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Impact of sarcopenia on overall survival and local relapse in head and neck cancer patients undergoing surgical excision

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Abstract. – OBJECTIVE: The purpose of this study is to evaluate the effect of sarcopenia on overall survival and local relapse in head and neck cancer patients undergoing surgical excision.

PATIENTS AND METHODS: This retrospective study includes head and neck cancer patients primarily treated with surgical excision in a tertiary care center. Patients were included if they had undergone an abdominal region Computer Tomography scan at least 45 days before the surgical excision. Hospital records were collected, and data analysis included patient demographics, comorbidities, tumor staging, surgical details, adjuvant therapy details, treatment complications, death records, and last follow-up appointment details.

RESULTS: In this retrospective study, 138 head and neck cancer patients were included, with 69.6% males and 30.4% females. The mean age was 60.2±12.3 years, and the average follow-up time was 54.3±16.3 months. Sarcopenia was present in 48.6% of patients and absent in 51.4%. Sarcopenic patients had a significantly lower mean age compared to non-sarcopenic patients ($p<0.05$). The proportion of larynx cancer was significantly lower in the sarcopenia group compared to the non-sarcopenia group ($p<0.05$). According to the American Joint Committee on Cancer (AJCC) staging, stage IV was significantly higher in the sarcopenia group ($p<0.05$). Local relapse was significantly higher in the sarcopenia group ($p<0.05$).

CONCLUSIONS: The findings of this study emphasize the importance of sarcopenia evaluation in determining prognosis and identifying patients who may benefit from specialized and intensive nutritional programs. Sarcopenia harms overall survival and local relapse in head and neck cancer patients.

Key Words:
Head and neck cancer, Sarcopenia, Overall survival, Skeletal muscle index, Nutritional status, Oncological outcomes.

Introduction

Head and neck cancer accounts for over 650,000 cases and 330,000 fatalities annually[1,2]. The prognosis of HNC depends on many factors such as age, performance status, weight, stage, and Human Papillomavirus (HPV) presence[3].

Sarcopenia is the age-related loss of muscle mass and strength. It is a progressive disease linked to an increased risk of adverse outcomes such as falls, fractures, physical impairment, and mortality[4]. Sarcopenia lowers the quality of life, mainly in the elderly[5], and it can be an indicator of malnutrition. Sarcopenia and oncology patients are closely associated since many oncological patients are prone to malnutrition.

In oncology, radiologically evaluated skeletal muscle mass was found to be a negative predictive and prognostic factor for patient survival[6]. Since muscle function tests are frequently not accessible, most retrospective research on sarcopenia in cancer patients only considers computed tomography (CT) assessed skeletal muscle mass[7]. As defined by CT imaging, sarcopenia evaluation at the third lumbar vertebra (L3) level has emerged as the gold standard of body composition analysis and muscle status evaluation[2,8].

Many studies have been performed[9-12] on head and neck cancer and sarcopenia concerning it. Sarcopenia may be a predictor of mortality in head and neck cancer patients and may indicate the prognosis of the patient[9-12]. Moreover, sarcopenia is an indicator of the wound-healing process, so it is closely related to the success of the surgery[9]. Furthermore, sarcopenia patients have more unplanned hospital admissions and hospital costs[11]. Head and neck cancer patients tend to get malnutrition due to dysphagia and surgical excision

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sites. Most of these studies highlight that this acquired malnutrition is a nasty prognostic factor for head and neck cancer patients.

Our study aims to demonstrate the effect of sarcopenia on the overall survival and recurrence of head and neck cancer patients.

Patients and Methods

This retrospective study includes head and neck cancer patients treated with surgical excision primarily in a tertiary care center. The ethics approval for the study was given by the Umraniye Research and Training Hospital Ethics Committee (number: 370, date: 24.11.2022). Patients were included in the study if they had had a CT scan of the abdominal region at least 45 days before the surgical excision. Hospital records were collected. Patient demography, comorbidities, tumor staging, surgical details, adjuvant therapy details, treatment complications, death records, and last follow-up appointment details were included in the analysis.

For sarcopenia evaluation, CT scans were done under equal circumstances. The acquisition (120 kV) and the reconstruction (5-mm slice thickness) were used in the same device. These CT scans were stored in the Picture Archiving and Communication System (PACS). Evaluations were done using PACS. Skeletal muscle was detected using Hounsfield units between -29 and 150 (Slice-o-Matic software, version 5.0; Tomovision, Magog, Canada). The radiology doctor chose two different cross sections (1 cm in between) at the level of L3.

