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Clinical impact of osteosarcopenia on mortality, physical function and chronic inflammation: a 9-year follow up cohort study

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ABSTRACT

Objective: This study aimed to determine the impact of osteosarcopenia on important clinical and functional outcomes in older adults.

Methods: 242 community-dwelling older adults from the study on ageing and longevity (ELLO data from 2009 to 2018). Subjects underwent body composition analysis by dual energy X-ray absorptiometry and bioelectrical impedance, and assessments for aerobic capacity and muscle strength including the incremental shuttle walking test (ISWT), 6-minutes walking test (6MWT), handgrip strength (HGS) and sit-to stand test (STS). Static balance was assessed by one-legged stance test (OLST) and chronic inflammation by IL-6 and tumor necrosis factor alpha (TNF-α). Osteosarcopenia was defined as low bone mineral density (BMD) (T-score<-1) combined with low phase angle (PhA). Comparisons were run with Students T test and Man-Whitney test. Survival probabilities were estimated using the Kaplan-Meier method. Receiver operating characteristic curve was used to analyze the association of PhA with mortality and to find the best cut-point.

Results: The proportion of individuals who died in a 9-year follow up was higher in individuals with Osteosarcopenia (25%) compared to without osteosarcopenia (9%) (p=0.015). Osteosarcopenia was associated with mortality (HR: 1.4; 95% CI 1.02 - 1.29; p = 0.0151). Subjects with osteosarcopenia compared to without it presented worse performance in the ISWT (514 ±19 m vs. 621 ± 16 m), 6MWT (515 ± 7 m vs. 538 ± 6 m, p< 0.05), OLST (13.5 ±10.2 s vs.16.7 ±8.3 s) and HGS (25 ± 7 Kg vs. 28 ± 9 K5); p< 0.05 for all. The cut point used to PhA was ≤ 6.07º for both male and female (AUC: 0.687; Sensibility: 64% and Specificity: 61% for mortality).

Conclusion: Osteosarcopenia diagnosed with low phase angle combined with low BMD is highly associated with mortality. Additionally, older adults with osteosarcopenia presented worse aerobic capacity, balance and muscle strength.

KEYWORDS

Osteosarcopenia, sarcopenia, older people, functionality, mortality.

INTRODUCTION

Osteosarcopenia is a new geriatric syndrome defined as a simultaneous presence of osteoporosis or osteopenia with sarcopenia[1]. Studies show characteristics overlapping signaling by similar biological pathways related to reduction in muscle and bone mass[1,2]. This interaction in both muscles and bones, observed in osteoporosis/osteopenia and sarcopenia, is classified as osteosarcopenia[3]. The prevalence of osteosarcopenia can increase the risk of falls and fractures, frailty, disability, becoming a growing medical and financial disease[3,4].

Osteosarcopenia is less prevalent in elderly population than sarcopenia, however this new geriatric syndrome has a greater negative impact on functionality and falls compared to

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sarcopenia alone[1,5]. The prevalence of osteosarcopenia may vary from 5 to 37% and it is higher in women and in individuals older than 80 years[6]. Despite the large prevalence and the negative consequences of osteosarcopenia on clinical variables, its impact on functionality and risk of mortality in older people are still lacking analyzed.

Osteosarcopenia is detected as the presence of osteoporosis or osteopenia combined with sarcopenia[1]. The clinical diagnosis of osteopenia or osteoporosis is well defined (T score <-1), both condition are defined as the loss of bone mineral density (BMD) compared to a reference population, according to the criteria of the World Health Organization (WHO)[7]. On the other hand, despite the significant increase in studies related to sarcopenia, there is no agreement among consensus on which measurement tools and cut off points should be used to better define the diagnosis of sarcopenia[8-11]. In addition the cut off points used to diagnose sarcopenia have been developed in populations other than Latin America[9-11], where there is still no consensus[12].

This disagreement between the different sarcopenia criteria[12] has influence on the diagnosis of osteosarcopenia[1]. For this reason, it would be important to use a single measurement associated with muscle mass and muscle function, in the definition of the "sarcopenia component" in the diagnosis of osteosarcopenia. In this context, the phase angle (PhA) is a variable that indicates the quality of the muscle and is associated with the diagnosis of sarcopenia[13].

The parameters for calculating PhA are derived from the bioelectrical impedance test (BIA), which is an easy, non-invasive and inexpensive method, with good accuracy and reliability to asses body composition[14]. To our knowledge, the clinical impact of osteosarcopenia on functional variables and mortality using PhA combined with low BMD have not been studied before. For this reason, the aim of this study was to determine the impact of a new and simple criteria to diagnose osteosarcopenia using low PhA and BMD, on mortality and on important clinical and functional outcomes in elderly people.

