Bone Mineral Density in Patients with Psoriatic Arthritis

BRUNO FREDIANI, ALESSANDRA ALLEGRI, PAOLO FALSETTI, LARA STORRI, STEFANIA BISOGNO, FABIO BALDI, PAOLO FILIPPONI, and ROBERTO MARCOLONGO

ABSTRACT. ***Objective.*** Little information is available concerning bone mass in patients with psoriatic arthritis (PsA): the existence of less severe periarticular osteoporosis is considered possible, but there are no data concerning the existence of systemic osteoporosis. We investigated bone mineral density (BMD) in patients with PsA.

Methods. We studied 186 patients with non-axial PsA and 100 healthy subjects, equally divided into 3 groups: women of child-bearing age, women in menopause, and men. No patient had previously received steroid treatment. In all patients, evaluation was made of disease duration, inflammation indices (erythrocyte sedimentation rate, C-reactive protein), functional indices (Steinbrocker scale), and the Health Assessment Questionnaire (HAQ). BMD was measured by fan-beam x-ray densitometry of the lumbar spine, femur, and total body (evaluating the whole skeleton, as well as the spine, trunk, and upper and lower limbs). Ultrasound densitometry of the heel was also performed.

Results. BMD was significantly lower in the arthritic than in the healthy subjects regardless of sex, menopausal status, or age, as expressed in g/cm^2 (lumbar spine 1.112 vs 1.326; femoral neck 0.870 vs 1.006; total body 1.125 vs 1.203) or by T and Z scores (lumbar T = –1.36, Z = –0.98; femoral neck T = –1.12, Z = –0.83; total body T = –1.09, Z = –0.65). Ultrasound densitometry of the heel was similarly altered (stiffness 96 vs 77; T –1.78; Z –1.29). Among the PsA patients, demineralization in at least one skeletal region was observed in 67% of premenopausal women (marked in 11%), 100% of postmenopausal women (marked in 47%), and 80% of the men (marked in 29%). In premenopausal women, demineralization did not correlate with the disease variables; in postmenopausal women and the men, it correlated with a decline in the functional indices and the HAQ score. This was confirmed by analysis of the relative risk of osteoporosis expressed in odds ratios (HAQ: 1.6; age: 1.4; years since menopause: 1.7).

Conclusion. Demineralization was observed in more than 2/3 of our PsA patients without axial involvement. This demineralization was not related to the indices of inflammation or disease duration, but there is a delayed correlation with HAQ score, as well as age and the number of years since menopause. (J Rheumatol 2001;28:138-43)

Key Indexing Terms:
PSORIATIC ARTHRITIS BONE MINERAL DENSITY INFLAMMATION INDICES
FUNCTIONAL INDICES HEALTH ASSESSMENT QUESTIONNAIRE

Reduced bone mass is a frequent finding in patients with rheumatoid arthritis (RA)[1,2]. This demineralization is initially limited to juxtaarticular bone and is probably related to articular inflammation and the various mediators involved in its genesis[3-6], but it subsequently spreads throughout the skeleton and is thought to be an extraarticular manifestation due to various factors, including disease activity and reduced mobility[1,7,8].

PsA may or may not be associated with cutaneous psoriasis, and it is negative for rheumatoid nodules and rheumatoid factor (RF). Nevertheless, symmetric or asymmetric oligoarticular or polyarticular PsA typically involves the distal interphalangeal joints and leads to the manifestation of dactylitis ("sausage finger") and enthesitis, which is also observed in other forms of arthritis[9,10].

Little information is available concerning bone mass in patients with PsA: it has been shown that the extent of periarticular osteoporosis is less than in those with RA[11], but there are few and substantially negative data concerning the occurrence of systemic osteoporosis[10,12-14].

Dual energy x-ray absorptiometry (DXA) is an accurate and reproducible method of measuring the bone mineral content of the spine, femur, and the body as a whole[15,16]. We measured bone mass using fan-beam DXA and ultrasound densitometry in 186 non-steroid treated PsA patients to investigate the presence of systemic osteoporosis.

MATERIALS AND METHODS

Study population. The PsA group. One hundred eighty-six patients with PsA

From the Institute of Rheumatology, University of Siena, Siena; and the Bone and Mineral Research Unit, University of Perugia, Perugia, Italy.