L3 skeletal muscles are transversus abdominis, internal oblique, external oblique, rectus abdominis, erector spine, psoas, and quadratus lumborum. Two cross sections' mean that the skeletal muscle area was calculated. This was described as the mean L3 skeletal muscle area (cm^2). Skeletal muscle index (SMI) was calculated by dividing L3's mean skeletal area by the patient's height (cm^2/m^2). Sarcopenia was described as SMI <52.4 cm^2/m^2 in men and <38.5 cm^2/m^2in women.

Statistical Analysis

In the descriptive statistics of the data, the mean, standard deviation, median maximum, lowest, highest, frequency, and ratio values were calculated. The distribution of variables was measured with the Kolmogorov-Smirnov test. In the analysis of quantitative independent data, the Independent sample *t*-test and Mann-Whitney U test were used. In the study of qualitative independent data, the Chi-square test was used. When the Chi-square test conditions were unmet, the Fischer test was used. The effect level was investigated using univariate and multivariate logistic regression. Cox regression (univariate-multivariate) and Kaplan Meier were used for survival analysis. The analysis was performed using the SPSS 28.0 program (IBM Corp., Armonk, NY, USA).

Results

In this retrospective study, 138 head and neck cancer patients were involved. Ninety-six of them (69.6%) were men, and 42 (30.4%) were women. The age average was 60.2±12.3 years. The average follow-up time was 54.3±16.3 months. Sixty-seven (48.6%) of the patients had sarcopenia, while seventy-one (51.4%) did not. Sixty-three (45.7%) of the patients had larynx cancer, 15 (10.9%) had oropharynx cancer, 48 (34.8%) had oral cavity cancer, 3 (2.2%) had salivary gland cancer, 6 (4.3%) had skin cancer, and 3 (2.2%) had paranasal sinus cancer. According to The American Joint Committee on Cancer (AJCC) staging, 33 (23.9%) patients were stage I, 18 (13%) were stage II, 33 (23.9%) patients were stage III, and 54 (39.1%) were stage IV. Ninety-three (67.4%) patients received radiotherapy, and 45 (32.6%) did not. Thirty-three (23.9%) patients had local relapses, and 105 (76.1%) patients did not (Table I).

The average age was 59.6±13.2 in sarcopenic patients and 60.7±11.4 in non-sarcopenic patients. In the sarcopenia group, the number of females was significantly higher than in the group without sarcopenia ($p<0.05$). In the sarcopenia group, 52 (77.6%) patients were male, and 15 (22.4%) were female. In the non-sarcopenia group, 44 (62.0%) patients were male, and 27 (38.0%) were female. Also, weight, height, and body mass index (BMI) were significantly lower in the sarcopenia group ($p<0.05$). The average height of the sarcopenic patients was 169.1±9.7 cm, and 166.0±8.7 cm in non-sarcopenic patients. The average weight of the sarcopenic patients was 69.3±12.6 kg, and 78.2±14.0 kg in non-sarcopenic patients. The BMI of the sarcopenic patients was 28.3±4.6, and it was 24.1±3.3 in non-sarcopenic patients (Table II).

The presence of larynx as the primary tumor site in the sarcopenia group was significantly lower than in the group without sarcopenia

Table I. Characteristics and demographics of patients.

		Min-Max	Median	Mean±sd	n%
Age		26.0 - 87.0	61.5	60.2 ± 12.3	
Sex	Male			96	69.6%
	Female			42	30.4%
Primary tumor site					
Larynx				63	45.7%
Oropharynx				15	10.9%
Oral cavity				48	34.8%
Salivary gland				3	2.2%
Skin				6	4.3%
Paranasal sinus				3	2.2%
AJCC Stage	I			33	23.9%
	II			18	13.0%
	III			33	23.9%
	IV			54	39.1%
Adjuvant RT	No			45	32.6%
	Yes			93	67.4%
Sarcopenia	(-)			71	51.4%
	(+)			67	48.6%
Local recurrence	(-)			105	76.1%
	(+)			33	23.9%
Postoperative follow up		20.0 - 83.0	56.0	54.3 ± 16.3	

American Joint Committee on Cancer (AJCC).

