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An Updated Hip Fracture Incidence Rate for Brazil: The Brazilian Validation Osteoporosis Study (BRAVOS)

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***Sergio Ragi Eis is deceased. This paper is dedicated to his memory**

Abstract

Summary: Hip fracture incidence rates in three representative geographic areas in Brazil over a period of 2 years (2010-2012) were assessed by the first time. Estimated incidence rates varied regionally, and markedly differed from those previously reported. Thus, national guidelines as well as FRAX Brazil should be revised in light of this new data.

Purpose: To determine the annual incidence of hip fractures in individuals aged 50 years and over, living in 3 cities located in different regions of the country. To investigate the age, gender and regional differences in fracture rates. Based on the obtained data, to estimate the national incidence of hip fractures resulting from osteoporosis, in order to improve prevention strategies.

Methods: Retrospective, observational study including all patients aged ≥ 50 years admitted in hospitals because of a hip fracture in three cities (Belem, Joinville and Vitoria) from representative geographic areas in Brazil from 2010 to 2012. Data were obtained from medical records in those cities. We analyzed incidence rates (crude and age- and gender-standardized rates) for hip fractures.

Results: There were 1,025 (310 in men and 715 in women) hip fractures in the over-50-year of the merged population from the three cities. The crude incidence rate for hip fracture was 103.3/100,000 (95% confidence interval [CI = 97.0; 109.7), in men 77.4/100,000 (95% CI= 68.8; 86.0) and in women 125.2/ 100,000 (95% CI=116.0; 134.4). Incidence standardized for age and gender was 105.9 cases per 100,000 persons per year (95% CI= 99.4; 112.4); 78.5 cases per 100,000 (95% CI= 69.8; 87.3) in men and 130.6 cases 100,000 women (95% CI= 121.0; 140.2) per year. Belem, located in equatorial region (latitude 1°27'S) had significantly lower crude and age-adjusted incidence than Joinville (latitude 26°18'S) and Vitoria (latitude 20°19'S), which were no different from each other. The incidence of fractures increased exponentially with age, and women had about twice the risk of fractures than men.

Conclusions: Hip fracture mainly affects elderly women and presents great variability in incidence between the different regions in Brazil. The incidence of hip fractures in Brazil differed markedly from that reported previously, so that national guidelines and FRAX model for Brazil should be revised.

Keywords: Hip Fractures; Epidemiology; Osteoporosis; Brazil; Population studies

1. Introduction

Osteoporosis, a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with a resulting increase in bone fragility and low trauma fractures [1] , is a considerable public health issue worldwide. In that scenario, hip fractures represent the most serious complication of osteoporosis and are associated with substantial morbidity, mortality, and health care cost [2].

The incidence of hip fracture rises markedly with age and, in most countries, the number of elderly individuals is set to increase due to cohort effects and increases in life expectancy[3] . Worldwide projections for the annual number of

hip fractures forecast a doubling by the year 2025 and a threefold increase by the year 2050 due to the changes in population demography alone[4] .

Information about hip fractures in Brazil is limited [5]. There are, however, four published regional reports on the incidence of hip fracture in different parts of Brazil which results were collated to estimate national data and supported the development of FRAX model for Brazil[6]. These independent studies used different methodologies and were undertaken in the cities Porto Alegre located in the South[7] , Marilia in the Southeast[8] , Sobral[9] and Fortaleza[10] in the Northeast regions of the country. Notwithstanding, there are several limitations in the use of those data. The issues include differences in study definitions of hip fracture, the methods used to capture individuals with hip fracture, and the generalizability of the populations used to generate national-specific fracture rates.

Therefore, the aim of the present study (BRAVOS Study-The Brazilian Validation Osteoporosis Study) is to update the hip incidence rates for Brazil with data which are more accurate and based on an expanded and representative national sampling rather than previous regional estimates.

