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Vertebral fracture assessment in Moroccan women: Prevalence and risk factors

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ABSTRACT

Introduction: Vertebral fracture assessment (VFA) is a fast, low-radiation technique which produces images that are of sufficient quality to be used to diagnose the presence of vertebral deformity consistent with fracture.
Objective: To study prevalence and risk factors of vertebral fractures using VFA in asymptomatic Moroccan women.
Methods: The study cohort consists of a population of 328 consecutive women aged over 50 (mean age, weight and BMI of 65 ± 6.5 (50–84) years, 72.0 ± 12.8 (42–125) and 29.4 ± 5.0 (17.1–45.8) kg/m^2, respectively). Lateral VFA images and scans of the lumbar spine and proximal femur were obtained by two technologists using a GE Healthcare Lunar Prodigy densitometer. Vertebral fractures were defined using a combination of Genant semiquantitative (SQ) approach and morphometry.
Results: 68% of vertebrae from T4–L4 and 75% from T8–L4 were adequately visualized on VFA. Vertebral fractures (grades 2 or 3) were detected in 25.6% (84/328) of these women. Thirty-two of women with VFA-identified fracture (38.0%) had only a single vertebral fracture, while the other 61.9% had two or more. Fractures were most common in the mid-thoracic spine and at the thoraco-lumbar junction. As would be expected, the prevalence of VFA-detected fractures increased with age and as BMD declined. Stepwise regression analysis showed that presence of vertebral fracture was mainly related to the spine osteoporotic status, age older than 65, history of peripheral fracture and more than six parities.
Conclusion: Vertebral fractures are common in asymptomatic Moroccan women and are related to age, low BMD, history of fracture and multiparity.

1. Introduction

Osteoporosis is a major public health burden worldwide and the rates of hip and other fractures are rapidly increasing in developing countries [1]. Vertebral fractures (VFs) are the most common osteoporotic fractures which are important to detect because they have been associated with reduced quality of life, increased morbidity and mortality, and increased risk of future vertebral and non-vertebral fractures [2,3]. The costs of these fractures are also high for society. Moreover, drugs that are available for treating osteoporosis, such as bisphosphonates or strontium ranelate, are effective at reducing the risk of further VFs and are recommended for use in this group of patients.

The standard method to assess vertebral fracture is radiography of the thoraco-lumbar spine. However, there is no gold standard for the definition of osteoporotic vertebral fracture [4]. A number of methods have been developed for interpretation of spinal X-rays, including the Genant semiquantitative method, which has been used as a surrogate gold standard in a number of key osteoporosis studies [5]. This approach is more objective and reproducible than other qualitative methods [6]. Vertebral morphometry using dual-energy X-ray absorptiometry (DXA) also known as vertebral fracture assessment (VFA) is a fast, low-radiation technique which produces images that are of sufficient quality to be used to diagnose the presence of vertebral deformity consistent with fracture [7,8]. VFA has demonstrated utility for vertebral visualization and thus is an important tool for fracture detection in women and men [9,10]. VFA offers "point of service" convenience for the patient when it is done at the same visit as for BMD measurement by DXA, with far less radiation than standard radiography [11]. The effective radiation dose for VFA is about 30–50 microSieverts (μSv) versus 1800–2000 μSv for a lateral thoracic and lumbar spine X-ray. By comparison, typical background radiation at sea level in the USA is about 7 μSv per day [12].

Clinical risk factors associated with VFs have been well studied in many populations [13–15] and in Moroccan men [16]. However, the epidemiology of VFs in women of the southern bank of the Mediterranean Sea and in Moroccan women in particular is still unknown. Thus, we aimed in the present study to evaluate the prevalence, risk factors and clinical characteristics associated with VFs in a cohort

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of asymptomatic women aged over 50 who had a VFA examination during their bone mineral density (BMD) testing.