B. Frediani, MD; A. Allegri, MD; P. Falsetti, MD; L. Storri, MD; S. Bisogno, MD; F. Baldi, MD; R. Marcolongo, MD, Institute of Rheumatology, University of Siena; P. Filipponi, MD, Bone and Mineral Research Unit, University of Perugia.

Address reprint requests to Dr. B. Frediani, Institute of Rheumatology, University of Siena, Ospedale Le Scotte, viale Bracci, 53100 Siena, Italia.

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diagnosed according to the criteria of Wright and Moll[10] were enrolled over a period of 12 months: 125 women (60 premenopausal, 65 postmenopausal) and 61 men. According to the subgroup classification[9], the patients had type 1, 3, or 4 peripheral arthritis; none presented with axial involvement (subgroup 5). All patients were seronegative for RF, and were treated only with nonsteroidal antiinflammatory drugs.

The exclusion criteria were current or previous treatment with corticosteroids, immunosuppressants, hormone replacement therapy, thyroxine, or vitamin D (or one of its active metabolites), and the presence of demineralizing diseases.

Control group. This consisted of 100 healthy subjects recruited from among the hospital staff and other volunteers: 68 women (33 premenopausal, 35 postmenopausal) and 32 men. These did not present any pathology, were not taking demineralizing drugs, and did not have any form of phlogistic or degenerative arthropathy. Exclusion criteria were the same as for the patient group.

Methods. A detailed history was taken of each patient, with particular reference to age, menopausal status, disease duration, current and/or previous treatments, and current or previous pathologies; their height and weight were measured, and a record was made of their Steinbrocker articular function index and the results of the modified Stanford Health Assessment Questionnaire (HAQ)[17]; blood samples were taken for the determination of the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and RF.

BMD was evaluated by means of fan-beam x-ray densitometry using a Lunar-Expert, version 1.72. This method allows rapid scanning of the total skeleton and/or particular skeletal regions, and provides radiograph-like images[18]. The following regions were evaluated: the lumbar spine (L2–L4), femur (neck, Ward's triangle, trochanter), and the total body, as a whole and in regional terms (total spine, total trunk, upper limbs, lower limbs). The results were expressed as g/cm^2. Further, bone mass was qualitatively evaluated by ultrasound densitometry of the heel using the Lunar-Achilles Plus[19], and the results expressed in terms of broadband ultrasound attenuation (BUA), speed of sound (SOS), and stiffness (theoretical entity matching both previous measurements). T scores (the difference between the BMD of the patient and that of young healthy adults corrected for the standard deviation) and Z scores (the difference between the BMD of the patient and that of healthy subjects of the same age) were used in the case of both DXA and ultrasound.

For diagnostic purposes, all patients underwent peripheral and axial radiography and articular echography of the small and large joints and the entheses.

Statistical analysis. Analysis was performed by subgroups based on sex and menopausal status. The mean BMD and stiffness were compared with those of the age matched control group (Z score) and young adults (T score). The HAQ results were used as a measure of disability and scored between 0 (normal) and 3.0 (severe disabilty); Steinbrocker's index was used as a measure of functional joint impairment and scored between 1 (normal) and 4 (severe functional impairment). Disease activity was measured using ESR and CRP.

Parametric tests included analysis of variance, Pearson's correlation coefficient, and t test for unpaired data. Nonparametric tests included Spearman's correlation coefficient and Mann-Whitney U-test. Bonferroni corrections were performed for multiple comparisons. In addition to univariate analysis, a multivariate analysis was carried out to establish the independent effects of the different covariates on bone mass (age, years since menopause, body mass index, disease duration, ESR, CRP, Steinbrocker index, HAQ score). To this end, a linear model was adopted in which BMD and stiffness were used to identify the independent variables predictive of osteoporosis.

RESULTS

Characteristics of the PsA group and the various subgroups based on sex and menopausal status are shown in Table 1.

The BMD of the total body, total body subregions, lumbar spine and femur, as well as the stiffness of the heel, were significantly less in the 3 PsA subgroups than in the controls (Figure 1).

Figure 2 shows the corresponding values in terms of T and Z scores, which were all negative and more altered at the level of the spine (total and lumbar) and heel.

