Men suffer vertebral fractures with similar spinal T-scores to women

L. del Rio[1], P. Peris[2], L. Jover[3], N. Guañabens[2], A. Monegal[2], S. Di Gregorio[1]

[1]CETIR Centre Mèdic Barcelona; [2]Rheumatology Service, Hospital Clínic, University of Barcelona, IDIBAPS; [3]Public Health Department, University of Barcelona, Spain.

Abstract

Objective

To evaluate the applicability of the WHO densitometric criteria for the diagnosis of spinal osteoporosis in men and to compare it with women with vertebral fractures, as well as to analyze the role of vertebral dimensions in the development of spinal fractures.

Methods

For these purposes we analyzed, using DXA, vertebral projected area and lumbar bone mineral density (BMD), as well as T and Z-scores in lumbar spine in a cohort of 66946 individuals; 2556 of these subjects had one or more atraumatic vertebral fracture (396 men and 2160 postmenopausal women).

Results

Men and women with fractures showed significantly lower mean BMD, T-score and Z-score values than individuals without fractures while vertebral dimensions were similar in both groups of patients. When comparing men and women with vertebral fractures, the former showed a significantly greater projected area (46.89±5.5 vs. 39.13±4.6 cm^2 $p<0.001$) and lumbar BMD (0.991± 0.21 vs. 0.938± t0.19 g/cm^2 $p<0.001$). However, the median lumbar T-score values were similar for both sexes (-2.3 in women vs. -2.2 in men; p: NS). In addition, a similar percentage of men and women with vertebral fractures showed T-score values <-2.5 in the lumbar spine (44% vs. 46%, p=NS).

Conclusion

We conclude that although men with vertebral fractures have greater vertebral dimensions and BMD than women, the lumbar T-scores are similar. Therefore, it seems reasonable to adopt the same T-score values for the diagnosis of osteoporosis in men and women.

Key words

Bone densitometry, vertebral fractures, T-score, male osteoporosis, osteoporosis.

Luis del Rio, MD; Pilar Peris, MD; Luis Jover, PhD; Nuria Guañabens, MD; Ana Monegal, MD; Silvana Di Gregorio, MD.

Please address correspondence to: Luis del Rio, CETIR Centre Mèdic, Londres 6, 08029 Barcelona, Spain. E-mail: ldelrio@cetir.es

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Introduction

While osteoporosis in women has been well documented, osteoporosis in men has received much less attention, although at present it is increasingly recognized as a problem in clinical practice. In fact, up to 30% of hip fractures occur in men, and a previous multicenter European study has shown that the prevalence of vertebral deformities is similar in both sexes (1). In 1994, the World Health Organization (WHO) formulated criteria for the diagnosis of osteoporosis based on the relationship between bone mineral density (BMD), expressed as T-score, and the risk of fracture, where a value for BMD -2.5 SD or more below the young adult average value would be indicative of osteoporosis (2, 3). However, the WHO proposals apply only to white postmenopausal women. At present, the usefulness of these criteria for the diagnosis of osteoporosis in men has not yet been established, and studies comparing BMD differences between genders with fractures are scarce (4).

Nevertheless, many of these studies showed a relationship between low BMD and risk of fracture in men (5-10). Likewise for women, the risk of having a new vertebral fracture is increased two-fold for each decrease in 1 SD (in lumbar spine BMD) below the normal age-matched mean BMD (5, 11, 12), whereas the relative risk for hip fracture was found to be three-fold (1.7 - 5.4) for each SD decrease in femoral neck BMD (6); the increase in the fracture risk is observed as much with young women as with elderly women (13). These data indicate that for both men and women, low BMD is an important predictor of incident vertebral fractures (14). In addition, Selby *et al.* (15) reported in a small study that men and women presented vertebral fractures with similar lumbar T-scores.

Different authors have proposed various BMD criteria for the diagnosis of osteoporosis in men, *i.e.*, using a value of BMD -2.5 SD or more below the young adult mean (T-score ≤ -2.5 for men) (16) or for practical purposes, considering a value of Z-score < -1 as an indication for therapy (11). Although the current status of the approach to the diagnosis of osteoporosis in men by BMD measurements is not totally established, it seems reasonable that until new data are available, gender-specific criteria should be used to select those men who would need control and treatment (17). Indeed recently, the International Society for Clinical-Densitometry (ISCD) Consensus recommended using a T-score below -2.5 (from male reference database) for the diagnosis of osteoporosis in men 65 years of age and older (18).

Moreover, it should be taken into account that men have bigger bones than women and bone size is an important determinant of skeletal strength. In fact, it has been previously shown that the smaller vertebral bodies of women suffer higher mechanical stress than those of men. These biomechanical disadvantages may contribute to the increased risk of vertebral fractures (19, 20).

