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ORIGINAL ARTICLE

The ultrasonographic measurement of muscle thickness in sarcopenia. A prediction study

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ABSTRACT

BACKGROUND: Sarcopenia is a common disease in the elderly. Although extensive research has been conducted on muscle mass and quality assessment tools, there are still certain drawbacks preventing their universal use.
AIM: The aim of this study was the evaluation of the thickness of head, neck, upper and lower limb muscles measured with ultrasonography, as a potential predictory tool in sarcopenia.
DESIGN: Prediction study.
SETTING: The Outpatient Sarcopenia Clinic of the Rehabilitation Department of the University Hospital of Patras.
POPULATION: Ninety-four individuals (27 men and 67 women) with a mean age of 75.6 years (SD=6.6), referred for sarcopenia screening, participated in this study.
METHODS: The muscle thickness was measured with transverse and longitudinal ultrasound scans bilaterally.
RESULTS: The thickness of the geniohyoid and medial head of gastrocnemius muscle in all ultrasound sections, and the thickness of the rectus femoris and vastus intermedius muscle, in specific sections, was found to be significantly decreased in patients with sarcopenia ($P<0.05$). The Receiver Operating Characteristic (ROC) curve analysis of the ultrasound muscle thickness measurements resulted in a significant association with sarcopenia. In the case of the geniohyoid muscle, the measured area under the ROC curve was found to be the highest (0.79). The optimal cut-off for the prediction of sarcopenia from the geniohyoid muscle was 0.65 cm with sensitivity equal to 75.0% and specificity equal to 66.7%.
CONCLUSIONS: The results of this study have shown that the thickness of the neck and lower limb muscles measured ultrasonographically can be utilized in the prediction of sarcopenia with high sensitivity and specificity.
CLINICAL REHABILITATION IMPACT: The prevalence of sarcopenia in the geriatric population and the rehabilitation wards is reported to be high. Therefore, an easy, fast, low cost and with no risk, widely available method such as ultrasonography could be an extremely valuable tool for the screening and follow-up of sarcopenia.

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KEY WORDS: Ultrasonography; Sarcopenia; Neck muscles; Muscle, skeletal; Quadriceps muscle.

In 2016, sarcopenia was recognized as a disease, which was assigned an ICD-10-CM code (M62.84), and was recently included as a health condition in the "Packages for Rehabilitation Interventions" by the World Health Organization.[1, 2] Sarcopenia has been characterised as a syndrome, associated with a significant functional decline, higher rate of falls, impaired ability to perform activities of daily living, a higher incidence of hospitalization, a higher mortality rate and a high economic burden when untreated.[3, 4] The prevalence of sarcopenia has been reported to range between 4.3% and 73.3%, depending on the screening tools, the criteria used to establish the diagnosis, and the study population.[4] Interestingly, the prevalence of sarcopenia was found to be 53.0% in the inpatient convalescent rehabilitation ward.[5]

The prompt diagnosis and management considering the ageing population are of paramount importance for sarcopenia.[6-9] The diagnosis of sarcopenia is based on the assessment of muscle strength, muscle mass and physical performance. However, there is no universal consensus on the assessment methods in clinical practice, and it is technically challenging to measure muscle mass and muscle quality accurately.[10]

The quantitative assessment of muscle mass can be performed by magnetic resonance imaging (MRI) and computed tomography (CT), which are considered as the gold-standards.[3, 11] However, these tools are not commonly used in daily clinical practice, mainly due to the high cost, lack of portability and, in case of CT, exposure to ionizing radiation. Dual-energy X-ray absorptiometry (DXA) is a more widely available method to determine full-body muscle mass.[3] A significant disadvantage of DXA is that equipment is not portable, limiting its use as a diagnostic or screening tool in the community.

The ultrasound muscle thickness measurement has been suggested as a useful tool in the early detection and monitoring of sarcopenia.[12] According to published studies, ultrasound is a reliable and valid tool for the assessment of muscle size in older adults.[13, 14] Commonly used measurements include muscle thickness, cross-sectional area, fascicle length, pennation angle, and echo-intensity.[15] Measuring muscle thickness can provide an estimate of the reduction in lean body mass.[16] Thickness and fascicle length values of medial gastrocnemius muscle have been proposed as alternative measurements for diagnosing/quantifying sarcopenia.[17] Equations for muscle mass prediction, based on multiple ultrasound muscle thickness measurements have been published.[18, 19]

A drawback of the ultrasonographic measurement techniques is that they present a degree of examiner dependency, which is higher in comparison with other imaging modalities used to measure muscle mass, such as DXA, CT scanning and MRI.[20] The orientation of the ultrasound transducer relative to the body surface, the compressive or shear stress on tissue through the force exerted by the examiner and the characteristics of the intervening subcutaneous adipose tissue can alter tissue dimensions and echo intensity. Changes in the ultrasound transducer orientation may result in measurement errors when estimating muscle size and ultrastructure features, such as the pennation angle.[21]

This study aims to investigate which muscles of the head, neck, upper and lower limbs present ultrasonographically detectable thickness changes in sarcopenic patients. More specifically, the aim was to define which side (dominant *versus* non-dominant) and ultrasound section (transverse *versus* longitudinal) presented the most significant thickness changes in each of the studied muscle groups of the sarcopenic patients and to evaluate the muscle thickness measurement, as a potential predictory tool in sarcopenia.

Materials and methods

Consecutive individuals over 60 years of age referred for sarcopenia screening to the Outpatient Sarcopenia Clinic of the Rehabilitation Department of Patras University Hospital, from June 2018 until December 2019, from municipal community centres for the elderly and other clinical settings were enrolled into this study. Individuals with a history of cranial or limb fracture and head, neck or limb surgery during the last twelve months, tremor, paresis, amputations, autoimmune disorders affecting the musculoskeletal system, individuals presenting head, neck or limb muscle atrophy due to peripheral neuropathies, and those under medication which could potentially affect muscle architecture and echogenicity (steroids) were excluded from the study.

The diagnosis of sarcopenia was made in accordance with the criteria and cut-off points proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) in the revised European consensus on definition and diagnosis.[3] More specifically, muscle strength was measured by a hand-held Jamar dynamometer. The best of the six grip strength measurements was used, with cut-off points <27 kg for men and <16 kg for women.[3, 22] The appendicular skeletal muscle mass (ASM) was measured by dual-energy X-ray absorptiometry (DXA); the cut-off point of ASM/height^2 was <7.0 kg/m^2 for men and <5.5 kg/m^2 for women.[3] The assessors of DXA did not have access to the clinical information or the results of ultrasonographic thickness measurements. Initially, this study was based on the available EWGSOP diagnostic criteria, published in 2010.[23] When the revised EWGSOP diagnostic criteria were published, the diagnosis of sarcopenia for the individuals already examined was also revised, following the new criteria. The study was approved by the Bioethics Committee of the University Hospital of Patras (registration number: 401, date 12/6/2018, chairperson: Alexandra Lekkou, M.D.) and was conducted according to the Declaration of Helsinki. All participants were informed in detail about this research and gave their written consent.

