oral malignancies according to the procedure codes of the *International Classification of Diseases Clinical Modification of 9th Revision Operations and Procedures* (ICD-9); (2) Those who underwent free-flap reconstruction surgery concurrently; (3) Complete imaging data, including head and neck enhancement CT, postoperative chest radiographs, and ultrasound of the lower extremities, are available at baseline and after surgery. Exclusion criteria: (1) Patients with a history of preoperative radiotherapy or chemotherapy; (2) Patients with co-morbidities of other malignancies; and (3) The medical record is incomplete and the key information available is unknown.

2.2 | Observation endpoints

The primary observational endpoint was the cumulative total complication rate at 1 month postoperatively, which was the ratio of the sum of individuals with one or more postoperative complications within 1 month postoperatively to the number of individuals in the included cohort, including respiratory, cardiovascular, surgery-related complications, and other complications not listed but judged clinically relevant to treatment. Complications were determined from the medical record book, ICD-9 codes during the hospitalization and follow-up period. Secondary observation endpoints included time in intensive care, postoperative hospital stay, and total cost of the current treatment.

2.3 | Exposure variables

This study aimed to identify predictors of postoperative complications, including age, gender, smoking, alcohol consumption, American Society of Anesthesiologists (ASA) score, clinical tumor stage, tumor site, type of free flap used, presence of tracheotomy, skeletal muscle index based on third cervical spine measurements, and presence of sarcopenia. Additionally, hemoglobin (HB), mean platelet volume (MPV), and platelet distribution width (PDW) in blood routine parameters were included in the analysis. Platelet count (PLT), lymphocyte absolute value (LYM), neutrophil absolute value (NEU), as well as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were also collected and analyzed to further investigate their impact on postoperative complications.

TABLE 1 Patient comorbidities according to the ASA score.

ASA PS classification	Definition	Adult examples[a], including, but not limited to
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Current smoker, social alcohol drinker, pregnancy, obesity (30 < BMI < 40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Recent (<3 months) MI, CVA, TIA or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, shock, sepsis, DIC, ARD, or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes	

[a]Patient comorbidities in this study were defined according to the examples provided in the ASA physical status classification system, rather than investigator-defined conditions.

2.4 | Definitions

A patient was deemed a tobacco/alcohol user for the purposes of this study if he or she had smoked or chewed tobacco/alcohol on a continuous basis within the previous 3 years. The ASA score (Table 1) was used to analyze preoperative complications recorded in patients' medical records.[10] This included chronic respiratory, circulatory, digestive, urinary, and metabolic diseases that may affect patient prognosis, such as diabetes, hypertension, chronic obstructive pulmonary disease, morbid obesity (defined as body mass index ≥40), active hepatitis, pacemaker implantation, moderate or severe decrease in ejection fraction, end-stage renal disease, myocardial infarction, cerebrovascular disease, transient ischemic attack, coronary artery disease/cardiac stent history, progressive myocardial ischemia, severe valve dysfunction, sepsis, disseminated intravascular coagulation, acute respiratory distress syndrome, and abdominal conditions. When one or more of these codes appeared in the medical record, it was considered that there were complications. The tumor site included the tongue, cheek, lip, gums, floor of the mouth, and jawbone. Cases where the tumor originated at the root of the tongue but extended to the oropharynx were also included in the analysis. The free flap types considered were forearm flap, anterolateral thigh flap, and fibula flap.

Surgical-specific complications in the study were defined as the presence of at least one of the following within the observation endpoint: septic drainage of the incision; spontaneous dehiscence of the incision that was intentionally opened or aspirated by the surgeon with a positive culture result or not cultured and the patient has a fever (temperature >38°C) with local pain or tenderness; and abscess or other evidence of infection involving deep tissue on gross anatomic, radiologic, or histopathologic examination; sepsis, central venous catheter infection, postoperative bleeding or hematoma or flap thrombosis. Postoperative pneumonia was defined as the presence of a new or progressive infiltrate on chest radiograph or CT scan combined with purulent sputum, leukocytosis (white blood cell count $>10*10^9$/L), or fever (temperature > 38°C). Other respiratory-related complications include imaging or clinically confirmed and documented pleural effusions, pulmonary atelectasis, acute bronchitis, or acute respiratory distress syndrome. Cardiovascular-related complications include ultrasound-confirmed deep vein thrombosis in the lower extremities, myocardial infarction, arrhythmias, heart failure. If the number of complications in a particular category was too small to cause significant bias in

