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The application of ultrasound sarcopenia index in sarcopenic population

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A R T I C L E I N F O

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A B S T R A C T

Background: Aging leads to progressive motor system decline, which can result in sarcopenia, defined as the age-related loss of muscle mass and function. Architectural changes, epitomized by a decrease in fascicle length (Lf) and muscle thickness (MT), provide a useful signature of sarcopenia. Their ratio (Lf/MT), named ultrasound sarcopenia index (USI), is a new parameter proposed for evaluating changes in muscle geometric proportions associated with muscle atrophy but lacks application in a sarcopenic population. This study aimed to explore vastus lateralis USI in a sarcopenic population.

Methods: In a sample of 139 older adults (54% females), recruited from Italy and Slovenia, we assessed muscle architecture using ultrasound imaging to measure Lf, MT, pennation angle (PA), and USI. We assessed handgrip strength, sit-to-stand test, and physical performance with timed up-and-go and gait speed. Appendicular lean mass was assessed with dual x-ray absorptiometry. Sarcopenia was classified using the EWGSOP2 and SDOC classifications.

Results: Sarcopenia prevalence was 15.1% and 30.9% when classified by the EWGSOP2 and SDOC classifications, respectively. Differences in muscle architecture were observed between sarcopenic and non-sarcopenic groups, with MT showing the largest effect size (Cohen's d EWGSOP2: 0.86; SDOC:0.77). USI was higher in sarcopenic compared to non-sarcopenic individuals classified with EWGSOP2 (5.33 ± 1.30 vs 4.59 ± 0.94, $p = .011$, Cohen's d:0.69), confirming its sensitivity in detecting sarcopenia.

Conclusion: We showed that increased USI values are associated with sarcopenia. This study shows USI as a sensitive, non-invasive marker for sarcopenia classification, supporting its use in clinical screening and monitoring of muscle changes in older adults.

1. Introduction

Aging is often characterized by declines in multiple domains, including muscular changes, mostly epitomized by sarcopenia, defined as the age-related decrease in muscle mass and muscle function (Cruz-Jentoft et al., 2019). Compared to normal aging, sarcopenic muscle undergoes changes of larger magnitudes, further impacting muscle function and performance and resulting in a decreased ability to perform daily life activities, and an increased risk of falls and fractures (Cruz-Jentoft et al., 2019). Several research groups have proposed classifications to classify sarcopenia (Bauer et al., 2019; Cruz-Jentoft et al., 2010; Bhasin et al., 2020; Fielding et al., 2011; Studenski et al., 2014; Chen et al., 2020) and in 2019 European Working Group on Sarcopenia in Older People updated their classification, where they presented a component of muscle quality in the third, confirmatory step (Cruz-Jentoft et al., 2019). Through the development of sarcopenia definition, most classifications included muscle mass as a key component in determining sarcopenia presence. However, in recent years, muscle strength and physical performance were put at the forefront of classification (Cruz-Jentoft et al., 2019) or even the only two components used in classification (Bhasin et al., 2020) making muscle function the primary component of sarcopenia.

Aging per se causes architectural changes in skeletal muscle, which are a relevant determinant of muscle function (Lieber and Fridé, 2000; Narici et al., 2003). These changes, such as alternations in fascicle length (Lf), pennation angle (PA), and muscle thickness (MT), have been well

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documented throughout aging research. For example, in comparison to younger adults, in older adults, Lf decreases by ~10% and PA decreases by ~13% (Narici et al., 2003). However, less is known about architectural changes in sarcopenia. While it is well known that sarcopenic muscles are overall smaller (Mitchell et al., 2012) in comparison to non-sarcopenic ones, to the best of the authors knowledge, PA and Lf have not been reported in a classified and diagnosed sarcopenic population in thigh muscles.

The underlying mechanisms of sarcopenia are complex and multifaceted. In order to improve definition, the concept of muscle quality was incorporated into the classification to reflect changes in muscle function that occur independently of muscle mass or size (Frontera, 2017). In recent studies, muscle quality is defined and assessed in different ways, e.g. combination of handgrip strength and appendicular skeletal mass (Barbat-Artigas et al., 2012; Brown et al., 2016) or bioelectrical impedance-derived phase angle (Nunes et al., 2019; Akamatsu et al., 2022).

