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Factors associated with low bone mineral density among white women

ABSTRACT

OBJECTIVE: To analyze whether the factors causing low bone mineral density among elderly women are the same as those observed in other age groups.

METHODS: A cross-sectional study was carried out on the medical records of a random sample of 413 white women seen at an imaging diagnostics service in a city of Southern Brazil, in 2003. Femoral bone mineral densities with adjustment using T-scores were used. The following variables were investigated: age, body mass index, tobacco smoking, alcohol consumption, milk consumption, physical activity and hormone replacement therapy. Univariate and multivariate unconditional logistic regression were used.

RESULTS: In the sample, 52.5% were up to 59 years old and 47.5% were 60 or over. The mean bone mineral density was 0.867 g/cm^2 (SD=0.151) for the femoral neck. Significant age-adjusted values were obtained for physical activity (adjusted OR=0.47; 95% CI: 0.23;0.97), body mass index greater than or equal to 30.0 kg/m^2 (adjusted OR=0.10; 95% CI: 0.05;0.21), alcohol consumption (adjusted OR=7.90; 95% CI: 2.17;28.75), low milk consumption (adjusted OR=3.29; 95% CI: 1.91;5.68) and hormone replacement (adjusted OR = 0.44; 95% CI: 0.21;0.90). Among the elderly women, body mass, milk consumption and physical activity were independent protection factors.

CONCLUSIONS: Advanced age, body mass, physical activity, milk and alcohol consumption were important factors in bone mass regulation. The influence of behavioral factors was maintained among the women of advanced aged, thus reinforcing the role of preventive measures in medical practice and public health promotion policies aimed at healthy aging.

KEY WORDS: Osteoporosis, epidemiology. Osteoporosis, prevention & control. Bone density. Women. Risk factors. Cross-sectional studies.

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INTRODUCTION

In more developed regions, decreasing mortality and fertility and increasing life expectancy have resulted in aging of the population and increasing rates of chronic-degenerative diseases like osteoporosis.[9]

This bone metabolic disorder is characterized by loss of bone mass and disorganization of bone microarchitecture, which makes bones more fragile. It is an important cause of fractures, which create the need to use health services.[5] Bone mass decreases with advancing age and more frequently affects women.[22] For these reasons, interest in this problem has been growing. New products, medications and technologies are being developed and incorporated

into medical care. Studies on factors associated with the occurrence of osteoporosis are also necessary for guiding preventive measures.

There are more studies on the occurrence of osteoporotic fractures than on associations between osteoporosis and low bone mineral density (BMD). Over recent years, several factors related to the occurrence of low BMD have been identified. These include the physical factors of advanced age, female sex, history of osteoporosis in the family, irregular menstrual cycles, early menopause, no history of pregnancies and the use of certain medications (corticosteroids, anticonvulsants, aluminum hydroxide, diuretics and anti-inflammatories). They also include the behavioral factors of low calcium intake, high protein, sodium and coffee intake, smoking, alcohol use and sedentary lifestyle.[6]

In most of these studies, the association of the factor was measured in isolation, without controlling for other characteristics that might have the potential to intervene. Thus, there is little knowledge of the influence that certain characteristics may have on the effect of factors that are associated with occurrences of this event.

The objective of the present study was to analyze whether the factors leading to low BMD among elderly white women are the same as those observed in other age groups.

METHODS

A cross-sectional study was carried out on BMD measurements made on women living in Santos, State of São Paulo, in 2003, who were attended at a specialized imaging diagnostics service. All of these women had been referred there by doctors, who had various specialties but were mainly gynecologists, geriatricians, general clinicians, rheumatologists and orthopedists.

In 2000, Santos had more than 417,000 inhabitants, of whom 15.6% were aged 60 years or over.* At the time of the study, densitometry examinations** were not being performed by any public institution, and were only done by three private imaging diagnostic clinics.

To calculate the sample size, the α error was set at 0.05 and the ß error at 0.2 (test with a power of 0.8), and the prevalence of the study variables was assumed to be 0.50. Since approximately 14 examinations per day were being performed at the diagnostics unit, a sampling fraction of 25% was defined. The first sampling day was taken to be the first working day in January. The second day drawn was the fourth working day after this first day, and so on. The days sampled were drawn at four-day intervals from January to June 2003. The sample was thus made up of the records corresponding to 32 working days that were drawn.

