



Prognostic Value of Baseline Cervical CT-derived Muscle Density as a Surrogate of Myosteatorsis in Patients with Head and Neck Cancer

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ABSTRACT

Objective: Head and neck cancer (HNC) is frequently associated with malnutrition, systemic inflammation, and sarcopenia. Computed tomography (CT)-derived body composition parameters may offer prognostic information beyond conventional clinical measures. We aimed to evaluate the associations of baseline body composition parameters with survival outcomes and treatment tolerance in patients with HNC.

Material and Methods: This retrospective cohort study included 57 patients with HNC treated with curative-intent radiotherapy-based approaches at a tertiary oncology center. Baseline clinical, laboratory, treatment, and imaging data were collected. Body composition analysis was performed on baseline contrast-enhanced cervical CT scans and included measurements of cervical total fat area (cTFA), muscle area, muscle index, and muscle density. Pre- and post-treatment changes were also assessed in 30 patients with paired imaging. Survival analyses for overall survival (OS) and progression-free survival (PFS) were performed using Kaplan-Meier and Cox regression methods.

Results: The median age was 60.7 years, and 77.2% of patients were male. Most patients had stage III-IV disease (87.7%). In the paired subgroup, cTFA, muscle area, and muscle density generally declined during treatment; however, these changes were small and did not reach statistical significance. Baseline cervical muscle density was not associated with survival when analysed as a continuous variable. Using exploratory, internally derived sex-specific receiver operating characteristic thresholds [≤ 39.1 Hounsfield unit (HU) for women, ≤ 39.5 HU for men], low muscle density showed an adjusted association with worse OS [hazard ratio (HR): 5.93; 95% confidence interval (CI): 1.52-23.15; $p=0.010$] and PFS (HR: 5.09; 95% CI: 1.56-16.62; $p=0.007$). Because these thresholds were derived within the same cohort and the number of women was small, these categorical analyses are hypothesis-generating. Low muscle density was associated with a greater requirement for enteral nutritional support and lower rates of chemotherapy completion.

Conclusion: In this small retrospective cohort, low baseline cervical muscle density was associated, after adjustment, with worse survival and reduced likelihood of treatment completion. These findings are exploratory and require external validation.

Keywords: Head and neck cancer; body composition; computed tomography; cervical CT; muscle density; myosteatorsis; total fat area; prognosis

INTRODUCTION

Head and neck cancer (HNC) is the seventh most common cancer worldwide, with approximately 792,280 new cases and 424,066 deaths globally in 2021.¹ Projections estimate continued increases in absolute case numbers through 2050, driven largely by population aging and growth.²

Patients with HNC constitute one of the malignancy groups at highest risk for malnutrition and sarcopenia because of the anatomical location of the tumor, the biological burden of the disease itself, and treatment-related toxicities.³ The reported prevalence of malnutrition in this population ranges from 26% to 74%, while sarcopenia has been described in 3.8% to 78.7% of cases.^{4,5} This vulnerability is driven by

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several overlapping mechanisms. First, nutrition-impact symptoms are extremely common, affecting at least 90% of patients, and include xerostomia, trismus, dysphagia, chewing difficulty, mucositis, taste alterations, and loss of appetite; moreover, tumors arising in the oral cavity, pharynx, and larynx directly compromise swallowing and oral intake.⁶ Second, radiotherapy and concurrent chemoradiotherapy further aggravate nutritional decline through toxicities such as mucositis, xerostomia, dysphagia, dermatitis, and dysgeusia, with the risk of malnutrition rising markedly during treatment and clinically meaningful weight loss frequently observed.^{7,8} Third, a substantial proportion of patients are already malnourished at the time of diagnosis, partly owing to pre-existing lifestyle and socioeconomic factors, including tobacco and alcohol use.⁹ In parallel, sarcopenia develops as a component of cancer-related cachexia through reduced protein and energy intake, chronic malnutrition, dysphagia, systemic inflammation, and physical inactivity, while surgery, radiotherapy, and chemotherapy may further accelerate muscle loss.¹⁰ Clinically, these disturbances are far from trivial: pre-treatment radiologic sarcopenia has been associated with inferior survival, greater treatment-related complications, more severe chemotherapy toxicity, longer radiotherapy interruptions, and increased dependence on nutritional tube support.^{10,11}