2. Materials and methods

2.1. Subjects

Three hundred and twenty-eight consecutive postmenopausal women aged 50 years and over who had no previous diagnosis of osteoporosis were entered into the study. Women were recruited prospectively with consent from our Rheumatology Department or addressed by private rheumatologists in Rabat area who were invited to participate in the study. General exclusion criteria were non-Caucasian origin and diseases, drugs, and other major determinants known to affect bone metabolism. Thus, we excluded subjects with gastrectomy, intestinal resection, recent hyperthyroidism or hyperparathyroidism, recent severe immobilization or treatment with corticosteroids (more than 3 months). Our institutional review board approved this study. The procedures of the study were in accordance with the Declaration of Helsinki, and formal ethics committee approval was obtained for the study. All the participants gave an informed and written consent. Each subject completed a standardized questionnaire designed to document putative risk factors of osteoporosis. History of fractures, lifestyle (alcohol consumption, gymnastics or jogging/walking, smoking) and diet (milk, yogurt, cheese) habits were also recorded. The women were asked whether they usually drank milk, coffee, or alcohol, if they ate cheese or yogurt, if they did gymnastics or jogging/walking, and if they smoked tobacco. Menstrual and reproductive history were assessed: all patients were menopausal since at least 1 year. Height and weight were measured in our center before DXA measurement, in light indoor clothes without shoes. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.

2.2. BMD measurement

Bone mineral density was determined by a Lunar Prodigy Vision DXA system (Lunar Corp., Madison, WI). The DXA scans were obtained by standard procedures supplied by the manufacturer for scanning and analysis. All BMD measurements were carried out by two experienced technicians. Daily quality control was carried out by measurement of a Lunar phantom. At the time of the study, phantom measurements showed stable results. The phantom precision expressed as the coefficient of variation percentage was 0.08. Moreover, reproducibility has been assessed recently in clinical practice and showed a smallest detectable difference of 0.04 g/cm^2 (spine) and 0.02 (hips) [17,18]. Patient BMD was measured at the lumbar spine (anteroposterior projection at L1–L4) and at the femurs (i.e., femoral neck, trochanter, and total hip). The World Health Organization (WHO) classification system was applied, defining osteoporosis as T-score ≤ -2.5 and osteopenia as $-2.5 < T$-score < -1. Study participants were categorized by the lowest T-score of the L1–4 lumbar spine, femur neck, or total femur using our reference values [19].

VFA was classified using a combination of Genant semiquantitative (SQ) approach and morphometry in the following manner: each VFA image was inspected visually by two clinicians (IG and AN who had a previous training session in VFA) to decide whether it contained a fracture in any of the visualized vertebrae. Each vertebra that was judged as fractured by visual inspection by any of the investigators was measured using built-in morphometry and assigned a grade based on Genant SQ scale [5], where grade 1 (mild) fracture is a reduction in vertebral height of 20–25%, grade 2 (moderate) a reduction of 26–40%, and grade 3 (severe) a reduction of over 40%. As most epidemiological studies defined fractures as grade 2 and higher, subjects with no fractures or with grade 1 fractures were included in the non-fracture group, whereas those with grade 2 or higher fractures were included in the fracture group.

Table 1
Characteristics of the population study ($n = 328$).

	Mean ± S.D.	Range
Age (years)	65 ± 6.5	50–84
Weight (kg)	72 ± 12.8	42–125
Height (m)	1.56 ± 0.1	1.38–1.71
BMI (kg/m^2)	29.4 ± 5.0	17.1–45.8
Number of parity	5.4 ± 2.6	0–13
Years since menopause	15.2 ± 8.5	1–38
BMD lumbar spine (g/cm^2)	0.921 ± 0.1	0.945–1.384
BMD total hip (g/cm^2)	0.860 ± 0.1	0.050–1.197
T-score lumbar spine (S.D.)	−2.0 ± 1.2	−5.2–1.9
T-score total hip (S.D.)	−1.3 ± 0.9	−4.2–1.4

2.3. Statistical analysis

Results are presented as means (S.D.) and categorical variables are expressed as frequencies. To compare patients with and without vertebral fractures, Chi-square test and student's t-test were used firstly. Potential risk factors were entered to a stepwise conditional binary regression analysis and the resulted odds ratios with 95% confidence intervals were reported. The level for significance was taken as $p \leq 0.05$. Excel 2007 and SPSS 15.0 were used for statistical analysis.

3. Results

3.1. Patient demographics

In this cohort of 328 women, the mean ± S.D. (range) age, weight and BMI were 65 ± 6.5 (50–84) years, 72.0 ± 12.8 (42–125) and 29.4 ± 5.0 (17.1–45.8) kg/m^2, respectively (Table 1). Sixty-one women (18.6%) had a history of traumatic peripheral fracture in younger age (radius = 33, tibia = 16, femur = 7, humerus = 5).

