The burden of osteoporosis in Brazil: regional data from fractures in adult men and women – The Brazilian Osteoporosis Study (BRAZOS)

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ABSTRACT

Objectives: The BRAZOS (The Brazilian Osteoporosis Study) study is the first epidemiological and population-based study carried out in a representative sample of Brazilian men and women, 40 years or older, with the objective of identifying the prevalence and main clinical risk factors (CRF) associated with low-impact fractures. This report shows the main results according to each region of the country. **Patients and Methods:** A total of 2,420 subjects (70% women) from 150 different cities in five geographic regions in Brazil, and from all different socio-economical classes were included in this study. Anthropometrical data, as well life style, previous fractures, nutritional status, physical activity, falls, and quality of life were evaluated by a quantitative individual survey. Low-impact fracture was defined as that resulting from a fall no greater than standing height of an individual. A $P < 0.05$ was considered significant. **Results:** Statistically significant differences in the prevalence of fractures among the five Brazilian regions according to gender or social class were not observed. However, in women, a higher incidence of fractures was observed in metropolitan areas than in rural areas, and a tendency for a higher frequency of fractures was observed in men from Northeastern states. Statistically significant differences among men from metropolitan areas or rural areas were not observed. **Conclusions:** Significant differences in the prevalence of low-impact fractures among the five different regions of Brazil were not observed, as well as its frequency or relevance of risk factors.

Keywords: Brazilian population, clinical risk factors, epidemiology, fracture, regional prevalence, osteoporosis.

INTRODUCTION

Osteoporotic fractures have high prevalence, representing an important public health problem in Brazil,[1] especially hip fractures, whose incidence increases with age,[2-4] being associated with deterioration of the quality of life and higher mortality.[5-7]

Early identification of clinical risk factors (CRF) associated with low bone density[8-10] and fractures[11-13] is fundamental for the management of patients at risk, especially the introduction of effective preventive, diagnostic, and therapeutic strategies.[14] Besides, they are low cost and easy to execute and implement, especially in developing countries.

As a rule, tools to detect individuals, especially postmenopausal white females, with low bone density in the spine and hips or spinal and non-spinal fractures, have a sensitivity and specificity around 75 to 95% and 35 to 60%, respectively.[8-13] However, males, postmenopausal females,

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and races other than Caucasian, have not been evaluated by the majority of the studies.

Very few consistent data on the prevalence and relevance of risk factors for higher risk of fracture secondary to osteoporosis, as well as the ingestion of nutrients related with bone health, are available in Latin America and Brazil. The objective of the present study was to identify those aspects in a representative sample of Brazilian females and males older than 40 years of age. Besides, this report emphasizes the regional differences in the prevalence of low-impact fractures in each of the five Brazilian regions.

PATIENTS AND METHODS

From March to April 2006, 2,420 individuals (725 males and 1695 females) older than 40 years, representative of all social-economic classes, were evaluated in a quantitative transversal investigation. Individuals with different schooling status and professions were also included in the study population. Interviews were done in person, at the house of the individual, carried out by a team trained for this end. The study evaluated 150 counties throughout the country, including towns with up to 20 thousand inhabitants, from 20 to 100 thousand, and above 100 thousand inhabitants. Family income was calculated in terms of minimum wage.

The size of the study population was calculated by a probabilistic sample representative of the Brazilian population, urban and rural, based on data of the IBGE (from Portuguese for Brazilian Institute of Geography and Statistics)[15] 2000 Census and 2003 PNAD (from Portuguese for National Home Sample Investigation).[16] selected in three stages, controlling for gender, age group, and profession. Homes were selected at random. Interviews were conducted in diurnal and nocturnal periods every day of the week, including Saturdays and Sundays, to maximize the presence of the target-population at home. The questionnaire was applied in approximately 50 minutes for each individual. Some distortions like gender and age were premeditated, aimed at including predominantly females and individuals older than 65 years, the main populations affected by osteoporosis, as well as obtaining more data with lower sampling error. The distribution of social classes, schooling, marital status, race, and religion mimicked the official data of the Brazilian government. Later, the data was weighed to recompose the distribution and proportionality of the Brazilian population.[15,16] The sampling error of the study showed 95% confidence interval of 2.2%, 90% power, and alpha error of 5%.

