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Longitudinal assessment of malnutrition by GLIM criteria and NRS-2002 screening in head and neck cancer patients undergoing radiotherapy or chemoradiotherapy: a prospective observational study

Müge Akmansu[1], Çağlar Güzel[1]

[1]Department of Radiation Oncology, Faculty of Medicine, Gazi University, Ankara, Türkiye

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ABSTRACT

Objective: This study aimed to examine the concordance between Global Leadership Initiative on Malnutrition (GLIM) criteria and Nutrition Risk Screening-2002 (NRS-2002) screening scores, and to describe longitudinal changes in anthropometric parameters and C3-derived skeletal muscle metrics, in patients with head and neck cancer (HNC) undergoing radiotherapy (RT) or chemoradiotherapy (CRT).

Methods: A total of 32 HNC patients undergoing RT or CRT were prospectively enrolled and assessed at baseline (Day 1) and at Week 5 of treatment, with all patients receiving standardized oral nutritional supplementation and weekly clinical monitoring throughout the study period. Anthropometric measurements, skeletal muscle mass (SMM) at the third cervical vertebra (C3), and nutritional status using the NRS-2002 and GLIM criteria were assessed at baseline (Day 1) and at the end of the fifth week of treatment.

Results: From the first day to the fifth week of anticancer treatment, the percentage of patients at risk of malnutrition (NRS-2002 scores ≥ 3) increased significantly from 40.6% to 71.9% (P = .002), while the prevalence of malnutrition based on GLIM criteria increased from 46.9% to 71.9% (P = .005). Despite nutritional support, significant reductions in body weight, BMI, and C3 cross-sectional muscle area all P < .05 were observed. NRS-2002 scores correlated significantly with GLIM classifications at baseline and at Week 5 (all P < .005). No significant associations were observed between C3-derived skeletal muscle parameters and either assessment tool.

Conclusions: Despite standardized nutritional supplementation and weekly clinical monitoring, significant declines in body weight, BMI, and C3 cross-sectional muscle area were observed during the five-week treatment period. The GLIM criteria identified a progressive increase in malnutrition prevalence, particularly in the severe (Stage 2) category. NRS-2002 scores showed stronger associations with anthropometric parameters than with SMM, suggesting potential limitations of SMM assessments in this patient population. These findings underscore the need for individualized, proactive nutritional management in HNC patients undergoing RT or CRT. The utility of C3-based skeletal muscle assessment as a monitoring tool during active treatment requires further validation in larger prospective studies.

Keywords: head and neck neoplasm, malnutrition, nutritional assessment, radiotherapy

Corresponding author: Caglar Guzel
Email: caglarguzel3@gmail.com

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Introduction

Head and neck cancer (HNC) is one of the cancer types with the highest prevalence of malnutrition, due to the compromising impact of lifestyle habits adopted prior to diagnosis as well as the location of the tumor on food intake, the hypercatabolic state induced by the malignancy itself and the toxicities of radiotherapy (RT) or chemoradiotherapy (CRT).[1,2]

Approximately 70% of weight loss in HNC patients involves the decrease in lean body mass (LBM), with skeletal muscle mass (SMM) being its primary component.[1,3] Reduced SMM is increasingly recognized as a critical factor contributing to poor short- and long-term outcomes in oncology, including diminished treatment tolerance, increased toxicity, and worse survival.[4,5] In clinical practice, the gold standard for SMM assessment is based on cross-sectional imaging at the third lumbar vertebra (L3); however, this is not routinely available in HNC patients.[1,3-6] Instead, SMM assessment at the third cervical vertebra (C3), which is typically included in HNC imaging protocols, has been validated as a reliable and cost-effective alternative, showing a strong correlation with L3 measurements.[7,8] Despite this, the diagnostic sensitivity of C3-based SMM assessments in identifying malnutrition remains limited, particularly in sarcopenic or nutritionally compromised patients.

Main Points

- Malnutrition progressed significantly during treatment, with GLIM-defined malnutrition prevalence increasing from 46.9% at baseline to 71.9% by Week 5 despite nutritional supplementation.
- The proportion of severely malnourished patients (GLIM Stage 2) tripled during the five-week treatment period.
- NRS-2002 scores increased in parallel with GLIM staging and were consistently associated with anthropometric deterioration, supporting their complementary use for early malnutrition identification and monitoring in routine clinical practice.
- Significant reductions in body weight, BMI, and C3 cross-sectional muscle area were observed during the five-week treatment period, confirming measurable anthropometric and regional muscle deterioration in this patient population.
- C3-based skeletal muscle parameters were not significantly associated with GLIM staging or NRS-2002 scores, and their role as a monitoring tool during active treatment requires further validation.

