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Ultrasound measurement of rectus femoris muscle thickness as a quick screening test for sarcopenia assessment

Rustani Kejda,
Postgraduate School of Geriatrics, University of Siena; Siena, Italy

Kundisova Lucia,
Postgraduate School of Public Health, University of Siena; Siena, Italy

Capecchi Pier Leopoldo,
Postgraduate School of Geriatrics, University of Siena; Siena, Italy

Nante Nicola,
Postgraduate School of Public Health, University of Siena; Siena, Italy

Bicchi Maurizio,
Postgraduate School of Geriatrics, University of Siena; Siena, Italy

Corresponding author: lucia.kundsiova@gmail.com

Highlights:

- The sensibility of the method in diagnosis of sarcopenia was 100%.
- ROC analysis showed high accuracy of the method (AUC resulted 0.9).
- This method is useful in elderly patients with functional or cognitive impairment.

ABSTRACT:

Introduction

Sarcopenia is a geriatric syndrome related to loss of muscle mass and function, leading to disability, frailty and higher mortality. According to *European Working Group on Sarcopenia in Older People* (EWGSOP) the diagnosis of sarcopenia requires the assessment of muscle mass, muscle force and function, that is time-consuming and not easily at hand in everyday clinical practice.

We propose the B-mode ultrasound measurement of muscle thickness as a quick screening test to assess the presence of sarcopenia.

Methods:

A cross-sectional study was realized, 119 patients (average age 82 years, 50.4% females) from the Department of Internal Medicine of the University Hospital of Siena (Italy) were enrolled. The diagnosis of sarcopenia was assessed according to EWGSOP criteria. Rectus femoris muscle (RFM) thickness (in cm) was measured by ultrasound B-mode scanning. Sensibility and specificity of the test was evaluated and Receiver Operating Analysis (ROC) was performed to assess the accuracy of

the test.

Results:

Average RFM thickness was 0.78 ± 0.26 , significantly lower in sarcopenic patients (0.55 ± 0.2 vs. 0.9 ± 0.3 ; Mann-Whitney; $p<0.001$) and females (0.7 ± 0.3 vs 0.86 ± 0.3 ; Mann-Whitney; $p<0.001$). The cut-off point of 0.7 cm for females and 0.9 cm for males was established as a threshold to assess the presence of sarcopenia by ultrasound. Sensibility of ultrasound measurement of RFM thickness was 100%, specificity 64%, positive predictive value (PPV) 64.3% and negative predictive value (NPV) 100%. ROC analysis was performed in order to quantify how accurately RFM thickness can discriminate between sarcopenia and non-sarcopenia state. AUC for all patients was 0.9 and after a comparative analysis for gender higher values for males (0.94 vs. 0.92) were observed.

Conclusion:

We suggest a screening test for sarcopenia based on the ultrasound measurement of RFM thickness, as a not invasive and easy to perform method even in elderly patients with functional or cognitive impairment.

Background

According to the *European Working Group on Sarcopenia in Older People* (EWGSOP), sarcopenia is defined as a "a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death" (Cruz-Jentoft, Landi, Topinkova, & Michel, 2010). It represents an important risk factor in elderly patients and is considered one of the main causes of invalidity and frailty (J. M. Bauer & Sieber, 2008).

The aetiology is multifactorial, and according to EWGSOP criteria it is classified in two groups: *primary* (age-related), and *secondary* (other causes or unknown origin). Muscle mass loss seems to be related to impaired protein turn-over (Nair, 1995), age-related impairment of endocrine system (Sakuma & Yamaguchi, 2012), and the "low-grade" chronic inflammation state, termed "*inflammageing*" (Franceschi et al., 2007). Fat tissue replaces muscle tissue, and adipocytes produce IL-6 e TNF- α and adipokines leptin and adiponectin, all involved in promoting of chronic inflammation. (Schaap et al., 2009)

Within some limits, age-related reduction of muscle mass is considered "physiological", it is important to recognize the moment when the process becomes progressive and disabling.

Sarcopenia can be asymptomatic for a long time, being masked by the relative stability of body weight, often non-corresponding with variations of fat tissue and muscle mass (J. Bauer et al.,

2013). Sarcopenia induces an impairment of both muscle mass and function and different techniques are suggested for detecting changes in these two parameters.

