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Prevalence and risk factors of radiographic vertebral fracture in postmenopausal Vietnamese women

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ABSTRACT

Background: Vertebral fracture is associated with an increased risk of atraumatic fracture and mortality. The prevalence of vertebral fractures among postmenopausal Caucasian women has been reported to range between 15% and 35%. Because there is no estimate of the magnitude of the problem in Vietnam, we undertook this study to estimate the prevalence and risk factors of vertebral fracture in Vietnam.
Methods: Radiographs were taken from 209 postmenopausal women aged between 50 and 85 years (average 62) who were randomly sampled from various districts in Ho Chi Minh City. The presence of vertebral fracture was assessed by the Genant's semi-quantitative method with two independent readers. Bone mineral density (BMD) at the lumbar spine (LS), femoral neck (FN) and whole body was measured by DXA (Hologic QDR4500). Anthropometric and clinical data were obtained by a standardized questionnaire.
Results: Among the 209 women, 48 were found to have at least one radiographic vertebral fracture, which yielded a prevalence of 23% (95%CI: 18–29%). Although fracture occurred in all vertebrae, most (83%) occurred at the L1–L5. Most fractures occurred at one vertebra, and only 12% occurred at multiple vertebrae. The prevalence increased with age such that it reached 39% among those aged 70+ years. There was no significant association between vertebral fracture and back pain, fall history, and dietary calcium intake. In simple log-binomial regression analysis, higher risk of vertebral fracture was associated with advancing age (prevalence ratio [PR] per 10 years: 1.40; 1.16–2.05) and lower lumbar spine BMD (PR per SD: 1.51; 1.18–1.92). In multivariable analysis, the two factors remained independently associated with fracture risk, with the area under the receiver operating characteristic curve being 0.66.
Conclusions: These data suggest that approximately one out of 4 postmenopausal women in Vietnam have a radiographic vertebral fracture, and this prevalence is as common as in Caucasian populations. The number of women needed to screen to identify one vertebral fracture is about 4 to 5, which seems to be cost-effective.

Introduction

Asymptomatic vertebral fracture is a silent consequence of osteoporosis and is the most common type of osteoporotic fracture. Vertebral fracture is associated with serious chronic outcomes, including substantial back pain, physical impairment and disability [1] which are in turn associated with reduced quality of life [2] and increased risk of mortality [3]. The presence of a vertebral fracture is an indicator of future atraumatic fracture risk [4,5], such that individuals with a pre-existing vertebral fracture have a 5-fold increase in subsequent fracture risk [6]. Therefore, recognizing individuals with a vertebral fracture is important because it helps identify patients at high risk of fractures for early intervention.

The prevalence and risk factors of asymptomatic vertebral fracture in Caucasians have been well documented. Several studies have suggested that among postmenopausal Caucasian women, the prevalence of vertebral fracture ranged between 15% and 35% [7], with a high variability among countries and ethnicities. Risk factors of morphometric vertebral fractures included advancing age, cigarette smoking, lack of physical activity, and low bone mineral density [1,5,8–11]. In recent years, several randomized clinical trials have been conducted in largely Caucasian women and showed that anti-resorptive treatment of women with a pre-existing vertebral fracture and/or low bone mineral density could reduce the risk of future vertebral fracture [12]. However, such an efficacy in Asian populations is still unclear, due to lack of randomized clinical trials in Asian populations, driven perhaps by inadequate data on the magnitude of osteoporotic fractures in Asia.

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Table 1
Demographic characteristics of participants.