2. Material and Methods

This study was conducted in three cities in Brazil, selected according to the following criteria: population between 400,000 and 1,300,00 inhabitants; existing hospital network and health system (both private and public systems) capable to treat hip fractures without need of population migration in search of treatment; and distribution of cities throughout the country, to cover the majority of country's macro regions. The selected cities were Belem, capital of the State of Pará (located in the North region of country) at latitude of 1°27′ (S), Vitoria-Vila Velha, twin cities in the state of Espirito Santo (Southeast region), at 20°19′(S) and Joinville, located in state of Santa Catarina (South region) at 26°18′(S).

This retrospective study comprised patients 50 years and older who lived in those three cities and experienced a hip fracture and received their care exclusively in one of the specific city hospitals from February 1, 2010 to May 30, 2012. Having the local ethics committee approved the study, training for the reviewers of the discharge lists, radiographs, and other records were performed, central review of records to confirm the diagnosis of hip fracture was established and hospital records of all patients with hip fracture, filed according to International Classification of Diseases, tenth edition (ICD-10), in the foregoing hospitals, were carefully reviewed to determine the incidence of hip fracture. The data obtained were abstracted from the emergency room and orthopedics wards, operation room logs and discharge sheet. All patients from those cities with hip fracture were identified using relevant codes and computerized hospital records saved under hip fracture. Fractured patients living outside the city and transferred to those hospitals for treatment were not included. Pathological fractures (those due to tumors, inflammation or Paget's disease of bone) were excluded. Cases of readmission, transfers to another unit, hospital or clinic were identified, and every duplicate record or data was eliminated.

Demographic data used for the calculation of sex and age rates were derived from the reports of the public authority of civil information, based on the 2010 national census[11]. The age specific incidence rates of hip fracture per 100,000 persons were calculated for each sex, 5-year age group, by dividing the numbers of hip fractures recorded during the

study period by the sum of the persons more than 50 years old during that period. To estimate the national incidence of hip fractures, incidence rates derived using the local populations were then merged by weight and extrapolated to the population of the regions using government estimates for the same year. The age-specific rates were then applied to the United Nations Standard Population (2010)[12] to calculate age-adjusted(standardized) rates for hip fracture. For this purpose, the direct method of standardization was used.

Data were analyzed using the SPSS for Windows V22.0 (SPSS, Chicago, IL, U.S.A.). The data was described by tables of frequency and graphics, stratified by gender, age and other variables of interest. Between-group comparisons were conducted using the chi-square test applying a Bonferroni correction approach for post hoc analysis after a statistically significant chi-squared test.

3. **Results**

3.1. **General data**

The population of the three cities, aged 50 yrs. or more during the period of the study, was 601,285 inhabitants, from those 338,134 were female (56.2%) and 263,150 (43.8%) were male, giving a sex ratio of 1.3:1. These individuals accounted for 19% of the total population (3,168,544) of those areas. From February 1, 2010 to May 30, 2012, a total of 1,025 cases of hip fractures were identified across the three cities, 310 in men and 715 in women aged 50 years or more. The median age and interquartile range (IQR) of the event was 78.8(IQR=71-85) years in women and 75.5(IQR=65-82) years in men (p <0,001).

3.2. **Crude incidence of Hip Fractures**

The number of hip fractures and calculated incidences from the three cities during the observation period are shown in Table 1. Belem showed significantly lower hip fracture crude incidence (56.2/100,000 inhabitants; 72.4 /100,000 for women; 34.9/ 100,000 for men) compared to Joinville (93.8/100,000 inhabitants; 117.2 /100,000 for women; 66.7/ 100,000 for men) and to Vitoria (102,0/100,000 inhabitants; 121.9/100,000 for women; 76.1/100,000 for men), with no statistically significant difference between Vitoria and Joinville (Table 2). The incidence of hip fractures stratified by age and sex for each region is shown in Figure 1.

The estimated crude incidence rates of hip fracture in Brazil, derived by using the three cities' populations merged by weight and extrapolated to the population of the regions, considering 100,000 inhabitants 50 years or older per year were 103.3/100,000 (95% confidence interval [CI = 97.0; 109.7). In men 77.4/100,000 (95% CI= 68.8; 86.1) and in women 125.2/ 100,000 (95% CI=116.0; 134.4). There is a significant difference in crude incidence between females and males, as incidence rate for women were consistently higher than that of men in all age segments, except at age 50-54 years and 65-69 years (Figure 2). Annual incidence rates increased exponentially with age in both genders.

