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Osteopenia/Osteoporosis and Its Association with Sarcopenia: EpiFloripa Aging Study 2013/2014

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Keywords
Sarcopenia · Bone mineral density · Older adults

Abstract
Objective: To verify the association between sarcopenia and osteopenia/osteoporosis in the older population from Florianópolis, Southern Brazil. ***Methods:*** A cross-sectional study with 598 older adults. The bone mineral density (BMD) was evaluated by total BMD, lumbar spine BMD (LS-BMD), femoral neck BMD (FN-BMD), and osteopenia/osteoporosis was defined when BMD (g/cm^2) <–1 standard deviation of the sample mean. Sarcopenia was identified by the appendicular muscle mass index (AMMI), by sex, when AMMI <7.26 kg/m^2 for men and <5.5 kg/m^2 for women. ***Results:*** Of the 598 subjects (63–93 years) in the sample, 65.4% were women. The proportion of altered BMD was 52.1% for total BMD, 62.5% for LS-BMD, and 70.9% for FN-BMD in women, while for men, altered BMD proportion was 29.3% for total BMD, 24.5% for LS-BMD, and 64.9% for FN-BMD. After adjustments, sarcopenia was associated with increased odds of altered LS-BMD (OR: 12.25; 95% CI: 3.66–40.96 and OR: 2.90; 95% CI: 1.30–6.48) and FN-BMD (OR: 5.59; 95% CI: 1.64–19.05 and OR: 7.95; 95% CI: 3.23–19.57), respectively for women and men. The association between sarcopenia and altered total BMD (OR: 11.08; 95% CI: 3.84–31.97) was observed only in women. ***Conclusion:*** The proportion of osteopenia/osteoporosis was higher in women. Sarcopenia was associated with osteopenia/osteoporosis in the population from Florianópolis, except for total BMD in men.

Osteopenia/osteoporose e sua associação com sarcopenia: Estudo EpiFloripa Idoso 2013/2014

Palavras Chave
Sarcopenia · Densidade mineral óssea · Idoso

Resumo
Objetivo: Verificar a associação entre sarcopenia e osteopenia/osteoporose em idosos de Florianópolis, Sul do Brasil. ***Métodos:*** Trata-se de estudo transversal com 598 idosos. A osteopenia/osteoporose foi identificada por meio da densidade mineral óssea (DMO) total, DMO coluna lombar (DMO-CL) e DMO colo do fêmur (DMO-CF), sen-

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do considerada alterada quando DMO (g/cm^2) <–1 desvio padrão da média da amostra. A sarcopenia foi identificada por meio do índice de massa muscular apendicular (IMMA, Kg/m^2), de acordo com o sexo, quando IMMA <7,26 kg/m^2 para homens e <5,5 kg/m^2 para mulheres. ***Resultados:*** Dos 598 indivíduos (63 a 93 anos) da amostra, 65,4% eram mulheres. A prevalência de osteopenia/osteoporose foi 52,1% para DMO-total, 62,5% para DMO-CL e 70,9% para DMO-CF nas mulheres. Para os homens, a osteopenia/osteoporose foi de 29,3% para DMO total, 24,5% para DMO-CL e 64,9% para DMO-CF. Após ajustes, a sarcopenia foi associada a maiores chances de DMO-CL alterada (OR: 12,25; IC 95%: 3,66–40,96 e OR: 2,90; IC 95%: 1,30–6,48) e DMO-CF alterada (OR: 5,59; IC 95%: 1,64–19,05 e OR: 7,95; IC 95%: 3,23–19,57), para mulheres e homens, respectivamente. A sarcopenia foi associada à DMO-total alterada (OR: 11,08; IC 95%: 3,84–31,97) apenas em mulheres. ***Conclusão:*** A prevalência de osteopenia/osteoporose foi maior entre as mulheres. Idosos sarcopênicos apresentam maiores chances de ter osteopenia/osteoporose, exceto para DMO total em homens.

Introduction

With the accelerated population aging and the tendency of involution of the bone and muscle tissues among older adults, the consequences of these muscular and bone changes are approaching the epidemic status [1].