Recently, Global Leadership Initiative on Malnutrition proposed global consensus-based universal criteria (GLIM criteria) for diagnosis and severity grading of malnutrition in adults in different clinical settings after individuals were determined to be at risk of malnutrition according to a validated nutritional screening tool.[9] The diagnosis of malnutrition is based on any combination of at least one phenotypic criterion (nonvolitional weight loss, low body mass index [BMI] or reduced muscle mass) and one etiologic criterion (reduced food intake or disease burden / inflammation), while the severity classification (stage 1 / moderate or stage 2 / severe) is based on the degree of loss for the phenotypic criteria.[9] Notably, given that they are currently developed as a consensus-based framework, the validity and reliability of these operational criteria need to be tested across different clinical populations.[10,11] However, to date, only a limited number of studies have investigated the prevalence of malnutrition according to GLIM specifically in the HNC setting.[10,12,13]

This study aimed to examine the concordance between GLIM staging and NRS-2002 scores prospectively and describe longitudinal changes in anthropometric parameters and C3-derived skeletal muscle metrics over the first five weeks of RT or CRT, in a real-world outpatient HNC cohort under standardized oral nutritional supplementation and weekly clinical monitoring.

To our knowledge, this represents one of the few prospective studies to simultaneously apply all three assessment modalities — GLIM criteria, NRS-2002 screening, and C3-based skeletal muscle metrics — within the same HNC cohort, thereby enabling a direct comparison of their concordance and methodological limitations under routine clinical conditions.

Methods

Study population

A total of 32 patients with HNC (median age 60 years, range 18-85 years, 81.3% were men) who received RT or CRT with concomitant nutritional support were included in this prospective longitudinal study conducted at a tertiary care radiation oncology clinic between April 2020 and April 2021. Patients were eligible if they were 18 years or older and provided written informed consent

after a detailed explanation of the study protocol. Exclusion criteria included prior anticancer treatment, secondary malignancies, or inability to complete the planned treatment protocol. Of the 58 patients initially screened, 26 were excluded due to prior anticancer treatment (n = 12), secondary malignancy (n = 6), inability to complete the planned treatment course (n = 5), or refusal to provide informed consent (n = 3). All 32 enrolled patients completed both assessment time points (Day 1 and Week 5) with no loss to follow-up. All patients received volumetric modulated arc therapy (VMAT) with standard fractionation (1.8–2 Gy per fraction). Patients undergoing CRT received concurrent weekly platinum-based chemotherapy according to institutional protocols; cetuximab-based regimens were not used in this cohort.

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study, which was conducted in accordance with the ethical principles stated in the 'Declaration of Helsinki' and approved by the institutional ethics committee. This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Assessments

Data on patient demographics (age, sex), comorbid diseases, smoking status, tumor characteristics (TNM stage, location) and treatment modality (definitive/adjuvant RT, CRT) were recorded at baseline. Data on anthropometrics (weight [kg], BMI [kg/m^2], mid-arm circumference [cm], calf circumference [cm]), SMM at the level of the third cervical vertebra (C3) including paravertebral cross-sectional muscle area (CSMA, cm^2) and skeletal muscle index (cm^2 / m^2), and nutritional status assessment via NRS-2002 and GLIM criteria were recorded on the first day and 5th week of anti-cancer treatment.

Study parameters

First-day vs. fifth-week data on anthropometrics, SMM and nutritional status (NRS-2002, GLIM) were compared. The correlation of NRS-2002 scores with anthropometrics and SMM as well as the change in NRS-2002 scores, anthropometrics and SMM according to the first day and fifth week GLIM classification groups were also evaluated. The characteristics of the patient and treatment were also evaluated according to anthropometric parameters, SMM, and nutritional status.

SMM assessment

Skeletal muscle mass was assessed by measuring cross-sectional muscle area at the C3 vertebral level on planning computed tomography (CT) scans obtained at baseline (Day 1) and at Week 5. All scans were acquired with a 2.5-mm slice thickness using the institutional radiotherapy simulation protocol.

Muscle contours were manually delineated at the C3 level according to previously validated anatomical landmarks and methodology.[8] Skeletal muscle tissue was segmented using Hounsfield unit thresholds of −29 to +150 HU and cross-sectional muscle area was calculated using the volume analysis tool of the treatment planning system (Eclipse v15.1, Varian Medical Systems).

CSMA was defined as the sum of the bilateral paravertebral muscles (PVM); the sternocleidomastoid muscles (SCM) were excluded from all measurements owing to the risk of contour inaccuracy in the presence of cervical lymph node involvement. The C3 skeletal muscle index (SMI) was calculated by dividing total CSMA by the square of the patient's height (cm^2/m^2).

Measurements were independently performed by two trained observers using a standardized segmentation protocol, both blinded to each other's measurements and to the patients' nutritional assessment results. To evaluate reproducibility, a randomly selected subset comprising 25% of the scans was reanalyzed. Intra- and interobserver agreement were assessed using a two-way random effects intraclass correlation coefficient (ICC) model with absolute agreement. The analysis demonstrated good reproducibility, with intraobserver ICC values of 0.86 (95% CI: 0.80–0.93) and interobserver ICC values of 0.82 (95% CI: 0.75–0.90).

Nutritional status assessment

Nutritional status assessment was based on NRS-2002 and GLIM criteria. Patients with NRS 2002 scores ≥ 3 were considered at risk of malnutrition that required nutritional intervention. Based on GLIM criteria, patients were classified as stage 1 (moderate malnutrition; weight loss: 5–10% within the past 6 months, or 10–20% beyond 6 months; low BMI: < 20 if < 70 years, < 22 if ≥ 70 years, reduced muscle mass: mild to moderate deficit) and stage 2 (severe malnutrition; weight loss: >10% within the past 6 months, or >20% beyond 6 months; low BMI: < 18.5 if <70 years, < 20 if ≥ 70 years; reduced muscle mass: severe deficit) [9].