The ultrasound images were acquired using the GE Logiq P9 ultrasound system equipped the ML6-15 linear array transducer (GE Healthcare GmbH, Freiburg, Germany). All image optimization modes were switched off, except the harmonic tissue imaging, to avoid alteration of image characteristics by software processing. The gain was set to 50, the dynamic range at 66 dB, the frequency at 10 MHz and all of them were kept constant throughout the examination. The depth was set at 3 cm for head and

neck muscles, 6 cm for rectus femoris and vastus intermedius muscles and 4 cm for all other muscles. Whenever required, the depth was increased to include the whole muscle in the image. The focal zones (up to six) were distributed evenly along with the depth of the image. A generous quantity of ultrasound gel (CLEAR ECO Supergel, Ceracarta S.p.A., Forlì, Italy) was used to achieve the optimal ultrasound beam coupling and to prevent deformation of the soft tissues due to transducer pressure during the examination. The ultrasound examination of all subjects was performed by the same experienced musculoskeletal sonographer (NB). The transducer was placed perpendicular to the skin and eventually slightly angled (in the elevational direction) to achieve the brightest echo from muscle fascia.

The goal of this study was to assess muscles involved in standing, ambulation, upper limb function and swallowing. Therefore, the following anatomical sites were selected: for the anterior arm muscles at two-thirds of the distance from the acromion to the elbow crease; for the rectus femoris muscle halfway along the line from the anterior–superior iliac spine to the superior pole of the patella; for the tibialis anterior muscle at one-quarter of the distance from the inferior pole of the patella to the malleolus lateralis[24] and at the bulkiest part of the medial head of gastrocnemius muscle.[25] The subjects were examined lying in a prone position for the gastrocnemius scans with the foot hanging off the examination bed and in a supine position for all other muscle groups of the lower and upper limbs. They were instructed to remain completely relaxed during ultrasound scanning and image recording, with the upper and lower limbs extended. The masseter muscle was examined at rest, with the subject in a sitting position. The probe was placed parallel to the mandibular margin, perpendicular to the skin surface, approximately midway between the zygomatic arch and the mandibular angle.[26, 27] The thickness of the masseter muscle was measured at the thickest part in both the transverse and longitudinal planes. Transverse and longitudinal sonograms were recorded from all muscles bilaterally. First, the transverse ultrasound section was acquired, and then the transducer was rotated to 90° to acquire the longitudinal section. The geniohyoid muscle thickness was measured with the transducer placed on the sagittal plane, between the symphysis menti and hyoid bone,[14] with the subject positioned as for the examination of the masseter muscles.

Muscle thickness was measured with the built-in electronic callipers of the scanner (Figure 1, 2). The geniohyoid muscle was measured between the deep and superficial muscle fascia; the masseter muscle was measured between

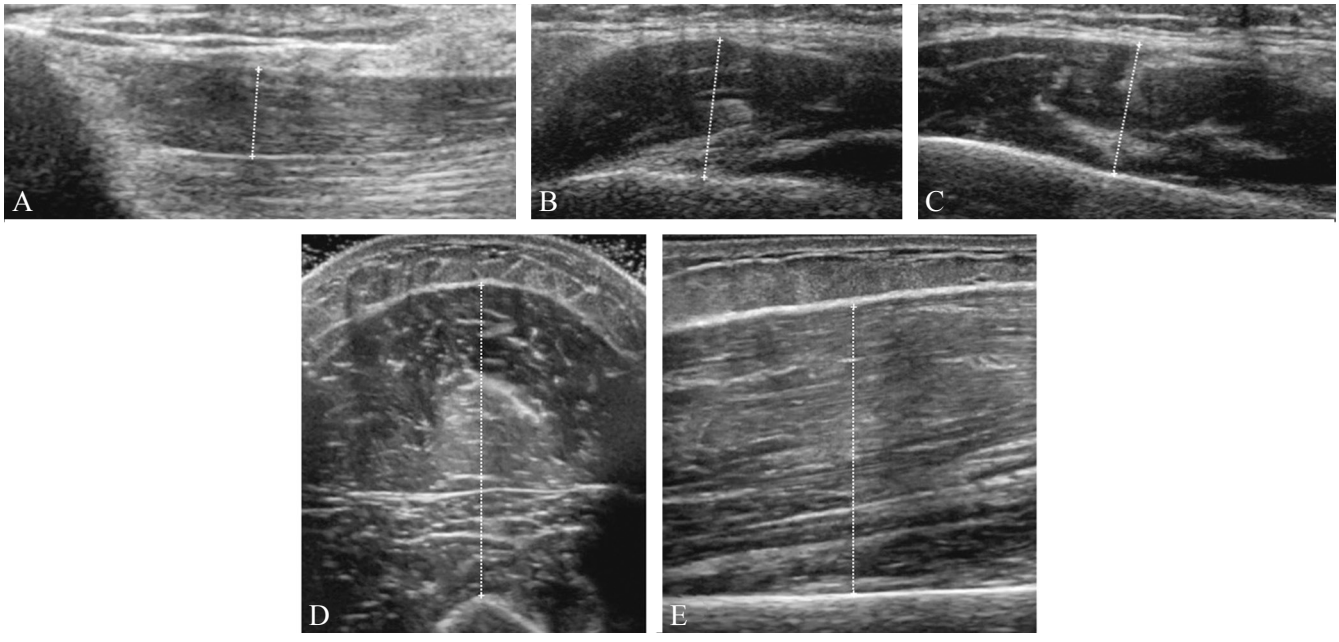

Figure 1.—Thickness measurement of the head, neck and upper limb muscles. The images present the placement of the electronic callipers for the geniohyoid muscle (A); masseter in the transverse (B) and longitudinal section (C); anterior arm muscles in the transverse (D) and longitudinal section (E).