The aim of this study was to evaluate the applicability of the WHO criteria for the diagnosis of spinal osteoporosis in men and to compare it with women. In addition, we studied the role of vertebral size in the development of vertebral fractures. For these purposes, we analyzed vertebral dimensions, BMD, as well as T- and Z-scores in lumbar spine in a large cohort of men and women with atraumatic vertebral fractures and in individuals without fractures.

Patients and methods

The study was carried out on 66642 individuals who were attending the Bone Metabolic Unit at our medical center for bone mass measurements; 2556 of these subjects had one or more vertebral fracture (396 men and 2160 postmenopausal women: aged 61±11 *vs.* 63±10 years), whereas the remaining 64086 individuals (61599 postmenopausal women and 2487 men: aged 56±8 *vs.* 57±3 years) did not have vertebral fractures.

All participants were investigated for fragility of skeletal fractures. Non-vertebral fractures were evaluated by means of a self-reported personal history of fracture, whereas vertebral fractures were recorded in all patients from the medical records. Since vertebral fractures associated with corticosteroid

treatment and alcoholism may occur with higher bone mass (21, 22), participants with vertebral fractures associated with corticosteroid treatment or with increased alcohol intake (> 100 gr alcohol/day) were not included in the study. Subjects on hormone replacement therapy, raloxifene or on bisphosphonate treatment were not used for the analysis.

A questionnaire was administered to all individuals by a trained nurse, which included details on previous skeletal fractures, previous diseases (especially related to processes which can affect bone metabolism), toxic habits (alcohol and tobacco consumption), physical activity, drug therapies and calcium intake.

In addition, height and weight were recorded in all patients. Bone mineral density (BMD) of the lumbar spine (L2-L4) was measured in all subjects by dual x-ray absorptiometry using a bone mineral analyzer DPX-L (Lunar Radiation Corporation, Madison WI) and was expressed in g/cm^2. The *in vitro* and *in vivo* coefficients of variation were 0.5% and 0.8%, respectively. The T-scores and Z-scores were calculated on the basis of BMD measurements performed in 832 healthy control subjects (308 male/524 female) between 20 and 79 years old. All subjects were of Mediterranean origin and were residents in the same geographical area. T-scores were obtained from individuals aged 20-39 years. In cases with one or more fractured vertebrae of the lumbar spine, only results from the remaining unfractured vertebrae were analyzed.

Osteoporosis was considered as a value for BMD that was -2.5 standard deviations or more below the young adult mean value (T-score < -2.5).

Vertebral dimensions were analyzed using dual-energy x-ray absorptiometry (DXA) as previously described by Vega *et al*. (23). In all individuals, measurements of vertebral projected area in L2-L4 were obtained, and the results were expressed in cm^2.

Statistical analysis

Between-group comparisons were performed by *t*-test for unpaired data. Due to the population distribution, the T-score was analyzed using the median. The proportion of fractured individuals with T-scores ≤ -2.5 was calculated, and the chi-square and/or Fisher exact tests were used to compare proportions between groups. The cumulative relative frequency of vertebral fracture was determined for each value of BMD and T-score and Z-score values, as well as for vertebral dimensions (width, height and area). This relative frequency represents the probability of vertebral fracture being present at or below that level of BMD or vertebral size. The Logit transformation of the cumulative relative frequency [In(frequency/1-frequency)] was used to analyze the results by linear regression, and the slope of this line reflected changes in the scatter of the distribution (15).

The subsequent analyses consider individuals with vertebral fractures, irrespective of the number of fractured vertebrae. Results are expressed as mean, median and standard deviation (SD), or as the 25-75-percentile intervals reference. *P*-values less than 0.05 were considered to be significant in hypothesis tests. Statistical analysis was undertaken using SPSS v 11.0

Results

Table I shows the distribution of individuals according to age, BMD and T-score and Z-score values, as well as vertebral dimensions. Men with vertebral fractures were slightly younger than women (61 ± 11 *vs*. 63 ± 10; $p<0.0001$). In addition, patients with vertebral fractures were older than patients without fractures (Table I). Mean BMD, T-score and Z- score values were significantly lower in men and women with vertebral fractures than in individuals without fractures, only women with vertebral fractures showed lower vertebral dimensions than the non fractured but the values were very close (Table I).

When comparing men and women with vertebral fractures, the former showed slightly although significantly greater mean values in vertebral dimensions ($p<0.0001$), BMD ($p<0.0001$) and lumbar T-score ($p<0.046$) (Table I). However, the median lumbar T-score values

Table I. Clinical characteristics, bone mineral density and vertebral dimensions from individuals with and without vertebral fractures (Mean ± SD).

