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RESEARCH PAPER

Ultrasound-derived muscle assessment system for older adults: a promising muscle mass estimation tool

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Abstract

Background: Quantitative assessment of muscle mass is a critical step in sarcopenia disease management. Expanding upon the use of ultrasound in foetal growth assessment, we established and validated an ultrasound-derived muscle assessment system for older adults at a risk of sarcopenia.
Methods: A total of 669 older adults were recruited in three cohorts in this cross-sectional study. In cohort 1($n = 103$), the most valuable sites for skeletal muscle mass index (SMI) estimation were located among 11 ultrasound scanning sites. An ultrasound-derived SMI estimating algorithm based on muscle thickness (MT) was obtained in the modelling group composed of cohorts 1 and 2 ($n = 309$). The reliability of the muscle mass estimation equation and the validity of the obtained cut-off values were verified in cohort 3 ($n = 257$), which was selected as the verification group.
Results: In the modelling group, the cut-off values of ultrasound-derived e-SMI for low SMI were 7.13 kg/m^2 for men and 5.81 kg/m^2 for women. In the verification group, the intraclass correlation between e-SMI and SMI was 0.885. The sensitivity of the e-SMI in detecting low SMI was 93.6% for men and 89.7% for women, and the negative predictive value was 94.9% for men and 94.7% for women. Combined with the handgrip strength and gait speed, the e-SMI had an overall diagnostic sensitivity of 92.7% and a specificity of 91.0% for sarcopenia.
Conclusion: The ultrasound-derived muscle assessment system can be a promising muscle mass estimation tool and a potential disease classification tool.

Keywords: ultrasound, muscle, sarcopenia, diagnosis, older people

Key Points

- Quantitative assessment of muscle mass is a critical step in sarcopenia disease management.
- We established an ultrasound-derived muscle assessment system based on three cohorts (hospital, community, ethnic groups).
- The ultrasound-derived muscle assessment system shows robustness in different patient populations within the region.

Introduction

Sarcopenia is an age-associated syndrome of decreased skeletal muscle mass and function [1, 2], and is related to poor prognosis outcome [3–5]. The prevalence of sarcopenia in people aged 65 and over has reached 20% or even higher [6–8]. Currently, sarcopenia can be diagnosed by low skeletal muscle mass index (SMI) plus low handgrip strength (HS) or low gait speed (GS).

According to the European Working Group on Sarcopenia in Older People [9] and the Asian Working Group for Sarcopenia (AWGS) [10], magnetic resonance imaging (MRI) and computed tomography (CT) are considered the gold standards for noninvasive muscle mass assessment. However, the high cost and lack of established normal values with these imaging techniques limit their clinical application. AWGS also recommended dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) as preferred muscle mass assessment methods. However, using DXA for community-dwelling older adults is not yet feasible in primary health care institutions. Moreover, DXA carries a potential radiation risk and is more expensive than BIA, discouraging its use in practice. Given the disadvantages of MRI, CT and DXA, BIA has become the first-choice diagnostic method for sarcopenia in many medical institutions. However, BIA also has some shortcomings, such as the results being affected by hydration status and water distribution in the body [11], and for older adults who have been engaged in manual labour, the thickened callosities in palms or feet may affect the measurement results [12].

Ultrasound is, however, widely available, portable and inexpensive. In the three decades of ultrasound in the assessment of sarcopenia, parameters including muscle thickness (MT), muscle cross-sectional area (CSA), echo intensity (EI), fascicle length (FL), pennation angle (PA) and muscle stiffness have been successively studied [13–15]. Abe et al. [16, 17] proposed a time-consuming method whereby whole-body multisite ultrasound is used to estimate muscle mass. Madden et al. [18] proposed a rapid point-of-care ultrasound protocol, and Narici et al. [15] innovatively proposed a qualitative and quantitative assessment of sarcopenia by combining the MT of the vastus lateralis with the corresponding FL and PA. However, the fitting effect for a single site is not robust enough. We posited that similar results could be achieved by evaluating MT at several valuable muscle sites, which can balance efficiency and effectiveness.

