

Assessment of Sarcopenia by Ultrasound. A Feasibility Study in Acutely Admitted Danish Geriatric Inpatients

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Abstract

Objective: Sarcopenia is a major geriatric syndrome diagnosed by assessing strength, quantity, and quality of muscles. We aimed to describe the feasibility of assessing sarcopenia by bedside assessment including the emerging tool ultrasound.

Materials and Methods: Participants were recruited consecutively among patients acutely admitted to the Department of Geriatrics, Odense University Hospital, Denmark. Ultrasound examination and handgrip-test (muscle strength) were performed at admission and minimum 5 days later. Muscle thickness of m. rectus femoris was measured and appendicular lean mass (ALM) (muscle quantity) was calculated using a validated regression model, two ultrasound scanning sites (dominant upper arm and thigh), and three anthropometric measures. Echo intensity was measured as an indicator of muscle quality.

Results: Out of 25 eligible participants, 17 were included. There was a significant ($p=0.002$) decline in m. rectus femoris thickness [1.7 cm (SD ± 0.2) to 1.6 cm (SD ± 0.3)], and a significant ($p=0.04$) decline in echo intensity [121.4 A.U (SD ± 18.4) to 133.6 A.U (SD ± 19.1)]. All ultrasound ALM and handgrip strength measurements showed non-significant declines. According to EWGSOP2's criteria, one participant was sarcopenic, while 12 met the threshold criteria by low handgrip strength. Thirteen participants had a lower handgrip strength compared to reference values from an age- and gender-matched normal population.

Conclusion: It is feasible to perform bedside assessments on geriatric inpatients. A short period of hospitalization may result in a significant reduction of localized muscle thickness and echo intensity. Further studies including validation by DXA scans are needed.

Keywords: Ultrasound, sarcopenia, handgrip strength, geriatric assessment, muscle assessment

Introduction

Sarcopenia is a skeletal muscle disorder and a major geriatric syndrome (1) characterized by the loss of muscle strength, endurance, and muscle mass (2,3). The prevalence of sarcopenia is reported as high as 30% in a community-dwelling population (1,4). In older adults this can lead to functional decline, impairing the ability to perform activities of daily living (5,6) and decreasing quality of life (7). Sarcopenia shows significant overlap with the frailty syndrome (8), as low handgrip strength (HGS) and slow gait speed are characteristics of both conditions (9). In addition, sarcopenia increases the risk of falls and fractures (10,11) as well as the rate of hospital admission and mortality (6,12), and carries a high personal, social, and economic burden

when untreated (8). Early identification of sarcopenia is therefore essential for effective prevention and treatment.

To address the need for standardization in identifying, examining, and treating sarcopenia, the EWGSOP2 developed guidelines in 2018 (8). These guidelines involve the assessment of muscle strength, muscle quantity, muscle quality, and physical performance as an indicator of severity (8). Muscle strength can be assessed by HGS, a simple, inexpensive measurement, and a powerful predictor of poor patient outcomes (8,13). Low HGS correlates moderately with low strength in other body compartments (14,15). Muscle quantity is usually assessed by gold-standard techniques such as magnetic resonance imaging (MRI), computed tomography (CT), and dual-energy

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X-ray absorptiometry (DXA) (8,16). In contrast, the assessment of muscle quality remains a conflicted area with little standardization (17), but consensus exists that muscle quality is of even greater importance than previously thought (8). Echo intensity (EI) is one of the functions evaluating muscle quality, and a high EI has been associated with poor muscle performance (18,19) and may be an indirect measure of adipocyte infiltration or fibrosis (19).

Ultrasound is a patient-safe and patient-centred method for examining various conditions and has shown great potential in examining muscle quantity and quality (8,20). Assessment of pennate muscles such as the quadriceps femoris can detect a decrease in muscle thickness (MT) and cross-sectional area (CSA) within the first week of critical illness in middle-aged adults (8,21). Studies in young adults have shown that muscle atrophy can be detected after 5 days (22,23). Compared to other imaging techniques ultrasound measurements are inexpensive and radiation-free. Furthermore, the device is mobile, examination can be done bedside (24), and requires minimal training (25).