Exclusion criteria were as follows: cognitive deficiency, such as neurological sequelae or senile dementia, that made it impossible for the individual to provide reliable and consistent answers, and more than two individuals older than 40 years were present in the same house.

A structured questionnaire, developed especially for this study and based on a review of the literature,[1-13] was the tool used to collect the data. Main aspects evaluated were age; demographic, anthropometric, and socio-economic data; general knowledge about osteoporosis; history of falls, and their circumstances, in the past year; personal and pathologic antecedents; history of fractures, and gynecological and reproductive history; family history of hip fractures after 50 years of age in first degree relatives; quality of life (SF-8);[17] and medications and associated diseases that were classified according to the 10th revision of the ICD (International Classification of Diseases). The nomenclature proposed by Burger was used to define early menopause.[18] Current and past lifestyle and current smoking (packs/year), alcohol ingestion,[19] and physical activities[20] were also evaluated in all individuals. Current sun exposure and in the last 12 months was defined as adequate if longer than 15 minutes without sunscreen, and more than five times a week.

Eating habits were investigated by 24-hour recollection, in which the individual was interviewed at home and gave a detailed report on the foods and drinks ingested the day before the interview.[21]

Low-impact fracture was defined as secondary to a fall no greater than standing height after the age of 50 years in axial (ribs and thoracic and/or lumbar vertebrae) and appendicular (forearm, humerus, and hip) sites. Traumatic fractures in non-characteristic sites of osteoporosis, such as face bones, skull, tibia or fibula, and femoral diaphysis, were excluded from the analysis. Chronic falls were defined as more than two falls n the last 12 months.[22] All questionnaires were reviewed by an independent supervisor and submitted to a process of critique and consistency. Inconsistent questionnaires were verified *in loco* or *post hoc* by telephone contact.

Individuals were informed about the study and those who agreed to participate signed an informed consent. The study protocol was analyzed and approved by the Research Ethics Committee of UNIFESP/EPM.

Anthropometric data was assessed with all individuals without shoes and wearing light clothes. The weight (kg) was determined by a portable anthropometric office scale (Filizola®). The height was measured using a standard tape measure. The body mass index (BMI) was calculated in kg/m^2.

Statistical analysis

Descriptive analysis, with mean and standard deviation, was used to assess the study variables. The Student *t* test was used to compare continuous parameters, and Simple Analysis of Variance (One-way ANOVA) followed by Tukey *post-hoc* test for multiple comparisons, was used for the comparison among three or more groups.

The correlation between continuous and categorical variables was analyzed by the Chi-square test. Division in categories was based on tercile distribution of the frequency of the sample for all continuous variables. Low-impact fracture was considered the dependent variable and all others were considered independent variables when elaborating the statistical model for logistic regression analysis.

The software SPSS/PC for Windows version 12 and SAS (Statistical Analysis System) for Windows version 8.02 were used for processing, analysis, and elaboration of all models. A level of significance of 5% ($P < 0.05$) was adopted in all statistical tests.

RESULTS

Tables 1 and 2 show the anthropometric and demographic data of the study population, older than 40 years of age, according to gender and the presence of low-impact fractures, respectively. Low impact fractures were present in 15.1% of the females and 12.8% of males. As a rule, women with fractures were significantly older and men with fractures weighed less. The mean age of menarche, with shorter menacme and higher number of children, was significantly higher in women with fractures.

According to the BMI, the majority of the study population above 40 years of age was classified as overweight (60% of males and 59% of females), especially in social classes A and B (Table 3). Regional differences in the prevalence of overweight and obesity were not observed in both genders. Age, weight, height, BMI, and socio-economic class showed equal and non-statistically significant distribution among the five Brazilian regions.

The most frequent disorders mentioned included hypertension (29%), back pain (18%), rheumatic diseases (14%), dyspepsia (13%), depression (11%), diabetes mellitus (8%), dyslipidemia (6%), and osteoporosis (6%). Approximately 33% of the study population did not report any comorbidity. As a rule, all diseases were more common in females, except for dyspepsia and diabetes mellitus, which were similar in both genders.