For the etiologic criterion, all patients were classified as meeting the criterion of 'disease burden/inflammation' on the basis of a confirmed active malignancy requiring anticancer treatment, consistent with the GLIM framework's guidance that cancer constitutes a chronic disease with systemic inflammation.

Nutritional intervention and monitoring

All patients received standardized nutritional counseling and oral nutritional supplements (ONS) starting at treatment initiation. Standard, commercially available balanced ONS formulations routinely used in clinical practice were prescribed (approximately 1.2–1.5 kcal/mL; 200–220 mL per serving), without disease-specific or protein-enriched formulations.

The initial prescription consisted of 2–3 bottles per day, with dose adjustments based on weekly body weight trends, treatment tolerance, and patient-reported intake.

Nutritional monitoring was performed weekly through structured face-to-face physician-led interviews (approximately 10 minutes each) during RT/CRT. Each interview included a symptom-directed assessment (dysphagia, odynophagia, mucositis, nausea, and taste alterations), a 24-hour dietary recall, and a pragmatic adherence evaluation based on patient-reported supplement consumption. Bottle counts were used to corroborate self-reported adherence where available.

Adherence to ONS was pragmatically categorized as acceptable when patients reported consuming approximately ≥75% of the prescribed amount on most days of the week. Given the pragmatic outpatient design, total caloric and protein intake from all dietary sources was not formally quantified.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY). Descriptive statistics were presented as means ± standard deviation (SD), medians (min-max), or percentages. The Shapiro-Wilk test was used to assess normality. Parametric data were analyzed using paired t-tests and one-way analysis of variance (ANOVA) with post hoc Tukey HSD tests, while non-parametric data were analyzed using the Mann-Whitney U test and Kruskal-Wallis test. Categorical variables were compared using the chi-square test, with the McNemar-Bowker test applied for time-based comparisons. Pearson's correlation coefficients were calculated for relationships between quantitative variables. $P < .05$ was considered statistically significant.

Results

Baseline characteristics

The study population included 32 HNC patients with a median age of 60 years (range: 18–85 years), of whom 81.3% were male. Hypertension and chronic obstructive pulmonary disease (COPD) were the most common comorbidities (18.8% each), and 37.5% of patients were active smokers. Most tumors were located in the larynx (56.3%) or oral cavity (21.9%), and the predominant histological subtype was squamous cell carcinoma (93.8%). Overall, 65.6% of patients had locally advanced diseases (T3-T4). A total of 68.8% of patients received CRT, while 31.3% underwent RT alone.

All patients were managed exclusively in an outpatient setting throughout the five-week treatment period. No patient required hospitalization, nasogastric tube feeding, percutaneous endoscopic gastrostomy (PEG), or parenteral nutritional support during the study. No grade 3 acute toxicity occurred that necessitated escalation of nutritional support or treatment interruptions longer than 2 days. Among the 32 enrolled patients, 27 (84.3%) demonstrated acceptable adherence to the prescribed ONS regimen (≥75% of the prescribed daily dose on most monitored days) based on weekly interview-based assessment. The remaining five patients (15.6%) reported suboptimal adherence, primarily attributable to nausea (n = 3), odynophagia (n = 1), and dysgeusia (n = 1).

Further baseline characteristics are detailed in Table 1.

Changes in anthropometrics and SMM during treatment

Between Day 1 and Week 5 of treatment, there were significant reductions in body weight (mean±SD: 69.38 ± 15.43 kg vs. 65.98 ± 16.08 kg, $P = .001$), BMI (23.83 ± 4.74 vs. 22.92 ± 4.68 kg/m², $P < .001$), and calf circumference (36.39 ± 3.12 cm vs. 35.66 ± 2.88 cm, $P < .001$) (Table 2). The percentage weight loss averaged 5.08% (mean ± SD: 5.08 ± 9.21%) across the study population, with significant differences observed between GLIM stages ($P = .004$).

Table 1. Baseline characteristics

Patient characteristics		
Age (year)	Mean (SD)	57.8 (15.1)
	Median (min-max)	60 (18-85)
Age group, n (%)	≤65 year	21 (65.6)
	>65 year	11 (34.4)
Sex, n (%)	Male	26 (81.3)
	Female	6 (18.8)
Comorbidity, n (%)	Hypertension	6 (18.8)
	Diabetes	4 (12.5)
	COPD	6 (18.8)
	Other	6 (18.8)
Active smoking, n (%)		12 (37.5)
Tumor characteristics, n (%)		
Histological subtype	Squamous cell carcinoma	30 (93.8)
	Undifferentiated	1 (3.1)
	Adeno-squamous	1 (3.1)
TNM Stage	0	1 (3.1)
	Stage I	4 (12.5)
	Stage II	6 (18.8)
	Stage III	5 (15.6)
	Stage IV	16 (50.0)
Treatment characteristics, n (%)		
Type of treatment	CRT	22 (68.8)
	RT	10 (31.3)
RT approach	Definitive	18 (56.3)
	Adjuvant	14 (43.8)
RT field	Nasopharynx	4 (12.5)
	Oropharynx	1 (3.1)
	Hypopharynx	1 (3.1)
	Larynx	18 (56.3)
	Oral cavity	7 (21.9)
	Unknown	1 (3.1)
RT Dosage	≤50 Gy	1 (3.1)
	>50 Gy	31 (96.9)

