Obesity, dynapenia and their combination: implications for bone mineral density in Brazilian adults−The Pró-Saúde Study

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Highlights

- Changes in body composition and function with aging starts nearly at forties.
- Bone status relationship with dynapenia and obesity was investigated in adults.
- Dynapenia alone was not associated with BMD in both men and women studied.
- Obesity and dynapenia interacted to influence BMD in women, but not in men.
- Results suggest a bone protective effect of higher fat mass in dynapenic women

Obesity, dynapenia and their combination: implications for bone mineral density in Brazilian adults − The Pró-Saúde Study

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Abstract

Objective: To evaluate bone mineral density (BMD) in the presence or absence of dynapenia and/or obesity in Brazilian adults. **Methods:** This is a cross-sectional study conducted in 502 adults (33-81 y; 51% women) participants of the Pró-Saúde Study, a cohort of civil servants at university campi in Rio de Janeiro, Brazil. Body composition and BMD were determined by dual energy X-ray absorptiometry (DXA). Handgrip strength was measured using a dynamometer. According to measures of handgrip strength (≤19 kg for women and ≤32 kg for men) and fat mass (> 30% and >40% for men and women, respectively), participants were classified into four groups: non-obese non-dynapenic, obese non-dynapenic, non-obese dynapenic and obese dynapenic. The association between BMD at each specific bone site and obesity, dynapenia, and their interaction was evaluated using a general linear model. **Results**: The prevalence of dynapenic obesity was 14% and 15.2% in men and women, respectively. Dynapenia alone was not associated with BMD at any site in both men and women. Obesity and dynapenia interacted to influence BMD in women ($P<0.05$). Total body, lumbar spine and femoral neck BMD were, respectively 6.3%, 9.3% and 10.4% higher in dynapenic obese women compared to their non-obese counterparts ($P<0.05$). In men, obesity, dynapenia, as well as their combination, were not associated with BMD at any site. **Conclusion:** Our results suggest that dynapenia, obesity, and their combination may affect bone mineral density in a gender-dependent manner. In the presence of dynapenia, fat mass appears to exert a protective effect on bone mineral density in women, but not in men.

Key words: low muscle strength, fat mass, bone mass, adults, DXA

Introduction

Gradual changes in body composition during the life course include decrease in skeletal muscle mass, traditionally referred as sarcopenia [1], as well as increase and redistribution in fat mass. These changes occur as consequence of physiologic adjustments in the endocrine and metabolic systems with aging [2], but may be accelerated by lifestyle habits, including physical inactivity and unhealthy diet [3]. Although muscle mass was being used as the main parameter when evaluating sarcopenia, it is now accepted that a broader set of functional tests, including muscle strength, can contribute to a more adequate diagnosis [4,5]. There is evidence that muscle strength may decrease faster than muscle mass, which suggests that the quality of the muscle may be compromised earlier with aging [6,7].

The term dynapenia has been proposed to describe the age-related reduction in muscle strength, dissociating the concept of mass reduction from the concept of muscle strength reduction [8-10]. The recently revised guidelines of European Working Group on Sarcopenia in Older People (EWGSOP) recognized that strength predicts adverse outcomes better than muscle mass information [5, 11-13]. Nevertheless, in that guideline, even though muscle strength comes to the forefront, the term sarcopenia was maintained. This may be due to the belief that sarcopenia is a well-known term and its replacement can lead to major conceptual misunderstanding [10].

Muscle, fat and bone tissues are metabolically interconnected [14,15] and share responses to hormonal factors including sexual steroids, insulin, insulin like growth factor I (IGF-I) and growth hormone (GH) [16]. Also, both muscle and body fat are sources of mechanical loading that can contribute to the maintenance of bone mineral density (BMD) [15,17,18]. It is well accepted that muscle mass is strongly and directly associated with BMD [19,20], although the relationship between muscle strength and BMD deserves more investigation. Some [7,21] but not all [22,23] studies suggest that muscle strength is directly associated with BMD independently of muscle mass. On the other hand, the effects of fat mass on bone mass are controversial, with published studies showing both direct, inverse and no associations with this outcome [19, 24-26] depending on population characteristics, especially gender.

Much less explored is the potential association between bone mass and the simultaneous occurrence of dynapenia and obesity. To our knowledge, only one study has examined dynapenic obesity in the context of low bone mass and fracture outcomes, and this study focused in elderly men and women [27]. They suggest that adipose tissue infiltration into muscles was associated with a higher incident hip fractures risk [27]. Moreover, given that dynapenia may confer low

BMD risk, it is possible that obese individuals with dynapenia do not demonstrate BMD equivalent to that of those with obesity alone [9].

Considering that changes in body composition and function with aging starts nearly at forties, and that studies addressing low muscle strength and fat mass excess relationship with bone status are usually conducted in elderly individuals, it is important to identify the presence of these outcomes earlier in life. Therefore, the aim of this study is to evaluate bone mineral density in the presence or absence of dynapenia and/or obesity in Brazilian adults.

Methods

Study design and population

This is a cross-sectional study conducted in a subsample of a cohort study of university civil servants in Rio de Janeiro, Brazil. Details on study population were previously described [28-30]. Briefly, concurrently with cohort phase 4 (2012-13), 520 participants of the baseline waves 1 and 2 (n=2444) – corresponding to about 20% of each strata of sex, age (<50 vs. 50+ yrs) and education level (less than high school vs. high school or more) from the cohort baseline – were invited to conduct additional evaluation that included an interview to obtain general and socioeconomic data, anthropometry and body composition assessment by dual energy x-ray absorptiometry (DXA). Seven participants did not perform DXA measurements and eleven did not perform handgrip strength test and therefore were excluded from the study. Thus, 502 participants (249 men and 255 women) were included in the current analyses. Based on previous reports [10,31] a sample of 446 individuals would be sufficient to estimate the prevalence of dynapenic obesity, assuming 95% CI. Additionally, with this sample size and based on previous studies [32,33] it was estimated that the minimum detectable differences between groups in LSBMD and in FNBMD were 0.116 and 0.090 g/cm2, respectively, assuming 95% CI and 80% power.

