

Diagnostic test accuracy of ultrasound for sarcopenia diagnosis: A systematic review and meta-analysis

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Abstract

Muscle ultrasound is an emerging tool for diagnosing sarcopenia. This review aims to summarize the current knowledge on the diagnostic test accuracy of ultrasound for the diagnosis of sarcopenia. We collected data from Ovid Medline, Embase and the Cochrane Central Register of Controlled Trials. Diagnostic test accuracy studies using muscle ultrasound to detect sarcopenia were included. Bivariate random-effects models based on sensitivity and specificity pairs were used to calculate the pooled estimates of sensitivity, specificity and the area under the curves (AUCs) of summary receiver operating characteristic (SROC), if possible. We screened 7332 publications and included 17 studies with 2143 participants (mean age range: 52.6–82.8 years). All included studies had a high risk of bias. The study populations, reference standards and ultrasound measurement methods varied across the studies. Lower extremity muscles were commonly studied, whereas muscle thickness (MT) was the most widely measured parameter, followed by the cross-sectional area (CSA). The MTs of the gastrocnemius, rectus femoris, tibialis anterior, soleus, rectus abdominis and geniohyoid muscles showed a moderate diagnostic accuracy for sarcopenia (SROC-AUC 0.83, 8 studies; SROC-AUC 0.78, 5 studies; AUC 0.82, 1 study; AUC 0.76–0.78, 2 studies; AUC 0.76, 1 study; and AUC 0.79, 1 study, respectively), whereas the MTs of vastus intermedius, quadriceps femoris and transversus abdominis muscles showed a low diagnostic accuracy (AUC 0.67–0.71, 3 studies; SROC-AUC 0.64, 4 studies; and AUC 0.68, 1 study, respectively). The CSA of rectus femoris, biceps brachii muscles and gastrocnemius fascicle length also showed a moderate diagnostic accuracy (AUC 0.70–0.90, 3 studies; 0.81, 1 study; and 0.78–0.80, 1 study, respectively), whereas the echo intensity (EI) of rectus femoris, vastus intermedius, quadriceps femoris and biceps brachii muscles showed a low diagnostic accuracy (AUC 0.52–0.67, 2 studies; 0.48–0.50, 1 study; 0.43–0.49, 1 study; and 0.69, 1 study, respectively). The combination of CSA and EI of biceps brachii or rectus femoris muscles was better than either CSA or EI alone for diagnosing sarcopenia. Muscle ultrasound shows a low-to-moderate diagnostic test accuracy for sarcopenia diagnosis depending on different ultrasound parameters, measured muscles, reference standards and study populations. The combination of muscle quality indicators (e.g., EI) and muscle quantity indicators (e.g., MT) might provide better diagnostic test accuracy.

Keywords diagnosis; meta-analysis; muscle depletion; muscle wasting; ultrasound imaging

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Introduction

Sarcopenia, a progressive muscle disorder characterized by loss of muscle mass and function, is associated with increased adverse health outcomes including functional disability, falls and mortality.¹ According to a recent systematic review, the prevalence of sarcopenia was 8–36% in younger adults and 10–27% in older adults based on different diagnostic criteria.²

Irrespective of the diagnostic criteria used, muscle mass measurement plays a crucial role in the diagnosis of sarcopenia. A review including 283 studies reported that 264 (93.3%) studies defined sarcopenia using muscle mass measurement and 198 studies (70%) defined sarcopenia using only low muscle mass (LMM).³ Dual-energy X-ray absorptiometry (DXA, used in 43.6% of the included studies), computed tomography (CT, used in 25.6% of the included studies) and bioelectrical impedance analysis (BIA, used in 19.3% of the included studies) are conventionally used to measure muscle mass.³ CT is a ‘gold standard’ for measuring muscle mass; however, it is expensive and associated with radiation exposure risk.⁴ Moreover, DXA and BIA can be used to only measure fat-free mass directly.⁴ Thus, these methods are not ideal for measuring muscle mass.

Recently, ultrasound has gained increasing attention for measuring muscle mass due to its safety, noninvasiveness, low cost and real-time characteristics.⁵ Additionally, ultrasound is portable, making it a valuable tool for researching sarcopenia in community-dwelling individuals. Ultrasound appears to be an accurate and reliable method with high reproducibility for the measurement of muscle mass.^{6–8} Muscle thickness (MT) and muscle cross-sectional area (CSA), two common ultrasound parameters for muscle mass, have been widely used in sarcopenia research.^{9,10} However, the cutoff points of ultrasound parameters for diagnosing sarcopenia have not been established. The updated version of the European Working Group on Sarcopenia in Older People Consensus (EWGSOP2)⁴ recommended ultrasound as a valid and reliable tool for measuring muscle mass, but further studies are required to assess its potential.

So far, six systematic reviews have addressed the use of ultrasound for measuring skeletal muscle.^{6,10–14} One of these reviews reported the validity of ultrasound-based models for predicting whole-body muscle mass,¹¹ one examined the reliability of sonoelastography to assess sarcopenia,¹³ two summarized the techniques used for muscle measurement using ultrasound in sarcopenia^{12,14} and the other two evaluated the validity and reliability of detecting muscle mass in older adults.^{6,10} Measurable diagnostic properties including sensitivity and specificity are essential for clinicians and researchers to evaluate and choose an optimal diagnostic tool. However, the diagnostic potential of ultrasound for sarcopenia has not been systematically reviewed. Therefore, this systematic review aimed to summarize the current information

on the diagnostic test accuracy (DTA) of any type of ultrasound for the diagnosis of sarcopenia.

Methods

We conducted and reported this review according to the Preferred Reporting Items for Systematic Review and Meta-Analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA).^{15,16} The database search, study selection, data extraction and risk of bias assessment were all performed by two authors (H.F. and W.Z.) independently, and any disagreement during the process was resolved by discussion with the arbitrator (M.Y.).

Databases and searches

The following databases were retrieved on 10 July 2021: Ovid Medline and Epub, Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations (from 1946), Embase (from 1974) and the Cochrane Central Register of Controlled Trials (June 2021). The following keywords and the corresponding Medical Subject Headings (MESH) terms were combined to search the databases: ‘sarcopenia’, ‘muscle atroph*’, ‘muscular atroph*’, ‘muscle mass*’, ‘muscle size*’, ‘muscle diameter*’, ‘muscle volume*’, ‘muscle thickness*’, ‘muscle wasting’, ‘ultrasonic’, ‘ultrasonography’, ‘ultrasound’, ‘sonography’, ‘ultrasono* imaging’, ‘echography’, ‘elastography’, ‘sonoelastography’ and ‘echo intensity’. Supporting Information, *Table S1* shows the detailed search strategy.