To locate ultrasound measurement sites valuable for quantitative assessment of the muscle mass of the older adults and to develop an ultrasound scanning programme that can quantitatively determine the muscle mass and evaluate site-specific muscle loss in older adults, we designed a cross-sectional study that included three cohorts. Cohort 1 was recruited from our medical institution to identify the most valuable sites for SMI estimation among the 11 ultrasound scanning sites. Cohort 2 was recruited in a community near our medical institution. The subjects of cohorts 1 and 2 together constituted the modelling group to form and adjust the SMI estimating equation parameters and determine the cut-off values of estimated SMI (e-SMI) for low SMI. Cohort 3 was recruited from communities in ethnic plateau areas to verify the reliability of the muscle mass estimation equation and the validity of the obtained cut-off values.

Methods

Study participants

Individuals were primarily included if they met the following criteria: (1) over 60 years of age; (2) patients with suspected sarcopenia, for example, who needed assistance with walking, rising from a chair, or climbing stairs; recently had a history of falls walking; recent unintentional weight loss. The exclusion criteria were as follows: (1) amputated arm or leg, (2) severe oedema, (3) implantable pacemaker, (4) impaired consciousness, poor general health or other reasons that would prevent the individual from completing the study. Severe oedema was defined oedema higher than knee level [19].

The study process was shown in Figure 1. Initially, cohort 1, including 103 hospitalized older adults from the National Clinical Research Center for Geriatrics in West China Hospital, was recruited between June 2020 and May 2021. Cohorts 2 and 3, which included 309 community-dwelling older adults and 257 older adults from ethnic plateau areas in western China, respectively, were recruited between July 2021 and May 2022.

Reference criteria for the diagnosis of sarcopenia followed the AWGS2019 criteria [10]: low muscle mass, low muscle strength and/or low physical performance. Low muscle mass was assessed using the Inbody 770 body composition analyser (Seoul, South Korea) to obtain the SMI (kg/m^2). Low muscle strength was determined based on HS, measured twice on the dominant hand using a handheld dynamometer (EH101; Camry, Zhongshan, China). The highest value was used for the analysis. Low physical performance was assessed by GS using a 4-m walk test.

Reference criteria (BIA, HS test and 4-m walking test) and ultrasound examinations were performed on all recruited participants. BIA was performed by a geriatrician. Ultrasound examinations were performed by two trained sonographers. To ensure comparability between different examinations, examinations of a particular participant were completed within the same day.

BIA measurement

The participants were instructed not to eat, exercise, or drink water within the 2 h before the BIA test, and they were asked to empty their bladder before measurement. During the measurement, participants were instructed to remove metal accessories such as watches, stand barefoot on the pedal, fit the round sensor onto their heel, straighten and separate their arms, and hold the electrodes with both hands. During the test, participants were asked to keep their armpit and arm