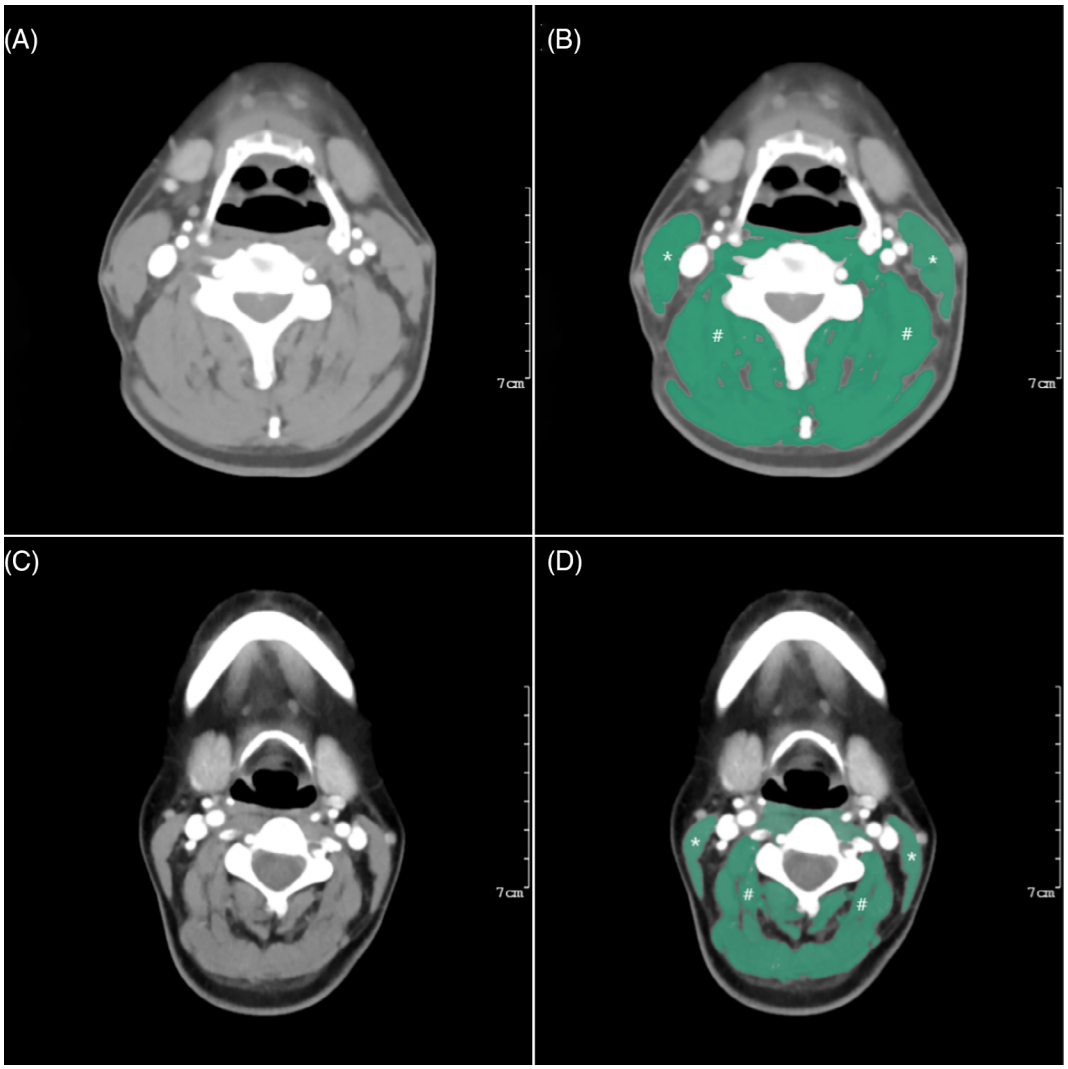

FIGURE 1 (A, B) Example of segmentation of skeletal muscle tissue at the level of the third cervical vertebra (C3) of a non-sarcopenia patient. Threshold for HU were set from −29 to +150, which corresponds with skeletal muscle density. Most of the skeletal muscle was selected automatically (green), while other densities such as bone structures and fat infiltration were excluded. However, the outside counts have to be manually adjusted for each region of interest to eliminate huge veins. The sternocleidomastoid muscle (*) and paravertebral muscles (#) are displayed. The measuring area is 58.97 cm^2. (C, D) CT sectional image of C3 level in a patient with sarcopenia. The measuring area is 21.40 cm^2. [Color figure can be viewed at wileyonlinelibrary.com]

the statistical analysis, they were not analyzed separately, but were combined in the total complications. Total complications were defined as the sum of individuals who experienced one or more postoperative complications.

The sarcopenia group (SA group) and the non-sarcopenia group (NS group) were divided according to the diagnostic criteria of sarcopenia. Diagnosis of sarcopenia: the area of skeletal muscle coverage is defined by measuring the paravertebral and sternocleidomastoid facet muscles on CT slices at the level of the third cervical vertebra (C3), using a threshold range of −29 to 150 Hounsfield unit (HU). The calculated skeletal muscle area at the level of C3 cross section area (C3 CSA) is converted to the area of the third lumbar vertebra (L3 CSA) according to the formula:[4]

(L3 CSA) = 27.304 + 1.363*(C3 CSA) − 0.671*age (year) + 0.640*weight (kg) + 26.442*gender(1 = male; 2 = female).

The value obtained by dividing the calculated L3 CSA by the square of height in meters is the skeletal muscle index (SMI; cm^2/m^2). SMI values <40.8 cm^2/m^2 for male and <34.9 cm^2/m^2 for female are diagnosed as sarcopenia.[11] The measured CT information was obtained from the hospital HIS system and its own area measurement tool. Figure 1 shows the contours of the sternocleidomastoid and paravertebral muscles, along with differences in

skeletal muscle appearance between sarcopenic and non-sarcopenic patients.

2.5 | Statistical analysis

Means and standard deviations were described for the continuous variable with the normal distribution, and medians (25th and 75th percentiles) were used for continuous variables with non-normal distribution. Categorical variables are described as percentages. The independent samples t-test and Wilcoxon rank-sum test were conducted for continuous variables and the Chi-square test was performed for qualitative variables. The logistic regression was conducted to evaluate the association of sarcopenia with complications. Model 1 incorporates macro indicators, including smoking, drinking, metabolic syndrome, and tumor stage. Model 2 further incorporates routine blood tests indicators based on Model 1. Sex, age, height, and weight were excluded from the model to avoid the effects of multicollinearity. Data tidying and modeling were implemented using R-studio (version 4.0.2). $p < 0.05$ was regarded as statistical significance.

3 | RESULTS

3.1 | General information of the research subjects

This cohort study included a total of 253 patients, comprising 195 males and 58 females, with a mean age of 52.2 years. Preoperative CT data were collected from all patients, with 44 patients diagnosed with sarcopenia after measurement and conversion. Additionally, preoperative ASA score, platelet count, white blood cell count, hemoglobin, mean platelet volume, and platelet distribution width data were collected from all patients. The locations of primary tumors in this cohort included buccal mucosa, gums, jaws, lips, floor of mouth, tongue, and tongue root extending to oropharynx, and 184 cases involved patients who underwent tracheotomy. Anterolateral thigh flap (ALT), fibula flap, and forearm flap were used in 149 cases, 22 cases, and 82 cases, respectively.

The occurrence of surgery-related complications was recorded in 87 patients postoperatively, including 51 cases of surgical incision infection from various causes, 13 cases of salivary fistula, five cases of postoperative hematoma, and 17 cases of flap thrombosis.

Postoperative imaging-confirmed respiratory complications were documented in 65 patients.

Two patients developed ventricular premature beats and acute non-ST-segment elevation myocardial infarction, respectively, and recovered with prompt treatment. Seven patients developed deep vein thrombosis and recovered after standard treatment. Other rare complications included one case of decubitus, two cases of urinary system infection, and one case of delirium.

Patients with sarcopenia had an intensive care time of 29.86 h and a mean postoperative hospital stay of 18.45 days, compared with 23.31 h and 15.84 days, respectively, in the control group. The total cost of hospitalization for patients with sarcopenia increased by 13.49% compared with the non-sarcopenic group.

General information of the study cohort is detailed in Table 2.

3.2 | Evaluation of outcomes and correlation analysis

The overall postoperative complication rate was 65.91% in the SA group and 51.67% in the control group, and the difference between the two groups was not statistically significant ($p = 0.097$). As shown in Table 3, among the included exposure factors, higher age, male, tobacco use, neutrophil count, and neutrophil/lymphocyte ratio were risk factors for total postoperative complications with $p < 0.05$.

Further analysis of respiratory-related complications showed that the percentage of respiratory-related complications after surgery was 45.45% in the SA group and 21.53% in the control group, with a statistically significant difference ($p = 0.002$). In addition, higher age and neutrophil values were also risk factors for postoperative respiratory complications ($p < 0.001$), while no other exposure factors were found to be statistically significant。.

