Evaluation of Two Proposals Based on Clinical Factors for Selecting Male Patients With Rheumatoid Arthritis That Should Undergo a Bone Densitometry

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Introduction. Criteria based on age, inflammation, and immobility have been proposed to identify which patients with rheumatoid arthritis (RA) should be examined by dual energy x-ray absorptiometry (DXA) to diagnose osteoporosis. Recently, a modified version of the criteria by including weight and the use of corticosteroids has been proposed. These two set of criteria have not been tested in male patients in a clinical setting.
Objective: To analyse, in a group of patients followed in a teaching hospital, the value of two proposals to select men with RA for bone densitometry.
Patients and method: Clinical and demographic data were collected from the charts of a total of 65 men with RA, submitted to the bone densitometry unit during a 4 year period. Bone mineral density (BMD) was measured in spine and femoral neck by DXA. Two set of criteria were tested: *a)* 3 item criteria (age, inflammation, and immobility), and *b)* 5 item criteria (age, inflammation, immobility, weight, and ever use of corticosteroids). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated
Results: Thirty-five (54%) patients fulfilled the 3 item criteria and 38 (59%) the 5 item criteria. For the diagnosis of osteoporosis using the 3 item criteria, the sensitivity was 62%, specificity 48%, PPV 23%, and NPV 83%; using the 5 item criteria the sensitivity was 90%, specificity 47%, PPV 23%, and NPV 96%.
Conclusions: The 5 item criteria are a more accurate tool to identify, in clinical practice, male patients with RA and osteoporosis than the 3 item criteria. It seems a good screening method for the selection of those patients with RA whose BMD should be assessed, as the sensitivity and NPV seem acceptable.

Key words: Male. Rheumatoid arthritis. Bone densitometry. Osteoporosis. Screening.

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Evaluación de dos propuestas basadas en factores clínicos para seleccionar a qué varones con artritis reumatoide debe realizarse una densitometría ósea

Introducción. En 1998, se propusieron unos criterios basados en la edad, la actividad de la enfermedad y el grado de inmovilidad para seleccionar a pacientes con artritis reumatoide (AR) tributarios de la realización de una densitometría. Con posterioridad, se ha postulado una versión modificada en la que se incluye, además, el peso y la toma de glucocorticoides. Hasta la actualidad no se ha comprobado su valor en pacientes varones en un contexto asistencial.
Objetivo: Analizar la utilidad de ambas propuestas en un grupo de varones con AR controlados de forma habitual en un hospital universitario.
Pacientes y método: Se incluyó a 65 varones con AR remitidos a la unidad de densitometría durante un período de 4 años. Mediante la revisión de las historias clínicas, se obtuvieron los datos clínicos y demográficos necesarios para llevar a cabo el estudio. La densidad mineral ósea en columna lumbar y en cuello femoral se evaluaron por absorciometría fotónica dual de fuente radiológica. Se calcularon la sensibilidad, la especificidad, el valor predictivo positivo (VPP) y el valor predictivo negativo (VPN) de la propuesta de 3 ítems (edad, inflamación e inmovilidad) y de la propuesta de 5 ítems (edad, inflamación, inmovilidad, peso y tratamiento con glucocorticoides).
Resultados: Del total, 32 (54%) pacientes cumplían los requisitos de la propuesta de 3 ítems y 38 (59%) los de la propuesta de 5 ítems. Para el diagnóstico de osteoporosis, con la propuesta de 3 ítems la sensibilidad fue del 62%; la especificidad, del 48%; el VPP, del 23%, y el VPN, del 83%, mientras que con la propuesta de 5 ítems fueron del 90, el 47, el 23 y el 96%, respectivamente.
Conclusiones: La propuesta de 5 ítems resulta más útil en la práctica asistencial que la propuesta de 3 ítems para decidir a qué varones con AR practicar una densitometría. La propuesta de 5 ítems puede ser un buen método de cribado, ya que los valores obtenidos en cuanto a sensibilidad y VPN parecen aceptables.

Palabras clave: Varones. Artritis reumatoide. Densitometría ósea. Osteoporosis. Cribado.

Introduction

There is an ample consensus on the use of dual energy x-ray absorptiometry (DXA) as the standard evaluation of bone mineral density (BMD). In fact, the operative diagnosis of osteoporosis is established according to this measurement technique.[1] Unfortunately, there are limitations in the use of bone densitometry, mainly as a consequence of the small number of measuring devices in public health facilities.

Generalized bone loss is one of the most frequent extra articular manifestations of rheumatoid arthritis (RA) and one of the main causes of morbidity and mortality.[2-7] A low BMD is associated, fundamentally, to inflammation, immobility, and steroid use.