METHODS

Population study

The present study was performed a longitudinal cohort design, which monitoring a single result (mortality) in older people from the study on aging and longevity (ELLO data from 2009 to 2018) from the community of Londrina, Paraná, Brazil. The research was approved by the Research Ethics Committee of *Universidade Norte do Paraná* (UNOPAR) for both study designs (PP / 0070/09 and PP 1,168,693). The collections and tests were performed at the UNOPAR. All participants signed an informed consent form.

The total sample of the EELO Project was 508 subjects, which is representative of the 43,610 citizens over 60 years of age who live in Londrina city. Subsequently, from the EELO program database, part of the sample was selected to measure the bone mineral density (BMD). Criterion considered for the BMD test was do not use medication that interferes with bone metabolism. We included older adults of both sexes, physically self-reliant according to the classification proposed by Spirduso functional status (levels 3 and 4). Therefore, individuals who performed the basic and instrumental activities of daily life were included. Also, we included older adults with normal cognitive level assessed by the mini-mental state examination questionnaire (> 17 points). We considered adults aged 60 years or over, in accordance with the recommendation of the WHO. Subjects with alcoholic habits, some decompensated chronic disease or physical limitation that would impair the understanding and performance of the tests involved in the study were excluded.

Body composition

The analysis of body composition was performed via dual energy absorptiometry by X-rays (DEXA) and bioimpedance (BIA). Muscle mass and BMD were assessed using DEXA (QDR 4500, Hologic Inc., Bedford, USA). BMD was assessed in the lumbar spine (L1-L4) and femoral neck. The interpretation for the diagnosis was made according to the WHO criteria, as follows: normal BMD with a T score of up to -1.0 SD, osteopenia T score of -1.0 to -2.4 SD and Osteoporosis T score ≤ -2 5 SD at any bone site[7].

Phase Angle was measured using bioelectrical impedance (Bio-dynamics 310TM; Biodynamics Corp., USA), after 10-hour of fasting. The test was performed on the dominant side of the individual with the patient in a supine position, the arms and legs were separated by approximately 30 degrees from a midline. The electrode placement sites were cleaned with alcohol. One electrode was placed in the hand and the other in the foot. After connecting the cables to the electrodes, the corresponding values were recorded. The calculation of the phase angle derived from the relationship between the direct measurements of reactance (Xc) and resistance (R) was calculated directly by the equation: PhA = arctangent (Xc / R). Osteosarcopenia in this study was defined as low bone mineral density (BMD) (T score <-1) [7], combined with low PhA (using the cutoff point calculated in this study).

Aerobic capacity

Aerobic capacity was assessed by the incremental shuttle walk test (ISWT) and the six-minute walk test (6MWT). In the ISWT, patients must walk quickly, at increasing speeds, on a 10 m course delimited by 2 cones (at the beginning and at the end). An audible signal, which represents a change in level, as well as an increase in the patient's speed during the test, with a total of 15 levels. The 6MWT was performed according to the American Thoracic Society standards. The patient cov-

ered the maximum possible distance walking in a linear path with 30 meters in length bounded by two cones, for 6 minutes. Standardized incentive phrases and information about the remaining test time were used. There were two evaluations with an interval of 30 minutes. The greater distance performed between the two attempts was analyzed.

Muscle strength

Muscle strength was assessed via handgrip strength testing (HST) and sit-to stand test (STS). The handgrip strength testing was assessed in the sitting position, using a Jamar hydraulic dynamometer (Sammons Preston Inc, Saint Paul, MN) with the forearm and wrist resting on the arms of the chair. Participants performed 3 attempts on each hand, alternating between them, with a 30-second rest between tests. The highest value was recorded and used for analysis. The STS indirectly assesses the strength of the lower limbs. The patient was instructed to sit completely in the chair, to stand up fully extending the knees, without performing postural compensations, keeping the arms crossed in front of the chest and should be performed repeatedly. The result is obtained by the total number of correct executions in the 30 second interval.

Static balance

Static balance was assessed by the one-legged support test (OLST), the test is performed with the patient in unipedal support on a stable platform with the eyes open. The best time of three attempts of the dominant leg was considered for the analysis.

Chronic Inflammation

Chronic inflammation was assessed from venous blood to measure interleukin 6 (IL-6) 24 and tumor necrosis factor alpha (TNF-α), after 10-hour of fasting. The Peprotech kit was used to measure IL-6 cytosine and the Abnova kit to measure TNF-α, the quantification of cytokines was performed using the flow cytometry technique according to previous studies[15].