One of the newly proposed methods that could assess muscle quality and be implemented in sarcopenia classification is the ultrasound sarcopenia index (USI), which was defined as a ratio between Lf and MT (Narici et al., 2021). This index is based on muscle architectural and geometrical changes that occur with aging, highlighting a disproportionate decrease in MT compared to the Lf decrease. Ultrasonographic assessment of muscle architecture seems particularly attractive when compared to other existing methods as it is inexpensive, widely available, does not involve ionizing radiation, and is portable, being able to be employed at the bed site (Seynnes et al., 2008; Reeves et al., 2004). In addition, USI has been shown to be independent of sex, body mass, and body height (Narici et al., 2021). However, it has not yet been applied to the sarcopenic population diagnosed according to the most established classifications, as the original article explored USI in groups of older adults with different levels of mobility, and those were later classified into sarcopenia levels according to USI values compared to a young non-sarcopenic population. The aim of our study was to (i) compare architectural characteristics of vastus lateralis (VL) between non-sarcopenic and sarcopenic older adults in groups of participants from two countries, classified with two diagnostic classifications, and (ii) apply the USI in a sarcopenic population.

2. Methods

2.1. Study design and participants

This cross-sectional study included a total of 139 older individuals (54% females), merging one group of 51 Slovenian older participants (53% females) and a group of 88 Italian older individuals (55% females). Participants were recruited from different settings: cultural centers, voluntary associations, nursing homes, community-dwelling groups, and retirement groups across Slovenia and Italy. Participants were included in the study when they were a) older than 65 years, b) were able to walk independently or with a walking aid, and c) were able to understand and follow given instructions. Participants were excluded if they were regular wheelchair users or very physically active (>4 sessions/week), and if they presented a history of serious lower limb musculoskeletal injuries in the last 12 months, severe metabolic and cardiopulmonary disorders, or neurological diseases. All participants provided informed written consent to this study, which was approved by the Slovenian National Medical Ethics Committee (ID: 0120–76/2021/6) for the Slovenian group and the Ethics Committee of the Department of Biomedical Sciences, University of Padova (Italy) (n. HEC- DSB/03–20) for the Italian group. Research has been performed in accordance with the Declaration of Helsinki.

2.2. Ultrasound imaging procedures

In all the participants, VL muscle architecture of the right leg was assessed by ultrasonography at rest by trained operators (K.P. or F.S.), using the same protocol (Narici et al., 2021). Measurements were performed with the participant lying supine on an examination table, using an ultrasound device (MyLab25 Gold or Mylab70, Esaote, Genoa, Italy), fitted with the same probe, a 7–10 MHz, 4.7 cm linear array transducer. The acquisition point was at the distal third (defined as 35% of the distance between the caudal part of the trochanter major and the distal boundary of the lateral femoral condyle) and mid-width of the VL muscle, identified as the mid-distance between the lateral and medial borders. This specific site was selected because it aligns with the region of the VL recommended for muscle biopsies, as it minimizes the risk of neurovascular damage (Narici et al., 2021). Three scans were collected and the best-quality image was analyzed. For all scans, transmission gel was used to ensure the acoustic contact and to keep the pressure on the skin to a minimum. Lf, PA, and MT were assessed manually using the ImageJ software (1.53v, National Institutes of Health, Bethesda, MD). Lf was measured using the segmented line tool using the manual linear extrapolation method. PA was determined as the insertion angle between the fascicle and the deep aponeurosis. MT was measured as the perpendicular distance between a deep aponeurosis and superficial aponeurosis in the proximal, central, and distal portions of the acquired image. For all the parameters, the mean of the three measures was used for statistical analysis. The ratio of Lf/MT was calculated to obtain the USI (Narici et al., 2021). An inter-operator class correlation (ICC) was calculated for 20 images for architectural parameters: Lf ICC = 0.872 (95% CI: 0.667–0.951), PA ICC = 0.812 (95% CI: 0.536–924), MT ICC = 0.988 (95% CI: 0.972–0.995) and for USI - ICC = 0.951 (95% CI 0.872–981). An example of a sarcopenic and non-sarcopenic muscle are presented in Fig. 1.