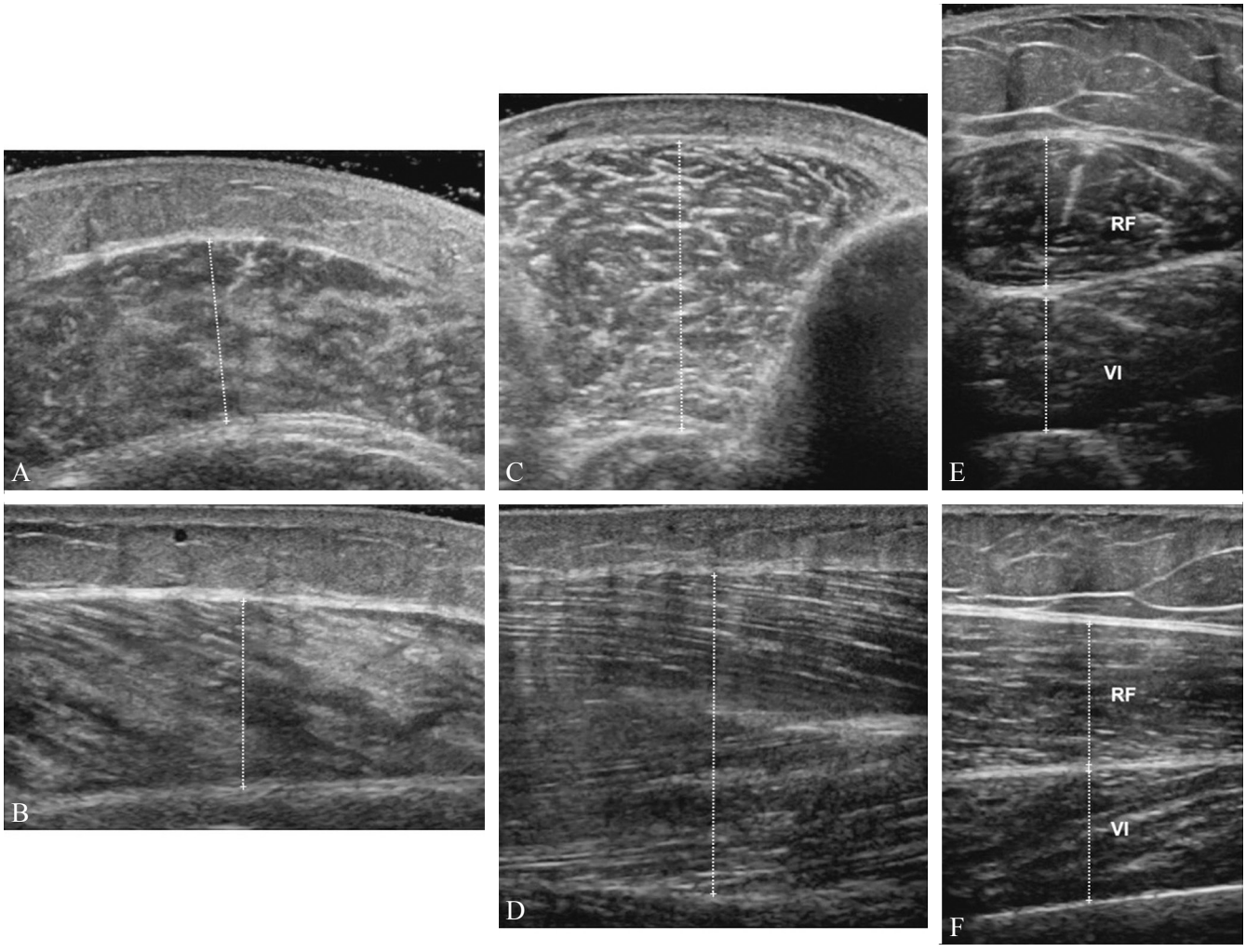

Figure 2.—Thickness measurement of lower limb muscles. The images present the placement of the electronic callipers for the medial head of gastrocnemius in the transverse (A) and longitudinal section (B); tibialis anterior in transverse (C) and longitudinal section (D); quadriceps femoris in the transverse (E) and longitudinal section (F).

the cortex of the mandible and the superficial fascia of the masseter. The anterior arm muscles were measured between the cortex of the humerus and the superficial fascia of the biceps. It should be noted that this measurement included the biceps brachii and the underlying brachialis muscle. The thickness of the rectus femoris was measured between its deep and superficial fascia; the vastus intermedius between the cortex of the femur and the superficial fascia of the vastus intermedius; the tibialis anterior between the interosseous membrane (next to the tibia) and the superficial fascia of the tibialis anterior; and the medial head of gastrocnemius between its deep and superficial fascia. Clinical information, grip strength and DXA results were not available to the performers of muscle thickness measurements.

Statistical analysis

Quantitative variables are expressed as mean value and standard deviation (SD). Qualitative variables are expressed as absolute and relative frequencies. For the comparison of means between two groups, the Student's *t*-test was used. For the comparisons of proportions, the χ^2 tests and Fisher's Exact tests were used. Ultrasonographically acquired measurements of muscle thickness were tested for their ability to predict sarcopenia using receiver operating characteristic (ROC) curves. The overall performance of the ROC analysis was quantified by computing the area under the curve (AUC). An area of 1 indicated perfect performance, while 0.5 indicated

a performance that was not different than chance. Using ROC analysis, the optimal sensitivity and specificity of various cut-off values for the prediction of sarcopenia were determined. A series of multiple logistic regression analysis was performed to identify the association of ultrasonographically acquired measurements of muscle thickness with sarcopenia, after adjusting for gender and age. Adjusted odds ratios with 95% confidence intervals were computed from the results of the logistic regression analyses. All reported P values are two-tailed. Statistical significance was set at P<0.05 and analyses were conducted using SPSS statistical software (version 22.0).

Results

A total of 103 subjects over 60 years of age were enrolled in the study as potentially eligible. Two individuals refused to undergo the full-body DXA scan and 7 were excluded, according to the exclusion criteria. The sample consisted

TABLE I.—*Demographic characteristics and muscle thickness measured ultrasonographically in the total sample and by gender.*

	Total sample (N.=94)	Women (N.=67; 71.3%)	Men (N.=27; 28.7%)	P
Age	75.6 (6.6)	75.1 (6.5)	76.9 (6.7)	0.223+
Dominant side, N (%)				
Right	91 (96.8)	65 (97.0)	26 (96.3)	1.000‡‡
Left	3 (3.2)	2 (3.0)	1 (3.7)	
BMI (kg/ m^2)	28.2 (4.6)	29.1 (4.3)	26 (4.7)	0.003+
BMI, N (%)				
Normal	20 (21.3)	10 (14.9)	10 (37.0)	0.018‡
Overweight/ obese	74 (78.7)	57 (85.1)	17 (63.0)	
Hand grip strength (kg)	22.5 (6.82)	20.37 (4.68)	27.71 (8.37)	<0.001+
Gait speed	0.89 (0.23)	0.87 (0.20)	0.95 (0.27)	0.096+
TA - Trans (D) (cm)	2.44 (0.37)	2.33 (0.29)	2.72 (0.40)	<0.001+
TA - Long (D) (cm)	2.57 (0.39)	2.47 (0.32)	2.81 (0.44)	<0.001+
TA - Trans (ND) (cm)	2.39 (0.36)	2.28 (0.29)	2.67 (0.37)	<0.001+
TA - Long (ND) (cm)	2.49 (0.37)	2.39 (0.33)	2.74 (0.36)	<0.001+
RF - Trans (D) (cm)	1.68 (0.34)	1.61 (0.29)	1.83 (0.41)	0.004+
VI - Trans (D) (cm)	1.30 (0.41)	1.25 (0.37)	1.43 (0.49)	0.050+
RF - Long (D) (cm)	1.56 (0.33)	1.52 (0.29)	1.66 (0.41)	0.065+
VI - Long (D) (cm)	1.30 (0.42)	1.24 (0.37)	1.46 (0.49)	0.023+
RF - Trans (ND) (cm)	1.64 (0.33)	1.58 (0.30)	1.77 (0.38)	0.012+
VI - Trans (ND) (cm)	1.25 (0.36)	1.21 (0.35)	1.37 (0.38)	0.055+
RF - Long (ND) (cm)	1.53 (0.33)	1.49 (0.31)	1.63 (0.36)	0.057+
VI - Long (ND) (cm)	1.25 (0.34)	1.20 (0.31)	1.36 (0.39)	0.041+
RF + VI - Trans (D) (cm)	2.98 (0.67)	2.86 (0.57)	3.27 (0.81)	0.008+
RF + VI - Long (D) (cm)	2.87 (0.68)	2.76 (0.59)	3.12 (0.83)	0.021+
RF + VI - Trans (ND) (cm)	2.89 (0.61)	2.79 (0.56)	3.14 (0.67)	0.011+
RF + VI - Long (ND) (cm)	2.77 (0.6)	2.69 (0.53)	2.99 (0.69)	0.024+
MHG - Trans (D) (cm)	1.66 (0.29)	1.66 (0.27)	1.66 (0.34)	0.980+
MHG - Long (D) (cm)	1.63 (0.28)	1.63 (0.25)	1.61 (0.34)	0.806+
MHG - Trans (ND) (cm)	1.70 (0.29)	1.70 (0.27)	1.70 (0.34)	0.947+
MHG - Long (ND) (cm)	1.67 (0.28)	1.67 (0.27)	1.65 (0.33)	0.757+
AAM - Trans (D) (cm)	2.81 (0.5)	2.64 (0.37)	3.23 (0.52)	<0.001+
AAM - Long (D) (cm)	2.67 (0.58)	2.57 (0.41)	2.94 (0.81)	0.004+
AAM - Trans (ND) (cm)	2.70 (0.51)	2.52 (0.40)	3.16 (0.47)	<0.001+
AAM - Long (ND) (cm)	2.67 (0.47)	2.53 (0.38)	3.04 (0.47)	<0.001+
MAS - Trans (Rt) (cm)	1.07 (0.19)	1.03 (0.19)	1.15 (0.18)	0.009+
MAS - Long (Rt) (cm)	1.01 (0.19)	0.99 (0.19)	1.06 (0.19)	0.110+
MAS - Trans (Lt) (cm)	1.07 (0.19)	1.03 (0.18)	1.19 (0.17)	<0.001+
MAS - Long (Lt) (cm)	1.03 (0.21)	0.98 (0.19)	1.16 (0.22)	<0.001+
GHY (cm)	0.69 (0.13)	0.67 (0.12)	0.73 (0.17)	0.057+