Data on sociodemographic characteristics and menopausal status were obtained by structured interviews. Postmenopausal status was defined as the self-reported cessation of natural menses for at least 12 months. Participants self-classified their race/skin color as white, brown, black, yellow, or indigenous − categories adopted by the Brazilian census [34].

Anthropometry and body composition

Total body mass and height were measured with subjects dressed in light clothes according with standard protocol [35]. Total body mass was measured to the nearest 0.1 kg, using a digital scale (Filizola, Brazil). Height was measured with a wall stadiometer to the nearest 0.1 cm (Seca, Brazil). Body mass index (BMI, kg/m^2) was derived.

Body composition was determined by dual energy X-ray absorptiometry (DXA) (Lunar iDXA, GE Healthcare, WI). Total fat (kg and %), total non-bone lean mass (TLM) (kg) and arms and legs lean mass (kg) were derived from DXA total body scan and estimated by the software enCore 2008 version 12.20. The sum of arms and legs lean mass was used to define appendicular lean mass (ALM). Skeletal muscle index (SMI) was calculated dividing ALM by squared height. Obesity was defined as total fat mass higher than 30% and 40% for men and women, respectively [36-38].

Visceral adipose tissue (VAT) was measured in a 5 cm wide region placed across the entire abdomen just above the iliac crest at a level that approximately coincided with the 4^{th} lumbar vertebrae on the whole body DXA scan by the software CoreScan VAT [39]. Data on VAT was expressed in absolute values (kg) and relative to total fat mass (%).

Handgrip strength measurement

Handgrip strength was measured using a hand dynamometer (Smedley, Takey). Each participant was asked to extend the arm at 45°, holding the hand dynamometer, and squeeze the handgrip with maximum strength. The test was performed twice on each hand with an interval of 10 – 15 seconds between measurements. The highest value of each side was used to represent handgrip strength. Dynapenia was characterized by low muscle strength defined based on the handgrip cut-off values of ≤19 kg for women and ≤32 kg for men, on at least one side evaluated. These cut-offs correspond to two standard deviations below the sex-specific means reference data for young adults, as proposed by EWGSOP [5,40].

BMD measurement

Bone mineral density (BMD, g/cm^2) of total body, lumbar spine (LS) (L1–L4) and femoral neck BMD were also measured by DXA. Low bone mass was considered when T score of the lumbar spine or femoral neck was -1.0 or less in postmenopausal women and men aged 50y and older. In premenopausal women and in men younger than 50y, Z score values below -2.0 were used to define low bone mass [41]. All DXA scans were performed by the same trained

operator, analyzed by the same certified clinical densitometrist and followed standard quality control procedures according to the manufacturer. Measurements on the calibration block (daily) and on the calibration spine phantom (weekly) supplied by the manufacturer had coefficients of variation <0.5%. Coefficients of variation derived from three repeated measurements in 50 subjects were 0.47%, 0.87% and 0.62% for total body, lumbar spine (L1–L4) and femoral neck BMD, respectively.

Data analyses

Combining the adopted criteria for definition of obesity and dynapenia, individuals were grouped in: non-obese non-dynapenic, obese non-dynapenic, non-obese dynapenic and obese dynapenic. Data were assessed for normality using the Kolmovorov-Smirnov test. Results are presented as mean ± standard deviation or adjusted mean ± standard error for continuous variables and as frequencies and percentages for categorical variables. The analyses were conducted in men and women separately. Mean values of continuous variables (except BMD) were compared between groups using one-way ANOVA. The influence of obesity, low muscle strength, and their interaction on BMD was evaluated using a general linear model, followed by Tukey post hoc test, with BMD at each specific bone site as dependent variables and the presence or absence of obesity and low muscle strength as fixed factors. Based on previously reported data [24], age, height, total lean mass, race and postmenopausal period (for women) were also included in the analyses as covariates. Frequency distributions of low and adequate bone mass between groups were compared by Chi-square test. All statistical analyses were conducted using the statistical package SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of study participants according to presence of obesity and low muscle strength are presented in **table 1**. In men, the prevalence of obesity and dynapenia were 54.6% and 25.3%, respectively. Dynapenic obesity was prevalent in 14% of male. Non-obese dynapenic men were older than those without dynapenia. Total body weight, BMI, total fat mass (absolute and relative) and VAT (absolute and relative) were higher in obese compared to non-obese groups ($P<0.05$), independent of presence of low muscle strength. TLM and ALM were highest ($p<0.001$) in obese non-dynapenic group. Additionally, SMI was higher in obese non-dynapenic

men compared to non-obese men (p<0.001) (table 1). Among women, prevalence of obesity and dynapenia were similar to that observed in men (60.4% and 24.7%, respectively). Dinapenic obesity was present in 15.2% of female participants. Mean age was higher in obese dynapenic compared to non-obese non-dynapenic women (p<0.05). Similar to the observed in men, total weight, BMI, total fat (absolute and relative) and VAT (absolute and relative) were higher in obese compared to non-obese women (P<0.05), independent of presence of dynapenia. Obese women presented higher TLM than non-obese dynapenic women (p<0.001). Additionally, obese women had higher SMI than their non-obese counterparts, independently of muscle strength status (table 1).

In men, obesity, dynapenia, as well as their interaction, were not associated with BMD at total body, lumbar spine and femoral neck (**Figure 1**). Mean BMD for total body, lumbar spine and femoral neck were similar within all men groups (Figure 1A, 1B, 1C). In women, obesity was associated with higher total body, lumbar spine and femoral neck BMD (p<0.01) (Figure 1). Dynapenia was not associated with BMD at any site. However, statistically significant interaction between obese status and muscle strength status was observed for BMD at total body, lumbar spine and femoral neck (p<0.05) (Figure 1). Mean BMD values at total body (Figure 1D) and lumbar spine (Figure 1E) were lower in non-obese dynapenic women compared to obese dynapenic women. Also, femoral neck BMD was lower in non-obese dynapenic women compared to obese women, independently of muscle strength status (Figure 1F) (P<0.05).

