ORIGINAL ARTICLE

Journal of Cachexia, Sarcopenia and Muscle (2023)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/jcsm.13362

Using magnetic resonance imaging to measure head muscles: An innovative method to opportunistically determine muscle mass and detect sarcopenia

Miguel German Borda[1,2,3], Gustavo Duque[4,5], Mario Ulises Pérez-Zepeda[6,7]*, Jonathan Patricio Baldera[1,8], Eric Westman[9], Anna Zettergren[10], Jessica Samuelsson[10], Silke Kern[10,11], Lina Rydén[10], Ingmar Skoog[10,11] & Dag Aarsland[1,12]

[1]*Centre for Age-Related Medicine (SESAM), Stavanger University Hospital, Stavanger, Norway;* [2]*Semillero de Neurociencias y Envejecimiento, Ageing Institute, Medical School, Pontificia Universidad Javeriana, Bogotá, Colombia;* [3]*Faculty of Health Sciences, University of Stavanger, Stavanger, Norway;* [4]*Research Institute of the McGill University Health Centre, Montreal, Québec, Canada;* [5]*Dr. Joseph Kaufmann Chair in Geriatric Medicine, Department of Medicine, McGill University, Montreal, Québec, Canada;* [6]*Instituto Nacional de Geriatría, Dirección de Investigación, Ciudad de México, México;* [7]*Centro de Investigación en Ciencias de la Salud (CICSA), FCS, Universidad Anáhuac México Campus Norte, Huixquilucan, México;* [8]*Escuela de Estadística de la Universidad Autónoma de Santo Domingo, Santo Domingo, República Dominicana;* [9]*Division of Clinical Geriatrics, Center for Alzheimer Research, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden;* [10]*Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden;* [11]*Department of Psychiatry, Cognition and Old Age Psychiatry, Sahlgrenska University Hospital, Mölndal, Sweden;* [12]*Department of Old Age Psychiatry, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, London, UK*

Abstract

Background Sarcopenia is associated with multiple adverse outcomes. Traditional methods to determine low muscle mass for the diagnosis of sarcopenia are mainly based on dual-energy X-ray absorptiometry (DXA), whole-body magnetic resonance imaging (MRI) and bioelectrical impedance analysis. These tests are not always available and are rather time consuming and expensive. However, many brain and head diseases require a head MRI. In this study, we aim to provide a more accessible way to detect sarcopenia by comparing the traditional method of DXA lean mass estimation versus the tongue and masseter muscle mass assessed in a standard brain MRI.

Methods The H70 study is a longitudinal study of older people living in Gothenburg, Sweden. In this cross-sectional analysis, from 1203 participants aged 70 years at baseline, we included 495 with clinical data and MRI images available. We used the appendicular lean soft tissue index (ALSTI) in DXA images as our reference measure of lean mass. Images from the masseter and tongue were analysed and segmented using 3D Slicer. For the statistical analysis, the Spearman correlation coefficient was used, and concordance was estimated with the Kappa coefficient.

Results The final sample consisted of 495 participants, of which 52.3% were females. We found a significant correlation coefficient between both tongue (0.26) and masseter (0.33) with ALSTI ($P < 0.001$). The sarcopenia prevalence confirmed using the alternative muscle measure in MRI was calculated using the ALSTI (tongue = 2.0%, masseter = 2.2%, ALSTI = 2.4%). Concordance between sarcopenia with masseter and tongue versus sarcopenia with ALSTI as reference has a Kappa of 0.989 ($P < 0.001$) for masseter and a Kappa of 1 for the tongue muscle ($P < 0.001$). Comorbidities evaluated with the Cumulative Illness Rating Scale were significantly associated with all the muscle measurements: ALSTI (odds ratio [OR] 1.16, 95% confidence interval [CI] 1.07–1.26, $P < 0.001$), masseter (OR 1.16, 95% CI 1.07–1.26, $P < 0.001$) and tongue (OR 1.13, 95% CI 1.04–1.22, $P = 0.002$); the higher the comorbidities, the higher the probability of having abnormal muscle mass.

Conclusions ALSTI was significantly correlated with tongue and masseter muscle mass. When performing the sarcopenia diagnostic algorithm, the prevalence of sarcopenia calculated with head muscles did not differ from sarcopenia calculated using DXA, and almost all participants were correctly classified using both methods.

Keywords dementia; diagnosis; geriatrics; H70; neurodegenerative disorders; sarcopenia

Received: 12 May 2023; Revised: 4 August 2023; Accepted: 20 September 2023
**Correspondence to: Mario Ulises Pérez-Zepeda, Instituto Nacional de Geriatría, Dirección de Investigación, Av. Contreras 428, Col. San Jerónimo Lídice, Alcaldía La Magdalena Contrera. CP. 10200, Ciudad de México, México. Email: mperez@inger.gob.mx*
Ingmar Skoog and Dag Aarsland shared last author.

Introduction

Age-related muscle wasting, clinically presented as sarcopenia, is a major driver of frailty, cognitive decline, falls and disability in older adults.[1–3] Although sarcopenia is a condition closely linked to the aging process, it is also considered multifactorial and influenced by various factors such as chronic illnesses, physical inactivity, inadequate nutrition and hormonal changes. This condition is widely recognized and characterized by multiple pathogenic pathways, including neuromuscular degeneration, loss of alpha motor units in the central nervous system and fat accumulation within muscle tissue.[3,4]

According to the European Working Group on Sarcopenia in Older People (EWGSOP), the diagnosis of sarcopenia includes muscle strength, muscle mass and physical performance.[5] Determining muscle strength and physical performance is simple, cheap and accessible with tests such as grip strength and gait speed, respectively.[3] On the other hand, assessment of muscle quantity requires tests such as dual-energy X-ray absorptiometry (DXA) (for lean mass) or whole-body magnetic resonance imaging (MRI), which are costly and sometimes impractical.