The 4-m usual walking speed test was used for measuring gait speed. Values are expressed as mean (SD).
Rt: right; Lt: left; D: dominant side; ND: non-dominant side; Long: longitudinal ultrasound scan; Trans: transverse ultrasound scan; TA: tibialis anterior; RF: rectus femoris; VI: vastus intermedius; MHG: medial head of gastrocnemius; AAM: anterior arm muscles; MAS: masseter; GHY: geniohyoid.
+Student's *t*-test; ‡Pearson's χ^2 test; ‡‡Fisher's Exact test.

of 94 individuals (27 men and 67 women) with a mean age of 75.6 years (SD=6.6). All diagnostic procedures for sarcopenia (clinical assessment, grip strength, DXA) and the ultrasonographic examination were completed within one week without any adverse event. The demographic characteristics and ultrasonographically measured muscle thickness of the total sample and by gender are presented in Table I. While men had a lower body mass index (BMI), they had higher values of muscle thickness in most of the ultrasound measurements, compared to women.

The muscle thickness measured on sections acquired from dominant and non-dominant sides was compared using paired *t*-tests. The results are presented in Table II. There were significant differences in the values between the dominant side *versus* non-dominant side concerning tibialis anterior muscle (transverse and longitudinal sections), vastus intermedius muscle (longitudinal section), medial head of gastrocnemius muscle (transverse and longitudinal sections) and the anterior arm muscles (transverse section).

Sixteen subjects (17.0%) were diagnosed with sarcopenia. A comparison of the demographic characteristics and ultrasonographically measured muscle thickness between those with and without sarcopenia is shown in Table III. Sarcopenia was more frequent in men and subjects with sarcopenia had lower BMI, handgrip strength values and gait speed (4-m usual walking speed test). The ultrasonographically measured muscle thickness of the vastus intermedius muscle — transverse and longitudinal sections (dominant side), vastus intermedius muscle — longitudinal section (non-dominant side), rectus femoris muscle — transverse and longitudinal sections (non-dominant side), medial head of gastrocnemius muscle — transverse and longitudinal sections (on both dominant and non-dominant sides) and geniohyoid muscle was found significantly low-

TABLE II.—*Comparison of muscle thickness measurements between dominant* versus *non-dominant sides.*

	Paired differences		P value
	Mean	SD	
TA - Trans	0.05	0.21	0.030
TA - Long	0.08	0.24	0.002
RF - Trans	0.04	0.23	0.099
VI - Trans	0.05	0.26	0.089
RF - Long	0.04	0.24	0.152
VI - Long	0.06	0.25	0.030
MHG - Trans	-0.04	0.17	0.013
MHG - Long	-0.04	0.18	0.020
AAM - Trans	0.11	0.28	<0.001
AAM - Long	0.00	0.43	0.997
MAS - Trans	-0.01	0.12	0.541
MAS - Long	-0.02	0.17	0.252

The values between dominant *versus* non-dominant sides were compared using paired *t*-tests. Long: longitudinal ultrasound scan.
Trans: transverse ultrasound scan; TA: tibialis anterior; RF: rectus femoris; VI: vastus intermedius; MHG: medial head of gastrocnemius; AAM: anterior arm muscles; MAS: masseter.

TABLE III.—*Demographic characteristics and muscle thickness measured ultrasonographically in subjects with and without sarcopenia.*

	No sarcopenia (N=78; 83.0%)	Sarcopenia (N=16; 17.0%)	P
Age	75.3 (6.6)	77.3 (6.4)	0.261+
Gender, N (%)			
Females	61 (78.2)	6 (37.5)	0.002‡
Males	17 (21.8)	10 (62.5)	
Dominant side, N (%)			
Right	75 (96.2)	16 (100)	1.000‡‡
Left	3 (3.8)	0 (0.0)	
BMI	28.8 (4.6)	25.5 (4)	0.008+
BMI, N (%)			
Normal	13 (16.7)	7 (43.8)	0.038‡‡
Overweight/obese	65 (83.3)	9 (56.2)	
Hand grip strength (kg)	23.44 (6.73)	17.98 (5.40)	0.003+
Gait speed	0.91 (0.23)	0.77 (0.19)	0.018+
TA - Trans (D) (cm)	2.45 (0.37)	2.42 (0.38)	0.803+
TA - Long (D) (cm)	2.57 (0.38)	2.55 (0.45)	0.861+
TA - Trans (ND) (cm)	2.39 (0.35)	2.41 (0.41)	0.852+
TA - Long (ND) (cm)	2.48 (0.36)	2.51 (0.45)	0.780+
RF - Trans (D) (cm)	1.70 (0.35)	1.56 (0.27)	0.115+
VI - Trans (D) (cm)	1.34 (0.41)	1.09 (0.38)	0.029+
RF - Long (D) (cm)	1.59 (0.34)	1.44 (0.31)	0.102+
VI - Long (D) (cm)	1.34 (0.42)	1.11 (0.38)	0.040+
RF - Trans (ND) (cm)	1.67 (0.33)	1.48 (0.31)	0.040+
VI - Trans (ND) (cm)	1.28 (0.37)	1.13 (0.32)	0.122+
RF - Long (ND) (cm)	1.56 (0.34)	1.38 (0.22)	0.049+
VI - Long (ND) (cm)	1.28 (0.35)	1.08 (0.25)	0.036+
RF + VI - Trans (D) (cm)	3.04 (0.68)	2.65 (0.56)	0.031+
RF + VI - Long (D) (cm)	2.93 (0.68)	2.55 (0.61)	0.039+
RF + VI - Trans (ND) (cm)	2.95 (0.61)	2.61 (0.55)	0.040+
RF + VI - Long (ND) (cm)	2.84 (0.61)	2.46 (0.38)	0.021+
MHG - Trans (D) (cm)	1.69 (0.28)	1.49 (0.30)	0.009+
MHG - Long (D) (cm)	1.66 (0.26)	1.45 (0.30)	0.005+
MHG - Trans (ND) (cm)	1.74 (0.27)	1.49 (0.29)	0.001+
MHG - Long (ND) (cm)	1.71 (0.27)	1.47 (0.26)	0.002+
AAM - Trans (D) (cm)	2.83 (0.49)	2.72 (0.52)	0.439+
AAM - Long (D) (cm)	2.68 (0.60)	2.64 (0.50)	0.813+
AAM - Trans (ND) (cm)	2.71 (0.53)	2.66 (0.44)	0.718+
AAM - Long (ND) (cm)	2.70 (0.48)	2.56 (0.39)	0.268+
MAS - Trans (Rt) (cm)	1.06 (0.19)	1.10 (0.23)	0.474+
MAS - Long (Rt) (cm)	1.02 (0.19)	0.98 (0.20)	0.374+
MAS - Trans (Lt) (cm)	1.06 (0.18)	1.12 (0.22)	0.292+
MAS - Long (Lt) (cm)	1.02 (0.21)	1.09 (0.22)	0.251+
GHY (cm)	0.71 (0.13)	0.58 (0.10)	<0.001+