Based on T or Z scores, low bone mass was prevalent in 28.5% and 28.2% of men and women respectively. Frequency distribution of low or adequate bone mass in the studied groups are presented in **table 2**. In non-dynapenic men, the distribution in low/adequate bone status differed by obesity status (p=0.009), with most individuals with low bone mass belonging to the non-obese group (Table 2). In contrast, among women, the distribution of low or adequate bone mass was significantly different (p=0.037) in obese and non-obese women in the presence of dynapenia (Table 2).

The frequencies of isolated or simultaneous occurrence of obesity and/or dynapenia and/or low bone mass are illustrated in **Figure 2**. Frequency of osteodynapenic obesity was 3.3% among men and 4.3% among women. Of note, 21.5% of the men and 23.9% of the women had none of the three studied conditions (obesity, dynapenia or low bone mass).

Discussion

In the present study, we evaluated BMD in relation to the presence or absence of obesity and/or dynapenia in a sample of Brazilian adults. We observed that dynapenia alone was not associated with BMD in both men and women studied. Nevertheless, an interaction between obesity and muscle strength status was observed in women suggesting a bone protective effect of having higher fat mass in those who were dynapenic.

DXA is recognized as the reference method for measurements of fat mass but it still lacks consensus in the establishment of cut-off points to group individuals in obesity categories [42-45]. Considering the proposed cut-offs of 30% for men and 40% for women [36-37], the population studied had a high frequency of obese individuals (almost 55% and 60% for men and women, respectively). Using the same cut-off values, studies conducted in Americans, Mexicans, Tasmanians and Vietnamese adults found highly variable prevalence of obesity, ranging from 14% to 53% in men and from 15% to 73% in women [19,37,44,46,47].

Data on prevalence of dynapenia also varies widely, with studies reporting frequencies from 4.4% to 43.8% in older populations [10,31,48,49]. Again, part of the variation has been attributed to the use of different cutoff points for low muscle strength evaluated by dynamometry [5,40,50,51]. Using the cutoffs recently proposed by EGWSOP [5,40], we found that dynapenia was present in 25.3% and 24.7% in men and women, respectively. These frequencies appear to be high, especially considering that the majority of the individuals (80%) was younger than 60 years old.

The simultaneous occurrence of obesity and dynapenia was firstly described by Bouchard and coworkers [12]. In that study, dynapenic obesity was associated with poor physical function in older adults [12]. More recent studies have been conducted investigating its association with many other unfavorable health outcomes including high mortality risk, cardiovascular disease, functional incapacity, risk of falls and fracture [10,27,31,48,52]. The prevalence of dynapenic obesity varies in a range between 4% to 17.6% considering several definitions and cut-offs for both obesity and dynapenia [10,13,27,31,48,52]. In the present study, the simultaneous presence of obesity and dynapenia affected 14% and 15.2% of men and women, respectively. One would expect dynapenic obesity to be less frequent among middle-aged participants (mean age ~53 years) in our study. However, its prevalence approached that observed in elderly populations, usually associated with higher muscle weakness.

The choice for using strength instead of muscle mass when investigating the muscle relationship with BMD was based on the faster decrease of strength with age, compared to

muscle mass loss [53,54]. In this adult population (mostly middle-aged), however, muscle strength status (dynapenic or not) was not associated with BMD in both men and women. Although the effect of dynapenic status on bones was not previously explored, several studies have reported positive correlation between muscle strength and BMD at total body and specific bone sites in elderly people, mainly in postmenopausal women [7,21-23]. Results of our correlation analysis showed a weak, but statistically significant direct association between muscle strength and BMD (total and specifics sites) in men ($r>0.115$, for all bone sites) and women ($r>0.184$, for all bone sites) that, however, disappeared after adjustment for muscle mass (data not shown). This is consistent with studies suggesting that the relationship between muscle strength and BMD may be muscle mass dependent [19,26,55].

The combination of obesity with low muscle strength has been associated with high mortality risk [13,48] and other health outcomes such as metabolic syndrome [31], cardiovascular disease [56], activities of daily living disability [10,13] and risk of falls [52]. However, to our knowledge, only one study, conducted in Tasmanian older adults, investigated the relationship between dynapenia combined with obesity and BMD [27]. The authors suggest that lower muscle strength, at least in the presence of obesity, results in less adverse effects for bone health in older women than men. Similarly, in the present study, we observed a higher BMD in the dynapenic obese women compared to their non-obese counterparts suggesting that the presence of obesity may benefit bone health in women when muscle strength is impaired. Based on frequencies of adequate bone mass in men, it appears that a slight advantage of obesity for non-dynapenic men may also occur.

The influence of obesity on bones has been extensively studied [20,24,26,57,58], with some evidence of a direct association between fat mass and BMD in women, mainly in those at the postmenopausal period [20,24]. Mechanisms explaining the potential beneficial effect of fat on women's BMD include the increased aromatization of androgen to estrogen in adipose tissue [59] as well as the high circulating levels of insulin, IGF-I, and leptin [60], which are usually associated with adiposity, but also appear to favor bone formation. Nevertheless, the effect of excess of fat on BMD remains controversial and other factors besides gender, such as age and ethnicity appear to influence in this relationship [26,57,58]. The ectopic fat accumulation in skeletal muscle in the form of intramuscular and intermuscular adipose tissue (IMAT) [61] is another topic that adds to the question whether the presence of obesity offsets or exacerbates the risk of osteoporosis in individuals with dynapenia [9]. IMAT is considered a major determinant of muscle weakness [62]. Although less investigated, there is also evidence that fat infiltration into muscle is associated with higher risk of hip fracture [63] and lower lumbar BMD [64].