Older adults with cognitive disorders represent a particularly vulnerable group, as their physical health assessments are often overlooked, and conditions such as sarcopenia are ignored, leading to missed opportunities for improving their clinical outcomes.[6–9] Measures of muscle mass in arms and legs usually are used to measure decline in muscle mass in sarcopenia, for example, appendicular lean soft tissue index (ALSTI). However, the muscles involved in mastication and swallowing, such as the tongue and masseters, can also serve as indicators of age-related muscle decline. The volume of these muscles can be easily assessed using head computed tomography (CT) scans and MRIs, which are often used to diagnose and monitor conditions such as dementia, stroke, head/neck cancer and traumatic brain injury and have been used to assess mortality risk in older adults with traumatic brain injury.[10] Our group recently showed that tongue muscle volume is associated with malnutrition, as well as lower hippocampal and grey brain volume.[11,12] We propose that these methods offer significant advantages as potential alternatives to measuring muscle quantity. However, it is essential to validate these techniques against the standard imaging methods (i.e., DXA) used for categorizing sarcopenia and ensure their accuracy and reliability.

This study proposes an innovative, practical and cost-effective approach to assessing muscle mass, setting it apart from the traditional methods and repurposing available image studies regularly performed in older persons with neurocognitive or other head conditions. Specifically, the study aims to evaluate whether the volumes of the masseter and tongue muscles correlate with the total appendicular lean mass (ALM) quantified by DXA and to determine the usefulness of these measures in diagnosing sarcopenia.

We hypothesize that the masseter muscles and the tongue could be effective alternatives for measuring muscle mass and diagnosing sarcopenia whenever head MRI is accessible.

Methods

Design and sampling

The present study is part of the H70 Birth Cohort Study in Gothenburg, Sweden. This is a comprehensive population study examining birth cohorts of older people in Gothenburg.[13] This study comprised one cohort born in 1944 (examined in 2014–2016 with a response rate of 72%; n = 1203).[13,14]

The participants were interviewed face to face, providing information on different topics: comorbidity, lifestyle behaviours, nutrition, functional performance, medications, cohabitation and education level. From the total of 1203 persons, we included 791 who had MRI images available, and from them, 251 individuals did not have good visualization of either the tongue or the masseter. A total of 495 individuals constituted the final sample, with correctly segmented images. See Supporting Information S1. Details of the design, recruitment, clinical and biomarker procedures are described elsewhere.[13]

Imaging

Scanning was conducted on a 3-Tesla Philips Achieva system (Philips Medical Systems) using a T1-weighted sequence with the following parameters: field of view: 256 × 256 × 160 voxels; voxel size: 1 × 1 × 1 mm^3; echo time: 3.2 ms; repetition time: 7.2 ms; and flip angle: 9°. Image organization and quality control were done through TheHiveDB system.[15] Tongue and masseter were manually segmented using 3D Slicer Version 5.2.1, by only one trained researcher to avoid variability. The first 20 images were re-analysed, showing good intra-rater reliability (*Figure 1*).[13]

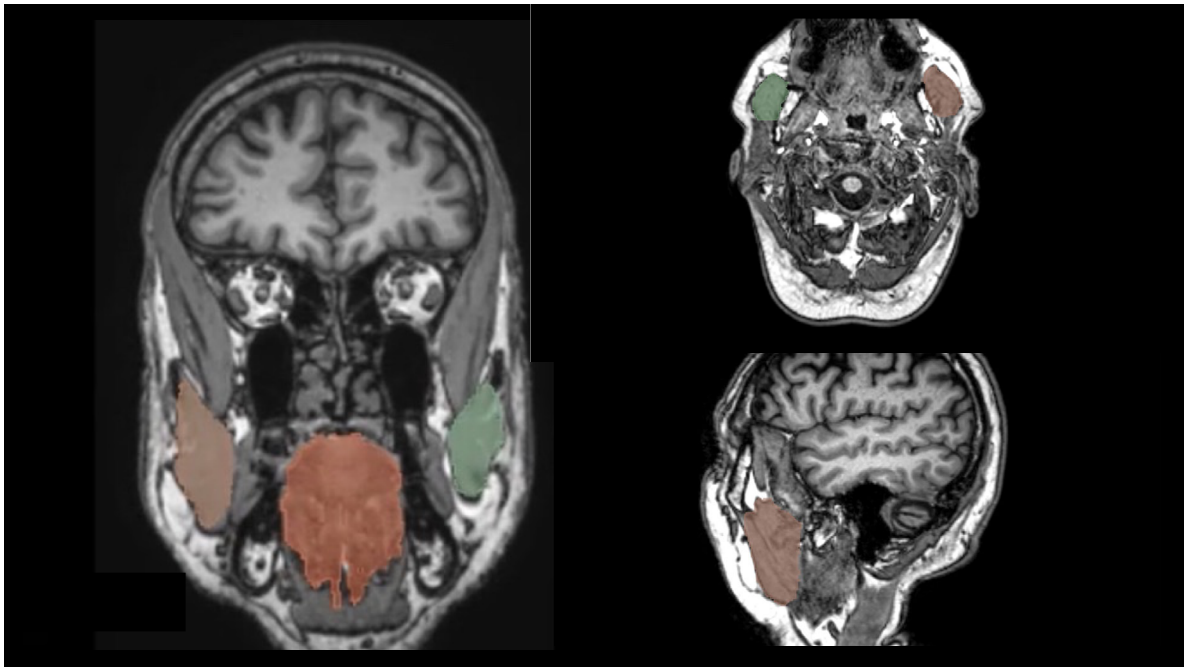

Figure 1 Segmentation of the tongue and the masseter using 3D Slicer.