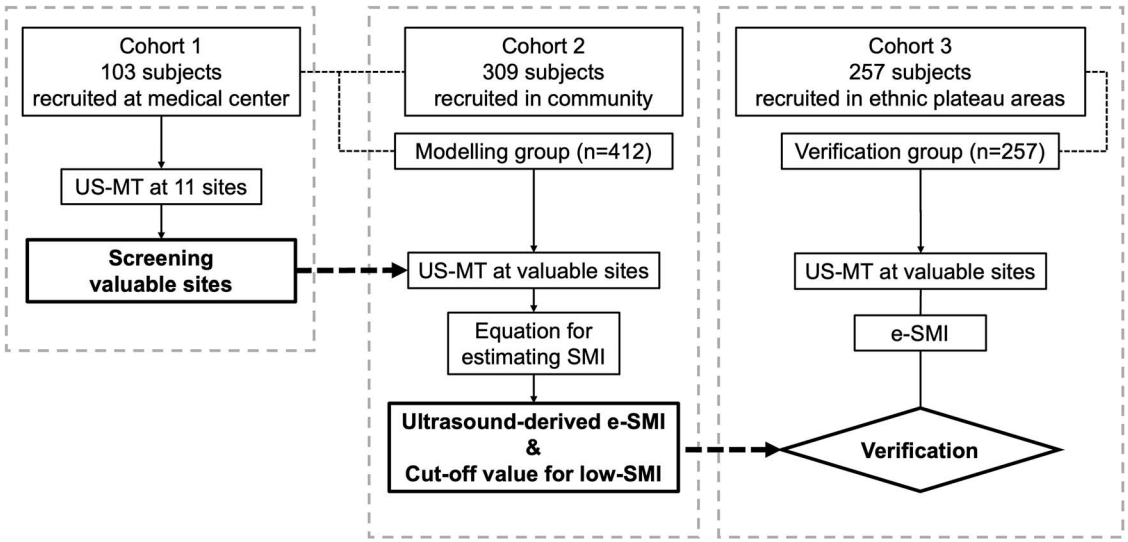

Figure 1. The flowchart of this study. SMI: skeletal muscle mass index; e-SMI: estimated-SMI; US: ultrasound; MT: muscle thickness; BIA: bioelectrical impedance analysis.

at an approximate 15° angle and to keep their inner thighs from touching each other. Participants were asked to remain quiet for the entire duration of the test, and each participant was tested only once.

Ultrasound examination

The sonographic equipment in cohort 1 was the Aixplorer Ultrasound system (SuperSonic Imagine, Aix-en-Provence, France), with an SL 10–2 multifrequency linear transducer. In cohorts 2 and 3, the equipment used was a Mindray M9 Portable Ultrasound Machine (Mindray, Shenzhen, China) with an SL 10–3 multifrequency linear transducer and a Mindray MX7 Portable Ultrasound Machine (Mindray, Shenzhen, China) with an SL 13–3 multifrequency linear transducer.

In cohort 1, MT was measured and recorded at 11 sites throughout the body, including the proximal upper extremity (sites 1 and 2), distal upper extremity (sites 3 and 4), abdomen (site 5), back (site 6), proximal lower extremity (sites 7 and 8), distal lower extremity (sites 9 and 10), waist (site 11). Specific scanning processes, measurement site localisation, corresponding muscle and standard images have been reported in a previous study [20]. In cohorts 2 and 3, only MT at valuable sites were measured and recorded. MT at each site was measured three times, and the average value was taken in the following statistical analysis.

Statistical analysis

Statistical analyses were performed using SPSS 24.0 software (IBM, Armonk, NY, USA), MedCalc software 20.0.4 (MedCalc Software Ltd, Ostend, Belgium) and GraphPad Prism 9.0.0 (GraphPad Software, San Diego, CA, USA). Continuous variables that conformed to a normal distribution were described as the means ± standard deviations, and a *t*-test was used to assess differences between groups. For other continuous variables, the median (25th percentile to 75th percentile) was used, and a Mann–Whitney *U* test was applied for comparison between groups in the case of nonnormally distributed continuous variables. The comparison of proportions was performed using the chi-square test or Fisher probabilities. Multiple linear regression with a stepwise method was used to screen for sites valuable for the estimation of SMI and to establish an estimating model of age, sex, BMI and MT under ultrasound for SMI (excluding parameters with *P*-values over 0.10). For the sexes in the regression, we assigned a value of 1 to males and 0 to females. The acquisition of e-SMI based on a multiple linear regression model and its corresponding 95% confident interval was completed by Eviews software (IHS Global INC, CA, USA). A Bland–Altman plot and intraclass correlation coefficient (ICC) were used to compare the difference and evaluate the consistency between the ultrasound- derived e-SMI and the SMI measured by BIA. Receiver operating characteristic (ROC) analysis was used to determine the cut-off values of the e-SMI for detecting low SMI status. The diagnostic 4-fold table and the corresponding sensitivity and specificity were used to assess the diagnostic accuracy of ultrasonography for low SMI and sarcopenia. A *P*-value of <0.05 was used to indicate statistical significance for two-sided tests.