For surgery-specific complications, the percentage of postoperative surgery-related complications was 29.55% in the SA group and 35.41% in the control group, with no statistically significant difference ($p = 0.457$). Male and tobacco use were risk factors for surgery-related complications (all P values <0.05).

Other complications were too few in number to be analyzed separately and were combined in the total complications.

3.3 | Multiple logistic regression model evaluation

To exclude the influence of confounding factors, a multifactorial analysis was further performed by including independent variables based on factors that may influence postoperative complications in clinical practice, and

TABLE 2 Basic characteristics.

	Total (%)	Sarcopenia (%)	None-Sarcopenia (%)	*p* value
Age				
Mean (SD)	52.17 (±12.39)	65.73 (±8.79)	49.32 (±11.09)	<0.001
Gender				
Male	195 (77.08)	20 (45.45)	175 (83.73)	<0.001
Female	58 (22.92)	24 (54.55)	34 (16.27)	
Drink				
No	193 (76.28)	36 (81.82)	157 (75.12)	0.441
Yes	60 (23.72)	8 (18.18)	52 (24.88)	
Smoking				
No	112 (44.27)	30 (68.18)	82 (39.23)	<0.001
Yes	141 (55.73)	14 (31.82)	127 (60.77)	
Stage				
I	18 (7.11)	3 (6.82)	15 (7.18)	0.121
II	62 (24.51)	5 (11.36)	57 (27.27)	
III	74 (29.25)	14 (31.82)	60 (28.71)	
IV	99 (39.13)	22 (50.00)	77 (36.84)	
Tracheostomy				
No	69 (27.27)	7 (15.91)	62 (29.67)	0.065
Yes	184 (72.73)	37 (84.09)	147 (70.33)	
ASA score				
Mean (SD)	1.92 (±0.73)	2.05 (±0.75)	1.89 (±0.72)	0.191
Type of free flap				
ALT[a] flap	149 (58.89)	32 (72.73)	117 (55.98)	0.082
Fibular flap	22 (8.70)	4 (9.09)	18 (8.61)	
Forearm flap	82 (32.41)	8 (18.18)	74 (35.41)	
Location				
Buccal	58 (22.92)	9 (20.45)	49 (23.44)	0.052
Gingival	19 (7.51)	4 (9.09)	15 (7.18)	
Jaw	5 (1.98)	3 (6.82)	2 (0.96)	
Lip	4 (1.58)	0 (0.00)	4 (1.91)	
Month Floor	19 (7.51)	2 (4.55)	17 (8.13)	
Tongue root[b]	15 (5.93)	6 (13.64)	9 (4.31)	
Tongue	133 (52.57)	20 (45.45)	113 (54.07)	
HB[c]				
Mean (SD)	137.95 (±18.20)	125.02 (±13.36)	140.67 (±17.93)	<0.001
MPV[d]				
Mean (SD)	10.45 (±1.01)	10.22 (±0.92)	10.49 (±1.02)	0.086
PDW[e]				
Mean (SD)	12.15 (±2.29)	11.47 (±2.06)	12.30 (±2.31)	0.011
PLR[f]				
Mean (SD)	135.60 (±61.96)	153.00 (±86.70)	131.94 (±54.95)	0.121
NLR[g]				
Mean (SD)	2.39 (±2.41)	2.52 (±1.52)	2.36 (±2.56)	0.331

TABLE 2 (Continued)

	Total (%)	Sarcopenia (%)	None-Sarcopenia (%)	*p* value
Total complication				
No	116 (45.85)	15 (34.09)	101 (48.33)	0.097
Yes	137 (54.15)	29 (65.91)	108 (51.67)	
Surgery-related complications				
No	166 (65.61)	31 (70.45)	135 (64.59)	0.492
Yes	87 (34.39)	13 (29.55)	74 (35.41)	
Respiratory-related complications				
No	188 (74.31)	24 (54.55)	164 (78.47)	0.002
Yes	65 (25.69)	20 (45.45)	45 (21.53)	

[a]Anterolateral thigh flap.
[b]Tongue root extending to oropharynx.
[c]Hemoglobin.
[d]Mean platelet volume.
[e]Platelet distribution width.
[f]Platelet-lymphocyte ratio.
[g]Neutrophil-lymphocyte ratio.

the results are shown in Table 4. Sarcopenia and smoking emerged as major risk factors in both models for overall and respiratory complications, increasing the risks over two-fold with p values under 0.05. Specifically, sarcopenia raised the odds of overall complications by 2.18 (confidence interval [CI] = 1.02–4.68, $p = 0.045$) and 2.43 (CI = 1.10–5.38, $p = 0.028$)-fold in models 1 and 2 respectively, and increased the odds of respiratory complications by 2.89 (CI = 1.31–6.37, $p = 0.008$) and 3.65 (CI = 1.56–8.57, $p = 0.003$)-fold. Smoking increased the likelihood of overall complications by 2.32- and 2.24-fold, and respiratory complications by 2.51- and 2.32-fold in the two models. While model 2 also identified NLR as a risk factor for respiratory complications (OR = 1.23, CI = 1.04–1.46, $p = 0.018$), no factors significantly impacted surgery-specific complications (all p values were above 0.05).

4 | DISCUSSION

In this retrospective cohort study, we evaluated various risk factors impacting short-term postoperative complications in oral cancer patients undergoing microsurgery. Our findings showed that CT-defined sarcopenia significantly increased the incidence of total postoperative complications and respiratory-associated complications in patients. These results suggest that treatment teams should pay more attention to the preoperative nutritional status of oral cancer patients to reduce the risk of complications.

Preoperative malnutrition can lead to wound dehiscence, anastomotic fistula, infection, delirium, increased mortality, and prolonged hospital stay. The Mini Nutritional Assessment (MNA) scale is commonly used as a simple preoperative nutritional status assessment tool,[12] based mainly on food intake, mobility, BMI, or leg circumference. Sarcopenia is also widely used as a nutritional status indicator and frailty evaluation tool. It is characterized by age-related loss of skeletal muscle mass and function, leading to reduced exercise capacity and shorter exercise time. The prevalence of sarcopenia ranges from 5%–13% in individuals aged 60–70 years to 11%–50% in those aged 80 years and above.[13] In patients with malignant tumors, sarcopenia is a common comorbidity that significantly impacts clinical diagnosis and prognosis. Malignancy promotes sarcopenia through tumor metabolism, systemic inflammation, and tumor-mediated effects such as weakness and decreased functional status.[14] Sarcopenia has been identified as a poor prognostic factor for postoperative complications and prognosis in various malignancies, including colorectal cancer, esophageal cancer, hepatocellular carcinoma, malignant melanoma, pancreatic cancer, and bladder cancer. It is highly correlated with postoperative outcomes and is an essential tool for preoperative analysis and evaluation.[15–17]

The diagnosis of sarcopenia is based on a clinical assessment of three conditions: muscle mass, muscle strength, and physical performance. The precise diagnosis is complex, but in clinical practice, computed tomography (CT) is commonly used. Skeletal muscle volume at the level of the third lumbar vertebra (L3) based on abdominal CT is often used in studies to assess sarcopenia, but this approach is not routinely performed in oral cancer patients. In recent years, studies have used a

TABLE 3 Univariate analysis of different types of complications.

