Bone 45 (2009) 808–813

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Bone mass, size and previous fractures as predictors of prospective fractures in an osteoporotic referral population

Fredrik Eklund [a], Anna Nordström [a,b], Ulf Björnstig [c], Peter Nordström [b,d,*]

[a] Department of Surgical and Perioperative Sciences, Sports Medicine, Umeå University, Umeå, Sweden
[b] Department of Community Medicine and Rehabilitation, Rehabilitation Medicine, Umeå University, Umeå, Sweden
[c] Department of Surgical and Perioperative Sciences, Surgery, Umeå University, Sweden
[d] Department of Community Medicine and Rehabilitation, Geriatrics, Umeå University, 90185 Umeå, Sweden

ARTICLE INFO

Article history:
Received 22 February 2009
Revised 27 May 2009
Accepted 23 June 2009
Available online 30 June 2009

Edited by: R. Recker

Keywords:
BMD
vBMD
Bone area
Fractures
Osteoporosis
Proximal femur

ABSTRACT

The influence of bone mass, bone size and previous low energy fractures upon prospective fractures has not been investigated in a referral osteoporotic population. We investigated the association between bone mass, bone size, previous fractures, body constitution, and prospective validated fractures in 5701 women and 1376 men, aged 30 years and older. Bone mass measurements of the femoral neck were collected at a single study center in Sweden. Most of the subjects were measured on suspicion of osteoporosis. Data on validated low energy retrospective and prospective fractures in the cohort were collected from the corresponding health care district. Bone mineral density (BMD, g/cm^2) and estimated volumetric BMD (vBMD, g/cm^3) were shown to be good independent predictors for fracture in both women and men (Hazard ratio per standard deviation decrease (HR) = 1.27–1.52, $p<0.05$). Bone size did not predict prospective fractures in either sex (HR = 0.91–0.99, $p>0.05$), and bone size completely explained the higher BMD in men than in women. In women, retrospective low energy fractures (HR = 1.78, $p<0.001$) and height (HR = 1.02, $p = 0.006$) were additional independent predictors of osteoporotic fractures after adjusting for age and BMD. In conclusion, we show that in a large osteoporotic referral population, age, BMD and previous fractures are independent predictors of prospective low energy fractures. These results add additional strength to the recent change in focus towards a multivariate analysis when assessing the future risk of fracture.

Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue that leads to an increased fracture susceptibility [1]. The resulting low energy fractures are a major public health concern, causing great suffering to those afflicted and placing a heavy burden on society and the healthcare system [2]. The incidence of osteoporosis is highest in women, but the incidence in men is expected to triple over the next 50 years [3]. Identifying persons at risk of sustaining osteoporotic fractures is crucial to their prevention.

The definition of osteoporosis widely used in clinics and clinical research was created by the World Health Organization (WHO), and was developed for Caucasian postmenopausal women. This definition was based solely on the measured bone mineral density (BMD, g/cm^2) [4]. However, BMD is a rather blunt risk factor for future fractures, as it has a low sensitivity and does not account for other risk factors such as previous fractures or falls [5]. Another very important factor not taken into account in the diagnosis of osteoporosis is age, a factor that predicts future fractures independently of BMD, making it likely to underestimate the risk of fractures in older patients and overrate the risk in younger patients [6]. Also, bone size could influence the risk of fractures. A larger bone diameter would in theory increase the moment of inertia, and thereby decrease the risk of fractures. However, the results from previous prospective studies are not conclusive on this matter [7–9].

Therefore, to better predict the risk of fractures, the WHO has recently developed a fracture risk assessment tool, FRAX, based on the results of a number of population-based studies from Europe, Australia, North America, and Asia. FRAX utilizes a number of clinical risk factors (CRFs) for fracture risk assessment, either with or without bone mineral density data. To our knowledge, these factors have not been investigated in a high-risk population, such as an osteoporotic referral population.

Thus, the aim of the present study was to investigate the relationship between bone mass, bone size, weight, height, age, previous fractures and fracture risk in men and women of different ages in an osteoporotic referral population.

Material and methods

Since 1991, bone mineral density (BMD, g/cm^2) and fat mass have been measured using dual-energy x-ray absorptiometry (DXA) at the

* Corresponding author. Fax: +46 90 135 692.
E-mail address: peter.nordstrom@idrott.umu.se (P. Nordström).

8756-3282/$ – see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.bone.2009.06.024

Sports Medicine Unit, in Umeå, Sweden. By the 31st of December 2006, BMD of the femoral neck was measured and validated in a total of 7834 subjects, consisting of 6273 women and 1561 men between 30 and 95 years of age. Of these subjects, 5701 women and 1376 men could be tracked to a fracture, death or were still living in the same health care district as of the end of the study (August 1st 2006). In the current study, data from these subjects was analyzed with respect to future fractures or previous fractures. Before BMD measurement, all subjects had body height and weight measured in light clothing. Height was measured to the nearest centimeter using a wall-mounted stadiometer and weight was measured to the nearest kilogram using a digital scale.

The most common reason for measurement of BMD was the presence of factors related to an increased risk of osteoporosis. During 2005, a total of 984 subjects had their femoral neck BMD measured at the Sports Medicine Unit. The most common causes of admission were that the subject had sustained a previous fracture (28%), a general suspicion of osteoporosis (16%), corticosteroid therapy (16%) and rheumatoid diseases (16%). Nineteen percent (19%) of subjects were not admitted, but were volunteers involved in different research projects.