Traditional anthropometric measures such as body surface area and body mass index (BMI) are easy to obtain but may fail to fully reflect clinically relevant changes in body composition. Two patients with similar BMI may have markedly different muscle mass, fat reserves, and metabolic vulnerability.¹² Cross-sectional imaging offers an opportunity to quantify body composition in a more objective manner. Parameters such as visceral fat area, muscle area, and muscle density may capture both nutritional reserve and cancer-related cachexia.¹³ Myosteatosis refers to fatty infiltration within skeletal muscle and reflects impairment in muscle quality rather than muscle quantity alone.¹⁴ It is commonly assessed by skeletal muscle radiodensity, typically expressed as the mean Hounsfield unit (HU) value of the skeletal muscle compartment on computed tomography (CT), with lower HU values indicating greater lipid infiltration.¹⁵ Sarcopenia by itself may therefore provide an incomplete picture, as loss of muscle mass and deterioration in muscle quality represent biologically distinct processes with independent prognostic implications.¹⁴ A substantial proportion of high-risk patients may remain unrecognized when evaluated separately. In HNC, a more comprehensive assessment may require the joint evaluation of both sarcopenia and myosteatosis on CT imaging, ideally using routinely acquired staging or

treatment-planning scans at the L3 or, when more practical, the C3 level.³ Although sarcopenia and cancer cachexia have been evaluated in several malignancies, data specifically addressing myosteatosis in HNC, particularly measurements derived from fat and cervical imaging, remain limited. Therefore, this study aimed to investigate the relationship between baseline body composition parameters and survival outcomes in patients with HNC. We also explored the interaction between imaging-derived body composition metrics and inflammatory-nutritional biomarkers.

MATERIAL AND METHODS

This retrospective observational cohort study was conducted in the Department of Medical Oncology at Ankara University Faculty of Medicine and included patients with HNC who were treated with curative-intent, radiotherapy-based approaches between September 2011 and October 2023. Eligible patients were identified retrospectively from the institutional database. Inclusion criteria were as follows: (1) histologically confirmed HNC; (2) curative-intent radiotherapy-based treatment; (3) pre-treatment cervical CT imaging suitable for body composition assessment; (4) baseline clinical and laboratory data; and (5) follow-up data for progression and/or survival analyses. Patients were excluded if they had missing key imaging data, inadequate follow-up information, poor-quality CT images precluding reliable body composition measurements, or concurrent malignancy that could confound outcome interpretation.

Clinical data were extracted retrospectively from electronic medical records. The following variables were collected: age, sex, smoking status and alcohol use status, Eastern Cooperative Oncology Group (ECOG) performance status, primary tumor site, TNM stage, treatment modality, radiotherapy dose and fractionation, chemotherapy regimen, treatment completion status, need for enteral nutritional support, treatment-related toxicities, such as mucositis and dysphagia, when available, progression status, date of progression, and date of death or last follow-up. Anthropometric parameters included height, weight, and BMI.

Inflammatory and nutritional indices were calculated as follows: neutrophil-to-lymphocyte ratio (NLR) = neutrophils / lymphocytes; platelet-to-lymphocyte ratio = platelets / lymphocytes; lymphocyte-to-monocyte ratio = lymphocytes / monocytes, when available; prognostic nutritional index (PNI) = $10 \times \text{albumin (g/dL)} + 0.005 \times \text{lymphocyte count (per mm}^3\text{)}$; systemic immune-inflammation index (SII) = $\text{platelets} \times \text{neutrophils} / \text{lymphocytes}$; and pan-immune-inflammation value (PIV) = $\text{platelets} \times \text{neutrophils} \times \text{monocytes} / \text{lymphocytes}$.¹⁶

This study was conducted in accordance with the ethical standards of the institutional research committee and the Declaration of Helsinki. The study was approved by the Ankara University Human Researchs Ethics Committee (approval no: İ06-612-25, date: 12.08.2025; decision number: 106-612-25). Given the retrospective design of the study and the use of anonymized clinical and imaging data, the requirement for written informed consent was waived.

Continuous variables were summarized as median and IQR.

candidate predictors. Multivariable models were then built for selected variables of interest, adjusting for age, sex, stage, ECOG performance status, NLR, and BMI. Given the limited number of events (18 deaths and 25 progression events), the full multivariable model is vulnerable to overfitting. As a sensitivity analysis, we fitted a parsimonious model that included only low muscle density and NLR, the covariates most consistently associated with the outcome. Missing data were limited to a small number of variables: C-reactive protein was available for 49 of 57 patients; alcohol history for 50; lactate dehydrogenase for 55; and albumin, PNI, and feeding tube/gastrostomy for 56 each. All other variables were complete. Missing values were not imputed. Analyses were performed on complete cases for the variables included in each model, and the number of patients contributing to each analysis is indicated in the corresponding tables.

