Frequency of Osteoporosis in 187 Men with Rheumatoid Arthritis Followed in a University Hospital

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ABSTRACT. ***Objective.*** Although there is relevant information on frequency of osteoporosis in women with rheumatoid arthritis (RA), data about male patients are limited. We evaluated the frequency of osteoporosis in a group of Spanish men with RA followed in a university hospital.

Methods. From the database of our bone densitometry unit, we searched for men with RA evaluated between January 1991 and December 2004 and identified 187 patients, 156 of whom were older than 50 years. Previously recorded demographic, disease, and treatment-related variables were collected. Bone mineral density (BMD) was measured by dual x-ray absorptiometry (DEXA). Osteoporosis was defined according to the criteria of the World Health Organization (WHO), recommended for postmenopausal Caucasian women, as a T score ≤ –2.5 SD, and the International Society for Clinical Densitometry (ISCD), which indicates the same diagnostic threshold, but only in men over age 50 years.

Results. BMD was lower than in the general population in both lumbar spine [Z score –0.41 ± 1.00 (95% CI –0.55 to –0.26)] and femoral neck [Z score –0.46 ± 0.95 (95% CI –0.60 to –0.31)]. When the WHO threshold for postmenopausal women was applied, frequency of osteoporosis was 13% at lumbar spine, 12% at the femoral neck, and 21% in at least one of the evaluated sites. When ISCD criteria were applied, the frequency of osteoporosis was 13%, 14%, and 23%, respectively.

Conclusion. Frequency of osteoporosis in men is considerably lower than that traditionally established in women with RA, independent of the diagnostic criteria applied. (J Rheumatol 2006;33:1472–5)

Key Indexing Terms:
RHEUMATOID ARTHRITIS OSTEOPOROSIS MALE DENSITOMETRY

A strong relation exists between bone mineral density (BMD) measured by dual energy x-ray absorptiometry (DEXA) and the risk of fracture[1]. Fracture risk increases with decreasing BMD, so that there is no exact cutoff point to differentiate a person who will experience fracture from one who will not[2].

The consensus definition[3] of osteoporosis expresses that low BMD is an important component of the risk of fracture. Further, the operative definition[4] is based on BMD status. In 1994, an expert panel of the World Health Organization (WHO) recommended thresholds of BMD in women to define low BMD, or osteopenia (T score between –1.01 and –2.49 SD), and osteoporosis (T score ≤ –2.5 SD).

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It is clear that the relation between fracture risk and bone density is best described as a gradient rather than a threshold. However, WHO thresholds are useful in clinical practice to give information on prognosis. Moreover, although risk factors independent of bone mass should also be considered, BMD status is the main factor in the decision on intervention, and WHO thresholds are used, in most cases, as cutoff points.

In men, there is no universally accepted cutoff point to classify a patient as osteoporotic. In practice, the WHO threshold for osteoporosis, recommended for postmenopausal Caucasian women, has been utilized. The International Society for Clinical Densitometry (ISCD), in a recent position paper[5], considers that osteoporosis may be diagnosed in postmenopausal women and in men age 50 years and older if the T score of the lumbar spine, total hip, or femoral neck is –2.5 or less. For BMD in women prior to menopause and in men younger than 50 years, Z scores, not T scores, are preferred. A Z score of –2 or lower is defined as "below the expected range for age" and a Z score above –2 is "within the expected range for age."

Rheumatoid arthritis (RA) is an important cause of secondary bone loss[6,7]; inflammation, decreased functional capacity, and corticosteroids have been identified as independent risk factors for low bone density[8-11]. It has been well established that the BMD status of patients with RA is lower

than in the general population, both in men[12] and women[13]. However, studies to date have mainly been conducted in women. While there is relevant information on frequency of osteoporosis in women with RA, data about male patients are limited[8,14].

We studied a group of Spanish patients followed in a university hospital to evaluate the frequency of osteoporosis in men with RA, according to both WHO and ISCD criteria.

MATERIALS AND METHODS

The study was performed at the rheumatology department of the Hospital Universitari de Bellvitge, a 1000 bed teaching hospital in Barcelona, Spain. The department has a unit for admissions and 4 outpatient clinics, one in the hospital and 3 in affiliated primary care health centers. In our area, patients with RA are usually referred to the rheumatology department for a specialized opinion. The department has an established protocol for evaluation and followup of patients with RA.