The prevalence of RA in the general population is high[8]; therefore, some authors call for a densitometry only in those cases that supposedly present a high risk of suffering osteoporosis. In this sense, Lems et al[9] have proposed certain criteria based on age (women older than 50 and men older than 60 years of age), disease activity (C reactive protein values [CRP] >20 mg/L or an erythrocyte sedimentation rate [ESR] >20 mm/h in a persistent manner) and the degree of mobility (Steinbrocker ≥3 or HAQ ≥1.25), to select patients that are candidates to undergo densitometry. This proposal is especially intended for patients that are not being treated with steroids, but it has also been applied to patients using glucocorticoids.[10]

Our group[11] has shown the value of the treatment of postmenopausal women affected by severe RA, with a high frequency of use of steroid treatment and a high prevalence of osteoporosis. It was estimated that they were useful as a screening method, due to the acceptable levels of sensibility and predictive value obtained in for the diagnosis of osteoporosis (86% and 79%, respectively). The utility of this proposal in males has not been proven.

Recently, Haugeberg et al[12] have evaluated, in a study with a population base that included women and men, a modified version of the proposal by the Amsterdam group,[9] which includes, additionally, the parameters of weight and steroid use. It can be applied to all patients affected by RA, independent of the fact that they are undergoing steroid treatment or not. With these modifications, the obtained results seem to be better when concerning patient selection.

The value of this proposal has not been proven in assistance care. A study is presented in which the utility of both proposals is analyzed in a group of male patients with RA, controlled by the common methods in a university hospital.

Patients and Methods

In a retrospective manner, all male patients with RA sent to the densitometry unit during a period of 4 years have been considered as study objects, when complying with the following criteria: *a)* more than 1 year with the disease; *b)* periodical follow-up in the departments outpatient clinic (3-6 visits/year); and *c)* absence of concomitant illness that could affect bone metabolism. Sixty-five patients were identified; all of them fulfilled the ACR 1987 criteria for the classification of RA.[13]

The clinical histories of the patients were reviewed with the objective of obtaining information on the following variables: age; duration of RA; steroid use in some moment of the disease; rheumatoid factor; CRP and ESR (considering the mean value of the determinations done during the past year), and functional capacity according to Steinbrocker and the score of the Spanish version of the Health Assessment Questionnaire[14] (considering the value reflected on the last visit of the patient).

BMD was evaluated (g/cm^2) in the lumbar spine (L2-4) and the femoral neck through DXA (Hologic Inc, Waltham, Massachusetts, United States). The T-score and the Z-score were established from the data obtained in the multicentric evaluation of bone mass in the Spanish population (MRPO)[15], carried out with Hologic® equipment and in which our hospital.

Height and weight were obtained from the densitometry result sheet, because they reflected the values obtained at the moment of exploration.

In each patient, the criteria proposed by Lems et al[9] and Haugeberg et al[12] were evaluated. In the proposal of Lems et al, a densitometry must be done to every patient that has at least 2 of the following 3 items: *a)* age >60 years, *b)* CRP ≥20 mg/L or ESR ≥20 mm/h, and *c)* functional capacity according to Steinbrocker ≥3 or HAQ≥1.25. In the proposal of Haugeberg et al[12] a densitometry must be carried out in all patients that have at least 3 of the following 5 items: *a)* age >60 years, *b)* CRP≥20 mg/L or ESR≥20 mm/h, *c)* functional capacity according to Steinbrocker ≥3 or HAQ≥1.25, *d)* weight <60 kg, and *e)* treatment with steroids in some moment of the illness.

A 2×2 table was employed to evaluate sensitivity, specificity, positive predictive value, and negative predictive value of both proposals for the diagnosis of osteoporosis (T-score ≤–2.5 standard deviations [SD]) established by DXA. Additionally, values for a T-score ≤–1 SD (osteopenia or low bone mass) and for a Z-score ≤–1 SD were calculated, because some authors[4] traditionally have considered this last cut-point to evaluate the state of the bone mineral density in men.

The categorization of each patient was done according to the lowest value obtained in both the regions analyzed.

In 6 patients with a bilateral hip prosthesis, only the lumbar spine BMD was analyzed.

Results

Demographic and clinical characteristics of patients included in the study are shown in Table 1.

The mean value ±SD of BMD in the lumbar spine was 0.925±0.160 g/cm^2; the mean T-score was −0.82±1.28 (95% confidence interval [CI], −1.13 to −0.51), and the mean value of the Z-score, −0.33±1.00 (95% CI, −0.58 to −0.08). In the femoral neck, the mean value of BMD was 0.750±0.129 g/cm^2; the mean T-score was −1.41±1.02 (95% CI, −1.68 to −1.14), and the mean Z-score, −0.33±1.0 (95% CI, −0.59 to −0.07).