Vertebral fractures were identified using VFA in 84 (25.6%); this group of women were older and had a statistically significant lower weight, height and lumbar spine and total hip BMD and T-scores and higher number of parity and years of menopause than those without a VFA-identified vertebral fracture (Table 2). One-third of women with VFs had a history of traumatic peripheral fracture in the young age versus 14% of women without VFs ($p < 0.0001$).

3.2. Vertebral visualization and fracture identification on VFA

In these 328 women, 68% of vertebrae from T4–L4 and 75% from T8–L4 were adequately visualized on VFA (Fig. 1). The percentage

Table 2
Comparison between patients with and without vertebral fractures.

	Patients without prevalent VF, $n = 244$	Patients with prevalent VF, $n = 84$	p
Age (years)	63.6 ± 6.0	69.1 ± 6.2	<0.001
Weight (kg)	72.2 ± 13.1	69.2 ± 11.6	0.02
Height (m)	1.56	1.55	0.03
BMI (kg/m^2)	29.6 ± 5.2	28.6 ± 4.4	NS
Number of parity	5.0	6.3	<0.001
Years since menopause	14.0 ± 8.2	18.7 ± 8.5	<0.001
Calcium intake <500 mg/d	126 (51.6)	58 (69.0)	<0.001
Low physical activity	184 (89.3)	75 (75.4)	0.015
History of fracture: n (%)	34 (13.9)	27 (32.1)	<0.0001
BMD lumbar spine (g/cm^2)	0.945 ± 0.1	0.851 ± 0.1	<0.001
BMD total hip (g/cm^2)	0.876 ± 0.1	0.816 ± 0.1	<0.001
T-score lumbar spine (S.D.)	−1.8 ± 1.2	−2.6 ± 1.2	<0.001
T-score total hip (S.D.)	−1.2 ± 0.9	−1.7 ± 0.9	<0.001

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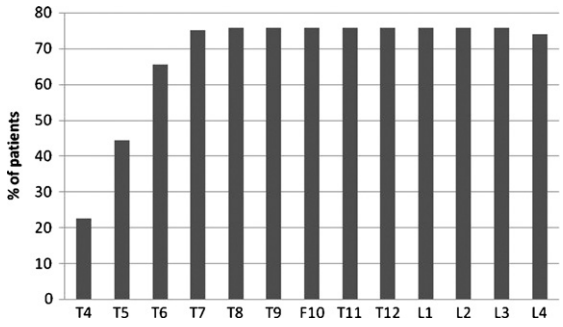

Fig. 1. Vertebral visualization using VFA.

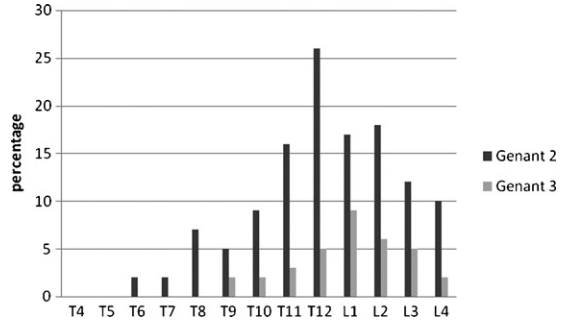

Fig. 2. VFA-identified fracture distribution.

of vertebrae not visualized at T4, T5, and T6 levels was 77.6%, 56.6%, and 35.4%, respectively. Vertebral fractures (grades 2 or 3) were detected in 25.6% (84/328) of these women. Thirty-two of women with VFA-identified fracture (38.0%) had only a single vertebral fracture, while the other 61.9% had two or more. Fractures were most common in the mid-thoracic spine and at the thoraco-lumbar junction (Fig. 2).

As would be expected, the prevalence of VFA-detected fractures globally increased with age and as BMD declined (Fig. 3). In this study population, 15% ($n = 52$) had normal BMD, 41% ($n = 134$) were osteopenic and 43% ($n = 142$) osteoporotic. The fracture prevalence was higher ($p < 0.0001$) in women with lower BMD (Fig. 4). Interestingly, a fracture was identified on VFA in 23% of women with normal spine BMD. Stepwise regression analysis showed that presence of vertebral fracture was mainly related to age older than 65, the spine osteoporotic status, history of fractures and more than six parities (Table 3).

