REVISTA BRASILEIRA DE REUMATOLOGIA

www.reumatologia.com.br

Original article

Factors associated with osteopenia and osteoporosis in women undergoing bone mineral density test☆

Ana Carolina Veiga Silva, Maria Inês da Rosa, Bruna Fernandes, Suéli Lumertz, Rafaela Maria Diniz, Maria Eduarda Fernandes dos Reis Damiani*

Universidade do Extremo Sul Catarinense, Criciuma, SC, Brazil

ARTICLE INFO

Article history:
Received 10 February 2014
Accepted 17 August 2014
Available online 27 November 2014

Keywords:
Osteoporosis
Dual-energy X-ray absorptiometry
Epidemiology
Metabolic bone diseases

ABSTRACT

The aim of this study was to determine the prevalence of osteopenia and osteoporosis in a female population, that had bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) in a specialized clinic in the south of Brazil. We conducted a cross-sectional study including 1871 women that performed scans between January and December 2012. We conducted a logistic regression analysis with all independent variables and outcomes (osteopenia, osteoporosis and fracture risk). According to DXA results, 36.5% of women had normal BMD, 49.8% were diagnosed with osteopenia and 13.7% with osteoporosis. Menopause and age over 50 years old were risk factors for osteopenia and osteoporosis while prior hysterectomy and BMI greater than 25 were protective factors. For the outcome of fracture at any site the risk factors were age over 50 years old, osteopenia and osteoporosis (OR = 2.09, 95% CI: 1.28–3.40) and (OR = 2.49, 95% CI: 1.65–3.74), respectively.

Fatores associados à osteopenia e osteoporose em mulheres submetidas à densitometria óssea

Palavras-chave:
Osteoporose
Densitometria
Epidemiologia
Doenças ósseas metabólicas

RESUMO

O objetivo deste estudo foi determinar a prevalência de osteopenia e osteoporose em uma população de mulheres que fizeram exames de densitometria em uma clínica especializada no sul do Brasil. Nós conduzimos um estudo transversal, incluindo 1.871 mulheres que se submeteram à densitometria óssea entre janeiro e dezembro de 2012. Foi feita uma análise de regressão logística com todas as variáveis independentes e os desfechos (osteopenia, osteoporose e risco de fraturas). A densitometria óssea foi diagnosticada como normal em 36,5% das mulheres, 49,8% com osteopenia e 13,7% com osteoporose. Estar na menopausa

☆ Institution: Universidade do Extremo Sul Catarinense – UNESC, Laboratory of Epidemiology.

* *Corresponding author.*
E-mail: mir@unesc.net (M.I. da Rosa).

http://dx.doi.org/10.1016/j.rbre.2014.08.011

e ter mais de 50 anos foram fatores de risco para osteopenia e osteoporose, enquanto ter feito histerectomia e apresentar índice de massa corporal (IMC) maior do que 25 foram fatores de proteção. Para o desfecho fratura em qualquer sítio, os fatores associados foram idade acima de 50 anos e osteopenia ou osteoporose, (OR = 2,09, intervalo de confiança [IC]: 1,28-3, 95%, 40) e (OR = 2,49, 95% CI: 1,65-3, 74), respectivamente.

Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro architectural deterioration of the bone tissue, resulting in increased risk of fracture due to bone fragility.[1] It was recently acknowledged as one of the main public health issues of developed countries.[2]

Osteoporosis is diagnosed by measuring the bone mineral density (BMD); a bone density that is 2.5 standard deviations (SD) or more below the young adult mean value (*t*-score <−2.5) indicates osteoporosis. Patients with bone density between 1 and 2.5 SD below average (*t*-score −1 to −2.5) are said to have osteopenia.[3]

In women, BMD decreases with age, presenting sharp drop during menopause. It is estimated that one in every two women in the UK from the age of 50 will suffer some kind of fracture during the remainder of her life.[4]

With increasing life expectancy and an aging population, it is anticipated that the impact of osteoporosis in the coming years will have a significant increase.[5] We should expect an economic burden for current and future public health system due to the high prevalence of osteoporosis and resulting fractures.[6]

The aim of this study was to determine the prevalence and factors associated with osteopenia and osteoporosis in women who have undergone bone mineral density test in a specialized service.