Inclusion and exclusion criteria

The inclusion criteria included (1) study population: men and women of any age and ethnicity; (2) index tests: any type of ultrasound that measured any muscle group in any anatomical location; (3) reference standards: sarcopenia could be defined using the European Working Group on Sarcopenia in Older People (EWGSOP1), the EWGSOP2, the International Working Group on Sarcopenia (IWGS), the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project, the Asian Working Group for Sarcopenia (AWGS 2014), the updated AWGS (AWGS 2019) or LMM alone; and (4) outcomes: studies that reported diagnostic properties: sensitivity, specificity, total accuracy, area under the curve (AUC) of receiver operating characteristic (ROC), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR), true-positive (TP), false-positive (FP), false-negative (FN) and true-negative (TN). The exclusion criteria included (1) reviews, editorials, meta-analyses, letters, case reports or se-

ries, conference abstracts, study protocols and comments; (2) non-English publications; and (3) duplicated publications.

Study selection

Two authors independently screened the titles and abstracts to identify potential eligible records. Then, two authors reviewed the full texts of these eligible publications according to the inclusion and exclusion criteria. The reasons for exclusion were recorded. The references of all included studies were also screened for potentially eligible studies.

Data extraction

The data were extracted from the included studies by two authors independently using a structured data extraction form. The following data were extracted: authors, publication year, country, study population, sample size, age, sex, reference standards for sarcopenia, type of transducer, measurement details (muscle group, probe, axis, measured bodyside, ultrasound parameters) and results (ultrasound parameter, cutoff values, TP, FP, TN, FN). If sufficient information was not available, the authors of the original studies were contacted via e-mail.

Methodological quality assessment

Two authors independently evaluated the methodological quality of each study according to the Quality Assessment of Diagnostic Accuracy Studies, Version 2 (QUADAS-2).¹⁷ The QUADAS-2 includes four key domains: (1) patient selection; (2) index test; (3) reference standard; and (4) flow and timing. Each domain evaluated the risk of bias and the first three also evaluated applicability.

Statistical analysis and data synthesis

To reduce the clinical heterogeneity, the index tests were divided based on the measured muscle groups (e.g., *rectus femoris* and *vastus intermedius*) and the ultrasound parameters (e.g., MT, CSA, echo intensity [EI] and fascicle length [FL]) into different categories including '*rectus femoris* MT' or '*vastus intermedius* CSA'.

If there were four or more studies available for a specific index test, then we performed a meta-analysis using the methods recommended by the Cochrane Diagnostic Test Accuracy Working Group.¹⁸ Bivariate random-effects models based on sensitivity and specificity pairs were used to calculate the pooled estimates of sensitivity, specificity, PLRs, NLRs, diagnostic odds ratios (DORs) and the AUCs of summary receiver operating characteristic (SROC), along with

the 95% confidence intervals (CIs). AUC is a global measure of test performance. Diagnostic accuracy was classified as low ($AUC < 0.7$), moderate ($0.7 \leq AUC < 0.9$) or high ($AUC \geq 0.9$).¹⁹

We did not conduct meta-analyses when there was an insufficient number of included studies ($n \leq 3$) for an index test. In these instances, we constructed 2×2 tables for each study and calculated sensitivity, specificity and AUC, along with the 95% CIs.

We used RevMan 5.4.1,²⁰ Stata Version 12.1 (Stata Corp, College Station, TX, USA) and MetaDTA Version 2.01^{21,22} in the statistical analyses and data synthesis.

Investigations of heterogeneity

The potential area of clinical heterogeneity included (1) study populations: healthy older adults, patients with different diseases and so forth; (2) index tests: different ultrasound parameters (MT, CSA etc.), different muscle groups (*rectus femoris*, *vastus intermedius* etc.), different probes and different body sizes (dominant, non-dominant or both); and (3) reference standards: EWGSOP1, EWGSOP2, AWGS 2014, AWGS 2019, FNIH, IWGS and LMM alone.

First, we summarized the clinical characteristics of the included studies to address these heterogeneities across studies (Table 1). Second, we present the main results based on the combination of the muscle group and ultrasound parameters, such as '*rectus femoris* MT'. Third, we used subgroup analyses to assess the impact of reference standards on the results, if possible. Last, for further exploration of potential sources of heterogeneity, we visually examined the forest plots of sensitivity and specificity, if possible.

Sensitivity analyses

We did not perform sensitivity analysis due to the lack of sufficient data for most involved index tests.

Assessment of reporting bias

We did not perform a quantitative assessment of reporting bias because of the insufficient number of included studies for each index test. Moreover, the consensus regarding the most robust approach to assessing reporting bias in DTA studies has not been established and there was uncertainty with respect to the application of standard approaches like funnel plots to DTA studies.^{40,41}

Table 1 Summary of studies regarding diagnostic performance of ultrasound for sarcopenia

Study	Country	Population	Age, years	N (men: women)	Reference standards	Probe	Axis	Measured body side	Index test	Cutoff value	AUC
Ayvicek 2019 ²³	Turkey	Geriatric outpatients	74	136 (46:90)	EWVGOP2-defined sarcopenia	Linear, 5–12 MHz	NA	NA	GM MT	12.3 mm	M: 0.90 F: 0.86
Barotzis 2020 ²⁴	Greece	Healthy older adults	75.6	94 (27:67)	EWVGOP2-defined sarcopenia	Linear, 10 MHz	Trans Long Long Trans Long Trans Long Trans Long Trans Long Sagittal NA	D D ND ND ND D D ND D D D D NA	VI MT VI MT VI MT RF MT RF MT RF + VI MT RF + VI MT RF + VI MT RF + VI MT GM MT GM MT GM MT GM MT GM MT GHY MT GM MT GM MT GM FL GM FL RA MT TA MT GM MT GM MT	10.1 mm 10 mm 11.3 mm 15.4 mm 15.9 mm 26.2 mm 28.4 mm 28 mm 26.1 mm 16.5 mm 16.1 mm 16.3 mm 17.2 mm 6.5 mm 17.1 mm 16.9 mm 34.7 mm 36.2 mm 7.5 mm 3.3 mm 14.7 mm 11.6 mm	0.67 0.66 0.67 0.68 0.68 0.67 0.66 0.69 0.69 0.70 0.74 0.73 0.79 0.83 0.80 0.78 0.68 0.85 0.83
Kuyumcu 2016 ²⁵	Turkey	Healthy older adults	73.1	100 (41:59)	EWVGOP1-defined sarcopenia	Linear, 5–12 MHz	NA	L R	GM MT GM MT	17.1 mm 16.9 mm	0.78 0.83
Sari 2020 ²⁶	Turkey	Patients with systemic sclerosis	52.6	93 (7:86)	LMMI-defined sarcopenia	Linear, 9–12 MHz	NA	L R	GM FL GM FL	34.7 mm 36.2 mm	0.80 0.78
Yuguchi 2020 ²⁷	Japan	Healthy older adults	72.4	195 (72:123)	LMMI-defined sarcopenia	Linear, 6 MHz	NA	R	GM MT	14.4 mm	0.48
Isaka 2019 ²⁸	Japan	Healthy older adults	75.8	60 (60:0)	LMMI-defined sarcopenia	Linear, 8 MHz	Trans	NA	SOL MT TIA MT GM MT	22.9 mm 14.4 mm 15 mm	0.76 0.82 0.82
Wang 2018 ²⁹	China	Healthy older adults	71.3	135 (39:96)	LMMI-defined sarcopenia	NA	Trans	R	RF MT	M: 15.1 mm F: 14.3 mm	M: 0.78 F: 0.65
Fukumoto 2021 ³⁰	Japan	Healthy older adults	75.4	204 (64:140)	LMMI-defined sarcopenia	Linear, 8–12 MHz	Trans	NA	VI MT RF + VI MT GM MT SOL MT GM + SOL MT RF + VI GM + SOL MT	M: 11.5 mm F: 9.1 mm M: 28.8 mm F: 23.4 mm M: 15.3 mm F: 14.2 mm M: 41.6 mm F: 37.5 mm M: 56.7 mm F: 53.7 mm M: 84.8 mm F: 76.2 mm	M: 0.67 F: 0.71 M: 0.78 F: 0.75 M: 0.80 F: 0.75 M: 0.78 F: 0.65 M: 0.84 F: 0.73 M: 0.85 F: 0.78

