Original article

Evaluation of the risk factors of asymptomatic vertebral fractures in postmenopausal women with osteopenia at the femoral neck

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A B S T R A C T

Objectives: To identify risk factors of asymptomatic vertebral fracture (aVF) in postmenopausal women with osteopenia at the femoral neck and to evaluate the association between the number of aVFs and the risk of major and hip osteoporotic fracture calculated with the FRAX® algorithm.

Study design: Epidemiological case-series study with data collected transversally.

Results: 728 postmenopausal women with osteopenia were included: 284 (39.0%) had aVF, of whom 200 (70.4%) had prior fragility fractures (FF). The likelihood of having an osteoporotic fracture in the next 10 years increased significantly with the number of aVF. The percentage of women with height loss, which was assessed as the difference between the greatest height reported by participants and that measured at inclusion, was higher in women with an aVF (OR 3.77, 95% CI 1.275–5.16, p < 0.05). Multivariate analysis showed that prior FF, height loss and race were factors associated with the presence of aVF.

Conclusions: In this group of postmenopausal women with osteopenia at the femoral neck, the presence of an aVF correlated with a higher risk of estimated major osteoporotic and hip fractures as calculated using the FRAX® algorithm. Height loss and prior FF were associated with the presence of aVF.

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1. Introduction

Osteopenia, as well as osteoporosis, are characterized by low bone mineral density (BMD) and abnormal bone architecture. According to the World Health Organization (WHO), osteopenia is defined as a Bone Mass Density (BMD) T score between −1.0 and −2.5 SD while osteoporosis is defined as a BMD T score ≤−2.5 SD [1].

Fragility fractures have been diagnosed in subjects with both osteoporosis and osteopenia. Common fracture sites are vertebrae, proximal femur, and distal forearm [2]. Vertebral fractures (VF) have been associated with reduced quality of life, increased morbidity and mortality, and increased risk of future vertebral and non-vertebral fractures [3,4]. Prospective data from spinal radiographs of postmenopausal women with osteoporosis show that VF are frequently undiagnosed worldwide [5,6]. Because they are frequently undetected, VF may remain untreated, leading to height loss, kyphosis, chronic back pain, and back-related functional disability [7–11]. In addition, large numbers, which exceed 30%, of vertebral fractures are asymptomatic (aVF) [12–14].

Almost 23% of osteopenic women without a history of FFs have at least one aVF and the incidence increases to 54% in osteopenic women with a previous FF [13]. Therefore, identification of aVFs is of primordial importance especially in patients without densitometric osteoporosis, a common situation where experts agree to preconize treatment.

In addition to low bone density, other authors have documented the relation between height loss and vertebral/hip fractures in osteopenic/osteoporosis patients [15–17].

The FRAX® algorithm, developed by the WHO, is a tool for assessing the risk osteoporosis-related fracture. The output of the algorithm is the 10-year probability of hip fracture and the 10-year probability of major fragility osteoporotic fracture (vertebral, forearm, hip, wrist, or shoulder) [18–21]. The aims of the present study were to identify risk factors of aVFs in postmenopausal women with osteopenia at the femoral neck and to evaluate the association between the number of aVFs and the risk of major and hip osteoporotic fracture calculated with FRAX® algorithm.
2. Patients and methods

2.1. Study design

Subanalysis of an epidemiological, case-series study with data collected transversally in which the frequency of FRAX® risk factors was analyzed in postmenopausal women with a diagnosis of osteoporosis at the femoral neck and with or without prior history of FF (FROSPE study) [13]. This was a clinical practice study in which women were consecutively recruited among those visiting gynecology clinics. During a six-month period, each participating gynecologist selected ten consecutive women with densitometric osteoporosis at the femoral neck, and with (5 women) or without (5 women) prior clinical FF. Patients were required to sign a written informed consent form before their inclusion in the study. The study protocol was approved by the institutional review board of Hospital Clínico San Carlos (Madrid, Spain), and the study was conducted in accordance with the principles of the Declaration of Helsinki.

2.2. Patients

Postmenopausal (surgical or natural, for more than a year) women, with age ranging between 40 and 90 years, were eligible for the study. Patients that were currently participating in a clinical trial were excluded from the study.