The records relating to the days drawn were checked with regard to whether the data and numbers had been filled out legibly and completely. The printouts contained the report on the BMD examination and the characteristics of the individuals who were examined, distributed in 16 fields filled in by the patient before undergoing the examination. These data were transcribed to a printed record card containing the coded variables and were input to an electronic spreadsheet in the software application EpiInfo 6.04d. A sample of 45 records was drawn out to check on the consistency of the typing input.

From the draw, 459 lumbar column and femoral neck examinations were identified. Nine of these were excluded: six in which the data were incomplete, two on male patients and one on a patient with a high degree of osteoarthrosis, i.e. severely abnormal BMD. Among the remaining 450 records, 37 corresponding to women who considered their skin color to be non-white were also excluded. The final sample consisted of 413 densitometric examinations of the lumbar column and femoral neck on white women aged between 30 and 85 years.

BMD was measured by means of the dual-energy x-ray absorptiometry examination (DXA). The densitometric measurements on the lumbar column (L2-L4) and femoral neck were performed on the Lunar DPX-IQ apparatus. The coefficient of variation over the period of these examinations was less than 2%. The measurements were classified by means of T-scores corresponding to the mean BMD for normal young women minus the patient's BMD, divided by the standard deviation (SD) of the mean for normal young women. The bone tissue was deemed normal when the observed BMD was not lower than one SD below the mean for the reference young adults. Osteopenia corresponded to an observed BMD between 1 and 2.5 SD below the reference, and osteoporosis was deemed present when the observed BMD was lower than 2.5 SD below the reference. The women whose BMD was 1 SD or more below the reference were deemed to present low BMD.[22] The BMD measurements from the femoral neck were used, since this is considered to be the most appropriate predictor for the risk of hip fracture for white women. This is the most important type of fracture from a public health point of view.[15]

* Instituto Brasileiro de Geografia e Estatística. Censo demográfico 2000: características gerais da população: resultados da amostra [Accessed on Jun 23, 2005]. Available at: http://www.ibge.gov.br/home/estatistica/populacao/

** Instituto Brasileiro de Geografia e Estatística. Pesquisa Assistência Médico-Sanitária. Brasília: 2002 [acesso em 23 jun 2005]. Disponível em: http://< www.ibge.gov.br>

Table 1. Characteristics of the study population. Santos, Southeastern Brasil, 2003.

Characteristic	N	%
Age group		
< 49	58	14.0
50 – 59	159	38.6
60 – 69	115	27.8
> 69	81	19.6
Body mass index		
Underweight (< 18.5)	4	1.0
Normal (18.5-24.9)	170	41.2
Overweight (25.0-29.9)	161	38.9
Obesity I (30.0-34.9)	63	15.3
Obesity II (35.0-39.9)	14	3.4
Morbid obesity (> 40.0)	1	0.2
Smoking		
No	307	74.3
Yes	106	25.7
Alcohol use		
No	382	92.5
Yes	31	7.5
Physical activity		
No	318	77.0
Yes	95	23.0
Milk consumption		
None	44	10.7
Little	178	43.1
Regular	161	39.0
High	30	7.2
Hormone replacement therapy		
No	323	78.2
Yes	90	21.8
Postmenopausal status		
No	235	56.9
Yes	178	43.1
Anti-inflammatories		
No	328	79.4
Yes	85	20.6
Corticoids		
No	393	95.2
Yes	20	4.8
Hormones		
No	392	94.9
Yes	21	5.1
Hyperthyroidism		
No	407	98.5
Yes	6	1.5
Hypothyroidism		
No	389	94.2
Yes	24	5.8
Asthma		
No	397	96.1
Yes	16	3.9
Fractures		
No	382	92.5
One region	29	7.0
More than one region	2	0.5
Prosthesis use		
No	407	98.5
Yes	6	1.5
Total	413	100.0

The demographic, physical and behavioral characteristics were obtained from reviewing the medical records. The variables analyzed were the patient's age at the time of the examination; body mass index (BMI, in kg/m^2); smoking (women who smoked cigarettes, independent of the daily quantity and duration of the habit); alcohol use (those whose daily consumption was more than two spirit measures or two cans of beer); milk consumption in four groups: no consumption, low (< 50 ml/day), regular (between 50 ml and 300 ml/day) and high (more than 300 ml/day); menopause (self-reported by the women aged less than 65 years); and physical activity (performing physical exercise with a mean duration of at least 30 minutes/day).