Methods

A cross-sectional study was made with 1871 women undergoing bone mineral density test in a specialized clinic from January 2012 to December 2012. The project was approved by the Research Ethics Committee of Universidade Extremo Sul Catarinense under Protocol No. 829 392 012.

Osteopenia and osteoporosis were diagnosed by *Dual-energy X-ray absorptiometry* (DXA), allowing the BMD to be measured with the GE Lunar Prodigy Primo equipment with software Encore version 13.20. The Lunar Prodigy series showed clinical accuracy even 40% higher compared to other systems. A study suggests that BMD measurement error is between 5% and 8%.[7]

DXA is considered the gold standard for measuring BMD and diagnosing osteopenia/osteoporosis. DXA results are presented by (1) absolute BMD values (g/cm^2): absolute values are important because they are used to monitor changes in BMD over time; (2) *t*-score, calculated in SD, taking as reference the mean BMD of peak bone mass in young adults. The diagnostic criteria proposed by the World Health Organization (WHO) in 1994, based on the following data: up to −1.0 SD, normal, from −1.1 to −2.49 SD, osteopenia, and below −2.5 SD, osteoporosis[8]; (3) Z-score, calculated on SD, taking as reference the mean BMD expected for individuals of same age, ethnicity and gender.

It is important to recognize that the DXA results described here are only valid when strict criteria for the exam, quality control and analysis of the images are observed. The professionals responsible for the acquisition of images, as well as for analyzing and interpreting them must act in accordance with recognized professional qualification programs in the country. The incorrect application of the method limits its use, as in all imaging tests.

General data were taken from the densitometry report and included measurement of weight and height, age, BMI, previous fractures, calcium intake, thyroid medication, menopause, hormone replacement therapy, symptoms of menopause, hysterectomy and oophorectomy. Age was categorized into percentiles: (1) 25th percentile: aged 51 years or less, (2) between 25th and 50th percentile: aged 52–57 years, (3) between 50th and 75th percentile: aged 58–65 years and (4) above the 75th percentile: aged 66 years or older. Other qualitative variables were dichotomized.

BMI was calculated using the formula weight (kg)/height^2 (m). The DXA data collected included BMD values (g/cm^2) of the femur neck, preferably the right one, the total femur and the mean value of the lumbar vertebrae (L1-L4).

Descriptive analysis of all variables was performed. A bivariate analysis was performed using the Pearson's chi-square test.

In the model building process, we observed the importance of each component through the likelihood ratio test. The −2log likelihood (*deviance*) value, which is a measure to determine how well the model fits the data, was used. Estimates per interval were calculated using 95% confidence level. All variables with $p < 0.25$ (univariate analysis) were candidates to enter the model, according to the method of Hosmer and Lemeshow. Only $p < 0.05$ variables remained in the model. In case any biologically important change was observed in the coefficient of estimated risk factor, comparing models with and without the risk factor, it was considered that the covariate would be a confounding factor, and if so, should remain in the model, even if its own coefficient was not significant. The method used to build the multivariable logistic regression model was the backward method, in which all the variables selected by the researchers enter the model, and selection is made by removing the least significant variable, one at a time, in an automatic sequence mode, based on statistical criteria. The estimates per interval were calculated using 95% confidence

Table 1 – Characteristics of the women that performed DXA scans from January to December, 2012, presented as frequency (%) or average (± SD).

Variable	Average ± SD or *n* (%)
Age (years old)	59.2 ± 10.5
Weight (kg)	68.7 ± 12.8
Height (m)	1.57 ± 0.06
Femoral neck BMD	0.89 ± 0.27 *t* score: −1.03
Total femoral BMD	0.93 ± 0.15 *t* score: −0.59
Lumbar spine BMD	1.0 ± 0.17 *t* score: −0.75
BMI (kg/m²)	27.7 ± 5.0
≥24.9 kg/m²	592 (34.9)
≥25 kg/m²	1104 (65.1)
Fractures (n = 104)	
Forearm	45 (43.3)
Ribs	24 (23.0)
Femur	22 (21.2)
Spine	13 (12.5)
Calcium intake	
Yes	595 (31.9)
No	1273 (68.1)
DXA diagnosis	
Normal	682 (36.5)
Osteopenia	932 (49.8)
Osteoporosis	257 (13.7)
Use of thyroid medication	
Yes	412 (22.1)
No	1455 (77.9)
Hysterectomy	
Yes	461 (24.9)
No	1392 (75.1)
Oophorectomy	
Yes	332 (18.1)
No	1506 (81.9)