2.3. Definition of fragility fracture and asymptomatic vertebral fracture

2.3.1. Definition of clinical FF

Prior FF was defined as a history of fracture in adult life that occurred spontaneously or a fracture caused by trauma that, in a healthy individual, would have not caused fracture (low impact fracture). FF included all those nonvertebral (all except for those in fingers and toes, face, and skull) and clinical vertebral fractures. The clinical diagnosis of a prior FF had to be documented in the patient’s medical records or through reports from emergency, trauma, or other services [13]. The concomitancy of an acute symptomatic episode plus the radiological confirmation was required in the case of clinical vertebral fractures.

2.3.2. Definition of aVF

aVFA was identified with a routine lateral X-ray of the thoracic and lumbar spine or vertebral fracture assessment, in conjunction with dual-energy X-ray absorptiometry (DXA), which was performed in all patients [22]. Those patients who already had a lateral X-ray made within the last year did not require another X-ray. The presence and the number of aVF were defined by investigator criteria based on the semiquantitative method developed by Genant et al., although the grade 1, 2 or 3 of the vertebral deformity was not registered [23]. Specialized radiologists in the participating centres performed diagnoses. Those images showing a poor vision at either the thoracic or the lumbar regions were repeated until vision was satisfactory.

2.4. Measurement of BMD and height loss

2.4.1. Measurement of BMD

BMD (g/cm²) was quantified with dual-energy X-ray absorptiometry (DXA) at the non-dominant proximal femoral neck and at the lumbar spine with the certified machines in use in the participating centres. Values were referred to the standard curves included in the respective machine software. The femoral neck was selected because this is the region used in the original characterization for osteopenia and osteoporosis by the WHO [1].

2.4.2. Measurement of height loss

Participants were asked to report their tallest height ever from memory. Participants’ height loss was calculated as tallest height ever minus current height.

2.5. Risk factors included in the analysis

2.5.1. Risk factors included in the FRAX® algorithm

The following risk factors were assessed: age; weight; height; prior FF, parental history of hip fracture; smoking status; use of corticosteroids; alcohol intake (three or more doses per day); rheumatoid arthritis; secondary osteoporosis, BMD (T score for the femoral neck).

2.5.2. Other factors analyzed

These factors included ethnicity, lifestyle habits (smoking, alcohol consumption and whether participants were sedentary; women were considered sedentary when their level of physical activity did not exceed the tasks usually performed by a housewife), family history of fractures (maternal history of fracture [apart from hip fracture, which was included in the FRAX® algorithm], fractures in first-degree relatives [parents and siblings]; height loss, T score (different location than femoral neck), date and type of menopause (surgical or natural), patient’s perception of her health status (excellent, very good, good, fair/poor), sight (excellent, very good, good, poor), and recent falls [number in the last year] [13].

2.6. Statistical considerations

For the description of continuous variables, the mean and standard deviation, the median and the interquartile range in the case of asymmetry and the maximum and minimum values observed were used. For the description of categorical variables, the number and percentage of patients per response category were used. The qualitative variables were compared using the chi-squared test and the quantitative variables using the Student t-test or variance analysis after study of variance homogeneity. Corresponding non-parametric tests were used in the event the established assumptions were not met. A multivariate logistic regression analysis was conducted to evaluate the factors associated with vertebral fractures. Adjusted OR and 95% confidence interval (CI) were calculated. For the statistical analysis, the SPSS version 15 for Windows statistical package was used. A level of statistical significance of \( p < 0.05 \) was used for all statistical tests performed.

3. Results

3.1. Patients’ characteristics

A total of 752 women were included in the study. Of those, 17 were excluded from the analysis because the BMD T-score was missing, and 7 due to incomplete X-ray/aVF data. Finally 728 patients that had completed X-ray and aVF data were analyzed. A total of 284 (39.0%) patients had aVF and 444 (61.0%) did not have any aVF. Remarkably, almost 30% of the population with no previous FF had detectable aVF. Table 1 shows the demographic characteristics of both populations, including FRAX® and non-FRAX® risk factors.