Other studies assessing sarcopenia use nonportable imaging tools (CT, MRI, or DXA) to assess muscle mass, but we have not been able to identify any previous studies assessing sarcopenia in geriatric inpatients using ultrasound. The aim of this study was to assess the feasibility of using ultrasound for diagnosing sarcopenia and to describe how muscle strength (HGS), muscle quantity (ultrasound-ALM and thickness of m. rectus femoris), and muscle quality (echo intensity) change in a population of acutely admitted geriatric patients hospitalized for a minimum of 5 days.

Materials and Methods

Study Design

This study was carried out as a single-center feasibility study.

Setting

A medical student (J.S.H) received training and supervision (written material, instructional videos, and two months of daily supervised scans prior to the start of this study) in carrying out all assessments including ultrasound by a physician (K.S.B) in geriatric medicine with large experience and certification in the use of point-of-care ultrasound.

Study Population

During May 2022 participants were recruited consecutively among patients acutely admitted to the Department of Geriatric Medicine, Odense University Hospital (OUH), Denmark. The department is a 32-bed acute medical ward treating frail, multimorbid older adults with acute medical conditions. Patients were eligible for inclusion if they consented to participate within

24 hours of admission and had an expected hospitalization of minimum 5 days.

Exclusion Criteria

Patients with known moderate or severe dementia, and patients who were cognitively impaired due to delirium and thus unable to provide informed consent were excluded, as were patients developing delirium after inclusion, and those discharged after less than 5 days of hospitalization.

Intervention

The following information was retrieved from the medical record in order to describe the health and functional level of the study population: Height, weight, body mass index, Barthel index [(BI)-100] (26,27) number of diseases, and diagnosis upon admission. Multimorbidity was assessed by the Charlson comorbidity score (CCI) (28). Frailty was assessed by the clinical frailty scale (CFS) at baseline (29,30).

All participants were informed orally and in writing about the purpose of the study. It was made clear to the participants that they could withdraw at any stage of the study, and that withdrawal would have no consequences for their treatment and care.

Participants went through an ultrasound examination and a handgrip measurement immediately after obtaining consent (baseline) and again immediately before discharge from the hospital, but not earlier than day 5 (follow-up). All patients discharged before day 5 were omitted. As the average in-hospital stay in the department is 6.7 days (personal communication), day 5 was chosen to obtain a representative geriatric population.

Ultrasound Examination

A CE-certified ultrasound device MindrayTE7 was used with the L14-6Ns probe for the 2-D real time B-mode ultrasound. All ultrasound measurements were done with the probe in a neutral tilt with a minimum of pressure applied and with a generous amount of conductive gel. The scanning sites were marked with a pen and three sets of measurements were performed, and the mean value used.

Quantitative Muscle Measures

B-mode ultrasound was carried out to quantify muscle mass by estimating ALM, which corresponds approximately to appendicular skeletal muscle mass (ASM) (8,24). An easily feasible and validated ultrasound scanning protocol with a high correlation to DXA estimates of ALM was chosen (24).

To calculate ALM via a validated regression model (24), two scanning sites (dominant upper arm and thigh) (A), and three anthropometric measures (B) were used as shown in Figure 1 and described in the appendix.

The participants' height in meters, weight in kilograms, gender, the measured MT, and anthropometric values were used in the equations listed in the appendix to calculate ultrasound-ALM (24).

In addition, MT of m. rectus femoris was obtained according to the recommendation by SARCUS (20). In short, with the patient in a neutral and horizontal position, B-mode ultrasound was carried out on the middle part of the muscle, defined as half the length from the trochanter major (upper landmark of the muscle) to the superior border of the patella (the lower landmark of the muscle) to measure MT defined as the distance between the upper and the lower muscle fascicle on a cross-sectional image.

Qualitative Muscle Measure

EI was used to assess muscle quality as recommended by SARCUS (20). EI is a function evaluating muscle quality from ultrasound imaging on a grey scale, ranging from black to white (18,19). We used the image obtained during measurements of m. rectus femoris MT, and performed EI analysis in ImageJ (Version 1.53t, National Institute of Health, USA, <http://rsb.info.nih.gov/ij>) as described in previous studies (31,32).