		Total complication			Surgery-specific complications			Respiratory-related complications		
	Total	No	Yes	*p* value	No	Yes	*p* value	No	Yes	*p* value
Age										
Mean (SD)	52.17 (±12.39)	49.59 (±11.47)	54.36 (±12.76)	0.004	51.90 (±12.47)	52.70 (±12.29)	0.632	50.31 (±11.54)	57.57 (±13.26)	< 0.001
Gender										
Male	195 (77.08)	81 (69.83)	114 (83.21)	0.016	121 (72.89)	74 (85.06)	0.041	140 (74.47)	55 (84.62)	0.122
Female	58 (22.92)	35 (30.17)	23 (16.79)		45 (27.11)	13 (14.94)		48 (25.53)	10 (15.38)	
Drink										
No	193 (76.28)	91 (78.45)	102 (74.45)	0.551	128 (77.11)	65 (74.71)	0.762	143 (76.06)	50 (76.92)	0.998
Yes	60 (23.72)	25 (21.55)	35 (25.55)		38 (22.89)	22 (25.29)		45 (23.94)	15 (23.08)	
Smoking										
No	112 (44.27)	60 (51.72)	52 (37.96)	0.031	81 (48.80)	31 (35.63)	0.047	87 (46.28)	25 (38.46)	0.312
Yes	141 (55.73)	56 (48.28)	85 (62.04)		85 (51.20)	56 (64.37)		101 (53.72)	40 (61.54)	
Stage										
I	18 (7.11)	9 (7.76)	9 (6.57)	0.801	11 (6.63)	7 (8.05)	0.892	16 (8.51)	2 (3.08)	0.059
II	62 (24.51)	31 (26.72)	31 (22.63)		42 (25.30)	20 (22.99)		52 (27.66)	10 (15.38)	
III	74 (29.25)	34 (29.31)	40 (29.20)		50 (30.12)	24 (27.59)		50 (26.60)	24 (36.92)	
IV	99 (39.13)	42 (36.21)	57 (41.61)		63 (37.95)	36 (41.38)		70 (37.23)	29 (44.62)	
Tracheostomy										
No	69 (27.27)	36 (31.03)	33 (24.09)	0.261	41 (24.70)	28 (32.18)	0.242	57 (30.32)	12 (18.46)	0.076
Yes	184 (72.73)	80 (68.97)	104 (75.91)		125 (75.30)	59 (67.82)		131 (69.68)	53 (81.54)	
Sarcopenia										
No	209 (82.61)	101 (87.07)	108 (78.83)	0.097	135 (81.33)	74 (85.06)	0.492	164 (87.23)	45 (69.23)	0.002
Yes	44 (17.39)	15 (12.93)	29 (21.17)		31 (18.67)	13 (14.94)		24 (12.77)	20 (30.77)	
ASA score										
Mean (SD)	1.92 (±0.73)	1.90 (±0.73)	1.93 (±0.73)	0.692	1.94 (±0.74)	1.87 (±0.71)	0.471	1.86 (±0.70)	2.08 (±0.80)	0.064
Type of free flap										
ALT[a]	149 (58.89)	65 (56.03)	84 (61.31)	0.131	99 (59.64)	50 (57.47)	0.111	105 (55.85)	44 (67.69)	0.251
Fibular	22 (8.70)	7 (6.03)	15 (10.95)		10 (6.02)	12 (13.79)		17 (9.04)	5 (7.69)	
Forearm	82 (32.41)	44 (37.93)	38 (27.74)		57 (34.34)	25 (28.74)		66 (35.11)	16 (24.62)	

TABLE 3 (Continued)

	Total	Total complication			Surgery-specific complications			Respiratory-related complications		
		No	Yes	*p* value	No	Yes	*p* value	No	Yes	*p* value
Location										
Buccal	58 (22.92)	30 (25.86)	28 (20.44)	0.911	35 (21.08)	23 (26.44)	0.321	46 (24.47)	12 (18.46)	0.411
Gingival	19 (7.51)	8 (6.90)	11 (8.03)		10 (6.02)	9 (10.34)		15 (7.98)	4 (6.15)	
Jaw	5 (1.98)	2 (1.72)	3 (2.19)		4 (2.41)	1 (1.15)		3 (1.60)	2 (3.08)	
Lip	4 (1.58)	1 (0.86)	3 (2.19)		1 (0.60)	3 (3.45)		4 (2.13)	0 (0.00)	
Month Floor	19 (7.51)	10 (8.62)	9 (6.57)		12 (7.23)	7 (8.05)		14 (7.45)	5 (7.69)	
Tongue root[b]	15 (5.93)	6 (5.17)	9 (6.57)		11 (6.63)	4 (4.60)		8 (4.26)	7 (10.77)	
Tongue	133 (52.57)	59 (50.86)	74 (54.01)		93 (56.02)	40 (45.98)		98 (52.13)	35 (53.85)	
HB[c]										
Mean (SD)	137.95 (±18.20)	137.65 (±18.63)	138.20 (±17.89)	0.941	137.68 (±19.21)	138.46 (±16.18)	0.961	138.68 (±17.27)	135.85 (±20.66)	0.341
MPV[d]										
Mean (SD)	10.45 (±1.01)	10.45 (±1.03)	10.45 (±0.99)	0.661	10.45 (±0.97)	10.44 (±1.08)	0.891	10.44 (±1.03)	10.47 (±0.93)	0.532
PDW[e]										
Mean (SD)	12.15 (±2.29)	12.15 (±2.31)	12.15 (±2.28)	0.761	12.16 (±2.19)	12.14 (±2.47)	0.811	12.15 (±2.33)	12.16 (±2.17)	0.561
PLR[f]										
Mean (SD)	135.60 (±61.96)	135.14 (±58.44)	136.00 (±65.00)	0.971	134.85 (±59.32)	137.04 (±67.04)	0.771	131.75 (±52.82)	146.75 (±82.42)	0.322
NLR[g]										
Mean (SD)	2.39 (±2.41)	2.12 (±2.09)	2.62 (±2.64)	0.004	2.40 (±2.83)	2.38 (±1.29)	0.051	2.12 (±1.76)	3.18 (±3.61)	<0.001

[a]Anterolateral thigh flap.
[b]Tongue root extending to oropharynx.
[c]Hemoglobin.
[d]Mean platelet volume.
[e]Platelet distribution width.
[f]Platelet-lymphocyte ratio.
[g]Neutrophil-lymphocyte ratio.