Some study limitations should be mentioned. The absence of information on physical activity habits, and dietary habits, which are recognized to influence our main outcome variables, may have limited our conclusions. Also, we did not incorporate IMAT information obtained by Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) techniques for the evaluation of muscle quality. Finally, the sample size was not powered to detect group differences in LSBMD lower than 11%, and FNBMD lower that 12%. On the other hand, considering that the only study evaluating bone status in dynapenic obesity was conducted in older people, a major strength of our study was the early investigation of middle-age men and women. It is important to highlight that almost five percent of participants shared on obesity, dynapenia and low bone mass.

Our results suggest that dynapenia, obesity, and their combination may affect bone mineral density in a gender-dependent manner. In the presence of dynapenia, fat mass may exert a protective effect on bone mineral density in women, but not among men. We herein reported that changes in body composition and muscle strength during the ageing process, seem to exert synergistic effects on BMD that may result in a lower risk of low BMD, especially among women. It is important to emphasize the early monitoring of these changes encourage developing treatment strategies to enhance muscle strength, prevent bone mass loss, and improve quality of life for a growing number of older adults.

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The authors' responsibilities were as follows: FFB and EF designed and supervised the study; AC conducted DXA analysis and interpretation; AC analyzed the data; AC and FFB wrote the paper and had primary responsibility for the final content. VW and EF contributed to the interpretation of results and critical review. All authors read and approved the final manuscript.

The authors have no conflicts of interest to declare.

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Ethical standards

The study was registered in the National Research Ethics System, was approved by the Ethics Committee of the Social Medicine Institute, at State University of Rio de Janeiro (CAAE : 04452412.0.0000.5260), and was carried out after participants‘ informed consent.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Evans WJ. What is sarcopenia? J Gerontol A Biol Sci Med Sci 1995; 50: 5-8. doi: 10.1093/gerona/50a.special_issue.5

[2] Jafari Nasabian P, Inglis JE, Reilly W, Kelly OJ, Ilich JZ. Aging human body: Changes in bone, muscle and body fat with consequent changes in nutrient intake. J Endocrinol 2017; 234(1):R37-R51. doi: 10.1530/JOE-16-0603

[3] Curtis E, Litwic A, Cooper C, Dennison E. Determinants of muscle and bone aging. J Cell Physiol 2015: 230(11):2618-2625. doi: 10.1002/jcp.25001

[4] Cruz-Jentoft AJ, Baeyens JP, Bauer JM et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010; 39(4):412-423. doi: 10.1093/ageing/afq034

[5] Cruz-Jentoft AJ, Bahat G, Bauer JM et al. Sarcopenia: revised European consensus on definition and diagnosis Age Ageing 2019; 48:16-31. doi: 10.1093/ageing/afy169

[6] Visser M, Goodpaster BH, Kritchevsky SB et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. J Gerontol A Biol Sci Med Sci 2005; 60:324–333. doi: 10.1093/gerona/60.3.324

[7] Ma Y, Fu L, Jia L et al. Muscle strength rather than muscle mass is associated with osteoporosis in older Chinese adults. J Formos Med Assoc 2018; 117 (2): 101-108. doi: 10.1016/j.jfma.2017.03.004

[8] Clark BC, Manini TM. Sarcopenia dynapenia. J Gerontol A Biol Sci Med Sci 2008; 63(8):829–34. doi: 10.1093/gerona/63.8.829

[9] Scott D, Daly RM, Sanders KM, Ebeling PR. Fall and fracture risk in sarcopenia and dynapenia with and without obesity: the role of lifestyle interventions. Curr Osteoporos Rep 2015; 13(4): 235-244. doi: 10.1007/s11914-015-0274-z

[10] Alexandre TS, Scholes S, Santos JLF, de Oliveira C. Dynapenic Abdominal Obesity as a Risk Factor for Worse Trajectories of ADL Disability Among Older Adults: The ELSA Cohort Study J Gerontol A Biol Sci Med Sci 2019; 4 (7): 1112–1118. doi: 10.1093/gerona/gly182.

[11] Newman B, Varant K, Visser M et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition cohort. J Gerontol A Biol Sci Med Sci 2006; 61(1):72–77. doi: 10.1093/gerona/61.1.72

[12] Bouchard DR and Janssen I. Dynapenic-Obesity and Physical Function in Older Adults. J Gerontol A Biol Sci Med Sci 2010; 65(1): 71-77. doi: 10.1093/gerona/glp159

[13] Rossi AP, Bianchi L, Volpato S et al. Dynapenic abdominal obesity as a predictor of worsening disability, hospitalization, and mortality in older adults: results from the InCHIANTI study. J Gerontol A Biol Sci Med Sci 2017; 72:1098–1104. doi: 10.1093/gerona/glw203.

[14] Armamento-Villareal R, Napoli N, Waters D et al. Fat, muscle, and bone interactions in obesity and the metabolic syndrome. Int J Endocrinol 2014: 247076. doi: 10.1155/2014/247076

[15] Locquet M, Beaudart C, Durieux N, Reginster JY, Bruyère O. Relationship between the changes over time of bone mass and muscle health in children and adults: a systematic review and meta-analysis. BMC Musculoskelet Disord 2019; 20(1), 429-42. doi: 10.1186/s12891-019-2752-4.

[16] Cederholm T, Cruz-Jentoft AJ, Maggi S. Sarcopenia and fragility fractures. Eur J Phys Rehabil Med 2013; 49: 111–117.

[17] Gonnelli S, Caffarelli C, Tanzilli T, Alessi C, Pitinca MT, Rossi S et al. The associations of body composition and fat distribution with bone mineral density in elderly Italian men and women. J Clin Densitom 2013; 16(2):168–77. doi: 10.1016/j.jocd.2012.02.013

[18] Leslie WD, Weiler HA, Lix LM, Nyomba BL. Body composition and bone density in Canadian White and Aboriginal women: the First Nations Bone Health study. Bone 2008; 42(5):990–5. doi: 10.1016/j.bone.2008.01.018

[19] Scott D, Shore-Lorenti C, McMillan L et al. Associations of components of sarcopenic obesity with bone health and balance in older adults. Arch Gerontol Geriatr 2018; 75: 125-131. doi: 10.1016/j.archger.2017.12.006.