COPD: chronic obstructive pulmonary disease; RT: Radiotherapy; CRT: Chemoradiotherapy

There was also a significant decrease in cross-sectional muscle area (CSMA) at the C3 vertebra level (4.76 ± 1.39 cm^2 vs. 4.46 ± 1.21 cm^2, P = .038), while changes in skeletal muscle index (SMI) were not statistically significant (P = .058). (Table 2)

Nutritional status at baseline and week 5

The prevalence of malnutrition based on GLIM criteria increased significantly from 46.9% at baseline to 71.9% by Week 5 (P = .005). Of these, the proportion of patients classified as severely malnourished (Stage 2) increased from 9.4% to 28.1%. Similarly, the percentage of patients at risk of malnutrition based on NRS-2002 scores (≥ 3) increased from 40.6% at baseline to 71.9% at Week 5 (P = .002). (Table 2)

Correlation of NRS-2002 scores with anthropometrics and SMM

Anthropometric parameters (body weight, BMI and mid-arm circumference) were correlated negatively with first day and 5th week NRS-2002 scores (r: ranged from -0.387 for mid-arm circumference to -0.609 for BMI; P ranged from .03 to < .001) and positively with first day and 5th week CSMA (r: ranged from 0.598 for mid-arm circumference to 0.699 for body weight; P < .001) and skeletal muscle index (r: ranged from 0.538 for mid-arm circumference to 0.648 for BMI; P ranged from .004 to < .001) measured at the level of C3. (Table 3)

No significant correlations were observed between NRS-2002 scores and C3-derived skeletal muscle parameters at either time point (all P > .05; Table 3).

Correlation of GLIM categories with anthropometrics and SMM

Staging based on GLIM criteria was negatively correlated significantly with both BMI (r = -0.391, P = .027) and midarm circumference (r = -0.356, P = .045) on the first day, while only with BMI (r = -0.435, P = .013) in the fifth week. By Week 5, only BMI retained statistical significance with GLIM classification. No significant correlation was observed between GLIM stages and SMM parameters. (Table 3).

Table 2. First day vs. 5th week data on anthropometrics, SMM and nutritional status

		First day		5th week		P value[1]
		Mean±SD	Median(min-max)	Mean±SD	Median(min-max)	
Anthropometrics						
Weight (kg)		69.38 ± 15.43	67.00 (45.00 - 95.00)	65.98 ± 16.08	65.20 (27.00 - 91.00)	.001
BMI (kg/m^2)		23.83 ± 4.74	23.65 (13.90 - 30.70)	22.92 ± 4.68	21.85 (14.00 - 31.20)	< .001
Mid arm circumference (cm)		29.78 ± 3.73	30.50 (21.00 - 35.50)	29.42 ± 3.80	30.00 (19.50 - 35.00)	.15
Calf circumference (cm)		36.39 ± 3.12	36.25 (31.00 - 43.00)	35.66 ± 2.88	36.25 (30.00 - 42.00)	< .001
SMM (C3)						
CSMA (cm^2)		4.76 ± 1.39	4.50 (2.30 - 7.40)	4.46 ± 1.21	4.45 (2.20 - 6.50)	.04
SMI (cm^2/m^2)		1.64 ± 0.46	1.60 (0.77 - 2.61)	1.54 ± 0.44	1.47 (0.80 - 2.48)	.06
Nutritional status						
NRS-2002 assessment						
Total score		2.31 ± 1.28	2.00 (1.00 - 5.00)	3.19 ± 1.31	3.00 (1.00 - 5.00)	< .001
Risk of malnutrition (≥3), n (%)		13 (40.6)		23 (71.9)		.002[2]
GLIM classification, n (%)						
Non-malnourished		17 (53.1)		9 (28.1)		.005[3]
Malnourished	Total	15 (46.9)		23 (71.9)		
	Stage 1	12 (37.5)		14 (43.8)		
	Stage 2	3 (9.4)		9 (28.1)		

BMI: Body mass index; SMM: Skeletal muscle mass; CSMA: Cross-sectional muscle area; SMI: Skeletal muscle index, NRS: Nutritional Risk Screening, GLIM: Global Leadership Initiative on Malnutrition

[1]Paired samples t test, [2]McNemar test, [3]McNemar-Bowker test

Change over time in nutritional status by GLIM assessment

When stratified by GLIM classification, 50% of patients who were moderately malnourished (Stage 1) at baseline progressed to Stage 2 by Week 5. Among the non-malnourished at baseline, 41.2% developed malnutrition (Stage 1 or 2) during treatment. (Table 4)

NRS-2002 scores, anthropometrics and SMM according to GLIM groups

Stage 1 and stage 2 vs. non-malnourished GLIM groups on the first day had a significantly higher first day (3.17 ± 1.03 and 4.00 ± 1.00 vs. 1.41 ± 0.62, P < .001) and 5th week (4.00 ± 0.74 and 4.67 ± 0.58 vs. 2.35 ± 1.12, P = .002) NRS-2002 scores.