2.3. Physical performance assessment

Physical performance was measured with habitual gait speed and the timed up-and-go test. The gait speed was measured over the 4 m, the participants started a meter behind the starting line and walked at their habitual speed. The test was repeated twice. Gait speed was calculated for both attempts, and the average was used in the analysis. Timed up-and-go test was done for the assessment of dynamic balance and functional mobility over the 3-m course (Podsiadlo and Richardson, 1991). The score consists of the time in seconds needed to stand up from the chair, walk three meters, pivot around the cone, return, and sit down again. The test was performed twice, and the average of both attempts was used in the analysis.

2.4. Sarcopenia screening and classification

Handgrip strength of the dominant hand was measured with a hydraulic dynamometer (Jamar Smart, Sammons Preston, USA) in a seated position, elbow flexed at 90°. The participants were instructed to squeeze the dynamometer three times with maximal effort. Average of the three attempts was used for the analysis. For the five sit-to-stand test (5STS), the participants were instructed to stand up from the chair to a fully extended position five times as fast as possible with their arms on their chest. Total time was measured with a stopwatch in seconds. For safety reasons, the chair was placed in front of the wall. A whole body scan was performed with the participant lying supine with legs and arms fully extended. Body composition was obtained using dual-energy X-ray absorptiometry (Lunar Prodigy, GE Medicals, Madison WI for the Slovenian group; Hologic Horizon™ QDR RSeries, Bedford, MA, USA for the Italian group). Appendicular lean mass was computed as the sum of arms and legs lean mass, and the sum was normalized to squared body height.

Participants were classified into sarcopenia groups according to the EWGSOP2 classification (Cruz-Jentoft et al., 2019) and the Sarcopenia Definition and Outcome Consortium (SDOC) classification (Bhasin et al., 2020). For both classifications, we used recently proposed modified cut-

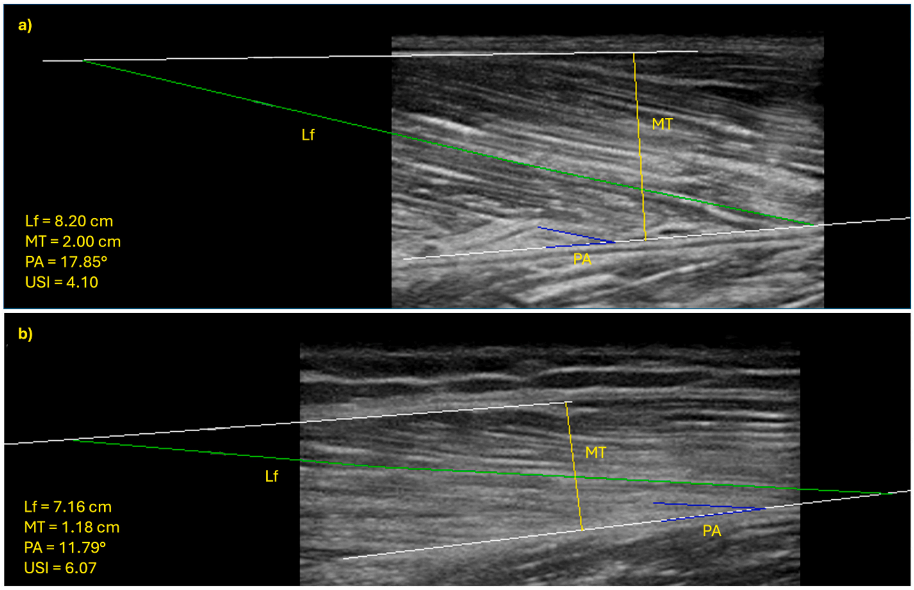

Fig. 1. An example of a a) non-sarcopenic and b) sarcopenic muscle with average values
Note: Lf: fascicle length, MT: muscle thickness, PA: pennation angle, USI: ultrasound sarcopenia index.

off points (Westbury et al., 2023) which leads to higher prevalence rates of sarcopenia while preserving the capacity to predict key health outcomes.