[20] Ho-Pham LT, Nguyen UD, Nguyen TV. Association between lean mass, fat mass, and bone mineral density: A meta-analysis. J Clin Endocrinol Metab 2014; 99(1): 30-38. doi: 10.1210/jc.2013-3190

[21] Tachiki T, Kouda K, Dongmei N et al. Muscle strength is associated with bone health independently of muscle mass in postmenopausal women: the Japanese population-based osteoporosis study. J Bone Miner Metab 2019; 37(1): 53-59. doi: 10.1007/s00774-017-0895-7

[22] Kim SW; Lee HA, Cho EH. Low handgrip strength is associated with low bone mineral density and fragility fractures in postmenopausal healthy Korean women. J Korean Med Sci 2012; 27: 744-747. doi: 10.3346/jkms.2012.27.7.744

[23] Li YZ, Zhuang HF, Cai SQ, Lin CK, Wang PW, Yan LS, Lin JK, Yu HM. Low grip strength is a strong risk factor of osteoporosis in postmenopausal women. Orthop surger 2018; 10(1):17-22. doi: 10.1111/os.12360

[24] Chain A, Crivelli M, Faerstein E, Bezerra, FF. Association between fat mass and bone mineral density among Brazilian women differs by menopausal status: The Pro-Saude Study. Nutrition 2017; 33, 14-19. doi: 10.1016/j.nut.2016.08.001

[25] Perna, S, Spadaccini D, Nichetti M, Avanzato I, Faliva MA, Rondanelli M. Osteosarcopenic visceral obesity and osteosarcopenic subcutaneous obesity, two new phenotypes of sarcopenia: Prevalence, metabolic profile, and risk factors. J aging Res 2018: 6147426 doi: 10.1155/2018/6147426

[26] Sutter T, Toumi H, Valery A, El Hage R, Pinti A, Lespessailles E. Relationships between muscle mass, strength and regional bone mineral density in young men. PloS one 2019; 14(3), e0213681. doi: 10.1371/journal.pone.0213681

[27] Scott D, Chandrasekara SD, Laslett LL, Cicuttini F, Ebeling PR, Jones G. Associations of sarcopenic obesity and dynapenic obesity with bone mineral density and incident fractures over 5–10 years in community-dwelling older adults. Calcifi Tissue Int 2016; 99(1):30-42. doi: 10.1007/s00223-016-0123-9

[28] Da Rocha TF, Hasselmann MH, Curioni CC, Bezerra FF, Faerstein E. Alcohol consumption is associated with DXA measurement of adiposity: the Pró-Saúde Study, Brazil. Eur J Nutr 2017; 56(5), 1983-1991. doi: 10.1007/s00394-016-1240-y

[29] Normando P, Santos-Rebouças C, Leung C, Epel E, Fonseca AC, Zembrzuski V, et al. Variants in gene encoding for vitamin D binding protein were associated with leukocyte telomere length: The Pró-Saúde Study. Nutrition. 2020; 71:110618. doi:10.1016/j.nut.2019.110618

[30] Oliveira N, Coelho GMO, Cabral MC, Bezerra FF, Faerstein E, Canella DS. Association of body image (dis)satisfaction and perception with food consumption according to the NOVA classification: Pró-Saúde Study. Appetite. 2020; 144:104464. doi:10.1016/j.appet.2019.104464

[31] Aubertin-Leheudre M, Anton S, Beavers DP. Dynapenia and metabolic health in obese and non-obese older adults aged 70 years and older: the life study. J Am Med Dir Assoc 2017; 18(4): 312–319. doi: 10.1016/j.jamda.2016.10.001

[32] Ilich JZ, Inglis JE, Kelly OJ, McGee DL. Osteosarcopenic obesity is associated with reduced handgrip strength, walking abilities, and balance in postmenopausal women. Osteoporos Int. 2015;26(11):2587- 2595. doi:10.1007/s00198-015-3186-y

[33] Chung JH, Hwang HJ, Shin HY, Han CH. Association between Sarcopenic Obesity and Bone Mineral Density in Middle-Aged and Elderly Korean. Ann Nutr Metab. 2016;68(2):77- 84. doi:10.1159/000442004

[34] Brasil. Instituto Brasileiro de Geografia e Estatística. IBGE Características étnicos-raciais da população: Um estudo das categorias de classificação de cor ou raça. Rio de Janeiro: IBGE; 2008.

[35] Lohman TG, Roche AF, Martorelli R. Anthropometric standardization reference manual. Champaign, Illinois. 1998

[36] Baumgartner RN, Wayne SJ, Waters DL, Janssen I, Gallagher D, Morley JE. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. Obes Res 2004; 12(12):1995-2004. doi: 10.1038/oby.2004.250

[37] Dufour AB, Hannan MT, Murabito JM, Kiel DP, McLean RR. Sarcopenia definitions considering body size and fat mass are associated with mobility limitations: The Framingham Study. J Gerontol A Biol Sci Med Sci 2013; 68(2):168-174. doi: 10.1093/gerona/gls109

[38] Yoonjoo J, Linton JA, Choi J et al. Association between Cigarette Smoking and Sarcopenia according to Obesity in the Middle-Aged and Elderly Korean Population: The Korea National Health and Nutrition Examination Survey (2008–2011). Korean J Fam Med 2019; 40(2):87-92. doi: 10.4082/kjfm.17.0078

[39] Micklesfield LA, Goedecke JH, Punyanitya M, Wilson KE, Kelly TL. Dual-Energy X-Ray performs as well as clinical computed tomography for the measurement of visceral fat. Obesity 2012; 20(5):1109-1114. doi: 10.1038/oby.2011.367.