In addition to these, other characteristics were observed: family history of osteoporosis; postmenopausal status; use of medications (anti-inflammatories, corticoids, hormones and hormone replacement therapy – HRT); presence of pathological conditions (hyperthyroidism, hypothyroidism, asthma and previous history of fractures); and prosthesis use.

The independent variables were selected on the basis of the Chi-square association test. Only the significant variables ($p<0.05$) were included in the multivariate analysis. The outcome was defined by low femoral BMD (osteopenia + osteoporosis), adjusted by the T-score. The effect of the independent variables was assessed by means of unconditional multiple logistic regression, with estimation of odds ratios (OR). This was analyzed for the whole sample and separately for the women aged up to 59 years and 60 years and over. For the modeling, the stepwise forward selection strategy was used. The significance level for inclusion of each variable in the logistic model was measured by means of the likelihood ratio test. To allow adjustment for the other variables, the criterion for inclusion in the final model of independent variables was a p-value$\leq$0.20. The Hosmer-Lemeshow test was used to assess the fit of the model. Independent variables excluded from the

final model were examined for possible interactions and collinearity.[12] The SPSS software was used to perform the statistical analyses.

The project was approved by the Research Ethics Committee of the Guilherme Álvaro State Hospital, which is accredited by the National Research Ethics Commission of the Brazilian National Health Board.

RESULTS

Among the records examined, most of the patients referred for densitometric evaluation had a supplementary health plan. The distribution of the sample characteristics is presented in Table 1. Out of the records, 52.5% were from women aged up to 59 years and 47.5% were 60 years or over. The mean age was 60.2 years (SD=9.9) and the mean BMD was 1.062 g/cm² (SD=0.176) for the lumbar column and 0.867 g/cm² (SD=0.151) for the femoral neck. Most of the women with BMI>29.9 kg/m² presented values indicative of type I obesity.[23]

T-score analysis for the femoral neck indicated that 44.8% of the patients were normal, 47% had osteopenia and 8.2% had osteoporosis. In relation to the lumbar column, 42.9% had normal bone, 37.8% had osteopenia and 19.4% had osteoporosis. Low BMD (osteopenia + osteoporosis) was presented by 42.2% of the women aged up to 59 years and 69.4% of the women aged 60 years and over (p<0.00).

To examine the factors related to declining BMD, the percentage distribution of bone condition (normal, osteopenic or osteoporotic) was analyzed according to the

Table 2. Percentage distribution of the variables analyzed, according to bone condition. Santos, Southeastern Brazil, 2003.

Variable		Femoral bone			
	N	Normal	Osteopenia	Osteoporosis	p*
Age group					
30 – 39	4	75.0	25.0	-	
40 – 49	54	59.2	35.2	5.6	
50 – 59	159	56.6	40.9	2.5	
60 – 69	115	37.4	55.6	7.0	
70 – 79	70	20.0	58.6	21.4	
80 and over	11	27.2	36.4	36.4	<0.00
Body mass index					
≤ 24,9	174	29.9	56.3	13.8	
25,0 – 29,9	161	50.9	44.1	5.0	
≥ 30,0	78	65.3	32.1	2.6	<0.00
Smoking					
No	307	49.5	42.7	7.8	
Yes	106	31.1	59.5	9.4	<0.00
Alcohol use					
No	382	47.4	44.7	7.9	
Yes	31	12.9	74.2	12.9	<0.00
Physical activity					
No	318	35.2	54.1	10.7	
Yes	95	76.8	23.2	-	<0.00
Milk consumption					
None	30	70.0	30.0	-	
Little	161	62.7	34.2	3.1	
Regular	178	32.0	57.9	10.1	
High	44	13.6	61.4	25.0	<0.00
Hormone replacement					
No	323	35.3	54.5	10.2	
Yes	90	78.9	20.0	1.1	<0.00

* χ^2 Pearson

T-scores found from evaluating the femoral bone site. The independent variables are presented in Table 2.

To measure the effect of the factors, the association of each factor with the femoral BMD was tested in the presence of the other characteristics, by means of multivariate analysis. Table 3 presents the results from this analysis. Significant adjusted OR values (with 95% CI) were obtained for physical activity, overweight (24.9<BMI<30.0), type I obesity (BMI≥30.0), alcohol use, little and no milk consumption, HRT and advanced age.

Although smoking was a statistically significant variable in univariate analysis, it lost its statistical significance (p>0.20) in the multivariate model. However, there were significant associations between the habit of smoking and the other exposure factors. The highest proportions of smokers were seen among the women who consumed less than 50 ml of milk per day, were younger, consumed alcohol regularly, did not practice physical activity, were not using HRT and presented BMI≤24.9 kg/m^2. Nonetheless, regarding these associations, none of the interactions between smoking and the other independent variables presented a statistically significant effect on the outcome.

