

## ORIGINAL RESEARCH

# The Validity of Muscle Ultrasound in the Diagnostic Workup of Sarcopenia Among Older Adults: A Scoping Review

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Purpose: Muscle ultrasound has emerged as a promising method in the diagnostic work-up of sarcopenia. The objective of this scoping review was to explore the validity of muscle ultrasound against the latest sarcopenia definitions among older adults.

Methods: We adhered to the PRISMA guidelines for scoping reviews. A systematic search of databases was performed by two independent reviewers. All articles comparing the performance of ultrasound to an internationally acknowledged sarcopenia definition among older adults (≥60 years) and published between 2019/01/01 (the year updated sarcopenia definitions were introduced) and 2023/ 11/15 were included. Data were extracted and collated by muscle and muscle parameters.

Results: Out of 2290 articles screened, six studies comprising 24 validity tests among a total of 1619 older adults (mean age 74.1 years, 52.2% female) were included. The validity tests investigated the rectus femoris (n = 7), biceps brachii (n = 5), gastrocnemius medialis (n = 4), tibialis anterior (n = 4), soleus (n = 3), and rectus abdominis (n = 1). The parameter muscle thickness (MT) (n = 14) was most commonly measured. The latest European and Asian sarcopenia definitions (EWGSOP2, AWGS2) were applied as reference standards in four validity tests each. None of the studies used the Sarcopenia Definition and Outcome Consortium (SDOC) criteria. The highest area under the curve AUC (0.92, 95% confidence interval [CI] 0.89–0.94) was found for the muscle thickness of the rectus femoris muscle. Due to substantial heterogeneity among the studies, pooling of data using a meta-analytic approach was not feasible. Conclusion: Limited number of studies have examined the validity of muscle ultrasound for diagnosing sarcopenia based on recent definitions among older adults. Thereby, muscle thickness of the rectus femoris showed promising results regarding validity. Further studies are needed to investigate the validity of key muscles and to validate muscle ultrasound among older hospitalized patients.

#### Keywords: geriatric assessment, muscle thickness, cross-sectional area, rectus femoris, POCUS, SARCUS, EWGSOP, AWGS, SDOC

#### Introduction

Sarcopenia is an age-related disease resulting in the loss of skeletal muscle mass, muscle function, and performance. <sup>1</sup> Its causes are multifactorial, including disuse, chronic disease, inflammation, mitochondrial dysfunction, and nutritional deficiencies.<sup>2</sup> The prevalence of sarcopenia ranges from 1% to 55%, influenced by factors such as the clinical setting, and sarcopenia definition (eg, diagnostic criteria, cut-off points).<sup>3,4</sup> Sarcopenia is associated with adverse clinical outcomes, such as functional decline, disability, falls, hospitalization, and mortality.<sup>5-7</sup> To mitigate these poor outcomes, early diagnosis and targeted interventions like resistance training are actively pursued.<sup>8,9</sup>

In the diagnostic work-up of sarcopenia, muscle mass is recognized as a key criterion. Over the last years, ultrasound has been increasingly used to measure muscle mass, taking advantage of its clinical feasibility and costefficiency. 11,12 Furthermore, ultrasound serves as a practical and noninvasive tool without radiation, making it applicable in community, hospital, and nursing home settings. 13 In various medical domains, particularly critical care, point-of-care

ultrasound (POCUS) has established itself as a reliable diagnostic method for predicting adverse outcomes.<sup>14</sup> Notably, the working group on ultrasound in sarcopenia (SARCUS) has recently emphasized the need to standardize muscle ultrasound, advocating for its increased utilization in the assessment of sarcopenia.<sup>11</sup>

However, evidence on the validity of muscle ultrasound to diagnose sarcopenia among older adults is limited. A systematic review published in 2017 showed that ultrasound is a reliable and valid tool for the assessment of muscle size in older adults. Another systematic review among adults found that muscle ultrasound showed a low-to-moderate diagnostic accuracy depending on the muscles and ultrasound measures used. Notably, these reviews did not incorporate studies employing the most recent sarcopenia definitions, nor did they encompass research findings from recent years. Meanwhile, updated sarcopenia definitions by the European Working Group on Sarcopenia in Older People (EWGSOP2, 2019), the Asian Working Group for Sarcopenia (AWGS2, 2019), and the Sarcopenia Definitions and Outcome Consortium (SDOC, 2020) have been proposed.