(Continues)

Table 1 (continued)

Study	Country	Population	Age, years	N (men: women)	Reference standards	Probe	Axis	Measured body side	Index test	Cutoff value	AUC
Matsuzawa 2021 ³¹	Japan	Haemodialysis patients	77.5	58 (36:22)	LMM-defined sarcopenia	Linear, 4–11 MHz	Trans	NA	RF CSA	M: 1.88 cm ² F: 1.43 cm ²	M: 0.88 F: 0.74
Wilkinson 2021 ³²	England	Patients with chronic kidney disease	62	113 (54:59)	LMM-defined sarcopenia	Linear, 7.5 MHz	Trans	R	RF CSA	M: 6.7 cm ² F: 5.7 cm ²	M: 0.70 F: 0.90
Sato 2020 ³³	Japan	Heart failure patients	74	69 (NA:NA)	AWGS 2014-defined sarcopenia	Linear, 12 MHz or sector	Trans	R	RF MT	15 mm	0.80
Rustani 2019 ³⁴	Italy	Internal medicine patients	82.8	119 (59:60)	EWGSOP1-defined sarcopenia	Linear, 5–7.5 MHz	Trans	R	RF MT	NA	0.9
Hida 2018 ³⁵	Japan	Healthy older adults	66.2	201 (99:102)	LMM-defined sarcopenia	Linear, 5–18 MHz	Trans	R	RF + VI MT	M: 36 mm F: 34 mm	M: 0.71 F: 0.74
Tada 2021 ³⁶	Japan	Rheumatoid arthritis patients	66.5	84 (18:66)	AWGS 2014-defined sarcopenia	Linear, 5–18 MHz	Trans	NA	RF + VI MT	M: 24.7 mm F: 19.7 mm	M: 0.83 F: 0.75
Yoshida 2020 ³⁷	Japan	Rheumatoid arthritis patients	NA	78 (0:78)	AWGS 2014-defined sarcopenia	Linear, 9.0 MHz	NA	Mean values of the left and right sides	BB rEI + CSA BB rEI BB CSA RF rEI + CSA RF rEI RF CSA	NA	0.85 0.69 0.81 0.85 0.67 0.78
Álvarez 2021 ³⁸	Spain	Healthy older adults	78.9	57 (24:33)	LMM-defined sarcopenia	Linear, 11.5 MHz	Trans Long	D	GM MT GM MT	18.5 mm 17.3 mm	0.79 0.83
Yamada 2017 ³⁹	Japan	Healthy older adults	80.2	347 (100:247)	LMM-defined sarcopenia	Linear, 7.5 MHz	NA	NA	RF MT VI MT RF + VI MT RF EI VI EI RF + VI EI	M: 13.4 mm F: 11.8 mm M: 14.4 mm F: 11.7 mm M: 28.8 mm F: 23.3 mm M: NA F: 58.2 NA NA	M: 0.70 F: 0.63 M: 0.66 F: 0.61 M: 0.68 F: 0.62 M: 0.52 F: 0.61 M: 0.48 F: 0.50 M: 0.49 F: 0.43

Abbreviations: AUC, area under the curve; AWGS, Asian Working Group for Sarcopenia; BB, biceps brachii; CSA, cross-sectional area; D, dominant side; EI, echo intensity; EWGSOP, European Working Group on Sarcopenia in Older People; F, female; FL, fascicle length; GHY, geniohyoid; GM, gastrocnemius; L, left; LMM, low muscle mass; Long, longitudinal ultrasound scan; M, male; MT, muscle thickness; N, sample size of the study; NA, not available; ND, non-dominant side; R, right; RA, rectus abdominis; rEI, recorrected EI; RF, rectus femoris; SOL, soleus; TA, transversus abdominis; TIA, tibialis anterior; Trans, transverse ultrasound scan; VI, vastus intermedius.

Results

Results of study selection

Figure 1 shows the PRISMA diagram for the study selection. A total of 7332 publications were retrieved initially. After removing the duplicates, the titles and abstracts of 4597 publications were screened. We excluded 4491 publications after the title and abstract screening. Then, the full texts of 106 publications were further assessed for eligibility. We excluded 89 studies for the reasons listed in Figure 1. Finally, we included 17 studies with a total of 2143 participants in this review.^{23–39}

Methodological quality of the included studies

The methodological quality assessment results of the included studies are summarized in Figure 2. All included studies had a high risk of bias.

Characteristics of the included studies

Table 1 presents the characteristics of the 17 included studies published between 2016 and 2021 and conducted in seven countries. Nine studies recruited healthy older adults,^{24,25,27–30,35,38,39} two studies recruited patients with kidney diseases,^{31,32} two studies recruited patients with rheumatoid arthritis,^{36,37} one study recruited geriatric outpatients,²³ one study recruited patients with heart failure,³³ one study recruited patients with systemic sclerosis²⁶ and one study recruited internal medicine patients.³⁴ The mean age of the study populations ranged from 52.6 to 82.8 years.