In order to assess muscle mass loss, EWGSOP suggests: Computed tomography (CT), Magnetic Resonance Imaging (MRI), Dual-energy X-ray Absorptiometry (DXA), and Bio-Impedance Analysis (BIA) (Cruz-Jentoft, Baeyens, et al., 2010). In the clinical practice, the use of these techniques is limited due to their cost, availability and facility of use. Ultrasound measurement of muscle mass can represent a quick and inexpensive method for detecting of muscle mass loss and qualitative changes (Sergi, Trevisan, Veronese, Lucato, & Manzato, 2016) even in the presence of acute and chronic diseases as imbalances in body fluids (Ticinesi, Meschi, Narici, Lauretani, & Maggio, 2017), being also comparable to other techniques such as DEXA, CT or MRI. (Nijholt, Scafoglieri, Jager-Wittenaar, Hobbelen, & van der Schans, 2017)

Several studies demonstrated that ultrasound measurement of the thickness of all four heads of quadriceps femoris muscle is highly reproducible in both sarcopenic and non-sarcopenic patients, and is also correlated with isometric maximum voluntary contraction force of quadriceps femoris muscle. The highest intra-class correlation coefficients were found for the large muscles as the quadriceps femoral muscle, probably because of the larger spatial resolution (Miyatani, Kanehisa, Kuno, Nishijima, & Fukunaga, 2002; Sanada, Kearns, Midorikawa, & Abe, 2006).

However, this technique has not yet been introduced as a diagnostic method for sarcopenia in the clinical practice, due to the absence of standardized protocols.

Aim of the study:

Aim of this paper was to assess the validity of the ultrasound measurement of the rectus femoris muscle (RFM) thickness as a screening test for sarcopenia.

Material and methods:

A cross-sectional study was carried out in the Department of Internal Medicine at the University Hospital of Siena (Italy) between February and November 2016. All recovered patients were asked to participate on the study, they were enrolled if they expressed their informed consent with participation. Patients were divided into two groups based on the presence of sarcopenia (sarcopenic and non-sarcopenic).

The diagnosis of sarcopenia was established using diagnostic criteria of the EWGSOP:

1. Muscle mass was assessed through anthropometric measures of mid-arm muscle circumference (MAMC) using the formula: $MAMC = \text{mid-arm circumference} - (3.14 \times \text{thickness of tricipital fold})$. Measurements were performed with Skinfold calliper FAT-1, on

- the right side of the patient. A low muscle mass was classified as MAMC <21.1 in males and <19.2 cm in females, as in the Sirente Study.
2. Muscle force was assessed by measuring handgrip strength (HS) by a digital dynamometer (DynX); HS was measured for both hands, and only the higher value was registered. Muscle strength was classified as impaired if $HS < 30$ kg for males, and $HS < 20$ kg for females;
 3. Physical performance was evaluated using gait speed measurement in 4 metres walking test, assessing a cut-off point for impaired physical performance at the speed $< 0,8$ m/sec for both sexes.

In addition to these techniques, ultrasound measurement of Rectus femoris muscle (RFM) thickness was performed in B-mode using linear multifrequent transducer (5-7.5 MHz, MyLab 25Gold-Esaote). RFM thickness was assessed on the right side of the patient, in a supine position with both knees extended and relaxed and toes pointing to the ceiling, at the halfway point between epicondylus lateralis and trochanter major of the femur. The transducer was placed perpendicularly to the long axis of the thigh with adequate use of contact gel and minimal pressure to avoid excessive compression of the muscle. All measurements were taken by the same physician in order to avoid inter-individual variability.

A set of three consecutive measurements was performed, and the average value was reported as RFM thickness. Data were reported in centimeters (cm) as means \pm standard deviation.

Statistical analysis:

Feasibility and reliability of the ultrasound measurement of RFM thickness as a quick “screening” test to establish the presence of sarcopenia were assessed by measuring method's SENSITIVITY: probability of “real sarcopenic patients” (whose diagnosis was established using the EWGSOP criteria) to be “positive” (identified by ultrasound measurement of RFM as “sarcopenic”), and method's SPECIFICITY: probability of “real non-sarcopenic” patients to result “negative” in the test. To achieve this aim, empirical cut-off points of RFM thickness values were established; RFM thickness value under the cut-off point was considered “positive”.