Stage 1 and stage 2 vs. non-malnourished GLIM groups on the 5th week also had significantly higher first day (2.50 ± 1.23 and 3.00 ± 1.41 vs. 1.33 ± 0.50, P = .012) and 5th week (3.50 ± 0.94 and 4.22 ± 0.67 vs. 1.67 ± 0.87, P < .001) NRS-2002 scores. (Table 5)

The 5th week vs. the first day NRS-2002 scores were significantly higher in non-malnourished (2.35 ± 1.12 vs. 1.41 ± 0.62, P = .001) and stage 1 malnourished (4.00 ± 0.74 vs. 3.17 ± 1.03, P = .005) patients based on the first day GLIM assessment, and in stage 1 (3.50 ± 0.94 vs. 2.50 ± 1.23, P < .001) and stage 2 (4.22 ± 0.67 vs. 3.00 ± 1.41, P = .005) malnourished patients based on the 5th week GLIM assessment. (Table 5)

SMM parameters did not differ significantly across GLIM groups at either assessment point (all P > .05; Table 5). Given the small number of patients within each GLIM subgroup, these comparisons should be considered exploratory.

Table 3. Correlation of NRS-2002 scores with anthropometrics and skeletal muscle assessment

		NRS-2002 score		GLIM-stage		C3 CSMA		C3 SMI	
		First day	5th week	First day	5th week	First day	5th week	First day	5th week
C3 CSMA	r	-0.060	-0.225	-0.099	-0.182	-	-	0.952	0.945
	p	.75	.22	.59	.33	-	-	**< .001**	**< .001**
C3 SMI	r	-0.087	-0.285	-0.185	-0.210	0.952	0.945	-	-
	p	.64	.11	.31	.25	**<.001**	**<.001**	-	-
Body weight	r	-0.527	-0.430	-0.252	-0.26	0.649	0.689	0.564	0.542
	p	.002	.01	.16	.15	**< .001**	**< .001**	**.001**	**.001**
Body mass index	r	-0.545	-0.609	-0.391	-0.435	0.622	0.674	0.630	0.648
	p	.001	< .001	.03	.01	**<.001**	**<.001**	**<.001**	**< .001**
Midarm circumference	r	-0.454	-0.387	-0.356	-0.19	0.661	0.598	0.635	0.538
	p	.009	.03	.05	.30	**< .001**	**< .001**	**< .001**	**.001**
Calf circumference	r	-0.335	-0.257	-0.109	-0.024	0.385	0.283	0.278	0.136
	p	.06	.16	.55	.90	.03	.12	.12	.46

CSMA: Cross-sectional muscle area; SMI: Skeletal muscle index
Pearson correlation analysis; r: correlation coefficient

Table 4. Comparison of the first day versus the fifth week of nutritional status based on GLIM assessment

	GLIM-5th week			P value
	Non-malnourished (n=9)	Stage 1 (n=14)	Stage 2 (n=9)	
GLIM-first day, n(%)				
Non-malnourished (n=17)	9 (100.0)	7 (50.0)	1 (11.1)	.005
Stage 1 (n=12)	0 (0.0)	7 (50.0)	5 (55.6)	
Stage 2 (n=3)	0 (0.0)	0 (0.0)	3 (33.3)	

McNemar-Bowker test

Patients classified as not malnourished on the first day and fifth week of GLIM evaluation had significantly higher BMI compared to stage 1 (25.80 ± 3.78 vs. 21.46 ± 4.87 kg/m2, P = .037) and stage 1 and stage 2 patients (26.79 ± 4.09 vs. 21.39 ± 4.29 and 21.44 ± 3.86, P = .009), respectively. (Table 5)

Characteristics of the patient and treatment according to study parameters

Females vs. males (median -1.50 vs. -1.00, P = .03) and patients who received CRT vs. RT (median -1.0 vs. 0.0, P = .030) had more marked deterioration in NRS-2002 scores, while definitive vs. adjuvant RT (72.2 vs. 28.6%, P = .02) was applied more frequently in non-malnourished patients based on first day GLIM (Table 6).

Age, smoking status and tumor stage had no significant influence on anthropometrics, SMM and nutritional status parameters (Table 6).