DXA, dual-energy X-ray absorptiometry; SD, standard deviation; *n*, number of individuals; BMD, bone mineral density; BMI, body mass index.

level. Interactions between variables were tested, and they were all nonsignificant at a 5% level of significance.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 18.0.

Results

The sample consisted of 1871 women who underwent DXA scan in a specialized private clinic in south of Santa Catarina. The average age was 59.2 ± 10.5 years, mean weight of 68.7 ± 12.8 and height of 1.57 ± 0.06. The mean BMI was 27.7 ± 5.0, 65.1% had a BMI > 25. The prevalence of fractures at any site was of 5.5%; the forearm and ribs being the most prevalent (Table 1). It was found that 31.9% of women were taking calcium, and 22.1% were on thyroid medication, 24.9% had previously had a hysterectomy, and 18.1%, an oophorectomy (Table 1).

According to the bone mineral density test diagnosis, 36.5% of women were normal, 49.8% had osteopenia and 13.7% had osteoporosis (Table 1).

Table 2 shows the prevalence of bone mass density in different subgroups, as well as the analysis of statistical significance using the chi-square test. The linear increase in osteopenia and osteoporosis was observed with advancing age ($p < 0.001$). The BMI, however, was inversely associated with reduced BMD ($p < 0.001$), i.e., women with higher BMI had less osteopenia or osteoporosis.

The correlations between the BMD measured at the spine, femur and femoral neck and the BMI were ($r = -0.133$, $p < 0.001$, $r = 0.590$ $p < 0.001$ and $r = 0.258$, $p < 0.001$), respectively.

The BMD at all sites had negative correlation with age (femoral neck $r = -0.220$, $r = -0.337$ total femur and lumbar spine $r = -0.015$, $p < 0.001$).

The multivariate regression had the following outcomes: osteoporosis, osteopenia and any fracture.

Table 3 shows the final logistic regression model for the first two outcomes, including the variables mean dichotomized age, menopause, BMI and hysterectomy. One can observe increased risk of osteoporosis for the variables age and menopause. Protection was found with an increased BMI and hysterectomy.

Table 4 shows the final fracture model, in which being older than 50 years old and presenting osteopenia/osteoporosis increase the chances of fractures at any site in 2.09 and 2.49, respectively, when compared to women aged 49 years or less and women with normal BMD.

Discussion

Our study used data from a clinic specialized in the diagnosis of osteoporosis, so the prevalence of osteopenia and osteoporosis cannot be extended to the general population, being restricted to a group of women referred for a DXA scan. In this case, the prevalence of osteoporosis should be overrated in relation to other population groups.

According to the DXA results, 36.5% of women had normal BMD, 49.8% were diagnosed with osteopenia and 13.7% with osteoporosis. The prevalence of osteopenia and osteoporosis found in our study showed a linear increase with age in the four age percentiles of the population studied.

The prevalence found in this study was lower than that found in the literature on similar studies conducted before the year 2000. In a study that assessed the prevalence of osteoporosis in Brazilian women, above the age of 50, and referred for bone density test, this prevalence was of 40%.[9] In the United States, a study with 600 patients at Wayne State University in Detroit, found a prevalence of 52%.[10]

The NHANES III study conducted between 1988 and 1994 by the Centers for Disease Control and Prevention gathered 3311 postmenopausal women above the age of 50 for proximal femur BMD examinations. The prevalence of osteoporosis and osteopenia verified was 18% and 50%, respectively.[11] In Sao Paulo state, a cross-sectional study with 4332 women over the age of 40, in a primary care service, found the prevalence of osteoporosis to be 33% and osteoporotic fractures of 11.5%($p < 0.05$),[12] while another study with 627 women over the age of 50 showed prevalence of osteoporosis in the lumbar spine and in femoral neck of 28.8% and 18.8%, respectively.[13]

Table 2 – Prevalence of bone mineral mass density in patients subgroups.