Osteopenia is characterized by low bone mineral density (BMD) and has been found in 5–50% of older adults [2–5]. As the bone tissue deteriorates, osteopenia can lead to a skeletal disease known as osteoporosis. Also, with advancing age, a decrease in muscle mass and function, recognized as sarcopenia, reaches 5–13% of those with 60–70 years of age and up to 50% among people over 80 years [2, 3, 6].

The literature has documented a few mechanisms on how sarcopenia and bone interact, through genetic, molecular [1, 7], mechanical [1, 6], and functional alterations [3, 6]. The complications of these conditions have a great socioeconomic impact on the population [8, 9]. The decline of muscle and bone strength presents manifestations in the reduction of mobility and functionality, greater predisposition to falls, fractures [10, 11], functional dependence, and increased morbidity and mortality risk [1, 12]. Older adults who present sarcopenia and osteoporosis generally require more health care and specialized long-term care, which represents high costs and considerable social impact [8, 9].

In Brazil, the few studies about sarcopenia and BMD at older ages are with outpatients [13], small samples [13–16], 80 years or older [16], overweight [17], and with different definition criteria [18]. Only the accumulation of work assigns some degree of consistency to the findings; therefore, the objective of the present study was to verify the association between sarcopenia and osteopenia/osteoporosis in older residents from the city of Florianópolis, Southern Brazil.

Methods

This study is part of the follow-up of the epidemiological research entitled "Conditions of Health of the Elderly in Florianópolis – EpiFloripa Aging Study," whose baseline was carried out in 2009/2010 and the follow-up in 2013/2014. The EpiFloripa Aging Study is a longitudinal, population- and household-based study with individuals aged 60 years or older living in the city of Florianópolis, Southern Brazil. The details of the study such as population and sampling were previously published, and so it will be presented briefly [19, 20]. It was a two-stage sampling strategy, the first stage was the urban census tracts of the city, stratified in ascending order of monthly average income of the head of the family, and the second stage was the households of these sectors. Both units were drawn systematically. If one of the households had two or more older adults, they would all be invited to participate in the study.

Data was collected through domiciliary (face to face) interviews with a structured questionnaire in netbooks to record the data. The consistency analysis of the data occurred weekly, and quality control was conducted by telephone through a reduced questionnaire application in 10% of the interviews (selected randomly). Participants from the follow-up (2013/2014) were invited to perform tests at the Health Sciences Center of the Federal University of Santa Catarina (UFSC).

The baseline sample consisted of 1,705 participants. To the follow-up, 3 interviews were excluded (2 duplicates data and 1 incompatible age) and 217 deaths were identified. From the 1,485 eligible participants, 159 were losses, 129 refused, and 1,197 (80.6%) were interviewed in 2013/2014. From the 1,197 participants, 604 (50.4%) participated in the tests, such as body composition, bone densitometry, and biological exams (vitamin D). Due to inappropriate information in the image tests, the analytical sample consisted of 598 individuals.

Between the 2013/2014 sample (1,197 participants) and the tests (598 participants), there were losses for the age group ($p < 0.001$), mostly 80 years or older, cognitive deficit ($p < 0.001$), and dependence on activities of daily living (ADL) ($p = 0.003$) (data not shown).

Dependent Variables

Osteopenia/osteoporosis was identified by BMD from total BMD, lumbar spine BMD (LS-BMD), and femoral neck BMD (FN-BMD). The evaluation of BMD (g/cm^2) was done with the dual energy X-ray absorptiometry (DXA; model Lunar Prodigy

Table 1. Description of the sample according to demographic, socioeconomic, lifestyle, health conditions, sarcopenia, and bone mineral density of older adults; Florianópolis, Southern Brazil, 2013/2014