Table II. Comparison between sarcopenic and non-sarcopenic groups.

		Sarcopenia (-)		Sarcopenia (+)			
		Mean.±sd/n-%	Median	Mean.±sd/n-%	Median	p	
Age		60.7 ± 11.4	62.0	59.6 ± 13.2	61.0	0.439	m
Sex	Male	44 62.0%		52 77.6%		**0.046**	χ^2
	Female	27 38.0%		15 22.4%			
Height		166.0 ± 8.7	166.0	169.1 ± 9.7	167.0	0.093	m
Weight		78.2 ± 14.0	78.0	69.3 ± 12.6	72.0	**0.001**	*t*
BMI		28.3 ± 4.6	27.2	24.1 ± 3.3	24.0	**0.000**	m
Primary tumor site							
Larynx		31 43.7%		32 47.8%		0.629	χ^2
Oropharynx		6 8.5%		9 13.4%		0.347	χ^2
Oral cavity		22 31.0%		26 38.8%		0.335	χ^2
Salivary gland		3 4.2%		0 0.0%		0.245	χ^2
Skin		6 8.5%		0 0.0%		**0.015**	χ^2
Paranasal sinus		3 4.2%		0 0.0%		0.245	χ^2
AJCC Stage	I	22 31.0%		11 16.4%			
	II	12 16.9%		6 9.0%			
	III	21 29.6%		12 17.9%		**0.001**	χ^2
	IV	16 22.5%		38 56.7%			
Adjuvant RT	No	24 33.8%		21 31.3%		0.758	χ^2
	Yes	47 66.2%		46 68.7%			
Local recurrence	(-)	59 83.1%		46 68.7%		**0.047**	χ^2
	(+)	12 16.9%		21 31.3%			

American Joint Committee on Cancer (AJCC), body mass index (BMI).

(p<0.05). The oropharynx, paranasal sinus, oral cavity, salivary gland, and skin were not significantly different between the two groups (p>0.05). In the sarcopenic group, 32 (47.8%) patients had larynx cancer, 9 (13.4%) had oropharynx cancer, and 26 (38.8%) had oral cavity cancer. In the non-sarcopenic group, 31 (43.7%) patients had larynx cancer, 6 (8.5%) had oropharynx cancer,

22 (31.0%) had oral cavity cancer, 3 (4.7%) had salivary gland tumor, 6 (8.5%) had skin cancer, and 3 (4.7%) had paranasal sinus cancer (Table II).

The presence of AJCC stage IV was significantly higher in the sarcopenia group ($p<0.05$) than in the other group. Postoperative radiotherapy was not very different between the two groups ($p>0.05$). Local relapse was significantly higher in the sarcopenia group ($p<0.05$) (Table II). In the sarcopenic group, 11 (16.4%) had AJCC stage I cancer, 6 (9.0%) had stage II cancer, 12 (17.9%) had stage III cancer, and 38 (56.7%) had stage IV cancer. In the non-sarcopenic group, 22 (31.0%) patients had stage I cancer, 12 (16.9%) had stage II cancer, 21 (29.6%) had stage III cancer, and 16 (22.5%) had stage IV cancer (Table II).

In the sarcopenic group, 46 (68.7%) patients received radiotherapy, and 21 (31.3%) did not. In the non-sarcopenic group, 47 (66.2%) received radiotherapy, and 24 (33.8%) did not. In the sarcopenic group, 21 (31.3%) patients had local relapse and 46 (68.7%) did not. In the non-sarcopenic group, 12 (16.9%) patients had a local relapse, and 59 (83.1%) did not (Table II).

In univariate logistic regression, sex, SMI/cm^2, AJCC stage, and postoperative radiotherapy were found to be significantly effective in differentiating relapse and non-relapse groups ($p<0.05$) (Table III). In multivariate logistic regression, AJCC stage and SMI/cm^2 were found to be independently significantly effective ($p<0.05$) (Table III).

In univariate Cox regression, age, height, weight, BMI score, and postoperative radiotherapy did not significantly affect survival time ($p>0.05$). SMI/cm^2, primary tumor site, and AJCC staging significantly affected disease-free survival time ($p<0.05$). In multivariate Cox regression, AJCC staging and SMI/cm^2 had a significant effect on disease-free survival time ($p<0.05$) (Table IV).