[40] Dodds RM, Syddall HE, Cooper R et al. Grip strength across the life course: normative data from twelve British studies. PLoS One 2014; 9(12): e113637. doi: 10.1371/journal.pone.0113637

[41] Petak S, Barbu CG, Yu EW, Fielding R, Mulligan K, Sabowitz B et al. The official positions of the international society for clinical densitometry: body composition analysis reporting. J Clin Densitom 2013; 16(4):508–519. doi: 10.1016/j.jocd.2013.08.018

[42] De Lorenzo A, Deurenberg P, Pietrantuono M et al. How fat is obese? Acta Diabetol 2003; 40:S254–S257. doi: 10.1007/s00592-003-0079-x

[43] Bouchard DR, Dionne IJ, Brochu M. Sarcopenic/obesity and physical capacity in older men and women: Data from the Nutrition as a Determinant of Successful Aging (NuAge) - the Quebec Longitudinal Study. Obesity 2009; 17(11):2082-2088. doi: 10.1038/oby.2009.

[44] Ho-Pham LT, Lai TQ, Nguyen MTT, Nguyen TV (2015) Relationship between Body Mass Index and Percent Body Fat in Vietnamese: Implications for the Diagnosis of Obesity. PLoS one 10(5): e0127198. doi: 10.1371/journal.pone.0127198

[45] Kim YM, Kim S, Won YJ, Kim SH. Clinical manifestations and factors associated with osteosarcopenic obesity syndrome: A cross-sectional study in Koreans with obesity. Calcif Tissue Int 2019; 105(1), 77-88. doi: 10.1007/s00223-019-00551-y.

[46] Scott D, Seibel M, Cumming R et al. Sarcopenic obesity and its temporal associations with changes in bone mineral density, incident falls and fractures in older men: The concord health and ageing in men project. J Bone Miner Res 2017: 32(3):575-583. doi: 10.1002/jbmr.3016

[47] Szlejf C, Parra-Rodríguez L, Rosas-Carrasco O. Osteosarcopenic obesity: Prevalence and its relation with frailty and physical performance in middle-aged and older women. J Am Med Dir Assoc 18(8):733.e1-733.e5. doi: 10.1016/j.jamda.2017.02.023

[48] Alexandre TS, Scholes S, Santos JF et al. Dynapenic abdominal obesity increases mortality risk among English and Brazilian older adults: a 10-year follow-up of the ELSA and SABE studies. J Nutr Health Aging 2018; 22(1):138-144. doi: 10.1016/j.jamda.2016.10.001

[49] Szlejf C, Suemoto CK, Lotufo PA et al. Association of sarcopenia with performance in multiple cognitive domains: results from the ELSA-Brasil study. J Gerontol A Biol Sci Med Sci 2019; 74(11):1805-1811. doi: 10.1093/gerona/glz118.

[50] McLean RR, Shardell MD, Alley DE, et al. Criteria for clinically relevant weakness and low lean mass and their longitudinal association with incident mobility impairment and mortality: the foundation for the National Institutes of Health (FNIH) sarcopenia project. J Gerontol 2014; 69(5), 576-583. doi: 10.1093/gerona/glu012.

[51] Studenski SA, Peters KW, Alley DE et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci 2014; 69(5):547-558. doi: 10.1093/gerona/glu010.

[52] Maximo RO, Santos LF, Perracinic MR et al. Abdominal obesity, dynapenia and dynapenic-abdominal obesity as factors associated with falls. Braz J Phys Ther 2019; 23(6):497-505. doi: 10.1016/j.bjpt.2018.10.009

[53] Delmonico MJ, Harris TB, Visser M et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. Am J Clin Nutr 2009; 90(6):1579–85. doi: 10.3945/ajcn.2009.28047

[54] Clark BC, Manini TM. What is dynapenia? Nutrition 2012; 28(5): 495-503. doi: 10.1016/j.nut.2011.12.002

[55] Wagner P, Chapurlat R, Ecochard R, Szulc P. Low muscle strength and mass is associated with the accelerated decline of bone microarchitecture at the distal radius in older men: the prospective STRAMBO study. J Bone Miner Res 2018; 33(9), 1630-1640. doi: 10.1002/jbmr.3456

[56] Tabibi H, As'habi A, Najafi I et al. Prevalence of dynapenic obesity and sarcopenic obesity and their associations with cardiovascular disease risk factors in peritoneal dialysis patients. Kidney Res Clin Pract 2018; 37(4): 404-413. doi: 10.23876/j.krcp.18.0064

[57] Hsu YH, Venners SA, Terwedow HA et al. Relation of body composition, fat mass, and serum lipids to osteoporotic fractures and bone mineral density in Chinese men and women. Am J Clin Nutr 2006; 83:146-154. doi: 10.1093/ajcn/83.1.146

[58] Zhao LJ, Jiang H, Papasian CJ et al. Correlation of obesity and osteoporosis: effect of fat mass on the determination of osteoporosis. J Bone Miner Res 2008; 23:17–29. doi: 10.1359/jbmr.070813

[59] Strugnell C, Dunstan DW, Magliano C, Zimmet PZ, Shaw JE, Robin MD. Influence of age and gender on fat mass, fat-free mass and skeletal muscle mass among Australian adults:

The Australian diabetes, obesity and lifestyle study (AusDiab). J Nutr Health Aging 2014; 18:540-546. doi: 10.1007/s12603-014-0464-x

[60] Reid IR. Fat and bone. Arch Biochem Biophys 2010; 503(1):20-2. doi: 10.1016/j.abb.2010.06.027.