For exploratory categorical analyses, low muscle density was defined using sex-specific ROC-derived cut-offs. All statistical tests were two-sided, and a p-value of <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 57 patients were included in the study. The median age was 60.7 years (range, 35.0-87.2), and 44 patients (77.2%) were male. Most patients had advanced-stage disease, with 50 (87.7%) presenting with stage III-IV disease. The most common primary tumor site was the larynx (n=36; 63.2%), followed by the oral cavity/oropharynx (n=12; 21.1%), the hypopharynx (n=5; 8.8%), and the nasopharynx (n=4; 7.0%). Regarding treatment modality, 33 patients (57.9%) underwent surgery followed by adjuvant radiotherapy, whereas 24 patients (42.1%) received definitive radiotherapy. Overall, 47 patients (82.5%) received concurrent chemoradiotherapy and 10 patients (17.5%) received radiotherapy alone (Table 1).

After a median follow-up of 29.3 months, 25 patients experienced disease progression and 18 died. Median PFS was 38.1 months, while median OS was 94.4 months. At baseline, the median BMI was 26.0 kg/m² (IQR: 22.9-29.1). Median inflammatory and nutritional indices were as follows: NLR, 2.56 (IQR: 1.89-3.71); PNI, 49.8 (IQR: 46-52.2); SII, 625.0 (IQR: 480.8-1057.6); and PIV, 437.0 (IQR: 275.0-668.6). Baseline imaging-derived body composition parameters included median values for cTFA of 29.3 cm² (IQR: 18.5-41.7), muscle area of 33.8 cm² (IQR: 27.3-39.4), and muscle density of 50.6 HU (IQR: 41.6-54.7) (Table 2).

Among the 30 patients with paired pre- and post-treatment CT measurements, body composition parameters showed

numerical declines during treatment. Median cTFA decreased from 32.6 to 25.4 cm², muscle area decreased from 34.7 to 33.9 cm², and muscle density decreased from 48.6 to 48.0 HU. The median percentage change was -6.3% for cTFA, -3.4% for muscle area, and -5.2% for muscle density (Table 3).

TABLE 1: Baseline demographic and clinical characteristics.

Characteristic	Overall cohort (n=57) (%)
Age, years, median (IQR)	60.7 (51.4-67.6)
Sex	
Male	44 (77.2)
Female	13 (22.8)
Smoking status	
Never	7 (12.3)
Current	22 (38.6)
Former	28 (49.1)
Alcohol use	
Yes	11 (19.3)
No	39 (68.4)
Missing	7 (12.3)
ECOG performance status	
0	7 (12.3)
1	46 (80.7)
2	3 (5.3)
3	1 (1.8)
Primary site	
Larynx	36 (63.2)
Oral cavity/oropharynx	12 (21.1)
Hypopharynx	5 (8.8)
Nasopharynx	4 (7.0)
Stage group	
Stage III-IV	50 (87.7)
Stage I-II	7 (12.3)
Treatment modality	
Surgery + adjuvant RT-based	33 (57.9)
Definitive RT-based	24 (42.1)
Radiotherapy course	
Concurrent chemoradiotherapy	47 (82.5)
Radiotherapy alone	10 (17.5)
RT dose, Gy (range)	66.0 (65.2-70.0)
RT fractions (range)	33 (33-35)
Concurrent chemotherapy regimen	
Cisplatin	38 (66.7)
Carboplatin	6 (10.5)
Cetuximab	2 (3.5)
CF (cisplatin + 5-FU)	1 (1.8)

Values are presented as median (IQR) or n (%).

ECOG: Eastern Cooperative Oncology Group; RT: Radiotherapy; fx: Fractions; CCRT: Concurrent chemoradiotherapy; 5-FU: Fluorouracil.

TABLE 2: Baseline laboratory and body composition characteristics.