The accuracy of ultrasound measurement of RFM thickness in assessing of the presence of sarcopenia was evaluated by Receiver Operating Characteristics analysis (ROC). The accuracy of the test was measured by the area under the ROC curve (AUC), an area close to 1 represents a perfect diagnostic test; an area of 0.5 represents a worthless test.

Statistical analysis was performed with Stata 12, and the level of significance was set at $p < 0.05$.

Results:

A total of 119 patients was enrolled; 50.4% were females, the average age was 82.8 ± 7 without any significant difference based on gender or presence of sarcopenia. Prevalence of sarcopenia was 38.7%, without difference between two sexes.

It was not possible to calculate an average mid-arm circumference, as the variable was coded in two groups (altered/normal) based on threshold value (21.1 cm for males, 19.2 cm for females).

Practically all sarcopenic patients resulted to have this value altered.

Average HS was 12.4 ± 8.4 , significantly higher in non-sarcopenic patients (14.6 ± 8.5 vs. 8.5 ± 6.5 ; Mann-Whitney; $p < 0.001$) and in males (15.5 ± 9.4 vs. 9.1 ± 5.5 ; Mann-Whitney; $p < 0.001$).

It was not possible to calculate an average gait speed, as the variable was coded into three groups (not walking, gait speed < 0.8 m/s, gait speed ≥ 0.8 m/s). Sarcopenic patients were more frequently collocated into groups with altered gait speed (chi-2; $p < 0.05$).

Average RFM thickness measured by ultrasound was 0.78 ± 0.26 , values were significantly lower in sarcopenic patients (0.57 ± 0.15 vs. 0.92 ± 0.23 ; Mann-Whitney; $p < 0.001$) and females (0.7 ± 0.3 vs. 0.86 ± 0.3 ; Mann-Whitney; $p < 0.001$). Due to remarkable differences in RFM thickness values between males and females, we proceeded with analysis stratified per gender, values are reported in Table 1.

Table 1: Values of RFM thickness measured by B-mode ultrasound for sarcopenic/non-sarcopenic patients and males/females; data are expressed as Means, Range, Median.

		<i>RFM thickness</i>		
		<i>Mean\pmStd. Dev.</i>	<i>Range</i>	<i>Median</i>
All patients	<i>All</i>	0.78 ± 0.26	0.3-1.5	0.80
	<i>Males</i>	$0.86 \pm 0.27^*$	0.3-1.5	0.90
	<i>Females</i>	0.69 ± 0.23	0.3-1.5	0.70
Sarcopenic patients	<i>All</i>	0.57 ± 0.15	0.3-0.9	0.52
	<i>Males</i>	$0.63 \pm 0.17^*$	0.3-0.9	0.60
	<i>Females</i>	0.50 ± 0.10	0.3-0.7	0.50
Non-sarcopenic	<i>All</i>	0.92 ± 0.23	0.5-1.5	0.90
	<i>Males</i>	$1.02 \pm 0.20^*$	0.6-1.5	1.00

patients	<i>Females</i>	0.82±0.20	0.5-1.5	0.82
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* Mann-Whitney, $p < 0.005$

The next step was to examine if the RFM thickness was correlated with results provided by other techniques used to detect muscle impairment (assessment of muscle mass and muscle force). Unfortunately it was not possible to perform a correlation between arm circumference and gait speed and RFM thickness, because both variables were not coded as continuous. A significant correlation between HS and RFM thickness was observed (Spearman's correlation coefficient $\rho = 0.5$; $p < 0.001$); the correlation was stronger and even more significant for males (Males $\rho = 0.6$; $p \leq 0.001$ vs. Females $\rho = 0.3$; $p < 0.05$).

Empirical cut-off points of RFM thickness values were established to identify "positive" patients; at first we decided to use the threshold of 0.5 cm for females and 0.6 cm for males. Using these cut-off points, sensitivity and specificity of the test resulted 63% and 93%, respectively. As sensitivity was the parameter of major interest in our study (need of identifying all subjects at risk for sarcopenia), the cut-off points were set to 0.7 cm and 0.9 cm for females and males, respectively, thus obtaining 100% sensitivity and 64% specificity; positive predictive value (PPV) resulted 64.3%, and negative predictive value (NPV) 100%.

ROC analysis was performed in order to quantify how accurately RFM thickness discriminates between sarcopenia and non-sarcopenia, AUC for all patients was 0.9 (Fig.1). Following comparative analysis for gender evidenced even a higher value for males (0.94 vs. 0.92) (Fig.2).