Muscle Strength Measure-HGS

Muscle strength was assessed by HGS (kg) using a Smedley dynamometer (TTM; Tokyo, Japan). The width of the handle was adjusted to fit the individual hand size, and HGS was measured using the dominant hand with the elbow in a 90°

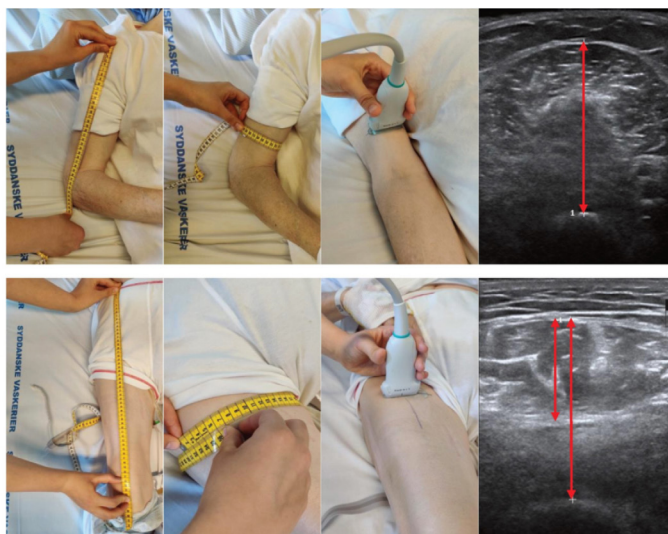


Figure 1. Qualitative and quantitative muscle measurements. The two scanning sites (dominant upper arm and thigh) and the anthropometric measures are demonstrated. UL measurements are shown together with the scanning sites and muscle thickness from the upper muscle fascicle to humerus (biceps) and femur (rectus femoris) are marked with a red arrow. The same applies to the muscle thickness of rectus femoris measured from the upper fascicle to the lower fascicle

position and the upper arm tight against the trunk. Depending on the participant's mobility, HGS was measured preferably standing, alternatively as sitting, or even in the supine position if the patient was unable to be in a vertical or sitting position, respectively. The best of three measurements with the dominant hand was used and matched to Danish reference values by Frederiksen et al. (15).

Data Management

The study was approved on April 28th, 2022, by the Data Protection Agency (journal nr: 21/50801). All data was stored in a secure Redcap Open database [OPEN (OP_1499)].

Statistics

Statistical analyses were carried out in Microsoft Excel version 2016 (Microsoft: Redmond Seattle USA). Normality was assessed using the Shapiro-Wilk test. Normally distributed data are presented as a mean \pm standard deviation (SD). Non-normally distributed data are presented as median with interquartile range (IQR). Results of numeric data were compared using paired t-test or Wilcoxon-rank sum test (analysis carried out in R-statistics version R-4.2.0 for Windows) depending on the normality of the data. As a limit for statistical significance, a two-sided $p < 0.05$ was chosen.

Reliability of Measurements

To assess the quality of ultrasound measurements, we estimated the intrarater reliability. As J.S.H was the only rater and performed three sets of measurements for each participant, we used the intra class coefficient (ICC) (2.1) model (33,34). As stated in the literature, we considered an ICC of 0.5 or less as poor, 0.5-0.75 as moderate, 0.75-0.9 as good and an ICC of 0.9 or above as excellent reliability (33).

Ethics

Ultrasound is a widely used non-invasive method and does not expose the participant to any radiation, nor does it provide any other physical harm.

The study has been approved by the Local Ethics Committee (Videnskabetisk Komité for Region Syddanmark) (S-20210100).

Results

In total, 25 participants were included in this study. Eight participants were excluded because of discharge before 5 days after baseline examination. The final sample comprised 17 participants (characteristics are presented in Table 1). The intrarater reliability using the ICC was calculated to 0.92.

Baseline Demographics

Median age was 85 years (IQR: 81-89), ranging from 60 to 93 years. The median length of hospitalization was 5 days (IQR:

5-7), ranging from 5 to 8 days. Nine participants were admitted because of an infection (53%), while two participants were admitted with rhabdomyolysis (12%), two with dehydration (12%), two with reduced general condition (12%), one with dyspnoea (6%) and one with hypotension (6%). The mean BI-100 was 52.1 (SD: ±30.1), the mean CFS was 5.1 (SD: ±1.17) and the mean CCI was 6.4 (SD: ±1.7).