TABLE 4 Multi-variate analysis of different types of complications.

	Total complication		Surgery-specific complications		Respiratory-related complications	
	Model 1	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Sarcopenia						
No						
Yes	2.18 (1.02–4.68, $p = 0.045$)	2.43 (1.10–5.38, $p = 0.028$)	1.01 (0.46–2.20, $p = 0.989$)	0.96 (0.42–2.15, $p = 0.912$)	2.89 (1.31–6.37, $p = 0.008$)	3.65 (1.56–8.57, $p = 0.003$)
Stage						
I (ref.[#])						
II	1.10 (0.36–3.36, $p = 0.862$)	1.15 (0.37–3.54, $p = 0.812$)	0.83 (0.26–2.64, $p = 0.752$)	0.80 (0.25–2.56, $p = 0.705$)	1.74 (0.33–9.29, $p = 0.515$)	1.88 (0.34–10.45, $p = 0.472$)
III	1.05 (0.34–3.18, $p = 0.938$)	1.07 (0.35–3.30, $p = 0.906$)	0.67 (0.21–2.13, $p = 0.497$)	0.64 (0.20–2.05, $p = 0.452$)	3.81 (0.76–19.16, $p = 0.105$)	3.95 (0.76–20.60, $p = 0.103$)
IV	1.08 (0.36–3.30, $p = 0.887$)	1.07 (0.35–3.29, $p = 0.910$)	0.93 (0.30–2.92, $p = 0.901$)	0.90 (0.29–2.86, $p = 0.865$)	2.51 (0.49–12.78, $p = 0.266$)	2.40 (0.45–12.71, $p = 0.303$)
Smoking						
No						
Yes	2.32 (1.25–4.31, $p = 0.007$)	2.24 (1.17–4.30, $p = 0.015$)	1.74 (0.92–3.28, $p = 0.088$)	1.78 (0.91–3.45, $p = 0.090$)	2.51 (1.19–5.26, $p = 0.015$)	2.32 (1.05–5.11, $p = 0.037$)
Drink						
No						
Yes	0.80 (0.39–1.62, $p = 0.529$)	0.76 (0.37–1.57, $p = 0.464$)	0.81 (0.39–1.67, $p = 0.560$)	0.81 (0.39–1.69, $p = 0.580$)	0.56 (0.24–1.27, $p = 0.166$)	0.51 (0.22–1.20, $p = 0.122$)
Tracheostomy						
No						
Yes	1.09 (0.47–2.50, $p = 0.839$)	1.10 (0.48–2.56, $p = 0.817$)	0.70 (0.30–1.65, $p = 0.415$)	0.69 (0.29–1.63, $p = 0.396$)	1.81 (0.66–5.02, $p = 0.252$)	1.84 (0.65–5.24, $p = 0.252$)
ASA score						
Mean ± SD	1.16 (0.79–1.71, $p = 0.461$)	1.16 (0.78–1.72, $p = 0.471$)	0.84 (0.56–1.27, $p = 0.416$)	0.83 (0.55–1.26, $p = 0.386$)	1.50 (0.97–2.32, $p = 0.068$)	1.51 (0.96–2.38, $p = 0.073$)

TABLE 4 (Continued)

	Total complication		Surgery-specific complications		Respiratory-related complications	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Type of free flap						
ALT[a] Flap (ref.)						
Fibular	1.98 (0.59–6.67, $p = 0.268$)	2.01 (0.59–6.83, $p = 0.264$)	2.55 (0.75–8.69, $p = 0.136$)	2.61 (0.76–8.95, $p = 0.127$)	0.63 (0.15–2.73, $p = 0.538$)	0.70 (0.16–3.03, $p = 0.633$)
Forearm	0.70 (0.37–1.30, $p = 0.259$)	0.71 (0.37–1.33, $p = 0.279$)	0.72 (0.37–1.39, $p = 0.326$)	0.73 (0.37–1.42, $p = 0.346$)	0.84 (0.39–1.81, $p = 0.653$)	0.86 (0.39–1.89, $p = 0.709$)
Location						
Buccal (ref.)						
Gingival	1.03 (0.29–3.74, $p = 0.961$)	0.98 (0.27–3.60, $p = 0.972$)	0.88 (0.23–3.28, $p = 0.845$)	0.86 (0.23–3.24, $p = 0.825$)	1.11 (0.22–5.76, $p = 0.897$)	0.95 (0.17–5.13, $p = 0.950$)
Jaw	0.73 (0.09–5.92, $p = 0.769$)	0.74 (0.09–6.03, $p = 0.780$)	0.17 (0.01–2.13, $p = 0.169$)	0.17 (0.01–2.14, $p = 0.170$)	2.17 (0.22–21.41, $p = 0.508$)	2.31 (0.23–22.74, $p = 0.474$)
Lip	2.41 (0.21–27.42, $p = 0.478$)	2.29 (0.20–26.75, $p = 0.509$)	4.54 (0.38–54.53, $p = 0.233$)	5.02 (0.41–61.85, $p = 0.208$)	0.00 (0.00-Inf, $p = 0.984$)	0.00 (0.00-Inf, $p = 0.984$)
Month floor	0.64 (0.18–2.30, $p = 0.491$)	0.65 (0.18–2.38, $p = 0.517$)	0.84 (0.22–3.15, $p = 0.796$)	0.85 (0.22–3.21, $p = 0.807$)	0.88 (0.20–3.98, $p = 0.870$)	0.94 (0.20–4.38, $p = 0.935$)
Tongue root[b]	1.19 (0.32–4.41, $p = 0.794$)	1.22 (0.32–4.56, $p = 0.772$)	0.70 (0.17–2.83, $p = 0.616$)	0.69 (0.17–2.82, $p = 0.603$)	1.86 (0.45–7.67, $p = 0.390$)	1.99 (0.46–8.56, $p = 0.357$)
Tongue	1.31 (0.54–3.21, $p = 0.550$)	1.25 (0.50–3.08, $p = 0.631$)	0.78 (0.31–1.94, $p = 0.593$)	0.80 (0.32–1.99, $p = 0.628$)	1.12 (0.39–3.24, $p = 0.831$)	1.03 (0.34–3.09, $p = 0.955$)
HB[c]						
Mean ± SD		1.01 (0.99–1.02, $p = 0.608$)		1.00 (0.98–1.02, $p = 0.851$)		1.01 (0.99–1.04, $p = 0.268$)
MPV[d]						
Mean ± SD		1.00 (0.35–2.87, $p = 0.996$)		1.17 (0.39–3.51, $p = 0.782$)		1.24 (0.35–4.41, $p = 0.740$)
PDW[e]						
Mean ± SD		1.02 (0.64–1.63, $p = 0.926$)		0.95 (0.59–1.54, $p = 0.830$)		0.97 (0.55–1.69, $p = 0.901$)
PLR[f]						
Mean ± SD		1.00 (0.99–1.00, $p = 0.427$)		1.00 (1.00–1.01, $p = 0.561$)		1.00 (0.99–1.01, $p = 0.907$)