DISCUSSION

Although the EWGSOP consensus provided valid and useful tools for the diagnosis of sarcopenia, nevertheless it has large limitations in the clinical settings. (Landi et al., 2012)

Particularly, hospitalized patients with chronic or acute diseases, depression or cognitive decline can hardly execute handgrip strength or gait speed tests. Regarding the muscle mass assessment, the techniques suggested by EWGSOP consensus are not always available in the clinical context or in extra-hospital settings such as nursing homes. (J. M. Bauer, Kaiser, & Sieber, 2008) In such situations, anthropometric measures represent a valid alternative, but they are quite time consuming. Therefore, the need for a rapid, reliable, and accurate tool led us to the evaluation of RFM thickness, measured by ultrasound, as a rapid screening test for sarcopenia. Our results seem very encouraging as this method demonstrated to be highly accurate, as confirmed by the excellent results of the ROC analysis. Certainly, after detecting "positive patients" with muscle thickness values under the cut-off points, the diagnosis should be confirmed using current validated

diagnostic criteria. It is necessary to establish the right cut-off point to identify correctly patients affected by sarcopenia.

The principal limitation of our study was the small sample size and the impossibility to examine a correlation between RFM thickness and arm circumference. Further research and evaluation of a diagnostic protocol are needed in order to establish the correct cut-off values.

CONCLUSION

Given the impact of sarcopenia on patients' quality of life (Tsekoura, Kastrinis, Katsoulaki, Billis, & Gliatis, 2017) and hospitalization-related costs, its early diagnosis and treatment should be accurately focused, also in terms of prevention of adverse outcomes. Therefore, future researches are needed to find a consensus on simple and valid tools that can be used for the diagnosis and screening of sarcopenia in everyday clinical practice.

For this purpose, we suggest a screening for sarcopenia, even in ambulatory settings, based on the ultrasound detection of RFM thickness, as a non-invasive and easy to perform technique even in elderly patients with functional or cognitive impairment. In our opinion, this method should be integrated with clinical evaluation and comprehensive geriatric assessment and may represent a very useful tool for the study of muscle mass and quality.

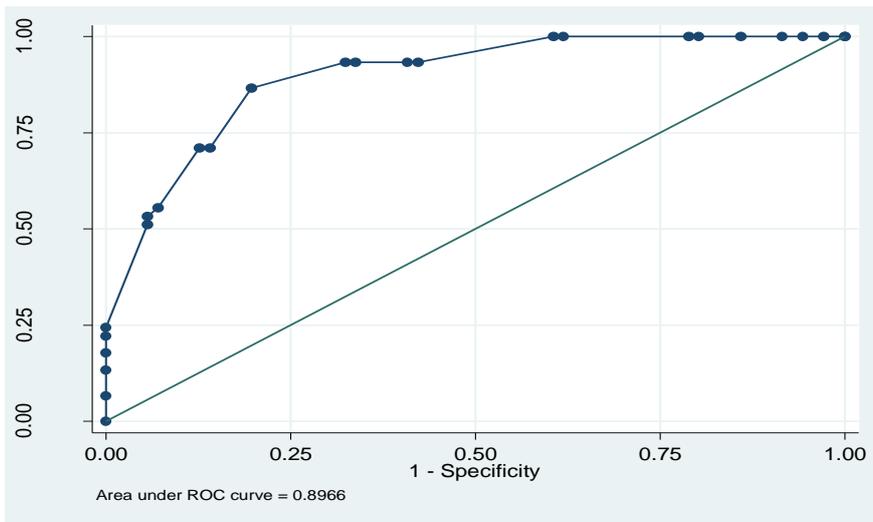
Conflict of interest: The authors declare no competing interests.

Ethical approval: Ethical approval was not required, informed consent of participants was obtained.