	Men with vertebral fractures (n=396)	Women with vertebral fractures (n=2160)	Men without vertebral fractures (n=2487)	Women without vertebral fractures (n=61599)
Age: years	61.03 (11.46) 0.000* 0.000***	63.44 (9.88) 0.000***	57.07 (13.19) 0.000***	56.30 (8.87)
Weight: kg	72.82 (12.64) 0.000*	65.35 (12.65)	72.53 (11.81) 0.000**	65.46 (10.53)
Height: cm	165.23 (7.23) 0.000* 0.007***	153.10 (6.55) 0.000***	166.31 (7.36) 0.000**	155.37 (6.22)
Lumbar Spine BMD g/cm^2	0.991 (0.214) 0.000* 0.000***	0.938 (0.192) 0.000***	1.052 (0.206) 0.000**	1.032 (0.180)
T-score	-2.0 (1.73) 0.046* 0.000***	-2.17 (1.60) 0.000***	-1.46 (1.67) 0.01**	-1.38 (1.50)
Z-score	-1.45 (1.60) 0.000* 0.000***	-0.63 (1.57) 0.000***	-0.98 (1.57) 0.000**	-0.26 (1.38)
Vertebral projected area: cm^2	46.89 (5.54) 0.000*	39.13 (4.63) 0.000***	46.70 (5.32) 0.000**	39.97 (4.16)

p^* : Differences between men and women with vertebral fractures
p^{**}: Differences between men and women without vertebral fractures
p^{***}: Differences between fractured and non-fractured patients compared by gender.

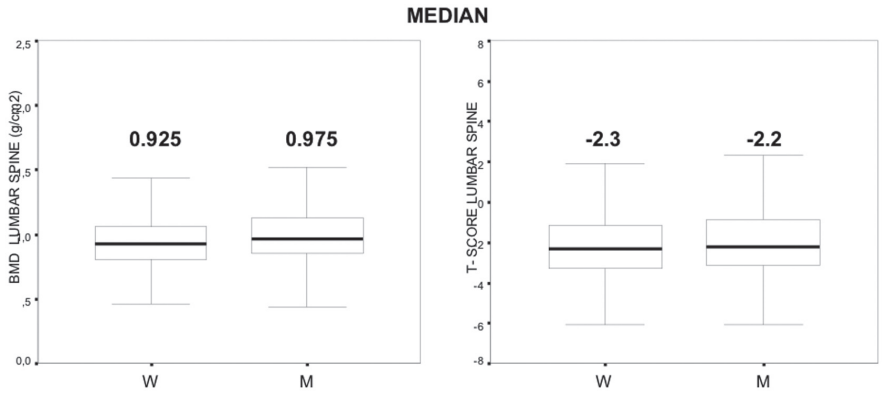

Fig. 1. Plots showing the median values (percentile 50) and 25-75 percentiles for lumbar BMD and lumbar T -score in men and women with vertebral fractures.

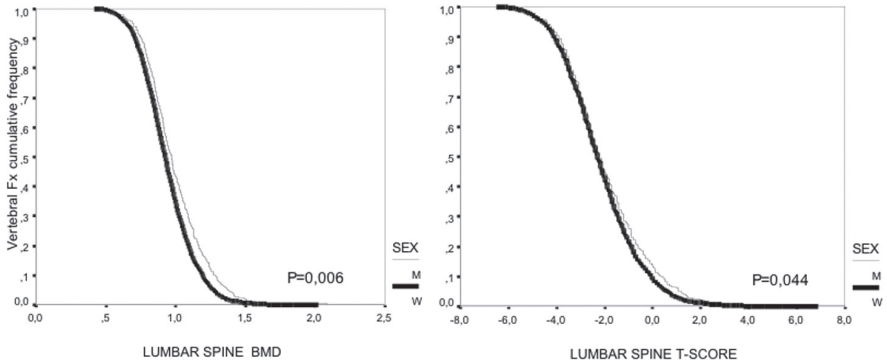

Fig. 2. Relationship between vertebral fracture cumulative frequency and lumbar BMD and T-score in men and women. The vertebral fracture cumulative frequency was higher in women with lower BMD, whereas was similar in both sexes when related to lumbar T-scores.

were similar in both groups of patients (men: -2.3 *vs*. women: -2.2, p = NS) (Fig. 1). Overall, 46% of women and 44% of men with vertebral fractures showed T-score values < -2.5 in the lumbar spine, $p = 0.657$ (NS).

