



# Sarcopenia measured with handgrip strength and skeletal muscle mass to assess frailty in older patients with head and neck cancer

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## ABSTRACT

**Objectives:** Patients with head and neck cancer (HNC) have a risk of sarcopenia which is associated with adverse health outcomes. Frailty is also associated with adverse outcomes and is diagnosed by a comprehensive geriatric assessment (CGA). Because a CGA is time-consuming and not all patients benefit from it, frailty screening questionnaires are used to select patients for CGA. Sarcopenia measurement may be a biomarker for frailty. Our objective was to examine the association between sarcopenia and a frailty screening questionnaire.

**Materials and Methods:** In this single-center retrospective study, 150 patients (≥ 60-years old) with HNC were reviewed. Sarcopenia was defined as the combination of reduced handgrip strength and loss of skeletal muscle mass, calculated as skeletal muscle index (SMI), according to the EWGSOP-criteria. Frailty screening was performed using the Geriatrics 8 (G8) questionnaire.

**Results:** The 150 patients included 101 men and 49 women. Frail patients were more likely to be sarcopenic at diagnosis. G8 frailty score showed a significant though weak correlation with SMI. Univariate regression analysis with frailty as a dependent variable distinguished comorbidity score, handgrip strength, SMI, and sarcopenia as significant. These variables were subjected to a multivariate analysis in which comorbidity score and SMI remained significant.

**Conclusion:** There is an association between sarcopenia and the G8 frailty screening questionnaire. Therefore, sarcopenia measurement could be interchangeable with the G8 frailty screening questionnaire. Further research should compare the gold standard for frailty, i.e. CGA, with sarcopenia.

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## 1. Introduction

Worldwide the annual incidence of head and neck cancer (HNC) accounts for more than 650,000 cases and 330,000 deaths [1]. Compared to patients with other malignancies, patients with HNC have a higher risk of severe malnutrition, mostly due to swallowing problems [2]. This could lead to sarcopenia. Sarcopenia is defined as a generalized and progressive loss of muscle function and skeletal muscle mass [3]. Previous studies showed that sarcopenia based on loss of skeletal muscle mass is present in 35.5–54.5% of patients with HNC and is related to adverse health outcomes [4,5]. For example, low skeletal muscle mass is associated with chemotherapy dose-limiting toxicity [6], increased incidence of postoperative complications, and decreased survival in

patients with HNC [7,8]. Patients with sarcopenia thus represent an important group that should be identified as they are at risk for complications of treatment and poor survival.

Frailty is also associated with poor outcomes and higher risks of treatment complications [9]. Frailty is often mentioned as an age-related syndrome of physiological decline and vulnerability, leading to an increased risk of adverse health outcomes [10]. A comprehensive geriatric assessment (CGA) that evaluates physical, psychological, functional, and social capabilities, and limitations of geriatric patients is the gold standard assessment for diagnosing frailty. In geriatric oncology, a CGA is used to detect disabilities, and comorbid conditions that potentially contribute to an older adult patient's vulnerabilities, which could predispose them to poor outcomes and treatment complications [11]. However, such assessments are time-consuming, leading many cancer specialists to seek a shorter screening tool that can separate fit older adults with cancer, who can receive standard cancer treatment, from vulnerable patients, who should subsequently receive a full assessment to guide tailoring of their treatment regimens [12]. One such tool is the Geriatrics 8 (G8) screening tool, which was developed specifically for older adults with cancer. Another potential predictor of toxicity and