Results

A total of 669 older adults were recruited for our study. There were certain differences in the demographic characteristics of the modelling group (cohorts 1 and 2) and verification group (cohort 3). There was a significant difference in the ethnic proportion between the two groups. The verification group (cohort 3) was recruited in ethnic plateau areas, where many communities were populated by ethnic minorities, including

Table 1. The demographic characteristics of the model group (cohorts 1 and 2) and verification group (cohort 3)

	Male		Female	
	Modelling group (n = 186)	Verification group (n = 125)	Modelling group (n = 226)	Verification group (n = 132)
Age (years)	71.0 (66.0–76.0)^{ns}	71.0 (68.0–74.0)	69.0 (66.0–72.5)*	71.0 (68.0–75.0)
BMI (kg/m^2)	24.3 (22.2–26.1)*	25.1 (22.9–27.6)	24.2 (22.1–26.4)*	25.0 (23.4–27.0)
Ethnic proportion (Han nationality/minority)	185/1*	42/83	226/0*	61/71
SMI (kg/m^2)	6.97 ± 0.69*	7.17 ± 0.69	5.80 ± 0.64*	5.97 ± 0.67
Proportion of low-SMI	97/186 (52%) *	47/125 (38%)	100/226 (44%) *	39/132 (30%)
Proportion of sarcopenia	38/185 (20%) ^{ns}	20/122 (16%)	37/226 (16%) ^{ns}	21/132 (16%)

BMI: body mass index; SMI: skeletal muscle mass index ns: no significant difference between the model group and verification group in this sex ($P > 0.05$). *Significant difference between the model group and verification group in this sex ($P < 0.05$).

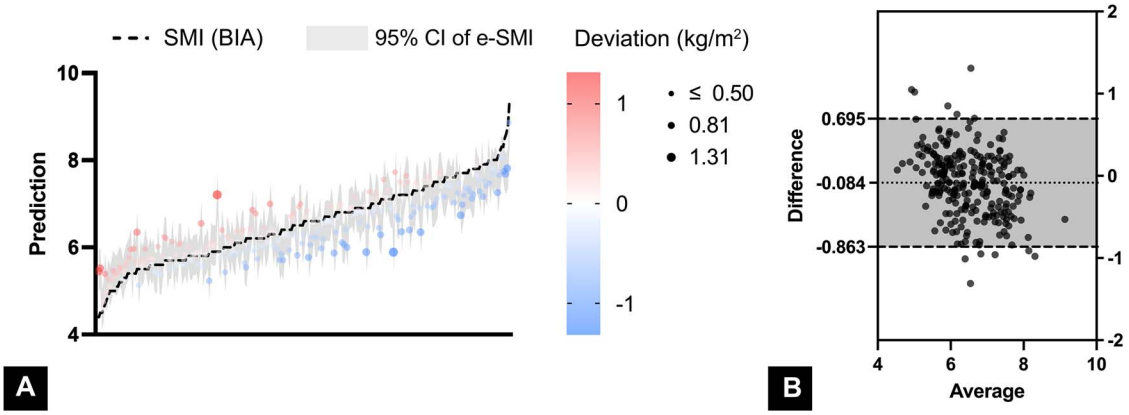

Figure 2. The consistency between ultrasound-derived e-SMI and BIA measured SMI. (A) A bubble chart of the deviation between e-SMI and SMI. The black dotted line represents the SMI, each bubble represents the corresponding e-SMI, and the grey interval represents the 95% CI for e-SMI. When e-SMI is higher than SMI, it appears as red bubbles, and when e-SMI is lower, it appears as blue bubbles. The larger the absolute value of the deviation is, the darker the colour and the larger the size of the bubbles. (B) Bland–Altman plots of the difference between ultrasound-derived e-SMI and BIA-measured SMI. The black dotted line in the middle represents the mean of the difference of e-SMI and SMI, and the grey intervals enclosed by the dotted lines at the upper and lower ends represent the 95% limits of agreement.