Ultrasound-measurements and HGS

All ultrasound-ALM medians showed a reduction from baseline to follow-up (Table 2), but none were significant. The same applies to HGS showing a non-significant reduction from a mean 16.5 kg (SD: ±9.6) at baseline to a mean 16.2 kg (SD: ±9.9) at follow-up. There was a significant (p=0.002) fall in the rectus femoris MT between baseline [1.7 cm (SD: ±0.2)] and follow-up [1.6 cm (SD: ±0.3)] (Figure 2 shows MT of m. rectus femoris at baseline and follow-up for each participant). Grey scale analysis revealed a significant (p=0.04) increase in EI from baseline [121.4 A.U (SD: ±18.4) and follow-up (133.6 A.U (SD: ±19.1)].

Sarcopenic Participants

Based on the ALM without circumference measures, one participant (6%) was categorized as sarcopenic by meeting both cut-off points made by the EWGSOP2 (8), i.e., low HGS (<27 kg and <16 kg men and women, respectively), and low muscle quantity (ASM <20 kg for men and <15 kg for women). When comparing to Danish gender, age, and height stratified reference values (15) thirteen participants (76%) had a lower HGS both at baseline and follow-up, while twelve participants (70%) had both at baseline and follow-up a lower HGS than the cut-off values for sarcopenic strength according to the EWGSOP2 (8).

Discussion

This study demonstrates that it is feasible to assess sarcopenia in a vulnerable population of acutely admitted geriatric patients by bedside ultrasound and anthropometric measures. Moreover,

although the population under study is small, we found a reduction in calculated ALM measurements, MT of rectus femoris, EI, and HGS from baseline to follow-up, i.e., after five days of admission, although only the reduction in MT (quantitative parameter) and EI (qualitative parameter) was significant. Thus, while an isolated significant difference is seen in the rectus femoris, there was no difference in overall ALM, which may be interpreted as a possible development of local sarcopenia during a short period of hospitalization and is in line

n	17
Age (years), median [IQR]	85 [81;89]
Female (%)	8 (47)
Days between 1. and 2. ultrasound scans, median [IQR]	5 [5;7]
Height (m), mean (SD)	1.7 (0.1)
Weight (kg), mean (SD)	72.5 (16.1)
BMI (kg/m ²), mean (SD)	25.0 (4.4)
Falls (within the last 12 months), median [IQR]	1 [1;2]
Arm dominance (%)	Right (100)
Leg dominance (%)	Right (94)
Primary diagnosis upon admission	
Infectious disease (%)	9 (53)
Rhabdomyolysis (%)	2 (12)
Dehydratio (%)	2 (12)
Reduced general condition (%)	2 (12)
Dyspnoea (%)	1 (6)
Hypotension (%)	1 (6)
Charlson comorbidity index, mean (SD)	6.4 (1.7)
Clinical frailty scale, mean (SD)	5.1 (1.2)
Barthel-100 index (Shahs version), mean (SD)	52.1 (30.1)
Data is presented as mean for normally distributed variables, median for non-normally distributed variables and numbers (%) for categorical variables. N: Number of individuals, BMI: Body mass index, SD: Standard deviation, IQR: Interquartile range	

	Baseline	Follow-up	
Ultrasound ALM with circumference measures (kg), mean (SD)	21.3 (4.24)	21.2 (4.1)	0.52
Ultrasound ALM (kg), mean (SD)	21.5 (4.0)	21.4 (3.8)	0.40
Ultrasound ALM/height ² (kg/m ²), median [IQR]	7.6 [6.5;7.9]	7.5 [6.8;7.9]	0.38
Muscle thickness (cm), mean (SD)	1.7 (0.2)	1.6 (0.3)	0.002*
Echo intensity (A.U), mean (SD)	121.4 (18.4)	133.6 (19.2)	0.04*
Handgrip strength (kg), mean (SD)	16.5 (9.6)	16.2 (9.9)	0.71
Data is presented as mean for normally distributed variables and median for non-normally distributed variables. P-values were tested using t-test (normally distributed variables), Wilcoxon's rank sum test (non-normally distributed variables). *Differences among measurements at baseline and follow-up was interpreted as significant if p<0.05. ALM: Appendicular lean mass, SD: Standard deviation, IQR: Interquartile range			