The ultrasound measurement methods varied across studies. For example, 16 included studies used linear array probes, whereas the other study did not provide this information.²⁹ The ultrasound frequencies ranged from 4 to 12 MHz (Table 1). Nine studies reported the probe position in the transverse axis, two studies reported the probe position in both the transverse and long axes and five studies did not report the probe position. Additionally, three studies measured both body sides, seven studies only measured the right side, one study only measured the dominant side and

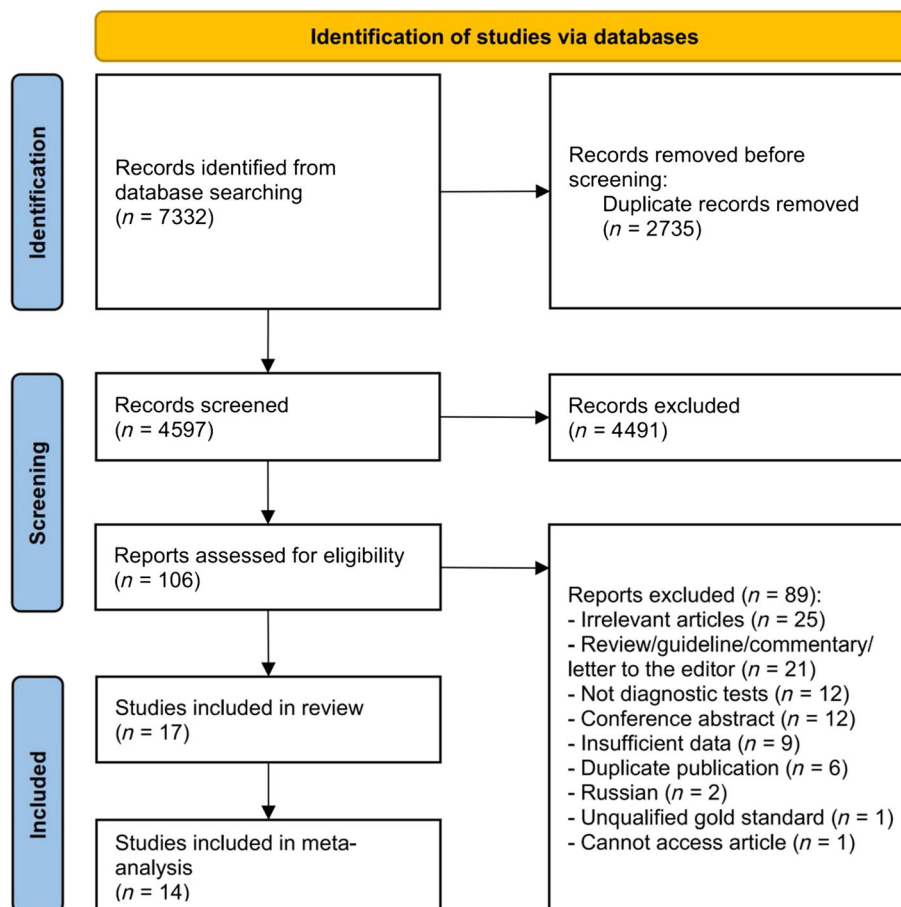


Figure 1 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram

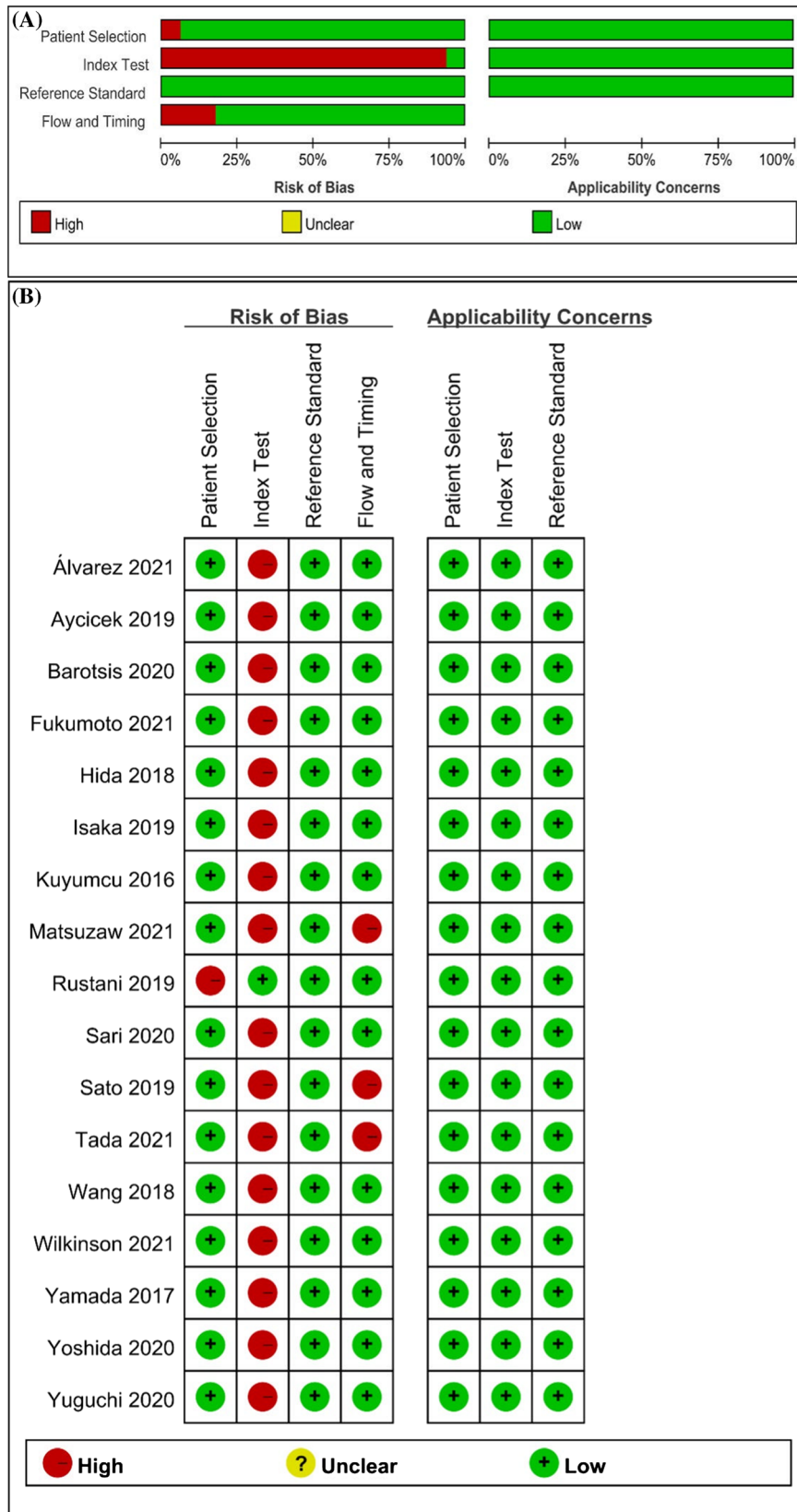


Figure 2 Summary of the risk of bias of the included studies according to the Quality Assessment of Diagnostic Accuracy Studies, Version 2 (QUADAS-2)