2.5. Statistical analysis

Statistical analysis was conducted in SPSS software (v 29.0.2.0, IBM, Chicago, IL, USA). Normality was assessed with the Shapiro-Wilk test and Levene's test was used for equality of variances. In cases of data non-normally distributed, an appropriate transformation was used, or a non-parametric alternative was used. Descriptive statistics differences were assessed with a *t*-test when normally distributed or non-parametric Mann-Whitney test when non-normally distributed. A two-sided independent samples t-test was conducted to compare muscle architecture parameters between sarcopenic and non-sarcopenic groups. Statistical significance was set at $p < .05$. A Cohen d effect size was reported when significance was reached and interpreted as small (Cohen d < 0.15), medium (0.15 < Cohen d < 0.35) and large effects (Cohen d > 0.75), respectively (Brydges, 2019). In addition, we have performed ROC analysis of USI predicting sarcopenia using EWGSOP2 and SDOC.

3. Results

There was no significant interaction between the origin of participants (i.e., Slovenia or Italy) and group (i.e., sarcopenic or non-sarcopenic) on USI (EWGSOP2: $F(1,123) = 0.073$, $p = .787$; SDOC: $F(1,122) = 2.385$, $p = .125$). Age emerged as a significant covariate in both models (EWGSOP2: $p = .031$, SDOC: $p = .032$), but its inclusion did not alter the interaction results. Therefore, data were pooled for all the analyses.

In the pooled sample of 139 participants, aged 78.23 ± 6.92 (54% females), sarcopenia prevalence was 15.1% with the EWGSOP2 classification and 30.9% with SDOC, respectively and sample characteristics are presented in Table 1.

Values of VL Lf, MT, and USI are reported in Table 2.

Higher USI values were observed regardless of the classification

Table 1
Descriptive statistics using sarcopenia classifications (EWGSOP2 and SDOC).

	Pooled	EWGSOP2		*p*-value (Cohen's d)	SDOC		p-value (Cohen's d)
	n = 139 (54% females)	Non-sarcopenic (*n* = 118)	Sarcopenic (*n* = 21)		Non-sarcopenic (*n* = 96)	Sarcopenic (*n* = 43)	
Age (years)	78.23 ± 6.92	77.26 ± 6.20	83.67 ± 8.34	<0.001[$]	75.92 ± 0.53	83.29 ± 1.23	<0.001[$]
Height (cm)	163.64 ± 10.09	163.59 ± 10.26	163.93 ± 9.27	0.888	164.91 ± 9.97	160.80 ± 9.88	0.026 (0.413)
Body mass (kg)	71.21 ± 13.89	72.96 ± 13.78	61.31 ± 9.95	<0.001 (0.400)	73.23 ± 13.77	66.70 ± 13.23	0.010 (0.416)
BMI (kg/m^2)	26.49 ± 3.99	27.16 ± 3.84	22.73 ± 2.52	<0.001 (0.716)	26.84 ± 0.40	25.76 ± 0.66	0.233[$]
ALM (kg)	18.43 ± 4.54	18.9 ± 4.54	15.76 ± 3.55	0.003 (0.712)	19.11 ± 0.48	17.08 ± 0.63	0.022[$]
ALM/ht^2 (kg/m^2)	6.79 ± 1.07	6.97 ± 1.02	5.80 ± 0.79	<0.001 (1.184)	6.93 ± 0.11	6.50 ± 0.15	0.062[$]
Hand grip strength (kg)	26.02 ± 9.26	26.82 ± 9.11	21.50 ± 8.98	0.007[$]	28.72 ± 0.90	20.53 ± 1.19	<0.001[$]
Timed up-and-go (s)	9.95 ± 6.77	9.13 ± 5.42	14.56 ± 10.84	0.015[$]	7.33 ± 0.15	14.22 ± 1.31	<0.001[$]
5 sit-to-stand (s)	12.97 ± 5.18	12.48 ± 4.92	15.68 ± 5.82	0.006[$]	11.08 ± 0.29	17.06 ± 1.03	<0.001[$]
Gait speed (m/s)	1.02 ± 0.28	1.05 ± 0.27	0.87 ± 0.31	0.016[$]	1.15 ± 0.20	0.74 ± 0.21	<0.001 (2.057)

[$] Non-parametric Mann-Whitney test, ALM: appendicular lean mass, ALM/ht^2: appendicular lean mass normalized to squared body height.