(Continues)

TABLE 4 (Continued)

	Total complication		Surgery-specific complications		Respiratory-related complications	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
NLR[g]						
Mean ± SD	1.16 (0.96–1.39, $p = 0.118$)		0.97 (0.84–1.11, $p = 0.651$)		1.23 (1.04–1.46, $p = 0.018$)	

Note: Model 1 was adjusted for smoking, drinking, Tracheostomy, ASA scoring, type of flap, tumor location and tumor stage. Model 2 further incorporates routine blood tests indicators based on Model 1. (ref. #): The first row serving as a reference value for a classification indicator.

[a]Anterolateral thigh flap.
[b]Tongue root extending to oropharynx.
[c]Hemoglobin.
[d]Mean platelet volume.
[e]Platelet distribution width.
[f]Platelet-lymphocyte ratio.
[g]Neutrophil–lymphocyte ratio.

method to assess skeletal muscle area on individual transverse sections of the cervical spine at the third cervical vertebra (C3) level.[18–20] This alternative has been shown to correlate strongly with L3 muscle measurements (R = 0.785) and is a reliable and economical option.[20,21] According to international consensus, sarcopenia is defined as an L3-SMI of <55 cm^2/m^2 in men and <39 cm^2/m^2 in women. However, we defined the cutoff value for sarcopenia as <40.8 cm^2/m^2 in men and <39 cm^2/m^2 in women based on a previous epidemiological study in a large Chinese population.[11] We believe that sarcopenia is more accurate and reasonable than SMI in evaluating the preoperative nutritional status of patients because it also considers gender.

The mechanisms by which sarcopenia affects postoperative complications are still poorly understood but may be related to increased inflammatory activity following immune senescence, inflammatory factors, and other peptides.[22] Additionally, sarcopenia is a feature of cachexia, a well-known precursor of poor prognosis. Most studies have focused on the effect of low skeletal muscle status on postoperative complications, and three observational studies have evaluated the relationship between preoperative sarcopenia and postoperative complications in patients with head and neck cancer. Findings from these studies have been mixed. For instance, Alwani's case–control study[23] of 168 oral cancer patients showed a significant increase in general and flap-specific complications in patients with sarcopenia ($p < 0.05$), but no significant association with bleeding, hematoma, or cardiovascular events. Another study from Japan by Nakamura[24] analyzed 106 cases of flap reconstruction for oral cancer and found that low skeletal muscle was an independent risk factor for postoperative infection. Jung's analysis[25] of 190 patients with oropharyngeal cancer showed that sarcopenia was one of the influencing factors for early complications within 6 months after surgery. However, Ansari's study[26] showed that patients with low skeletal muscle were not significantly more likely to have postoperative complications than those without low skeletal muscle (odds ratio 1.28, $p = 0.73$). In our study, patients in the sarcopenia group had a significantly higher overall postoperative complication rate compared with the control group and a 3.65-fold increased risk of respiratory-related complications. Smoking and neutrophil/lymphocyte ratio were also identified as risk factors. Interestingly, there was no statistically significant correlation between the presence of sarcopenia and surgery-specific complications. This finding contrasts with Jones' study[27] finding a link between cachexia and worse postoperative outcomes in head and neck cancer patients. This differing result can be explained by several potential reasons. Jones' study included not only oral

cancer but also oropharyngeal, hypopharynx and laryngeal cancer. The grouping criteria also differed, as we categorized patients based on muscle mass measured with CT scans, while Jones' study used combined clinical criteria to define cachexia. Most importantly, the two studies had different criteria for judging surgery-related complications. It is possible that broad-spectrum antibiotics effectively prevent infections in the operative area, and surgery-specific complications may depend more on intraoperative asepsis, proper management of physiological dead space, tight wound closure, adequate drainage, and postoperative wound care. These factors could not be quantitatively evaluated in our retrospective study.

A number of tools have been developed to predict postoperative complications, and the ASA scoring system is a commonly used standard for evaluating patients' preoperative state. In this cohort, comorbidity assessment was also based on the ASA evaluation system. However, in order to avoid statistical collinearity, only the ASA score was included in the calculation. Studies[28,29] have shown that a higher ASA score in major surgery for head and neck cancer should be monitored more closely for the development of postoperative respiratory complications. In this cohort, the p-value of this parameter was 0.06, which is not statistically significant. This may be related to differences in subjective grading of general condition by anesthesiologists. The analysis results also did not suggest that the type of flap or location of primary tumor had a significant impact on postoperative complications. The research team believes that this result is related to the serious imbalance in the proportion of various types of flaps and tumor sites in the cohort. The operation of a fibula flap is complicated, and the risk of postoperative complications is greater than that of a soft tissue flap, but it only accounts for 8.7% of the sample. There is also an uneven distribution of primary tumors, with buccal mucosa cancer and tongue cancer accounting for more than 75% of the total sample. This unbalanced distribution can bias the statistical results, although it can be corrected through statistical methods. Our confidence in the research findings is tempered by caution, and further data is necessary to ensure a uniform distribution of study subjects.

Short-term postoperative complications in this study were limited to 1 month postoperatively, when patients were not undergoing follow-up radiotherapy for the time being, to exclude the effect of follow-up treatment on surgical complications. Surgery-specific complications from radiation therapy include both short-term wound inflammation and may lead to radiation osteomyelitis, the latter often recurring years later, while bone marrow suppression from chemotherapy is also a common complication. These data were not available in its entirety, and the treatments were not homogenous, so the study team did not include them in the analysis. The effect of low SMI or sarcopenia on the delay or interruption of radiotherapy has been reported in previous studies,[30,31] and we are concerned about this possibility. However, it remains unclear whether the high incidence of short-term postoperative complications in this group of cases would further affect the conduct of radiotherapy. Further analysis is necessary to fully understand this issue.