4. Discussion

This is the first study on the prevalence of asymptomatic VFs in the Moroccan population of women aged 50 years and over. About 25% of asymptomatic women over 50 had a previously undiagnosed

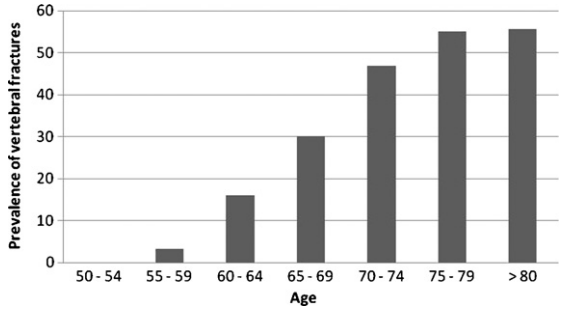

Fig. 3. Vertebral fractures prevalence (%) based on age group (years).

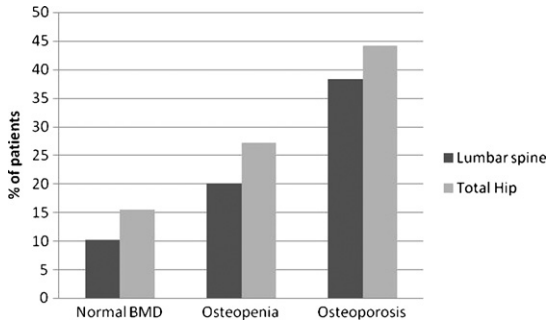

Fig. 4. Vertebral fractures prevalence (%) based on BMD.

vertebral deformity (we found that the prevalence of vertebral fractures was similar in these countries and, when pooled, increased from 3.2% in women aged 54–59 to 55.6% in women over 80). This prevalence of VFs in our population is similar to figures reported in western Caucasian populations as reported in a recent review [20] where prevalence of VFs (grades 2 and 3) is between 18% and 26%. Regional variations in the prevalence of VFs have been previously reported in multicenter studies in Europe where a threefold range difference was found. The European Prevalence Osteoporosis Study (EPOS) reported a higher prevalence in Scandinavian countries (Norway 23.7 and Sweden 27.8) and lower rates for some cities of Southern Europe (Madrid 14.9), Mediterranean countries (Turkey, 15.9), and Russia (12.7) [21]. Moreover, the prevalence distribution of VFs in our population study (55% among women over 75) seemed to be higher than in most European populations. One explanation to this finding is that spine BMD values were found to be lower in normal healthy Moroccans than in European/US women (especially in women over 50 where the difference was about 10–12%) whereas hip BMD values were comparable [19].

The spine is a key fracture site [22]; however, it has been estimated that only 30% of vertebral fractures receive clinical attention (which means that the majority of patients with vertebral fractures remain undetected) [23,24]. It appears that only those patients with the most severe vertebral fractures come to clinical attention (it is likely that this is due to higher levels of back pain and disability). Moreover, even VFs that are visible on X-rays are commonly not reported by radiologists [25]. Under-diagnosis of vertebral fractures on spine X-rays has been observed worldwide, with false negative interpretation rates of about 45% in North America, 46% in Latin America, and 29% in Europe/South Africa/Australia [26]. As many VFs are clinically unappreciated, but convey increased risk for future fracture, knowledge of existing fracture status is necessary for the optimal assessment of fracture risk [27,28].

Spine X-rays are considered the gold standard for vertebral fracture detection. However, VFA offers advantages including patient convenience, lower radiation exposure, cost-effectiveness and ease of directly integrating knowledge of bone density and fracture status into prediction of future fracture probability, and thus in the therapeutic decision [12,29–31]. The main limiting factor in utilizing VFA is the legibility of the vertebrae. Consistent with other studies [29,31–33], image quality was particularly poor in the upper thoracic spine (T4–T7). However, so few osteoporotic fractures occur at this level [9].

Table 3
Multiple logistic regression analysis.