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poor outcomes is sarcopenia [13]. Zwart et al. found that sarcopenia as measured by skeletal muscle mass on screening CTs was a potential biomarker for frailty in patients with HNC. In their study low skeletal muscle mass, was independently associated with frailty screening based on the G8 questionnaire [14]. However, Williams et al. were unable to find an association between sarcopenia, based on skeletal muscle mass, and frailty diagnosed with the Carolina Frailty Index in older adult patients with cancer [15]. Dunne et al., in their investigation of 100 older adults with cancer found no significant association between skeletal muscle mass, as measured at the level of the third third lumbar vertebral body, and any components of the CGA. [16]. Zwart et al. [14] and Dunne et al. [16] conducted only skeletal muscle mass measurements on CT of the third cervical or lumbar vertebrae to determine sarcopenia. According to the criteria of the European Working Group on Sarcopenia in Older People (EWGSOP) sarcopenia is a combination of muscle function and skeletal muscle mass [3]. The association between sarcopenia and frailty could possibly be improved when a combination of skeletal muscle mass and muscle function, examined with handgrip strength, is used to assess sarcopenia [3]. The aim of this study was to examine the association between sarcopenia, defined as reduced handgrip strength and loss of skeletal muscle mass, and frailty screening, as assessed by the G8 questionnaire in older adults with HNC.

## 2. Materials and Methods

### 2.1. Ethical Approval

The design of this study was approved by the Medical Ethical Research Committee of the University Medical Center Utrecht (approval ID 17-365/C). All procedures in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration (Version 2008) and its later amendments or comparable ethical standards. All data were handled according to general data protection regulation (GDPR).

#### 2.1.1. Patients and Study Design

In this single-center retrospective study, older adult patients ( $\geq 60$ -years old) with pathologically proven HNC diagnosed between September 2018 and January 2020 records were reviewed. In our clinic, these patients routinely undergo handgrip strength measurement and fill out the G8 questionnaire on their first outpatient clinic visit. Patients were included if they had a geriatric assessment screening (G8), handgrip strength measurement, and had recent ( $< 4$  weeks) pre-treatment imaging scans (CT or MRI) of the head and neck. This resulted in an initial inclusion of 180 patients. Patients were excluded due to insufficient quality of diagnostic imaging (incomplete imaging at the time of diagnoses (fifteen), presence of artifacts (twelve), no reliable

differentiation between muscle and surrounding tissue (three) which impaired measurements of skeletal muscle mass. This resulted in the final inclusion of 150 patients.

Relevant demographic and clinical variables were collected from patients' medical records: age, sex, body mass index (BMI), weight loss in the past six months, smoking status, alcohol use, comorbidity as evaluated by the Adult Comorbidity Evaluation-27 index (ACE-27), tumor localization, tumor type (primary, second primary or recurrence), histology, the *TNM stage according to the 8th edition of the UICC tumor classification* of malignant tumors and imaging technique (CT or MRI) were scored.

#### 2.1.2. Definition of Sarcopenia

As recommended by the EWGSOP we used the combination of low muscle function, as determined by handgrip strength measurements, and low muscle quantity, as determined by skeletal muscle mass, for the diagnosis of sarcopenia [3].

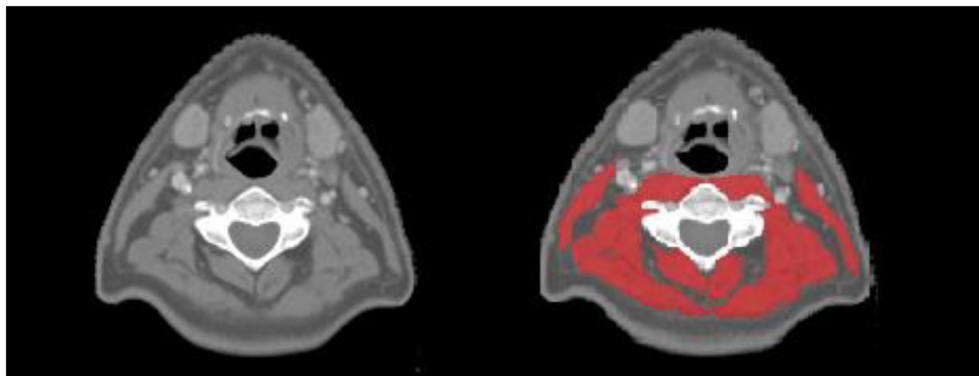
#### 2.1.3. Muscle Function

Overall muscle function is strongly related to handgrip strength [17]. Handgrip strength was measured using a Jamar hydraulic handheld dynamometer according to the recommendations of the American society of hand therapists (ASHT) and expressed in kilograms (kg). Patients were asked to squeeze maximally with each hand. The average score of the left and right hands was used for analysis. Patients had low handgrip strength if the handgrip strength was below twenty-seven kg (men) or below sixteen kg (women) [3].