Anthropometry

Body weight and height were measured using a calibrated electronic scale and a stadiometer, respectively. These values were used to calculate body mass index (BMI). Body composition was analysed with a Lunar Prodigy DXA scanner used for the 70-year-olds. The scans produced results for lean soft tissue, which was further transformed into ALSTI, which is a measurement used in clinical and research settings to assess muscle mass in the arms and legs. It is a ratio of the appendicular lean soft tissue (ALST) mass (i.e., the sum of the lean tissue mass in the arms and legs) to the square of the individual's height. The scanners were cross calibrated using a double scan of 33 subjects, with the iDXA ALSTI measurements calibrated using a regression equation.[16]

Muscle strength and physical performance

Physical performance tests included the self-selected and maximum gait speed, measured in metres per second over a 30-m indoor distance with a standing start.[17,18] Additionally, the distance achieved during a 6-min indoor walking test was recorded in metres. Grip strength was assessed using a Martin Vigorimeter and a JAMAR dynamometer (sub-sample), with the shoulder joint maintained in a neutral position. The test was repeated three times for each hand, and the highest value from the dominant hand was used as the outcome.[13] Results are reported in kilopascal as provided by the study and as previously reported by Wallengren et al.[16]

Sarcopenia definition

Sarcopenia was diagnosed using the revised operational definitions proposed by the EWGSOP[3] in 2019. The first stage, possible sarcopenia, was defined as low muscle strength. The second stage, confirmed sarcopenia, was identified by the presence of both low muscle strength and low muscle mass. Finally, severe sarcopenia was defined by the presence of low muscle mass, low muscle strength and low physical performance.[3] Muscle strength was determined using handgrip with a cut point of $<$27 kg in men and $<$16 kg in women. Low muscle mass with DXA was defined using a conversion equation to estimate the ALM, and computed ALM divided by standing height in metre squared (i.e., ALM/height^2) = ALSTI (kg/m^2) a cut point of $<$7 kg/m^2 in men and $<$6 kg/m^2 in women was used. Finally, physical performance was estimated with gait speed and a cut point of $<$0.8 m/s[19] (see *Table 1*).[16]

Tongue and masseter volumes were regressed against the lean mass measured by DXA, and those in the 20th percentile of residual value were considered to have abnormal muscle mass. A similar method has been previously used to determine low muscle mass.[20] The cut points following this method can be found in *Table 1*.

DOI: 10.1002/jcsm.13362

Table 1 Cut points for the different muscle measures

Variable	Cut-offs	
	Male	Female
Appendicular lean soft tissue (kg/m^2)	7	5.5
Gait speed of 30 m (m/s)	0.8	
Handgrip strength (kPa)	69	59
Tongue volume (cm^3)[a]	−0.763	−0.715
Masseter volume (cm^3)[a]	−0.787	−0.680
Masseter and tongue volumes (cm^3)[a]	−0.784	−0.694

[a]Lowest 20th percentile for the residuals resulting from regressing tongue and masseter muscles with dual-energy X-ray absorptiometry.

Covariates

We included demographic factors such as sex and age. Comorbidities were assessed using the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) scored by research nurses based on the face-to-face interviews with the participants.[21] Problems with teeth or dental prosthesis (percentage) and average of own teeth in your upper and lower jaws were considered based on the participants' self-report. These variables were deemed crucial to providing a more accurate and complete understanding of the association between masseter and tongue muscle volumes and total appendicular body lean mass.

Statistical analysis

The first step included describing the variables and estimating percentages for categorical variables and means/standard deviation (SD) for continuous variables. Second, bivariate analysis assessed the difference between sarcopenia groups by calculating Pearson's χ^2 test for categorical variables and Student's *t*-test for continuous variables. Finally, to analyse the correlation between the muscles ALST (kg/m^2), tongue volume (cm^3), masseter volume (cm^3) and masseter and tongue volumes (cm^3), the Spearman correlation coefficient was used (at least 0.8 [very strong], 0.6 up to 0.8 [moderately strong], 0.3–0.5 [fair] and <0.3 [poor]).[22,23] Additionally, concordance was estimated with the Kappa coefficient comparing each muscle mass measure, using the same muscle strength and physical performance test for all. Receiver operating characteristic (ROC) analysis was included to assess the accuracy of the alternative muscle measurements compared with ALSTI, stratified by sex, and for all the population for each muscle (i.e., tongue and masseters). Finally, a logistic regression analysis between the different ways to assess muscle mass and independent variables was performed.

The R software Version 4.2.1 and STATA 17.0 were used for all statistical analyses.