Variable	BMD				
	Normal	Osteopenia	Osteoporosis	*p*-value[a]	
	n (%)	*n* (%)	*n* (%)	Osteopenia vs. normal	Osteoporosis vs. normal
Total	682 (36.5)	932 (49.8)	357 (13.7)		
Age		16.4 (10)	19.7 (12)	<0.001	<0.001
Up to 51	264 (55.9)	193 (40.8)	16 (3.3)		
52–57	196 (42.6)	213 (46.3)	51 (11.1)		
58–65	143 (30.4)	256 (54.4)	71 (15.2)		
66 or older	79 (16.9)	270 (57.7)	119 (25.4)		
BMI				<0.001	<0.001
Up to 24.9	164 (27.7)	304 (51.4)	124 (20.9)		
25–29.9	219 (38.8)	277 (49.2)	68 (12.0)		
30–34.9	166 (45.1)	172 (46.7)	30 (8.2)		
35–39.9	45 (40.2)	54 (48.2)	13 (11.6)		
40 or more	18 (41.9)	20 (46.5)	5 (11.6)		
Menopause				<0.001	<0.001
Yes	481 (71.0)	797 (86.2)	235 (92.5)		
No	196 (29)	128 (13.8)	19 (7.5)		
HRT					
Yes	105 (15.8)	147 (16.3)	35 (13.8)	0.770	0.470
No	561 (84.2)	754 (83.7)	218 (86.2)		
Fractures				0.002	<0.001
Yes	22 (3.2)	63 (6.8)	34 (13.3)		
No	659 (96.8)	865 (93.2)	222 (86.7)		

[a] *p*-value, chi-square test; BMD, bone mineral density; BMI, body mass index; HRT, hormone replacement therapy.

In both male and female individuals, there is a balance between bone formation and resorption, but this becomes progressively negative with increasing age. Age-related bone loss begins immediately after the peak bone mass, but most of the bone loss occurs after the age of 65. Men, however, are less likely to develop osteoporosis than women, for two reasons: first, they gain more bone mass during puberty and, second, they lose less bone mass during aging, because, unlike women, men do not experience a sudden loss of estrogen. Elderly living at retirement homes are at greater risk. Eighty-five percent of women living in nursing homes over age 80 have osteoporosis.[14]

Our results showed a linear increase of osteopenia and osteoporosis with advancing age. In addition to the effects on bone mass, the aging also increases the risk of fractures, regardless of the bone mass, and an increase of 20 years of age means a fourfold risk of fractures.[15]

Oxidative stress (OS) is a common mechanism of pathogenesis of various degenerative diseases associated with aging, including osteoporosis.[16,17] An increase in reactive oxygen species (ROS) was implicated in decreased bone formation associated with advancing age, as well as increased resorption

Table 3 – Logistic regression model, considering the outcome variable – osteopenia vs. normal and osteoporosis vs. normal.

Variable	Adjusted OR (CI 95%)	
	Osteopenia	Osteoporosis
Age		
50 years or older	2.80 (2.20–3.57)	6.34 (4.36–9.23)
Up to 49 years old	1.00	1.00
BMI		
25 or more	0.46 (0.36–0.59)	0.22 (0.15–0.32)
Up to 24.9	1.00	1.00
Hysterectomy		
Yes	0.67 (0.52–0.87)	0.61 (0.41–0.92)
No	1.00	1.00
Menopause		
Yes	2.17 (1.63–2.88)	3.33 (1.92–5.77)
No	1.00	1.00

CI, confidence interval; BMI, body mass index.

Table 4 – Final logistic regression model, considering the outcome variable – any fracture.