#### 2.1.4. Skeletal Muscle Mass

Skeletal muscle mass was measured in all patients at the level of the third cervical vertebrae (C3) as cross-sectional muscle area (CSMA) on CT or MRI imaging before initiating treatment. The axial slice of the imaging which showed both transverse processes and the entire vertebral arc was selected for the segmentation of muscle tissue (Fig. 1). For CT imaging, muscle area was defined as the pixel area between the radiodensity range of  $-29$  and  $+150$  Hounsfield units (HU), which is specific for muscle tissue [18]. For MRI, muscle area was manually segmented, and fatty tissue was manually excluded. Segmentation of muscle tissue was manually performed using the commercially available software package SliceOmatic (version 5.0, Tomovision, Canada). The first author (CM) performed skeletal muscle mass measurements in all 150 patients.

The cross-sectional muscle area at the level of C3 was converted to CSMA at the level of L3 using a formula published by Swartz et al. [19]. The lumbar skeletal muscle index (SMI) was calculated by correcting skeletal muscle mass at the level of L3 for height. Patients



**Fig. 1.** Example of segmentation of skeletal muscle tissue at the level of the third cervical vertebra (C3) [5]. Figure shows two identical axial computed tomography (CT) slides at the level of C3; left shows the muscle tissue unsegmented, right shows both sternocleidomastoid and paravertebral muscles segmented in red.

had a low SMI if this value was below 43.2 cm<sup>2</sup>/m<sup>2</sup>; this cut-off value was established in a separate cohort of patients with HNC [6].

### 2.1.5. Frailty

For frailty screening, we used the G8 frailty questionnaire. This frailty screening tool consists of eight items which cover multiple geriatric domains, including nutritional status, physical capacity, mood, and polypharmacy. The G8 is specifically designed for older adult patients with cancer. Scores range from zero to seventeen, with scores  $\leq$  fourteen representing potential frailty [13].

### 2.2. Statistical Analysis

Data analyses were performed using IBM SPSS statistics 25. Baseline clinical characteristics were collected and continuous data are represented as mean  $\pm$  standard deviation (SD). Categorical data are represented as a number and percentage of total. The skeletal muscle mass, was presented dichotomously as low SMI and normal SMI based on previously published specific cut-offs for SMI. Muscle function was presented dichotomously as low muscle function and normal muscle function based on previously published gender-specific cut-offs for handgrip strength. Sarcopenia was presented dichotomously as sarcopenic (if patients had a low muscle function and low SMI) and non-sarcopenic (all other patients).

Frailty was presented dichotomously as frail and non-frail based on previously published cut-offs for the G8 frailty screening questionnaire.

Correlation between SMI, handgrip strength and the G8 frailty score were analyzed with bivariate Pearson's  $r$ -correlation coefficients. Independent sample  $t$ -tests or Chi-square statistics were used for analyzing differences between the frequencies of each categorical variable with the presence or absence of frailty and presence or absence of sarcopenia.

Univariate logistic regression analyses were performed, with frailty or sarcopenia as dependent variables and the baseline variables as independent variables. Variables were selected based on clinical relevance. Variables that were statistically significant ( $p < 0.05$ ) in the univariate regression were included in the multivariate logistic regression with odds ratios (ORs) and 95% CI's provided.

## 3. Results

### 3.1. Patient Characteristics

In total 150 patients with HNC diagnosed between September 2018 and January 2020 were included. Patient characteristics are presented in Table 1. The majority of the patients (67%) were male. Stage IV was the most common stage (43%). Of the included patients, 60 patients (40%) were screened as frail according to the G8 questionnaire. The majority of the patients (61%) had low SMI at diagnosis. Low handgrip strength at diagnosis was seen in a minority of the included patients (22%). Of the included patients, 21 patients (14%) were sarcopenic, as defined by low handgrip strength and low SMI. The mean time between G8 questionnaire and handgrip strength measurement (first consultation) and the CT/MRI scan was 1.8 weeks.