The mean age of menarche and menopause was 13 ± 1.8 and 47 ± 5.1 years, respectively. Approximately 35% of females were in the menopause. Prolonged corticotherapy was observed in 4% of the sample. Almost 25% of the study population used some type of medication that knowingly affects mineral and calcium metabolism, especially hormone replacement therapy (15%) and biphosphonates (4%). Statistically significant differences among social classes, age group, and Brazilian region were not observed.

In the past 12 months, only 24% of the study population exercised regularly, especially individuals of social classes A/B and in Southern and Southeastern Brazil (30%) ($P < 0.05$). Current smoking was referred by approximately 25% of the cohort, especially men (28% *vs.* 21%). Almost half of the male population (47%) referred drinking regularly in the past year, especially in A/B classes. The majority of the women (53%) did not ingest alcoholic beverages regularly. The last two life habits did not show statistically significant differences among Brazilian regions or socio-economic classes.

Men with fractures smoked a mean of 18.4 ± 0.78 packs/year, and men without fracture smoked a mean of 6.19 ± 2.26

Table 1
Anthropometric characteristics of the Brazilian population older than 40 years of age according to the presence of low-impact fractures

		Males		Females		
	Total	Without fracture	With fracture	Without fracture	With fracture	P*
Age (years)	59.6 ± 13.5	54.6 ± 0.35	55.4 ± 2.3	55.3 ± 0.33	63.6 ± 1.55*	0.007
Weight (kg)	67.2 ± 14.6	74.8 ± 0.44	70.4 ± 1.68	65.9±0.46	65.5 ± 1.9	< 0.001
Height (m)	1.59 ± 0.09	1.68 ± 0.002	1.68 ± 0.009	1.57 ± 0.002	1.56 ± 0.01	< 0.001
BMI (kg/ m^2)	26.4 ± 5.05	26.3 ± 0.14	25.1 ± 0.66	26.6 ± 0.15	27.1 ± 0.84	0.951

BMI: body mass index; *Student *t* test.

Table 2
Demographic data of the adult Brazilian population according to gender

	Total N (%)	Men N (%)	Women N (%)
Marital status			
Married	1.331 (55%)	383 (52.8)	948 (55.9)
Widow/er	629 (26)	182 (25)	447 (26.4)
Single	242 (10)	81 (11.2)	161 (9.5)
Divorced	97 (4)	36 (5)	61 (3.6)
Separated	97 (4)	36 (5)	61 (3.6)
Undefined	24 (1)	7 (1)	17 (1)
Race			
Caucasian	1.210 (50)	363 (50.1)	847 (50)
Mulatto	678 (28)	203 (28)	475 (28)
African-descent	315 (13)	95 (13)	220 (13)
Native Brazilian	169 (7)	50 (6.9)	119 (7)
Asian	24 (1)	7 (1)	17 (1)
Other	24 (1)	7 (1)	17 (1)
Social class			
AB	315 (13)	87 (12)	228 (13.4)
C	774 (32)	239 (33)	535 (31.6)
DE	1.331 (55)	399 (55)	932 (55)

packs/year ($P < 0.001$). Statistically significant differences in smoking between women with and without fracture (7.86 ± 0.42 *versus* 7.14 ± 1.62 packs/year, respectively) were not observed.

Regular physical activity was significantly lower in men and women with fractures than in those without fracture (16.9 *versus* 44.8% and 8.1 *versus* 32.7%, respectively). A family history of hip fractures after 50 years of age was more common among women with fractures (14.5 *versus* 7.1%, $P = 0.037$), but a significant correlation was not observed in males. Prior use of birth control pills was higher in women without fractures (50.1 *versus* 33.9%, $P = 0.009$). Oophorectomy and early menopause were more common in women with fractures (20.4 *versus* 8.2%, respectively) ($P = 0.02$). Current use of corticosteroids, daily sun exposure, and drinking did not show statistically significant differences between both genders regarding the presence of low-impact fractures. Hormone replacement therapy, hysterectomy, and the presence of amenorrhea did not differ between women with and without fractures.