Variables	Women (n = 391), mean age (SD) = 72.5 (6.2)		Men (n = 207), mean age (SD) = 72.0 (6.4)	
	n	% (95% CI)	n	% (95% CI)
Education level				
No formal education	26	6.2 (3.7–10.2)	14	5.2 (2.7–9.8)
1–4 years	155	39.2 (31.4–47.5)	60	24.5 (2.49–31.7)
5–8 years	72	18.4 (14.0–23.6)	34	20.2 (13.6–29.0)
9–11 years	70	18.5 (14.1–23.9)	24	16.9 (11.8–23.6)
12 or more	67	17.7 (13.0–23.7)	75	33.1 (28.8–41.2)
Alcohol consumption				
No	270	69.0 (62.5–74.8)	76	33.7 (25.9–42.5)
Moderate	97	24.4 (19.2–30.4)	64	29.2 (22.4–37.0)
High	24	6.6 (4.0–10.7)	67	37.1 (28.4–46.8)
Smoking habit				
Never	300	74.7 (67.9–80.5)	75	31.0 (24.5–38.3)
Former and stopped	68	19.7 (14.8–25.6)	111	58.4 (51.3–62.3)
Current	23	5.6 (3.4–9.1)	21	10.6 (66.5–16.4)
Physical activity				
Insufficiently active	192	48.5 (42.3–54.8)	64	27.3 (20.0–35.9)
Physically active	199	51.5 (45.2–57.7)	143	72.7 (64.0–79.9)
Dependency on activities of daily living				
No	276	70.4 (62.5–77.3)	167	82.14 (22.7–37.5)
Yes	115	29.6 (22.7–37.5)	37	17.86 (11.4–26.9)
Falls (last year)				
No	260	66.1 (61.2–70.7)	160	76.1 (68.6–82.3)
Yes	131	33.9 (29.3–38.8)	47	23.9 (17.7–31.4)
Sarcopenia				
No	328	83.0 (77.1–87.6)	148	71.2 (62.3–78.6)
Yes	63	17.0 (12.4–22.9)	59	28.8 (21.3–37.7)
Total BMD				
Normal	191	47.9 (40.3–55.5)	140	71.0 (61.7–77.3)
Altered	199	52.1 (44.5–59.6)	67	29.0 (22.7–36.3)
Lumbar spine BMD				
Normal	150	37.5 (30.7–44.8)	147	75.48 (67.1–82.3)
Altered	240	62.5 (55.2–69.3)	60	24.52 (17.7–32.9)
Femoral neck BMD				
Normal	108	29.1 (23.4–35.4)	69	35.0 (25.7–45.6)
Altered	282	70.9 (64.6–76.6)	138	64.9 (54.3–74.2)
Vitamin D				
Normal	101	30.5 (23.6–38.5)	93	43.4 (36.2–50.8)
Hypovitaminosis	271	69.5 (61.5–76.4)	106	56.6 (49.2–63.8)
Seasons				
Spring	55	15.7 (10.7–22.4)	29	18.0 (11.6–26.7)
Summer	44	9.4 (6.2–14.1)	19	9.5 (5.4–16.1)
Autumn	178	52.6 (42.9–62.1)	97	46.5 (36.6–56.8)
Winter	95	22.3 (16.1–30.0)	54	26.0 (19.0–34.5)

SD, standard deviation; BMD, bone mineral density; 95% CI, 95% confidence interval.

Advance by General Electric). The mean values of each BMD from the sample of this study were calculated and according to the consensus of the World Health Organization [21] considered as normal when up to –1 standard deviation (SD) of the mean. Osteopenia/osteoporosis was defined by BMD <–1 SD of the sample mean (osteopenia: –1 to –2.5 SD, and osteoporosis: <–2.5 SD) [14].

All participants received information on the purpose of the test before the evaluation and were asked to remove metal objects. Participants also received instructions to remain immobile and silent during the procedure, which was repeated if necessary. The examination was carried out according to DXA manual, and it lasted an average of 15 min for the total body scan, lumbar spine densitometry, and femoral neck densitometry.

Independent Variable

Sarcopenia was identified through muscle mass analysis from DXA. The criteria was appendicular skeletal muscle index (ASMI) ≤2 SD, according to a reference population mean of young adults in the Rosetta study, by sex [22]. The cut-off points for inadequate ASMI (kg/m^2) (sarcopenia) were <7.26 kg/m^2 for men and <5.5 kg/m^2 for women, considering sarcopenia (no/yes). We used the ASMI formula proposed by Baumgartner et al. [22]: ASMI (kg/m^2) = lean muscle mass of the arms (kg) + lean muscle mass of the legs (kg)/height^2 (m).