#### 3.1.1. Correlation Analysis of Sarcopenia and Frailty Score

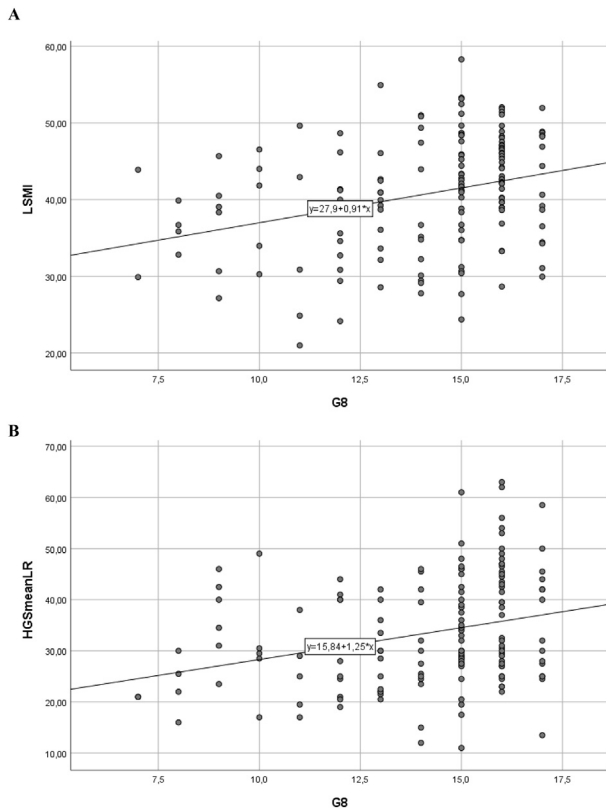
SMI showed a significant though weak correlation with the G8 frailty score ( $r = 0.252$ ,  $p < 0.01$ ). handgrip strength showed a significant but weak correlation with the G8 frailty score ( $r = 0.284$ ,  $p < 0.01$ ). A stronger and significant correlation was identified between SMI and the handgrip strength ( $r = 0.512$ ,  $p < 0.01$ ). Scatterplots, with SMI, handgrip strength, and the G8 frailty score are presented in Fig. 2.

As seen in Table 1, statistically significant differences were seen between patients with and without frailty in the presence of sarcopenia,

**Table 1**  
Characteristics of HNC patients with and without frailty [1].

	Total N = 150		Frail N = 60		Non Frail N = 90		$\chi^2$	p-value
Age (years) (M, SD)	70.3	7.26	71.5	8.7	69.5	6.0	NA	0.137
Sex (n, %)								
Male	101	67	36	60	65	72	2.445	0.118
Female	49	33	24	40	25	28		
Weight loss 6 months prior to diagnosis (n, %)								
Non	117	78	40	66	77	86	13.230	<b>0.001*</b>
<10%	26	17	13	22	13	14		
$\geq 10\%$	7	5	7	12	0	0		
BMI (kg/m <sup>2</sup> ) (n, %)								
<20	53	35	26	43	27	30	21.027	<b>0.000*</b>
20–24.9	9	6	9	15	0	0		
25–29.9	64	43	20	33	44	49		
$\geq 30$	24	16	5	9	19	21		
Smoker (n, %)								
No	26	17	10	17	16	18	1.669	0.434
Former	73	49	26	43	47	52		
Current	51	34	24	40	27	30		
Alcohol use (n, %)								
No	29	18	11	18	18	20	0.267	0.875
Yes	101	62	40	67	61	68		
Former	20	12	9	15	11	12		
ACE-27 score (n, %)								
Non	49	33	12	20	37	41	11.934	<b>0.008*</b>
Mild	54	36	21	35	33	37		
Moderate	29	19	15	25	14	15		
Severe	18	12	12	20	6	7		
Localization (n, %)								
Oral cavity	32	21	13	22	19	21	5.401	0.714
Nasal cavity	6	4	3	5	3	3		
Nasopharynx	6	4	2	3	4	5		
Oropharynx	37	25	19	31	18	20		
Hypopharynx	11	7	5	8	6	7		
Larynx	29	19	10	17	19	21		
Salivary glands	17	11	5	9	12	13		
Skin	2	1	0	0	2	2		
Unknown primary	10	7	3	5	7	8		
Type of tumor (n, %)								
Primary	143	95	59	98	84	93	2.122	0.346
Recurrent	1	1	0	0	1	1		
Second primary	6	4	1	2	5	6		
Histology (n, %)								
Squamous	119	79	50	82	69	77	1.335	0.513
Adenocarcinoma	18	12	5	9	13	14		
Other	13	9	5	9	8	9		
TNM Stage (n, %)								
I	23	15	8	13	15	17	8.008	<b>0.046**</b>
II	30	20	6	10	24	27		
III	33	22	14	23	19	21		
IV	64	43	32	54	32	35		
Type of imaging (n, %)								
CT	92	61	39	65	53	59	0.567	0.451
MRI	58	39	21	35	37	41		
Low muscle function (n, %)								
No	117	78	43	72	74	82	2.337	0.126
Yes	33	22	17	28	16	18		
Low SMI (n, %)								
No	58	39	14	23	44	49	9.914	<b>0.002*</b>
Yes	92	61	46	77	46	51		
Sarcopenia (n, %)								
No	129	86	47	78	82	91	4.882	<b>0.027**</b>
Yes	21	14	13	22	8	9		