3.2. **Annual incidence of hip fractures standardized by Age and Sex**

The standardized annual incidence of hip fracture per 100,000 persons in Belem, Joinville and Vitoria was 60.9(95% CI= 55.0-66.0), 116.2 (95% CI= 100.6;131.8) and 106.6 (95% CI= 96.1;117.1), respectively. As shown in Table 2,

the differences in incidence between regions after adjusting for age and gender were similar to those found when analyzing crude incidence data, with Belem showing again the lowest incidence and no statistically significant difference in standardized hip fracture incidence between Vitoria and Joinville.

During the study period, the age standardized annual incidence of hip fractures in population ≥50 years (merged by weight population of the three regions) was 105.9 cases per 100,000 persons per year (95% CI= 99.4; 112.4); 78.5 cases per 100,000 (95% CI= 69.8; 87.3) in men and 130.6 cases 100,000 women (95% CI= 121.0; 140.2) per year.

4. Discussion

This study characterizes for the first time the hip fracture incidence in Brazil from the age of 50 years upwards, based on data from three representative geographic areas in Brazil over a period of 2 years (2010-2012). As expected, hip fracture incidence increased progressively with age in both sexes. At younger ages, incidence rates were higher in men than in women but were substantially higher in women at older ages. The majority of hip fractures occurred in men and women aged 70 years or more. In spite of sharing the same pattern of increasing incidence of hip fractures with age and bimodal distribution by gender (higher rates at younger ages in men and while the rates were higher in women at older ages), the overall crude hip fracture rates in men and women aged 50 years and older were dissimilar among the three cities. Belem presented a statistically significant lower hip fracture incidence rate than Vitoria and Joinville.

Some hypotheses may be proposed to explain the variation in hip fracture incidence rates, crude and standardized by age and sex, observed among the three cities in this study. Those hypotheses include differential exposure to risk factors such as sunlight and differences in ethnic factors. There are differences in geographical latitude among the 3 cities: Belem is located closest to Ecuador line, whereas Vitoria and Joinville are closer to Tropic of Capricorn. The cutaneous synthesis of vitamin D is dependent on the suitable UV photon reaching a 7-dehydrocholesterol molecule, which is influenced, among others variables, by the solar zenith angle according to latitude[13] . Differences in geographical latitude could suggest that 25(OH)D declines with increasing distance from the equator could, at least in part, to explain the incidence of fractures in those cities with increasing distance from the equator (Vitoria and Joinville) than that observed in Belem[14]. A Brazilian nationwide study demonstrated that Vitamin D insufficiency increased as a function of latitude in Brazil, with percentage of deficiency of Vitamin D occurrence progressively increasing with more southern latitudes[15]. Latitude seems to be more relevant for Vitamin D status than skin color, since in northern regions the prevalence of Afro-American descendants and/or mixed race are greater than in the southern ones[16].

Despite the Brazilian population has a high degree of miscegenation [ethnic background or skin color], it shows significant distribution amongst different regions: in Joinville, there is a predominance of whites (84%) followed by browns (14%) and blacks (3%) races; Belem shows predominance of browns (65%), followed by whites (28%) and then blacks (7%); Vitoria is comprised browns (51%), whites (42%) and blacks (8%) .The 2010 national census highlighted the persistence of differences in the distribution of ethnic different groups, with a higher concentration of African descendants in the North and Northeast and whites in the Southeast and South[16]. Ethnicity and race influence

the epidemiology of fractures, with data demonstrating highest fracture rates in Caucasian population[17]. Therefore, the predominance of Caucasian population in Joinville and Vitoria, unlike Belem, could be one of the determinants of higher risk of hip fractures on those cities. Those regions also present important differences in lifestyle and socioeconomic factors: differences in physical activity could underlie the differences in hip fracture rates in urban (predominantly in South and Southeast regions) versus rural settings (predominantly in North)[18]. For example, Xia et al. hypothesized that the rapid increasing rates of hip fracture in Beijing could reflect increased urbanization which is characterized by increased reliance on cars and buses instead of walking or cycling[19]. In addition, other changes in urban environments such as the increase in hard surfaces upon which to fall, sitting in chairs rather than on the floor could also play a role[17] .