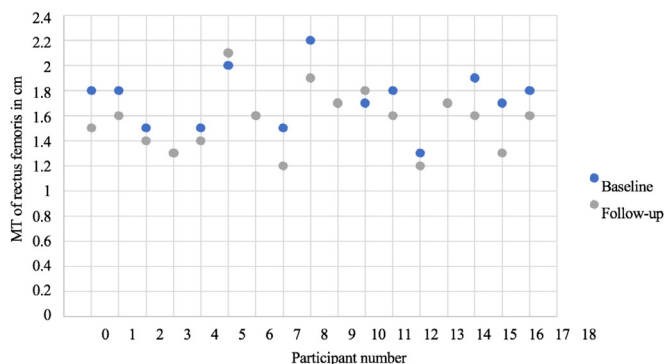


Figure 2. Muscle thickness (MT) of m. rectus femoris at baseline and follow-up for each participant

with findings from a study on hospitalized hip fracture patients using a similar method (35). To our knowledge, no previous studies have described ultrasound assessed sarcopenia in non-fracture geriatric inpatients.

A minimum of 5 days was chosen since the median length of stay at the department of geriatric medicine, OUH is 6.7 days (personal communication). Other studies in younger adults have shown that muscle atrophy can be detected after 5 days of bed rest (8,22,23), and dramatic changes in muscle mass occur within 4–6 weeks of bed rest in healthy individuals (22), which indicates that a significant change in ALM may first be identified after a longer period of hospitalization.

The participants in this study were all older adults without dementia and delirium, but with a moderate degree of frailty [mean CFS score: 5.1 (SD 1.2)]. By excluding patients with dementia and delirium it may be questioned whether the studied population is representative. If more vulnerable participants, i.e., those with cognitive impairment, dementia, and delirium, were included, the muscle assessments may have been lower, as sarcopenia is associated with dementia, mild cognitive impairment, and cognitive decline (36). However, we do not know whether the decline during at least 5 days of bed rest for these patients would affect the rate of decline in muscle status more than cognitively intact older patients. Another factor is, that acute illness in most cases starts in the preceding days before the acute hospitalization with bed rest at home. Ideally, the baseline measurements should have been performed at home when the first signs of illness with reduced physical activity or bed rest began. Furthermore, at the department of geriatrics, OUH, there is a very high focus on good nutrition, mobilisation, and physiotherapy, which may contribute to preventing deterioration of muscle functions and only a minor reduction in ALM.

Both equations of ALM (ALM with circumferences and the “abbreviated” version) were used since the reliability of circumference assessments can be compromised by clinical conditions like oedema (24) and changes in body composition

in older patients (37). When comparing the ALM estimates without circumferences, only one participant (6%) met the EWGSOP2 criteria for being sarcopenic (ASM <20 kg for men and <15 kg for women) (8). In an acute hospital setting with older adults (>65 years), the prevalence of EWGSOP-defined sarcopenia was 10% (1,38), which is in line with our results based on a much smaller sample. In contrast, another Danish study based on geriatric out-patients referred for falls assessment or general geriatric assessment, the prevalence of sarcopenia was 26% according to the criteria from the EWGSOP (39), which may be explained by a longer period of disabling conditions (falling, fear of falling, uncovered non-acute somatic disease) leading to a more sedentary lifestyle and sarcopenia.

Thirteen participants (76%) had lower HGS both at baseline and follow-up compared to reference values adjusted for gender, age, and height (15). Following the EWGSOP2 recommendation the number was 12 (70%). However, the EWGSOP2 recommendation takes only into account the gender, not the height and age, and there is no recommendation of which hand-dynamometer to use, nor definitions of HGS cut-offs for the varying hand-dynamometers. Looking at the prevalence of sarcopenia when based on strength (HGS) in this study, the prevalence is much higher compared to the prevalence of sarcopenic muscle mass (ALM). Studies have shown that the greatest decline in muscle strength occurs in the earliest stages of bed rest (23). Furthermore, it has been shown that a decline in muscle strength happens much faster than muscle atrophy during the first 2 weeks of bed rest (23), which underlines the fact that rectus femoris was a significant statistical parameter, not HGS. However, the finding of rectus femoris atrophy needs to be controlled in a larger population of geriatric inpatients.