The 4-m usual walking speed test was used for measuring gait speed. Values are expressed as mean (SD).
Rt: right; Lt: left; D: dominant side; ND: non-dominant side; Long: longitudinal ultrasound scan; Trans: transverse ultrasound scan; TA: tibialis anterior; RF: rectus femoris; VI: vastus intermedius; MHG: medial head of gastrocnemius; AAM: anterior arm muscles; MAS: masseter; GHY: geniohyoid.
+Student's *t*-test; ‡Pearson's χ^2 test; ‡‡Fisher's Exact test.

er in subjects with sarcopenia. The sum of rectus femoris and vastus intermedius muscle thickness was significantly lower in subjects with sarcopenia for both sections and sides.

Concerning comorbidity, diabetes mellitus, thyroid disease, chronic obstructive pulmonary disease, coronary artery disease and osteoporosis were present in 25.6%, 35.9%, 2.6%, 2.6% and 16.7% of the patients without sarcopenia, respectively. The corresponding proportion of diabetes mellitus, thyroid disease, chronic obstructive pulmonary disease, coronary artery disease and osteoporosis was 37.5%, 31.3%, 0%, 0% and 31.3% in patients with sarcopenia, respectively and no significant differences were found in comparison to those without sarcopenia (P>0.05). Regarding medication, the proportion of those without sarcopenia receiving statins, antihypertensives and antidepressants was 37.2%, 46.0% and 13.0%, respectively, while the proportion of those with sarcopenia receiving statins, antihypertensives and antidepressants was 31.3%, 62.5% and 6.3%, respectively and no significant differences were found (P>0.05).

Table IV presents the ROC analysis results in the prediction of sarcopenia from the ultrasound muscle thickness measurements, which revealed a significant association with sarcopenia. The highest AUC value was found for the geniohyoid muscle, and it was equal to 0.79 (Figure 3). The optimal cut-off for the prediction of sarcopenia from the geniohyoid muscle was 0.65 cm with sensitivity equal to 75.0% and specificity equal to 66.7%. AUCs for the medial head of gastrocnemius muscle — longitudinal section (dominant side), medial head of gastrocnemius muscle — transverse section (non-dominant side) (Figure 4), and medial head of gastrocnemius muscle — longitudinal section (non-dominant side) (Figure 5) ranged from 0.70 to 0.74, and the optimal cut-off values were 1.61, 1.63 and 1.72 cm, respectively. The AUCs for the sum of rectus femoris and vastus intermedius muscle, on both sections and sides, were significant and ranged from 0.66 to 0.69.

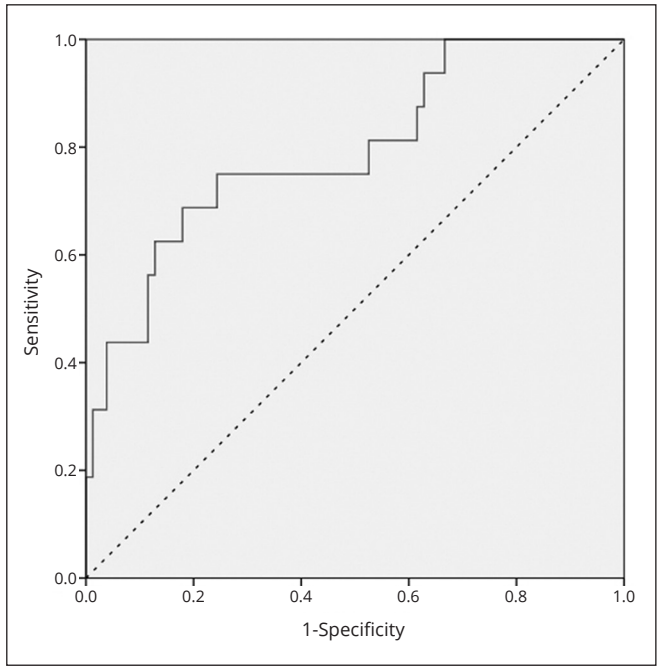

Figure 3.—ROC analysis for the prediction of sarcopenia from geniohyoid muscle thickness.

TABLE IV.—*ROC analysis results for the prediction of sarcopenia from ultrasonographically measured muscle thickness.*

	AUC (95% CI)	P	Cut-off	Sensitivity (%)	Specificity (%)
VI - Trans (D) (cm)	0.67 (0.53-0.81)	0.031	1.01	50.0	84.6
VI - Long (D) (cm)	0.67 (0.52-0.81)	0.039	1.00	50.0	82.1
RF - Trans (ND) (cm)	0.67 (0.53-0.82)	0.033	1.54	68.8	65.4
RF - Long (ND) (cm)	0.68 (0.56-0.80)	0.026	1.59	81.3	51.3
VI - Long (ND) (cm)	0.66 (0.51-0.79)	0.050	1.13	62.5	64.1
RF + VI - Trans (D) (cm)	0.68 (0.54-0.81)	0.026	2.62	70.0	76.0
RF + VI - Long (D) (cm)	0.67 (0.53-0.81)	0.034	2.84	75.0	60.0
RF + VI - Trans (ND) (cm)	0.66 (0.51-0.81)	0.050	2.80	63.0	58.0
RF + VI - Long (ND) (cm)	0.69 (0.57-0.81)	0.019	2.61	63.0	66.0
MHG - Trans (D) (cm)	0.69 (0.55-0.84)	0.015	1.65	75.0	56.4
MHG - Long (D) (cm)	0.70 (0.56-0.84)	0.013	1.61	75.0	61.5
MHG - Trans (ND) (cm)	0.74 (0.61-0.86)	0.003	1.63	75.0	67.9
MHG - Long (ND) (cm)	0.73 (0.62-0.85)	0.003	1.72	87.5	52.6
GHY (cm)	0.79 (0.67-0.92)	<0.001	0.65	75.0	66.7

ROC: receiver operating characteristic. AUC: area under the curve. D: dominant side; ND: non-dominant side; Long: longitudinal ultrasound scan; Trans: transverse ultrasound scan;
VI: vastus intermedius; RF: rectus femoris; MHG: medial head of gastrocnemius; GHY: geniohyoid.