In our study, when incidence of hip fracture in Brazil is calculated from the merged three representative geographic areas after weighting adjustments, it is significantly lower than that reported previously by our group in a prior study where data from four older epidemiologic Brazilian studies were collated to estimate national data on the incidence of hip fracture incidence[6] (Table 3). This trend is similar to that observed in other international studies[20]. One such study of female residents of Ontario (Canada), showed that age-adjusted incidence of hip fractures fell by 20% between 1992 and 2005[21].

A number of different hypotheses may explain this decrease[22]. First, current emphasis on osteoporosis prevention, diagnosis and treatment programs, demonstrated, for instance, by the 10-fold increase in the number of densitometries performed in Ontario from 37,000 in 1992 to 404,000 in 2001, in addition to the rise in the number of antiresorptive treatments prescribed: 13,000 in 1996 and 226,000 in 2003[23]. In a recent study, Kern et al[24] demonstrate that screening for osteoporosis is associated with a statistically significant reduction in incidence of hip fractures compared to standard medical management. In Brazil, where the constitution guarantees universal access to health care, diagnosis and treatment has been implemented since 2002 when bone densitometry and treatment for osteoporosis (bisphosphonates and raloxifene) have been regularly available in our public health system[25].

The second reason for these incidence rate differences is the recognized methodological limitations from the previous Brazilian studies. There were large differences among those studies in criteria of case identification and capture; lack of access to radiographs, and other records; absence of a central review of data to confirm the diagnosis of hip fracture and to avoid double counting may have led to an overestimation of the actual descriptive epidemiology of hip fracture in our country[6].

Wide international differences in age-standardized hip fracture rates worldwide have been reported, varying by at least 10-fold[20]. Some of the variability in these reports is explained, in part, by differences in the time frame during which fractures were captured for each specific country, the representativeness of the population of interest, racial groups and regions included (urban vs. rural), accuracy of the capture of fractures, and differences in reference population used for standardization[26]. However, some ecological studies do not suggest important roles for these risk factors with the possible exception of physical activity on the risk of falling[27 28 29]. Notwithstanding all of the above, the highest fracture rates are consistently reported in northern European countries and North America, and the lowest rates in

some, but not all, countries in South America and Asia[30]. Based on age-standardized annual incidence of hip fracture for men and women combined (Table 3), Brazil belongs to an intermediate-risk country for hip fracture and similar is to Colombia in Latin America or Saudi Arabia in Middle East[6]. We should stress, however, that low fracture rates reported in this study should not be taken as indicating that osteoporosis is not a serious problem in Brazil. Several studies have described the economic burden of these fractures in Brazil[31,32,33]. A recent publication estimated, in 2018, that fractures caused by osteoporosis in Brazil amounted to an economic burden of approximately 309 million USD[33]. Moreover, a cross-sectional study of 2,344 individuals over 40 years of age, residents of rural and urban areas of 150 cities in Brazil (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[34]. Regarding mortality related to hip fractures in Brazil, a prospective study published in 2009 investigated the mortality rate in the first year after hip fractures, as well as the factors associated with mortality in Brazilian patients. Mortality rates were 35%, with most of those deaths (74.4%) occurring after hospital discharge. 43.3% of the men and 31,8% of the women died (31.8%) within the first year after fracture[35].