The strength of this small study is that the ICC showed a value of 0.92, indicating an excellent reliability (33). As no other investigator was involved in the measurements interrater reliability could not be assessed. Considering that ultrasound is easily available, can be done bedside (20), and can be carried out after a few weeks of training (25), ultrasound should have a greater place in the diagnosis of sarcopenia. The MT measurements are easy to perform, and no equipment restrictions exist (24).

Study Limitations

A major limitation of this study is the relatively small sample size and the exclusion of the most vulnerable patients with dementia or delirium. Therefore, our results should be interpreted with caution. The prevalence of sarcopenia could have been higher if patients with these diagnoses had been included, as well as a larger sample size, and including patients with longer bedrest would increase the validity of the estimated prevalence as well as the representativeness of this patient group. Also, the muscle mass assessments by ultrasound and circumference

measurements of the geriatric in-patient population should be validated by DXA scans. In addition, we cannot rule out that small alterations in the contrast-enhancement software on the ultrasound device could have interfered with the results of the EI-measurements.

Conclusion

Our study suggests that it is feasible to perform assessment of sarcopenia using bedside assessments of geriatric inpatients and even a short period of hospitalization (5 days) seems to result in a significant reduction in both MT and EI of the m. rectus as measured by ultrasound, thereby suggesting a process of sarcopenia in a large muscle that has important functions for keeping normal posture and balance. Future studies addressing hospitalized geriatric patients should validate the bedside muscle quantity assessment by DXA scan, as well as doing in-home assessment for sarcopenia after discharge, to see how muscles of geriatric patients are affected by longer immobilisation and sedentary living during convalescence and rehabilitation.

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Ethics

Ethics Committee Approval: The study has been approved by the Local Ethics Committee (Videnskabsetisk Komité for Region Syddanmark) (S-20210100).

Informed Consent: All participants were informed orally and in writing about the purpose of the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.K.B., K.A.R., Concept: J.S.H., K.K.B., K.A.R., Design: J.S.H., K.K.B., K.A.R., Data Collection or Processing: J.S.H., Analysis or Interpretation: J.S.H., K.K.B., Literature Search: J.S.H., K.K.B., K.A.R., Writing: J.S.H., K.K.B., K.A.R.