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REFERENCES:

- Bauer, J., Biolo, G., Cederholm, T., Cesari, M., Cruz-Jentoft, A. J., Morley, J. E., . . . Boirie, Y. (2013). Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. *J Am Med Dir Assoc*, *14*(8), 542-559. doi: 10.1016/j.jamda.2013.05.021
- Bauer, J. M., Kaiser, M. J., & Sieber, C. C. (2008). Sarcopenia in nursing home residents. *J Am Med Dir Assoc*, *9*(8), 545-551. doi: 10.1016/j.jamda.2008.04.010
- Bauer, J. M., & Sieber, C. C. (2008). Sarcopenia and frailty: a clinician's controversial point of view. *Exp Gerontol*, *43*(7), 674-678. doi: 10.1016/j.exger.2008.03.007
- Cruz-Jentoft, A. J., Baeyens, J. P., Bauer, J. M., Boirie, Y., Cederholm, T., Landi, F., . . . European Working Group on Sarcopenia in Older, P. (2010). Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*, *39*(4), 412-423. doi: 10.1093/ageing/afq034
- Cruz-Jentoft, A. J., Landi, F., Topinkova, E., & Michel, J. P. (2010). Understanding sarcopenia as a geriatric syndrome. *Curr Opin Clin Nutr Metab Care*, *13*(1), 1-7. doi: 10.1097/MCO.0b013e328333c1c1
- Franceschi, C., Capri, M., Monti, D., Giunta, S., Olivieri, F., Sevini, F., . . . Salvioli, S. (2007). Inflammaging and anti-inflammaging: a systemic perspective on aging and longevity emerged from studies in humans. *Mech Ageing Dev*, *128*(1), 92-105. doi: 10.1016/j.mad.2006.11.016
- Landi, F., Liperoti, R., Fusco, D., Mastropaolo, S., Quattrociocchi, D., Proia, A., . . . Onder, G. (2012). Prevalence and risk factors of sarcopenia among nursing home older residents. *J Gerontol A Biol Sci Med Sci*, *67*(1), 48-55. doi: 10.1093/gerona/blr035
- Miyatani, M., Kanehisa, H., Kuno, S., Nishijima, T., & Fukunaga, T. (2002). Validity of ultrasonograph muscle thickness measurements for estimating muscle volume of knee extensors in humans. *Eur J Appl Physiol*, *86*(3), 203-208.
- Nair, K. S. (1995). Muscle protein turnover: methodological issues and the effect of aging. *J Gerontol A Biol Sci Med Sci*, *50 Spec No*, 107-112.
- Nijholt, W., Scafoglieri, A., Jager-Wittenaar, H., Hobbelen, J. S. M., & van der Schans, C. P. (2017). The reliability and validity of ultrasound to quantify muscles in older adults: a systematic review. *J Cachexia Sarcopenia Muscle*, *8*(5), 702-712. doi: 10.1002/jcsm.12210
- Sakuma, K., & Yamaguchi, A. (2012). Sarcopenia and age-related endocrine function. *Int J Endocrinol*, *2012*, 127362. doi: 10.1155/2012/127362
- Sanada, K., Kearns, C. F., Midorikawa, T., & Abe, T. (2006). Prediction and validation of total and regional skeletal muscle mass by ultrasound in Japanese adults. *Eur J Appl Physiol*, *96*(1), 24-31. doi: 10.1007/s00421-005-0061-0
- Schaap, L. A., Pluijm, S. M., Deeg, D. J., Harris, T. B., Kritchevsky, S. B., Newman, A. B., . . . Health, A. B. C. S. (2009). Higher inflammatory marker levels in older persons: associations with 5-year change in muscle mass and muscle strength. *J Gerontol A Biol Sci Med Sci*, *64*(11), 1183-1189. doi: 10.1093/gerona/ghp097
- Sergi, G., Trevisan, C., Veronese, N., Lucato, P., & Manzato, E. (2016). Imaging of sarcopenia. *Eur J Radiol*, *85*(8), 1519-1524. doi: 10.1016/j.ejrad.2016.04.009
- Ticinesi, A., Meschi, T., Narici, M. V., Lauretani, F., & Maggio, M. (2017). Muscle Ultrasound and Sarcopenia in Older Individuals: A Clinical Perspective. *J Am Med Dir Assoc*, *18*(4), 290-300. doi: 10.1016/j.jamda.2016.11.013
- Tsekoura, M., Kastrinis, A., Katsoulaki, M., Billis, E., & Gliatis, J. (2017). Sarcopenia and Its Impact on Quality of Life. *Adv Exp Med Biol*, *987*, 213-218. doi: 10.1007/978-3-319-57379-3_19

Fig.1: ROC analysis for accuracy of ultrasound measurement of RFM thickness in the diagnosis of sarcopenia.**Fig. 2: ROC analysis for gender.**