4.1. Limitations and Strengths of the study

The use of retrospective study design and data collection may be considered as a limitation of our study as prospective study design and data collection in general is considered to be of a higher reliability. Additionally, we cannot be completely sure that the regions studied are fully representative of the Brazilian national population. Nevertheless, our study has several strengths. It is the first study developed to assess the hip fracture incidence in Brazil by the inclusion of multiples cities (representing a better national sampling rather than previous isolated regional estimates[6]) under the same protocol and including both private and public health systems. It seems reasonable to work on the assumption of representativeness, particularly as the gender and age distributions are similar to national data (data not shown). Moreover, the study methodology was developed to minimize the potential limitations of its retrospective data collection. The diagnoses of fragility hip fracture were validated by thoroughly examining all medical records and X-ray reports. Further we also excluded from our retrospective analysis readmissions due to complications or revisions and we conducted systematic database reviews throughout the study in order to exclude over identification of cases (double counting).

5. Conclusions

To our knowledge, it is the first study planned to estimate the hip fracture incidence in Brazil using data from 3 cities intending to represent a better national sampling. The age standardized annual incidence of hip fractures in population ≥50 years in the merged three regions was 105.9/ 100,000 persons per year; 78.5/ 100,000 men and 130.6/100,000 women per year. These incidences are lower from those found in previous studies used to build the FRAX Brazil. In addition, there was a significant difference between the geographic locations, with lower incidences in the northern regions compared to the southern ones. Sociodemographic, life styles and climatic characteristics may explain the

differences found in hip fracture incidence observed among the cities in this study. These data may better estimate the public health impact of hip fractures and may be used to adjust the model of FRAX Brazil.

Declarations

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Conflict of interest: The authors declare that they have no conflict of interest in respect to this work.

Ethics approval: The ethics committees of the institutions where the research took place approved the study.

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Table 1: Annual Incidence of hip fractures (Feb/2010-May/2012) per 100,000 inhabitants (in the year 2011) according to age and gender in the three cities

Region	BELEM						JOINVILLE						VITORIA					
Sex	Women			Men			Women			Men			Women			Men		
	Hip Fractures	Population	Incidence	Hip Fractures	Population	Incidence	Hip Fractures	Population	Incidence	Hip Fractures	Population	Incidence	Hip Fracture	Populatior	Incidence	Hip Fracture:	Population	Incidence
Age(y)																		
50-54	8	50.627	7,0	5	42.996	5,2	2	15.457	5,8	2	15.043	5,9	5	26.293	8,5	10	22.381	19,9
55-59	21	39.264	23,8	6	32.365	8,2	4	12.512	14,2	8	11.541	30,8	13	21.002	27,5	10	17.533	25,3
60-64	29	30.372	42,4	13	23.673	24,4	9	8.807	45,4	6	7.779	34,3	15	15.555	42,9	11	12.277	39,8
65-69	26	22.381	51,6	12	16.425	32,5	6	5.829	45,7	10	4.864	91,4	11	11.068	44,2	22	8.498	115,1
70-74	32	16.778	84,8	12	11.500	46,4	10	4.607	96,5	8	3.440	103,3	42	8.896	209,8	14	6.186	100,6
75-79	46	11.772	175,7	13	7.076	81,7	30	3.250	410,3	11	2.103	232,4	65	6.949	415,7	26	4.281	269,9
80-84	62	7.996	344,6	29	4.236	304,3	34	2.215	682,1	12	1.109	481,0	48	4.661	457,7	16	2.535	280,5
85-89	57	3.851	657,8	13	1.972	298,0	32	1.055	1.348,4	8	526	676,2	39	2.237	774,7	15	1.128	591,1
90-94	12	1.924	277,2	5	756	294,0	13	382	1.511,9	3	164	812,7	25	962	1.155,2	4	382	464,8
95-99	10	948	468,6	3	253	644,6	3	96	1.677,4	2	43	2.565,4	6	384	866,9	1	85	610,5
TOTAL	303	185.914	72,4	111	141.251	34,9	143	54.212	117,2	70	46.611	66,7	269	98.008	121,9	129	75.287	76,2

Table 2: Incidence rates(per 100,000, with 95% confidence intervals) of hip fractures in patients ≥ 50 years, crude and standardized*