Therefore, this study aims to contribute to recent advances in the field of sarcopenia clarifying the role of muscle ultrasound in the context of the most updated definitions of sarcopenia. The specific aim of this scoping review was to explore and summarize the validity of muscle ultrasound to identify sarcopenia based on an internationally acknowledged definitions among older adults.

#### **Methods**

The methodology for this scoping review was based on the recommendations by the PRISMA extension for scoping reviews by Tricco et al.<sup>20</sup> The review included the following five key phases: (1) identifying the research question, (2) identifying relevant studies, (3) study selection, (4) charting the data, and (5) collating, summarizing, and reporting the results.

#### Research Question

This scoping review was guided by the question: "What is the current evidence on the validity of ultrasound for muscle assessment to diagnose sarcopenia in older adults?"

# Data Sources and Search Strategy

A systematic literature search was performed in PubMed and Embase for studies published between 2019/01/01 and 2023/11/15. The search strategy consisted of the combination of "ultrasound", "sarcopenia", and "older". The detailed search strategy is shown in the appendix (<u>Table S1</u>). The time frame was chosen to ensure the inclusion of the most recent literature on the application of ultrasound for muscle assessment in sarcopenia since the publication of updated definitions.

# Eligibility Criteria

Eligible for our scoping review were original and published studies investigating muscle ultrasound in the diagnostic workup of sarcopenia in adults aged 60 years and older. We included studies that compared the performance of ultrasound to an internationally acknowledged sarcopenia diagnosis tool according to Stuck AK et al.<sup>6</sup> Studies performed in both outpatient and inpatient settings were eligible.

We excluded secondary research including systematic reviews, umbrella reviews, scoping reviews, and literature reviews. Furthermore, letters and editorials and all non-English articles were excluded. Studies investigating osteosarcopenia and sarcopenic obesity were not included since definitions differ from diagnostic criteria for sarcopenia. Studies including patients with specific diseases (eg, renal failure, critically ill patients) were excluded, as we wanted to evaluate the role of muscle ultrasound in the assessment of primary sarcopenia (and not secondary sarcopenia). Finally, studies investigating muscle elasticity were not included.

## Screening

Two independent reviewers (A.K.E, J.S.S) conducted the abstract and full-text screening using Rayyan (<a href="https://www.rayyan.ai/">https://www.rayyan.ai/</a>). Cohen's kappa of inter-rater agreement was 0.73. Discrepancies were resolved through discussion. Zotero (Corporation for Digital Scholarship, version 6.0.30) was used to manage the literature.

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## Data Summary and Synthesis

Data from the included studies were extracted by one reviewer (J.S.S) using a standardized data extraction sheet. The extracted data entailed study characteristics (author, year of publication, study design, country, size of the study, setting), participant characteristics (mean age, the proportion of females, the proportion of patients with sarcopenia), ultrasound characteristics (type of ultrasound machine, type of ultrasound probe, muscle(s) and muscle parameter(s) evaluated, reliability), and descriptive data on the sarcopenia definition (diagnostic criteria for sarcopenia and methods to assess for the diagnostic sarcopenia components). For each validity test, we further extracted data on the muscle, muscle parameter, and reference standard used to define sarcopenia. Moreover, we extracted the corresponding estimates on the reliability (intraclass correlation coefficient [ICC] and estimates on validity (specificity, sensitivity, positive and negative likelihood ratios). Results of Odds ratio [OR], and Area under the curve [AUC]) were retrieved for each validity test. If there were multiple models (unadjusted and adjusted) for odds ratio reported, the fully adjusted model or adjusted model was extracted. The results of the validity tests were extracted for each evaluated muscle, and muscle parameter (eg, muscle thickness [MT], muscle cross-sectional area [CSA]), respectively.