Discussion

Although several studies have investigated GLIM criteria in HNC patients[10,12,13], the present study adds to this literature by simultaneously incorporating longitudinal C3-based skeletal muscle assessment alongside both GLIM staging and NRS-2002 monitoring within a prospective real-world outpatient cohort. This integrated,

Table 5. NRS-2002 scores, anthropometrics and SMM according to the first day and fifth week GLIM classification

	GLIM- first day				GLIM-5th week			
	Non-malnourished	Malnourished			Non-malnourished	Malnourished		
		Stage 1	Stage 2	p value[2]		Stage 1	Stage 2	P value[2]
NRS-2002 scores, mean±SD								
First day	1.41 ± 0.62	3.17 ± 1.03	4.00 ± 1.00	<.001	1.33 ± 0.50	2.50 ± 1.23	3.00 ± 1.41	.01
5th week	2.35 ± 1.12	4.00 ± 0.74	4.67 ± 0.58	.002	1.67 ± 0.87	3.50 ± 0.94	4.22 ± 0.67	< .001
p value[1]	.001	.005	.18		.08	<.001	.005	
Difference	-0.94 ± 0.90	-0.83 ± 0.83	-0.67 ± 0.58	.86	-0.33 ± 0.50	-1.00 ± 0.78	-1.22 ± 0.97	.053
Anthropometrics, mean±SD								
Body weight (kg)	73.82 ± 13.64	63.50 ± 16.35	67.67 ± 18.72	.21	75.80 ± 13.29	60.41 ± 16.74	64.83 ± 14.35	.08
BMI (kg/m^2)	25.80 ± 3.78	21.46 ± 4.87	22.17 ± 5.73	.04	26.79 ± 4.09	21.39 ± 4.29	21.44 ± 3.86	.009
Calf circumference (cm)	36.82 ± 2.84	35.75 ± 3.03	36.50 ± 5.63	.67	36.51 ± 2.55	34.68 ± 2.68	36.33 ± 3.32	.24
Mid-arm circumference (cm)	31.32 ± 3.05	27.71 ± 3.93	29.33 ± 3.21	.030	31.33 ± 3.16	28.18 ± 4.20	29.44 ± 3.24	.15
SMM, mean±SD								
C3 CSMA (cm^2)	4.94 ± 1.33	4.48 ± 1.54	4.83 ± 1.40	.69	4.81 ± 1.14	4.37 ± 1.19	4.23 ± 1.37	.58
C3 SMI (cm^2/m^2)	1.73 ± 0.45	1.51 ± 0.49	1.59 ± 0.43	.47	1.71 ± 0.44	1.52 ± 0.46	1.39 ± 0.39	.31

BMI: Body mass index; SMM: Skeletal muscle mass; CSMA: Cross-sectional muscle area; SMI: Skeletal muscle index
[1]Paired samples t test, [2]One way ANOVA

Table 6. Characteristics of the patient and treatment according to anthropometrics, SMM, and nutritional status

	Difference (first day score - 5th week score), mean±SD				GLIM-first day, n(%)			GLIM-5th week, n(%)		
	BMI (kg/m²)	C3 CSMA (cm²)	C3 SMI (cm²/m²)	NRS-2002 score	Non-malnourished	Stage 1	Stage 2	Non-malnourished	Stage 1	Stage 2
Sex										
Female	1.40 ± 0.87	0.25 ± 0.18	0.08 (0.03 - 0.18)	-1.50 (-2.00 -1.00)	3 (50.0)	3 (50.0)	0 (0.0)	1 (16.7)	2 (33.3)	3 (50.0)
Male	0.80 ± 1.29	0.32 ± 0.88	0.10 (-0.95 - 0.66)	-1.00 (-3.00 - 0.00)	14 (53.8)	9 (34.6)	3 (11.5)	8 (30.8)	12 (46.2)	6 (23.1)
p value	.29[1]	.86[1]	.96[2]	.03[2]	.60[3]			.41[3]		
Age group										
<65 year	1.15 ± 1.28	0.31 ± 0.50	0.11 ± 0.18	-1.00 (-3.00 - 0.00)	12 (57.1)	7 (33.3)	2 (9.5)	6 (28.6)	8 (38.1)	7 (33.3)
> 65 year	0.45 ± 1.03	0.29 ± 1.20	0.08 ± 0.43	0.00 (-2.00 - 0.00)	5 (45.5)	5 (45.5)	1 (9.1)	3 (27.3)	6 (54.5)	2 (18.2)
p value	.12[1]	.96[1]	.87[1]	.11[2]	.79[3]			.60[3]		
Smoking										
No	0.91 ± 1.12	0.28 ± 0.94	0.05 (-0.95 - 0.66)	-1.00 (-2.00 - 0.00)	10 (50)	8 (40)	2 (10)	5 (25)	9 (45)	6 (30)
Yes	0.92 ± 1.45	0.34 ± 0.50	0.13 (-0.17 - 0.55)	-0.50 (-3.00 - 0.00)	7 (58.3)	4 (33.3)	1 (8.3)	4 (33.3)	5 (41.7)	3 (25)
p value	.98[1]	.84[1]	.86[2]	.35[2]	.90[3]			.87[3]		
Disease stage										
Early stage (stage I-II)	0.68 ± 0.91	0.20 (-0.40 - 1.50)	0.07 (-0.16 - 0.55)	-0.50 (-2.00 - 0.00)	6 (60)	4 (40)	0 (0)	4 (40)	4 (40)	2 (20)
Advanced (stage III-IV)	0.95 ± 1.36	0.40 (-2.50 - 2.10)	0.13 (-0.95 - 0.66)	-1.00 (-3.00 - 0.00)	10 (47.6)	8 (38.1)	3 (14.3)	5 (23.8)	9 (42.9)	7 (33.3)
p value	.58[1]	.70[2]	.75[2]	.24[2]	.44[3]			.60[3]		
RT approach										
Definitive	0.79 ± 1.46	0.20 (-2.50 - 1.50)	0.07 (-0.95 - 0.55)	-0.50 (-3.00 - 0.00)	13 (72.2)	5 (27.8)	0 (0)	7 (38.9)	7 (38.9)	4 (22.2)
Adjuvant	1.06 ± 0.89	0.35 (-0.60 - 2.10)	0.12 (-0.23 - 0.66)	-1.00 (-2.00 - 0.00)	4 (28.6)	7 (50.0)	3 (21.4)	2 (14.3)	7 (50)	5 (35.7)
p value	.56[1]	.78[2]	.70[2]	.50[2]	.02[3]			.30[3]		
Treatment										
CRT	1.20 ± 1.37	0.25 (-2.50 - 2.10)	0.08 (-0.95 - 0.66)	-1.00 (-3.00 - 0.00)	11 (50)	8 (36.4)	3 (13.6)	4 (18.2)	10 (45.5)	8 (36.4)
RT	0.26 ± 0.41	0.25 (-0.40 - 1.50)	0.09 (-0.16 - 0.55)	0.00 (-1.00 - 0.00)	6 (60)	4 (40)	0 (0)	5 (50)	4 (40)	1 (10)
p value	.006[1]	.54[2]	.58[2]	.03[2]	.47[3]			.12[3]		

