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# Vertebral fracture risk factors in postmenopausal women over 50 in Valencia, Spain. A population-based cross-sectional study

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ABSTRACT

*Purpose:* This study aims to estimate the prevalence of risk factors for osteoporotic vertebral fracture and analyze the possible associations between these factors and the presence of densitometric osteoporosis and prevalent morphometric vertebral fracture.
*Methods:* Data from a population-based cross-sectional sample of 804 postmenopausal women over the age of 50 years old living in the city of Valencia (Spain) were used. The women were interviewed to identify the prevalence of osteoporotic fracture risk factors and underwent a densitometry and a dorsolumbar spine X-ray.
*Results:* The most prevalent risk factors were densitometric osteoporosis (31.7%), history of parental hip fracture (19.4%), hypoestrogenism (19%), and body mass index (BMI) $\geq$30 kg/m$^2$ (35.2%). After adjusting for all covariables, densitometric osteoporosis was associated with increased age [odds ratio (OR)$_{65–69\ years}$: 2.84, 95% confidence interval (CI): 1.75–4.61; OR$_{70–74\ years}$: 4.01, 95% CI: 2.47–6.52; OR$_{75+\ years}$: 5.96, 95% CI: 3.27–10.87] and inversely associated with high BMI (OR$_{25.0–29.9}$: 0.51, 95% CI: 0.34–0.76; OR$_{\geq 30}$: 0.30, 95% CI: 0.19–0.46). Morphometric vertebral fracture was associated with age (OR$_{65–69\ years}$: 2.04, 95% CI: 1.03–4.05; OR$_{70–74\ years}$: 4.05, 95% CI: 2.11–7.77; OR$_{75+\ years}$: 8.43, 95% CI: 3.97–17.93), poor educational level (OR: 1.70, 95% CI: 1.06–2.72) and with densitometric osteoporosis and BMI $\geq$30 kg/m$^2$ (OR: 3.35, 95% CI: 1.85–6.07).
*Conclusions:* The most prevalent osteoporotic fracture risk factors were having a high BMI and the presence of densitometric osteoporosis. A higher risk of morphometric vertebral fracture in women with both low bone mineral density and high BMI was found. This association, if confirmed, has important implications for clinical practice and fracture risk tools. We also found a higher risk in women with a poor educational level. More attention should be addressed to these populations in order to control modifiable risk factors.


## Introduction

Osteoporosis is a multi-factorial skeletal disease characterized by low bone mass and a deterioration of the macro and microarchitecture of bone tissue, which leads to increased bone fragility and susceptibility to fracture. Osteoporosis is a silent disease, yet has a major clinical impact because of its association with an increased risk of fracture. Whereas hip fractures are the most serious and costly, vertebral fractures are the most common form of osteoporotic fractures, with population prevalence estimates in Spain between 20% and 30% in post-menopausal women over the age of 50 years old [1,2]. Studies in other countries show figures between 35% and 50% [3–5], prevalence being highly dependent on the definition of vertebral fracture (clinical, morphometric, radiological degree of deformity) and the sample used, as prevalence increases with age, patients recruited in specialist clinics, and in patients with rheumatoid arthritis, lupus and other diseases.

While fractures of the vertebrae are underdiagnosed and undertreated [6–8], they often occur earlier than hip fractures in disease progression, and vertebral fractures are associated with an increased risk of both future vertebral and nonvertebral fractures [9–11]. Hence, 20% of women who have had a recent vertebral fracture will have a new fracture within a year [12]. Having had one or more vertebral fractures has been related to lower survival rates [13,14], and vertebral fracture also causes chronic back pain, limitations in daily living activities and poorer quality of life [15–17].

Today it is widely accepted that in addition to bone mineral density (BMD), several clinical risk factors are strongly related to osteoporotic fractures, and in recent years several risk assessment tools have been proposed for estimating the probability of osteoporotic fractures and

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for identifying high-risk patients [18,19]. Risk factors used in these assessment tools include, among others, low BMD, personal history of previous osteoporotic fracture, parental history of hip fracture, low body mass index (BMI), regular alcohol intake, smoking, sedentary life, personal history of falls, low calcium intake, early menopause, hypogonadism, some osteopenic diseases and use of glucocorticoids.

While the relationship between the presence of these risk factors and the incidence of hip fracture or major osteoporotic fracture (hip, forearm, clinical vertebral) has been widely studied [20–22], the relationship with the presence of morphometric vertebral fracture is less well-known [11,23,24], in part because of the logical scarcity of surveys performing systematic spine radiographs in general population samples. Although the different osteoporotic fractures share several common risk factors, we could also expect some differences according to location, both in the importance of the factors and in the strength of their association with the risk of each specific fracture.

The FRAVO study is a population-based cross-sectional study conducted in Valencia (Spain), primarily designed to estimate the prevalence of densitometric osteoporosis and vertebral fracture in postmenopausal women [1]. All participating women were interviewed to identify the prevalence of osteoporotic fracture risk factors, and they underwent a densitometry and a dorsolumbar spine X-ray. We used data from the FRAVO study to describe the prevalence of risk factors for osteoporotic vertebral fracture among post-menopausal women over 50 years old living in Valencia (Spain), and to analyze the possible associations between these factors and the presence of densitometric osteoporosis and prevalent morphometric vertebral fracture.