#### Results

Through our systematic literature search strategy, 2893 records were identified (Figure 1). After duplicate removal, 2290 records remained for abstract screening. Of those, 94 full texts were screened, which resulted in the inclusion of six publications comprising 24 validity tests in this scoping review.

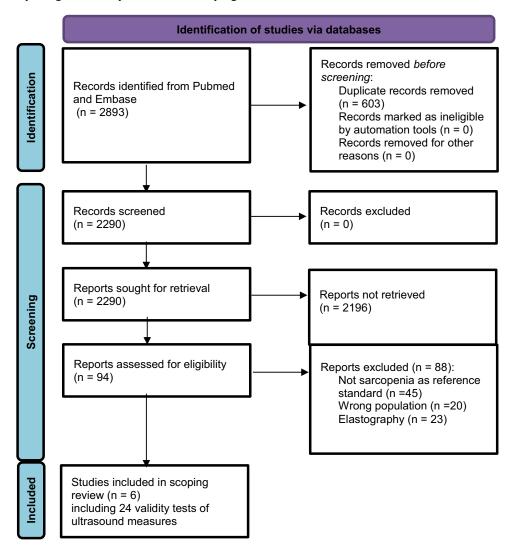


Figure I Flow chart.

## Study Characteristics

Data from six observational studies are described in this scoping review (Table 1). These were conducted in Asia (Taiwan, Thailand, China, Japan) and in Europe (Italy and Turkey). Three studies were performed in the outpatient setting<sup>21–23</sup>, one study in the inpatient setting,<sup>24</sup> and two study studies did not report the clinical setting.<sup>25,26</sup> Overall, data of a cumulative number of 1619 older adults consisting of mostly healthy individuals is described. The mean age was 74.1 (standard deviation [sd] 5.3) years and 52.2% were female. The proportion of patients with sarcopenia ranged between  $10.8\%^{25}$  and  $38.7\%^{24}$  (n = 5), while one study did not report the proportion of sarcopenic patients in their study.<sup>26</sup>

Methods to assess sarcopenia differed between studies. Muscle mass was evaluated by dual-energy x-ray absorptiometry (DXA), <sup>23,25</sup> or bioelectrical impedance analysis (BIA), <sup>21,22,26</sup> or mid-arm muscle circumference. <sup>24</sup> Grip strength was determined with a dynamometer in all six studies. Physical performance was measured by gait speed using the 10 m walk test, the 4 m walk test, the five times sit-to-stand test, or a "sarcopenia leg strength-testing chair". Ozturk et al<sup>21</sup> did not assess physical performance. Detailed study characteristics are shown in the appendix (Table S2).

#### Characteristics of Muscle Ultrasound

Overall, six muscles (rectus femoris, gastrocnemius medialis, tibialis anterior, soleus, biceps brachii, rectus abdominis) and five different muscle parameters (muscle thickness [MT], cross-sectional area [CSA], muscle volume [MV], echo intensity [EI], and fat thickness [FT]) were evaluated. Sonographic cut-off values applied to define low muscle mass are listed in Table 2. The type of ultrasound machine differed between the individual studies (Appendix, Table S3).

The intra-rater reliability of muscle ultrasound was evaluated in three<sup>21,22,26</sup> of the six included studies (Table 1). The intraclass coefficient (ICC) ranged from 0.95 to 0.96 for the rectus femoris MT and from 0.86 to 0.82 for the gastrocnemius medialis MT between studies. No study evaluated inter-rater reliability.

## Results of Validity Tests

In the 24 validity tests, the rectus femoris was the most frequently tested muscle (n = 7). Concerning muscle parameters, muscle thickness (n = 14) was investigated in the majority of validity tests. The bubble chart (Figure 2) summarizes the number of validity tests performed for each muscle and muscle parameter, respectively. Detailed results of the validity tests including sensitivity, specificity, positive likelihood value (PLV), negative likelihood value (NLV), odds ratio (OR), and area under the curve (AUC) are displayed in Table 2. The following diagnostic criteria were used as a reference standard for the diagnosis of sarcopenia: AWGS1 (n = 15, 62.5%), AWGS2 (n = 4, 16.7%), EWGSOP1 (n = 1, 4.2%), EWGSOP2 (n = 4, 16.7%).