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References

- Cruz-Jentoft AJ, Landi F, Schneider SM, Zúñiga C, Arai H, Boirie Y, Chen LK, Fielding RA, Martin FC, Michel JP, Sieber C, Stout JR, Studenski SA, Vellas B, Woo J, Zamboni M, Cederholm T. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing* 2014;43:748-759.
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M; 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;39:412-423.
- Perkisas S, Bastijns S, Baudry S, Bauer J, Beaudart C, Beckwée D, Cruz-Jentoft A, Gasowski J, Hobbelen H, Jager-Wittenaar H, Kasiukiewicz A, Landi F, Malek M, Marco E, Martone AM, de Miguel AM, Piotrowicz K, Sanchez E, Sanchez-Rodriguez D, Scafoglieri A, Vandewoude M, Verhoeven V, Wojszel ZB, De Cock AM. Application of ultrasound for muscle assessment in sarcopenia: 2020 SARCUS update. *Eur Geriatr Med* 2021;12:45-59.
- Landi F, Liperoti R, Fusco D, Mastropaolo S, Quattrociochi D, Proia A, Russo A, Bernabei R, Onder G. Prevalence and risk factors of sarcopenia among nursing home older residents. *J Gerontol A Biol Sci Med Sci* 2012;67:48-55.
- Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. *J Cachexia Sarcopenia Muscle* 2016;7:28-36.
- Yagi T, Inoue T, Ogawa M, Shimada Y, Heguri Y, Okada R, Iwata S, Kishimoto M. Sarcopenia affects activities of daily living recovery and hospitalization costs in older adults in convalescent rehabilitation wards. *Eur Geriatr Med* 2021;12:1237-1245.
- Beaudart C, Biver E, Reginster JY, Rizzoli R, Rolland Y, Bautmans I, Petermans J, Gillain S, Buckinx F, Dardenne N, Bruyère O. Validation of the SarQoL®, a specific health-related quality of life questionnaire for Sarcopenia. *J Cachexia Sarcopenia Muscle* 2017;8:238-244.
- Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; 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.
- Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146-M156.
- Schaap LA, van Schoor NM, Lips P, Visser M. Associations of Sarcopenia Definitions, and Their Components, With the Incidence of Recurrent Falling and Fractures: The Longitudinal Aging Study Amsterdam. *J Gerontol A Biol Sci Med Sci* 2018;73:1199-1204.
- Yeung SSY, Reijniers EM, Pham VK, Trappenburg MC, Lim WK, Meskers CGM, Maier AB. Sarcopenia and its association with falls and fractures in older adults: A systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle* 2019;10:485-500.
- Koon-Yee Lee G, Chun-Ming Au P, Hoi-Yee Li G, Chan M, Li HL, Man-Yung Cheung B, Chi-Kei Wong I, Ho-Fun Lee V, Mok J, Hon-Kei Yip B, King-Yip Cheng K, Wu CH, Cheung CL. Sarcopenia and mortality in different clinical conditions: A meta-analysis. *Osteoporos Sarcopenia* 2021;7:S19-S27.
- Leong DP, Teo KK, Rangarajan S, Lopez-Jaramillo P, Avezum A Jr, Orlandini A, Seron P, Ahmed SH, Rosengren A, Kelishadi R, Rahman O, Swaminathan S, Iqbal R, Gupta R, Lear SA, Oguz A, Yusuf S, Zatońska K, Chifamba J, Igumbor E, Mohan V, Anjana RM, Gu H, Li W, Yusuf S; Prospective Urban Rural Epidemiology (PURE) Study investigators. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet* 2015;386:266-273.
- Beaudart C, McCloskey E, Bruyère O, Cesari M, Rolland Y, Rizzoli R, Araujo de Carvalho I, Amuthavalli Thiyagarajan J, Bautmans I, Bertière MC, Brandi ML, Al-Daghri NM, Burlet N, Cavalier E, Cerreta F, Cherubini A, Fielding R, Gielen E, Landi F, Petermans J, Reginster JY, Visser M, Kanis J, Cooper C. Sarcopenia in daily practice: assessment and management. *BMC Geriatr* 2016;16:170.
- Frederiksen H, Hjelmborg J, Mortensen J, McGue M, Vaupel JW, Christensen K. Age trajectories of grip strength: cross-sectional and longitudinal data among 8,342 Danes aged 46 to 102. *Ann Epidemiol* 2006;16:554-562.
- Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. *Proc Nutr Soc* 2015;74:355-366.