Mortality

Mortality and causes of death were obtained from the Mortality Information Center (MIC) of the Municipal Health Department of Londrina, Brazil from March 2009 to December 2018. In the case of older adults who were part of the EELO data collection in Londrina and moved to other regions of Brazil and died elsewhere, the information on their death was made through the national MIC.

Statistical Analysis

The parametric distribution of the continuous variables was checked using the Kolmogorov-Smirnov test and the graphical procedures (normal probability plot). Descriptive statistics were used to describe the demographic and clinical characteristics of the patients and other potentially confounding variables. Continuous variables were presented as the mean and standard deviation (SD), and categorical variables were presented as the number and percentage. The comparison of the clinical variables (aerobic capacity, balance, muscle strength and inflammation) was performed with the Student's t, U Mann-Whitney tests and Chi-square test to compare categorical variables. The receiver's operational characteristic curve (ROC) was used to detect the best cutoff point for PhA with mortality. Survival probabilities were estimated using the Kaplan-Meier curves and Mantel-Cox analysis to compare survival curves between those subjects with and without osteosarcopenia at 9 years. The statistical significance was considered as $p < 0.05$, and the analysis was performed using SPSS software (IBM Co., USA) and GraphPad Prism 6.0 (GraphPad Software, San Diego, CA, USA).

RESULTS

Of the 323 subjects who met the inclusion criteria for BMD, 43 were not found, 29 refused to participate, and 9 died before performing the BMD evaluation. Finally, the study included 242 subjects (age: 68 ± 6 years; women 77%; body mass index 27.6 ± 4Kg / m2). Most of the individuals presented BMI equal or higher than 25 Kg/m^2 (72.7%), Regarding prevalence of comorbidities, 58.6% presented hypertension, 20% diabetes and 11.9% osteoporosis. Other variables are reported in the Table 1.

The ROC analysis in PhA to mortality is presented in Figure 1. The cutoff point detected for PhA was ≤ 6.07º for both male and female (AUC: 0.687; Sensibility: 64% and Specificity: 61% for mortality).

The clinical impact of osteosarcopenia detected using this cutoff point combined with low BMD (T score <-1) is presented in Figure 2. Individuals with osteosarcopenia compared to those without it presented worse performance in the ISWT (514 ±19 m versus 621 ± 16 m; p< 0.001), 6MWT (515 ± 7 m versus 538 ± 6 m; p=0.015), OLST (13.5 ±10.2 s versus 16.7 ±8.3 s; p=0.012) and HGS (25 ± 7 Kg versus 28 ± 9 Kg; p=0.0006). No significant difference was observed in STS (p=0.84), IL-6 (p=0.18), TNF-α (p=0.26).

The overall survival proportion analysis between those subjects with and without osteosarcopenia during in a 9-year follow-up was presented in the Figure 3. The proportion of subjects who died in a 9-year follow-up was higher in the osteosarcopenia group (25%) compared to those without osteosarcopenia (9%). The presence of osteosarcopenia was associated with higher risk of mortality HR: 1.4 (95% CI 1.02 - 1.29; p = 0.015).

Table 1. Characteristics of the individuals

VARIABLES	N= 242
Age (years)	68 ± 5.8
Female, n (%)	168 (70%)
BMI (Kg/m^2)	s27.6 ± 4.6
BMI Classification	
< 18.5	4 (1.7%)
18.5 - <25	62 (25.6%)
25 - <30	106 (43.8%)
> 30	70 (28.9%)
Comorbidities	
Hypertension	142 (58.6%)
Diabetes	49 (20.2%)
Osteoporosis	29 (11.9%)
Body Composition	
BMD lumbar spine (T-score)	-1.29 ± 1.52
BMD femoral neck (T-score)	-1.69 ± 1.03
SMI (Kg/m^2)	8 ± 1.5
Phase angle (º)	6.25 ± 0.86
Aerobic capacity	
ISWT (m)	584.5 ± 195.5
6MWT (m)	529.8 ± 67.7
Muscle strength	
HGS (Kg)	26.7 ± 8.1
SST (rep)	11.74 ± 2.25
Static balance	
OLST(sec)	15.6 ± 9.8
Chronic inflammation	
IL-6 (pg/mL)	10476 (5944-20589)
TNF-α (pg/mL)	7.81 (1.9-17.3)

BMI: body mass index; SWT: shuttle walking test; 6MWT: 6 minutes walking test; OLST: one legged stance test; SST: sit to stand; IL6: interleukin 6; TNF-α : tumoral necrosis alpha.