No studies have elaborated on the specific mechanisms by which sarcopenia affects respiratory complications, but it is thought to be related to the systemic inflammatory state. Growing evidence suggests that higher levels of inflammatory markers are associated with physical decline in older adults.[32] Recent evidence also supports the association between sarcopenia and systemic inflammatory status with poor prognosis of malignancy.[33,34] In head and neck cancer studies, two retrospective cohort studies[35,36] included serum inflammatory markers such as PLR and NLR as variables to analyze the effect of sarcopenia on overall survival. The study by Cho[36] showed a significant impact on 3-year survival in patients receiving radiotherapy for advanced tumors with combined NLR improvement in sarcopenia. These studies focus on the influence of inflammatory markers on survival, but evaluations of short-term postoperative complications are deficient. The lack of detailed studies on the specific mechanism of sarcopenia affecting respiratory complications may be related to systemic inflammation. More and more evidence show that higher levels of inflammatory markers are related to physical decline in the elderly. Although studies have shown the relationship between sarcopenia and systemic inflammatory state with poor prognosis of malignant tumors, the evaluation of short-term postoperative complications remains limited.

Growing evidence suggests that higher levels of inflammatory markers are associated with physical decline in older adults. Recent evidence also supports a relationship between sarcopenia and systemic inflammatory state with poor prognosis of malignant tumors. In head and neck cancer studies, two retrospective cohort studies[34,35] included serum inflammatory markers such as PLR and NLR as variables to analyze the influence of skeletal muscle reduction on overall survival rate. A study by Cho[36] showed that among patients with advanced cancer who received radiotherapy, sarcopenia combined with an improvement in NLR significantly impacted the 3-year survival rate. However, while these studies focused on the influence of inflammatory markers on survival, evaluations of short-term postoperative complications were insufficient. Blood routine parameters were included in this study as they are easily obtainable in retrospective cohorts and can serve as emerging inflammatory markers in specific tumors. While classic inflammatory markers such as C-reactive protein (CRP),

interleukin-6 (IL-6), procalcitonin (PCT) and serum amyloid A (SAA) have been confirmed to be sensitive in clinical practice, not all cases in the cohort were tested for these markers. Blood routine parameters are routinely obtained before operations and are increasingly being explored as inflammatory markers. Platelet-related parameters have also been studied for their relationship with certain cancers and sepsis. However, because MPV, PDW, and PLT are easily influenced by age, smoking, obesity, and the use of anticoagulant drugs, further high-quality research is needed to determine or use composite parameters. The role of leukocyte-related parameters in the tumor inflammatory microenvironment is also a research hotspot. NLR and PLR have been revealed to be related to the inflammatory reaction and prognosis in head and neck cancer and may become new verification markers.[9,37] Previous studies have focused on evaluating PLR, NLR, or MLR as prognostic markers for head and neck cancer patients. A meta-analysis[8] of published studies showed that NLR elevation was associated with worse prognosis in most studies, but the relationship between PLR, MLR, and prognosis is less well-established, with conflicting results reported in the literature. For inflammatory lesions, NLR is the most studied biomarker in COVID-19 for pulmonary infections, and its predictive value for severe progression and mortality has been confirmed by multiple studies.[38–40] The results of this study suggest that NLR mainly affects respiratory-related complications, and subsequent studies need to collect values of different inflammatory markers through prospective cohort studies for further analysis.

No different nursing measures for patients with sarcopenia and non-sarcopenia were observed in this cohort. All patients who underwent surgery for head and neck cancer, regardless of sarcopenia status, received similar standardized care programs after surgery, including the application of broad-spectrum antibiotics, maintenance of oral hygiene, adequate drainage, and nutrition, such as increasing protein intake to improve muscle quality. The results of this study emphasize the necessity of screening high-risk cases. The development of patient complications significantly prolonged postoperative hospitalization time and increased hospitalization expenses. Preoperative evaluation of sarcopenia by CT can predict short-term postoperative complications, and the medical team should pay extra attention to the overall situation of these cases.

5 | LIMITATION

The number of certain complications in this cohort was too small. Cardiovascular events, venous thrombosis, and other related complications were only recorded in a few cases and, although included in the total complications, could not be analyzed separately. In addition, the retrospective study was limited by the indicators available in medical records, which were not complete. Data on patients' leg circumference, grip strength, walking speed, and mental status were unavailable, requiring a follow-up prospective design to obtain better results.

6 | CONCLUSION

This study reviewed the relationship between preoperative sarcopenia and short-term postoperative complications in patients undergoing flap reconstruction for oral cancer at a single medical center in the last 3 years. Our analysis showed a 2.32-fold increased risk of total postoperative complications and a 3.65-fold increased risk of respiratory-related complications in patients who developed preoperative sarcopenia, but no significant effect on surgery-specific complications.

ACKNOWLEDGMENT

This research is supported by the Basic Research Program of Shenzhen Innovation Council (JCYJ20210324110014037) and Shenzhen Clinical Research Center for Oral Diseases (20210617170745001-SCRC202201001).

CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests.

DATA AVAILABILITY STATEMENT

The data for this project are available by request for academic purposes via the senior author.

ORCID

Hongyu Yang https://orcid.org/0000-0003-4547-9775

REFERENCES

1. Chamoli A, Gosavi AS, Shirwadkar UP, et al. Overview of oral cavity squamous cell carcinoma: risk factors, mechanisms, and diagnostics. *Oral Oncol*. 2021;121:105451.
2. Papadopoulou SK. Sarcopenia: a contemporary health problem among older adult populations. *Nutrients*. 2020;12(5):1293.
3. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):16-31.
4. Swartz JE, Pothen AJ, Wegner I, et al. Feasibility of using head and neck CT imaging to assess skeletal muscle mass in head and neck cancer patients. *Oral Oncol*. 2016;62:28-33.
5. Zwart AT, van der Hoorn A, van Ooijen PMA, Steenbakkers R, de Bock GH, Halmos GB. CT-measured skeletal muscle mass used to assess frailty in patients with head and neck cancer. *J Cachexia Sarcopenia Muscle*. 2019;10(5):1060-1069.