[61] Aguiari P, Leo S, Zavan B et al. High glucose induces adipogenic differentiation of muscle-derived stem cells. Proc Natl Acad Sci 2008; 105(4):1226–1231. doi: 10.1073/pnas.0711402105

[62] Perkisas S, De Cock AM, Verhoeven V, Vandewoude M. Intramuscular adipose tissue and the functional components of sarcopenia in hospitalized geriatric patients. Geriatrics 2017; 2(1):11. doi: 10.3390/geriatrics201001

[63] Lang T, Cauley JA, Tylavsky F, Bauer D, Cummings S, Harris TB. Computed tomographic measurements of thigh muscle cross- sectional area and attenuation coefficient predict hip fracture: the health, aging, and body composition study. J Bone Miner Res 2010; 25(3): 513-519. doi: 10.1359/jbmr.090807

[64] Zhao, Y, Huang M, Sosa MS et al. Fatty infiltration of paraspinal muscles is associated with bone mineral density of the lumbar spine. Arch Osteoporos, 2019: 14(1):99. doi: 10.1007/s11657-019-0639-5.

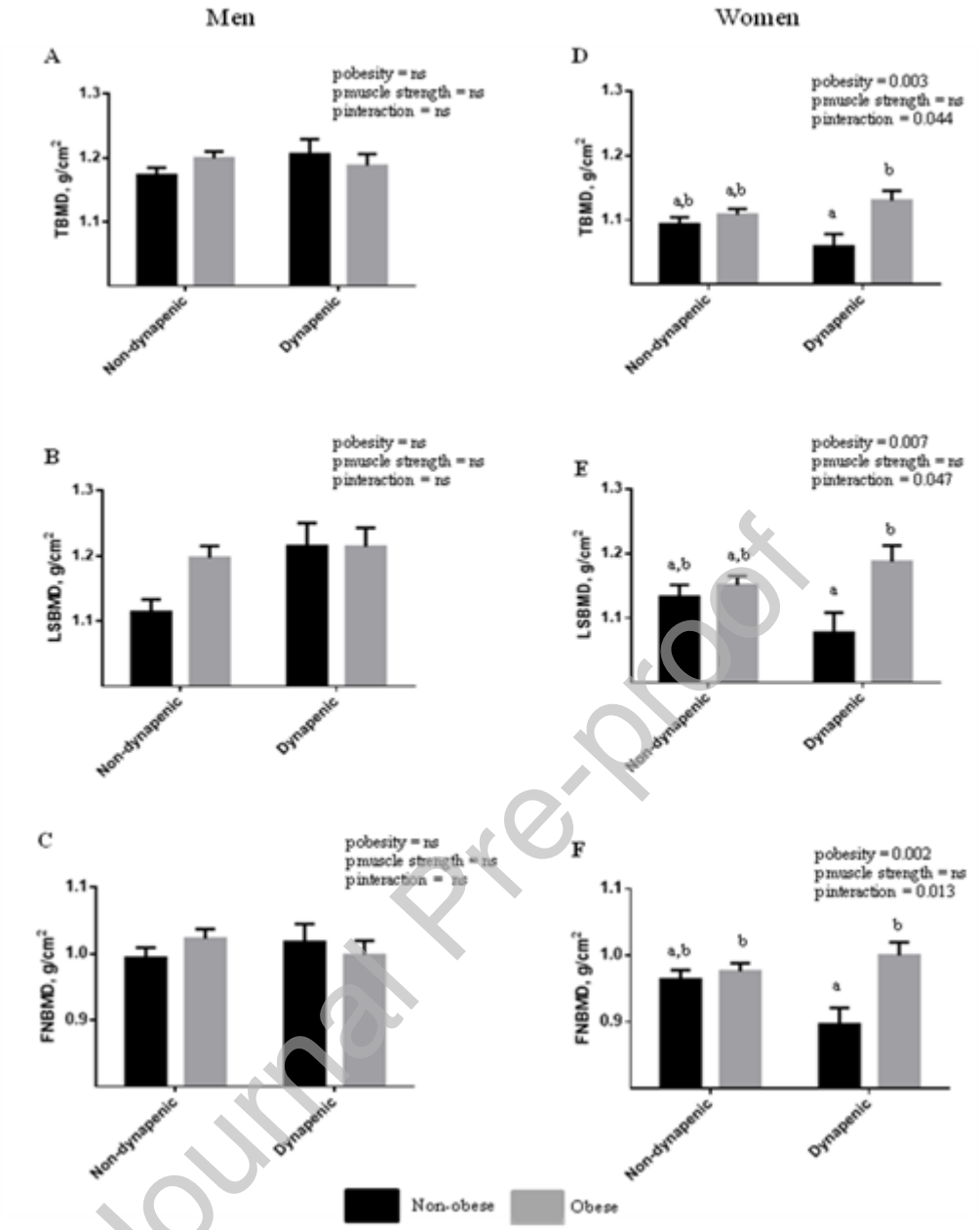

Figure 1: Association of obesity, dynapenia and their interaction with bone mineral density (BMD) at total body (TBMD) (A,D), lumbar spine (LSBMD) (B,E) and femoral neck BMD (FNBMD) (C,F), by gender: Pró-Saúde Study, Brazil, 2012-13.
*P-value obtained by a general linear model, followed by Tukey post hoc test with adjustment for age, height, total lean mass, race and postmenopausal period (only for women). Different letters indicate statistical significance between groups.

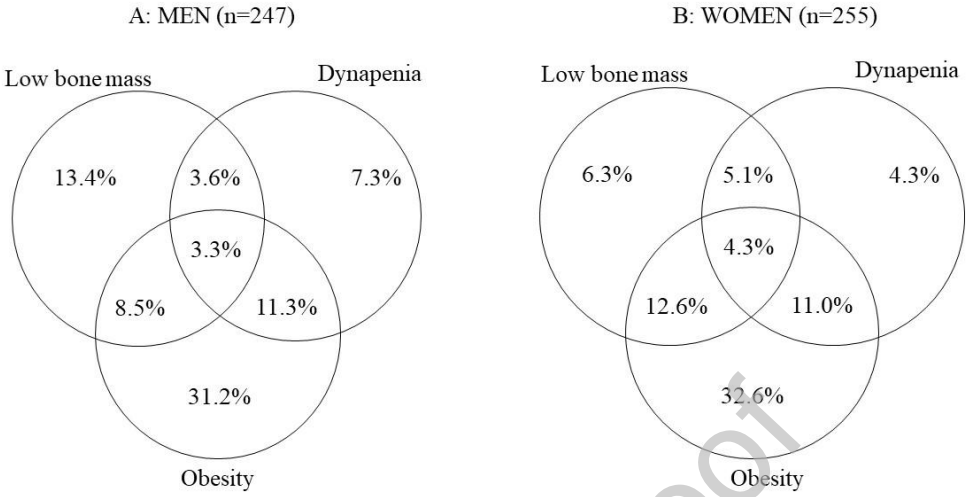

Figure 2: Frequency of obesity, dynapenia and low bone mass and their combinations in the men (A) and women (B) studied.