Twenty (31%) patients had a normal BMD in both the lumbar spine and the femoral neck; 13 (20%) had osteoporosis in at least 1 of the 2 measured areas; 32 (49%) presented a T-score ≤−1 SD and 22 (34%), a Z-score ≤−1 SD; 39 (60%) were older than 60 years; 37 (57%) presented a CRP ≥20 mg/L or an ESR≥20 mm/h; 23 (35%), a HAQ≥1.25 or a Steinbrocker functional capacity of ≥3; 8 (12%) weighed less than 60 kg; and 58 (89%) had received treatment with steroids in some point of their illness.

Seven (11%) patients that did not comply with any of the criteria proposed by Lems et al; 23 (35%) complied with 1 item; 29 (45%) with 2 items; and 6 (9%) with the 3 of them. Therefore, 35 (54%) patients complied with 2 or 3 items and were susceptible to undergo a densitometry.

Two patients (3%) had none of the criteria proposed by Haugeberg et al; 8 (12%) complied with 1 item; 17 (26%), 2 items; 31 (48%), 3 items; 5 (8%), 4 items; and 2 (3%), 5 items. Therefore, 38 (59%) patients complied with 3, 4 or 5 items and were susceptible to undergo a densitometry.

Table 2 shows sensitivity, specificity, PPV, and NPD of the criteria proposed by Lems et al (3 item criteria) and Haugeberg et al (5 item criteria) for the diagnosis of osteoporosis (T-score ≤−2,5 SD) and for the identification of patients with a T-score ≤−1 SD or a Z-score ≤−1 SD.

TABLE 1. Demographic and Clinical Characteristics of 65 Males With Rheumatoid Arthritis Included in the Study*

Age, y	62.3±12.2
Weight, kg	71.8±11.3
Height, cm	165±7.4
Body mass index, kg/m^2	26.4±3.6
Duration of illness, y	10±8
Positive rheumatoid factor, n	54 (83%)
HAQ 0.87±0.8	
ESR, mm/h	23.2±19.1
CRP, mg/L	19.6±21.6
Steinbrocker functional capacity, n	
I	27(41.5%)
II	27 (41.5%)
III	8 (12%)
IV	3 (5%)
Glucocorticosteroid treatment, n	58 (89%)

*HAQ indicates Health Assessment Questionnaire; CRP, C reactive protein; ESR, erythrocyte sedimentation rate.

TABLE 2. Sensitivity, Specificity, and Predictive Values of the Criteria Proposed by Lems et al[9] (3 Items) and Haugeberg et al[12] (5 items) for 3 Different Cut Points of Bone Mineral Density*

	T-score ≤−1 SD, %	T-score ≤−2,5 SD, %	Z-score ≤−1 DS, %
Sensitivity			
3 items	56	62	50
5 items	62	90	57
Specificity			
3 items	50	48	44
5 items	48	47	40
Positive predictive value			
3 items	71	23	31
5 items	68	24	34
Negative predictive value			
3 items	33	83	63
5 items	41	96	63

*SD indicates standard deviation.

Discussion

In the present study, the utility of two proposals of clinical criteria to select male patients with RA, candidates for bone densitometry, has been analyzed. This study was carried out in an assistance context and must be interpreted in light of two considerations. First, no systematical indication for carrying out a densitometry in every patient undergoing periodic control; in the department, there is a certain tendency to not carry out the exploration in elderly patients with advance disease. Second, it is estimated that the percentage of patients that undergo treatment with steroids is higher than usual; it is very probable that, more or less, there is a selection bias in which the densitometry has been ordered with a greater frequency in patients treated with steroids. Taking this into account, the study can result interesting because it analyzes the proposals of Lems et al and Haugeberg et al in a clinical setting.

The demographic and clinical characteristics of the patients that were selected for this study are very similar to those included in the population study of the Norwegian authors,[12] done in 52 men, except in the percentage of patients undergoing steroid treatment (62% and 89%).

Of the results obtained for the present study one can deduce that the 5 item proposal constitutes a more useful tool to identify the patients with osteoporosis than the initial, 3 item proposal. The sensibility or the 3 cut-points applied was clearly larger when the proposal of Haugeberg et al was applied. This proposal can be a good screening method when deciding what male patients with RA will undergo a densitometry; the results obtained regarding sensibility and PPV are acceptable. Besides, their application does not involve an appreciable increment of the number of explorations that must be done with respect to the 3 item proposal.

In spite of the elevated number of patients that had undergone steroid treatment in some moment of their disease, the frequency of osteoporosis in the present series is low (20%). This circumstance emphasizes that not all male RA patients treated with steroids undergo a relevant bone mass loss. Because of this, the selection criteria proposed by Haugeberg et al, easily applied in the daily practice, result of special interest.

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