The patients were divided into 3 groups on the basis of their lumbar and/or femoral BMD (expressed as T scores): group 1 included subjects with a T score above –1 (normal); group 2 those with a T score between –1 and –2.5 (osteopenic); and group 3 those with a T score below –2.5 (osteoporotic). The percentage of patients in each group is shown in Figure 3; demineralization was observed in at least one skeletal district in 67% of the premenopausal women (56% osteopenic and 11% osteoporotic), 100% of the postmenopausal women (53% and 47%), and 80% of the men (51% and 29%).

Among the premenopausal women, BMD and stiffness correlated only with the body mass index (BMI) ($r = 0.34$, $p = 0.004$ for lumbar BMD; $r = 0.28$, $p = 0.006$ for femoral BMD; $r = 0.30$, $p = 0.004$ for heel stiffness).

Among the menopausal women, BMD and stiffness correlated not only with BMI, but also with age ($r = 0.45$, $p = 0.008$

Table 1. Characteristics of healthy subjects (control) and patients with PsA.

Characteristics	Male, mean (SD)		Premenopausal Female, mean (SD)		Postmenopausal Female, mean (SD)		Total, mean (SD)	
	Control	PsA	Control	PsA	Control	PsA	Control	PsA
N	32	61	33	60	35	65	100	186
Age, (yrs)	53.5 ± 11.8	54.5 ± 12.2	36.6 ± 6.0	37.1 ± 7.0	64.5 ± 5.7	63.9 ± 6.8	63.1 ± 5.7	63.4 ± 6.2
Years of menopause					10.8 ± 4.8	10.3 ± 4.7	10.8 ± 4.8	10.3 ± 4.7
Height, (cm)	168.3 ± 6.1	169.7 ± 6.3	158 ± 4.0	159 ± 4.0	156.9 ± 3.7	157.2 ± 3.9	162.4 ± 5.0	162.6 ± 5.2
Weight, (kg)	75.2 ± 5.5	74.3 ± 6.2	58.2 ± 4.0	59.3 ± 6.0	56.9 ± 5.3	57.7 ± 5.7	66.6 ± 6.2	66.8 ± 6.1
BMI, (kg/m^2)	22.9 ± 2.8	23.2 ± 3.4	21.7 ± 2.5	21.8 ± 2.3	20.8 ± 2.8	20.9 ± 3.1	22.2 ± 2.7	22.3 ± 2.8
Disease duration, mo		47 (6–63)		21 (6–37)		55 (12–120)		42 (7–66)
ESR	6 ± 2	22 ± 9	4 ± 2	18 ± 5	9 ± 5	24 ± 7	6 ± 4	21 ± 7
CRP	0.2 ± 0.05	1.2 ± 0.6	0.3 ± 0.04	1.3 ± 0.4	0.2 ± 0.04	1.6 ± 0.5	0.2 ± 0.04	1.3 ± 0.5
Steinbrocker	1 ± 0	1.8 ± 0.6	1 ± 0	1.4 ± 0.5	1 ± 0	2.4 ± 0.9	1 ± 0	1.8 ± 0.8
HAQ	0 ± 0	0.4 ± 0.1	0 ± 0	0.3 ± 0.1	0 ± 0	1.1 ± 0.4	0 ± 0	0.6 ± 0.1