Variable	Overall cohort (n=57)
BMI, kg/m ²	26.0 (22.9-29.1)
Hb, g/dL	13.7 (12.1-14.9)
CRP, mg/L	12.0 (4.3-36.1)
Albumin, g/L	40.8 (37.7-43.0)
LDH, U/L	173.0 (153.5-196.0)
NLR	2.56 (1.89-3.71)
PNI	49.8 (46.0-52.2)
SII	625.0 (480.8-1057.6)
PIV	437.0 (275.0-668.6)
Baseline cTFA, cm ²	29.3 (18.5-41.7)
Baseline muscle area, cm ²	33.8 (27.3-39.4)
Baseline muscle density, HU	50.6 (41.6-54.7)

cTFA denotes cervical total fat area, defined as VAT + SAT on baseline cervical CT. Values are presented as medians (IQR).
 BMI: Body mass index; Hb: Hemoglobin; CRP: C-reactive protein; LDH: Lactate dehydrogenase; NLR: Neutrophil-to-lymphocyte ratio; PNI: Prognostic nutritional index; SII: Systemic immune-inflammation index; PIV: Pan-immune-inflammation value; cTFA: Cervical total fat area; HU: Hounsfield unit; IQR: Interquartile range; SAT: Subcutaneous adipose tissue; VAT: Visceral adipose tissue.

Baseline cervical muscle density was not statistically significant when analyzed as a continuous variable. However, using exploratory sex-specific ROC-derived cut-offs, low muscle density was associated with worse OS in univariable Cox regression analysis [hazard ratio (HR): 3.60; 95% confidence interval (CI): 1.31-9.88; $p=0.013$] and remained independently associated with OS after adjustment for age, sex, stage, ECOG performance status, BMI, and NLR (HR: 5.93; 95% CI: 1.52-23.15; $p=0.010$). Low muscle density was also associated with worse PFS in univariable Cox analysis (HR: 2.54; 95% CI: 1.04-6.25; $p=0.042$) and in the multivariable model (HR: 5.09; 95% CI: 1.56-16.62; $p=0.007$) (Table 4). In a parsimonious sensitivity model adjusting only for NLR, low muscle density remained associated with worse OS (HR: 7.44; 95% CI: 2.37-23.33; $p=0.001$) and PFS (HR: 3.82; 95% CI: 1.50-9.74; $p=0.005$), and these estimates had narrower CIs than those from the fully adjusted model. Kaplan-Meier analyses showed similar findings, with significant separation between the curves for both OS (log-rank $p=0.008$) and PFS (log-rank $p=0.035$) (Figure 2). The ROC-derived thresholds identified a small high-risk subgroup with high specificity but modest sensitivity. For OS, sensitivity and specificity were 33.3% and 89.7%, respectively; for PFS, they were 28.0% and 90.6%, respectively.

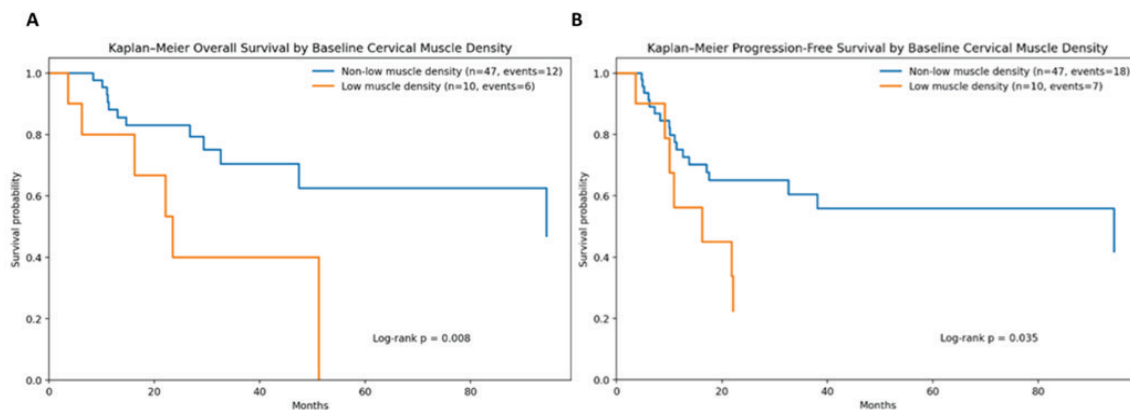


FIGURE 2: Kaplan-Meier curves for overall survival (OS) and progression-free survival (PFS) according to baseline cervical muscle density. Low muscle density was defined using exploratory sex-specific ROC-derived cut-offs (≤ 39.1 HU for women and ≤ 39.5 HU for men). Patients with low baseline cervical muscle density had significantly worse OS and PFS than other patients in the cohort. Survival curves were compared using the log-rank test (OS, $p=0.008$; PFS, $p=0.035$).

