Value of clinical factors in selecting postmenopausal women with rheumatoid arthritis for bone densitometry

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Abstract

Objective—**Criteria to decide which patients with rheumatoid arthritis (RA) should be examined by dual energy *x* ray absorptiometry (DXA) are currently not available. The rheumatologists from Amsterdam have proposed preliminary criteria based on clinical risk factors (age, disease activity, and functional status). These criteria are preliminary and not widely accepted but might be helpful in practice. The value of the proposal in a group of Spanish postmenopausal women with RA is analysed.**

Methods—**DXA (lumbar spine and femoral neck) was performed in 128 patients recruited from a clinical setting, and the proposed criteria were applied. T and Z scores were established for a Spanish reference population.**

Results—**The mean (SD) age of the patients was 61.3 (10.7) and mean duration of the postmenopausal period 14.5 (10.1) years. Mean duration of RA was 13.7 (7.7) years. Mean C reactive protein was 22 (21) mg/l; mean erythrocyte sedimentation rate 26 (18) mm/1st h; and mean Health Assessment Questionnaire score 1.25 (0.79). Ninety (70%) patients fulfilled the proposed criteria. Their sensitivity for the diagnosis of osteoporosis (T score $\leqslant -2.5$ SD) was 86% and their specificity, 43%. Positive predictive value was 54% and negative predictive value, 79%.**

Conclusions—**The proposed criteria seem a good screening method for the selection of those patients with RA whose bone mineral density should be assessed as the sensitivity and negative predictive value are acceptable.**

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Dual energy *x* ray absorptiometry (DXA) is the most commonly used method of measuring bone mineral density (BMD); it has been shown to be a good predictor of the future risk of fracture. Unfortunately, the generalised use of DXA is limited as it is expensive and time consuming, is not portable, and is available only in specialised clinics.

Generalised bone loss is recognised as an extra-articular complication in rheumatoid arthritis (RA).[1] There is compelling evidence that this bone mass reduction is associated with an increased risk of fracture.[2][3]

DXA is the preferred technique for assessing the presence of low BMD in patients with RA.

However, the prevalence of RA in the general population is high and it is, therefore, necessary to use DXA to investigate only those patients at high risk of osteoporosis.

Criteria to decide who should be evaluated are currently not available. Of interest, Lems and Dijkmans[4] presented a proposal from rheumatologists in Amsterdam based on clinical risk factors (age, disease activity, and functional status) strongly associated with low BMD in patients with RA. This proposal is a set of preliminary criteria to promote a discussion on osteoporosis in RA; they are not widely accepted guidelines. However, it is interesting and may be helpful in daily rheumatological practice until more definite criteria are available.

We have undertaken, in a group of Spanish postmenopausal women, a study to evaluate the value of the proposed criteria as a screening method to identify the patients with RA who should be examined by DXA.

Methods

Over a period of 12 months all postmenopausal women who were receiving regular follow up (three to six visits each year) for RA at the outpatient clinic of our rheumatology department and who fulfilled the inclusion criteria were asked to participate. The inclusion criteria were (*a*) duration of RA longer than one year; (*b*) duration of postmenopausal period longer than one year; and (*c*) absence of concomitant diseases that might affect BMD. Patients with current or past treatment with 7.5 mg/day or above of prednisone were excluded. Consent was obtained from 128 patients. All the included patients fulfilled the 1987 criteria of the American Rheumatism Association for RA diagnosis.[5]

The medical charts of the patients were reviewed in order to record the data about (*a*) age; (*b*) duration of the postmenopausal period; (*c*) duration of RA; (*d*) rheumatoid factor; and (*e*) C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in the 1st hour; the mean of the determination of CRP and ESR in the past year was calculated.

BMD (g/cm^2) was measured at the lumbar spine (L2-4) and femoral neck by DXA using a Hologic - QDR 1000 unit (Hologic Inc, Waltham, Mass). Calibration with a lumbar spine phantom was performed daily and with a femoral phantom weekly. T and Z scores were established in comparison with a reference healthy Spanish population.[6] World Health Organisation[7] criteria were used for the diagnosis of osteoporosis (T score $\leqslant -2.5$ SD).

On the same day that BMD assessment was made, the Spanish version[8] of the Health Assessment Questionnaire (HAQ) was applied and Steinbrocker's score was established.

Proposed criteria from rheumatologists in Amsterdam were evaluated in each patient. These criteria are the following: (*a*) high disease activity, defined as mean CRP above 20 mg/l or persistently increased ESR above 20 mm/1st h, or both; (*b*) high age, defined for women as >50 years and for men as >60 years; and (*c*) immobility, defined as HAQ ≥1.25 or Steinbrocker's score ≥3, or both. If two or more criteria are present evaluation of BMD is recommended.

The results are expressed as mean (SD). Confidence interval (CI) was used to assess the difference between the mean Z score at each site and the general population; p values <0.05 were considered significant. A 2 × 2 table was used to evaluate the sensitivity, the specificity, and the positive and negative predictive values of the proposed criteria for the diagnosis of osteoporosis established by DXA. Additionally, their value for a T score ≤−1 (low bone mass) and for a Z score ≤−1 was also calculated.

The patient's ascription to each category was made using the lowest value of the two regions explored.

Results

Table 1 summarises the clinical characteristics of the 128 patients included in the study.