From the database of our bone densitometry unit, we searched for men with RA who were evaluated between January 1991 and December 2004; only data relating to first evaluation were considered. Patients included in the study fulfilled the following criteria: (1) duration of RA longer than 1 year; (2) regular followup for RA (3 to 6 visits per year) at the outpatient clinic of our rheumatology department; and (3) absence of concomitant diseases that might affect BMD. We identified 187 patients; all fulfilled the American Rheumatism Association 1987 revised classification criteria for RA[15].

The medical charts of these patients were reviewed to record data on: (1) age, (2) body mass index, (3) duration of RA, (4) rheumatoid factor, (5) Steinbrocker score, (6) ever-use of corticosteroids, and (7) cumulative dose of corticosteroids.

BMD (g/cm^2) was measured at the lumbar spine (L2–L4) and femoral neck by DEXA (Hologic Inc., Waltham, MA, USA). Calibration with a lumbar spine phantom is performed daily and with a femoral phantom weekly. T score (comparison with healthy subjects of the same sex with peak bone mass) and the Z score (comparison with age and sex matched healthy controls) were established by comparison with data from a study of BMD at the lumbar spine and femoral neck in a Spanish population performed by the Multicentre Research Project on Osteoporosis (MRPO)[16]. The aim of the study was to generate standard curves for BMD at both sites. The total sample size was 2442 subjects of both sexes stratified according to survival rates, demographic distribution by local regions, and sex ratio in the Spanish population. BMD measurements were performed with a Hologic QDR device. The MRPO members considered that the results obtained were representative of BMD values in the Spanish population. In 13 patients with bilateral hip prosthesis, only lumbar BMD was available.

Confidence intervals (CI) were used to assess the difference between the mean Z score at each site and the general population. Differences between patients with normal BMD and patients with a T score ≤ –1 SD were assessed by analysis of variance and chi-squared tests.

RESULTS

Table 1 shows the demographic and clinical characteristics of the patients included in the study; Table 2 presents data on their densitometric status.

Fifty-seven (30%) patients had a T score > –1 SD (normal BMD) in both lumbar spine and femoral neck. Patients with a T score > –1 SD (normal BMD) both in the lumbar spine and the femoral neck were younger (55.52 ± 12.44 vs 62.45 ± 12.78 yrs; $p < 0.01$), had a shorter duration of RA (7.18 ± 7.01 vs 9.89 ± 8.35 yrs; $p < 0.05$), had a higher body mass index (27.39 ± 3.61 vs 25.72 ± 3.68; $p < 0.01$), and presented a better functional class ($p < 0.01$) than patients with a T score ≤ –1 SD in at least one of the evaluated sites.

Table 1. Demographic and clinical characteristics of patients. Data are presented as mean ± SD (range) or N (%).

Age, yrs	60.34 ± 13.04 (20–87)
Height, cm	165.11 ± 7.05 (142–189)
Weight, kg	71.55 ± 11.34 (45–113)
Body Mass Index, kg/m^2	26.22 ± 3.73 (17.36–39.10)
Disease duration, yrs	9.08 ± 8.05 (1–34)
Rheumatoid factor positive	152 (81)
Steinbrocker's score*	
I	58 (33)
II	85 (48.5)
III	24 (14)
IV	8 (4.5)
Ever corticosteroid treatment	135 (72)
Mean cumulative dose, g**	7.9 ± 8.4 (0.1–36)

* Available data on 175 patients. ** Available data on 109 patients.

Table 2. Densitometric status of patients. Data are presented as mean ± SD (95% confidence intervals).

	Lumbar Spine	Femoral Neck
BMD (g/cm^2)	0.914 ± 0.154	0.739 ± 0.120
T-score	–0.98 ± 1.24	–1.38 ± 1.00
	(95 CI –1.15 to – 0.80)	(95 CI –1.53 to – 1.23)
Z-score	–0.41 ± 1.00	–0.46 ± 0.95
	(95 CI –0.55 to –0.26)	(95 CI –0.60 to –0.31)

Table 3 shows the percentage of patients assigned to each T score and Z score category for BMD status at the lumbar spine and femoral neck; data are presented for the whole series and for the 2 age ranges considered. In the whole series, when WHO thresholds for postmenopausal women were applied, frequency of osteoporosis was 13% at lumbar spine, 12% at femoral neck, and 21% in at least one of the evaluated sites. When we considered only men aged 50 years and older, the frequency of osteoporosis was 13% at lumbar spine, 14% at femoral neck, and 23% in at least one of the evaluated sites.