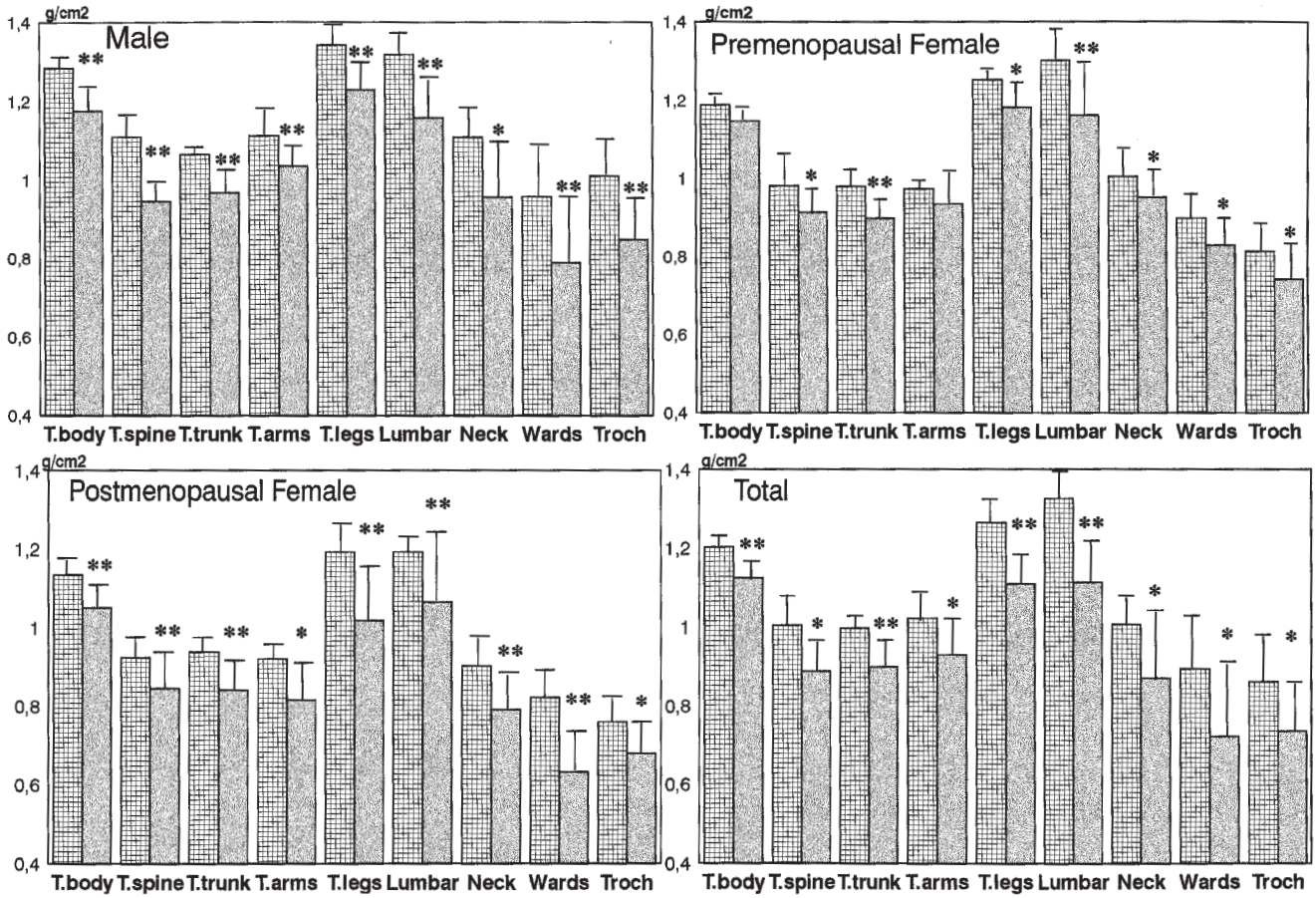

Figure 1. Bone mineral density (g/cm^2) and ultrasound results (stiffness) in healthy control subjects (▦) and patients with psoriatic arthritis ( ) affecting different skeletal regions. *p < 0.05 (PsA vs control); **p < 0.01 (PsA vs control).

for lumbar BMD; r = 0.46, p = 0.009 for femoral BMD; r = 0.51, p = 0.003 for heel stiffness); years since menopause (r = 0.51, p = 0.004; r = 0.55, p = 0.002; r = 0.60, p = 0.0008, respectively); Steinbrocker index (r = 0.53, p = 0.002; r = 0.52, p = 0.006; r = 0.54, p = 0.002); and HAQ (r = 0.36, p = 0.04; r = 0.34, p = 0.05; r = 0.39, p = 0.03).

Among the men, BMD and stiffness correlated with BMI, age, Steinbrocker index, and HAQ.

There was no correlation with ESR, CRP, or disease duration in any of the 3 subgroups.

A multivariate analysis was carried out to analyze the independent effects of the covariates on bone mass, using a linear model to identify the predictors of osteoporosis in the 186 patients as a whole and in the subgroups. In the patients as a whole, HAQ, age, and BMI were significant predictors of bone mass, as were years since menopause in the menopausal women. The only significant predictor among the premenopausal women with PsA was BMI.