Seven validity tests ( $n = 4 \text{ studies}^{21-24}$ ) investigated the rectus femoris. Thereof, four validity tests measured the MT, two tests the CSA, and one test the MV. The highest AUC (0.92, 95% confidence interval [CI] 0.89–0.94) was found for the MT of the rectus femoris muscle using AWGS2 as the reference definition.<sup>22</sup>

The gastrocnemius medialis was evaluated in four validity tests (n = 2 studies) assessing MT, EI, and the MT/EI index. For MT, the AUC ranged from 0.71 (95% CI 0.61–0.79) in males to 0.82 (95% CI 0.76–0.87) in females.

The tibialis anterior was investigated in four validity tests ( $n = 1 \text{ study}^{26}$ ). The predictive validity of the EI of the tibialis anterior was significantly associated with sarcopenia (OR 4.9, 95% CI 1.74–19.10). The strongest association for the tibialis anterior was described by the index of MT/EI (OR 11.1, 95% CI 2.73–45.46).

Three validity tests for the soleus muscle were identified ( $n = 1 \text{ study}^{26}$ ). The strongest association with sarcopenia was described for the index of MT/EI (OR 2.11; 95% CI 1.17–4.39).

Five validity tests were performed for the biceps brachii muscle (n = 1 study<sup>25</sup>) assessing MT, CSA, and FT.

One validity test investigated the rectus abdominis MT ( $n = 1 \text{ study}^{21}$ ) using a cut-off value of 7 mm in men, and 6.6 mm in women, respectively. The corresponding AUC was moderate for both men (0.68; 95% CI 0.55–0.84) and women (0.70, 95% CI 0.54–0.90).

**Table I** Characteristics of Included Studies (n = 6)

Author (year)	Country	Number of participants (n)	Study participants	Mean age (years)	Proportion female (%)	Proportion sarcopenia (%)	Reference standard	Number of validity tests	Muscle measured (sonographic muscle parameter)	Reliability/
Ozturk (2022) <sup>21</sup>	Turkey	313	Outpatient,65+, healthy	79.0ª	59.5% <sup>b</sup>	13.4%	EWGSOP2	4	GM (MT) RF (MT) RF (CSA) RA (MT)	0.92 0.96 0.96 0.94
Chen (2022) <sup>23</sup>	Taiwan	91	Outpatient, no age restriction, able to walk ≥10m	68.3	61.5%	36.0%	AWGS2	3	RF (MT) RF (CSA) RF (MV)	n.r. n.r. n.r.
Sri-on (2022) <sup>22</sup>	Thailand	857	Outpatient, 60+, able to walk ≥6m	70.0	68.6%	22.2%	AWGS2	I	RF (MT)	0.95
Li (2020) <sup>25</sup>	China	179	Setting n.r., 60+, no muscular pathologies	69.0°	72.6%	10.8% <sup>d</sup>	AWGSI	5	BB (MT) BB (CSA) BB (CSA Equation 1) <sup>e</sup> BB (CSA Equation 2) <sup>f</sup> BB (FT)	n.r. n.r. n.r. n.r. n.r.
Isaka (2019) <sup>26</sup>	Japan	60	Setting n.r., no age restriction, healthy, able to walk without assistive device	75.8	0%	n.r.	AWGSI	10	GM (MT) GM (EI) GM (MT/EI) <sup>g</sup> TA (MT) TA (EI) TA (MT/EI) <sup>g</sup> TA (MT+EI) SOL (MT) SOL (EI) SOL (MT/EI) <sup>g</sup>	0.86 0.85 n.r. 0.96 0.95 n.r. n.r. 0.85 n.r.
Rustani (2019) <sup>24</sup>	Italy	119	Inpatient, no age restriction	82.2	50.4%	38.7%	EWGSOPI	I	RF (MT)	n.r.