	OR 95% CI	p
Age ≥65 years	3.93 [2.19–7.07]	<0.001
BMD lumbar spine ≤−2.5	3.04 [1.73–5.35]	<0.001
History of fracture	2.75 [1.41–5.33]	0.003
Number of parity ≥6	2.13 [1.22–3.73]	0.008

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This study is the first large descriptive evaluation of VFA in a population of asymptomatic Moroccan women and documents that vertebral fractures are common when searched systematically. As could be expected, the prevalence of VFs in this cohort of women was higher in those of older age and with lower BMD. Importantly, approximately 27% of women with osteopenia and 10% of women with normal BMD who otherwise may not have been identified as being at greater fracture risk were found to have unappreciated evident vertebral fracture (grades 2 and 3). It is well known in postmenopausal women that about half of fractures occur in patients without densitometric osteoporosis and that other factors than BMD may play a role. In this case, recognition of VFs by imaging of the spine change the patient's diagnostic classification, estimation of fracture risk, and threshold for pharmacological intervention as treatment of patients with prevalent VFs reduces the risk of future fractures even when the baseline *T*-score is above the osteoporosis diagnostic cutpoint of −2.5. Thus, these data suggest that *T*-score (i.e., osteopenia) by DXA should receive consideration as an indication for performance of VFA in elderly women as it is now recommended by the ISCD [34]. The most intriguing finding from our study is that prevalent VFs were related to high parity. However, we have already shown that the number of parities was among the most important risk factors of osteoporosis in Moroccan women [35]. In the other hand, classical risk factors for fracture such as smoking, alcohol, low calcium intake and low physical activity were found to be non-significant in multivariate analysis. Smoking and alcohol intake are rare in Moroccan women over 50 (2 ex smokers and 0 alcohol intake in our series) whereas low calcium intake and low physical activity are common and were frequently observed both in fractured and non-fractured women in our study.

Vertebral deformities can be due to developmental abnormalities, Scheuermann's disease sequelae, and degenerative changes. Attention must be paid on osteoporotic depressions of the central end plates of the vertebrae, as osteoarthritic changes occur only on the anterior part of the vertebrae. The main difficulties are related to isolated short anterior vertebral heights at the midthoracic spine. The interpretation of such deformities must take into account degenerative changes of adjacent discs, and the presence of deformities of similar appearances on contiguous vertebrae, both signs being more in favor of a non-osteoporotic origin of the deformity. Vertebral fractures are unlikely to have identical aspect and occur more frequently to non-contiguous vertebrae, although these signs are not specific of osteoporosis. Thus, as we did in our study, the use of the semiquantitative method for fractures assessment needs a first step of visual identification of non-fracture deformities or normal variants, otherwise the method may be less specific than the quantitative approach.

Fractures of the spine are associated with reduced pulmonary function, chronic back pain, loss of height, kyphosis, loss of self-esteem, abdominal discomfort, disability, loss of independence, and death [36]. The mortality rate of 5 years after a clinical VF is about 20% greater than expected, with mortality rates higher for men than women. Mortality rates increase with the number of VFs [37]. New VFs, even those that are not recognized clinically (i.e., morphometric fractures), are associated with substantial increases in back pain and functional limitations [38]. The presence of a VF increases the relative risk of future VFs by about 4.4-fold, and increases the risk of fragility fractures at other skeletal sites as well [39,40]. The presence of a VF is a risk factor for future fracture that is independent of BMD [41]. Thus, many societies interested in osteoporosis management recommend that patients with a prior VF receive drug therapy regardless of BMD *T*-score [42].

Our study has strengths and limitations. The assessment of fracture was carefully conducted using standard procedures of acquisition, and standard reading of all VFA. All the morphometric assessments were made by two experienced investigators after training sessions and after a previous global visualization. Before diagnosis of fracture, a non-osteoporotic origin was considered for each deformity. However, even history of trauma was inquired, we cannot exclude that some subjects did not report remote traumas. The main limitation lies in the procedures used to select subjects, who were all volunteers and ambulatory, and presumably healthier than the general population. The Rabat population may not be adequately representative of the whole population. However, since the population living in the area of Rabat is a balanced mixture of the various regions constitutive of the country, we believe the impact on prevalence estimate is limited.

In summary, VFA is a technology than can reliably and accurately diagnose vertebral fractures with greater patient convenience, less radiation exposure, and lower cost than spine X-rays. The information obtained by VFA would improve management of osteoporotic patients diagnosed only on BMD results as the diagnosis of asymptomatic VFs would allow the indication of anti-osteoporotic treatments. Our results support the recommendation to perform VFA in elderly women referred for DXA measurement especially for women over 65, with history of fractures, more than six parities and when BMD is low.

Conflict of interest

All the authors state that there is no conflict of interest.

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