BMI, HAQ, and age were significant predictors of bone mass among the men with PsA.

In a subsequent phase, in the patients as a whole, a logistic model was prepared in which the presence of osteoporosis (a T score below –2.5) in at least one skeletal site was the dependent variable. In this model, age, HAQ, years since menopause, and BMI were all significantly associated with osteoporosis. An impaired HAQ and BMI remained significantly associated with osteoporosis also after correction for age and the number of years since menopause (Table 2).

Tables 3 and 4 show BMD and stiffness in the premenopausal and menopausal women with PsA, subdivided on the basis of whether they had normal or altered indices of disease activity, the HAQ score or articular function, and the absence or presence of cutaneous psoriasis.

There was a clear reduction in bone mass among the premenopausal women with abnormal ESR values and an altered HAQ (at the level of the total body and lumbar spine).

Among the menopausal women, bone mass was reduced in the presence of an altered HAQ and Steinbrocker index score (BMD was significantly reduced at the level of the total body, the femur, and the heel, but not the lumbar spine).

DISCUSSION

There are no data revealing the presence of osteopenia or osteoporosis in correlation with PsA, with few studies on the

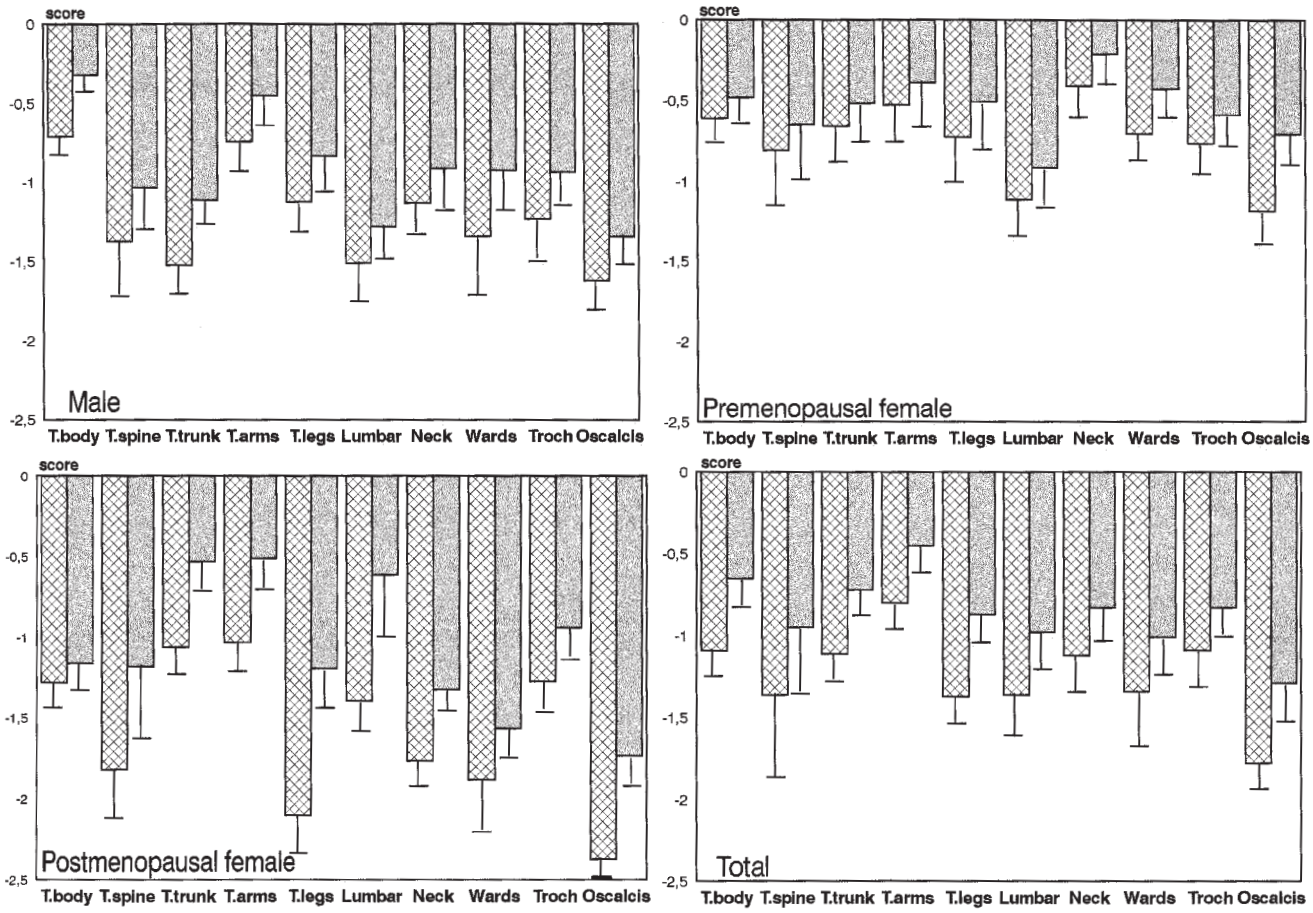

Figure 2. Bone mineral density and ultrasound results expressed as T(▨) and Z(▩) scores in skeletal regions of patients with psoriatic arthritis.

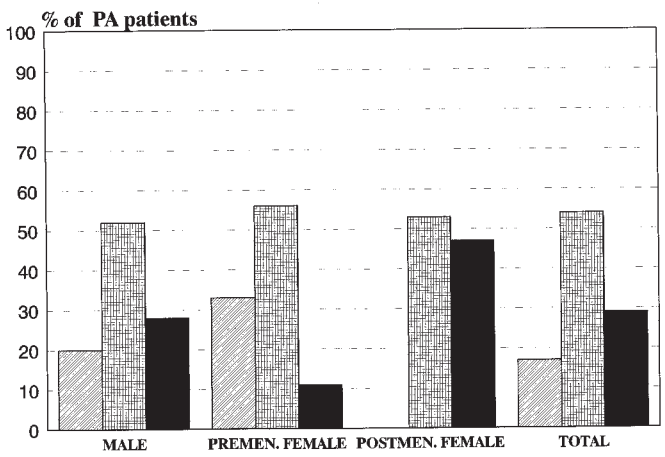

Figure 3. Percentage of normal (▨), osteopenic (▦), and osteoporotic subjects (■) defined on the basis of T scores in patients with psoriatic arthritis.