DISCUSSION

To our knowledge, this study represents the pioneering analysis of the impact of osteosarcopenia on mortality and various clinical outcomes. Subjects with osteosarcopenia exhibited notable declines in physical performance, muscle strength, aerobic capacity, static balance, and a heightened risk of mortality. These findings underscore the utility of utilizing PhA and BMD as metrics for assessing muscle and bone mass, respectively. These measurements enable the identification of subjects with impaired functional performance and an elevated mortality risk over a 9-year follow-up period.

These results emphasize the critical importance of early detection of this geriatric syndrome due to its great impact on the health of older adults. Furthermore, this study has identified a new cut-off point for PhA ≤ 6.07º to detect risk of mortality in older people. The clinical diagnosis of this new geriatric syndrome holds significant clinical relevance, as it has been associated with a greater propensity for functional decline and fractures in comparison to individuals with sarcopenia, osteoporosis, or osteopenia, as delineated in both our current investigation and prior research[5,16].

The clinical measurements utilized for detecting osteosarcopenia can be separated in those utilized for "osteo" and "sarcopenia" component[1]. We used PhA to assess the "sarcopenia component" given its well-documented associations with diverse clinical variables[17-19]. PhA reflects the muscle quality, related to muscle mass and muscle strength[20,21]. Lower PhA values may indicate compromised cell integrity or even cell death, whereas higher values correspond to intact cell membranes, indicative of good health status[20,22]. PhA seems to be reliable in detecting changes in clinical parameters over time, which, in turn, could contribute to the understanding of its prognostic utility[23]. In addition, previous studies have shown associations between PhA with hospitalization and mortality in older adults[23], particularly among those with chronic diseases[24,25]. Therefore, phase angle is a measurement highly associated with important clinical variables in older people.

The association between PhA and mortality has been well-stablished in the scientific literature. A recent systematic review with 11,534 patients with varying clinical conditions demonstrated correlations between PhA and mortality, with reported cutoff points ranging from 3.2º to 7.8º [17]. This variability in PhA value can be attributed to the diverse populations of the studies included in this systematic review[17]. The proposed cutoff points are tailored to specific study cohorts and might not be universally applicable to general clinical practice[18,19]. For this reason, the identification of population-specific cutoff points assumes paramount significance. Therefore, we have identified the cutoff point for PhA ≤ 6.07º, which is a little higher than other previous cutoff points for Brazilian population[17,26]. These previous studies have in-

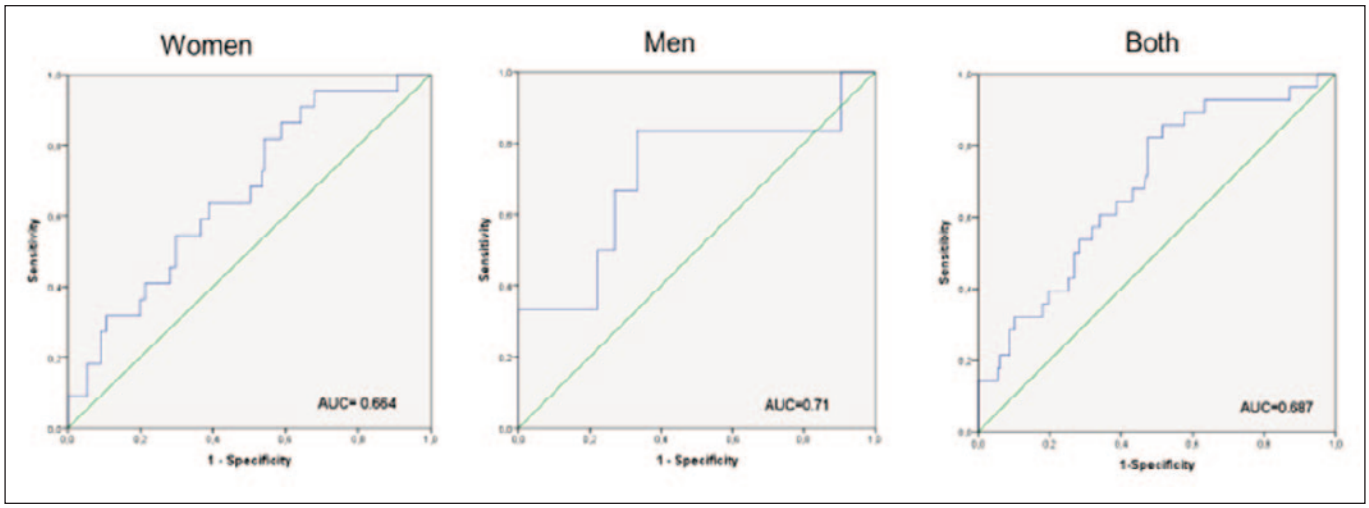

Figure 1. Receiver operating characteristic curve (ROC) in phase angle to mortality