	All ($n=209$)	Vegetarian ($n=104$)	Omnivore ($n=105$)	p-value[a]
Age (years)	62 (10)	62 (10)	62 (9)	0.9541
Weight (kg)	53 (8)	54 (7)	53 (9)	0.5962
Height (cm)	149 (6)	149 (6)	148 (6)	0.1528
Body mass index (kg/m^2)	24 (3)	24 (3)	24 (4)	0.7888
Femoral neck BMD (g/cm^2)	0.63 (0.11)	0.64 (0.11)	0.62 (0.11)	0.1723
Lumbar spine BMD (g/cm^2)	0.76 (0.14)	0.77 (0.14)	0.74 (0.15)	0.1498
Dietary calcium intake (g/day)[b]	443 (333, 652)	**387 (294, 485)**	**589 (398, 853)**	**<.0001**
Morning exercise (n; %)	162 (77.5)	81 (77.8)	81 (77.1)	0.8978
Hypertension (n; %)	60 (28.7)	24 (23.1)	36 (34.3)	0.0733
Cardiovascular disease (n; %)	7 (3.4)	4 (3.9)	3 (2.9)	0.7212
Diabetes mellitus (n; %)	14 (6.7)	9 (8.6)	5 (4.8)	0.2685
Osteoarthritis (n; %)	38 (18.2)	20 (19.2)	18 (17.1)	0.6956
Back pain (n; %)	128 (61.2)	68 (65.4)	60 (57.1)	0.2214
Prior fracture (n; %)	46 (22.0)	24 (23.1)	22 (21.0)	0.7109
History of fall (n; %)	21 (10.1)	14 (13.5)	7 (6.7)	0.1072

Values are mean (SD); unless otherwise specified.
BMD, bone mineral density.
Significant values are shown in bold-faced.
[a] Comparison between vegetarian and omnivorous groups.
[b] Median (Q1, Q3).

Limited data accumulated during the past two decades have shown that Asian women, on average, have lower bone mineral density (BMD) than their Caucasian counterparts, but paradoxically, the incidence of fractures in Asian women is lower than in Caucasian women. Although the prevalence of vertebral fractures in Asia has not been well documented, recent epidemiologic studies in Japan, Thailand and Hong Kong observed a prevalence of 10 and 30%, respectively [8,13–18]. Moreover, under-reporting and recognition of vertebral fractures leading to lack of clinical care has been a complicating factor in the management of osteoporosis in Asian countries. Vietnam is a relatively large country in Southeast Asia with a population of 86 million, and like many other countries in the region, there is virtually no fracture data in Vietnam. In an effort to contribute to the international literature of vertebral fracture, we undertook this study to estimate the prevalence and risk factors of vertebral fractures in postmenopausal Vietnamese women.

Materials and methods

Study design and participants

The study setting was Ho Chi Minh City (formerly Saigon), a major city and an economic hub in Vietnam. The city has a population of 6.4 million, with a density of 7943 people per square mile (www.hochiminhcity.gov.vn, date of access: 10 July 2008). The current annual average GDP of the City was $2180 (GDP adjusted for Purchasing Power Parity was $10,870).

The study was designed as a cross-section investigation, and part of a study that examined the effect of veganism on bone health. We randomly selected 20 temples and monasteries in Ho Chi Minh City, and then sent a letter of invitation to invite all nuns aged 50 or above to participate in the study. In the next step, we randomly sampled households around each temple or monastery and a similar letter of invitation was sent out to female members of the households. The sample size of this study was calculated based on BMD as the primary outcome. Under the assumption that the difference in bone mineral density between vegetarians and omnivores was 0.05 g/cm^2 (a difference of clinical relevance), and given that the between-subjects standard deviation of bone mineral density is around 0.12 g/cm^2, we estimated that a sample size of ~91 individuals in each group was required to have a power of 80% to detect the difference at the confidence interval of 95%. Ultimately, 105 nuns and 105 women aged 50 years or above participated in the study. The sample size is also statistically adequate to estimate a "true" prevalence of vertebral fracture of 20% with a sampling variability of 5%.

None of the participants had any disease deemed to affect osteoporosis (such as hyperthyroidism, hyperparathyroidism, renal failure, malabsorption syndrome, alcoholism, chronic colitis, multimyeloma, leukemia, and chronic arthritis) or previous use of therapies that interfere with bone metabolism (e.g., glucocorticoid, heparin, warfarin, thyroxin, and estrogen).

