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Association of preoperative low skeletal muscle mass with postoperative complications after selective neck dissection

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Abstract. Skeletal muscle mass (SMM) is an emerging predictive and prognostic factor in head and neck cancer patients. The aim of this study was to investigate the predictive value of low SMM for postoperative complications in clinically T1–2 oral cavity cancer patients undergoing selective neck dissection. A retrospective study in clinically T1–2 oral cavity cancer patients who underwent selective neck dissection between 2011 and 2017 was performed. The predictive value of low SMM for the occurrence of postoperative complications and prolonged hospital stay was evaluated. SMM was measured using pre-treatment imaging (computed tomography or magnetic resonance imaging) at the level of the third cervical vertebra (C3). In total, 53 patients were included, of whom 42 (79.2%) had low SMM. Patients with low SMM were not significantly more likely to experience postoperative complications (odds ratio 1.28, $P = 0.73$) when compared to patients without low SMM. No statistically significant difference in mean duration of hospital stay was seen between these patient groups. In conclusion, low SMM was found not to predict postoperative complications in T1–2 oral cavity cancer patients who underwent neck dissection.

Keywords: sarcopenia; neck dissection; mouth neoplasms; postoperative complications; length of stay.

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Oral cancer is among the top 10 most common malignancies worldwide[1]. Surgery, often followed by postoperative (chemo)radiotherapy, is a curative treatment option for patients with oral cavity cancer. Research on postoperative morbidity and survival in head and neck cancer (HNC) patients undergoing surgery with curative intent has largely focused on factors such as anatomical extension, nodal stage, comorbidities, functional status, and age[2]. Identifying risk factors in individual patients may allow surgeons to more effectively discern those at higher risk of complications and develop strategies for risk factor modification and timely recognition.

The assessment of body composition and its impact on postoperative outcomes, survival, and disease progression in various types of cancers is increasingly being

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studied[3,4]. Specifically the state of muscle mass depletion, termed sarcopenia, has been related to negative outcomes in a variety of cancers. In cancer patients, low skeletal muscle mass (SMM) has been related to a higher rate of postoperative complications, longer hospital stay, and decreased survival[4,5]. In oncological patients, SMM is rarely assessed during routine clinical practice.

Recent studies have demonstrated the predictive and prognostic value of low SMM in HNC patients. Most surgical research papers have demonstrated its prognostic value for patients with locally advanced HNC, which often necessitates wide surgical resection with free flap reconstruction[6,7]. However, little is currently known of the effects of low SMM in patients with early stage HNC who undergo surgery.

SMM is most commonly assessed on abdominal computed tomography (CT) imaging at the level of the third lumbar vertebra (L3). However, abdominal CT is not routinely performed in preoperative management protocols and the follow-up of HNC patients, and is thus not readily available for the assessment of SMM without leading to an increased patient burden or health care-related costs. A novel SMM assessment method at the level of the third cervical vertebra (C3) has been published and validated[8]. Magnetic resonance imaging (MRI) or CT imaging at the level of C3 is almost always available in patients with HNC, enabling the evaluation of SMM.

The objective of this study was to investigate whether preoperative low SMM, as measured using CT or MRI at the level of C3, is associated with the development of postoperative complications and a prolonged hospital stay in patients with early stage oral cavity cancer undergoing surgery, including neck dissection.

Materials and methods

Ethical approval

The design of this study was approved by the Medical Ethics Research Committee of the University Medical Center Utrecht (approval ID 17-365/C). All procedures in this study were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Patients and study design

A retrospective study was performed of all consecutive patients who underwent surgery for oral cavity squamous cell carcinoma clinically staged as T1 or T2 and a unilateral selective neck dissection (levels I–III/IV), between 2011 and 2017, in the Department of Oral and Maxillofacial Surgery and the Department of Head and Neck Surgical Oncology of the University Medical Center, Utrecht, the Netherlands. Clinical staging was recorded using the seventh edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Handbook[9].