subject[13,14]. In particular, the only quantitative study[13] was based on neutron activation rather than DXA and involved a small number of patients with PsA in comparison with a much larger number of subjects with RA. Further, the results are questionable, since total body calcium in the patients with RA was reduced in comparison with controls but not in comparison with the PsA subjects; the same can be said about the loss of total calcium after one year, which was significant in comparison with baseline only in the RA and not in the PsA patients. This suggests that the size of the PsA sample was insufficient to detect a demineralization that was less than that observed in patients with RA.

Our data, which relate to a larger population and are based on commonly used densitometric evaluations, indicate that patients with PsA have significantly less systemic bone mass than normal subjects.

We studied nonsteroid treated patients with nonaxial PsA, including men and premenopausal women in order to exclude the negative effect of sex and estrogen deficiency on bone mass. In comparison with young adults (T score), bone mass was reduced in 2/3 of the premenopausal women, 100% of the menopausal women, and 80% of the men, although only some (ranging from 11% to 47%) presented outright osteoporosis.

The demineralization was confirmed by the comparison with age matched normal subjects (Z score).

The reduction in bone mass affected all the skeletal seg-

Table 2. Variables determining a significant relative risk of osteoporosis in at least one skeletal region.

	OR	CI	p	OR (corrected for age and years of menopause)	CI	p
Age	1.4	1.04–1.75	0.01	—	—	—
Years of menopause	1.7	1.11–2.45	0.005	—	—	—
HAQ	1.6	1.07–2.12	0.007	1.5	1.12–1.99	0.009
BMI	0.72	0.66–0.88	0.009	0.79	0.68–0.89	0.01

Table 3. Bone mineral density (g/cm^2) in premenopausal women with PsA divided on the basis of normal (1) or altered (2) variables.