Variable	Adjusted OR (CI 95%)
Age	
50 years or older	2.09 (1.28–3.40)
Up to 49 years old	1.00
BMD	
Osteopenia/osteoporosis	2.49 (1.65–3.74)
Normal	1.00

BMD, bone mineral density; CI, confidence interval.

associated with estrogen deficiency.[16] In line with this evidence, increased ROS production in osteoblasts stimulates apoptosis and decreased bone formation. As of the fourth decade, the bone formation is lower than the resorption.[18] Serum levels of the insulin-like growth hormone that modulates the effect of the GH in the bone also decrease with age.[19]

Our study showed a higher prevalence of forearm, rib, hip and spine fractures, respectively. According to the literature, the vertebral fracture is the most common clinical manifestation of osteoporosis. Most of these fractures (about two thirds) are asymptomatic, diagnosed as an incidental finding on X-ray.[20] Hip fractures are relatively common in osteoporosis and affects 15% of women and 5% of men at the age of 80. Subchondral insufficiency fractures of the femoral head, resulting in osteopenia, can lead to rapid loss of cartilage and space-destructive osteoarthritis.[21] In addition to that, fractures of the distal radius (Colles' fractures) may also occur and are more common in women after menopause, while the risk of hip fracture increases exponentially with age.

Our results show an inverse correlation between the BMI and the risk of osteopenia and osteoporosis. Published studies show that low body weight (less than 58 kg) is associated with an increased risk of osteoporosis and fractures. Weight losses after the age of 50 in women increases the risk of hip fracture, while weight gains decreases this risk.[22,23]

Menopause was also a risk factor with statistical significance in our study. The rate of bone loss in women with postmenopausal hypoestrogenism is probably around 0.5% and 1.5% per year, with a small percentage of women who are "fast bone losers" and can lose 3%–5% of bone mass per year. The rate of bone loss is highly dependent on hormonal factors, environmental and genetic factors. In a longitudinal study with 272 healthy pre- and perimenopausal women, there was no bone loss in women beyond the menopause, while an accelerated bone loss was observed in the 2–3 years prior to the cessation of menstruation, with significant correlation between the rate of bone lost and the elevation of follicle-stimulating hormone (FSH) and markers of bone metabolism.[24–26]

We also found that hysterectomy would be a protective factor for osteopenia and could not find a plausible explanation for this protection, since it goes against the literature, which reports a decrease in bone mass after hysterectomy.[27–29] This variable is independent of the oophorectomy, which was analyzed apart and showed no statistical significance. This analysis may be biased, since confounding factors, such as the lifestyle and the reproductive history of the patients, were not controlled.