Patients were included if they had imaging of the head and neck, either CT or MRI scans, obtained less than 1 month before surgery. Clinical and demographic data were collected from the medical records. Data collected included age at surgery, sex, body mass index (BMI), smoking history, tumour localization, pathological tumour stage, comorbidity as expressed by the Adult Comorbidity Evaluation-27 (ACE-27) score, duration of hospitalization, and occurrence of complications. Patients were excluded if they underwent reconstruction with local or free flaps, bilateral neck dissection, or a marginal or segmental mandibular resection.

All surgical procedures were performed by experienced head and neck surgeons. All postoperative complications were scored according to the Clavien–Dindo classification of surgical complications during the hospitalization[10].

Skeletal muscle mass measurement

SMM was measured as the muscle cross-sectional area (CSA) on pre-treatment CT or MRI of the head and neck area at the level of the third cervical vertebra (C3). The axial slide of the imaging, which showed both transverse processes and the entire vertebral arc, was selected for segmentation of the muscle tissue. For CT imaging, the muscle area was defined as the pixel area between the radiodensity range of −29 and +150 Hounsfield Units (HU), which is specific for muscle tissue. For MRI, the muscle area was manually segmented and fatty tissue was manually excluded. The CSA was calculated as the sum of the delineated areas of the paravertebral muscles and both sternocleidomastoid muscles. Segmentation of the muscle tissue was performed manually using the commercially available software package sliceOmatic (Tomovision, Magog, Quebec, Canada) by a single researcher (E.A.) who was blinded to the patient outcomes. An example of segmentation at the level of C3 is shown in Fig. 1.

The CSA at the level of C3 was converted to CSA at the level of L3 using a previously published formula (Formula 1 below)[8]. The lumbar skeletal muscle index (LSMI) was calculated by correcting SMM at the level of L3 for squared height, as shown in Formula 2 below. Low SMM was defined as a LSMI below 43.2 cm^2/m^2; this cut-off value was determined in a separate cohort of head and neck cancer patients[11].Formula 1: CSA at L3 (cm^2) = 27.304 + 1.363 × CSA at C3 (cm^2) − 0.671 × Age (years) + 0.640 × Weight (kg) + 26.442 × Sex (Sex = 1 for female and 2 for male)
Formula 2: LSMI (cm^2/m^2) = CSA at L3/length (m^2)

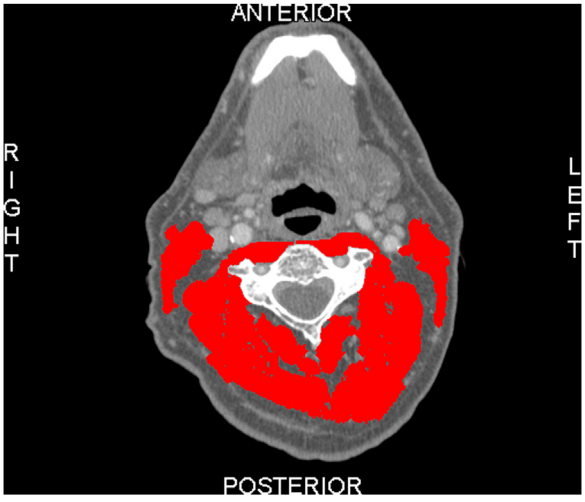

Fig. 1. Example of delineation of the paravertebral and sternocleidomastoid muscles at the level of C3.

Table 1. General characteristics of patients with and without low skeletal muscle mass (SMM).