	ESR		CRP		Psoriasis		Steinbrocker		HAQ	
	1	2	1	2	1	2	1	2	1	2
Total body	1.211	1.149**	1.199	1.161	1.175	1.179	1.177	1.176	1.212	1.147**
	(0.071)	(0.062)	(0.069)	(0.088)	(0.072)	(0.069)	(0.088)	(0.069)	(0.073)	(0.062)
Lumbar spine	1.221	1.176*	1.201	1.195	1.198	1.200	1.201	1.197	1.227	1.170**
	(0.157)	(0.163)	(0.177)	(0.181)	(0.163)	(0.179)	(0.159)	(0.162)	(0.147)	(0.158)
Femur neck	0.977	0.939	0.969	0.945	0.958	0.956	0.956	0.960	0.975	0.940
	(0.159)	(0.157)	(0.139)	(0.151)	(0.132)	(0.161)	(0.133)	(0.127)	(0.153)	(0.157)
Os calcis	84	86	86	85	87	84	86	86	84	86
(stiffness)	(11.4)	(12.3)	(9.1)	(12.7)	(11.9)	(15.1)	(11.7)	(13.8)	(12.8)	(12.5)

*p < 0.05 (2 vs 1); **p < 0.01 (2 vs 1).

Table 4. Bone mineral density (g/cm^2) in menopausal women with PsA divided on the basis of normal (1) or altered (2) variables.

	ESR		CRP		Psoriasis		Steinbrocker		HAQ	
	1	2	1	2	1	2	1	2	1	2
Total body	1.076	1.011*	1.069	1.019*	1.044	1.049	1.063	1.028*	1.077	1.011**
	(0.088)	(0.057)	(0.065)	(0.071)	(0.055)	(0.072)	(0.059)	(0.089)	(0.078)	(0.063)
Lumbar spine	1.101	1.076	1.099	1.079	1.084	1.092	1.099	1.078	1.104	1.072*
	(0.179)	(0.168)	(0.166)	(0.173)	(0.151)	(0.208)	(0.167)	(0.166)	(0.179)	(0.177)
Femur neck	0.858	0.837	0.862	0.832	0.850	0.844	0.861	0.834*	0.860	0.815*
	(0.122)	(0.144)	(0.144)	(0.169)	(0.159)	(0.141)	(0.160)	(0.145)	(0.122)	(0.140)
Os calcis	75	74	73	75	75	74	78	71*	74	74
(stiffness)	(10.9)	(14.2)	(14.3)	(13.9)	(14.2)	(13.6)	(11.9)	(13.2)	(13.6)	(12.7)

*p < 0.05 (2 vs 1); **p < 0.01 (2 vs 1).

ments even in the young premenopausal women, although it was more marked or in any case densitometrically more detectable, at the level of the trunk (particularly the spine) and heel. It is known that these 2 sites are, respectively, partially and completely trabecular. PsA related osteoporosis thus seems to have the typical characteristics of postmenopausal osteoporosis. The femur was also greatly involved only in the postmenopausal subjects. However, the prevalent impairment of the heel also provides an indication concerning the presence of a qualitative alteration in the trabecular microarchitecture.

The biohumoral indices of inflammation did not correlate with the bone mass of our patients, and were therefore not predictive. Only the young premenopausal women with an altered ESR were more demineralized, and then not in all sites.

Among premenopausal women, the only factor other than arthritis aggravating osteoporosis seems to be BMI, which also correlated with demineralization in the other subgroups, together with age and the number of years since menopause.

PsA related osteoporosis is therefore influenced by risk factors that are simultaneously generic and typical of all primary forms of osteoporosis.

In general, our patients did not present severe impairment of the HAQ or articular function, although these worsened with age. Nevertheless, after correcting for age, both variables (but particularly HAQ score) were determinants of generalized demineralization in PsA.

In our population, in comparison with the other variables, disease duration did not have any particular weight in determining the loss of bone mass.

In conclusion, unlike the few previous studies and despite

the limitations of its transversal design, our study based on the use of more sophisticated quantitative and qualitative instrumental evaluations shows that patients with PsA have a reduced total skeletal BMD, which becomes more marked with age, estrogen deficiency, and an impaired HAQ, and on which an increase in the indices of phlogosis has a limited and only initial importance. Longitudinal studies are needed to confirm these results.

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