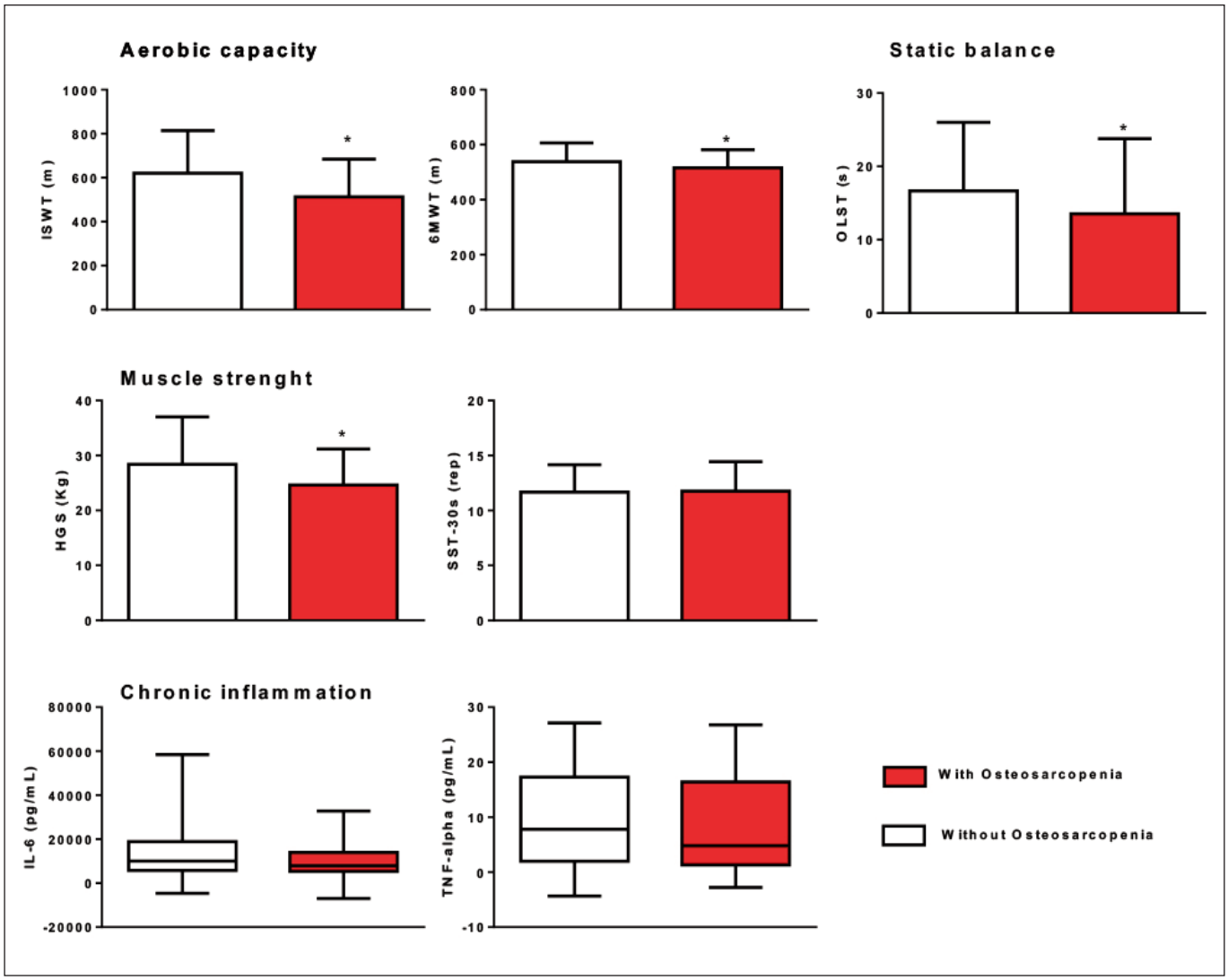

Figure 2. Comparison between older people with and without osteosarcopenia

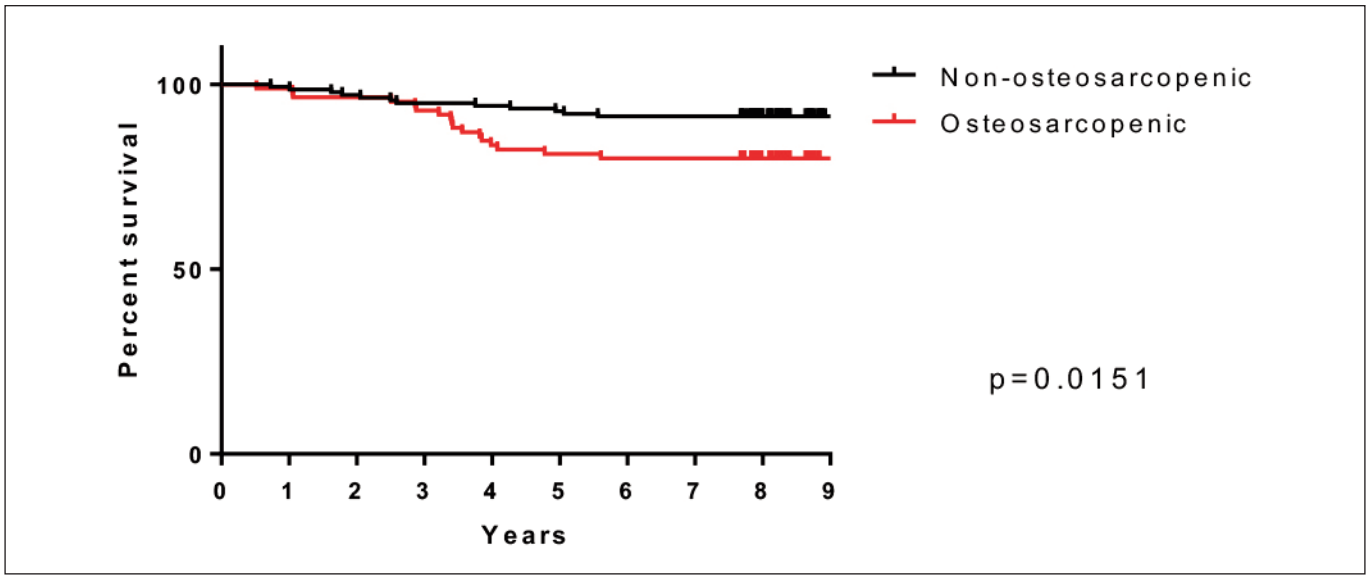

Figure 3. Survival proportion between the groups in a 9-year follow-up

cluded individuals with other clinical conditions (i.e. hospitalized patients, septic patients) and with different range of follow-up (from 1 month to 25 months)[17,26]. Our study, in contrast, centered on older individuals without functional disability or chronic decompensated diseases, and featured a more extensive follow-up period.

Electrical bioimpedance emerges as a pivotal tool for PhA determination, as it enables the identification of low muscle mass and sarcopenia among the elderly[20,21]. While consensus predominantly favors dual-energy X-ray absorptiometry (DEXA) for measuring muscle mass, studies have elucidated correlations between bioimpedance-derived parameters and DEXA[27]. Bioimpedance analysis is an easy, non-invasive and inexpensive method, with good accuracy and reliability to asses body composition and PhA[14]. On the other hand, in light of our findings, using PhA to measure the "sarcopenia component" combined with low BMD, can diagnose osteosarcopenia faster, lower cost and less invasively. PhA could be a useful tool for the diagnosis of osteosarcopenia because there are different reference values for each sarcopenia criterion in the elderly population, and there is not agreement between them[28]. Given the heterogeneity of reference values for sarcopenia criteria among the elderly population, PhA emerges as a potent tool for the effective detection of this novel geriatric syndrome, thereby enabling preemptive interventions to mitigate functional deterioration and mortality in this population.

Older people with geriatric syndromes are characterized with increased reaction time, greater postural oscillation in the orthostatic position and decreased effectiveness of motor strategies of postural balance, which are associated with risk of falls and fractures[29]. In addition, studies mention a progressive decrease in body weight from the age of 65 years and attribute the loss of body mass, especially to decreased food intake, difficulty in chewing and changes in body composition related to aging, such as increased deposition of fat, loss of bone mass and muscle mass, further contributing to diminished physical and functional performance[30]. Osteosarcopenia exacerbates these declines, as corroborated by prior investigations[1,5], thereby suggesting a potentially greater negative impact compared to other geriatric syndromes like sarcopenia or frailty[1]. Our study substantiates that older adults afflicted by osteosarcopenia experience pronounced declines in physical performance, muscle strength, aerobic capacity, static balance, and an elevated mortality risk. Considering these cumulative insights, early diagnosis of osteosarcopenia becomes imperative in older adults to forestall future functional impairment and mortality.