Statistical significant differences are in bold.



**Fig. 2.** Scatterplots for skeletal muscle index, handgrip strength and frailty scores. The figure illustrates the correlation of skeletal muscle index (SMI) and G8 frailty scores (A); handgrip strength (HSG) and frailty scores (B).

low SMI, amount of comorbidity as evaluated by the ACE-27 score, and TNM stage. Frail patients were more likely to be sarcopenic (combination of low handgrip strength and low SMI) at diagnosis (22% versus 9%,  $p < 0.05$ ), to have low SMI at diagnosis (77% versus 51%;  $p < 0.01$ ), to have a severe comorbidity defined by the ACE-27 score (20% versus 7%;  $p < 0.01$ ), and to have a stage IV disease (54% versus 35%;  $p < 0.05$ ).

Statistically significant differences were found between patients with and without sarcopenia for frailty measured by the G8, age at diagnosis, and comorbidity scores as evaluated by the ACE-27 score (Table 2). Sarcopenic patients were more likely being frail (22% versus 9%,  $p < 0.05$ ), to be older of age at diagnosis (mean 77 years versus 69 years;  $p < 0.01$ ), and to have a mild ACE-27 score (57% versus 32%;  $p < 0.01$ ).

### 3.1.2. Univariate and Multivariate Logistic Regression

Univariate and multivariate logistic regression analysis with frailty or sarcopenia as the dependent variable was performed. Table 3 shows the univariate regression analysis with frailty as the dependent variable which distinguished ACE-27 score (OR 6.17, 95% CI 1.90–20.00,  $P = 0.002$ ), handgrip strength (OR 0.94, 95% CI 0.90–0.97,  $P < 0.000$ ), SMI (OR 0.92, 95% CI 0.87–0.96,  $P < 0.000$ ), and sarcopenia (OR 2.84, 95% CI 1.10–7.34,  $P = 0.032$ ) as significant variables for predicting frailty. These significant variables were subjected to two different multivariate analyses. The first with sarcopenia and the second with hand grip strength and SMI because of assumed multicollinearity. In the first multivariate analysis only ACE-27 score (OR 5.47, 95% CI 1.67–17.98,  $P = 0.005$ ) remained significant. In the second ACE-27 score (OR 8.08, 95% CI 2.21–29.60,  $P = 0.003$ ) and SMI (OR 0.92, 95% CI 0.86–0.98,  $P = 0.006$ ) remained significant.