17. Correa-de-Araujo R, Harris-Love MO, Miljkovic I, Fragala MS, Anthony BW, Manini TM. The Need for Standardized Assessment of Muscle Quality in Skeletal Muscle Function Deficit and Other Aging-Related Muscle Dysfunctions: A Symposium Report. *Front Physiol* 2017;8:87.
18. Watanabe Y, Yamada Y, Fukumoto Y, Ishihara T, Yokoyama K, Yoshida T, Miyake M, Yamagata E, Kimura M. Echo intensity obtained from ultrasonography images reflecting muscle strength in elderly men. *Clin Interv Aging* 2013;8:993-998.
19. Wu J, Luo H, Ren S, Shen L, Cheng D, Wang N. Enhanced echo intensity of skeletal muscle is associated with poor physical function in hemodialysis patients: a cross-sectional study. *BMC Nephrol* 2022;23:186.
20. Perkisas S, Baudry S, Bauer J, Beckwée D, De Cock AM, Hobbelen H, Jager-Wittenaar H, Kasiukiewicz A, Landi F, Marco E, Merello A, Piotrowicz K, Sanchez E, Sanchez-Rodriguez D, Scafoglieri A, Cruz-Jentoft A, Vandewoude M. Application of ultrasound for muscle assessment in sarcopenia: towards standardized measurements. *Eur Geriatr Med* 2018;9:739-757.
21. Puthuchery ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, Hopkinson NS, Phadke R, Dew T, Sidhu PS, Velloso C, Seymour J, Agley CC, Selby A, Limb M, Edwards LM, Smith K, Rowleron A, Rennie MJ, Moxham J, Harridge SD, Hart N, Montgomery HE. Acute skeletal muscle wasting in critical illness. *JAMA* 2013;310:1591-1600.
22. Bloomfield SA. Changes in musculoskeletal structure and function with prolonged bed rest. *Med Sci Sports Exerc* 1997;29:197-206.
23. Marusic U, Narici M, Simunic B, Pisot R, Ritzmann R. Nonuniform loss of muscle strength and atrophy during bed rest: a systematic review. *J Appl Physiol (1985)* 2021;131:194-206.
24. Barbosa-Silva TG, Gonzalez MC, Bielemann RM, Santos LP, Costa CDS, Menezes AMB; COCONUT Study Group, Brazil. $2 + 2 (+ 2) = 4$: A new approach for appendicular muscle mass assessment by ultrasound. *Nutrition* 2021;83:111056.
25. Tillquist M, Kutsogiannis DJ, Wischmeyer PE, Kummerlen C, Leung R, Stollery D, Karvellas CJ, Preiser JC, Bird N, Kozar R, Heyland DK. Bedside ultrasound is a practical and reliable measurement tool for assessing quadriceps muscle layer thickness. *JPEN J Parenter Enteral Nutr* 2014;38:886-890.
26. Mahoney FI, Barthel DW. Functional Evaluation: The Barthel Index. *Md State Med J* 1965;14:61-65.
27. Ryg J, Engberg H, Mariadas P, Pedersen SGH, Jorgensen MG, Vinding KL, Andersen-Ranberg K. Barthel Index at hospital admission is associated with mortality in geriatric patients: a Danish nationwide population-based cohort study. *Clin Epidemiol* 2018;10:1789-1800.
28. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373-383.
29. Fournaise A, Nissen SK, Lauridsen JT, Ryg J, Nickel CH, Gudex C, Brabrand M, Poulsen LM, Andersen-Ranberg K. Translation of the updated clinical frailty scale 2.0 into Danish and implications for cross-sectoral reliability. *BMC Geriatr* 2021;21:269.
30. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005;173:489-495.
31. Rech A, Radaelli R, Goltz FR, da Rosa LH, Schneider CD, Pinto RS. Echo intensity is negatively associated with functional capacity in older women. *Age (Dordr)* 2014;36:9708.
32. Wilhelm EN, Rech A, Minozzo F, Radaelli R, Botton CE, Pinto RS. Relationship between quadriceps femoris echo intensity, muscle power, and functional capacity of older men. *Age (Dordr)* 2014;36:9625.
33. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med* 2016;15:155-163.
34. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull.* 1979;86:420-428.
35. Sanz-Paris A, González-Fernandez M, Hueso-Del Río LE, Ferrer-Lahuerta E, Monge-Vázquez A, Losfablos-Callau F, Sanclemente-Hernández T, Sanz-Arque A, Arbones-Mainar JM. Muscle Thickness and Echogenicity Measured by Ultrasound Could Detect Local Sarcopenia and Malnutrition in Older Patients Hospitalized for Hip Fracture. *Nutrients* 2021;13:2401.
36. Beeri MS, Leugrants SE, Delbono O, Bennett DA, Buchman AS. Sarcopenia is associated with incident Alzheimer's dementia, mild cognitive impairment, and cognitive decline. *J Am Geriatr Soc* 2021;69:1826-1835.
37. Camina Martín MA, de Mateo Silleras B, Redondo del Río MP. Body composition analysis in older adults with dementia. Anthropometry and bioelectrical impedance analysis: a critical review. *Eur J Clin Nutr* 2014;68:1228-1233.
38. Gariballa S, Alessa A. Sarcopenia: prevalence and prognostic significance in hospitalized patients. *Clin Nutr* 2013;32:772-776.
39. Christensen MG, Piper KS, Dreier R, Suetta C, Andersen HE. Prevalence of sarcopenia in a Danish geriatric out-patient population. *Dan Med J* 2018;65:A5485.