Notes: aln sarcopenic group, 71 years in comparative non-sarcopenic group. bln sarcopenic group, 65.3 years in non-sarcopenic group. 'In females, 70 years in males. aln females, 16.3% in males. eprediction equation consisting of age, gender and CSA for sarcopenia: logit(P) = -7.542 + 0.125\*age - 1.584\*gender (man=0, woman=1) - 0.449\*CSA, P = elogit(P) /1+elogit(P). prediction equation consisting of BMI, FT, MT, and CSA is: logit(P) = 2.416-0.095\*BMI -0.798\*FT + 0.231\*MT - 0.693\*CSA, P = elogit(P) / I + elogit(P).

gMT/EI Index was determined by the division of MT and EI.

Abbreviations: EWGSOP 2, European Working Group on Sarcopenia in Older People 2019; EWGSOP1, European Working Group on Sarcopenia in Older People 2010; AWGS2, Asian Working Group for Sarcopenia 2019; AWGS1, Asian Working Group for Sarcopenia 2014; GM, Gastrocnemius medialis; RF, Rectus femoris; RA, Rectus abdominis; BB, Biceps brachii; TA, Tibialis anterior; SOL, Soleus; MT, muscle thickness; CSA, cross-sectional area; MV, muscle volume; FT, fat thickness; El, echo intensity; ICC, intraclass correlation coefficient; n.r., not reported.

**Table 2** Results of Validity Tests (n = 24)

Muscle and muscle parameter	Author, Year	Reference standard for sarcopenia (method of muscle mass measurement)	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	OR (95% CI)	AUC (95% CI)	Sonographic Cut-off value
Rectus femoris MT	Ozturk 2022	EWGSOP2 (BIA)	88.2% (m) 80.0% (f)	60.6% (m) 61% (f)	28.8 (m) 22.5 (f)	96.6 (m) 65.6 (f)	0.73 (0.64-0.84) <sup>a</sup> * 0.80 (0.68-0.93) <sup>b</sup> *	0.74 (0.64–0.82) (m) 0.76 (0.70–0.82) (f)	≤15.5mm (m) ≤13.0cm (f)
	Chen 2022	AWGS2 (DXA)	n.r.	n.r.	n.r.	n.r.	n.r.	0.64 (m), 0.78 (f)	n.r.
	Sri-On 2022	AWGS2 (BIA)	90.9% <sup>c</sup>	92.2% <sup>d</sup>	76.6 <sup>e</sup>	97.3 <sup>f</sup>	n.r.	0.92 (0.89–0.94)	≤II.0mm (m) ≤I0.0mm (f)
	Rustani 2019	EWGSOPI (mid-arm muscle circumference)	100%	64%	64.3	100	n.r.	0.90, 0.94 (m), 0.92 (f)	≤9.0mm (m) ≤7.0mm (f)
Rectus femoris CSA	Ozturk 2022	EWGSOP2 (BIA)	64.7% (m) 68.0% (f)	81.1% (m) 74.1% (f)	39.3 (m) 27.9 (f)	92.4 (m) 94.0 (f)	0.54 (0.42–0.70) <sup>a</sup> * 0.60 (0.44–0.80) <sup>b</sup> *	0.77 (0.68–0.85) (m) 0.77 (0.70–0.82) (f)	≤5.2 cm² (m) ≤4.3 cm² (f)
	Chen 2022	AWGS2 (DXA)	n.r.	n.r.	n.r.	n.r.	n.r.	0.86 (m), 0.76 (f)	n.r.
Rectus femoris MV	Chen 2022	AWGS2 (DXA)	n.r.	n.r.	n.r.	n.r.	n.r.	0.83, 0.89 (m), 0.80 (f)	n.r.
Gastrocnemius medialis	Ozturk 2022	EWGSOP2 (BIA)	70.6% (m) 96% (f)	63.8% (m) 65.5% (f)	26.1 (m) 28.2 (f)	92.3 (m) 99.1 (f)	0.71 (0.63-0.80) <sup>a</sup> * 0.77 (0.67-0.90) <sup>b</sup> *	0.71 (0.61–0.79) (m) 0.82 (0.76–0.87) (f)	≤13.8mm (m) ≤13.9mm (f)
MT	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	0.62 (0.15–2.59) <sup>8**</sup> (m)	0.76 (0.70–0.82) (f)  0.64 (m), 0.78 (f)  0.92 (0.89–0.94)  0.90, 0.94 (m), 0.92 (f)  0.77 (0.68–0.85) (m) 0.77 (0.70–0.82) (f)  0.86 (m), 0.76 (f)  0.83, 0.89 (m), 0.80 (f)	≤14.4mm
Gastrocnemius medialis El	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	3.35 (0.75–1.42) <sup>g</sup> * (m)	n.r.	≥40.7 AU
Gastrocnemius medialis MT/EI Index	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	I.25 (0.96–I.76) <sup>E*</sup> (m)	n.r.	n.r
Tibialis Anterior MT	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	5.08 (1.87-20.81) <sup>8*</sup> (m)	n.r.	≤14.4mm
Tibialis anterior El	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	<b>4.88 (1.74–19.10)</b> <sup>8*</sup> (m)	n.r.	≥59 AU
Tibialis anterior MT/El Index	Isaka 2019	AWGS1 (BIA)	n.r.	n.r.	n.r.	n.r.	<b>2.99 (1.47–7.84)</b> <sup>g*</sup> (m)	n.r.	n.r
Tibialis anterior Combination MT, EI <sup>h</sup>	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	II.14 (2.73–45.46)* (m)	n.r.	≤14.4mm ≥40.7 AU
Soleus MT	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	I.37 (0.55–3.37) <sup>8</sup> * (m)	0.76	≤22.9mm
Soleus El	Isaka 2019	AWGSI (BIA)	n.r.	n.r.	n.r.	n.r.	1.99 (0.81–5.46) <sup>8*</sup> (m)	n.r.	≥63.2 AU