In the sarcopenic group (60.78 months), disease-free survival time was significantly lower than in the non-sarcopenic group (72.28 months) ($p<0.05$) (Table V). Cumulative survival was lower in the sarcopenic group (Figure 1).

Discussion

Nutritional problems and weight loss are common in patients with head and neck cancer. The consequence of malnutrition may be more significant than expected. Sarcopenia and loss of muscle may appear due to individual factors (being elderly, having malnutrition due to conditions such as cancer). Also, it may be present because systemic inflammatory mechanisms that lead to

Table III. Logistic regression analysis.

	Univariate Model			Multivariate Model		
	OR	95% CI	p	OR	95% CI	p
Sex	2.407	1.068 - 5.428	**0.034**			
AJCC stage	1.877	1.251 - 2.816	**0.002**	1.525	1.010 - 2.330	**0.049**
Adjuvant RT	2.659	1.009 - 7.008	**0.048**			
SMI/cm²	0.931	0.893 - 0.970	**0.001**	0.942	0.901 - 0.985	**0.009**

Logistic Regression (Forward LR), American Joint Committee on Cancer (AJCC), Skeletal muscle index (SMI).

Table IV. Cox regression analysis.

	Univariate Model			Multivariate Model		
	OR	95% CI	p	OR	95% CI	p
Age	1.015	0.986 - 1.045	0.320			
Height	0.978	0.941 - 1.017	0.260			
Weight	0.980	0.956 - 1.006	0.129			
BMI	0.957	0.880 - 1.042	0.313			
Primary tumor site	1.342	1.068 - 1.687	**0.012**			
AJCC stage	1.787	1.238 - 2.579	**0.002**	1.48	1.024 - 2.139	**0.037**
Adjuvant RT	2.378	0.981 - 5.761	0.055			
SMI/cm²	0.943	0.912 - 0.974	**0.000**	0.952	0.917 - 0.987	**0.008**

Cox Regression (Farward LR), American Joint Committee on Cancer (AJCC), Body mass index (BMI), Skeletal muscle index (SMI).

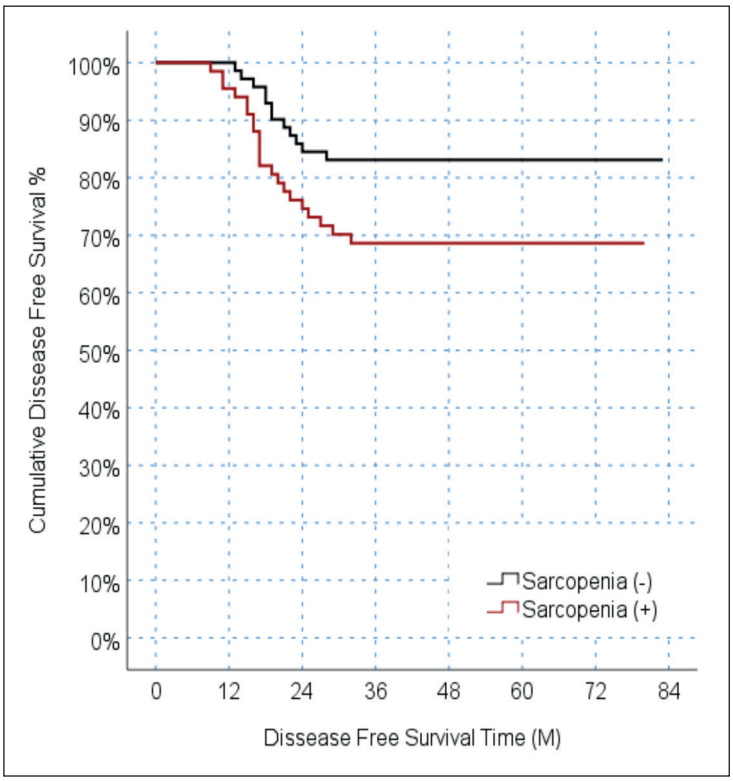

Figure 1. The disease-free survival is longer in the sarcopenia group compared to the non-sarcopenia group.

cachexia may be active in earlier stages of the disease before the patient is diagnosed.