Table 2
Values of muscle architecture parameters in non-sarcopenic and sarcopenic groups classified with EWGSOP2 and SDOC.

		Non-sarcopenic	Sarcopenic	p-value	Cohen's d
EWGSOP2	Fascicle length (cm)	7.58 ± 1.27	7.52 ± 1.21	0.869	
	Pennation angle (°)	15.12 ± 2.95	14.41 ± 3.04	0.346	
	Muscle thickness (cm)	1.68 ± 0.31	1.41 ± 0.35	<0.001*	0.855
	USI	4.59 ± 0.94	5.33 ± 1.30	0.011*	0.688
SDOC	Fascicle length (cm)	7.65 ± 1.18	7.37 ± 1.44	0.269	
	Pennation angle (°)	15.07 ± 2.99	14.86 ± 2.92	0.707	
	Muscle thickness (cm)	1.71 ± 0.30	1.47 ± 0.34	<0.001*	0.767
	USI	4.55 ± 0.85	5.01 ± 1.33	0.082	

EWGSOP2: European Working Group on Sarcopenia in Older People revised classification, SDOC: Sarcopenia definition and outcomes consortium classification; USI: ultrasound sarcopenia index.
* $p < .05$.

used, however, they reached significance ($p = .011$) only when using EWGSOP2 (Fig. 2).

We performed an ROC analysis and found that ROC = 0.673 (95% CI: 0.524–0.823) which can be considered as moderate predictive value. In addition, we performed a ROC analysis of USI predicting sarcopenia using SDOC, we found ROC = 0.566 (95% CI: 0.438–0.694), which is not considered an acceptable predictive value.

4. Discussion

The aim of our study was twofold: to compare architectural characteristics of VL between non-sarcopenic and sarcopenic older adults, classified with two different sarcopenia definitions (EWGSOP2 and SDOC), and to explore the USI in a population clinically classified for sarcopenia. The main findings of our study are that: (i) MT but not PA, and Lf differed between the two groups, (ii) the USI was greater in the sarcopenic group.

4.1. Differences in muscle thickness and architecture in sarcopenia

We found smaller VL MT in individuals with clinically diagnosed sarcopenia compared to non-sarcopenic older adults. Previous studies showed that MT predicts clinical and functional outcomes (Casey et al., 2022) and decreases with aging (Narici et al., 2003; Vezzoli et al., 2019). This decrease was previously reported to be more pronounced in sarcopenic individuals in the gastrocnemius medialis than in non-sarcopenic individuals (Kuyumcu et al., 2016; Ticinesi et al., 2017). Studies that looked into strength decline in aged populations found strong correlations between MT and muscle strength (Strasser et al., 2013; Selva Raj et al., 2017), which is the main pillar of current sarcopenia classifications. Our findings suggest that MT is sensitive to changes in sarcopenia also in the thigh muscle. This is also supported by literature suggesting that MT is strongly associated with muscle volume assessed by magnetic resonance imaging (Franchi et al., 2018), the gold standard to assess muscle mass, which has been the main component to classify sarcopenia throughout the development of sarcopenia definition.