Table 4 shows the univariate regression analysis with sarcopenia as dependent variables distinguished age (OR 3.68, 95% CI 1.27–10.64,  $P = 0.016$ ) and G8 (OR 2.84, 95% CI 1.10–7.34,  $P = 0.032$ ) as significant

**Table 2**  
Characteristics of HNC patients with and without sarcopenia [2].

	Total N = 150		Sarcopenic N = 21		Non Sarcopenic N = 129		$\chi^2$	p-value
Age (years) (M, SD)	70.3	7.26	77	8.6(SD)	69	6.4(SD)	NA	<b>0.000*</b>
Sex (n, %)								
Male	101	67	12	57	89	69	1.153	0.283
Female	49	33	9	43	40	31		
Weight loss 6 months prior to diagnosis(n, %)								
Non	117	78	16	76	101	78	1.376	0.503
<10%	26	17	3	14	23	18		
≥ 10%	7	5	2	10	5	4		
BMI (kg/m <sup>2</sup> ) (n, %)								
<20	53	35	10	48	43	33	4.576	0.206
20–24.9	9	6	0	0	9	7		
25–29.9	64	43	10	48	54	42		
≥ 30	24	16	1	4	23	18		
Smoker (n, %)								
No	26	17	4	19	22	17	0.050	0.975
Former	73	49	7	33	44	34		
Current	51	34	10	48	63	49		
Alcohol use (n, %)								
No	29	18	4	19	25	19	0.706	0.703
Yes	101	62	13	62	88	68		
Former	20	12	4	19	16	13		
ACE-27 score (n, %)								
Non	49	33	0	0	49	38	12.19	<b>0.007*</b>
Mild	54	36	12	57	42	32		
Moderate	29	19	6	29	23	18		
Severe	18	12	3	14	15	12		
Localization (n, %)								
Oral cavity	32	21	5	24	27	21	4.716	0.787
Nasal cavity	6	4	0	0	6	5		
Nasopharynx	6	4	0	0	6	5		
Oropharynx	37	25	4	19	33	25		
Hypopharynx	11	7	1	5	10	8		
Larynx	29	19	5	24	24	19		
Salivary glands	17	11	4	19	13	10		
Skin	2	1	0	0	2	1		
unknown primary	10	7	2	9	8	6		
Type of tumor (n, %)								
Primary	143	95	21	100	122	94	1.195	0.550
Recurrent	1	1	0	0	1	1		
Second primary	6	4	0	0	6	5		
Histology (n, %)								
Squamous	119	79	17	81	102	80	0.154	0.926
Adenocarcinoma	18	12	2	9	16	12		
Other	13	9	2	10	11	8		
TNM Stage (n, %)								
I	23	15	6	29	17	13	4.228	0.238
II	30	20	2	9	28	22		
III	33	22	4	19	29	22		
IV	64	43	9	43	55	43		
Type of imaging (n, %)								
CT	92	61	12	57	80	62	0.181	0.671
MRI	58	39	9	43	42	38		
Low muscle function (n, %)								
No	117	78	0	0	117	91	86.58	<b>0.000*</b>
Yes	33	22	21	100	12	9		
Low SMI (n, %)								
No	58	39	0	0	58	45	15.39	<b>0.000*</b>
Yes	92	61	21	100	71	55		
G8 Frailty questionnaire (n, %)								
Not frail > 14	129	86	47	78	82	91	4.882	<b>0.027**</b>
Frail ≤ 14	21	14	13	22	8	9		

Statistical significant differences are in bold.



**Table 3**

Univariate and multivariate logistic regression analysis for analyzing variables associated with frailty in patients with HNC [3].

Frailty	Univariate analysis			Multivariate analysis					
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Age (years)									
<70	Ref.								
≥ 70	1.20	0.62–2.29	0.594						
Sex									
Male	Ref.								
Female	1.73	0.87–3.46	0.120						
ACE-27 score									
Non	Ref.			Ref.			Ref.		
Mild	1.96	0.84–4.59	0.120	1.62	0.67–3.94	0.289	1.90	0.75–4.81	0.173
Moderate	3.30	1.24–8.78	<b>0.017**</b>	2.80	1.03–7.63	<b>0.044**</b>	3.59	1.21–10.60	<b>0.002*</b>
Severe	6.17	1.90–20.00	<b>0.002*</b>	5.47	1.67–17.98	<b>0.005*</b>	8.08	2.21–29.60	<b>0.003*</b>
TNM Stage									
I	Ref.								
II	0.47	0.14–1.62	0.231						
III	1.38	0.46–4.16	0.565						
IV	1.88	0.70–5.04	0.212						
Handgrip strength	0.94	0.90–0.97	<b>0.000*</b>				0.97	0.93–1.02	0.207
SMI	0.92	0.87–0.96	<b>0.000*</b>				0.92	0.86–0.98	<b>0.006*</b>
Sarcopenia									
No	Ref.			Ref.					
Yes	2.84	1.10–7.34	<b>0.032**</b>	2.29	0.83–6.28	0.109			