Variables	Low SMM $n = 42$ (79.2%)	Without low SMM $n = 11$ (20.8%)	*P*-value
Sex, *n* (%)			0.74
Female	16 (38.1%)	5 (45.5%)	
Male	26 (61.9%)	6 (54.5%)	
Age (years), mean ± SD	66.7 ± 12.5	58.2 ± 16	0.06
BMI (kg/m^2), mean ± SD	23.8 ± 3.4	29.9 ± 7.4	0.0001
Smoker, *n* (%)			0.97
No	27 (64.3%)	7 (63.6%)	
Current/former	15 (35.7%)	4 (36.4%)	
ACE-27 score, *n* (%)			0.31
1 (None)	12 (28.6%)	4 (36.4%)	
2 (Mild)	18 (42.9%)	2 (18.2%)	
3 (Moderate)	12 (28.6%)	5 (45.5%)	
4 (Severe)	0	0	
pTNM stage, *n* (%)			0.05
I	14 (33.3%)	1 (9.1%)	
II	14 (33.3%)	8 (72.7%)	
III	9 (21.4%)	0 (0%)	
IV	5 (11.9%)	2 (18.2%)	
Localization, *n* (%)			0.19
Floor of mouth	10 (23.8%)	3 (27.3%)	
Tongue	18 (42.9%)	5 (45.5%)	
Gingiva	7 (16.7%)	0 (0%)	
Buccal mucosa	4 (9.5%)	2 (18.2%)	
Retromolar area	3 (7.1%)	1 (9.1%)	

BMI, body mass index; SD, standard deviation.

Table 2. Postoperative complications after selective neck dissection.

Complication	*n*	%
Wound infection	2	3.8
Seroma	2	3.8
Chyle leak	2	3.8
Electrolyte disturbance	2	3.8
Blood transfusion	1	1.9
Glycaemic dysregulation	1	1.9
Hypertension	1	1.9
Kidney failure – ICU management	1	1.9
Orocutaneous fistula	1	1.9
Pneumonia	1	1.9
Pneumonia – ICU management	1	1.9
Postoperative bleed	1	1.9
Delirium	1	1.9

ICU, intensive care unit.

Statistical analysis

The data analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated: continuous variables with a normal distribution were presented as the mean with standard deviation (SD), while variables with a skewed distribution were presented as the median with interquartile range (IQR); categorical variables were presented as frequencies and percentages. A binary logistic regression model was used for the univariate analysis. Those variables that were found to be statistically significant were included in the multivariate analysis of surgical complications. Statistical significance was evaluated at the 0.05 level using two-sided tests.

Results

Fifty-three evaluable patients were identified who had undergone surgical treatment for a T1 or T2 oral cavity cancer including neck dissection and who had pre-treatment CT or MRI available. Clinical and demographic data of the study population are presented in Table 1.

Skeletal muscle mass

Of these 53 included patients, 42 (79.2%) had low SMM. Low SMM was significantly associated with BMI ($P = 0.0001$) and TNM stage ($P = 0.05$) (Table 1).

Postoperative complications

Table 2 shows the postoperative complications that occurred. Of the 53 included patients, 36 (67.9%) had no surgical complications (Clavien–Dindo grade 0), eight (15.1%) had a grade 1 surgical complication, six (11.3%) had a grade 2 surgical complication, and three (5.7%) had a severe surgical complication indicated by a Clavien–Dindo grade of 3a or above. The median length of hospital stay was 7 days, IQR 5.5–8.5 days.

Association between low SMM and postoperative complications and length of hospital stay

The risk of developing postoperative complications was higher for patients with low SMM; however this was not statistically significant (odds ratio 1.28, $P = 0.73$) (Table 3).

The mean duration of hospital stay was longer in patients with low SMM (mean 10.8 days, SD 3.1 days) when compared to patients without low SMM (mean 7.6 days, SD 3.93 days); however this difference was not significant ($P = 0.60$).

Discussion

Although many studies have reported a higher risk of postoperative complications in cancer patients with low SMM, this study found that in clinically staged T1–2 oral cavity cancer patients who underwent surgery including selective neck dissection, no difference in complications was found between patients with and without low SMM. The combination of a high

Table 3. Logistic regression analysis—predictors of any postoperative complication (Clavien–Dindo grade 1–5).