Qiang, Tibetan or Hui groups. Therefore, the proportion of the minority in the verification group was significantly higher than that in the modelling group recruited in the plains. For the overall muscle mass, the SMI of the verification group was higher than that of the modelling group, and the proportion of low SMI was lower (38 vs. 52% for men and 30 vs. 44% for women). Despite this, there was no significant difference in the proportion of older adults diagnosed with sarcopenia between the two groups. The detailed comparison is shown in Table 1.

By screening data on subjects from cohort 1 who underwent ultrasound scans at 11 sites, we obtained four valuable sites located in the proximal and distal segments of the upper and lower extremities for muscle mass estimation. We then established a muscle mass estimation equation based on MT at these four sites, BMI, age and sex. The model and parameters are shown in the Supplementary Table S1. The ICC between ultrasound-derived e-SMI and BIA-measured SMI was 0.885, and the the consistency and difference are shown in Figure 2.

Additionally, we divided the participants into a low-SMI group and a normal SMI group according to SMI < 7 kg/m^2 (male) and SMI < 5.7 kg/m^2 (female) determined by BIA in the modelling group, and drew ROC curves to determine the cut-off value of the ultrasound-derived e-SMI for low-SMI in male and female older adults. The ROC curve of the e-SMI for the diagnosis of low-SMI is reported in the Supplementary Table S2. The cut-off value was 7.13 kg/m^2 for men and 5.81 kg/m^2 for women, with AUCs of 0.879 and 0.831, respectively.

Based on this cut-off value, we diagnosed low SMI status and sarcopenia in the verification group, and compared it with the results of the BIA diagnosis as a reference standard. As shown in Table 2, the sensitivity of ultrasound in diagnosing low SMI was 93.6% (44/47) for men and 89.7% (35/39) for women, the specificity was 71.8% (56/78) for men and 77.4% (72/93) for women, and the negative predictive value (NPV) was 94.9% (56/59) for men and 94.7% (72/76) for women. Combined with HS and GS, the new protocol has an overall

Table 2. The diagnostic efficiency of ultrasound in low SMI and sarcopenia. Among them, three men were excluded for the absence of HS data, and one man was excluded for the absence of GS data

			US-based diagnosis	
			+	−
Low SMI	BIA-based diagnosis (men)	+	44	3
		−	22	56
	BIA-based diagnosis (women)	+	35	4
		−	21	72
Sarcopenia	BIA-based diagnosis (men)	+	19	1
		−	8	93
	BIA-based diagnosis (women)	+	19	2
		−	11	100

BIA: bioelectrical impedance analysis; US: ultrasound; SMI: Skeletal muscle mass index +: positive, −: negative

diagnostic sensitivity of 92.7% and a specificity of 91.0% for sarcopenia.

Discussion

Our results showed that the ultrasound-derived e-SMI shows a high diagnostic accuracy for low SMI in older adults, and the sensitivity of ultrasound in diagnosing low SMI was 93.6% for men and 89.7% for women. Both in the plains and plateaus, our two cohort validation results suggest the accuracy of the ultrasound-derived e-SMI.

The older adults in cohorts 1 and 2, which constitute the modelling group, are mainly from urban communities, while the older adults in cohort 3 (verification group) are mostly from highland areas. We observed a certain difference in the MT at specific sites and muscle mass of the two groups. The older adults in the verification group usually had a thinner MT at the proximal extremity and a thicker MT at the distal extremity, a higher SMI and, correspondingly, a lower incidence of low SMI. We speculate that this may be affected by differences in ethnic composition. A previous study based on between healthy Japanese and German men have found that there are certain differences in the age-related, site-specific muscle loss in different ethnic groups [21]. In addition, most of the older adults in the verification group live in mountainous areas and usually do physical labour, and greater activity may delay the progression of age-related muscle loss, which may explain the result that older women in the verification group had a higher median age but a higher mean SMI than the modelling group.