The tumor-derived factors that affect muscle tissue have been studied in preclinical models[13,14]. The most common way of diagnosing sarcopenia is low muscle quantity evaluation in CT and SMI calculation[7,8]. The current study analyzed the impact of sarcopenia, diagnosed with SMI, on head and neck cancer patients. It confirmed that local relapse was higher in sarcopenic head and neck cancer patients, and overall survival time was lower in the same group. These findings highlight the significance of sarcopenia and its clinical use.

Many studies have been done in literature on sarcopenia and oncology patients. Specifically, in head and neck cancer patients, many studies[15-18] show that sarcopenia is a bad prognostic factor. Especially, those receiving radiotherapy have a poorer prognosis[8]. In our research, we found that patients receiving radiotherapy are significantly more likely to have local relapse. Fattouh et al[17] highlighted that patients with pre-treatment obesity have better overall survival. Our study found that BMI is not significantly associated with overall survival time. We would have expected that it would be significantly correlated. BMI was found to be lower in sarcopenic patients, unsurprisingly.

Cho et al[18] carried out a study that included 221 patients with head and neck cancer and searched for the predictive effects of sarcopenia with systemic inflammation in patients who had chemoradiotherapy. They found that sarcopenia and systemic inflammation together decrease overall survival. However, sarcopenia alone did not reduce survival[19]. On the other hand, in our study, disease-free survival time was significantly lower in sarcopenic patients[3,9].

When sarcopenic and non-sarcopenic patients were compared, it was unsurprisingly found that the local relapse percentage was higher in the sarcopenic group. Since sarcopenic patients have a poorer prognosis, as explained in the previous paragraph, they likely have a higher relapse percentage.

Sarcopenic patients had a higher percentage of receiving radiotherapy when compared to the non-sarcopenic group. This was an expected result since sarcopenic patients have a poorer prognosis and are more likely to receive adjuvant treatment.

Our study showed that AJCC stage IV patients had the highest percentage in the sarcopenic group, as expected. Stone et al[9] assessed 260 patients with head and neck cancer and found a similar result. The percentage of patients with sarcopenia is shown to be higher in AJCC category IV. Sarcopenia may be an independent prognostic factor

for overall survival, especially in patients with locally advanced disease[3,19,20-22]. They retrospectively analyzed squamous cell carcinoma patients and found that. They also showed that sarcopenic patients are prone to have a higher clinical stage (category IV) than nonsarcopenic patients. People who are not malnourished and have a healthy muscle status probably will have a better prognosis if they are diagnosed with head and neck cancer.

Cadoni et al[21] searched prognostic factors, and they found out that the larynx, as the primary site of the tumor, has a better overall survival time when compared to other sites[21]. Our study found that larynx cancer patients occupied a percentage of the sarcopenic group. Since sarcopenic patients have a poorer prognosis, this was an expected result.

Limitations

There are several limitations in this study. Abdominal computed tomography is generally deducted from positron emission tomography. However, it is not routine imaging for head and neck cancer patients. Therefore, a substantial number of these patients were not included in this study, which might have caused a selection bias. Our study is retrospective; therefore, we could not evaluate all variables and possible confounders.

For this reason, the study might contain information and confounding biases. Since patients' dietary habits can be variable, they may have been incorporated into the study. Moreover, this study was conducted in one tertiary care center and cannot be generalized to all head and neck cancer patients.

Conclusions

The findings of this study emphasize the importance of sarcopenia evaluation in determining prognosis and identifying patients who may benefit from specialized and intensive nutritional programs. Sarcopenia harms overall survival and local relapse in head and neck cancer patients. As sarcopenia led to a reduction in survival at both 2 and 5 years. In addition, sarcopenia was found to cause a higher local recurrence rate and was associated with AJCC stage IV. Moreover, the results prove that sarcopenia evaluation is a valuable prognostic method. This can help with the early diagnosis of patients who especially need intensive nutritional support.

Conflict of Interest

The authors declare no conflict of interest.

Informed Consent

The authors declare that the patients included in the study signed informed consent forms to use their medical information in the studies.

Ethics Approval

The ethics approval for the study was given by the Umraniye Research and Training Hospital Ethics Committee (number: 370, date: 24.11.2022).

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Authors' Contribution

Each author participated in planning, designing, writing and editing the study, as well as in the literature search and gave active intellectual support.

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Availability of Data and Materials

All data for this study are presented in this paper.

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