HU: Hounsfield unit; ROC: Receiver operating characteristic

TABLE 3: Changes in body composition during treatment in patients with paired CT measurements.

Variable	Baseline	Post-treatment	Absolute change	Percentage change, %	p-value
cTFA, cm ²	32.6 (19.7-43.0)	25.4 (17.8-37.4)	-1.5 (-12.7-6.3)	-6.3 (-40.1-23.1)	0.102
Muscle area, cm ²	34.7 (29.9-39.2)	33.9 (27.0-37.8)	-1.1 (-5.1-4.3)	-3.4 (-16.6-14.7)	0.730
Muscle density, HU	48.6 (42.1-56.7)	48.0 (40.6-52.5)	-2.4 (-6.6-0.9)	-5.2 (-10.8-1.9)	0.066

Paired analyses were performed on 30 patients who had both baseline and post-treatment CT measurements. Values are medians (IQR). p-values from Wilcoxon signed-rank tests.

cTFA: Cervical total fat area; HU: Hounsfield unit; CT: Computed tomography; IQR: Interquartile range.

Using the same exploratory sex-specific ROC-derived thresholds, patients with low baseline cervical muscle density were more likely to require enteral nutritional support than those in the remaining cohort (100.0% vs. 68.1%; $p=0.049$). Among patients receiving concurrent chemoradiotherapy, low muscle density was also associated with a markedly lower rate of chemotherapy completion (22.2% vs. 73.7%; $p=0.007$). No significant associations were observed for mucositis, dysphagia, use of feeding tube or gastrostomy, or radiotherapy completion, although radiotherapy interruption tended to be more frequent in the low-density group (20.0% vs. 2.1%; $p=0.076$). Exploratory toxicity analyses did not demonstrate statistically significant associations between low muscle density and treatment-related toxicities. Myosteatosis was not significantly associated with grade ≥ 2 or grade ≥ 3 overall toxicity, mucositis, dysphagia, or thrombocytopenia. However, low baseline cervical muscle density showed a trend toward higher rates of neutropenia (40.0% vs. 12.8%; $p=0.064$) and overall hematologic toxicity (40.0% vs. 14.9%; $p=0.089$) (Table 5).

DISCUSSION

The present study suggests that baseline cervical CT-derived muscle density may provide clinically relevant prognostic information for patients with HNC who were treated with curative-intent radiotherapy-based approaches. Exploratory sex-specific thresholds identified a subgroup with markedly worse OS and PFS. Although low muscle density remained associated with OS and PFS after adjustment, the CIs were wide, reflecting the small number of events, and the fully adjusted estimates should be regarded as imprecise. A parsimonious model restricted to low muscle density and NLR yielded a consistent association with narrower intervals, but this provides only partial reassurance and does not confirm independence. These multivariable results are, therefore, exploratory and hypothesis-generating. By contrast, isolated measures of cervical fat area and muscle index did not yield a comparatively consistent signal. Taken together, these findings imply that muscle quality may be more informative than muscle quantity alone in this setting and

TABLE 4: Baseline prognostic analyses for OS and PFS.

Panel A. Univariable Cox regression analyses.

Variable	OS HR (95% CI)	p	PFS HR (95% CI)	p
Age, per year	1.05 (1.01-1.10)	0.027	1.01 (0.98-1.05)	0.515
Sex, male vs female	1.17 (0.38-3.56)	0.783	1.22 (0.46-3.25)	0.693
Advanced stage, III-IV vs. I-II	0.34 (0.11-1.08)	0.067	0.38 (0.14-1.02)	0.055
ECOG performance status	0.70 (0.20-2.40)	0.566	0.68 (0.23-1.96)	0.472
BMI, kg/m ²	0.95 (0.85-1.06)	0.338	0.96 (0.88-1.05)	0.371
NLR	1.30 (1.07-1.57)	0.008	1.30 (1.09-1.55)	0.003
PNI	0.979 (0.915-1.047)	0.533	0.958 (0.908-1.011)	0.121
SII	1.060 (1.008-1.116)	0.025	1.034 (0.987-1.083)	0.157
cTFA, cm ²	1.01 (0.98-1.05)	0.393	1.02 (0.99-1.04)	0.247
Muscle index, cm ² /m ²	0.93 (0.77-1.12)	0.442	0.98 (0.84-1.14)	0.790
Muscle density, HU, continuous	1.00 (0.95-1.06)	0.874	0.99 (0.95-1.03)	0.637
Low muscle density, ROC-defined	3.60 (1.31-9.88)	0.013	2.54 (1.04-6.25)	0.042

Panel B. Multivariable Cox regression analyses.