While our study did not reveal disparities in inflammatory biomarkers, it is important to note that this does not necessarily negate the presence of chronic inflammation among osteosarcopenic individuals, as previously documented in the literature[4]. Our analysis encompassed only two biomarkers (IL6 and TNF-α). Therefore, there are other biological pathways that are needed to be investigated in future studies.

The strengths of this study that must be considered, including a robust sample size, an extensive follow-up period, a comprehensive array of evaluated variable, and the utilization of gold-standard measures for muscle mass and bone mineral density. Nonetheless, as a limitation of this study, although it explored mortality for 9 years, not all variables were monitored longitudinally and only two inflammatory biomarkers were used. Future studies should adopt a longitudinal approach encompassing a broader spectrum of clinical variables, thereby advancing our comprehension of this syndrome's definition and its associations with diverse clinical outcomes.

CONCLUSION

Elderly people with osteosarcopenia diagnosed with low phase angle combined with low bone mineral density exhibited pronounced worse aerobic capacity, balance and muscle strength and higher risk of mortality. Moreover, the established cutoff point for phase angle in this study holds potential applicability among older adults, showcasing robust sensitivity and specificity for predicting mortality over a 9-year follow-up period.

REFERENCE

1. Sepúlveda-Loyola W, Phu S, Bani Hassan E, Brennan-Olsen SL, Zanker J, Vogrin S, et al. The Joint Occurrence of Osteoporosis and Sarcopenia (Osteosarcopenia): Definitions and Characteristics. J Am Med Dir Assoc 2020;21:220–5. https://doi.org/10.1016/j.jamda.2019.09.005.
2. Kawao N, Kaji H. Interactions between muscle tissues and bone metabolism. J Cell Biochem 2015;116:687–95. https://doi.org/10.1002/jcb.25040.
3. Huo YR, Suriyaarachchi P, Gomez F, Curcio CL, Boersma D, Muir SW, et al. Phenotype of Osteosarcopenia in Older Individuals With a History of Falling. J Am Med Dir Assoc 2015;16:290–5. https://doi.org/10.1016/j.jamda.2014.10.018.
4. Hirschfeld HP, Kinsella R, Duque G. Osteosarcopenia: where bone, muscle, and fat collide. Osteoporos Int 2017;28:2781–90. https://doi.org/10.1007/s00198-017-4151-8.
5. Drey M, Sieber CC, Bertsch T, Bauer JM, Schmidmaier R, Group TF intervention, et al. Osteosarcopenia is more than sarcopenia and osteopenia alone. Aging Clin Exp Res 2016;28:895–899.
6. Zanker J, Duque G. Osteosarcopenia: the Path Beyond Controversy. Curr Osteoporos Rep 2020;18:81–4. https://doi.org/10.1007/s11914-020-00567-6.
7. Kanis J a. Assessment of osteoporosis at the primary health care level. World Health 2007:339.
8. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: An Undiagnosed Condition in Older Adults. Current Consensus Definition: Prevalence, Etiology, and Consequences. International Working Group on Sarcopenia. J Am Med Dir Assoc 2011;12:249–56. https://doi.org/10.1016/j.jamda.2011.01.003.
9. Cruz-Jentoft AJ, Landi F, Topinková E, Michel JP. Understanding sarcopenia as a geriatric syndrome. Curr Opin Clin Nutr Metab Care 2010;13:1–7. https://doi.org/10.1097/MCO.0b013e328333c1c1.
10. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: Consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc 2014;15:95–101. https://doi.org/10.1016/j.jamda.2013.11.025.
11. Cesari M, Landi F, Vellas B, Bernabei R, Marzetti E. Sarcopenia and physical frailty: Two sides of the same coin. Front Aging Neurosci 2014;6:1–4. https://doi.org/10.3389/fnagi.2014.00192.
12. Sepulveda Loyola WA, Suziane Probst V. Sarcopenia, definición y diagnóstico. Rev Chil Ter Ocup 2020;20:259. https://doi.org/10.5354/0719-5346.2020.53583.
13. Norman K, Wirth R, Neubauer M, Eckardt R, Stobäus N. The bioimpedance phase angle predicts low muscle strength, impaired quality of life, and increased mortality in old patients with cancer. J Am Med Dir Assoc 2015;16:173.e17-173.e22. https://doi.org/10.1016/j.jamda.2014.10.024.
14. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM, et al. Bioelectrical impedance analysis - Part I: Review of principles and methods. Clin Nutr 2004;23:1226–43. https://doi.org/10.1016/j.clnu.2004.06.004.
15. Sepúlveda-Loyola W, F. Vilaca Cavallari Machado, Castro LA De, Baltus THL, Morelli NR, Bonifácio KL, et al. Is oxidative stress associated with disease severity, pulmonary function and metabolic syndrome in chronic obstructive pulmonary disease? Rev Clínica Española 2019. https://doi.org/10.1016/j.rceng.2019.04.009.
16. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002;50:889–96. https://doi.org/10.1046/j.1532-5415.2002.50216.x.
17. Garlini LM, Alves FD, Ceretta LB, Perry IS, Souza GC, Clausell NO. Phase angle and mortality: a systematic review. Eur J Clin Nutr 2019;73:495–508. https://doi.org/10.1038/s41430-018-0159-1.
18. Norman K, Stobäus N, Zocher D, Bosy-Westphal A, Szramek A, Scheufele R, et al. Cutoff percentiles of bioelectrical phase angle predict functionality, quality of life, and mortality in patients with cancer. Am J Clin Nutr 2010;92:612–9. https://doi.org/10.3945/ajcn.2010.29215.
19. Llames L, Baldomero V, Iglesias ML, Rodota LP. Valores del ángulo de fase por bioimpedancia eléctrica; Estado nutricional y valor pronóstico. Nutr Hosp 2013;28:286–95. https://doi.org/10.3305/nh.2013.28.2.6306.
20. Selberg O, Selberg D. Norms and correlates of bioimpedance phase angle in healthy human subjects, hospitalized patients, and patients with liver cirrhosis. Eur J Appl Physiol 2002;86:509–16. https://doi.org/10.1007/s00421-001-0570-4.
21. Norman K, Pirlich M, Sorensen J, Christensen P, Kemps M, Schütz T, et al. Bioimpedance vector analysis as a measure of muscle function. Clin Nutr 2009;28:78–82. https://doi.org/10.1016/j.clnu.2008.11.001.
22. Barbosa-Silva MCG, Barros AJD. Bioelectrical impedance analysis in clinical practice: A new perspective on its use beyond body composition equations. Curr Opin Clin Nutr Metab Care 2005;8:311–7. https://doi.org/10.1097/01.mco.0000165011.69943.39.
23. Mella De Cuevas KM, Sepúlveda-Loyola W, Araya-Quintanilla F, de Barros Morselli J, Molari M, Probst VS. Association between clinical measures for the diagnosis of osteosarcopenia with functionality and mortality in older adults: longitudinal study. Nutr Clin y Diet Hosp 2022;42:143–51. https://doi.org/10.12873/423sepulveda.
24. Abad S, Sotomayor G, Vega A, Pérez de José A, Verdalles U, Jofré R, et al. El ángulo de fase de la impedancia eléctrica es un pre-