Baseline differences between the modelling and verification groups and possibly differences in the distribution of specific muscle mass undoubtedly posed a challenge to our algorithm, but our results showed that the ultrasound-derived muscle mass estimating equation exhibits impressive robustness. The ultrasound-derived e-SMI had a high consistency with the SMI determined by BIA (ICC = 0.885), and the results of the Bland–Altman plot analysis also showed that the SMI obtained by the two methods had a good consistency, suggesting that ultrasound not only can be used for the quantitative assessment of muscle mass but also has the potential to be an alternative to muscle mass obtained by BIA. However, as our SMI estimation equation is constructed based on multiple linear regression, this determines that our estimation is conservative, especially for those subjects with extremely low or high SMI, our estimates would inevitably have overestimates and underestimations, which can also be observed in the bubble chart.

In the following ROC analysis, we found a preliminary cut-off value for the diagnosis of low SMI using ultrasound in the older adults in the modelling group, and then extrapolated it to the verification group. In the modelling group, the AUCs of the e-SMI for the diagnosis of low SMI in men and women were 0.879 and 0.831, respectively, which was consistent with previous speculation. In previous studies, Fukumoto et al. [22] studied the rectus femoris, femoris intermedius, gastrocnemius and soleus muscles of the lower extremities in a Japanese population and found that the sum of the MTs at the four sites and the AUC for the diagnosis of low SMI in men and women were 0.849 and 0.776, respectively. Although the upper extremity muscles were not included in this study, the diagnostic accuracy for low SMI and the differences between men and women were similar to the results of this study. Sex differences in age-related muscle loss were observed and studied in numerous studies [23–25], and the altered contraction of the muscle fibre [26] and differences in hormone levels and the corresponding regulatory axes [27–30] were considered to be potential influencing factors. In the verification group, the sensitivity of ultrasound in diagnosing low SMI was 93.6% for men and 89.7% for women, and the NPV was 94.9% for men and 94.7% for women. When we attempted to substitute ultrasound-derived e-SMI for traditional BIA-determined SMI in the sarcopenia diagnostic workflow, we found that the new protocol had an overall diagnostic sensitivity of 92.7% and a specificity of 91.0% for sarcopenia. High sensitivity, excellent NPV and good availability all suggest that the four-site ultrasound scanning protocol can be an effective tool for the detection of low-SMI and community screening of sarcopenia. It should be noted that although we designed cohorts for different regions and different ethnic groups, these cut-off values were obtained in a Chinese population of non-obese individuals. However, differences in body composition were observed between the older adults in Asia and Europe or other regions [21, 31, 32], and an increased BMI in older adults may also lead to increased muscle volume and CSA [33]. Additionally, there may be some limitation of BIA for the assessment of body fat in severe obesity [34, 35]. We believe that the cut-off value may need to be adjusted and validated before being applied to other countries and regions.

In addition to high diagnostic accuracy, ultrasound offers great flexibility. On the one hand, ultrasound can quantitatively estimate muscle mass and make an initial diagnosis of low SMI even with MT at a single site [18, 20, 36],