Results

The sample was constituted of 52.3% females. Overall, muscular volumes and grip strength were significantly higher in men. Probable sarcopenia was diagnosed in 11.3% (n = 88), confirmed sarcopenia in 2.4% (n = 19) and severe sarcopenia in 2.2% (n = 11) using ALSTI. Sarcopenia confirmed using the tongue was 2% (n = 10), and that using the masseter was 2.2% (n = 11). The complete report of the descriptive results stratified by sex can be found in *Table 2*.

Correlation between the different muscle measures

Significant correlation coefficients were found between both tongue and masseter muscle volumes with total appendicular lean tissue mass: masseter volume (Rho 0.33, P-value < 0.001), tongue volume (Rho 0.26, P-value < 0.001) and combined masseter and tongue volumes (Rho 0.30, P-value < 0.001) (see *Figure 2* and Supporting Information S2).

The ROC curve was calculated: ALSTI with tongue (area under the curve [AUC] 0.499, 95% confidence interval [CI] 0.42–0.58) and ALSTI with masseters (AUC 0.507, 95% CI 0.41–0.574). ROC curves and AUC by sex can be found in Supporting Information S3.

Concordance of sarcopenia between masseter and tongue muscle measures and appendicular lean soft tissue index

A high concordance was found when comparing sarcopenia diagnosis using the two classifications: For sarcopenia with the masseter, muscle Kappa was 0.989 (P-value < 0.001), with only one participant being misclassified. A Kappa statistic of 1 was obtained with sarcopenia using the tongue muscle (P-value < 0.001) (see *Table 3*).

Associations between the different ways to assess muscle mass and independent variables were calculated. Comorbidities evaluated with the CIRS were significantly associated with all the muscle measurements: ALSTI (odds ratio [OR] 1.16, 95% CI 1.07–1.26, P < 0.001), masseter (OR 1.16, 95% CI 1.07–1.26, P < 0.001) and tongue (OR 1.13, 95% CI 1.04–1.22, P = 0.002); the higher the comorbidities, the higher the probability of having abnormal muscle mass. In addition, the BMI was also significant: ALSTI (OR 0.73, 95% CI 0.65–0.82, P < 0.001), masseter (OR 0.73, 95% CI 0.65–0.82, P < 0.001) and tongue (OR 0.73, 95% CI 0.66–0.81, P < 0.001); the lower the BMI, the higher the probability of having abnormal muscle mass. See complete information in Supporting Information S4.

Table 2 Frequency and distribution of the studied variables according to sex

	Males	Females	Overall	
	(*N* = 377)	(*N* = 414)	(*N* = 791)	*P*-value
Age, mean (SD)	70.5 (0.258)	70.5 (0.268)	70.5 (0.263)	0.887
BMI (kg/m^2), mean (SD)	26.3 (3.72)	26.1 (4.82)	26.2 (4.34)	0.593
CIRS-G, mean (SD)	5.68 (3.67)	6.01 (3.99)	5.86 (3.85)	0.246
Problems with teeth or dental prosthesis (%)				
No	327 (86.7%)	359 (86.7%)	686 (86.7%)	0.944
Yes	49 (13.0%)	53 (12.8%)	102 (12.9%)	
Missing	1 (0.3%)	2 (0.5%)	3 (0.4%)	
Average of own teeth in your upper jaw, mean (SD)	1.83 (0.379)	1.84 (0.369)	1.83 (0.374)	0.686
Average of own teeth in your lower jaw, mean (SD)	1.85 (0.356)	1.88 (0.320)	1.87 (0.338)	0.178
Tongue volume (cm^3), mean (SD)	75.4 (30.3)	58.6 (25.8)	65.0 (28.7)	<0.001
Total masseter volume (cm^3), mean (SD)	43.3 (17.9)	31.9 (13.9)	37.3 (16.9)	<0.001
Total masseter and tongue volumes (cm^3), mean (SD)	120 (43.8)	91.3 (37.4)	102 (42.3)	<0.001
Appendicular lean soft tissue (kg/m^2)	7.85 (0.792)	6.23 (0.636)	6.98 (1.08)	<0.001
Gait speed of 30 m (m/s)	1.31 (0.178)	1.30 (0.169)	1.30 (0.173)	0.688
Handgrip strength (kPa)	86.1 (16.5)	74.7 (13.4)	80.2 (16.0)	<0.001
Sarcopenia with appendicular lean soft tissue (kg/m^2)				
Sarcopenia probable (%)				
No	332 (88.3%)	361 (89.1%)	693 (88.7%)	0.797
Yes	44 (11.7%)	44 (10.9%)	88 (11.3%)	
Sarcopenia confirmed (%)				
No	359 (97.0%)	398 (98.0%)	757 (97.6%)	0.503
Yes	11 (3.0%)	8 (2.0%)	19 (2.4%)	
Sarcopenia severe (%)				
No	359 (97.3%)	398 (98.3%)	757 (97.8%)	0.493
Yes	10 (2.7%)	7 (1.7%)	17 (2.2%)	
Sarcopenia with tongue volume (cm^3)				
Sarcopenia probable (%)				
No	166 (88.8%)	278 (90.3%)	444 (89.7%)	0.707
Yes	21 (11.2%)	30 (9.7%)	51 (10.3%)	
Sarcopenia confirmed (%)				
No	182 (96.8%)	308 (98.7%)	490 (98.0%)	0.251
Yes	6 (3.2%)	4 (1.3%)	10 (2.0%)	
Sarcopenia severe (%)				
No	182 (97.3%)	308 (98.7%)	490 (98.2%)	0.433
Yes	5 (2.7%)	4 (1.3%)	9 (1.8%)	
Sarcopenia with masseter volume (cm^3)				
Sarcopenia probable (%)				
No	166 (88.8%)	278 (90.3%)	444 (89.7%)	0.707
Yes	21 (11.2%)	30 (9.7%)	51 (10.3%)	
Sarcopenia confirmed (%)				
No	182 (96.8%)	307 (98.4%)	489 (97.8%)	0.391
Yes	6 (3.2%)	5 (1.6%)	11 (2.2%)	
Sarcopenia severe (%)				
No	182 (97.3%)	307 (98.4%)	489 (98.0%)	0.620
Yes	5 (2.7%)	5 (1.6%)	10 (2.0%)	
Sarcopenia with total masseter and tongue volumes (cm^3)				
Sarcopenia probable (%)				
No	166 (88.8%)	278 (90.3%)	444 (89.7%)	0.707
Yes	21 (11.2%)	30 (9.7%)	51 (10.3%)	
Sarcopenia confirmed (%)				
No	182 (96.8%)	308 (98.4%)	490 (97.8%)	0.251
Yes	6 (3.2%)	4 (1.3%)	10 (2.0%)	
Sarcopenia severe (%)				
No	182 (97.3%)	308 (98.7%)	490 (98.2%)	0.433
Yes	5 (2.7%)	4 (1.3%)	9 (1.8%)	