Table 4 presents the multivariate analysis according to age groups (up to 59 years and 60 years and over). Among the women aged less than 60 years, milk consumption, alcohol use, BMI and HRT presented significant effects on low BMD when controlled for physical activity. The exposure of the sample to alcohol use and HRT was low from the age of 60 years onwards. BMI, milk consumption and physical activity maintained the significant effects (p≤0.05) that were presented on the whole sample. Smoking habit was not kept in the multivariate model in either of the groups because it lost its statistical significance (p>0.20).

DISCUSSION

Greater chance of the occurrence of low BMD was associated with advanced age, little or no milk consumption, alcohol consumption and tobacco use. On the other hand, physical activity, overweight or type I

Table 3. Multivariate analysis on the variables associated with low bone mineral density among white women, according to adjusted and unadjusted odds ratios. Santos, Southeastern Brazil, 2003.

Variable	N	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Age					
< 60	217	1.00		1.00	
≥ 60	196	3.08 (2.05;4.62)	<0.00	4.84 (2.63;8.92)	<0.00
Milk consumption					
High/regular	191	1.00		1.00	
Little	178	3.75 (2.44;5.78)	<0.00	3.29 (1.91;5.68)	<0.00
None	44	11.19 (4.50;27.80)	<0.00	12.22 (4.01;37.19)	<0.00
Alcohol use					
No	382	1.00		1.00	
Yes	31	6.07 (2.08;17.68)	<0.00	7.90 (2.17;28.75)	<0.00
Smoking					
No	307	1.00			
Yes	106	2.17 (1.36;3.46)	<0.00	*	
Body mass index					
Underweight/normal	174	1.00		1.00	
Overweight	161	0.41 (0.26;0.64)	<0.00	0.22 (0.12;0.41)	<0.00
Obesity	78	0.23 (0.13;0.40)	<0.00	0.10 (0.05;0.21)	<0.00
Hormone replacement therapy					
No	323	1.00		1.00	
Yes	90	0.15 (0.08;0.25)	<0.00	0.44 (0.21;0.90)	0.03
Physical activity					
No	318	1.00		1.00	
Yes	95	0.16 (0.10;0.28)	<0.00	0.47 (0.23;0.97)	0.04

* Not included in the adjusted model because statistical significance was lost (p>0.20)

Table 4. Multivariate analysis on factors associated with low bone mineral density among white women, according to age group. Santos, Southeastern Brazil, 2003.

Variable	Age group					
	< 60 years			≥ 60 years		
	N	Adjusted OR (95% CI)	p	N	Adjusted OR (95% CI)	p
Milk consumption						
High/regular	100	1.00		91	1.00	
Little	89	2.85 (1.21;6.67)	<0.00	89	3.72 (1.79;7.69)	<0.00
None	28	14.24 (3.23;62.66)	<0.00	16	16.30 (1.94;137.24)	0.01
Alcohol use						
No	188	1.00		194	*	
Yes	29	6.98 (1.91;25.59)	<0.00	2	*	
Smoking						
No	130	**		177	**	
Yes	87	**		19	**	
Body mass index						
Underweight/normal	107	1.00		67	1.00	
Overweight	75	0.30 (0.14;0.66)	<0.00	86	0.19 (0.08;0.48)	<0.00
Obesity	35	0.05 (0.01;0.21)	<0.00	43	0.12 (0.04;0.33)	<0.00
Hormone replacement therapy						
No	133	1.00		190	*	
Yes	84	0.40 (0.18;0.89)	0.01	6	*	
Physical activity						
No		1.00		184	1.00	
Yes		0.53 (0.22;1.28)	0.16	12	0.25 (0.06;1.00)	0.05

* Not included in the adjusted model – analysis category with N<10
** Not included in the adjusted model because statistical significance was lost (p>0.20)

obesity and HRT showed a protective effect.

Other studies have confirmed associations between low BMD and little milk consumption[10] and between low BMD and alcohol consumption habits.[6,13,18] Physical activity[14] and HRT[5] have been identified in the scientific literature as protective effects.