We found no differences in Lf between groups, regardless of the classification used, supporting the theory that MT declines more than Lf in sarcopenia (Narici et al., 2021). Similar results in VL have also been confirmed by others (Bres et al., 2023). Changes in Lf with aging have been less uniform, but one possible explanation could lie within the length of a muscle and consequently Lf. This length is limited by muscle's attachment into the proximal and distal tendons, and although Lf has been shown to decrease with age (Kubo et al., 2003), this decline is likely restricted by fixed tendon insertions into the bone. Secondly, Lf represents the number of sarcomeres in series (Narici et al., 2003; Mitchell et al., 2012), and from our results, we could suggest that sarcopenic muscle does not show shorter Lf when compared to non-sarcopenic ones. Even though a decline of Lf was found to be associated with aging, our results indicate that as sarcopenia progresses, the decrease in MT surpasses that of Lf, which confirms previous findings of Narici et al (Narici et al., 2021).

Similarly, we found no differences between the groups in PA. PA reflects sarcomeres in parallel and is generally viewed as a mechanism for accommodating more contractile elements along the deep aponeurosis (Narici et al., 2016; Sarto et al., 2021). Our finding is consistent with previous research showing that VL PA in sarcopenic individuals does not differ from non-sarcopenic ones (Bres et al., 2023). However, when comparing younger and older adults, PA has been shown to

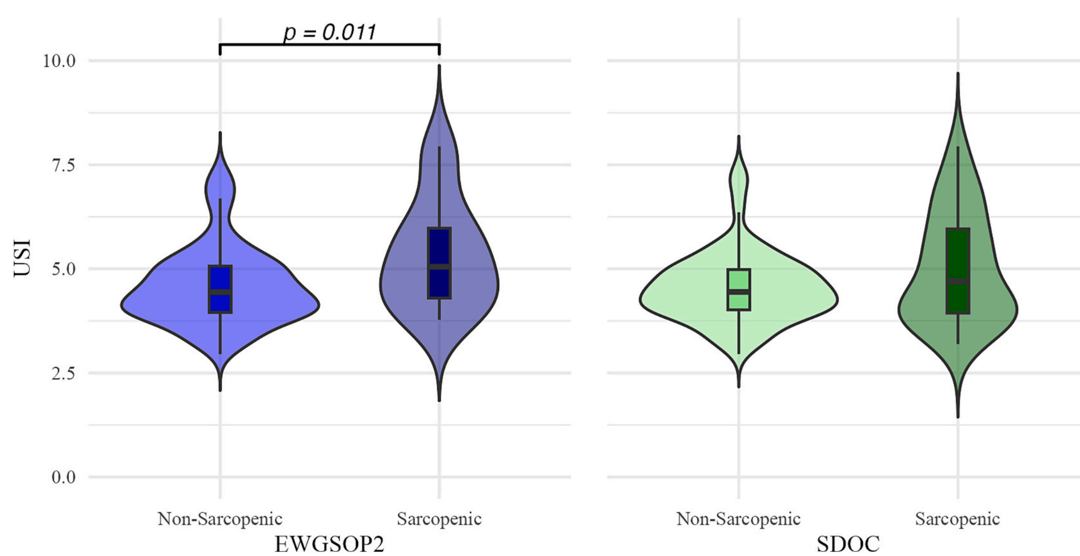

Fig. 2. USI values in sarcopenic and non-sarcopenic groups classified with EWGSOP2 and SDOC
Note: USI: ultrasound sarcopenia index; EWGSOP2: European Working Group on Sarcopenia in Older People; SDOC: Sarcopenia Definition and Outcome Consortium.

decrease with aging (Narici et al., 2003). Conversely, PA has been shown to increase with strength training (Suetta et al., 2008) and thus with hypertrophy. Therefore, considering the reduced muscle mass typically observed in sarcopenic adults, a decrease in PA might be expected. However, our findings do not show differences in PA values between sarcopenic and non-sarcopenic individuals. The lack of difference in PA is indeed surprising given that an increase in the ratio of Lf/MT predicts a decrease in PA since Lf/MT is the cosecant of PA. We did observe lower absolute values of PA in sarcopenic groups, however these were not large enough to be significant. As the literature in the area between sarcopenic and non-sarcopenic individuals is scarce, this would benefit from being explored in a larger cohort.