Statistical significant differences are in bold.

variables associated with sarcopenia. These significant variables were subjected to a multivariate analysis in which age (OR 3.65, 95% CI 1.25–10.71,  $P = 0.018$ ) and G8 (OR 2.81, 95% CI 1.06–7.43,  $P = 0.037$ ) remained significant.

#### 4. Discussion

This retrospective study, conducted in 150 patients with HNC, showed that there is an association between sarcopenia and frailty as

**Table 4**

Univariate and multivariate logistic regression analysis for analyzing variables associated with sarcopenia in patients with HNC [4].

Sarcopenia	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age (years)						
<70	Ref.			Ref.		
≥ 70	3.68	1.27–10.64	<b>0.016**</b>	3.65	1.25–10.71	<b>0.018**</b>
Sex						
Male	Ref.					
Female	0.59	0.23–1.54	0.286			
Weight loss 6 months prior to diagnosis						
Non	Ref.					
<10%	0.82	0.22–3.06	0.772			
≥ 10%	2.52	0.45–14.13	0.292			
BMI (kg/m <sup>2</sup> )	0.97	0.86–1.08	0.563			
TNM Stage						
I	Ref.					
II	0.20	0.04–1.12	0.067			
III	0.39	0.10–1.58	0.188			
IV	0.46	0.14–1.49	0.197			
G8 Frailty						
No	Ref.			Ref.		
Yes	2.84	1.10–7.34	<b>0.032**</b>	2.81	1.06–7.43	<b>0.037**</b>

Statistical significant differences are in bold.

assessed by the G8. There is also a significant but weak correlation between sarcopenia and frailty, based on the G8 frailty screening instrument. To our knowledge, this study is the first that used the novel definition of the EWGSOP for sarcopenia, defined as skeletal muscle mass and muscle function, and its correlation with frailty screening questionnaires in patients with HNC. Zwart et al. found also a low but significant correlation between skeletal muscle mass, defined as SMI, and frailty ( $r = 0.38$ ,  $P < 0.001$ ) [14]. In contrast to our study, they defined sarcopenia based on only SMI. We included muscle function as well. In our study, skeletal muscle mass, defined as SMI, was more significantly associated with G8 frailty screening compared to sarcopenia, defined as the combination of skeletal muscle mass and muscle function. Based on both studies, skeletal muscle mass may be interchangeable with the G8 frailty screening questionnaire. However, G8 is a more global assessment and sarcopenia looks at a very specific geriatric syndrome. Moreover, at this moment G8 is easier to collect from patients than manually analyzing a CT scan using specific software.

Since a comprehensive geriatric assessment takes about 60–90 min, and more importantly, not all patients will necessarily benefit from a CGA, a short prognostic tool that can separate fit older patients, who can receive standard cancer treatment, from vulnerable patients, who may benefit from a CGA and need tailoring of their treatment regimens would be of use. G8 is a fast screening tool of only eight simple questions and has a high sensitivity for diagnosing frailty, but a poor specificity and negative predictive value [12]. Fast assessment of skeletal muscle mass on CT needs specific software and takes about 5–10 min, limiting incorporating skeletal muscle mass into clinical practice in real-time. It is expected that automated methods, e.g. automated computed tomography segmentation, will accelerate body composition research and, eventually, facilitate the integration of body composition measures into clinical care [20].