The effect on BMD in the presence of more than one independent variable has been evaluated by some researchers.[1,3,7,17,20] The discussions on this information help in understanding the relationships between the exposure factors and the relative importance of each factor in producing the outcome. Among the characteristics analyzed, advanced age,[1,3,7] low BMI[1,3,7] and postmenopausal status[7,20] have been highlighted as risk factors in the presence of other variables. High BMI[4,8,17,20] and HRT[17,20] have been highlighted as associated protective factors, independent of the presence of other variables.

For other factors, including smoking, calcium intake, alcohol consumption and physical activity, the effect on the outcome has not been confirmed in certain studies through multivariate analysis. The reasons for these controversial results may be connected with the specific characteristics and limitations of each investigation. The most common reasons relate to the type of sample (only women aged 46 to 54 years in one study[20]) and its size (only 90 women in a study in Iran[1]). Moreover, these differences may be related to low frequency of occurrence of certain exposure factors, thus diminishing the statistical power of the test for detecting associations.

The correlation between smoking and reduced BMD results from the increase in osteoclastic activity produced by cigarettes.[19,21] Tanaka* found that smoking was a risk factor, independent of when in life the individual had had this habit, among a sample of men aged 50 years and over.

* Tanaka T. Fatores de risco para osteoporose em fêmur proximal em homens com idade igual ou maior de 50 anos [dissertação de mestrado]. São Paulo: Faculdade de Saúde Publica da USP, 2000.

In the multivariate analysis carried out in the present study, smoking did not present statistical significance ($p>0.20$) for it to remain in the adjusted model. Although the smoking habit showed associations with some independent variables, no interaction that would result in an important effect on the outcome was observed in the multivariate analysis.

In the present study, physical activity and overweight or type I obesity were protective factors for BMD among the women aged 59 years and over. These findings reinforce the hypothesis that the bone tissue needs to be subjected to tension with a certain regularity for it to be maintained, and that a sedentary lifestyle is related to decreased BMD and worsening of bone quality, with the consequent appearance of osteopenia and osteoporosis. On the other hand, the body's weight interacts with sexual hormones to maintain bone mass, thereby protecting against the adverse effects of estrogen deficiency on bone composition. Milk consumption of less than 50 ml per day remained significantly associated with low BMD, thus indicating that lack of calcium may have an important effect on women of advanced age.

In a longitudinal study carried out among elderly people in the Netherlands, Burger el al[4] found an association with body mass and smoking. Unlike among men, calcium intake among women did not show any association with the outcome. In another study with the same design, involving 800 elderly people (67 to 90 years old), Hannan et al[11] found that weight loss and alcohol use were risk factors for bone loss, while HRT and weight gain were protective factors. However, BMD was not affected by caffeine, physical activity, calcium intake and serum levels of vitamin D, thus indicating that other risk factors might be more important for this age group.[11] On the other hand, modest alcohol consumption among elderly women and higher levels of physical activity among elderly men signified a protective effect in a longitudinal study in the United Kingdom.[8]

Some of the results presented in this study must be interpreted with care. The information on the use of HRT did not take into account the length of exposure to this therapy, or the age of menarche. Serum calcium assaying and renal function evaluation would be necessary in order to safely rule out diseases affecting bone metabolism. Milk derivatives and other sources of calcium were not taken into consideration, nor were medications that might interfere with calcium absorption (certain antibiotics and anti-inflammatories, and medications containing corticosteroids for asthma). Caffeine consumption was not evaluated: this substance may interfere with calcium absorption in the intestine and calcium excretion in urine.[2] Some women who start on HRT or other antireabsorptive therapy may have to discontinue because of side effects, and this situation was not adequately documented in the questionnaires. The data on alcohol use, smoking and physical activity were distributed into only two categories, which left room for residual confounding in the multivariate analysis. The magnitude of the effect must be viewed with caution, given that for high-frequency outcomes, the OR may represent an overestimate.[16]

Another point to be considered is the diversity of methods and techniques used in epidemiological studies on BMD. The present study only made use of data from dual-energy x-ray absorptiometry examinations. The data on physical and behavioral characteristics were considered to be historical data and were gathered at the time of the densitometric examination. It was accepted that these were exposure factors that characterized the recent past of the sample examined, and therefore that they did not contribute towards the outcome under investigation.

Despite these limitations, it can be concluded that advanced age, body mass, physical activity and milk and alcohol consumption are important in regulating BMD. Among elderly women, associations with body mass, physical activity and milk consumption were confirmed, thus indicating that these also have an effect at this important stage of life. The findings provide reinforcement for the role that preventive measures have in medical practice and for the relevance of defending health policies that promote healthy aging.

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