Cities	Men		Women		Both genders	
	Crude (95%CI)	Standardized(95%CI)	Crude (95%CI)	Standardized(95%CI)	Crude (95%CI)	Standardized(95%CI)
Belem	34.9 (28.4-41.4)	39.0 (31.8-46.3)	72.4 (64.2-80.59)	80.6 (71.5-89.6)	56.2 (50.8-61.6)	60.9 (55.0-66.8)
Joinville	66.7 (51.1-82.3)	85.2 (65.3-105.26)	117.2 (98.0-136.4)	146.2 (122.2-170.2)	93.8 (81.2-106.5)	116.2 (100.6-131.8)
Vitoria	76.1 (63.0-89.2)	81.7 (67.2-95.8)	121.9 (107.4-136.5)	129.6 (114.1-145.1)	102.0 (92.0-112.1)	106.6 (96.1-117.1)

* Standardized incidence rate/100,000 persons ≥ 50 years (United Nation Standard Population 2010)

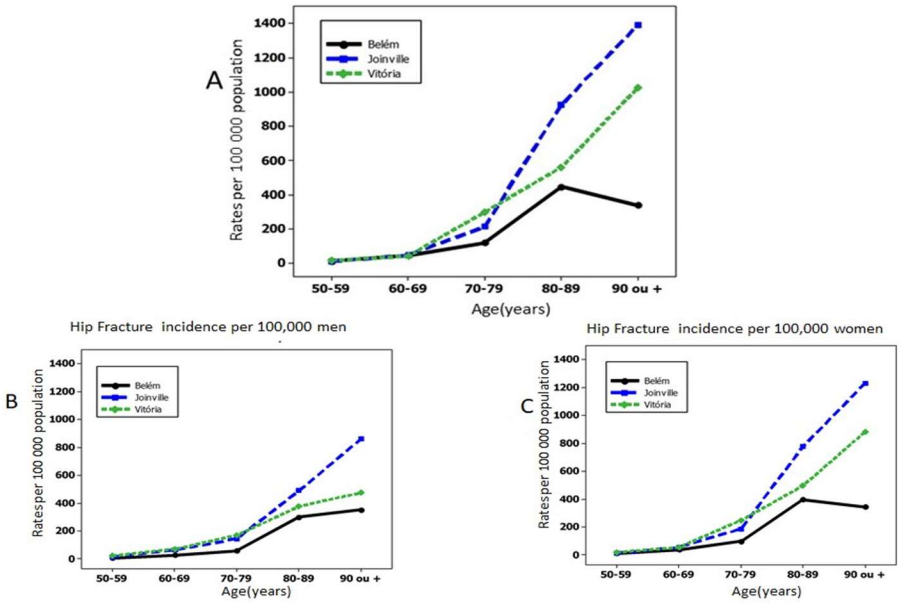

Figure 1. Incidence rate of hip fracture per 100,00 per year by sex and age in Belem, Joinville and Vitoria. A: Both genders; B: Men; C: Women

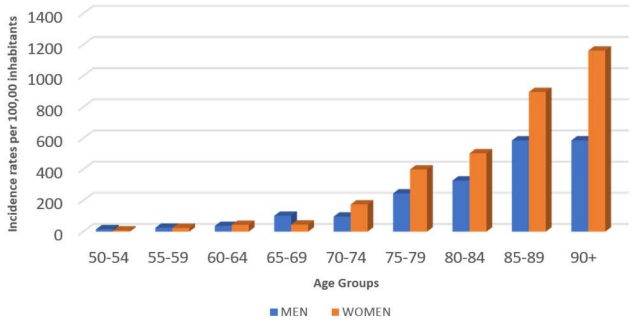

Figure 2. Crude incidence rates of hip fractures among males and females

Table 3. Age-standardised hip fracture rates (/100,000) in previous Brazilian studies[6], Bravos Study and international scenario[30]

Country	Women	Men
Argentina	390	124
Brazil	190	77
Brazil (Bravos Study)	130	78
Canada	290	131
Colombia	127	78
Denmark	574	290
France	291	126
Hong Kong	324	148
Lebanon	315	114
Nigeria	2	2
Philippines	133	48
Saudi Arabia	135	77
Sweden	539	247
United Kingdom	349	140