Soleus MT/El Index	Isaka 2019	AWGS1 (BIA)	n.r.	n.r.	n.r.	n.r.	<b>2.11 (1.17–4.39)</b> <sup>8</sup> * (m)	n.r.	n.r.
Biceps brachii Equation <sup>i</sup>	Li 2020	AWGSI (DXA)	n.r.	n.r.	n.r.	n.r.	n.r.	0.82 (0.73–0.92)	n.r. <sup>i</sup>
Biceps brachii Equation <sup>j</sup>	Li 2020	AWGSI (DXA)	n.r.	n.r.	n.r.	n.r.	n.r.	0.80 (0.69–0.92)	n.r. <sup>j</sup>
Biceps brachii CSA	Li 2020	AWGSI (DXA)	n.r.	n.r.	n.r.	n.r.	0.47 (0.23-0.96)*	n.r.	n.r.
Biceps brachii MT	Li 2020	AWGSI (DXA)	n.r.	n.r.	n.r.	n.r.	1.31 (0.96–1.78)	n.r.	n.r.
Biceps brachii FT	Li 2020	AWGSI (DXA)	n.r.	n.r.	n.r.	n.r.	0.56 (0.28–1.10)	n.r.	n.r.
Rectus abdominis MT	Ozturk 2022	EWGSOP2 (DXA)	58.8% (m) 84.0% (f)	81.5% (m) 58.8% (f)	37.0 (m) 22.3 (f)	91.5 (m) 96.3 (f)	0.68 (0.55-0.84)* 0.70 (0.54-0.90)*	0.69 (0.59–0.77) (m) 0.74 (0.67–0.80) (f)	≤7mm (m) ≤6.6mm (f)

Notes: Significant ORs are displayed in **bold print**. \* indicates a positive association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis. \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis. \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound muscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound nuscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound nuscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound nuscle measurement and the sarcopenia diagnosis \*\* indicates a negative association between ultrasound nuscle sarcopenia diagnosis \*\* indicates a negative association between ultrasound nuscle sarcopenia diagnosis \*\* indicates a negative association between ultrasound nuscle sarcopenia