Assessment of vertebral fracture

Standard lateral and anterio-posterior lumbar spine radiographs were taken with a 101.6 cm tube-to-film distance and were centered at L2. Radiographic fracture (referred as vertebral fracture in this study) was ascertained by the Genant's semi-quantitative (SQ) method with three independent readers (who are authors of this paper). The first author initially read the radiographs. After that, two readers (NDN and TVN) independently read the same radiographs. If there was a difference in reading between the readers, the assessment in a joint consensual reading was done. The kappa coefficient among readers was 0.67. The SQ criteria were also used to determine the severity of vertebral fractures (mild, moderate or severe). A fracture

Table 2
Prevalence (%) of radiographic vertebral fractures in postmenopausal women.

	n/total	Prevalence (95% CI)
Any vertebral fracture	48/209	23.0 (17.8, 29.1)
By age group		
50–59	18/105	17.1 (11.1, 25.5)
60–69	10/52	19.2 (10.8, 31.9)
70+	20/51	39.2 (27.0, 52.9)
By bone mineral density[a]		
Non-osteoporosis	23/141	16.3 (11.1, 23.3)
Osteoporosis	25/68	36.8 (26.3, 48.6)
Grade of fracture		
1	29/48	60.4 (46.3, 73.0)
2	12/48	25.0 (14.9, 38.8)
3	7/48	14.6 (7.2, 27.2)
Number of fractured vertebrae		
1	42/48	87.5 (75.3, 94.1)
2	5/48	10.4 (4.5, 22.2)
5	1/48	2.1 (0.1, 10.9)

[a] Bone mineral density (BMD) measured at the lumbar spine; osteoporosis: BMD T-scores ≤ -2.5.

Table 3
Risk factors of radiographic vertebral fractures (bivariate analysis).

Factor	Unit of comparison	Prevalence ratio (95% CI)
Age (years)	+10	**1.40 (1.11, 1.76)**
Weight (kg)	+8	1.10 (0.86, 1.41)
Height (cm)	−6	1.14 (0.89, 1.47)
BMI (kg/m^2)	+3	1.20 (0.94, 1.53)
Femoral neck BMD (gm^2)	−0.11	1.25 (0.96, 1.63)
Lumbar spine BMD (g/cm^2)	−0.14	**1.51 (1.18, 1.92)**
Dietary calcium intake (g/day)	+300	1.10 (0.92, 1.31)
Prior fracture	Yes	1.61 (0.96, 2.70)
Back pain	Yes	1.15 (0.68, 1.94)
Veganism	Yes	0.93 (0.56, 1.53)

BMI, body mass index; BMD, bone mineral density.
Significant values are shown in bold-faced.

was considered mild (grade 1) if having a 20–25% reduction in vertebral anterior, middle and/or posterior height; moderate (grade 2) if a reduction of 25–40% in height; and severe (grade 3) if a reduction >40% in height was observed.

Bone mineral density measurement

BMD was measured at the lumbar spine (LS), femoral neck (FN) and whole body (WB) in all participants. The measurement was done with a dual energy X-ray absorptiometry (DXA) densitometer (Hologic QDR 4500). The precision error (%CV) in our laboratory was 2% for lumbar spine and 1.8% for femoral neck BMD, and 1.5% for whole body BMD. The densitometer was standardized by a standard phantom every time before measurement is undertaken.

Data collection

Clinical data such as blood pressure, pulse, and reproductive history data (i.e. parity, age of menarche, and age of menopause), clinical history (i.e. previous fracture, previous falling, previous and current use of pharmacological therapies) were obtained by a standardized questionnaire. The questionnaire also solicited data on physical activity and lifestyle factors. The women were asked to report their past and current habits of cigarette smoking, alcohol use, and coffee drinking.