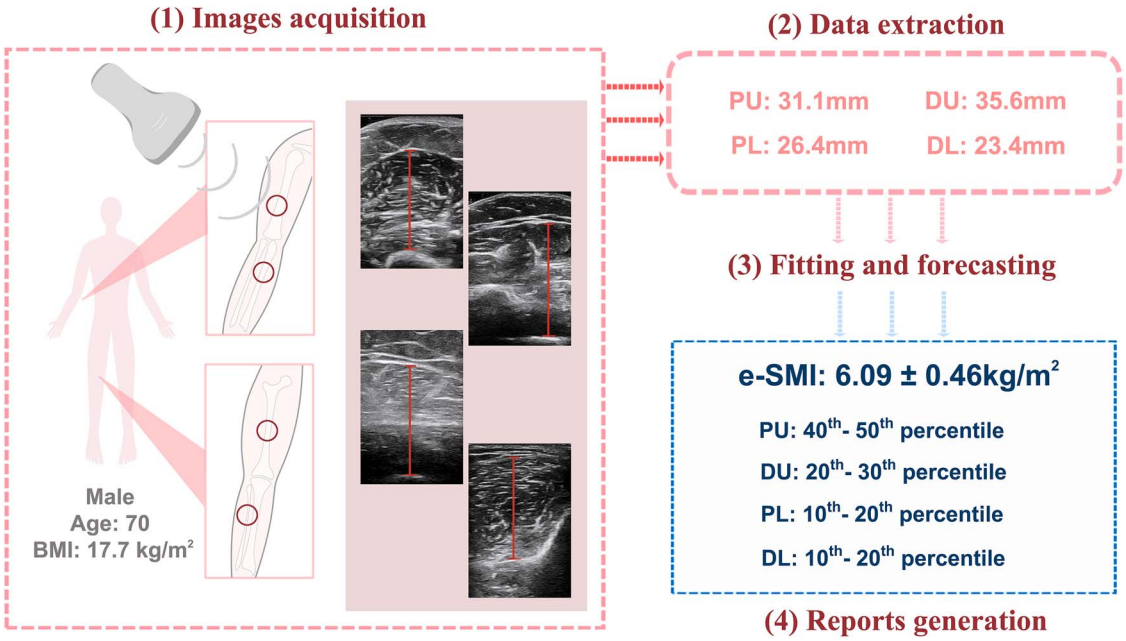

Figure 3. Workflow diagram of the ultrasound-derived muscle assessment system. We measured and input the MT at the target sites to obtain the e-SMI value and determine whether the muscle loss was located in the upper extremity or lower extremity, proximal or distal. PU: proximal upper extremity; DU: distal upper extremity; PL: proximal lower extremity; DL: distal lower extremity; SMI: skeletal muscle mass index.

which suggests that point-of-care ultrasound might be used to achieve rapid exclusion of low SMI. On the other hand, the sites included in this four-site ultrasound scanning protocol are located in the proximal and distal segments of the upper and lower extremities. As shown in Figure 3, we developed a system similar to ultrasonic foetal growth assessment that can be applied to the estimation of muscle mass and muscle mass loss in older adults. By measuring the MT of an older adult at four sites and comparing them with their respective percentiles (preliminary percentiles based on data from 669 older adults in this study were reported in Supplementary Table S3), we can obtain the estimated SMI value and locate the site-specific muscle loss at the same time and distinguish the muscle loss of the older adults into upper or lower extremity, proximal or distal types, etc. A more detailed classification of low SMI or sarcopenia may provide imaging evidence supporting the study of sarcopenia disease prognosis in the future.

This study has several advantages. It was a three-cohort study with strict quality control, representative of different patient populations within the region (hospital, community, ethnic groups), which makes the study more robust. We not only compared ultrasound with muscle mass but also combined the grip strength to diagnose sarcopenia according to the sarcopenia reference standard (AWGS 2019).

However, there are some limitations to this work. First, the ultrasound-derived muscle assessment system was built on BIA. Since BIA was also built on MRI or DXA, this may introduce potential errors to this system. Further research will need to be undertaken to reference ultrasound to MRI or DXA, and the protocol and cut-off value may need to be adjusted and validated before being applied to other countries and regions. Second, BIA can be performed with minimal training as compared with ultrasound, and more efforts on image analysis and artificial intelligence could be made in the future to fully exploit the potential of the ultrasound-derived muscle assessment system.

Conclusion

The ultrasound-derived muscle assessment system has a high diagnostic accuracy for detecting low SMI and sarcopenia and good consistency with BIA results in community-dwelling older adults, which suggests that it can be a promising muscle mass estimation tool and a potential disease classification tool.

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Declaration of Conflicts of Interest: None.

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Guideline Checklist: The authors have completed the STROBE guideline checklist.

Ethical Statement: This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of West China Hospital of Sichuan University (No. 2020[258] and 2021[1509]), and informed consent was obtained from all participants.

Data Sharing Statement: The data used to support the findings of this study are available from the corresponding author upon request.

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