6. van Rijn-Dekker MI, van den Bosch L, van den Hoek JGM, et al. Impact of sarcopenia on survival and late toxicity in head and neck cancer patients treated with radiotherapy. *Radiother Oncol*. 2020;147:103-110.
7. Picca A, Coelho-Junior HJ, Calvani R, Marzetti E, Vetrano DL. Biomarkers shared by frailty and sarcopenia in older adults: a systematic review and meta-analysis. *Ageing Res Rev*. 2022;73:101530.
8. Kumarasamy C, Tiwary V, Sunil K, et al. Prognostic utility of platelet-lymphocyte ratio, neutrophil-lymphocyte ratio and monocyte-lymphocyte ratio in head and neck cancers: a detailed PRISMA compliant systematic review and meta-analysis. *Cancer*. 2021;13(16):4166.
9. Nakayama M, Gosho M, Hirose Y, et al. Modified combination of platelet count and neutrophil "to" lymphocyte ratio as a prognostic factor in patients with advanced head and neck cancer. *Head Neck*. 2018;40(6):1138-1146.
10. Hurwitz EE, Simon M, Vinta SR, et al. Adding examples to the ASA-physical status classification improves correct assignment to patients. *Anesthesiology*. 2017;126(4):614-622.
11. Zhuang CL, Huang DD, Pang WY, et al. Sarcopenia is an independent predictor of severe postoperative complications and long-term survival after radical gastrectomy for gastric cancer: analysis from a large-scale cohort. *Medicine*. 2016;95(13):e3164.
12. Pereira-da-Silva L, Virella D, Fusch C. Nutritional assessment in preterm infants: a practical approach in the NICU. *Nutrients*. 2019;11(9):1999.
13. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian working Group for Sarcopenia. *J Am Med Dir Assoc*. 2014;15(2):95-101.
14. Roubenoff R, Hughes VA. Sarcopenia: current concepts. *J Gerontol A Biol Sci Med Sci*. 2000;55(12):M716-M724.
15. Reisinger KW, van Vugt JL, Tegels JJ, et al. Functional compromise reflected by sarcopenia, frailty, and nutritional depletion predicts adverse postoperative outcome after colorectal cancer surgery. *Ann Surg*. 2015;261(2):345-352.
16. Iritani S, Imai K, Takai K, et al. Skeletal muscle depletion is an independent prognostic factor for hepatocellular carcinoma. *J Gastroenterol*. 2015;50(3):323-332.
17. Okumura S, Kaido T, Hamaguchi Y, et al. Impact of preoperative quality as well as quantity of skeletal muscle on survival after resection of pancreatic cancer. *Surgery*. 2015;157(6):1088-1098.
18. Wendrich AW, Swartz JE, Bril SI, et al. Low skeletal muscle mass is a predictive factor for chemotherapy dose-limiting toxicity in patients with locally advanced head and neck cancer. *Oral Oncol*. 2017;71:26-33.
19. Bozkurt G, Elhassan HA, Mahmutoglu AS, et al. Neck muscle mass index as a predictor of post-laryngectomy wound complications. *Ann Otol Rhinol Laryngol*. 2018;127(11):841-847.
20. Bril SI, Wendrich AW, Swartz JE, et al. Interobserver agreement of skeletal muscle mass measurement on head and neck CT imaging at the level of the third cervical vertebra. *Eur Archiv Oto-Rhino-Laryngol*. 2019;276(4):1175-1182.
21. Jung AR, Roh JL, Kim JS, Choi SH, Nam SY, Kim SY. Efficacy of head and neck computed tomography for skeletal muscle mass estimation in patients with head and neck cancer. *Oral Oncol*. 2019;95:95-99.
22. Nieman DC. Special feature for the Olympics: effects of exercise on the immune system: exercise effects on systemic immunity. *Immunol Cell Biol*. 2000;78(5):496-501.
23. Alwani MM, Jones AJ, Novinger LJ, et al. Impact of sarcopenia on outcomes of autologous head and neck free tissue reconstruction. *J Reconstr Microsurg*. 2020;36(5):369-378.
24. Nakamura H, Makiguchi T, Yamaguchi T, Suzuki K, Yokoo S. Impact of sarcopenia on postoperative surgical site infections in patients undergoing flap reconstruction for oral cancer. *Int J Oral Maxillofac Surg*. 2020;49(5):576-581.
25. Jung AR, Roh JL, Kim JS, Choi SH, Nam SY, Kim SY. The impact of skeletal muscle depletion on older adult patients with head and neck cancer undergoing primary surgery. *J Geriatr Oncol*. 2021;12(1):128-133.
26. Ansari E, Chargi N, van Es RJJ, Dieleman FJ, Van Cann EM, de Bree R. Association of preoperative low skeletal muscle mass with postoperative complications after selective neck dissection. *Int J Oral Maxillofac Surg*. 2022;51:1389-1393.
27. Jones AJ, Davis KP, Novinger LJ, et al. Postoperative consequences of cancer cachexia after head and neck free flap reconstruction. *Head Neck*. 2022;44(7):1665-1677.
28. Clark JR, McCluskey SA, Hall F, et al. Predictors of morbidity following free flap reconstruction for cancer of the head and neck. *Head Neck*. 2007;29(12):1090-1101.
29. L'Esperance HE, Kallogjeri D, Yousaf S, Piccirillo JF, Rich JT. Prediction of mortality and morbidity in head and neck cancer patients 80 years of age and older undergoing surgery. *Laryngoscope*. 2018;128(4):871-877.
30. Ganju RG, Morse R, Hoover A, TenNapel M, Lominska CE. The impact of sarcopenia on tolerance of radiation and outcome in patients with head and neck cancer receiving chemoradiation. *Radiother Oncol*. 2019;137:117-124.
31. Findlay M, Brown C, De Abreu LR, 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(6):811-821.
32. Walker GE, Marzullo P, Ricotti R, Bona G, Prodam F. The pathophysiology of abdominal adipose tissue depots in health and disease. *Horm Mol Biol Clin Investig*. 2014;19(1):57-74.
33. Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. *Lancet Oncol*. 2014;15(11):e493-e503.
34. Shachar SS, Williams GR, Muss HB, Nishijima TF. Prognostic value of sarcopenia in adults with solid tumours: a meta-analysis and systematic review. *Eur J Cancer*. 2016;57:58-67.
35. Yamahara K, Mizukoshi A, Lee K, Ikegami S. Sarcopenia with inflammation as a predictor of survival in patients with head and neck cancer. *Auris Nasus Larynx*. 2021;48(5):1013-1022.
36. Cho Y, Kim JW, Keum KC, Lee CG, Jeung HC, Lee IJ. Prognostic significance of sarcopenia with inflammation in patients with head and neck cancer who underwent definitive chemoradiotherapy. *Front Oncol*. 2018;8:457.
37. Jank BJ, Haas M, Dunkler D, et al. Analysis of perioperative platelet indices and their prognostic value in head and neck cancer patients treated with surgery and postoperative radiotherapy: a retrospective cohort study. *J Clin Med*. 2019;8(11):1858.

38. Fois AG, Paliogiannis P, Scano V, et al. The systemic inflammation index on admission predicts In-hospital mortality in COVID-19 patients. *Molecules*. 2020;25(23):5725.
39. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J Infect*. 2020;81(1):e6-e12.
40. Seyit M, Avci E, Nar R, et al. Neutrophil to lymphocyte ratio, lymphocyte to monocyte ratio and platelet to lymphocyte ratio to predict the severity of COVID-19. *Am J Emerg Med*. 2021;40:110-114.

How to cite this article: Lin B, Lin J, Wang F, et al. Computed tomography-defined sarcopenia as a risk factor for short-term postoperative complications in oral cancer patients with free flap reconstruction: A retrospective population-based cohort study. *Head & Neck*. 2023;1-16. doi:10.1002/hed.27479