Table 1: Descriptive characteristics of study participants according to presence of obesity and dynapenia: Pró-Saúde Study, Brazil, 2012-13.

	Non-obese non-dynapenic	**Obese non-dynapenic**	**Non-obese dynapenic**	**Obese dynapenic**	**P-value***
Men					
N	86	100	27	36	
Age (y)	51.94±,7.47[b]	51.24±7.81[b]	57.37±7.29[a]	52.78±7.86[a,b]	0.003
Weight (kg)	74.16±9.17[b]	91.36±14.19[a]	69.21±11.90	85.72±14.00[a]	<0.001
Height (m)	1.73±0.06[a,b]	1.74±0.06[a]	1.70±0.08[b]	1.72±0.07[b]	0.009
BMI (kg/m²)	24.76±3.01[b]	30.31±3.95[a]	23.97±2.98[b]	29.57±4.20[a]	<0.001
Absolute TFM (kg)	18.59±4.56[b]	32.05±7.26[a]	17.53±5.29[b]	30.57±8.27[a]	<0.001
Relative TFM (%)	24.76±4.11[b]	34.81±3.36[a]	24.82±4.33[b]	35.28±4.57[a]	<0.001
VAT (kg)	0.98±0.51[b]	2.27±0.91[a]	0.98±0.52[b]	2.09±0.94[a]	<0.001
VAT (%)	5.01±2.02[b]	6.98±1.89[a]	5.34±1.91[b]	6.74±2.03[a]	<0.001
TLM (kg)	52.71±5.57[b]	56.32±7.78[a]	48.92±6.85[b]	52.36±7.35[b]	<0.001
ALM (kg)	25.40±3.28[b]	27.09±4.51[a]	23.00±3.89[c]	24.88±3.93[b,c]	<0.001
SMI (kg/m²)	8.47±1.08[b]	8.97±1.18[a]	7.98 ± 1.04[b]	8.57±1.07[a,b]	<0.001
Right HS (kg)	42.97±5.59[a]	43.45±5.91[a]	32.63±6.29[b]	32.32±5.46[b]	<0.001
Left HS (kg)	40.54±4.98[a]	41.00±5.73[a]	29.35±3.03[b]	27.98±4.54[b]	<0.001
Women					
n	77	115	24	39	
Age	51.38±7.21[b]	53.12±8.02[a,b]	55.29±8.26[a,]	55.77±8.49[a]	0.020
Weight (kg)	63.91±9.46[b]	77.63±11.78[a]	58.07±9.59[b]	77.31±17.81[a]	<0.001
Height (m)	1.61±0.07[a]	1.61±0.06[a]	1.58±0.07[a,b]	1.57±0.07[b]	0.016
BMI (kg/m²)	24.69±2.85[b]	30.14±4.62[a]	23.18±3.40[b]	31.14±5.93[a]	<0.001
Absolute TFM (kg)	23.48±4.36[b]	35.27±7.57[a]	20.40±4.80[b]	35.87±12.03[a]	<0.001
Relative TFM (%)	36.60±2.83[b]	45.10±3.43[a]	34.80±3.97[b]	45.67±4.61[a]	<0.001
VAT (kg)	0.58±0.34[b]	1.27±0.63[a]	0.53±0.32[b]	1.25±0.70[a]	<0.001
VAT (%)	2.39±1.22[b]	3.51±1.34[a]	2.47±1.24[b]	3.36±1.15[a]	<0.001
TLM (kg)	38.19±5.41[a,b]	40.06±4.86[a]	35.63±5.16[b]	39.21±6.39[a]	0.001
ALM (kg)	17.37±2.91[b]	18.49±2.66[a]	16.03±2.56[b]	17.86±3.05[a,b]	<0.001
SMI (kg/m²)	6.70±0.88[b]	7.17±0.09[a]	6.40±0.89[b]	7.20±0.98[a]	<0.001
Right HS (kg)	26.56±4.55[a]	26.19±3.99[a]	17.85±4.43[b]	17.94±3.69[b]	<0.001
Left HS (kg)	26.28±7.49[a]	24.78±3.73[a]	16.03±3.00[b]	16.32±2.90[b]	<0.001

BMI: Body mass index; TFM: Total fat mass; VAT: Visceral adipose tissue; TLM: Total lean mass; ALM: Appendicular lean mass; SMI: Skeletal muscle index; HS: Handgrip strength. Data expressed as mean ± SD. *P-value obtained by one-way Anova followed by Tukey test. Different letters in the same row indicate statistical significance between groups.

Table 2: Frequency distribution of low or adequate bone mass in the according to presence of obesity and dynapenia, by gender: Pró-Saúde Study, Brazil, 2012-13.

	Non-obese non- dynapenic	Obese non- dynapenic	Non-obese dynapenic	Obese dynapenic
Men				
Bone mass				
Low	33 (38.4)	21 (21.0)	9 (33.3)	8 (22.2)
Adequate	53 (61.6)	79 (79.0)	18 (66.7)	28 (77.8)
P-value*	0.009		0.242	
Women				
Bone mass				
Low	16 (20.8)	32 (27.8)	13 (54.2)	11 (28.2)
Adequate	61 (79.2)	83 (72.2)	11 (45.8)	28 (71.8)
P-value*	0.175		0.037	

Data expressed as n (%). *P-value obtained by by Chi-square test