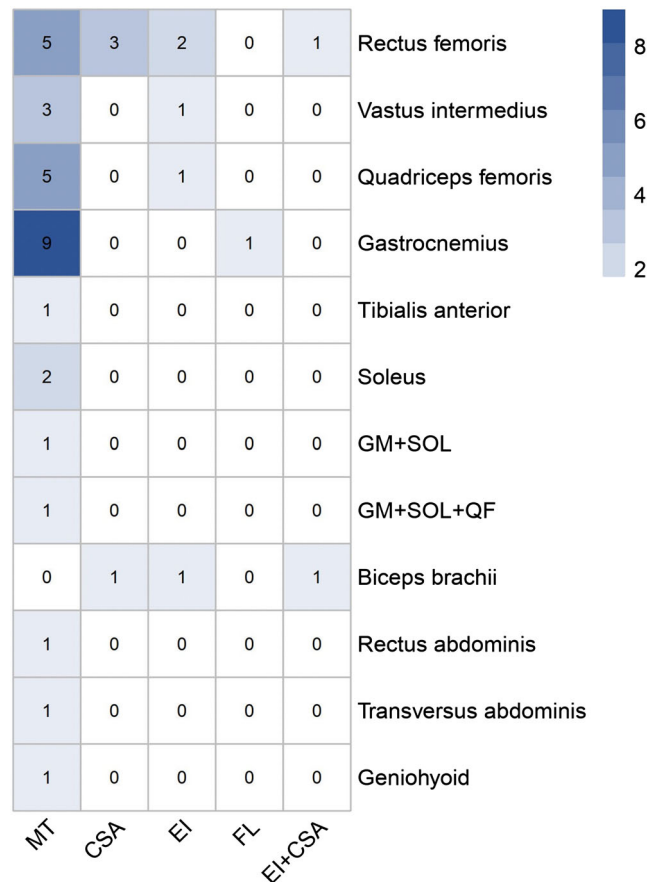


Figure 3 Summary of the muscles and ultrasound parameters measured in the included studies. CSA, cross-sectional area; EI, echo intensity; FL, fascicle length; GM, *gastrocnemius*; MT, muscle thickness; QF, *quadriceps femoris*; SOL, *soleus*

the other six studies did not report it. Ten included studies (59%)^{26–28,30,32,33,35–38} reported inter- and intra-rater reliability. The intraclass correlation coefficients ranged from 0.73 to 0.99.

As for reference standards, ten studies^{26–32,35,38,39} defined sarcopenia only based on LMM, two studies^{23,24} used the EWGSOP2, two studies^{25,34} used the EWGSOP1, two studies^{33,36} used the AWGS 2014 and one study³⁷ used the AWGS 2019 (Table 1).

Figure 3 summarizes the muscle groups and ultrasound parameters used in the included studies. *Gastrocnemius*, *rectus femoris* and *quadriceps femoris* were the most widely measured muscle groups. As for ultrasound parameters, MT was the most frequently used ultrasound parameter, followed by CSA and EI.

Results of diagnostic test accuracy

Table 2 shows the results of the overall and subgroup analyses of the DTA of different ultrasound parameters for sarcopenia. Figure 4 presents the results of the bivariate meta-analysis for the sensitivity and specificity. Moreover,

Figure 5 shows the SROC curves of ultrasound measurements of various muscles for sarcopenia diagnosis.

Muscle thickness for diagnosing sarcopenia

Gastrocnemius muscle thickness Nine studies^{23–30,38} assessed the diagnostic value of *gastrocnemius* MT for sarcopenia. The sensitivity ranged from 70% to 100%, and the specificity ranged from 16% to 85%. One study was excluded from the meta-analysis due to insufficient data.³⁸ Thus, the meta-analysis of the other eight studies showed that the pooled sensitivity and specificity were 82% (95% CI 71–90%) and 64% (95% CI 48–77%), respectively. The SROC-AUC was 0.83 (95% CI 0.79–0.86). The results of subgroup analysis according to different reference standards are listed in Table 2.

Rectus femoris muscle thickness Five studies^{24,30,33,34,39} assessed the diagnostic value of *rectus femoris* MT for sarcopenia. The sensitivity ranged from 62% to 87%, and the specificity ranged from 61% to 81%. The meta-analysis of the five studies demonstrated that the pooled sensitivity was 72% (95% CI 62–81%) and the pooled specificity was 72% (95% CI 64–79%). The SROC-AUC was 0.78 (95% CI 0.74–0.82) (Table 2).

Table 2 Overall and subgroup analyses for diagnostic accuracy of ultrasound for sarcopenia

Overall and subgroup analyses	Pooled sensitivity	Pooled specificity	Pooled PLR	Pooled NLR	Pooled DOR	SROC-AUC ^a
Gastrocnemius MT (8 studies) ²⁵	0.82 (0.71–0.90)	0.64 (0.48–0.77)	2.27 (1.59–3.26)	0.28 (0.18–0.43)	8.20 (4.40–15.28)	0.83 (0.79–0.86)
EWGSOP1-defined sarcopenia ^{23,24}	1.00 (0.79–1.00)	0.64 (0.53–0.74)	NA	NA	NA	NA
EWGSOP2-defined sarcopenia ^{23,24}	0.81 (0.60–0.92)	0.73 (0.49–0.89)	3.03 (1.27–7.22)	0.26 (0.10–0.70)	11.58 (2.00–66.88)	NA
LMM-defined sarcopenia ^{26–30}	0.82 (0.67–0.91)	0.59 (0.38–0.78)	2.02 (1.31–3.14)	0.30 (0.18–0.49)	6.79 (3.49–13.24)	0.81 (0.77–0.84)
Rectus femoris MT (5 studies) ³⁴	0.72 (0.62–0.81)	0.72 (0.64–0.79)	2.57 (1.80–3.67)	0.39 (0.26–0.58)	6.66 (3.14–14.12)	0.78 (0.74–0.82)
EWGSOP1-defined sarcopenia ²⁴	0.87 (0.74–0.95)	0.79 (0.68–0.88)	NA	NA	NA	NA
EWGSOP2-defined sarcopenia ²⁴	0.69 (0.41–0.89)	0.65 (0.54–0.76)	NA	NA	NA	NA
AWGS 2014-defined sarcopenia ³³	0.77 (0.56–0.91)	0.81 (0.67–0.92)	NA	NA	NA	NA
LMM-defined sarcopenia ^{30,39}	0.62 (0.54–0.70)	0.67 (0.58–0.74)	1.88 (1.43–2.49)	0.56 (0.44–0.72)	3.35 (2.02–5.57)	NA
Quadriceps femoris MT (4 studies) ²⁴	0.63 (0.54–0.71)	0.77 (0.57–0.90)	2.75 (1.33–5.72)	0.48 (0.36–0.65)	5.69 (2.16–14.97)	0.64 (0.60–0.69)
EWGSOP2-defined sarcopenia ²⁴	0.69 (0.41–0.89)	0.76 (0.65–0.85)	NA	NA	NA	NA
AWGS 2014-defined sarcopenia ^{30,39}	0.53 (0.29–0.76)	0.95 (0.87–0.99)	NA	NA	NA	NA
LMM-defined sarcopenia ^{30,39}	0.67 (0.54–0.78)	0.62 (0.53–0.71)	1.78 (1.21–2.61)	0.53 (0.33–0.84)	3.36 (1.45–7.80)	NA
Vastus intermedius MT (3 studies) ²⁴	0.62 (0.55–0.69)	0.70 (0.55–0.81)	2.04 (1.29–3.23)	0.55 (0.42–0.72)	3.73 (1.85–7.55)	NA
EWGSOP2-defined sarcopenia ²⁴	0.50 (0.28–0.72)	0.85 (0.75–0.91)	NA	NA	NA	NA
LMM-defined sarcopenia ^{30,39}	0.63 (0.55–0.70)	0.61 (0.56–0.66)	1.61 (1.36–1.92)	0.61 (0.49–0.75)	2.65 (1.82–3.88)	NA
Rectus femoris CSA (3 studies) ³⁷	0.84 (0.65–0.94)	0.69 (0.57–0.78)	2.68 (1.99–3.61)	0.23 (0.11–0.51)	11.55 (4.75–28.09)	NA
AWGS 2019-defined sarcopenia ^{31,32}	0.85 (0.69–0.95)	0.59 (0.43–0.74)	NA	NA	NA	NA
LMM-defined sarcopenia ^{31,32}	0.84 (0.51–0.96)	0.76 (0.64–0.85)	3.44 (2.14–5.51)	0.21 (0.06–0.81)	16.16 (3.20–81.71)	NA