BMI: Body mass index; CSMA: Cross-sectional muscle area; SMI: Skeletal muscle index; RT: radiotherapy; CRT: Chemoradiotherapy
[1]Independent samples t test, [2]Mann-Whitney U test, [3]χ^2 test

multimodal approach enables a direct comparison of assessment tools and muscle metrics under routine clinical conditions, which has not been systematically reported in previous studies focusing primarily on malnutrition prevalence.

Malnutrition remains a significant concern in HNC patients due to the combined effects of tumor biology, treatment-related toxicities, and decreased oral intake.[14-16] The baseline malnutrition prevalence observed in this study (46.9%) is consistent with prior research, reflecting the inherent nutritional vulnerability of this patient population.[10,15,17] By Week 5, prevalence increased to 71.9%, consistent with evidence that malnutrition frequently worsens during anticancer treatment owing to the cumulative mucosal and systemic toxicities of RT or CRT, including mucositis, dysphagia, and anorexia.[12,13]

NRS-2002 scores correlated significantly with GLIM-based malnutrition stages at baseline, and this concordance was maintained through Week 5 of treatment. These findings support the feasibility of applying GLIM criteria to prospectively identify patients at high nutritional risk prior to anticancer treatment, including those with severe malnutrition (Stage 2) who are at higher risk of postoperative complications and 90-day all-cause mortality.[9,18,19]

In addition, NRS-2002 scores were significantly associated with body weight, BMI and mid-arm circumference, whereas GLIM-defined malnutrition was significantly correlated with BMI alone at both time points. This pattern likely reflects the dominant role of low BMI as the most frequently met GLIM phenotypic criterion in this cohort, given that the majority of patients had BMI values near or below the GLIM threshold (<20 kg/m² for patients under 70 years). Weight loss and reduced muscle mass criteria, while clinically present, may have been less consistently met or may not have reached phenotypic threshold severity in all patients at baseline.[20,21]Similarly, Steer et al. reported that GLIM-defined malnutrition in HNC patients was significantly associated with BMI alone.[10]

The lack of significant association between GLIM classification and C3-derived muscle parameters may reflect the short observation period, limited sample size, and methodological challenges of detecting early muscle changes during active RT/CRT rather than a true lack of biological relationship.

In the present cohort, despite standardized ONS prescription aligned with ESPEN recommendations and weekly clinical monitoring, significant declines in body weight, BMI, and C3 CSMA were observed throughout the five-week treatment period. However, as total dietary intake from all sources was not formally quantified, the degree to which individual patients met recommended energy and protein targets cannot be confirmed; the observed nutritional deterioration should therefore be interpreted in the context of prescribed but incompletely verified nutritional support. These findings highlight the limitations of standard ONS-based interventions in HNC patients, particularly those with severe baseline nutritional deficits. Prior studies have reported similarly mixed results regarding the efficacy of ONS alone in maintaining nutritional status during RT or CRT, and nutritional strategies incorporating proactive measures — such as prophylactic enteral feeding or intensive individualized dietary counseling — may better address the complex needs of this population.[22-26]

CRT was associated with greater declines in BMI and nutritional status compared with RT alone, reflecting the heightened toxicity of combined treatments. This is consistent with prior evidence identifying CRT as a major risk factor for nutritional deterioration, owing to its exacerbation of mucositis, dysphagia, and gastrointestinal symptoms.[12,27-30] Early and intensive nutritional intervention is therefore essential to minimize treatment interruptions and improve clinical outcomes in these patients.[12,22,29]