Variable	Adjusted OS HR (95% CI)	p	Adjusted PFS HR (95% CI)	p
Age, per year	1.08 (1.01-1.15)	0.032	0.99 (0.95-1.04)	0.733
Sex, male vs female	0.25 (0.06-1.08)	0.063	0.62 (0.20-1.96)	0.415
Advanced stage, III-IV vs. I-II	0.35 (0.07-1.83)	0.213	0.27 (0.07-1.09)	0.065
ECOG performance status	0.74 (0.23-2.42)	0.622	0.87 (0.34-2.23)	0.768
BMI, kg/m ²	0.85 (0.73-0.99)	0.031	0.95 (0.87-1.04)	0.255
NLR	1.58 (1.16-2.14)	0.003	1.40 (1.11-1.76)	0.005
Low muscle density, ROC-defined	5.93 (1.52-23.15)	0.010	5.09 (1.56-16.62)	0.007

Reference category for stage is stage I-II.

*Adjusted for age, sex, stage, ECOG performance status, BMI, and NLR.

Low muscle density was defined using exploratory sex-specific ROC-derived cut-offs (≤ 39.1 HU for women and ≤ 39.5 HU for men).

OS: Overall survival; PFS: Progression-free survival; HR: Hazard ratio; CI: Confidence interval; BMI: Body mass index; NLR: Neutrophil-to-lymphocyte ratio; PNI: Prognostic nutritional index; cTFA: Cervical total fat area; HU: Hounsfield unit; ECOG: Eastern Cooperative Oncology Group; ROC: Receiver operating characteristic.

TABLE 5: Treatment tolerance, supportive care, and toxicity according to low muscle density.

Variable	Low muscle density, n/N (%)	Non-low muscle density, n/N (%)	p
Enteral nutritional support	10/10 (100.0)	32/47 (68.1)	0.049
Chemotherapy completion (among CCRT)	2/9 (22.2)	28/38 (73.7)	0.007
Feeding tube/gastrostomy	2/10 (20.0)	2/44 (4.5)	0.152
Mucositis	7/10 (70.0)	27/47 (57.4)	0.724
Dysphagia	7/10 (70.0)	34/47 (72.3)	1.000
Radiotherapy interruption	2/10 (20.0)	1/47 (2.1)	0.076
Radiotherapy completion	9/10 (90.0)	47/47 (100.0)	0.175
Any grade ≥ 2 toxicity	5/10 (50.0)	19/47 (40.4)	0.720
Any grade ≥ 3 toxicity	2/10 (20.0)	5/47 (10.6)	0.593
Dermatitis	2/10 (20.0)	24/47 (51.1)	0.095
Hematologic toxicity	4/10 (40.0)	7/47 (14.9)	0.089
Neutropenia	4/10 (40.0)	6/47 (12.8)	0.064
Thrombocytopenia	0/10 (0.0)	3/47 (6.4)	1.000

CCRT: Concurrent chemoradiotherapy.

that myosteatosis-like changes captured on routine cervical imaging may reflect a biologically meaningful dimension of host vulnerability. This observation is clinically plausible in the context of HNC. Prognosis in this disease is shaped not only by tumor burden and stage but also by the patient's nutritional reserve, inflammatory state, and capacity to tolerate intensive local therapy. Fatty degeneration within skeletal muscle may represent a more complex and advanced derangement than simple loss of muscle mass, reflecting impaired muscle composition, chronic catabolism, and reduced physiologic resilience.¹⁴ This may help explain why patients with low baseline muscle density in our cohort were more likely to require enteral nutritional support and substantially less likely to complete concurrent chemotherapy as planned. In this regard, cervical muscle density may function as an imaging marker that captures both nutritional fragility and treatment vulnerability. An unexpected finding in our study was that advanced stages (III-IV) were associated with HRs below 1 for both outcomes. This is unlikely to represent a protective effect of advanced disease and most probably reflects the small and imbalanced stage distribution: only 7 patients had stage I-II disease, and this subgroup had a higher observed event rate than the stage III-IV group (OS events 4/7 vs. 14/50; PFS events 5/7 vs. 20/50). The stage estimate is therefore unstable and should be interpreted with caution.