Conclusion

Our study showed that the prevalence of osteopenia is greater than that of osteoporosis and that old age and menopause are risk factors for both outcomes, while BMI above 25 and prior hysterectomy were protective factors. For the fracture outcome, the statistically significant risks were age above 50 years old and osteopenia or osteoporosis.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy (2001). JAMA. 2001;285:785–95.
2. World Health Organization. Burden of disease in DALYs by cause, sex, and mortality stratum in WHO regions, estimates for 2002. The World Health Report changing history. Geneva: World Health Organization; 2004. p. 126–31.
3. World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva: World Health Organization; 1994. p. 1–129. Technical Report Series no. 843.
4. Van Staa TP, Dennison EM, Leufkens HG, Cooper C. Epidemiology of fractures in England and Wales. Bone. 2001;29:517–22.
5. Lane NE. Epidemiology, etiology, and diagnosis of osteoporosis. Am J Obstet Gynecol. 2006;194:S3–11.
6. Hopkins RB, Tarride JE, Leslie WD, Metge C, Lix LM, Morin S, et al. Estimating the excess costs for patients with incident fractures, prevalent fractures, and nonfracture osteoporosis. Osteoporos Int. 2012 [Epub ahead of print].
7. Kuiper JW, Van Kuijk C, Grashuis JL, Ederveen AG, Schutte HE. Accuracy and the influence of marrow fat on quantitative CT and dual-energy X-ray absorptiometry measurements of the femoral neck in vitro. Osteoporos Int. 1966;6:25–30.
8. Kanis JA, WHO Study Group. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Synopsis of a WHO Report. Osteoporos Int. 1994;4:368–81.
9. Torres R, Marcelino C, Vieira L, Bandeira F. Prevalência de osteoporose em 1441 mulheres encaminhadas para determinação da densidade óssea. Arq Bras Endocrinol Metabol. 1998;42:S182.
10. Nelson D, Molloy R, Kleerekoper M. Prevalence of osteoporosis in women referred for bone density testing: utility of multiple skeletal sites. J Clin Densitom. 1998;1:5–12.
11. Looker AC, Orwoll ES, Johnston CC, Lindsay R, Wahner H, Dunn W. Prevalence of low femoral bone in older U.S. adults from NHANES III. J Bone Miner Res. 1997;12:1761–8.
12. Pinheiro MM, dos Reis Neto ET, Machado FS, Omura F, Yang JHK, Szejnfeld J, et al. Fatores de risco para fratura por osteoporose e baixa densidade óssea em mulheres na pré e pós-menopausa. Rev Saúde Pública. 2010;44:479–85.
13. Pinheiro MM, Reis N, Machado ET, Felipe FS, Yang O, Szejnfeld JH, et al. Risk factors for osteoporotic fractures and low bone density in pre and postmenopausal women. Rev Saude Publica. 2010;44:479–85.
14. Bandeira FC, Freese E. Prevalência de osteoporose e fraturas vertebrais em mulheres na pós-menopausa atendidas em serviços de referência. Rev Bras Epidemiol. 2007;10:86–98.
15. Vu MQ, Weintraub N, Rubenstein LZ. Falls in the nursing home: are they preventable? J Am Med Dir Assoc. 2006;7: S53.
16. Hui SL, Slemenda CW, Johnston CC Jr. Age and bone mass as predictors of fracture in a prospective study. J Clin Invest. 1988;81:1804.
17. Balaban RS, Nemoto S, Finkel T. Mitochondria, oxidants, and aging. Cell. 2005;120:483.
18. Manolagas SC. From estrogen-centric to aging and oxidative stress: a revised perspective of the pathogenesis of osteoporosis. Endocr Rev. 2010;31:266.

19. Lips P, Courpron P, Meunier PJ. Mean wall thickness of trabecular bone packets in human liac crest: changes with age. Calciforme Tissue Res. 1978;26:13–7.
20. Rudman D, Kutner MH, Rogers CM, Lubin MF, Fleming GA, Bain RP. Impaired growth hormone secretion in the adult population: relation to age and adiposity. J Clin Invest. 1981;67:1361–9.
21. Lindsay R, Silverman SL, Cooper C, Hanley DA, Barton I, Broy SB, et al. Risk of new vertebral fracture in the year following a fracture. JAMA. 2001;285:320–3.
22. Yamamoto T, Bullough PG. The role of subchondral insufficiency fracture in rapid destruction of the hip joint: a preliminary report. Arthritis Rheum. 2000;43:2423.
23. Green AD, Colón-Emeric CS, Bastian L, Drake MT, Lyles KW. Does this woman have osteoporosis? JAMA. 2004;292:2890–900.
24. Villareal DT, Fontana L, Weiss EP, Racette SB, Steger-May K, Schechtman KB, et al. Bone mineral density response to caloric restriction-induced weight loss or exercise-induced weight loss: a randomized controlled trial. Arch Intern Med. 2006;166:2502–10.
25. Chapurlat RD, Garnero P, Sornay-Rendu E, Arlot ME, Claustrat B, Delmas PD. Longitudinal study of bone loss in pre- and perimenopausal women: evidence for bone loss in perimenopausal women. Osteoporos Int. 2000;11:493–8.
26. Park HA, Lee JS, Kuller LH, Cauley JA. Effects of weight control during the menopausal transition on bone mineral density. J Clin Endocrinol Metab. 2007;92:3809.
27. Warming L, Hassager C, Christiansen C. Changes in bone mineral density with age in men and women: a longitudinal study. Osteoporos Int. 2002;13:105–12.
28. Hreshchyshyn MM, Hopkins A, Zylstra S, Anbar M. Effects of natural menopause, hysterectomy and oophorectomy on lumbar spine and femoral neck bone densities. Obstet Gynecol. 1988;72:631–8.
29. Watson NR, Studd JW, Garnett T, Savvas M, Milligan P. Bone loss after hysterectomy with ovarian conservation. Obstet Gynecol. 1995;86:72–7.