The most common sites of low-impact fractures were the distal forearm (30%), hip (12%), humerus (8%), ribs (6%), and spine (4%). Statistically significant differences in the presence of low-impact fractures among Brazilian regions, according to gender or social class, were not observed. However, among females, a higher incidence of fractures was observed in metropolitan regions than in rural areas, and men in Northeastern Brazil showed a tendency for higher incidence of fractures (Table 4). Statistically significant differences in the incidence of fractures were not observed between men from state capitals and smaller towns. Note that 70% of the women and 85% of the men had already had a low-impact fracture and did not know the diagnosis of the disease that caused bone fragility, osteoporosis.

After adjusting for potential confounding variables, clinical risk factors significantly associated with low-impact fractures in women can be seen in Table 5. The model showed excellent adjustment by the Hosmer-Lemeshow method ($P = 0.513$). In men, after adjustment for potential confounding variables, clinical risk factors with significant association are listed in Table 6. The model showed excellent adjustment ($P = 0.93$). Socio-demographic and anthropometric parameters, as well as drinking, did not reach statistical significance.

Table 3
Nutritional status of adult Brazilian men and women according to the body mass index (BMC) and World Health Organization (WHO, 1998) classification

BMI (kg/m²)	Below 18.5 (under weight)	18.5 to 24.9 (normal)	25 to 29.9 (overweight)	30 to 34.9 (grade I obesity)	35 to 39.9 (grade II obesity)	Over 40 (grade III obesity)
Gender						
Male	3%	37%	43%*	13%	3%	1%
Female	3%	39%	36%*	15%	5%	3%
Social class						
AB	2%	34%	44%*	16%	3%	2%
C	2%	39%	37%*	15%	6%	2%
DE	3%	40%	39%*	13%	3%	2%

*P< 0.05; BMI: body mass index.

DISCUSSION

The main clinical risk factors for fractures secondary to osteoporosis, in men and women, in Brazil were not well known, being usually extrapolated from international studies. The BRAZOS study (Brazilian Osteoporosis Study) is the first population-based epidemiological study designed to identify the main clinical risk factors associated with low-impact fractures in a representative sample of the adult Brazilian population.

The results of the present study showed that a sedentary life style, smoking, poor quality of life, and diabetes mellitus are the most relevant CRF for low-impact fractures in Brazilian men. In women, the most important CRF were advanced age, early menopause, sedentary life style, poor quality of life, higher phosphorus ingestion, diabetes mellitus, falls, chronic use of benzodiazepines, and family history of hip fractures after 50 years of age in first-degree relatives. Those risk factors reflect the involvement of several aspects in the determination of a higher risk of fracture, such as heredity (family history of fractures), life style (physical activity, smoking, nutrition) quality of life, falls, and aging with deterioration of bone quality.

Although CRF in high-risk populations for osteoporosis and fractures have been well established, especially in international studies,[5,8-13] its prevalence in the general population has not been clearly analyzed. The BRAZOS study investigated risky behavior for fractures in individuals with and without associated diseases and with and without the concomitant presence of medications, characterizing a real population – "real life" – and not only the population at higher risk for osteoporosis and fracture.

In Brazil, some retrospective or transversal studies, with a cohort representative of the Brazilian population, found several risk factors associated with low bone density, such as lack of hormone replacement therapy after menopause, low sun exposure, drinking, low calcium intake, sedentary life style, family history of osteoporosis, smoking, underweight and short stature, advanced age, low schooling, late menarche, early menopause, and lower body mass index.[6,23-25] The present study did not evaluate risk factors associated with bone density; however, our results allow the conclusion that those risk factors are very similar to those related with low-impact fractures. Pinheiro *et al*.[26] showed that the main CRF associated with osteoporosis-induced fractures in any skeletal site, in 275 postmenopausal women, after statistical adjustments, included family history of hip fracture, advanced age, and underweight. They also showed that the association of CRF with bone mass

Table 4
Prevalence of low-impact fractures in men and women in different Brazilian regions

	Homens (%)	Mulheres (%)
North	13.1	12.2
Northeast	21.8**	15.3
Midwest	13.8	10.5
Southeast	13.9	16.2
South	10.6	13.8
Metropolitan	13.9	17.0*
Rural (conutry side)	11.6	12.8

*P < 0.05; **P = 0.06.