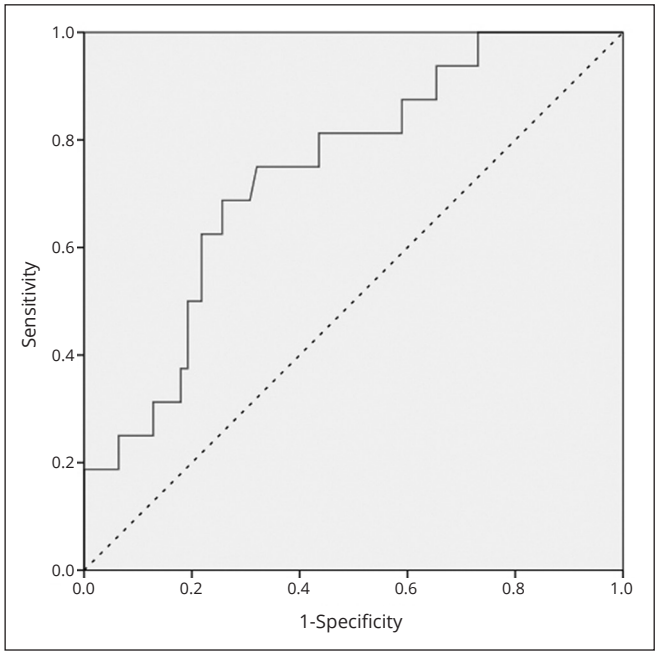

Figure 4.—ROC analysis for the prediction of sarcopenia from medial head of gastrocnemius muscle thickness - transverse section (non-dominant side).

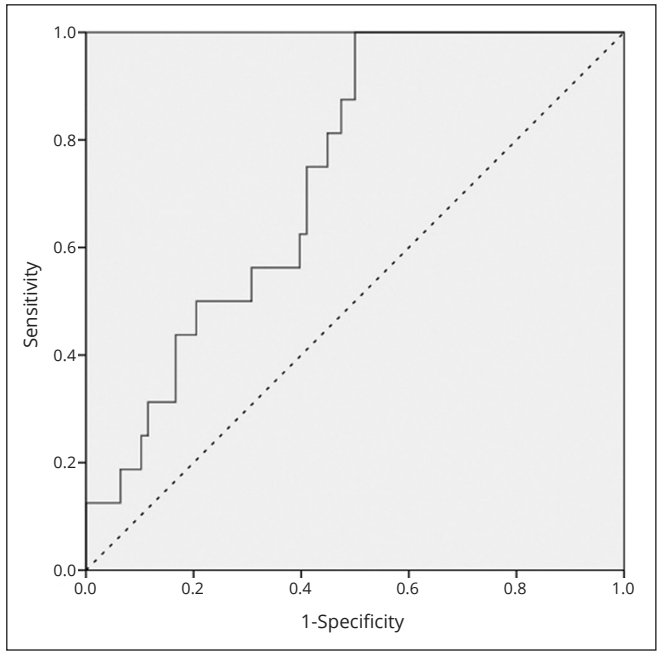

Figure 5.—ROC analysis for the prediction of sarcopenia from medial head of gastrocnemius muscle thickness - longitudinal section (non-dominant side).

Logistic regression models were performed for sarcopenia predictive ultrasound muscle thickness measurements, using the cut-off values from ROC analyses (Table V). After adjusting for gender and age, it was found that cases with vastus intermedius muscle — transverse section (dominant side) thickness less than 1.01 cm had 9.47 times greater odds for having sarcopenia. Similarly, cases with vastus intermedius muscle — longitudinal section (dominant side) thickness of less than 1 had 6.33 times greater odds for having sarcopenia. The likelihood of sarcopenia was 11.9 and 6.9 times greater in those with rectus femoris muscle — transverse section (non-dominant side) thickness less than 1.54 cm and rectus femoris muscle — longitudinal section (non-dominant side) with a thickness less than 1.59 cm, respectively. Vastus intermedius muscle — longitudinal section (non-dominant side) thickness less than 1.13 cm and medial head of gastrocnemius muscle — transverse section (dominant side) thickness less than 1.65 cm were associated with 6.92 and 4.52 times greater odds for sarcopenia. Logistic regression models also revealed that subjects with a thickness of the medial head of gastrocnemius muscle — longitudinal section less than 1.61 cm and those with a thickness of the medial head of gastrocnemius muscle — transverse section (non-dominant side) less than 1.63 cm were associated with a significantly greater likelihood for sarcopenia. Furthermore, the medial head of the gastrocnemius muscle — longitudinal section (non-dominant side) thickness less than 1.72 cm and the geniohyoid muscle thickness less than 0.65 were also predictive for sarcopenia as indicated from the adjusted odds ratios that were equal to 8.49 and 6.72, respectively. The sum of rectus femoris and vastus intermedius muscle (on both sections and sides) also had a significant association with sarcopenia in logistic regression analysis.

Discussion

Various ultrasound techniques have been used in the assessment of muscle mass in sarcopenic individuals.[15, 28, 29] Measurement of muscle thickness on ultrasound scans is a simple, easy and fast method to estimate muscle mass, which does not require any postprocessing with the use of special software and is less likely to be equipment dependent. To the best of our knowledge, this is the first ultrasound study that investigates changes in muscle thickness of the head, upper and lower limb muscles, on both transverse and longitudinal ultrasound sections from the dominant and non-dominant side of the body in patients with sarcopenia.

The results of this study have shown that the muscle

TABLE V.—*Odds ratios and 95% confidence intervals for the prediction of sarcopenia from ultrasound parameters as derived from logistic regression models.*

	OR (95% CI)+	P
VI - Trans (D) (cm)		
>1.01 (reference)		
≤1.01	9.47 (2.24-40.08)	0.002
VI - Long (D) (cm)		
>1.00 (reference)		
≤1.00	6.33 (1.67-23.99)	0.007
RF - Trans (ND) (cm)		
>1.54 (reference)		
≤1.54	11.90 (2.29-61.85)	0.003
RF - Long (ND) (cm)		
>1.59 (reference)		
≤1.59	6.90 (1.40-33.89)	0.017
VI - Long (ND) (cm)		
>1.13 (reference)		
≤1.13	6.92 (1.59-30.11)	0.010
RF + VI - Trans (D) (cm)		
>2.62 (reference)		
≤2.62	9.41 (2.22-39.88)	0.002
RF + VI - Long (D) (cm)		
>2.84 (reference)		
≤2.84	8.44 (1.89-37.68)	0.002
RF + VI - Trans (ND) (cm)		
>2.80 (reference)		
≤2.80	4.94 (1.19-20.38)	0.027
RF + VI - Long (ND) (cm)		
>2.61 (reference)		
≤2.61	4.59 (1.25-16.81)	0.022
MHG - Trans (D) (cm)		
>1.65 (reference)		
≤1.65	4.52 (1.09-18.79)	0.038
MHG - Long (D) (cm)		
>1.61 (reference)		
≤1.61	3.92 (1.01-15.34)	0.050
MHG - Trans (ND) (cm)		
>1.63 (reference)		
≤1.63	11.34 (2.38-53.94)	0.002
MHG - Long (ND) (cm)		
>1.72 (reference)		
≤1.72	8.49 (1.63-44.2)	0.011
GHY (cm)		
>0.65 (reference)		
≤0.65	6.72 (1.78-25.44)	0.005