Among men younger than 50 years, BMD was below the expected range for their age in 10% at the lumbar spine, 6% at femoral neck, and 13% in at least one of the evaluated sites.

DISCUSSION

In a group of Spanish patients we analyzed the frequency of osteoporosis in men with RA, according to WHO and ISCD criteria. As expected, men with RA presented a lower BMD than the general Spanish population. As described in women[9], patients with normal BMD were significantly younger, had a higher BMI and shorter disease duration, and a better functional class.

When we applied the classical WHO criteria, the obtained frequency of osteoporosis was low, despite high prevalence of corticosteroid treatment: 13% at lumbar spine, 12% at femoral neck, and 21% in at least one of the evaluated sites. When we

Table 3. Number (%) of patients assigned to each T-score and Z-score categories from the bone mineral density status at the lumbar spine and femoral neck. Classification by age distribution.

Lumbar Spine	< 50 yrs n: 31	> 50 yrs n: 156	Overall Series n:187
T score ≥ –1 SD	21 (68)	76 (49)	97 (52)
T score between –1.01 SD and –2.49 SD	7 (22)	59 (40)	66 (35)
T score ≤ –2.5 SD	3 (10)	21 (13)	24 (13)
Z score < –1	6 (19)	45 (29)	51 (27)
Z score < –2	3 (10)	8 (5)	11 (6)
Femoral Neck	n: 31	n: 143*	n: 174*
T score ≥ –1 SD	17 (55)	46 (32)	63 (36)
T score between –1.01 SD and –2.49 SD	14 (45)	77 (54)	91 (52)
T score ≤ –2.5 SD	0	20 (14)	20 (12)
Z score < –1	12 (39)	41 (29)	53 (30)
Z score < –2	2 (6)	2 (1)	4 (2)

* Thirteen patients had bilateral prosthesis in this age group.

considered only men aged 50 years and older, as recommended by ISCD, no substantial change in the frequency of osteoporosis was found: 13% at lumbar spine, 14% at femoral neck, and 23% in at least one of the evaluated sites.

To our knowledge, only 2 previous articles have been published in which, in male RA patients, osteoporosis has been defined using a T score ≤ –2.5 SD as a cutoff. Haugeberg, *et al*'s[8] nice population-based study performed in 52 men obtained a frequency of osteoporosis of 13% at lumbar spine, 17% at femoral neck, and 23% in at least one region of measurement; the characteristics of that series were similar to those we present except for the frequency of corticosteroid treatment (62%). Lodder, *et al*'s study[14] of 87 men with low to moderately active RA who were mainly naive for corticosteroid treatment found osteoporosis in 8% at lumbar spine and 3.5% at femoral neck.

Clearly, the frequency of osteoporosis in male RA patients is considerably lower than in female patients with RA. The frequencies in a previous study of our group[17] performed with 111 postmenopausal women treated with low-dose corticosteroids were 34% at lumbar spine, 34% at femoral neck, and 47% in at least one evaluated region. Similarly, in an interesting, multicenter cross-sectional study performed in Italy by Sinigaglia, *et al*[9], the frequency of osteoporosis in 925 women was 28.8% at lumbar spine, 36.2% at femoral neck, 27.8% at proximal radius, and 45.4% in at least one region of measurement.

We do not have a full explanation for the considerable difference in frequency of osteoporosis between male and female patients with RA. It is likely that the effects of deleterious factors for bone are not the same in male versus female patients; moreover, it is possible that criteria for classification of osteoporosis should be different in both genders.

Our study was performed in a clinical setting and should be interpreted in light of several considerations. First, we did not systematically get BMD assessment in our patients. The series does not include all patients with regular followup in the outpatient clinic; we are confident that in our department a trend exists to avoid the performance of bone densitometry in older men with advanced disease. Second, we estimate that in our series there is a slight overrepresentation of corticosteroid treatment. It is feasible that a selection bias exists because the densitometry was probably indicated more frequently in patients receiving corticosteroids. Third, the ISCD recommends consideration of the L1–L4 BMD value and the worst BMD result of 2 proximal femur measurements (total hip and femoral neck), whereas in our department, we routinely evaluate L2–L4 and femoral neck measurement. However, we think that the effect of this circumstance on the value of the study is less relevant.

Despite these limitations, our results may be useful to establish a clinical approach to determine frequency of osteoporosis in male patients with RA. According to the data we obtained, it seems necessary to design studies that assess both densitometric and radiological findings (presence of fractures), in order to establish a BMD value to classify male patients with RA as osteoporotic.

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