Table 5
Final logistic regression model for females older than 40 years according to the presence of low-impact fractures

	OR	95% CI	P
Advanced age	1.6	1.06-2.4	0.037
Family history of hip fractures	1.7	1.1-2.8	0.03
Early menopause	1.7	1.02-2.9	0.04
Sedentary life style	1.6	1.02-2.7	0.05
Poor quality of life (SF-8) (physical component)	1.9	1.2-2.9	0.006
Higher phosphorus intake (adjusted for calories)	1.9	1.2-2.9	0.003
Chronic use of benzodiazepines	2.0	1.2-3.6	0.01
Falls in the past year	2.4	1.2-5.0	0.017
Diabetes mellitus	2.8	1.01-8.2	0.05

Table 6
Final logistic regression model for males older than 40 years according to the presence of low-impact fractures

	OR	IC 95%	P
Poor quality of life (SF-8) (physical component)	3.2	1.7-6.1	< 0.001
Smoking	3.5	1.28-9.77	0.014
Diabetes mellitus	4.2	1.27-13.7	0.018
Sedentary life style	6.3	1.1-36.1	0.039

measurements could improve the discrimination of patients at higher risk for osteoporotic fractures.

In a recent study, Siqueira *et al*.[27] evaluated 3,214 individuals in Pelotas, RS, Brazil, and observed that the risk factors with stronger association with low-impact fractures included a history of osteoporosis, falls in the last year, male gender, Caucasians or mulattoes, and low schooling. The prevalence of fractures throughout life was almost twice as higher (28.3%) than that observed in the BRAZOS study (14.4%). The prevalence of fractures throughout life was 37.5% in men, mainly secondary to sports and outdoor activities ($P < 0.001$). Interestingly, the risk of fractures in the past year was 50% higher in men than in women ($P = 0.09$). In the present study, the prevalence of fractures due to bone fragility was significantly higher in women (15.1%) than in men (12.8%), which is similar to other studies.[2-8] The study in Southern Brazil included younger individuals (20 years of age and older) than our study, as well as trauma-related and non-traumatic fractures. Those aspects could have contributed for the higher prevalence of fractures in males and younger individuals. Similarly, Caucasians, mulattoes, and individuals of African descent reported a higher prevalence of fractures (28.8%, 31.2%, and 22.3%, respectively, $P < 0.03$). In our national sampling, statistically significant differences regarding race were not observed. This could be explained by the elevated degree of racial mixing in the country. Rio Grande do Sul might have a higher proportion of Caucasians and other less mixed races due to peculiarities and differences in the type of colonization (German and Italian).

Unlike other studies,[12,13] the present did not demonstrate any association among anthropometric data and low-impact fractures in both genders, although we were careful to accurately measure the height and weight of all the individuals evaluated. Some considerations should be done to explain this finding, especially the inclusion criteria – an elevated proportion of younger individuals (34% in the 40 to 50 years age group), as well as the elevated number of overweight and obesity, characterizing a general population and not one at high risk for osteoporosis and fractures. Robbins *et al*.[28] evaluated other large epidemiological studies (WHI – Women's Health Initiative, n = 11,390 women; CHS – Cardiovascular Health Study, n = 1,578 men and women; and EPIDOS – *Epidemiologie de l'Ostoporose*, n = 7,598 women) and they were also unable to demonstrate the predictive value of the BMI on bone density, although they have not investigated the influence on fracture rate.