+Odds Ratio (95% Confidence Interval) adjusted for age and gender.
D: dominant side; ND: non-dominant side; Long: longitudinal ultrasound scan; Trans: transverse ultrasound scan; VI: vastus intermedius; RF: rectus femoris; MHG: medial head of gastrocnemius; GHY: geniohyoid.

thickness of the geniohyoid muscle was significantly lower in subjects with sarcopenia. In a previous study, the tongue muscle mass was found to be smaller in patients with sarcopenic dysphagia.[30] The researchers have used a different methodology compared to the one used in this research and have studied a population presenting sarcopenic dysphagia. However, the conclusions are in accordance as it concerns the usability of ultrasound in the detection of muscle mass loss of tongue muscles. Furthermore, the method used in this study presented a sensitivity equal to 75.0% and specificity equal to 66.7% in the prediction of sarcopenia from the geniohyoid muscle thickness measurements. The measurement of the geniohyoid muscle thickness presents several advantages from a technical point of view. The image acquisition is fast, simple and does not require advanced operator skills. Moreover, there is no need to undress the patient, and the examination does not require complex patient positioning. The portability of the ultrasound and the availability of ultrasound equipment based on smartphones or tablets could make this technique ideal in the prediction — screening for sarcopenia, both in the community and the inpatient wards.

In the study by Kuyumcu *et al.* published in 2016, the muscle thickness of the gastrocnemius muscle was found to be lower in sarcopenic elderly.[25] The researchers have studied the medial head of the gastrocnemius muscle on transverse ultrasound scans acquired from both lower limbs, and the diagnosis of sarcopenia was based on muscle mass measurement by bioimpedance analysis (BIA). Even though in this study, the revised EWGSOP[3] criteria have been used to establish the diagnosis of sarcopenia and DXA for the estimation of muscle mass loss, the results are in line with the results of the study by Kuyumcu *et al.* The capability of ultrasound to detect muscle mass loss in sarcopenia does not seem to depend on the diagnostic protocol followed in the diagnosis of sarcopenia. Moreover, our results have shown that both transverse and longitudinal ultrasound sections from either the dominant or non-dominant side of the body presented a statistically significant decrease in muscle thickness in sarcopenic individuals. Therefore, if the ultrasonographically measured muscle thickness is adopted as a reference technique in muscle mass estimation for the diagnosis of sarcopenia, only one ultrasound section from the medial head of gastrocnemius muscle could suffice, reducing the examination duration and cost significantly.

Strasser *et al.* reported that the thickness measurement of the vastus intermedius and vastus medialis muscle could be an accurate and bedside tool in the diagnosis and course of sarcopenia.[31] Indeed, the ROC analysis of this study has shown that the ultrasound muscle thickness measurements of the vastus intermedius and rectus femoris muscle can be used for the prediction of sarcopenia. However, the significance of the effect varies according to the muscle, body side and scan type.

The statistical analysis performed in this study has

shown that the likelihood of sarcopenia was 11.9 times greater in individuals with low rectus femoris muscle thickness on the transverse section (non-dominant side). Similarly, subjects with low muscle thickness of the medial head of gastrocnemius on the transverse section (non-dominant side) presented 11.34 times greater likelihood for sarcopenia. Furthermore, low muscle thickness of the medial head of gastrocnemius muscle on longitudinal ultrasound section (non-dominant side) and the geniohyoid muscle was also predictive for sarcopenia as indicated from the adjusted odds ratios.

The thickness of the masseter, anterior arm and tibialis anterior muscles did not present a statistically significant decrease in sarcopenic compared to non-sarcopenic individuals. The hypothesis considered is that these muscles might be either less vulnerable to sarcopenia or more prone to fatty infiltration. Further studies on the echotexture of the muscles mentioned above could elucidate the causes of this observation.

According to the literature, there is no consensus or clear recommendation concerning which side of the body should be preferred for the assessment of sarcopenia using ultrasound muscle measurements.[32] The results of this study indicate statistically significant differences in muscle thickness between the dominant *versus* non-dominant sides, for specific muscles and sections (Table II). This fact has to be taken into consideration in the interpretation of ultrasound quantitative studies, as their results might be side-dependent and probably not reproducible on the opposite side.

Previous studies have shown that ultrasound is a valid and reliable tool in the assessment of muscle mass.[13, 14, 33] Under this perspective, ultrasound could be used to monitor the changes in muscle thickness in the course of sarcopenia and to evaluate the effectiveness of interventions. The integration of machine learning techniques in musculoskeletal ultrasonography is an emerging and promising field.[34-36] Computer aided diagnostic systems could help in reducing examination time and increasing the accuracy of the measurements.

Limitations of the study

This study presents some limitations. Firstly, the size of the sample was relatively small, especially as this concerns the male subjects; therefore, further studies would be required to obtain safer conclusions. Another limitation is that the regional/national cut-off values (for grip strength and DXA) in the diagnosis of sarcopenia were not available for our study population. Instead, the cut-off points recommended by EWGSOP2[3] for the harmonization of sarcopenia studies were used for this study. Finally, one should take into consideration that the results of this study were based on specific ultrasound equipment, image acquisition techniques and measurement methodology. Validation studies are required before applying them in different settings. Future research should investigate the role of ultrasonography in the diagnosis of primary *versus* secondary sarcopenia, as well as the potential influence of medication on its diagnostic accuracy.

Conclusions

The results of this study have shown that the ultrasonographically measured thickness of the neck and lower limb muscles can be used for predicting sarcopenia with high sensitivity and specificity. Further research, based on larger-scale studies, is required to thoroughly investigate the role of ultrasonography as a diagnostic tool for sarcopenia and to validate cut-off values in the assessment of muscle mass quantity and quality.

References

1. Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. J Cachexia Sarcopenia Muscle 2016;7:512–4.

2. Rauch A, Negrini S, Cieza A. Toward strengthening rehabilitation in health systems: methods used to develop a WHO package of rehabilitation interventions. Arch Phys Med Rehabil 2019;100:2205–11.

3. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, *et al.*; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16–31.

4. Beaudart C, Zaaria M, Pasleau F, Reginster JY, Bruyère O. Health outcomes of sarcopenia: a systematic review and meta-analysis. PLoS One 2017;12:e0169548.