The association between body composition and outcome should also be interpreted within the broader framework of cancer-related systemic inflammation and metabolic decline. In HNC, reduced oral intake, mucosal toxicity, dysphagia, and inflammatory activation often coexist and reinforce one another, accelerating deterioration in body composition over time.¹⁷ These findings support the potential

value of incorporating cervical CT-based body composition assessment into routine baseline evaluation, particularly because such imaging is already obtained in standard care. Identifying patients with very low muscle density before treatment may allow earlier dietitian involvement, closer supportive monitoring, and more individualized treatment planning.¹⁸ Even though the cut-off-based analyses in the present study remain exploratory, they point toward a clinically relevant phenotype that deserves further validation in larger prospective cohorts. Importantly, the ROC-derived cut-offs observed in our cohort (39.1 HU for women and 39.5 HU for men) were remarkably close to previously proposed sex-specific SMA attenuation thresholds reported by Kim et al.¹⁹ (39.9 HU for women and 40.2 HU for men). This proximity supports the biological plausibility of our findings and suggests that the prognostic signal identified in our study may not be purely data-driven, despite the exploratory nature of the cut-off selection. This reassurance is limited; however, the cut-offs were derived within the same cohort by ROC analysis and are therefore subject to optimism, particularly for women, who numbered only 13. When combined with the absence of an association when muscle density was modelled continuously, these findings are best regarded as hypothesis-generating, and cervical CT-based myosteatosis thresholds will require external validation before clinical use.

Existing evidence increasingly supports the prognostic relevance of muscle quality in HNC, although the strength and consistency of this association have varied across cohorts. In one of the earlier studies focusing specifically on this issue, Findlay and colleagues reported that pre-treatment myosteatosis was an independent predictor of worse OS in a 98-patient cohort, while post-treatment sarcopenia also

retained independent prognostic significance.²⁰ That study further highlighted the clinical and economic consequences of adverse body composition, showing substantially higher costs related to unplanned hospital admissions among patients with sarcopenia.²⁰ In a subsequent and larger cohort of 277 patients, the same group observed a very high prevalence of myosteatosis and sarcopenia; however, malnutrition emerged as an even stronger independent prognostic factor than either imaging-defined abnormality alone.²¹ Notably, the coexistence of sarcopenia and myosteatosis was associated with more frequent unplanned admissions and longer hospital stays, emphasizing that these body composition phenotypes may be particularly relevant when interpreted alongside broader markers of nutritional compromise.²¹ Other studies have similarly suggested that muscle quality may carry prognostic value beyond muscle quantity alone. Shaver et al.²² found that pre-treatment myosteatosis was associated with increased long-term mortality, while Ahern et al.²³ reported that the combined presence of post-treatment sarcopenia and myosteatosis was linked to poorer 5-year OS. In a related study, Roberti et al.²⁴ showed that intramuscular adipose tissue predicted PFS independently of muscle area, supporting the notion that compositional deterioration within muscle may be biologically and clinically distinct from loss of muscle mass. This distinction is important, because it implies that patients with apparently preserved muscle quantity may still harbor a high-risk muscle phenotype if radiodensity is low. Taken together, these findings suggest that myosteatosis is not merely a passive correlate of advanced disease, but may reflect an early and clinically meaningful manifestation of host vulnerability. This interpretation is also in line with the broader concept proposed by Kumar¹⁴, who described myosteatosis as a potentially early muscle phenotype that may precede overt cachexia and therefore represent a strategic point for intervention. By contrast, studies centered primarily on skeletal muscle depletion, such as the report by Grossberg et al.²⁵, have confirmed the adverse prognostic effect of muscle loss but also reinforce the need to distinguish muscle quantity from muscle quality. Viewed in this context, our assessment of cervical muscle density extends a growing body of evidence suggesting that the prognostic value of CT-based body composition in HNC may depend as much on qualitative muscle changes as on absolute muscle mass.