Abbreviations: BMI, body mass index; CIRS-G, Cumulative Illness Rating Scale for Geriatrics.

Discussion

In this population-based study of older persons (70 years and older), we found that head muscles (masseter and tongue) could be useful surrogates of general muscle mass to assess sarcopenia in older adults.[13] These findings could be beneficial for clinical practice to detect sarcopenia in patients who need head imaging for their primary conditions (e.g., dementia, stroke, trauma and cancer). Employing this method enhances the value of the measurement by boosting the clinical validity of the imaging study without adding costs or major complexities (i.e., repurposing).[24] This provides a tool for

DOI: 10.1002/jcsm.13362

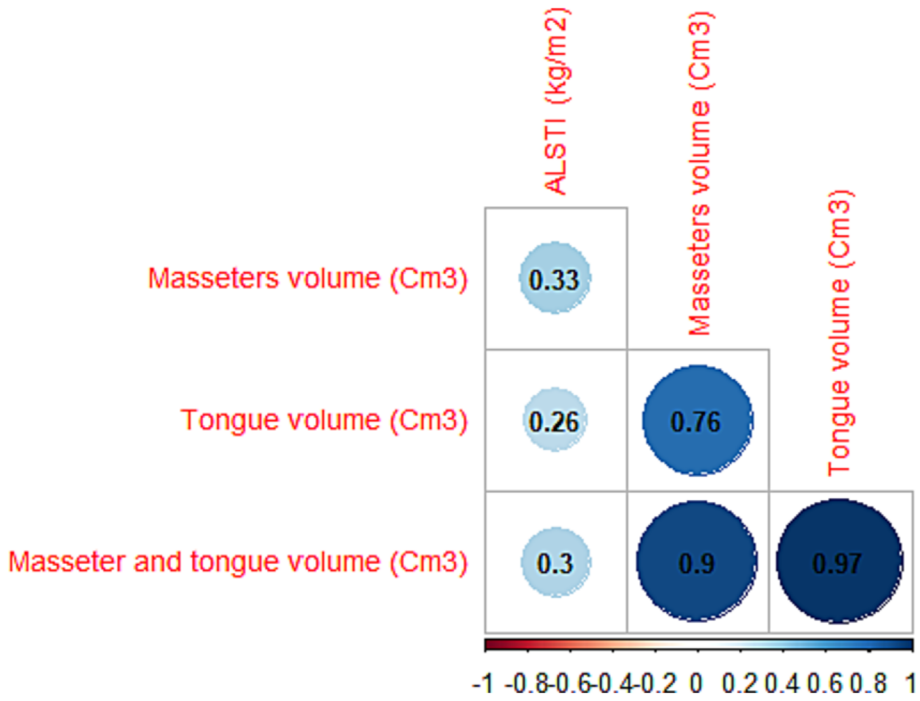

Figure 2 Correlations of masseter and tongue muscles against appendicular lean soft tissue index (ALSTI). All correlations had a *P*-value < 0.001. See Supporting Information S2.

Table 3 Sarcopenia concordance between the different muscle measures with appendicular lean soft tissue index as reference

Variable	Sarcopenia with appendicular lean soft tissue (kg/m^2)			Kappa index	*P*-value
	No sarcopenia	Sarcopenia probable	Sarcopenia confirmed		
Sarcopenia with tongue volume (cm^3)					
No sarcopenia	444	0	0	1.000	<0.001
Sarcopenia probable	0	41	0		
Sarcopenia confirmed	0	0	10		
Sarcopenia with masseter volume (cm^3)					
No sarcopenia	444	0	0	0.989	<0.001
Sarcopenia probable	0	40	1		
Sarcopenia confirmed	0	0	10		
Masseter and tongue volumes (cm^3)					
No sarcopenia	444	0	0	1.000	<0.001
Sarcopenia probable	0	41	0		
Sarcopenia confirmed	0	0	10		

general practitioners or physicians in several specialties to identify low muscle and refer to further studies and interventions.