Variables Adjustment

The adjustment variables, based on the literature [23, 24], were: age (continuous), education level in years (no formal education, 1–4, 5–8, 9–11, and 12 or more years), smoking habit (never smoked, former smoker and stopped, current smoker), consumption of alcoholic beverage, leisure and transportation physical activity, falls in the last year, dependency on ADL, and vitamin D (25 hydroxy).

To verify the consumption of alcoholic beverages (does not consume, non-abusive consumption, and abusive consumption), we used the first three questions of the questionnaire The Alcohol Use Disorders Identification Test *(*AUDIT) [25]. The leisure and transportation physical activity evaluation was measured by the long version of the International Physical Activity Questionnaire (IPAQ) [26] (insufficiently active [<150 min weekly of leisure and transportation physical activity] and physically active [≥150 min weekly of leisure and transportation physical activity]). The investigation of falls in the last year was through the question: "Have you suffered any fall in the last year?" categorized as yes or no. To evaluate the dependency on ADL [27] the Brazilian Questionnaire of Multidimensional Functional Evaluation was used, adapted from the questionnaire Old Americans Resources and Services (BOMFAQ/OARS): no (no dependence or dependence on up to 3 activities) and yes (dependence on 4 or more activities).

For the evaluation of vitamin D (25 hydroxy), blood samples were collected after fasting of 8 h. The serum samples were immediately frozen, and the vitamin D analyzed between November 2016 and April 2017 by microparticle chemiluminescence method (CMIA)/Liaison. The vitamin levels were classified according to the Brazilian Society of Endocrinology and Metabolism (Sociedade Brasileira de Endocrinologia e Metabologia – SBEM) [28] recommendations, as normal (30–100 mg/mL) and hypovitaminosis (<30 mg/mL). As vitamin D status is partially dependent on exposure to sunlight, which results in higher serum 25-OHD levels in spring/summer, compared to the fall/winter season, we used the season when the blood test was taken in the adjusted analysis.

Data Analysis

Descriptive analyses (proportion) were performed for all variables, and logistic regression was used to estimate the crude and adjusted odds ratios with their respective 95% confidence interval (CI). We considered three adjustments models in the association for sarcopenia and each BMD variable: model 1 adjusted by age and schooling; model 2 adjusted for age, schooling, smoking, alcohol consumption, physical activity, falls and functional dependence; model 3 adjusted for age, schooling, smoking, alcohol consumption, physical activity, falls, functional dependence, vitamin D, and season. The level of statistical significance was 5%.

Data was analyzed on the statistical program Stata 13.0 (Stata Corp., College Station, EUA). We considered the effect of the sample design by conglomerates and the sample weight with the command *svy*.

Results

Of the 598 subjects (63–93 years) in the sample, 65.4% were women. Table 1 shows the sociodemographic characteristics, lifestyle, health conditions, and BMD of the sample, stratified by sex. Men and women were predominantly physically active older adults, without ADL dependency, with no history of falls in the last year, and with hypovitaminosis D. Most women had 1–4 years of schooling, did not consume alcohol, and never smoked. Most men had 12 years or more of schooling, high alcohol consumption, and were former smokers. The proportion of women and men with sarcopenia was 17.0% (95% CI: 12.4–22.9) and 28.8% (95% CI: 21.3–37.7), respectively.

There was a predominance of women with osteopenia/osteoporosis in total BMD (52.1%; 95% CI: 44.5–59.7), LS-BMD (62.5%; 95% CI: 55.2–69.3), and FN-BMD (70.9%; 95% CI: 64.5–76.6). For men, among the characteristics related to osteopenia/osteoporosis, altered FN-BMD (64.9%; 95% CI: 54.4–74.2) was the most prevalent (Table 1).