Abbreviations: AWGS, Asian Working Group for Sarcopenia; CSA, cross-sectional area; DOR, diagnostic odds ratio; EWGSOP, European Working Group on Sarcopenia in Older People; LMM, low muscle mass; MT, muscle thickness; NA, not available; NLR, negative likelihood ratio; PLR, positive likelihood ratio; SROC-AUC, area under the curve of summary receiver operating characteristic.

^aSROC-AUC could only be calculated when the data were from ≥4 original studies.

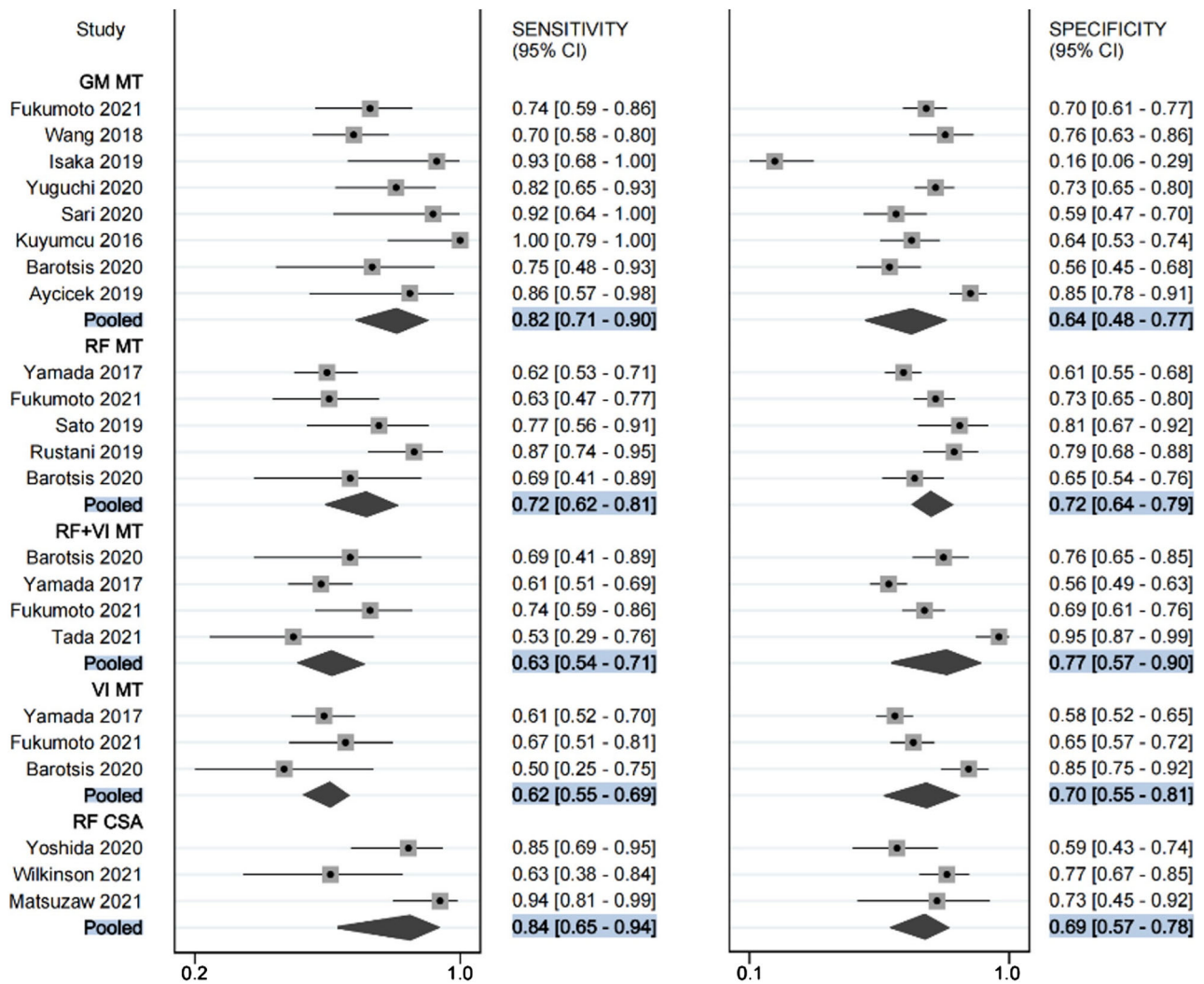


Figure 4 Forest plots of sensitivity and specificity of different ultrasound measurements for diagnosing sarcopenia. CI, confidence interval; CSA, cross-sectional area; GM, *gastrocnemius*; MT, muscle thickness; RF + VI, *quadriceps femoris*; RF, *rectus femoris*; VI, *vastus intermedius*

***Vastus intermedius* muscle thickness** Three studies^{24,30,39} assessed the diagnostic value of *vastus intermedius* MT for sarcopenia. The sensitivity ranged from 50% to 67%, and the specificity ranged from 58% to 85%. The meta-analysis of the three studies indicated that the pooled sensitivity was 62% (95% CI 55–69%) and the pooled specificity was 70% (95% CI 55–81%) (Table 2).