C3 cross-sectional muscle area (CSMA) has been proposed as a practical alternative to L3-based skeletal muscle assessment in HNC patients, given its routine availability on planning CT imaging.[7,8] In this study, C3 CSMA declined significantly during treatment, whereas changes in the skeletal muscle index (SMI) did not reach statistical significance, and neither parameter was significantly correlated with GLIM staging or NRS-2002 scores. The lack of significant association between GLIM classification and C3-derived muscle parameters may reflect the short observation period, limited sample size, and methodological challenges inherent to detecting early muscle changes during active RT/CRT, rather than a true absence of biological relationship. Similar constraints have been reported in prior studies evaluating C3-based assessments, particularly regarding sensitivity to small but clinically meaningful muscle losses.[31]

A further consideration is the potential influence of local radiotherapy-related tissue changes on C3 muscle

measurements. In the acute treatment phase, soft tissue edema and early lymphatic alterations within the irradiated neck region could theoretically affect cross-sectional area estimates. However, clinically relevant RT-induced skeletal muscle atrophy and volumetric changes are generally reported months to years after treatment completion rather than within the first weeks of therapy.[32,33] For this reason, the Week 5 assessment time point was intentionally selected to capture early treatment-related nutritional changes while minimizing exposure to long-term structural RT effects. Nevertheless, the possibility that local treatment-related tissue changes may partially confound C3 CSMA measurements cannot be entirely excluded and should be considered when interpreting these results.

By incorporating percentage weight loss and skeletal muscle metrics (CSMA and SMI) into the assessment, this study adds to the growing evidence supporting GLIM as a robust tool for malnutrition diagnosis and staging. The findings further suggest that GLIM can identify patients at higher risk of adverse outcomes, such as those with severe malnutrition (Stage 2), a subgroup often overlooked in routine clinical care.

This study has several limitations. First, the relatively small sample size (n = 32), heterogeneous distribution of tumor subsites (larynx 56.3%, oral cavity 21.9%, other 21.8%), range of treatment indications (definitive vs. adjuvant RT/CRT), and single-center design limit the generalizability of these findings. Additionally, the predominantly male cohort (81.3%) may reduce applicability to female HNC patients, in whom body composition thresholds for muscle depletion may differ. Second, total energy and protein intake from all dietary sources were not formally quantified. Although weekly structured interviews included a 24-hour dietary recall and pragmatic adherence assessment, the accuracy of patient-reported supplement consumption is subject to recall bias. Third, although C3-based measurements were performed using a standardized protocol with high reproducibility, local RT-related tissue changes may partially influence neck-level muscle estimates. Fourth, the absence of a control group precludes definitive conclusions regarding the effectiveness of nutritional support in mitigating malnutrition progression. Finally, given the small number of patients within each GLIM subgroup, subgroup-level findings should be interpreted as exploratory.

Future studies with larger cohorts and more robust methodologies are needed to validate these findings and explore the utility of GLIM criteria in predicting long-term clinical outcomes.

In conclusion, our findings revealed deterioration in anthropometrics, C3 CSMA, and NRS-2002 scores along with no change or even deterioration in baseline malnourished status according to GLIM in most HNC patients under anticancer treatment. Although all patients received standardized ONS prescription and weekly monitoring, progression of malnutrition was still observed during treatment. This likely reflects the complex multifactorial nature of nutritional decline in HNC, where treatment-related symptoms, inflammation, and catabolic stress may overcome nutritional interventions, particularly when nutritional intake cannot be strictly quantified in routine outpatient settings. NRS-2002 scores were significantly correlated with GLIM-based stages at baseline and the relationship between the two tests also maintained its significance over time, whereas neither GLIM stages nor NRS-2002 scores were associated with SMM parameters (C3 CSMA and skeletal mass index) within the short observation period. These findings suggest that anthropometric and clinical screening tools remain central in early nutritional monitoring, while the role of C3-based measurements requires further validation in larger studies with longer follow-up.

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Author contributions

Conception and design: M.A.; Data acquisition: M.A., C.G.; Data analysis: M.A., C.G.; Data interpretation: M.A., C.G.; Drafting of the manuscript: M.A.; Critical revision of the manuscript: M.A., C.G. All authors reviewed the results, approved the final version of the manuscript, and agreed to be accountable for all aspects of this study.

Ethical approval

This study was approved by the Gazi University Ethics Committee (Date: March 16, 2020, Decision/Protocol No: 452). Informed consent was obtained from all participants involved in this study.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable requests subject to institutional regulations and applicable ethical/privacy restrictions.

Conflict of interest

The authors declare the following potential conflict of interest: M.A. reports a relationship with Turkish Society for Radiation Oncology (TROD) that includes: unpaid Board Member.

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Generative AI statement

The authors declare that during the preparation of this study, the following AI-assisted technology was used: ChatGPT-5, OpenAI on 18/12/2025. Extent of Use: AI-assisted technology was used only for language editing, grammar and clarity improvement, and proofreading. It was not used for study conception or design, data collection, data extraction, statistical analysis, data interpretation, figure generation, or creation of scientific conclusions. All AI-assisted suggestions were critically reviewed and edited by the authors, who take full responsibility for the integrity, accuracy, originality, and final content of the manuscript. The authors confirm that they have critically reviewed and edited any AI-generated content and take full responsibility for the integrity, accuracy, and originality of the publication. The authors certify that the original human contribution is maintained and that AI-assisted tools are not listed or cited as authors.

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