The associated characteristics between BMD and sarcopenia, for women and men, are presented in Table 2. For women, sarcopenia was positively associated with all altered BMD characteristics even after the adjustments in models 1, 2, and 3. In model 3 (final), women with sarcopenia had, respectively, 11.08 (95% CI: 3.48–31.97), 12.25 (95% CI: 3.66–40.96), and 5.59 (95% CI: 1.64–19.05) times to present osteopenia/osteoporosis in total BMD, LS-BMD, and FN-BMD. For men, data from the crude and adjusted analysis showed sarcopenia was associated with osteopenia/osteoporosis except according to total BMD. In the adjusted analysis, in model 3, men with sarcopenia had 2.90 (95% CI: 1.30–6.48) and 7.95 (95% CI: 3.23–19.57) higher chance of having osteopenia/osteoporosis in LS-BMD and FN-BMD, respectively.

Table 2. Crude and adjusted analysis about sarcopenia associated with bone mineral density in women and men; Florianópolis, Southern Brazil, 2013/2014

Variables	Crude analysis		Model 1		Model 2		Model 3	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Women								
Total BMD								
Sarcopenia		≤0.001		≤0.001		≤0.001		≤0.001
No	1		1		1		1	
Yes	10.70 (4.51–25.41)		11.25 (4.22–30.00)		9.96 (3.44–28.86)		11.08 (3.84–31.97)	
Lumbar spine BMD								
Sarcopenia		≤0.001		≤0.001		≤0.001		≤0.001
No	1		1		1		1	
Yes	11.41 (4.37–29.78)		12.52 (4.50–34.82)		10.86 (3.44–34.22)		12.25 (3.66–40.96)	
Femoral neck BMD								
Sarcopenia		≤0.001		≤0.001		0.004		0.006
No	1		1		1		1	
Yes	7.66 (2.87–20.44)		8.43 (2.77–25.64)		5.88 (1.77–19.51)		5.59 (1.64–19.05)	
Men								
Total BMD								
Sarcopenia		0.373		0.698		0.659		0.491
No	1		1		1		1	
Yes	1.33 (0.70–2.53)		1.14 (0.59–2.21)		1.16 (0.59–2.29)		1.26 (0.64–2.47)	
Lumbar spine BMD								
Sarcopenia		0.008		0.016		0.021		0.010
No	1		1		1		1	
Yes	2.59 (1.29–5.20)		2.70 (1.21–6.04)		2.73 (1.16–6.41)		2.90 (1.30–6.48)	
Femoral neck BMD								
Sarcopenia		≤0.001		≤0.001		≤0.001		≤0.001
No	1		1		1		1	
Yes	5.23 (2.47–11.06)		5.67 (2.53–12.74)		6.72 (2.82–16.02)		7.95 (3.23–19.57)	

BMD, bone mineral density; 95% CI, 95% confidence interval; OR, odds ratio. Model 1: adjusted by age, schooling. Model 2: adjusted for age, schooling, smoking, alcohol consumption, physical activity, falls, and ADL dependency. Model 3: adjusted for age, schooling, smoking, alcohol consumption, physical activity, falls, ADL dependency, vitamin D, and season.

Discussion

In this study, the proportion of altered osteopenia/osteoporosis was 52.1% for total BMD, 62.5% for LS-BMD, and 70.9% for FN-BMD in women, while for men, altered BMD proportion was 29.3% for total BMD, 24.5% for LS-BMD, and 64.9% for FN-BMD. After adjustments, sarcopenia was positively associated with altered BMD for LS-BMD and FN-BMD characteristics in both sexes, and with total BMD only for women.

The results of this study showed a high proportion of osteopenia/osteoporosis, especially among women, as verified by other studies [29, 30]. In the study of Camargo et al. [29], the proportion of osteopenia of FN-BMD and osteoporosis was 57.4 and 12.8% in men, and 56.5 and 22.2% in women from São Paulo, Brazil, respectively. Pereira et al. [14] diagnosed 33.8% of men in the Federal District, Brazil, with osteoporosis, and 47.5% with osteopenia, totaling 81.3% of the sample with abnormal BMD. Gonçalves et al. [30], in Portugal, identified a proportion of osteopenia and osteoporosis, respectively, of 50 and 11% in women, and 32 and 2% in men. It is worth noting that separate samples were used.

A possible explanation for men to present a higher proportion of sarcopenia is their greater muscle mass, but also their greater loss of muscle mass with the advancement of age [31]. The muscle loss is due to the decline of growth hormone, insulin-related growth factor 1, and testosterone [32].