5. Yoshimura Y, Wakabayashi H, Bise T, Tanoue M. Prevalence of sarcopenia and its association with activities of daily living and dysphagia in convalescent rehabilitation ward inpatients. Clin Nutr 2018;37(6 Pt A):2022–8.

6. Özçakar L, Ata AM, Quittan M, Michail X. A 'musculoskeletal look' to sarcopenia: where do/should the physical and rehabilitation medicine physicians (physiatrists) stand? Int J Rehabil Res 2018;41:95–6.

7. Dent E, Morley JE, Cruz-Jentoft AJ, Arai H, Kritchevsky SB, Guralnik J, *et al.* International clinical practice guidelines for sarcopenia (ICFSR): screening, diagnosis and management. J Nutr Health Aging 2018;22:1148–61.

8. Hojan K, Milecki P, Molińska-Glura M, Roszak A, Leszczyński P. Effect of physical activity on bone strength and body composition in breast cancer premenopausal women during endocrine therapy. Eur J Phys Rehabil Med 2013;49:331–9.

9. Huang SW, Ku JW, Lin LF, Liao CD, Chou LC, Liou TH. Body composition influenced by progressive elastic band resistance exercise of sarcopenic obesity elderly women: a pilot randomized controlled trial. Eur J Phys Rehabil Med 2017;53:556–63.

10. Buckinx F, Landi F, Cesari M, Fielding RA, Visser M, Engelke K,

et al. Pitfalls in the measurement of muscle mass: a need for a reference standard. J Cachexia Sarcopenia Muscle 2018;9:269–78.

11. Beaudart C, McCloskey E, Bruyère O, Cesari M, Rolland Y, Rizzoli R, *et al.* Sarcopenia in daily practice: assessment and management. BMC Geriatr 2016;16:170.

12. Can B, Kara M, Kara Ö, Ülger Z, Frontera WR, Özçakar L. The value of musculoskeletal ultrasound in geriatric care and rehabilitation. Int J Rehabil Res 2017;40:285–96.

13. Nijholt W, Scafoglieri A, Jager-Wittenaar H, Hobbelen JS, van der Schans CP. The reliability and validity of ultrasound to quantify muscles in older adults: a systematic review. J Cachexia Sarcopenia Muscle 2017;8:702–12.

14. Shimizu S, Hanayama K, Metani H, Sugiyama T, Abe H, Seki S, *et al.* Retest reliability of ultrasonic geniohyoid muscle measurement. Jpn J Compr Rehabil Sci 2016;7:55–60.

15. Ticinesi A, Meschi T, Narici MV, Lauretani F, Maggio M. Muscle Ultrasound and Sarcopenia in Older Individuals: A Clinical Perspective. J Am Med Dir Assoc 2017;18:290–300.

16. Pillen S, van Alfen N. Skeletal muscle ultrasound. Neurol Res 2011;33:1016–24.

17. Takai Y, Ohta M, Akagi R, Kato E, Wakahara T, Kawakami Y, *et al.* Applicability of ultrasound muscle thickness measurements for predicting fat-free mass in elderly population. J Nutr Health Aging 2014;18:579–85.

18. Minetto MA, Caresio C, Menapace T, Hajdarevic A, Marchini A, Molinari F, *et al.* Ultrasound-based detection of low muscle mass for diagnosis of sarcopenia in older adults. PM R 2016;8:453–62.

19. Abe T, Fujita E, Thiebaud RS, Loenneke JP, Akamine T. Ultrasound-derived forearm muscle thickness is a powerful predictor for estimating DXA-derived appendicular lean mass in Japanese older adults. Ultrasound Med Biol 2016;42:2341–4.

20. Tosato M, Marzetti E, Cesari M, Savera G, Miller RR, Bernabei R, *et al.* Measurement of muscle mass in sarcopenia: from imaging to biochemical markers. Aging Clin Exp Res 2017;29:19–27.

21. Harris-Love MO, Monfaredi R, Ismail C, Blackman MR, Cleary K. Quantitative ultrasound: measurement considerations for the assessment of muscular dystrophy and sarcopenia. Front Aging Neurosci 2014;6:172.

22. Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C, *et al.* A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 2011;40:423–9.

23. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, *et al.*; European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010;39:412–23.

24. Arts IM, Pillen S, Schelhaas HJ, Overeem S, Zwarts MJ. Normal values for quantitative muscle ultrasonography in adults. Muscle Nerve 2010;41:32–41.

25. Kuyumcu ME, Halil M, Kara Ö, Çuni B, Çağlayan G, Güven S, *et al.* Ultrasonographic evaluation of the calf muscle mass and architecture in elderly patients with and without sarcopenia. Arch Gerontol Geriatr 2016;65:218–24.

26. Serra MD, Duarte Gavião MB, dos Santos Uchôa MN. The use of ultrasound in the investigation of the muscles of mastication. Ultrasound Med Biol 2008;34:1875–84.

27. Park KM, Choi E, Kwak EJ, Kim S, Park W, Jeong JS, *et al.* The relationship between masseter muscle thickness measured by ultrasonography and facial profile in young Korean adults. Imaging Sci Dent 2018;48:213–21.

28. Stringer HJ, Wilson D. The role of ultrasound as a diagnostic tool for sarcopenia. J Frailty Aging 2018;7:258–61.

29. Sanabria SJ, Martini K, Freystätter G, Ruby L, Goksel O, Frauenfelder T, *et al.* Speed of sound ultrasound: a pilot study on a novel technique to identify sarcopenia in seniors. Eur Radiol 2019;29:3–12.

30. Ogawa N, Mori T, Fujishima I, Wakabayashi H, Itoda M, Kunieda K, *et al.* Ultrasonography to measure swallowing muscle mass and quality in older patients with sarcopenic dysphagia. J Am Med Dir Assoc 2018;19:516–22.

31. Strasser EM, Draskovits T, Praschak M, Quittan M, Graf A. Association between ultrasound measurements of muscle thickness, pennation angle, echogenicity and skeletal muscle strength in the elderly. Age (Dordr) 2013;35:2377–88.

32. Perkisas S, Baudry S, Bauer J, Beckwée D, De Cock AM, Hobbelen H, *et al.* Application of ultrasound for muscle assessment in sarcopenia: towards standardized measurements. Eur Geriatr Med 2018;9:739–57.

33. Barotsis N, Tsiganos P, Kokkalis Z, Panayiotakis G, Panagiotopoulos E. Reliability of muscle thickness measurements in ultrasonography. Int J Rehabil Res 2020. [Epub ahead of print]

34. Katakis S, Barotsis N, Kastaniotis D, Theoharatos C, Tsiganos P, Economou G, *et al.* Muscle type and gender recognition utilising high-level textural representation in musculoskeletal ultrasonography. Ultrasound Med Biol 2019;45:1562–73.

35. Molinari F, Caresio C, Acharya UR, Mookiah MR, Minetto MA. Advances in quantitative muscle ultrasonography using texture analysis of ultrasound images. Ultrasound Med Biol 2015;41:2520–32.

36. Caresio C, Salvi M, Molinari F, Meiburger KM, Minetto MA. Fully Automated Muscle Ultrasound Analysis (MUSA): Robust and Accurate Muscle Thickness Measurement. Ultrasound Med Biol 2017;43:195–205.

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