Anthropometrical parameters including age, weight, and standing height were obtained. Body weight was measured by using an electronic balance with indoor clothing without shoes. Height was determined without shoes on a portable stadiometer with mandible plane parallel to the floor.

The study was approved by the Ethics Committee of the Pham Ngoc Thach University of Medicine and informed written consent was obtained from each participant.

Data analysis

The primary purpose of analysis was to assess the prevalence and risk factors of vertebral fracture. We estimated the prevalence of vertebral fracture and 95% confidence interval estimated by Wilson's score method which is a recommended method [19]. The magnitude of association between a risk factor and vertebral fracture was assessed by prevalence ratio (PR) instead of odds ratio, because the latter is difficult to interpret and tends to overestimate an association when the prevalence is more than 10% [20,21]. To estimate the prevalence ratio for risk factors, we used the log-binomial model [22], which has been considered a reliable method [23]. The prevalence ratio, both unadjusted and adjusted for potential covariates, was used to compare the prevalences between groups of interest. The R program was used for the statistical analysis [24,25].

Results

The final analysis was based on 209 women, after excluding 1 woman whose spinal radiograph was not appropriately taken. Characteristics of participants stratified by group are shown in Table 1. The average age for all women was 62 years (range: 50–85). The average BMI was 24 kg/m^2 (range: 15–34), with 28% ($n=59$) being within the "overweight" range (25 and 30 kg/m^2), and 2.4% ($n=5$) obese (greater than 30 kg/m^2). Using the WHO's criteria, the prevalence of osteoporosis (i.e., femoral neck BMD *T*-scores ≤ -2.5) in the entire sample was 35/210 or 17% (95% confidence interval: 12 to 22%). However, the prevalence increased with advancing age such that it reaches 40% by the age of 70 and above.

Among the women, 48 were found to have at least one radiographic vertebral fracture, yielding a prevalence of 23% (95%CI: 18–29%). There was no significant difference in fracture prevalence between vegans (22.1% or 23/104) and omnivores (23.8% or 25/105). Furthermore, there were no significant differences between vegetarian and omnivorous groups in terms of anthropometric and BMD measurements, lifestyles and morbility. However, dietary calcium intake in vegans was significantly lower than omnivores (Table 1). Therefore, it was decided to combine data from the two groups into a single sample for subsequent analyses.

On average, women with a vertebral fracture were older (65 vs. 61 years old, $p=0.007$) and had lower lumbar spine BMD (0.70 vs. 0.78 g/cm^2, $p=0.002$) than women without fracture. There were, however, no significant differences in other clinical and lifestyle factors between the two groups.

Further analyses of fracture by severity status are shown in Table 2. 60% of all fractures were classified as grade 1, whereas 25% and ~11% were grade 2 and grade 3, respectively. The majority of fracture cases occurred at one vertebra (88%) and 2 vertebrae (10%). The prevalence of fracture among the 50–59 years age group was 17%, which was significantly lower than among those aged 70+ years (40%).

The risk of fracture was significantly associated with advancing age (PR per 10 years: 1.4; 1.1–1.8) and lower lumbar spine BMD (PR per SD: 1.5; 1.2–1.9). However, none of the remaining factors was significantly associated with fracture (Table 3). In multivariable