Measurements of bone mass

Bone mineral content (BMC, grams), bone area (cm^2) and BMD, were measured in the femoral neck using dual-energy x-ray absorptiometry (DXA). The width of the neck box was standardized to 15 mm. To estimate the volumetric bone mineral density (vBMD, g/cm^3) of the femoral neck, it was assumed that this site is cylindrical in shape. The vBMD was calculated by dividing the BMC by the estimated volume [10]. From 1991 to 1998, a Lunar DPX-L machine was used, and from 1998 onward a Lunar IQ (GE-Lunar, GE Healthcare, USA) was used. The coefficient of variation (CV, SD/mean) was determined by scanning one person several times on the same day, with repositioning between each scan. Accordingly, the CV values were approximately 1% for the different estimates of femoral neck BMD and BMC. Calibrations of the equipment were performed each day using a standardized phantom to detect drifts in the measurements and to test machine functions. The equipment was also evaluated regularly using a spine phantom. No drifts in BMD were detected. The same technician performed more than 90% of all the scans during the 15 years of follow-up. The two different machines were also cross-calibrated by scanning two persons several times with both machines on the same day. Based upon this calibration, 0.1 g was subtracted from all femoral neck BMCs and 0.04 cm^2 was added to all femoral neck areas performed in the Lunar DPX-L.

Fracture data

All subjects admitted to the Emergency Department at the University Hospital of Northern Sweden, Umeå, since 1985, have been registered in an *Injury database*. This database has been digitized since 1993, and a total of about 30,000 fractures have been registered and validated [11]. These fractures cover the same health care district as where the BMD measurements were performed. In the present study, both retrospective and prospective fracture data were collected from this database and matched to location. Fractures resulting from high-energy trauma such as vehicle-related accidents and falls from one level to another were excluded.

The study protocol was approved by the Ethical Committee of the Medical Faculty, Umeå University, Umeå, Sweden.

Statistical analysis

Differences between subjects with and without prospective fractures were investigated using a Student's *t*-test for independent samples. To investigate the independent relationship between the different variables and prospective fractures, Cox regression analysis was used. The study endpoint was 2006-08-01, date of fracture or date of death, whichever came first. Date of death was collected through registers. Receiver–operator curves were compared for fractures in relation to osteoporosis, previous fractures, osteoporosis or previous fractures, and osteoporosis or previous fractures and age as a continuous variable. The incremental (likelihood ratio) χ^2 values were compared to estimate significant differences. For this purpose, the independent variables linear predictor scores were used (X^x Beta), i.e., the sum of the product of mean-centered covariate values and their corresponding parameter estimates for each case. All statistical tests were two-sided. The SPSS package (version 14.0; SPSS Inc., Chicago, IL, USA) and SAS (version 9, SAS Institute Inc., Cary, NC, USA) were used for the statistical analyses. The significance level was set to 0.05.

Results

In the present study, we analyzed a number of risk factors in relation to the prospective risk of fractures in a cohort consisting of 5701 women and 1376 men. The total follow-up time of the cohort was 38,084 person–years, or a mean of 5.4 years. During that time, 666 women and 106 men had at least one validated prospective fracture. These fractures included only low energy fractures. The type and number of first time prospective and retrospective fractures included for men and women is presented in Table 1. A total of 120 women and 11 men also had at least one prospective hip fracture (data not shown). The relationship between different bone variables and whether or not the subject sustained a prospective fracture is illustrated in Figs. 1A–C.

Table 2 shows the different parameters of bone mass and body constitution in relation to whether subjects experienced a prospective fracture or not during the follow-up time. Both men and women who sustained any osteoporotic fracture during the follow-up period were

Table 1
Type and number of prospective and retrospective low energy fractures in 5701 women and 1376 men during a mean of 5.4 years of follow-up.

	Women ($n=5701$)		Men ($n=1376$)	
	(n)	(%)	(n)	(%)
Prospective fractures				
Head	6	0.9		
Clavicula	10	1.5	1	0.9
Thorax/Ribs	37	5.6	15	14.2
Spine	43	6.5	9	8.4
Pelvis	14	2.1	5	4.7
Shoulder/Humerus	78	11.7	14	13.2
Elbow	22	3.3	1	0.9
Forearm/Wrist	189	28.4	11	10.4
Hand/Fingers	35	5.3	10	9.4
Hip	82	12.3	11	10.4
Femur	11	1.7	3	2.8
Knee	23	3.5	3	2.8
Tibia	16	2.4	7	6.6
Foot joint	59	8.9	11	10.4
Foot/Toes	41	6.2	5	4.7
Retrospective fractures				
Head				
Clavicula	11	1.0	4	2.6
Thorax/Ribs	39	3.4	7	4.6
Spine	51	4.4	20	13.2
Pelvis	17	1.5	3	2.0
Shoulder/Humerus	107	9.3	12	7.9
Elbow	23	2.0	2	1.0
Forearm/Wrist	512	44.4	35	23.0
Hand/Fingers	41	3.6	13	8.6
Hip	95	8.2	21	13.8
Femur	7	0.6	3	2.0
Knee	27	2.3	3	2.0
Tibia	46	4.0	7	4.6
Foot joint	118	10.2	15	9.9
Foot/Toes	59	5.1	7	4.6