***Quadriceps femoris* muscle thickness** Five studies^{24,30,35,36,39} measured *quadriceps femoris* MT, which is equal to the sum of *rectus femoris* MT and *vastus intermedius* MT. The sensitivity of *quadriceps femoris* MT for diagnosing sarcopenia varied from 53% to 74% and the specificity varied from 56% to 95%. One study was not included in the meta-analysis due to insufficient data.³⁵ Thus, the meta-analysis of the four included studies indicated that the pooled sensitivity was 63% (95%

CI 54–71%) and the pooled specificity was 77% (95% CI 57–90%). The SROC-AUC was 0.64 (95% CI 0.60–0.69) (Table 2).

***Tibialis anterior* muscle thickness** One study²⁸ reported that *tibialis anterior* MT showed a sensitivity of 87% and a specificity of 71% for diagnosing LMM-defined sarcopenia with an AUC of 0.82.

***Soleus* muscle thickness** Two studies^{28,30} assessed the diagnostic value of *soleus* MT for sarcopenia. Fukumoto et al.³⁰ reported that the AUC of *soleus* MT for diagnosing LMM-defined sarcopenia was 0.78 in men and 0.65 in women. The sensitivity was 76.9% in men and 60.0% in women, and the specificity was 65.3% in men and 66.4% in women. Similar results were obtained in another study (AUC 0.76, sensitivity 80%, specificity 67%).²⁸

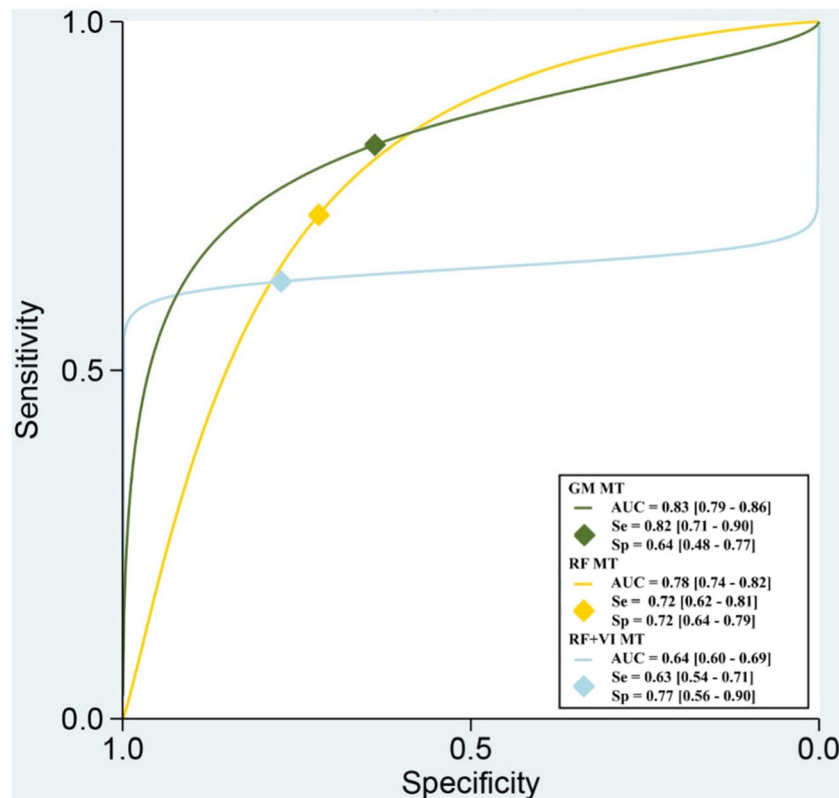


Figure 5 Summary receiver operating characteristic curves of different ultrasound measurements for diagnosing sarcopenia. AUC, the area under the curve; GM MT, the muscle thickness of *gastrocnemius*; RF MT, the muscle thickness of *rectus femoris*; RF + VI MT, the muscle thickness of *quadriceps femoris*; Se, sensitivity; Sp, specificity

Rectus abdominis muscle thickness One included study reported that *rectus abdominis* MT demonstrated an AUC of 0.76 for diagnosing LMM-defined sarcopenia with a sensitivity and specificity of 92.3% and 50.0%, respectively.²⁶

Transversus abdominis muscle thickness In one included study, *transversus abdominis* MT showed an AUC of 0.68 with a sensitivity and specificity of 76.9% and 52.5%, respectively, for diagnosing LMM-defined sarcopenia.²⁶

Geniohyoid muscle thickness *Geniohyoid* MT showed an AUC of 0.79, with sensitivity and specificity of 75.0% and 66.7%, respectively, for diagnosing EWGSOP2-defined sarcopenia.²⁴

Total muscle thickness of multiple muscle groups Fukumoto et al.³⁰ reported that the AUC of the total MT of *gastrocnemius* and *soleus* for diagnosing LMM-defined sarcopenia was 0.84 in men and 0.73 in women. The sensitivity was 84.6% in men and 70.0% in women, and the specificity was 73.5% in men and 63.6% in women. The total MT of *quadriceps femoris*, *gastrocnemius* and *soleus* for diagnosing LMM-defined sarcopenia was 0.85 in men and 0.78 in women. The sensitivity was 92.3% in men and 66.7% in women, and the specificity was 72.3% in men and 76.1% in women.

Cross-sectional area for diagnosing sarcopenia

Rectus femoris cross-sectional area Three studies^{31,32,37} measured *rectus femoris* CSA. The sensitivity ranged from 63% to 94%, and the specificity ranged from 59% to 77%. The pooled sensitivity was 84% (95% CI 65–94%), and the pooled specificity was 69% (95% CI 57–78%) (Table 2).

Biceps brachii cross-sectional area Yoshida and Kumon³⁷ reported that the AUC of *biceps brachii* CSA for diagnosing AWGS 2014-defined sarcopenia was 0.81 with a sensitivity and a specificity of 82% and 72%, respectively.

Echo intensity for diagnosing sarcopenia

Rectus femoris echo intensity Yamada et al.³⁹ reported that *rectus femoris* EI was not a good ultrasound parameter for diagnosing LMM-defined sarcopenia (AUC 0.52, 95% CI 0.39–0.65 in men; AUC 0.61, 95% CI 0.53–0.69 in women). Yoshida and Kumon³⁷ substituted *rectus femoris* EI with the subcutaneous fat thickness. The AUC of *rectus femoris* EI for diagnosing AWGS 2014-defined sarcopenia was 0.67 (95% CI 0.54–0.79) with a sensitivity of 61% and a specificity of 71%.