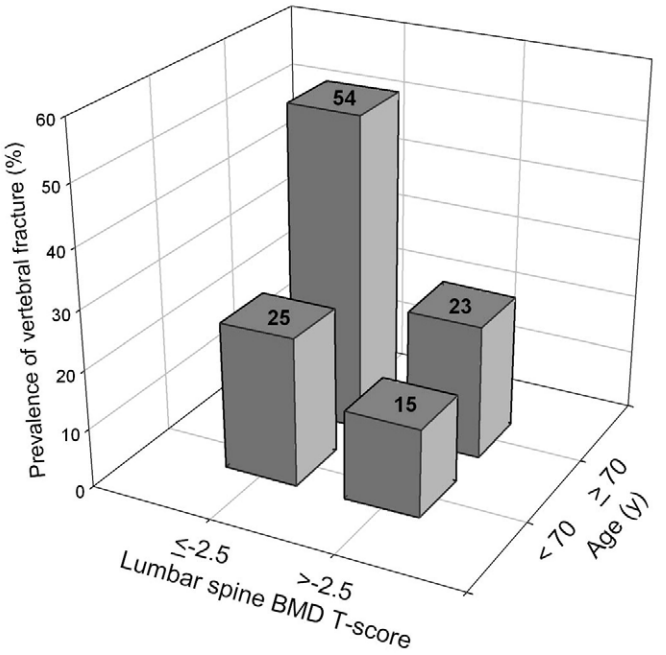

Fig. 1. Prevalence of radiographic vertebral fracture, stratified by LSBMD *T*-score and age.

analysis, only advancing age and lower lumbar spine BMD remained independently and significantly associated with increased risk of vertebral fracture. Analysis of regression diagnostics showed that the effect of age were non-linear (data not shown); therefore, age was categorized into two groups (<70 years and older groups). Women aged 70 years or older were more likely to sustain vertebral fracture compared to their younger counterparts (PR: 1.83, 95% CI: 1.12–3.00). Women with low BMD had higher risk of sustaining fracture (PR: 1.40, 95% CI: 1.07–1.84) independent of age. Area under the receiver operating characteristic curve of this two-factor model was 0.66.

Prevalence of vertebral fracture was further explored based on age and LSBMD *T*-score. The prevalence of vertebral fracture was highest among individuals with age of 70+ years and osteoporotic BMD (53.6%; 95% CI, 35.8–70.5) compared to those younger with normal BMD (15.1%; 95% CI, 9.8–22.6) (Fig. 1).

Discussion

Although vertebral fractures are recognized as a *prima facie* of osteoporosis, it is difficult to assess its magnitude in the general population since the fracture is a "silent" condition. Despite the prevalence and consequence of vertebral fractures having been well documented in Caucasian populations, there is a dearth of data in Asian countries, wherein by 2050 more than 50% of all fractures in the world is projected to occur. In this first ever study in Vietnam, by analyzing radiographs of a random sample of postmenopausal women, we found that approximately a quarter of women had asymptomatic vertebral fracture. Because vertebral fracture is associated with increased risks of subsequent non-vertebral fracture and mortality, this prevalence represents a significant public health burden in the country.

The prevalence of vertebral fracture in this population is comparable to that observed in Caucasian populations. In a recent study of 337 individuals aged 50 years or older without non-vertebral fracture in the United Kingdom, 25% was found to have vertebral fracture [26]. In the Study of Osteoporotic Fracture, the prevalence of vertebral fracture among women aged 65+ years was approximately 20% [27]. In the European Vertebral Osteoporosis Study in 19 European countries with more than 15,000 individuals aged 50–79 years, the radiographic prevalence of vertebral fracture ranged between 6 and 21% [7]. This between-countries variability in the prevalence was also observed in 5 South American countries (Latin American Vertebral Osteoporosis Study) where the average prevalence of vertebral fracture among women aged 50+ years was 15% [28].

In the present study, we found that the frequency of fracture was more common at the lumbar than at the thoracic spine. This finding is consistent with observations from other Asian populations among whom the ratio of vertebral fracture at the lumbar spine to thoracic spine was 1.4 in native Japanese, but was 0.51 in Japanese women living in Hawaii and 0.55 in Caucasian women [13]. It is not clear why such a difference exists, but it could be that previous studies did not assess fracture at L5 [29]. In our study population and other Asian population [30], fracture at L5 is common, especially in women. It could also be that fracture at the thoracic spine is more commonly underestimated compared to that at the lumbar spine [31].