The interest in the role of sarcopenia in oncology has been increasing over the past decade. Several articles exhibit the negative impact of sarcopenia on adverse health outcomes [21]. Frailty is also related to adverse health outcomes [9]. Sarcopenia and frailty are linked to each other, even though the treatments and suggested underlying concepts differ. Treatment of sarcopenia is focused on

combining exercise and adequate protein intake to increasing muscle mass and strength, while frailty is focused on a broader set of physical and non-physical domains [22].

Thereby several definitions of frailty are in use, depending on how frailty is measured [23]. The majority of frailty tools have been based upon one of two concepts of frailty; physical phenotype (Fried) or the multiple deficit model (Rockwood) [24,25]. Additionally, several definitions of sarcopenia are used i.e. the EWGSOP- or IWGS-criteria [26]. But more recent proposals for the definition of sarcopenia include muscle function in addition to muscle mass [3,27]. Studies using a physical definition of frailty tend to show more similarities with sarcopenia [28,29]. So, both the concepts of frailty and sarcopenia are evolving, and there is still no full consensus on which to use in clinical practice.

It is also important that frailty screening tools should be used to determine which patients should benefit from a CGA; not to diagnose frailty. The CGA is the current gold standard test for defining frailty. The G8 frailty screening questionnaire has insufficient discriminative power [12], and it is not yet known if assessment of skeletal muscle mass is suitable for screening of patients who need to undergo a CGA [12]. This needs to be investigated by comparing skeletal muscle mass with the CGA. Research in muscle density is another interesting field, as recently, muscle density on CT imaging was reported to be more associated with frailty than muscle mass [15].

As mentioned before, previous studies indicate that sarcopenia, based on loss of skeletal muscle mass, occurs in 35.5–54.5% of the patients with HNC [4,5]. In our cohort, sarcopenia was based on a combination of handgrip strength and at CT/MRI measured skeletal muscle mass. Using those two factors the prevalence of sarcopenia in our cohort was only 14%, likely due to the small prevalence of low handgrip strength. Reiss et al. reported on the consequences of applying the new EWGSOP2 guideline instead of the former EWGSOP1 guideline for sarcopenia diagnosis in older adults and expressed their concerns regarding missing sarcopenic patients due to the novel EWGSOP definition in which lower cut-off values for handgrip strength measurements are used [30].

Our study has limitations. The use of two different imaging techniques may raise concerns. Either CT or MRI imaging were used for the assessment of skeletal muscle mass, to maximize the number of patients that could be included. But recent research shows that these two different imaging modalities show significant correlation in quantifying skeletal muscle mass when measured by CSA at the level of C3 [31]. Other limitations of our study are its retrospective and small nature.

Our study also has important strengths. First, the study was performed in a large group of 150 patients. Second, because G8 and handgrip strength are routinely obtained at our institution, a consecutive series of patients were available for analysis. Third, the main observer (CM) was not aware of the diagnoses of frailty or sarcopenia in the patients. Fourth, a short period between the first consultation with G8 questionnaire and handgrip strength measurement and quantification of skeletal muscle mass was found (1.8 weeks). Fifth, all the segmentation of muscle tissue was manually performed by the first author. Because an excellent inter-observer agreement for skeletal muscle mass measurement at the level of C3 was demonstrated, these SMI measurement findings can be used globally to select patients for potential suitable therapy [32].

In conclusion, in this study there was an association between sarcopenia and frailty assessed by the G8. Therefore, assessment of skeletal muscle mass may be used as an alternative screening tool for the G8 questionnaire for frailty screening, i.e. selection of patients who need a full CGA. Further research should ideally retest our findings in a larger, prospective cohort study and test for associations between sarcopenia and a full CGA.

## Author Contribution

Study concepts: C.D.A. Meerkerk, N. Chergi, R. de Bree

Study design: C.D.A. Meerkerk, N. Chergi, R. de Bree

Data acquisition: C.D.A. Meerkerk

Quality control of data and algorithms: C.D.A. Meerkerk, N. Chergi

Data analysis and interpretation: C.D.A. Meerkerk

Statistical analysis: C.D.A. Meerkerk

Manuscript preparation: C.D.A. Meerkerk, N. Chergi

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## Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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