Abbreviations: m, males; f, females; DXA, dual energy x-ray absorptiometry; BIA, bioelectrical impedance analysis; EWGSOP 2, European Working Group on Sarcopenia in Older People 2010; AWGS2, Asian Working Group for Sarcopenia 2019; AWGS1, Asian Working Group for Sarcopenia 2019; AWGS1, Asian Working Group for Sarcopenia 2014; GM, Gastrocnemius medialis; RF, Rectus femoris; RA, Rectus abdominis; BB, Biceps brachii; TA, Tibialis anterior; SOL, Soleus; MT, muscle thickness; CSA, cross-sectional area; MV, muscle volume; FT, fat thickness; EI, echo intensity; ICC, intraclass correlation coefficient; n.r., not reported.

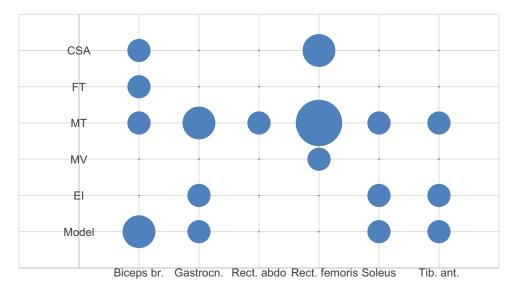


Figure 2 Bubble chart presenting the number of validity tests performed for each muscle and muscle parameter\* (n=24).

Notes: \*The area of the bubble represents the number of validity tests that were performed for the type of muscle and muscle parameter, respectively. The size of the following bubble equals n = 1 validity test.

Abbreviations: Biceps br., Biceps brachii; Gastrocn., Gastrocnemius; Rect. Abdo, Rectus abdominis; Rect. Femoris, Rectus femoris; Tib. ant., tibialis anterior; MT, Muscle thickness; CSA, cross-sectional area; MV muscle volume; El, Echointensity, FT, Fat thickness; Model, Models entail equations (eg, MT/El Index) that were established by the study teams to predict sarcopenia (Details in Table 2).

#### Discussion

This scoping review identified six muscles and five muscle parameters, respectively, that were tested for the predictive validity of ultrasound in diagnosing sarcopenia among older adults. Specifically, muscle thickness or cross-sectional area of the rectus femoris muscle was investigated most frequently. The latest sarcopenia definitions by the European and Asian Societies (EWGSOP2, AWGS2) were used in a third of all validity tests as a reference standard.

Our scoping review adds important findings to the current literature. We found a limited number of studies investigating the validity of muscle parameters using ultrasound to diagnose sarcopenia based on the latest internationally acknowledged definitions of sarcopenia in older adults. These include the European (EWGSOP2) and the Asian (AWGS2) sarcopenia definitions that were published in 2019. We did not identify studies using the latest definition introduced by the American Sarcopenia Definitions and Outcomes Consortium (SDOC) published in 2020. Previous reviews and meta-analyses (Nijolt et al, <sup>16</sup> Perkisas et al, <sup>11</sup> Fu et al <sup>17</sup>) summarized results based on former definitions of sarcopenia (eg, muscle mass only). Moreover, these studies primarily focused on the diagnosis of sarcopenia among adults at a younger age.

In our scoping review, we identified a majority of validity tests investigating the rectus femoris. This observation aligns with the findings of a prior review conducted by Fu et al, <sup>17</sup> wherein a substantial proportion of investigations also focused on the rectus femoris. A plausible rationale for this observation may be the clinical significance of this lower extremity muscle. The rectus femoris is a pivotal player in the regulation of gait and mobility. Furthermore, the accessibility of the rectus femoris is favorable for point-of-care ultrasound assessment. In contrast, the accessibility of the calf muscles may be impeded by the presence of compression stockings and requires specific patient positioning.