## Methods

### *Design*

Population-based cross-sectional study conducted between February 2006 and March 2007, primarily designed to estimate the population prevalence of vertebral fracture and densitometric osteoporosis.

### *Population and sample*

The study population was post-menopausal women over the age of 50 years old living in the city of Valencia, Spain, excluding women with cognitive impairment, physical impediment preventing a woman from going to the radiology center by her own means, race other than Caucasian and unwillingness to participate in the study. The methods of the FRAVO study have been fully described elsewhere [1]. Briefly, 1758 women were selected through an age-stratified (50–54, 55–59, 60–64, 65–69, 70–74 and 75+ years) random sample from the residents of Valencia, and invited to participate in the study. Only 1314 women confirmed receipt of the invitation letter (74.7%), and of these 76 presented at least one exclusion criteria, 371 declined to participate and 43 did not keep their appointments for the examinations, leaving 824 women participating in the study. In 19 cases the spine X-ray or the densitometry was not available.

### *Variables and definitions*

Information about socio-demographic characteristics, lifestyle and risk factors for vertebral fracture was collected using an interviewer-administered questionnaire. Among other variables, it included the subject's age, place of birth, educational level (no studies, primary, secondary/university), weight and height, stratifying BMI as low (<20 kg/m$^2$), normal (20.0–24.9 kg/m$^2$), overweight (25.0–29.9 kg/m$^2$) and obesity (30 kg/m$^2$ or more), age of menopause, hypoestrogenism (menopause before 45 years old, and primary or secondary amenorrhea over one year), history of parental hip fracture, prior non-vertebral osteoporotic fracture, treatment with glucocorticoids (for at least 3 months in the previous year), other drugs that decrease bone mass (lithium, anticonvulsants, high dose thyroxin, immunosuppressive treatment), smoking (≥20 cigarettes/day), alcohol intake (≥17 IU/week; an international unit-IU of alcohol is defined as 10 ml or approximately 8 g of ethanol), dietary calcium intake (<500 mg/day), and other secondary causes of osteoporosis (gastrectomy, bowel resection, inflammatory bowel disease, thyroidectomy, diabetes mellitus, chronic liver disease, chronic obstructive pulmonary disease, rheumatoid arthritis, transplantation, chronic kidney failure).

Spinal radiographs were performed using standardized techniques and two radiologists, blind to all data concerning the patients, performed the semiquantitative evaluation of the radiographs using the Genant method [25] to standardize the diagnosis of fractures. Each of the vertebrae, from T4 to L4, was classified based on Genant's score. Densitometric examinations were performed with two calibrated densitometers (dual-energy X-ray absorptiometry or DXA central) for the lumbar spine and the femoral neck. Using the World Health Organization (WHO) osteoporosis classification criteria based on T-scores [26], BMD results were classified as normal, osteopenia or osteoporosis.

Using the FRAX® tool calibrated for Spain (www.shef.ac.uk/FRAX/index.htm), we estimated the 10-year risk of major osteoporotic fracture (clinical spine, hip, forearm or humerus fracture) and the 10-year risk of hip fracture for each patient [27]. Data in the FRAX® web were introduced by the research team and calculations were based on the gender, age, BMI, personal history of previous fracture (with and without taking into account the results of the study X-ray exploration), parent history of fracture, current smoking, use of glucocorticoids, rheumatoid arthritis, other osteopenic diseases, alcohol intake and BMD measurement. In accordance with the FRAX® recommendations, missing values were considered as normal.

### *Ethical aspects*

All of the participating women were informed of the study's characteristics and risks (basically, those associated with exposure to X-rays), and all gave signed informed consent prior to their enrolment. The study was approved by the Ethics Committee for Clinical Research of the primary care departments in Valencia and Castellon. Because the study data could be clinically useful, we communicated the results of the densitometric and X-ray examinations to the patients, with a recommendation to visit their primary care doctor when pertinent.

### *Analysis*

First, we present the prevalence estimates of women who present the different risk factors as means or percentages, with their corresponding 95% confidence intervals (95% CI). 95% CI were calculated using the normal approximation for means and the exact binomial method for proportions. In order to provide population estimates, the figures in the sample were weighted for age according to the population distribution in Valencia in 2006 [28]. Bivariate logistic regression models were carried out to estimate the bivariate associations between risk factors and densitometric osteoporosis or prevalent morphometric vertebral fractures.

Finally, multivariable logistic regression models were built for both dependent variables (densitometric osteoporosis and morphometric vertebral fracture). We constructed an initial model with all associated variables in the bivariate model and the clinically relevant ones and used backward-forward stepwise methods to remove non-significant variables (with a removing probability of 0.10 and an entry probability of 0.05). The goodness-of-the-fit was evaluated using the C-Statistic (the area below the Receiver Operating Characteristic — ROC curve) for discrimination and the Hoshmer–Lemeshow test for calibration. High alcohol intake was not analyzed in the bivariate or multivariate analysis due to its very low prevalence (n = 3); in the multivariate analysis, and because of the presence of collinearity, BMD was introduced as a dichotomic variable (osteoporosis vs. normal and osteopenic). All