Our findings indicate that diabetes mellitus (DM) is related with a higher risk of low-impact fractures in men and women. Studies on the skeletal involvement in diabetes are controversial, since this disorder can affect bone health by several pathophysiological mechanisms, some of them contradictory, such as changes in the levels of insulin and IGF-1, accumulation of glycation end products, decreased renal function, obesity, hypercalciuria associated with glucosuria, decreased intestinal absorption of calcium, inappropriate homeostatic response in PTH secretion and complex changes in vitamin D regulation, angiopathy, inflammation, and neuropathy. As a rule, DM type I is associated with a reduction in bone density and higher risk of osteoporotic fractures, and DM type II is associated with greater bone mass, but with a higher risk of fractures, especially non-spinal fractures, due to bone fragility. In both cases, it is important to consider the influence of gender, age, weight, mass of adipose tissue, treatment, and duration of the disease. Thus, aspects related to bone quality and remodeling, as well as extra-skeletal factors related to falls and neuropathic problems secondary to microangiopathic complications, may be involved. Recently, some authors have demonstrated that chronic hypoestrogenism favors a higher expression of PPARγ in postmenopausal women and, consequently, greater differentiation of totipotent mesenchymal cells in adipocytes instead of osteoblasts, affecting bone formation. Thus, they believe that DM could represent the spectrum of another bone disease – "diabetic osteodystrophy" – and not osteoporosis.[29,30]

A higher number of falls showed significant direct association with a higher risk of low-impact fractures, even after adjusting for dizziness, postural hypotension, and the use of anti-vertigo drugs, anticonvulsants, antidepressants, and benzodiazepines.[31] In the FRISK study, the number of falls in the past year had an important role on the final score of greater risk of fractures[13]. A recent metanalysis to evaluate the risk of fractures in individuals using psychotropic drugs showed that benzodiazepines, antidepressants, non-barbituric anticonvulsants, barbituric anticonvulsants, anti-psychotics, hypnotics, and opioids have a higher risk of fractures.[32]

Brazilian studies[33,34] with men older than 50 years indicated a positive and significant correlation between bone density and current and past physical activities, even after adjusting for age and BMI. A prospective cohort of 5,995 elderly men found a high prevalence of smoking (59%) and drinking (47%), and mean BMI similar to that of the present study (26.9 kg/m^2). It also reported a higher incidence of low-impact fractures (17%) than that of the BRAZOS study (12.8%).[35] Sedentary life style and current smoking showed a significant correlation with a higher risk of low-impact fractures in men and women in the BRAZOS study, indicating that the incentive for regular

exercises and to quit smoking could be a simple, relevant, and low-cost measure for the prevention of fractures in our population.

The BRAZOS study showed a strong association between poor quality of life and the presence of low-impact fractures, both in men and women older than 40 years of age, emphasizing that patients with osteoporosis and fractures have a higher incidence of chronic pain, decreased physical capacity, reduction in social activities, decreased perception of well-being, and depressed mood than individuals without fractures. On the other hand, significant associations with mental aspects, similar to what was seen with other questionnaires,[36-38] were not observed.

The present study had some limitations, such the absence of X-rays of the thoracic and lumbar spine to identify pauci-symptomatic fractures. The prevalence data could be overestimated, since they were only referred by the individuals, without complementary exams – clinical (determination of the blood pressure) and laboratorial (fasting blood glucose and serum cholesterol levels, for instance) – to confirm those reports. However, although laboratorial exams were not carried out, it is important to emphasize that a detailed clinical evaluation of secondary causes of osteoporosis was undertaken. Thus, we can guarantee that associated diseases, except for diabetes mellitus, were not related with a higher risk of low-impact fractures after statistical adjustments.

The prevalence of osteoporosis should be higher than that observed in the BRAZOS study (6%), since bone densitometry was not done. Besides, since a high rate of low-impact fractures was observed in the present study and by using the WHO[39] definition of osteoporosis, in which the diagnosis of established osteoporosis can be made in the presence of fractures resulting from minimal trauma, the prevalence of osteoporosis should have been at least 12.8%, in men, and 15.1%, in women.

The objective of this study was to identify adult Brazilian individuals at higher risk of fractures secondary to bone fragility in whom the institution of preventive and health promotion measures should be a priority. Besides, using a simple and fast clinical evaluation, clinical risk factors more strongly associated with fractures in this study – age, family history of fractures, physical activity, smoking, falls, quality of life, nutritional status, presence of diabetes mellitus, and chronic use of benzodiazepines – could help select individuals in whom bone densitometry should be made, separating individuals at higher risk from those at lower risk of fractures, and in those who had already done a bone densitometry, the treatment decision could have better fundament, regardless of the region of the country.

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