dictor de supervivencia a largo plazo en pacientes en diálisis. Nefrologia 2011;31:670–6. https://doi.org/10.3265/Nefrologia.pre2011.Sep.10999.

25. Maddocks M, Kon SSC, Jones SE, Canavan JL, Nolan CM, Higginson IJ, et al. Bioelectrical impedance phase angle relates to function, disease severity and prognosis in stable chronic obstructive pulmonary disease. Clin Nutr 2015;34:1245–50. https://doi.org/10.1016/j.clnu.2014.12.020.
26. Alves FD, Souza GC, Clausell N, Biolo A. Prognostic role of phase angle in hospitalized patients with acute decompensated heart failure. Clin Nutr 2016;35:1530–4. https://doi.org/10.1016/j.clnu.2016.04.007.
27. Marini E, Buffa R, Saragat B, Coin A, Toffanello ED, Berton L, et al. The potential of classic and specific bioelectrical impedance vector analysis for the assessment of sarcopenia and sarcopenic obesity. Clin Interv Aging 2012;7:585–91. https://doi.org/10.2147/CIA.S38488.
28. Phu S, Al Saedi A, Zanker J, Bani Hassan E, Vogrin S, Duque G. Agreement Between Initial and Revised European Working Group on Sarcopenia in Older People Definitions. J Am Med Dir Assoc 2019:2018–20. https://doi.org/10.1016/j.jamda.2018.11.026.
29. Lajoie Y, Gallagher SP. Predicting falls within the elderly community: Comparison of postural sway, reaction time, the Berg balance scale and the Activities-specific Balance Confidence (ABC) scale for comparing fallers and non-fallers. Arch Gerontol Geriatr 2004;38:11–26. https://doi.org/10.1016/S0167-4943(03)00082-7.
30. Moriguti JC, Moriguti EK, Ferriolli E, de Castilho Cação J, Iucif N, Marchini JS. Involuntary weight loss in elderly individuals: assessment and treatment. Sao Paulo Med J 2001;119:72–7. https://doi.org/10.1590/S1516-31802001000200007.