DXA is one of the reference standards for quantifying body composition,[3] providing different body composition parameters, such as fat mass, fat-free mass and bone density. However, DXA has important limitations to be considered as the optimal imaging method for sarcopenia. For instance, in patients who have limited mobility, particularly in acute situations, conducting DXA scans can be challenging, costly and inconvenient. As DXA only reports lean mass, other more accurate methods of specifically quantifying muscle mass are still needed.

The other reference tool is whole-body MRI. It is a powerful tool for assessing body composition and identifying muscle loss. Unlike DXA, MRI is not limited by mobility issues, making it a useful alternative for patients who cannot undergo DXA scans. However, whole-body MRI is a more complex imaging technique requiring specialized equipment and expertise, making it more expensive and less accessible than DXA in many settings. Additionally, accessibility is an issue not only for these two instruments but also for bioelectrical impedance analysis (BIA). A study by Trevino-Aguirre et al. in 2014 aimed to assess the availability and use of DXA and BIA for the evaluation of sarcopenia by geriatricians in Belgium and Latin America; it was found that the availability

of both methods was very limited.[25] On the other hand, anthropometric variables (i.e., calf circumference) are inexpensive and accessible methods for estimating muscle mass but have important limitations. It may not accurately estimate muscle mass in individuals who are obese or have abnormal body fat distribution or even have pitting oedema.[26] Furthermore, the equations used to calculate muscle mass from anthropometric measurements are population specific and may not be suitable for individuals of different ethnic or racial backgrounds. Additionally, measurements can be affected by various factors such as clothing, posture and hydration status, leading to inconsistencies in results. Recently, ultrasonography has been proposed as a useful resource due to its non-invasive nature, cost-effectiveness and ability to be performed at the point of care.[27] However, it requires trained professionals, specialized equipment and extra time. There are concerns about reproducibility in individuals with higher body fat levels, as ultrasonography may encounter difficulties in accurately measuring muscle thickness due to interference from adipose tissue.[28]

As a result, utilizing imaging studies commonly employed to assess other medical conditions could enhance the screening for sarcopenia and increase the treatment of this usually overlooked condition.[10] Regional CT and MRI could become accurate and more practical non-invasive methods to quantify muscle volume. CT and MRI slices of predefined width can be analysed for different tissues by manual segmentation or automated software, such as the one used in our research. In this way, the volumes of individual or muscle groups can be determined. Regarding the clinical applications of this innovative approach, preliminary data from our teams in Norway, Australia and Canada have validated the use of CT/MRI image analysis software.[29]

Several studies have demonstrated the utility of head muscles in clinical settings.[30] Low masseter muscle cross-sectional area was associated with worse survival in individuals with squamous cell carcinoma of the head and neck.[31] Another study showed how measuring these muscles increased prognostic accuracy for post-operative long-term survival in carotid endarterectomy patients.[32] In another study, a lower volume of the masseter muscle predicted post-operative pneumonia in patients with oesophageal cancer.[33] Hwang et al. reported that the masseter muscle, analysed via CT, showed a statistically significant association with systemic nutritional biomarkers, adding evidence on the path of sarcopenia genesis.[34]

Our group recently reported that the tongue muscle volume was associated with hippocampal and total grey volume in people with Lewy body dementia[12] and with malnutrition in people with mild Lewy body dementia and Alzheimer's disease.[11] Other investigations have described the association of tongue muscle mass and strength with whole-body muscle.[35,36]

While our study provides valuable insights into the relationship between muscle volume and head muscles, it is important to acknowledge its limitations. While some factors may impact the volume of mastication and deglutition muscles, oral health problems like edentulism and prosthetic issues were evaluated and were not associated with muscle volume (as displayed in Supporting Information S3); other relevant conditions such as bruxism were not assessed in this study. The study sample consisted of older individuals from a specific geographic area, which may limit the generalizability of the findings to other populations. The cross-sectional design limits the ability to establish causality or determine the temporal sequence of events. Furthermore, some of the information in the study relies on self-reported data, which can be subject to social desirability bias, memory recall bias and other cognitive biases. However, it is worth noting that the sample population consisted of relatively young and cognitively healthy older adults, and the objective of the study was primarily focused on physical measures. Some limitations to the automated segmentation approach include thresholds and the operator's experience. However, in this study, only one person performed all the segmentations to reduce operator variability. 3D Slicer measures have been verified against gold standards in the past, exhibiting excellent inter- and intra-rater reliability, as well as good reliability and validity.[37] The correlation between volume of the tongue and masseter with ALSTI was moderate–fair but significant.[22] The relationship between the variables may be non-linear, which means that correlation coefficients cannot necessarily be able to fully capture the complexity of this type of relationship. This could be a reason for not having a high correlation coefficient. However, the correlation coefficient used can still provide trustable information about the strength and direction of the relationship between the studied variables. And when combining this muscle measure with other muscle strength or performance criteria, the sarcopenia approximation seems to have very good correlation.

Although our aim was to establish a correlation between two different measurements rather than predict what DXA reports, we still calculated AUC. The low AUC observed could be attributed to various factors, including the need for a better gold standard, the fact that muscles in the head have different functions than those in the appendicular regions and the comparison of a single muscle to several groups of them. Despite the low AUC values, our results can still be extrapolated to the clinic because, with a reasonable degree of certainty, we can say that if there is something abnormal with the tongue or masseter muscles, it is probable that the body's other muscles are also abnormal. This, added to the demonstrated ability of these muscles to predict adverse outcomes, justifies further interventions and examinations for the patients with low muscle mass in the tongue or masseter.[11,32,38] Finally, sensibility and specificity were not

calculated because populational cut points for masseter and tongue do not exist.