The positive association between sarcopenia and altered BMD is consistent with previous studies [4, 33]. Several potential mechanisms for sarcopenia, as well as the relation between sarcopenia and altered BMD, have been investigated to explain this association [6]. In the study of Bijlsma et al. [2], in both older men and women, sarcopenia (MMA/height^2) was associated with BMD.

Muscles and bones present genetic, molecular [1], mechanical [1, 6], and functional [6] interactions. However, the area related to mechanical interaction is the most accepted and recognized [1]. The muscles are connected to the bones and it involves movements through an active contraction. By their direct physical connection, the muscles expose the bone to a great variety of mechanical stimulus [1]. For individuals with sarcopenia, this relation is modified, and it can be explained by the way sarcopenia can lead to a reduction of bone resistance, due to the reduction of the mechanical load to the skeleton [7]. The weaker muscles will produce less maximum force, due to decreased mechanical stimulation, which leads to reduced bone remodeling [34, 35]. Recent findings suggest that decreased muscle mass may deteriorate bone microarchitecture [36]. The interest in muscle/bone relationship, as well as muscle biology, has increased in recent years. Nevertheless, physiological and pathological mechanisms related to these tissues remain unclear [6].

The results also showed that sarcopenia was associated with altered total BMD only in women. Postmenopausal hormone changes, especially estrogen deficiency, are risk factors for osteoporosis [4, 37]. The decrease in estrogen levels affects the acceleration of reabsorption activity and increases bone turnover [38]. It leads to impairment and imbalance of bone activity, with a negative balance of calcium especially in the mandible, maxilla, and long bones [39], which are the main bones evaluated in the total scan in bone densitometry.

A possible explanation for the association between sarcopenia and BMD of the femoral neck and lumbar spine, and not for total body BMD in men, is that femoral neck and lumbar spine are considered the gold standard for the diagnosis of osteoporosis [40], these being the most evaluated regions, as well as the distal third of the radius due to the risk of fracture. This result may have occurred due to the calculation of density measurement, in addition to the fact that age-related bone loss differs according to the skeletal regions or specific areas assessed [41].

This study has limitations and strengths. One of the limitations refers to the cross-sectional design, which precludes inferences about the outcome. The losses of participation on the tests may lead to selection bias. The participants who attended had better health conditions than those who refused, which may lead to underestimation of the proportion of sarcopenia and altered BMD, underestimating the found associations. Another limitation includes the lack of indicators of muscular strength and motor performance for the definition of sarcopenia, which were not available for analysis. Also, other important minerals for bone and muscle health, such as phosphate, calcium, iron, magnesium, potassium, as well as interleukin 6, parathyroid hormone, growth hormone [5], and tumor necrosis factor-alpha were not evaluated.

The main strengths of the study include the evaluation of body composition, bone densitometry, and laboratory tests using standardized procedures, as well as the application of questionnaires with validated scales. Also, this study has one of the largest samples of older adults in a population-based survey conducted in Brazil to investigate sarcopenia using the gold standard established in the literature, which is difficult to see in population studies.

The results of this study reinforce the importance of studying sarcopenia and osteopenia/osteoporosis in the

older population, due to its clinical and health implications, and may be used to support the clinical practice of health professionals in different areas, as well as contributing to health actions.

Final Considerations

The proportion of osteopenia/osteoporosis differed between the sexes, with higher values for women, considering the three measurements. For men, only the FN-BMD had a high proportion of osteopenia/osteoporosis. Sarcopenia was positively associated with osteopenia/osteoporosis, in both sexes, except for total BMD in men.

The combination of sarcopenia and osteopenia/osteoporosis can have a social and economic impact, due to its complications in the health of the affected population. The results show the importance of studying these characteristics in the older population. It can collaborate with the implementation of health actions capable of preventing, stimulating early diagnosis of the population at risk, treating, and even rehabilitating them.

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Statement of Ethics

The project was approved by the Committee of Ethics in Research with Human Beings of the Federal University of Santa Catarina (CAAE No. 16731313.0.0000.0121). All participants signed the Informed Consent Terms.

Conflict of Interest Statement

The authors declare no conflict of interest.

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