We found a limited number of validity tests investigating the echo intensity of different muscles. The highest OR at 4.88 was found for the tibialis anterior muscle. Of note, the combination of measuring the MT and EI of the tibialis anterior muscle resulted in an even higher OR of 11.14. Similarly, Fu et al<sup>17</sup> reported that in the biceps brachii, the diagnostic validity of EI alone (AUC 0.69) and of the CSA alone (AUC 0.81) was lower than the AUC of the combination of the two muscle parameters (0.85).

Interestingly, we found a number of studies investigating intra-rater reliability, but none of the studies assessed interrater reliability. Nonetheless, Nijholt et al<sup>16</sup> and Perkisas et al<sup>11</sup> previously identified muscle ultrasound as a technique

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demonstrating both high inter- and intra-rater reliability. Similarly, a cross-sectional study by Lanza et al<sup>27</sup> found that inter-rater agreement (ICC 0.850) and intra-rater agreement (ICC 0.90) were high.

The present scoping review has notable strengths. Methodologically, adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards for scoping reviews<sup>20</sup> was maintained, thereby ensuring a rigorous and valid research approach. Furthermore, our inclusion criteria specifically targeted studies that examined the validity of muscle ultrasound in predicting sarcopenia, with a strict reliance on internationally acknowledged sarcopenia definitions. Lastly, a noteworthy contribution of this scoping review is its exclusive focus on the older adult population, addressing a literature gap pertaining to age-specific considerations in the domain of muscle ultrasound and sarcopenia.

There are several limitations to our study. First, we found a limited number of studies and substantial variation regarding the methodological approach to investigate muscle parameters, and to assess sarcopenia between studies. Therefore, results could not be pooled using a meta-analytical approach. Second, we cannot exclude that we missed an article meeting our selection criteria. However, we used a broad and predefined search strategy and had two reviewers for independent screening and selection of articles.

Third, our scoping review explicitly focuses on validity results against currently acknowledged sarcopenia definitions in older adults. Thus, our results cannot be extrapolated to younger populations or to findings from studies using different criteria to measure sarcopenia (eg, muscle mass only). Fourth, there may be other factors influencing results of validity tests, as, for example, the study setting, the definitions of sarcopenia applied. Moreover, our review does not comprise methods applied for derivation of cut-off points of ultrasound parameters. Finally, the results of our scoping review are limited to the data of the original studies that were included.

Several implications arise from our study. While our scoping review does not definitively answer the question of which muscle and ultrasound parameter are most valid in the diagnostic work-up of sarcopenia, it does highlight key findings. The rectus femoris emerged as the most frequently assessed muscle in terms of validity for sarcopenia according to acknowledged definitions, showing promising results of AUC in four studies. Our analysis revealed a scarcity of studies within the older adult population, coupled with substantial heterogeneity in methodological approaches across studies. Specifically, there is only a limited number of validity studies (one-third of studies in this review) which applied the most recent European and Asian sarcopenia definitions (EWGSOP2, AWGS2), while the latest American definition of sarcopenia (SDOC) is yet to be evaluated. Therefore, future investigations should align with recommendations outlined by Perkisas et al<sup>11</sup> emphasizing the standardization of ultrasound methodology and the application of internationally acknowledged definitions of sarcopenia. This standardization is crucial for enabling meaningful comparisons between studies, potentially facilitating a meta-analytical approach. Moreover, ultrasound measures frequently differ by sex and are affected by anthropometric measures. Therefore, ultrasound indices have been proposed such as the Ultrasound Sarcopenia Index providing a marker independent of sex, height and body mass.<sup>28</sup>

Finally, there is a recognized need for additional studies to explore the added value of qualitative muscle parameters assessed through ultrasound, such as echo intensity. Gaining insights into these aspects will significantly enhance our overall comprehension of the diagnostic potential of ultrasound, ultimately contributing to advance effective diagnostic strategies for sarcopenia.

#### Conclusion

In conclusion, this scoping review highlights the limited availability of studies examining the validity of muscle ultrasound for diagnosing sarcopenia based on recent definitions among older adults. Muscle thickness of the rectus femoris showed most promising results regarding validity. Further observational studies are needed to confirm these findings and to validate ultrasound among older adults in the inpatient setting.

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