The study's large sample size is a notable strength that enhances the statistical power and precision of the findings. In addition, the use of DXA to measure sarcopenia represents a significant strength as it is considered the reference standard for this assessment. These findings have important implications for developing more accessible and practical methods for diagnosing sarcopenia in a variety of healthcare settings, ultimately benefiting both patients and clinicians.

Conclusions

Understanding the aging process of muscles remains an ongoing area of interest in caring for older adults. Researchers have been exploring alternative methods for measuring muscle mass since the early stages of research on sarcopenia.[39] With the limitations of traditional techniques, such as MRI and DXA, there is a need for accessible and practical approaches that healthcare providers can implement. Our study highlights the potential of measuring tongue and masseter muscle volumes, which can be readily obtained from head imaging studies, as a useful alternative for assessing muscle mass and improving the detection and management of sarcopenia.

Acknowledgements

We extend our heartfelt gratitude to all the participants, researchers and technical staff whose invaluable contributions have made the H70 study possible. Additionally, we would like to express our special thanks to Santiago Salazar for his exceptional assistance with imaging processing. The authors of this manuscript certify that they comply with the ethical guidelines for authorship and publishing in the *Journal of Cachexia, Sarcopenia and Muscle*.[40]

SK was financed by grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF agreement (ALFGBG-965923, ALFGBG-81392 and ALFGBG-771071); the Alzheimerfonden (AF-842471, AF-737641, AF-929959 and AF-939825); the Swedish Research Council (2019-02075); Stiftelsen Psykiatriska Forskningsfonden; Stiftelsen Demensfonden. In addition, this paper represents independent research supported by the Norwegian government, through hospital owner Helse Vest (Western Norway Regional Health Authority). Also, this study was funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author (s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Conflict of interest statement

SK has served on scientific advisory boards and/or as consultant for Geras Solutions and Biogen. GD has served on the advisory board for TSI Pharmaceuticals and SRW. The other authors have no conflicts of interest to declare.

Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

References

1. Lisko I, Kulmala J, Annetorp M, Ngandu T, Mangialasche F, Kivipelto M. How can dementia and disability be prevented in older adults: where are we today and where are we going? *J Intern Med* 2021; **289**:807–830.
2. Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. *J Cachexia Sarcopenia Muscle* 2016;**7**: 512–514.
3. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;**48**:16–31.
4. Roubenoff R. Sarcopenia: a major modifiable cause of frailty in the elderly. *J Nutr Health Aging* 2000;**4**:140–142.
5. Beaudart C, Reginster JY, Slomian J, Buckinx F, Dardenne N, Quabron A, et al. Estimation of sarcopenia prevalence using various assessment tools. *Exp Gerontol* 2015;**61**:31–37.
6. Beeri MS, Leugrans SE, Delbono O, Bennett DA, Buchman AS. Sarcopenia is associated with incident Alzheimer's dementia, mild cognitive impairment, and cognitive decline. *J Am Geriatr Soc* 2021;**69**: 1826–1835.
7. Dumurgier J, Artaud F, Touraine C, Rouaud O, Tavernier B, Dufouil C, et al. Gait speed and decline in gait speed as predictors of incident dementia. *J Gerontol A Biol Sci Med Sci* 2017;**72**:655–661.
8. Burns JM, Johnson DK, Watts A, Swerdlow RH, Brooks WM. Reduced lean mass in early Alzheimer disease and its association with brain atrophy. *Arch Neurol* 2010;**67**: 428–433.
9. Peng TC, Chen WL, Wu LW, Chang YW, Kao TW. Sarcopenia and cognitive impairment: a systematic review and meta-analysis. *Clin Nutr* 2020;**39**:2695–2701.
10. Tanabe C, Reed MJ, Pham TN, Penn K, Bentov I, Kaplan SJ. Association of brain atrophy and masseter sarcopenia with 1-year mortality in older trauma patients. *JAMA Surg* 2019;**154**:716–723.
11. Borda MG, Bani Hassan E, Weon J, Wakabayashi H, Tovar-Rios DA, Oppedal K, et al. Muscle volume and intramuscular fat of the tongue evaluated with MRI predict malnutrition in people living with dementia: a five-year follow-up study. *J Gerontol A Biol Sci Med Sci* 2022;**77**:228–234.
12. Borda MG, Castellanos-Perilla N, Tovar-Rios DA, Ferreira D, Duque G, Aarsland D. Tongue muscle mass is associated with total grey matter and hippocampal volumes in Dementia with Lewy bodies. *Arch Gerontol Geriatr* 2022;**100**:104647.