For both genders there was a sigmoid relationship between the cumulative frequency of vertebral fracture and bone mass, expressed as BMD or T-score values (Fig. 2). Lower BMD and T-scores were associated with an increased percentage of cumulative vertebral fractures with a similar trend in both sexes. The curves were very close in men and women for both BMD and lumbar T-scores (Fig. 2). When these results were expressed as the Logit of vertebral fracture frequency, a significant correlation between the Logit of fracture frequency and BMD was obtained in both sexes (Fig. 3). The slopes of the regression lines were slightly different between sexes, indicating that there is a gender-based difference in the distribution of bone mass in fractured patients.

Discussion

The results obtained in this study of a large cohort of individuals, show that men and women with vertebral fractures present low-grade differences in T-score values. In addition, almost half of fractured patients, men and women, showed a lumbar T-score lower than -2.5 and the cumulative percentage of vertebral fracture according to T-score was very close in both genders. Since the approach to the diagnosis of osteoporosis by BMD is to define a cut-off for BMD that captures most patients with osteoporotic fracture, our data suggest that the current WHO criteria for osteoporosis may also be applied to men (2).

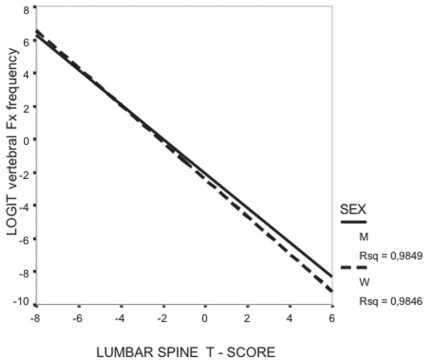

Fig. 3. Relationship between the Logit transformed vertebral fracture cumulative frequency and the lumbar T-score in men and women. No significant differences in cumulative vertebral fracture frequency can be observed between sexes when expressed by lumbar T-score.

Although in men with vertebral fractures, the mean lumbar T-score was slightly higher than that observed in fractured women, the values were very close, nearly -2, and the median T-score values were similar in both sexes (-2.3 in women *vs*. -2.2 in men) with slightly lower BMD measurements in women, of the order of 0.05 g/cm^2 less. Our results are in accordance with previous data reported in smaller cohorts showing comparable lumbar T-score values for men and for women with vertebral fractures (15). Moreover, in the present series the relationship between the cumulative frequency of vertebral fractures and bone mass, expressed as BMD or T-score, was similar in both sexes. It is possible that the selection of our patients could have contributed to these results, since traumatic vertebral fractures, those associated with the use of glucocorticoids and with alcohol abuse, were not included in the study, factors that can be associated with the development of fractures with higher BMD (21, 22).

In the present study, vertebral size was not related to vertebral fractures. Although women with vertebral fractures showed smaller vertebral projected area than those without fractures, the mean values of vertebral projected area present low-grade differences in both groups of patients. The high number of individuals included in our series could partly explain this finding. Thus, studies with very large samples may detect significant differences in non-relevant differences. It is well known that bone size is another determinant of skeletal strength. Thus, Gilsanz *et al*. reported (19) that the cross-sectional areas of vertebral bodies in adult women were 25% smaller than those of healthy men; as a consequence, the estimated mechanical stress in vertebral bodies was

30%-40% greater in women for equivalent applied loads. Some authors have considered the reduction in vertebral width as a probable contributor to vertebral fractures in men, indicating that some men with fractures would have failed to achieve full bone size during maturity or ageing (23, 24). In addition, smaller bones have been described as a predisposing factor for developing stress fractures in male recruits (25). Although our data did not support these findings, we cannot discard this hypothesis, since other methods such as computed tomography would be more accurate for evaluating vertebral dimensions.

Despite the advantages of the large sample size, this study has some weaknesses. There is a selection bias in our study population, because participants were referred for osteoporosis testing. Therefore BMD values are probably lower than in the general population. However, this is not likely to affect the results of the BMD and structural abnormality data in patients with vertebral fractures. Additional limitations of the present study are the inability to differentiate the patients who suffered clinical vertebral fractures from those with asymptomatic vertebral fractures and the absence of the evaluation of the number of vertebral fractures. Although it is well known that subjects with vertebral fractures have an increased risk of new vertebral fractures, BMD is an independent risk factor and our aim was to identify densitometric cut-off values in order to evaluate the risk of fracture. Finally, the selection of the patients with vertebral fractures could be criticized since vertebral fractures were assessed by reviewing the medical reports. However, the large number of individuals included in the study, as well as the consistent results observed in both groups of patients in both genders suggests that this selection criteria was fairly selective.

In conclusion, this study suggests that, as a conceptual definition, it is appropriate to apply the same T-score as a cut-off value for the diagnosis of osteoporosis in both men and postmenopausal women.

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