Variables	Univariate analysis		
	OR	95% CI	*P*-value
Sex			
Male	Ref.		
Female	0.34	0.09–1.26	0.11
Age	1.05	0.99–1.1	0.08
BMI	0.98	0.87–1.11	0.78
Low SMM	1.28	0.32–5.13	0.73
Stage			
Early (I and II)	Ref.		
Advanced (III and IV)	0.48	0.14–1.62	0.24
ACE-27			
1 (None)	Ref.		
2 (Mild)	1.9	0.38–9.0	0.44
3 (Moderate)	3.9	0.8–18.6	0.09
4 (Severe)	NA		

BMI, body mass index; CI, confidence interval; OR, odds ratio; NA, not applicable; SMM, skeletal muscle mass.

incidence of low SMM (79.2%) and low complication rate (32.1%) in a small specific cohort of 53 patients may have contributed to this finding. The high incidence of SMM is in line with the previously reported incidence of 69% in T1–2 oropharyngeal cancer patients[12]. In the present study, patients with high risk factors, i.e. reconstruction with local or free flaps, bilateral neck dissection, or marginal or segmental mandibular resection, were excluded. Surgery with a low complication risk may be less susceptible to the deleterious effects of low SMM.

Low SMM may be particularly predictive of complications in high risk groups. In surgical procedures with a higher risk of complications, low SMM has been shown to be predictive of postoperative complications. In a study of 235 patients who underwent total laryngectomy, the complication rate was 64.3% (Clavien–Dindo, any grade), and 27.2% of patients developed a pharyngocutaneous fistula[13]. Patients with low SMM (46.4%) who underwent total laryngectomy had more pharyngocutaneous fistulas than patients without low SMM (34.9% vs 20.6%; $P = 0.02$). In a study of 122 patients treated with free flap reconstruction after oral cancer resection, the rate of surgical site infection was 24.6%[14]. Low SMM was present in 25.4% of patients and was an independent significant risk factor for recipient site infection (18.7% vs 41.9%; $P = 0.011$). In a study of 78 patients who underwent mandibular reconstruction with a microvascular free fibula flap after oral cavity cancer resection, any complication occurred in 78.2% of patients and free fibula flap-related complications in 23.1% of patients[6]. Patients with low SMM (61.5%) had an increased risk of free fibula flap-related complications (hazard ratio 4.3, $P = 0.02$) and severe postoperative complications (Clavien–Dindo grade 3 or 4) (hazard ratio 4.0, $P = 0.02$).

In various publications on patients with low SMM undergoing surgery for different types of solid organ cancer including HNC, it has been shown that those with low SMM have a significantly longer hospital stay and significantly higher hospital costs than patients with normal SMM[11,13,15]. In the present study, patients with low SMM had a longer hospital stay than patients with normal SMM, however this was not found to be significant. This may also be due to the aforementioned combination of study characteristics.

In this study, SMM was measured at the level of C3, since imaging at this anatomical site is almost always readily available as part of a HNC workup. Both CT scans and MRI scans of the head and neck area were included to evaluate SMM, since some patients did not have CT scans as part of their workup. Most published studies on SMM in patients with cancer have been performed using CT imaging. A recently published brief report by our group demonstrated the interchangeability and equivalence in accuracy of the two imaging methods for evaluating SMM[16].

Important limitations of this study are its retrospective nature and the insufficiently large cohort to statistically detect significant differences in the potentially clinically relevant parameters. Since the patients in this study were treated within the same institution, it is difficult to generalize the findings to other institutions.

In conclusion, low SMM was not found to be correlated with postoperative complications and prolonged hospitalization in patients undergoing a selective neck dissection for clinically early stage oral cavity cancer. Surgery with a low complication risk may be less susceptible to the deleterious effects of low SMM.

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Competing interests

The authors have no conflict of interest to declare.

Ethical approval

This study was approved by the Medical Ethics Research Committee of the University Medical Center Utrecht (METC UMCU 17-365/C).

Patient consent

Informed consent was waived by the Medical Ethics Research Committee, University Medical Center Utrecht.

Availability of data and material

The data that support the findings of this study are available from the corresponding author (RB) upon reasonable request.

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