The association between low cervical muscle density and treatment tolerance in our cohort is consistent with the broader literature linking adverse body composition to increased treatment vulnerability in HNC. Prior studies have shown that low skeletal muscle mass is associated with higher rates of dose-limiting chemotherapy toxicity, longer radiotherapy interruptions, and greater need for supportive

care during chemoradiotherapy.^{3,26-28} This relationship may be partly explained by altered pharmacokinetics in patients with reduced muscle reserve; for example, lower skeletal muscle mass may reduce the distribution volume of cisplatin and increase systemic exposure, thereby contributing to treatment-limiting toxicity.²⁹ In our study, patients with low cervical muscle density were more likely to require enteral nutritional support and less likely to complete concurrent chemotherapy, suggesting that muscle quality may capture a clinically relevant dimension of treatment resilience. Although most individual toxicity endpoints were not statistically significant, trends toward higher rates of neutropenia and hematologic toxicity further support the possibility that low muscle density identifies a subgroup with reduced physiologic reserve during intensive treatment. These observations should, however, be interpreted with caution: the low-muscle-density group included only 10 patients; most individual toxicity endpoints did not reach statistical significance; and the associations with borderline *p*-values may be unstable. They are therefore best regarded as hypothesis-generating. These findings reinforce the need for early nutritional assessment, proactive dietitian involvement, and close multidisciplinary monitoring in patients with adverse body composition before treatment initiation.⁴

This study has several strengths. It was based on real-world clinical data and incorporated subgroup-level longitudinal imaging assessments alongside clinical and laboratory variables, thereby allowing a more integrated evaluation of host-related prognostic factors. In addition, the study focused on cervical CT-derived muscle quality, an area that remains relatively underexplored in the HNC literature. To our knowledge, the prognostic relevance of cervical myosteatosis has not been sufficiently characterized; this study therefore provides a novel perspective by examining muscle density at a clinically accessible cervical level using routinely available imaging.

Study Limitations

Several limitations should be acknowledged when interpreting the present findings. First, the retrospective, single-center nature of the study may have introduced selection bias and limited the generalizability of the results. Second, the sample size was relatively modest, which restricts statistical power, particularly for subgroup and exploratory analyses. Third, the cohort included different head and neck tumor subsites and treatment approaches, introducing a degree of clinical heterogeneity that may have influenced outcome patterns. In addition, some variables were not available for all patients, and missing data may have affected the robustness of certain analyses. The timing of both baseline

and post-treatment imaging was not completely uniform across the cohort, reflecting real-world practice rather than a strictly standardized protocol, and this variability may have influenced the observed changes in muscle and fat measures in the paired analysis. Interobserver agreement (e.g., intraclass correlation coefficient) was not formally assessed. Measurements were obtained using a shared, predefined segmentation protocol; however the absence of a quantified analysis of agreement is a limitation, and future studies should report reader reproducibility. Additionally, HPV status was not available for the majority of patients in this cohort; given the established prognostic relevance of HPV in oropharyngeal cancer, the absence of this variable is a limitation and may have introduced residual confounding into outcome analyses. Finally, several categorical body composition thresholds, particularly those used in exploratory analyses, were cohort-derived and should, therefore, be interpreted with caution until validated in larger external datasets. Low muscle density appears to provide clinically relevant prognostic information in HNC. Prospective validation in larger cohorts is warranted.

CONCLUSION

Baseline cervical muscle density may provide clinically relevant prognostic information in HNC. In our cohort, very low muscle density was associated with inferior survival, reduced treatment completion, and increased supportive care requirements. These findings support the potential value of cervical CT-derived myosteatosis assessment as a practical marker of host vulnerability in routine clinical care. Prospective validation in larger and more homogeneous cohorts is warranted.

Ethics

Ethics Committee Approval: The study was approved by the Ankara University Human Researchs Ethics Committee (approval no: İ06-612-25, date: 12.08.2025; decision number: 106-612-25).

Informed Consent: Given the retrospective design of the study and the use of anonymized clinical and imaging data, the requirement for written informed consent was waived.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.E., Meh.K., H.B., H.A.Y., Concept: E.E., Meh.K., H.B., H.A.Y., Design: E.E., Meh.K., H.B., H.A.Y., Data Collection or Processing: E.E., M.K., Meh.K., E.Y., H.B., H.A.Y., Analysis or Interpretation: E.E., M.K., Meh.K., E.Y., H.B., H.A.Y., Literature Search: E.E., Meh.K., H.B., H.A.Y., Writing: E.E., Meh.K., H.B., H.A.Y.

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