Asian women, on average, have lower bone mineral density than Caucasian women, but the risk of vertebral fracture in Asian women was either equivalent to or even higher than their Caucasian counterparts. For instance, among Thai women over the age of 50 years, approximately 36% was found to have an existing morphometric vertebral fracture [14]. In Taiwanese women aged 65+ years, the prevalence was somewhat lower (20%) [16], which is comparable to those estimates in Hong Kong [8]. However, in the Beijing Osteoporosis Project, the prevalence of morphometric vertebral fracture increased from 5% in women aged 50–59 years to 37% in women aged 80+ years [15]. There is a substantial variation in the prevalence of vertebral fracture among populations. It is possible that part of the variation could be due to differences in population characteristics and methods of assessment [32]. Indeed, at present, there is no single best method for assessing vertebral fracture[33] and the concordance between methods of assessment was modest, with the concordance coefficient ranging from 0.53 to 0.68 [34]. Taken together, our estimate of the prevalence of asymptomatic vertebral fracture is within the international variability ranges.

In this study, approximately 17% women had osteoporosis (e.g. femoral neck BMD *T*-scores ≤ -2.5). Moreover, 32% of women either had osteoporosis or vertebral fracture. In other words, if the International Osteoporosis Foundation guideline of treatment is adopted [12], then about one-third of postmenopausal women are eligible for treatment by virtue of the presence of fracture or osteoporosis. Although the anti-fracture efficacy has been demonstrated in randomized clinical trials in largely Caucasian women with a pre-existing vertebral fracture and/or osteoporosis [35], it is not clear whether the same efficacy exists in Asian populations. This is an area that requires further study and analysis.

Given that vertebral fracture is associated with increased risk of further non-vertebral fractures [3–5,27], increased risk of pre-mature mortality [3], and reduced quality of life [36], it is important to identify individuals at high risk for intervention. The question then is how many women should be screened to identify one case of fracture? In this study, since the prevalence of fracture is 23%, it means that approximately 4 to 5 postmenopausal women need to undergo vertebral morphometric screening in order to detect one woman who might be considered for an appropriate intervention. Since the cost of radiographic assessment is relatively low, it seems cost-effective to screen postmenopausal women for vertebral fracture.

However, at present, there is no non-invasive screening tool that can reliably identify individuals at high risk of fracture. In the absence of a screening tool, it seems useful to consider the use of risk factors as a means to identify high risk women. In this study, we found that advancing age and lower lumbar spine bone mineral density were independent risk factors of vertebral fractures. We found that the risk of vertebral fracture among women aged 70+ years (40%) was more than two times higher than that among women aged 50–59 years. Furthermore, the risk of vertebral fracture among osteoporotic women (~40%) was two-fold higher than non-osteoporotic women. In combination, the highest prevalence of vertebral fracture was virtually observed among individuals aged 70+ with osteoporotic BMD (54%). These findings are also consistent with previous findings in Caucasian population [37] and Chinese population [8]. However, the area under the receiver operating characteristic curve of the model with age and BMD as risk factors was only 0.66, which is not optimal for screening purposes. Thus, future research should be directed toward the development of prognostic models for identifying individuals at high risk of asymptomatic vertebral fracture.

The present finding must be interpreted within the context of strengths and limitations. A major strength of this study is that the women were randomly sampled from the general population, which increases the study's external validity. The radiographs were carefully read by three independent readers using a standard (Genant's) method. However, even though the sample size was adequate to estimate a prevalence of 20%, the sample size was inadequate for subgroup analysis. The participants were essentially urban women, whose lifestyle and nutritional status might be different from rural women; thus, the findings may not be extrapolated to rural populations.

In summary, these data suggest that undiagnosed vertebral fracture in Vietnamese postmenopausal women aged 50 years or above was 23%, which is comparable to that of Caucasian women. Consequently, the number needed to screen to detect one fracture case was 4 to 5. Although age and lumbar spine bone mineral density were significant risk factors of vertebral fracture, the two factors did

not have adequate discriminatory predictive value for prognosis of fracture.

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