13. Rydberg Sterner T, Ahlner F, Blennow K, Dahlin-Ivanoff S, Falk H, Havstam Johansson L, et al. The Gothenburg H70 Birth Cohort Study 2014–16: design, methods and study population. *Eur J Epidemiol* 2019;**34**:191–209.
14. Wetterberg H, Ryden L, Ahlner F, Falk Erhag H, Gudmundsson P, Guo X, et al. Representativeness in population-based studies of older adults: five waves of cross-sectional examinations in the Gothenburg H70 Birth Cohort Study. *BMJ Open* 2022;**12**:e068165.
15. Muehlboeck JS, Westman E, Simmons A. TheHiveDB image data management and analysis framework. *Front Neuroinform* 2014;**7**:49.
16. Wallengren O, Bosaeus I, Frandin K, Lissner L, Falk Erhag H, Wetterberg H, et al. Comparison of the 2010 and 2019 diagnostic criteria for sarcopenia by the European Working Group on Sarcopenia in Older People (EWGSOP) in two cohorts of Swedish older adults. *BMC Geriatr* 2021;**21**:600.
17. Bohannon RW. Comfortable and maximum walking speed of adults aged 20–79 years: reference values and determinants. *Age Ageing* 1997;**26**:15–19.
18. Skillbäck T, Blennow K, Zetterberg H, Skoog J, Rydén L, Wetterberg H, et al. Slowing gait speed precedes cognitive decline by several years. *Alzheimers Dement* 2022;**18**: 1667–1676.
19. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010;**39**:412–423.
20. Delmonico MJ, Harris TB, Lee JS, Visser M, Nevitt M, Kritchevsky SB, et al. Alternative definitions of sarcopenia, lower extremity performance, and functional impairment with aging in older men and women. *J Am Geriatr Soc* 2007;**55**:769–774.
21. Parmelee PA, Thuras PD, Katz IR, Lawton MP. Validation of the Cumulative Illness Rating Scale in a geriatric residential population. *J Am Geriatr Soc* 1995;**43**:130–137.
22. Chan YH. Biostatistics 104: correlational analysis. *Singapore Med J* 2003;**44**: 614–619.
23. Dancey CP, Reidy J. *Statistics without maths for psychology*, Eighth ed. Harlow, England; New York: Pearson; 2020.
24. Mombelli A. Clinical parameters: biological validity and clinical utility. *Periodontol 2000* 2000;**2005**:30–39.
25. Trevino-Aguirre E, Lopez-Teros T, Gutierrez-Robledo L, Vandewoude M, Perez-Zepeda M. Availability and use of dual energy X-ray absorptiometry (DXA) and bio-impedance analysis (BIA) for the evaluation of sarcopenia by Belgian and Latin American geriatricians. *J Cachexia Sarcopenia Muscle* 2014;**5**:79–81.
26. Perez-Zepeda MU, Gutierrez-Robledo LM. Calf circumference predicts mobility disability: a secondary analysis of the Mexican health and ageing study. *Eur Geriatr Med* 2016;**7**:262–266.
27. Madden KM, Feldman B, Arishenkoff S, Meneilly GS. A rapid point-of-care ultrasound marker for muscle mass and muscle strength in older adults. *Age Ageing* 2021; **50**:505–510.
28. Fu H, Wang L, Zhang W, Lu J, Yang M. Diagnostic test accuracy of ultrasound for sarcopenia diagnosis: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle* 2023;**14**:57–70.
29. Bani Hassan E, Demontiero O, Vogrin S, Ng A, Duque G. Marrow adipose tissue in older men: association with visceral and subcutaneous fat, bone volume, metabolism, and inflammation. *Calcif Tissue Int* 2018;**103**:164–174.
30. Katsuki M, Kakizawa Y, Nishikawa A, Yamamoto Y, Uchiyama T, Agata M, et al. Temporal muscle and stroke—a narrative review on current meaning and clinical applications of temporal muscle thickness, area, and volume. *Nutrients* 2022;**14**:687.
31. McGoldrick DM, Yassin Alsabbagh A, Shaikh M, Pettit L, Bhatia SK. Masseter muscle defined sarcopenia and survival in head and neck cancer patients. *Br J Oral Maxillofac Surg* 2022;**60**:454–458.
32. Oksala NKJ, Lindstrom I, Khan N, Pihlajaniemi VJ, Lyytikainen LP, Pienimaki JP, et al. Pre-operative masseter area is an independent predictor of long-term survival after carotid endarterectomy. *Eur J Vasc Endovasc Surg* 2019;**57**:331–338.
33. Kamada T, Ohdaira H, Ito E, Takahashi J, Nakashima K, Nakaseko Y, et al. Association between masseter muscle sarcopenia and postoperative pneumonia in patients with esophageal cancer. *Sci Rep* 2022;**12**:16374.
34. Hwang Y, Lee YH, Cho DH, Kim M, Lee DS, Cho HJ. Applicability of the masseter muscle as a nutritional biomarker. *Medicine* 2020;**99**:e19069.
35. Sugiya R, Higashimoto Y, Shiraishi M, Tamura T, Kimura T, Chiba Y, et al. Decreased tongue strength is related to skeletal muscle mass in COPD patients. *Dysphagia* 2022;**37**:636–643.
36. Nakazawa Y, Kikutani T, Igarashi K, Yajima Y, Tamura F. Associations between tongue strength and skeletal muscle mass under dysphagia rehabilitation for geriatric out patients. *J Prosthodont Res* 2020;**64**: 188–192.
37. Lo Giudice A, Ronsivalle V, Gastaldi G, Leonardi R. Assessment of the accuracy of imaging software for 3D rendering of the upper airway, usable in orthodontic and craniofacial clinical settings. *Prog Orthod* 2022;**23**:22.
38. Uhlich R, Hu P. Sarcopenia diagnosed using masseter muscle area predictive of early mortality following severe traumatic brain injury. *Neural Regen Res* 2018;**13**: 2089–2090.
39. Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. *Proc Nutr Soc* 2015;**1-12**:355–366.
40. von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for publishing in the *Journal of Cachexia, Sarcopenia and Muscle*: update 2021. *J Cachexia Sarcopenia Muscle* 2021;**12**:2259–2261.