Mean lumbar BMD was 0.856 (0.144) g/cm^2, mean lumbar T score was −1.74 (1.38), and mean lumbar Z score was −0.21 (1.01) (95%CI −0.39 to −0.03; p <0.05). At the femoral neck, mean BMD was 0.645 (0.116) g/cm^2, mean T score −1.74 (1.13), and mean Z score −0.57 (0.99) (95%CI −0.75 to −0.39; p <0.05).

DXA showed that 20 (16%) patients had normal BMD both in the lumbar spine and the femoral neck. Fifty six (44%) patients had osteoporosis in at least one of the evaluated sites. One hundred and eight (84%) patients had a T score ≤−1 and 51 (40%) patients a Z score ≤−1.

A hundred and thirteen (88%) patients were aged more than 50 years; 71 (55%) patients presented a CRP above 20 mg/l or an ESR above 20 mm/1st h, or both; 69 (54%) patients had an HAQ ≥1.25 or a Steinbrocker's score ≥3, or both.

Five (4%) patients did not fulfil any of the proposed criteria from the rheumatologists of

Table 1 *Clinical characteristics of 128 postmenopausal women with RA. Values are expressed as mean (SD) or No [%]*

Age (years)	61.3 (10.7)
Duration of postmenopausal period (years)	14.5 (10.1)
Duration of rheumatoid arthritis (years)	13.7 (7.7)
Rheumatoid factor positive	96 [75]
Treatment with low dose corticosteroids	109 [85]
Erythrocyte sedimentation rate (mm/1st h)	26 (18)
C reactive protein (mg/l)	22 (21)
Health Assessment Questionnaire	1.25 (0.79)
Steinbrocker's score	
1	33 [26]
2	51 [40]
3	40 [31]
4	4 [3]

Table 2 *Sensitivity, specificity, and predictive values of the proposed criteria for each category*

	T score ≤−1	T score ≤−2.5	Z score ≤−1
Sensitivity (%)	75	86	78
Specificity (%)	60	43	36
PPV* (%)	91	54	45
NPV* (%)	31	79	71

*PPV = positive predictive value; NPV = negative predictive value.

Amsterdam; 34 (27%) fulfilled one criteria; 47 (37%), two criteria; and 42 (33%), three criteria. Thus 89 (70%) patients fulfilled two or three criteria.

Table 2 shows the sensitivity, specificity, positive predictive value, and negative predictive value of the proposed criteria for the diagnosis of osteoporosis and for the identification of the patients with a T score ≤−1 or a Z score ≤−1.

Discussion

We have evaluated the proposal from rheumatologists in Amsterdam in a group of Spanish postmenopausal women with RA. Our study should be interpreted in the light of several considerations. The patients included are recruited from a clinical setting. Their characteristics probably do not represent the complete underlying population of patients with RA in the community. Unfortunately, there is not an available population based study which defines the overall characteristics of Spanish patients with RA.

As expected, BMD of patients was lower than that of the general population. The percentage of osteoporosis was higher than that seen in a recent population based study by Haugeberg *et al* which evaluated the magnitude of the problem in Norway.[9] Possibly, examination of BMD reduction in a series of patients who are referred to a rheumatology unit overestimates the problem and establishes a selection bias. Risk factors associated with low BMD in RA are especially prevalent in patients with aggressive disease, who are the subjects usually followed up in a hospital; a large percentage of these subjects had high disease activity and a high degree of immobility, two of the criteria proposed by the rheumatologists in Amsterdam.[4]

The proposal is extensive for both male and female patients. We examined only postmenopausal women as it seems that this group of patients with RA are particularly susceptible to osteoporosis. They are usually older than 50; thus one of the criteria is nearly always present and thus not useful.

The proposed criteria focus particularly on patients with RA not treated with corticosteroids, though it might be also useful in patients receiving this treatment.[10] Eighty five per cent of our patients are currently treated with low dose corticosteroids; this overrepresentation of corticosteroid treatment is a consequence of the kind of patients included in the study, periodically followed up in a teaching hospital who present with high clinical severity.

Our results suggest that the proposal of the rheumatologists in Amsterdam may be a

screening method to decide which postmenopausal women with RA should be investigated for osteoporosis; the sensitivity and the negative predictive value obtained seem acceptable in clinical practice. Specificity and positive predictive value were low, probably reflecting the fact that multiple factors play a part in the pathogenesis of osteoporosis in patients with RA.

In practice, identification of patients with a T score ≤−1 or with a Z score ≤−1 may be as important as osteoporosis when considering treatment or prevention. In fact, the importance of different cut off levels has not been definitively clarified in patients with RA in relation to subsequent fractures. Thus we tested the sensitivity and specificity as well as predictive values of the proposed criteria in our patient group also considering these two end points.

Recently, Kvien *et al* published an interesting population based study which examined relations among osteoporosis and low bone mass and demographic and clinical variables in patients with RA, in an attempt to develop a data driven clinical tool for the identification of patients at high risk for osteoporosis.[11] The logistic regression analysis models could only predict osteoporosis with a sensitivity of 50–60% and a specificity of 80–90% at the various measurement sites, and low bone mass with a sensitivity and specificity of about 70%. The authors stated that a consideration of demographic and disease markers may be of some help in predicting the presence of osteoporosis or low bone mass, but a combination of markers cannot be used as a clinical tool with sufficient sensitivity and specificity for the identification of osteoporosis or low bone mass in patients with RA.

A population based study to analyse the value of the proposal from the rheumatologists in Amsterdam would be particularly welcome in order to establish a comparison with the results obtained in our study.

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