4.2. Differences in the USI in sarcopenia

The sarcopenic group presented higher USI values compared to the non-sarcopenic counterparts. The first study introducing USI (Narici et al., 2021) justified its use by suggesting that if changes in Lf and MT occurred at the same rate, USI would remain unchanged. Similar to observations from the original authors, we have confirmed that the decrease in MT exceeds that in Lf (see above), resulting in an increased USI. The same article proposed a cut-off value for USI being above 4.76, which holds true for both of our sarcopenic classifications (EWGSOP2: 5.33 ± 1.30 and SDOC: 5.01 ± 1.33).

Notably, the USI results differed depending on the sarcopenia classification used. When using the EWGSOP2 classification, differences between groups were observed, whereas when using the SDOC classification, statistical significance was not reached. A key distinction between these two classifications lies in their criteria: EWGSOP2 includes a muscle mass component, while SDOC does not. This suggests that the presence of a muscle mass criterion may play a crucial role in detecting variations in muscle characteristics assessed by USI. The lack of observed differences with SDOC classification could indicate that muscle strength and function alone may not fully capture the structural muscle changes that USI reflects. At the same time, our findings highlight the need for standardization in sarcopenia definition (Coletta and Phillips, 2023), as using different classifications could lead to different outcomes.

Given that sarcopenia involves not just muscle mass loss but also a component of muscle quality (Cruz-Jentoft et al., 2019), USI, considering changes in muscle geometric proportions rather than muscle size, provides a crucial advantage over traditional imaging methods. This makes USI a relevant tool for sarcopenia and a potential diagnostic tool to improve classification and risk stratification in older adults. It has been previously shown that USI is not affected by sex, body mass, and height differences, which makes it a valuable and easy-applicable metric in clinical settings.

Lastly, the ROC analysis showed that when sarcopenia was diagnosed with EWGSOP2, USI demonstrated a moderate predictive value (AUC = 0.673; 95% CI: 0.524–0.823). Although this level of discrimination is not sufficient for diagnostic use alone, it suggests that USI may capture relevant muscle characteristics associated with sarcopenia as defined by EWGSOP2. These findings support the potential role of ultrasound-derived indices as complementary tools for the assessment of muscle health.

In contrast, when SDOC was used, the predictive performance of USI was poor (AUC = 0.566; 95% CI: 0.438–0.694). This limited discriminative ability is consistent with our results, in which SDOC classification did not reveal significant differences between groups. One possible explanation is that the SDOC definition places greater emphasis on functional measures (e.g., grip strength and gait speed) and does not incorporate direct measures of muscle mass. As USI primarily reflects muscle architectural properties assessed by ultrasound, its predictive value may be more closely aligned with frameworks that incorporate muscle mass, such as EWGSOP2.

Importantly, there is currently no gold standard definition of sarcopenia. Because ROC analysis requires a clearly defined reference standard to classify individuals as diseased or non-diseased, the estimated performance of USI depends on the used classification. As a result, differences between sarcopenia definitions can substantially influence ROC outcomes and limit the generalizability of the findings. Therefore, the interpretation of the present ROC analysis should be considered within the context of the specific diagnostic frameworks applied. Overall, these findings suggest that while USI shows some promise as a marker related to sarcopenia, its predictive capacity may be considered modest and seems to depend on the diagnostic framework used. Further studies with larger samples are needed to determine optimal thresholds and to evaluate whether USI can enhance current sarcopenia screening or assessment strategies when combined with functional measures.

5. Conclusions

In conclusion, our study highlights key differences in VL architecture between sarcopenic and non-sarcopenic older adults. For the first time, we showed that increased USI values are associated with sarcopenia, supporting USI's potential as a diagnostic tool. Future research should explore its broader clinical applications and contribute to standardizing sarcopenia classification. This index has been explored only on VL, however it would be beneficial to explore its potential on other muscle groups.

CRediT authorship contribution statement

Katarina Pus: Writing – original draft, Validation, Project administration, Investigation, Formal analysis, Data curation, Conceptualization. **Fabio Sarto:** Writing – review & editing, Writing – original draft, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Marco Narici:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization. **Boštjan Šimunič:** Writing – review & editing, Supervision, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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