Vastus intermedius echo intensity Yamada et al.³⁹ reported that *vastus intermedius* EI was not a good ultrasound param-

eter for diagnosing LMM-defined sarcopenia (AUC 0.48, 95% CI 0.36–0.61 in men; AUC 0.50, 95% CI 0.42–0.58 in women).

Quadriceps femoris echo intensity Yamada et al.³⁹ also reported that *quadriceps femoris* EI was not a good ultrasound parameter for diagnosing LMM-defined sarcopenia (AUC 0.49, 95% CI 0.35–0.61 in men; AUC 0.43, 95% CI 0.35–0.51 in women).

Biceps brachii echo intensity Yoshida and Kumon³⁷ reported that the AUC of *biceps brachii* EI for diagnosing AWGS 2014-defined sarcopenia was 0.69 (95% CI 0.58–0.81) with a sensitivity of 67% and a specificity of 70%.

Fascicle length for diagnosing sarcopenia

Gastrocnemius fascicle length Kuyumcu et al.²⁵ reported that *gastrocnemius* FL had a moderate diagnostic accuracy for sarcopenia (right calf: sensitivity 76.9%, specificity 71%, AUC 0.78; left calf: sensitivity 76.9%, specificity 81%, AUC 0.80).

Combination of cross-sectional area and echo intensity for diagnosing sarcopenia

Yoshida and Kumon³⁷ reported that the combination of EI and CSA of *biceps brachii* showed an AUC of 0.85 (95% CI 0.77–0.94) for diagnosing AWGS 2014-defined sarcopenia. The discriminative performance was superior to that of EI alone (AUC 0.69) and CSA alone (AUC 0.81). Similar results were found for the combination of EI and CSA of *rectus femoris* (Table 1).³⁷

Discussion

Our review summarized the current evidence regarding the DTA of muscle ultrasound for diagnosing sarcopenia. The MTs of the *gastrocnemius*, *rectus femoris*, *tibialis anterior*, *soleus*, *rectus abdominis* and *geniohyoid* muscles measured by ultrasound showed a moderate diagnostic accuracy for sarcopenia, whereas the MTs of *vastus intermedius*, *quadriceps femoris* and *transversus abdominis* muscles showed a low diagnostic accuracy. The *rectus femoris* CSA, *biceps brachii* CSA and *gastrocnemius* FL also showed a moderate diagnostic accuracy, whereas the EIs of *rectus femoris*, *vastus intermedius*, *quadriceps femoris* and *biceps brachii* muscles showed a low diagnostic accuracy.

Operators' techniques and experience may have a significant impact on ultrasound measurement results.^{9,14} However, approximately half of the included studies (41%) did not report the data regarding inter- and intra-rater reliability. Additionally, the clinical and methodological heterogeneities were significant across the included studies, including the study populations, the reference standards and the ultrasound measurements (e.g., the type of ultrasonographic probe, the position of the probe, measured body side, body position and measuring points). Thus, the pooled data

should be interpreted cautiously. Moreover, the data from different studies can not be directly compared. The Sarcopenia through Ultrasound (SARCUS) Working Group recently published two consensus^{9,14} to standardize the ultrasound measurements for assessing appendicular muscles, which might be useful for future studies in this field and the implementation of muscle ultrasound in clinical practice. The SARCUS consensus, however, do not specify the cutoff points of ultrasound parameters for different muscle groups to diagnose sarcopenia due to a lack of evidence. Further studies are needed to establish the optimal cutoff points for different ultrasound parameters in various populations.

Our review demonstrated that lower extremity muscles (e.g., *gastrocnemius*, *rectus femoris* and *quadriceps femoris*) were the most widely measured muscles by ultrasound for diagnosing sarcopenia, whereas upper extremity muscles (e.g., *biceps brachii*), head muscles (e.g., *geniohyoid*) and trunk muscles (e.g., *rectus abdominis*) were less evaluated (Figure 2). The reason may be that the lower extremity muscles are easier to measure and are more closely associated with mobility and activities of daily living than the trunk or head muscles.⁴² Currently, the best muscle group to reflect the whole-body muscle mass has not been identified.

Our review revealed that the most common ultrasound parameter for diagnosing sarcopenia was MT, followed by CSA.⁴³ Both MT and CSA represent the muscle quantity. Additionally, some included studies reported EI, an ultrasound parameter reflecting muscle quality. In the context of muscle ultrasound, muscle quality refers to the relative presence of different components of muscle tissue (e.g., muscle, vascular, fibrous and adipose tissue).⁹ Muscle quality has recently been considered as important as muscle quantity for defining sarcopenia.^{4,44,45} This is further supported by our results that demonstrated that the combination of CSA and EI of *biceps brachii* appeared to be better than CSA or EI alone for diagnosing sarcopenia.³⁷ Similarly, the combination of MT and EI of *tibialis anterior* had a better diagnostic value for sarcopenia than MT and EI alone.²⁸ These findings should be validated in different muscle groups in various study populations.

Our systematic review has several limitations. First, although we performed subgroup analyses for the main results based on different reference standards, we were unable to perform further analyses to explore the impact of other clinical heterogeneity on the meta-analysis results because of the insufficient number of studies. Second, current evidence of ultrasound for sarcopenia diagnosis focused on limb muscles. Future studies may address other muscle groups, including the head, neck, thoracic (especially diaphragm), pelvic and hand muscles. Third, only two included studies addressed EI and one included study addressed FL for diagnosing sarcopenia. All three studies were of poor methodological quality. Therefore, caution should be paid

for when explaining the relevant results. Fourth, we only included English publications, which may have resulted in selection bias. Fifth, some new ultrasound parameters, such as pennation angle, muscle contraction potential and muscle microcirculation, have been associated with sarcopenia.^{13,46,47} However, the included studies in our review did not address these parameters. Finally, some new ultrasound technologies, such as panoramic ultrasound imaging⁴⁸ and ultrasonic elastography,⁴⁷ have been applied in sarcopenia research, but our review did not include relevant studies.

In conclusion, muscle ultrasound shows a low-to-moderate diagnostic accuracy for sarcopenia diagnosis depending on different ultrasound parameters, measured muscles, reference standards and study populations. Lower extremity muscles are commonly studied and MT is the most widely measured ultrasound parameter, followed by CSA. The limited evidence indicates that the combination of muscle quality indicators (e.g., EI) and muscle quantity indicators (e.g., CSA) might provide better diagnostic accuracy, but more evidence is required to validate this finding. However, we did not identify the studies on the diagnostic accuracy of new ultrasound technologies (e.g., elastography and panoramic ultrasound imaging) for sarcopenia, which should be explored further in the future.

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Conflict of interest

None declared.

Online supplementary material

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

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