Performance of Risk Indices for Identifying Low Bone Mineral Density and Osteoporosis in Mexican Mestizo Women with Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** We evaluated the utility of 6 generic and 2 specific risk indices for identifying low bone mineral density (BMD) or osteoporosis in women with rheumatoid arthritis (RA); and their correlation with 10-year probability of fractures as assessed with the World Health Organization fracture risk assessment (FRAX) tool.

Methods. Mexican Mestizo women with RA were evaluated in this cross-sectional study using 6 generic indices [Simple Calculated Osteoporosis Risk Estimation (SCORE); Osteoporosis Risk Assessment Instrument (ORAI); Osteoporosis Self-Assessment Tool; Age, Body Size, No Estrogen; Osteoporosis Index of Risk (OSIRIS); and Guidelines of the US National Osteoporosis Foundation], 2 specific indices (Amsterdam and modified Amsterdam), and FRAX. BMD results on dual-energy x-ray absorptiometry (DEXA) at the lumbar spine and femoral neck were considered the "gold standard." Sensitivity, specificity, and predictive values (PV) of the indices and their correlations with FRAX results were estimated.

Results. Among 191 patients, 46 had osteoporosis (24.1%) and 119 had low BMD (62.3%). For predicting osteoporosis, SCORE showed the highest sensitivity (96%), whereas OSIRIS (87%) and ORAI (82%) showed the highest specificities. OSIRIS also had the greatest positive PV (92%). The specific indices had low sensitivity and low specificity (Amsterdam, 50% and 79%, respectively; modified Amsterdam, 56% and 70%). All the indices had a low but significant correlation with FRAX.

Conclusion. These findings support the use of some generic indices to identify patients with RA who should undergo DEXA testing. Currently available specific indices did not perform satisfactorily. New specific risk indices for osteoporosis in RA should be developed to increase sensitivity and specificity for predicting osteoporosis. (First Release Dec 15 2011; J Rheumatol 2012;39:247–53; doi:10.3899/jrheum.110467)

Key Indexing Terms:
OSTEOPOROSIS RISK INDICES DIAGNOSTIC TESTS
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Rheumatoid arthritis (RA) is a systemic chronic inflammatory disorder that affects synovial joints, leading, in severe cases, to functional impairment and disability[1]. Around one-fifth of postmenopausal patients with RA have osteo-

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porosis, and one-third have reduced bone mass in their hips[2]. Osteoporosis in RA is multifactorial, and its causes include medications (mainly corticosteroids); factors related to RA, such as disease activity, impairment in function with limited mobility, and cytokines that stimulate bone resorption; and general factors, such as age, female sex, and postmenopausal status[3,4]. In patients with RA, earlier identification of subgroups with low bone mineral density (BMD) and other risk factors for osteoporosis is required because the development of osteoporotic fractures in these patients is increased compared with the general population. One study identified that patients with RA had a relative risk (RR) of 2.0 for hip fracture and 2.4 for spine fracture compared with controls[5].

The presence of osteoporosis, as identified by dual-energy x-ray absorptiometry (DEXA), is the best predictor of fracture in patients with RA[6]. Nevertheless, there are limitations to performing central DEXA on every patient with RA, mostly related to costs. Further, in countries where equipment availability is limited, the assistance of clinical decision tools is needed to determine who needs osteoporosis screening with DEXA. Clinicians therefore need instruments to help them identify patients at higher risk for osteoporosis to make the use of DEXA more cost-effective. A recent study investigated the performance of 6 generic indices and 2 specific instruments for predicting osteoporosis at the femoral neck in postmenopausal Australian women with RA[7]; however, most of the subjects were white. It remains unknown whether the performance of these indices is similar in other races and for regions of the body other than the femoral neck, such as the lumbar spine. To date, no study has evaluated the performance of osteoporosis risk indices for identifying low BMD or osteoporosis in Hispanics with RA; and no studies have determined whether these indices correlate with the 10-year probability of hip fractures or other major fractures as evaluated by the fracture risk assessment (FRAX) tool developed by the World Health Organization (WHO). The aim of our study was to evaluate and compare the utility of 6 generic indices and 2 RA-specific indices for detecting low BMD and osteoporosis in Mexican Mestizo women with RA, and to correlate their scores with FRAX assessments.

MATERIALS AND METHODS

Study sample. This cross-sectional study evaluated 191 consecutive women who were diagnosed with RA from March 2007 to March 2009. These patients were referred from an outpatient rheumatology clinic in a secondary care center in Guadalajara, Mexico (Hospital General Regional 110, IMSS). Inclusion criteria were as follows: age ≥ 18 years at entry; self-identified race Mexican Mestizo; fulfillment of the 1987 criteria of the American College of Rheumatology for the diagnosis of RA[8]; and no previous BMD measurement. Patients were excluded if they were pregnant, had an overlap syndrome, were receiving bisphosphonates or parathyroid hormone therapy, or had a comorbidity associated with low BMD, such as diabetes mellitus, thyroid disease, or chronic renal failure.

Our study was approved by the Research and Ethics Board of our hospital. All patients provided written informed consent.

Clinical assessment. Each patient was interviewed using a structured questionnaire to record demographic information, general risk factors for osteoporosis (i.e., age, body weight, and height), clinical characteristics of RA, and RA treatment. At the time of the evaluation, 2 trained researchers assessed RA disease activity, including joint tenderness and 28-joint swelling counts. Morning stiffness and disease activity as perceived by the patient and the physician were assessed with visual analog scales ranging from 0 to 100 mm. Functioning was assessed using the Spanish modified version of the Health Assessment Questionnaire-Disability Index (HAQ-DI)[9]. Global functional status was evaluated according to the Steinbrocker classification[10]. Rheumatoid factor and C-reactive protein (CRP) were measured by nephelometry using commercial kits. Erythrocyte sedimentation rate (ESR, mm/h) was measured using the Wintrobe method.

Risk indices for osteoporosis. Two types of currently available osteoporosis risk indices were used: (1) generic instruments useful for comparing patients with 1 or more suspected risk factors for osteoporosis, which can be performed for a wide range of diseases, or even in patients with no known chronic disease; and (2) specific osteoporosis risk indices that focus on problems associated with a particular disease such as RA.

Generic indices. The following 6 generic indices were evaluated in the study:

1. Simple Calculated Osteoporosis Risk Estimation (SCORE)[11]. This index was designed in Canada for postmenopausal women and includes the following risk factors: age, race, RA, history of fractures in people ≥ 45 years old, estrogen treatment, and weight. To calculate SCORE, 5 points are added for race other than black; 4 points are added for RA (all the patients in our study met this criterion); 4 points are added for each type of nontraumatic fracture (hip, wrist, or ribs only) after 45 years of age, to a maximum of 12 points; 3 points are added for each decade of age (3 times the first digit of age); 1 point is added if the woman has never received estrogen therapy; and 1 point is subtracted for each 4.5 kg of body weight (body weight in pounds is divided by 10 and truncated to yield an integer). The threshold for the SCORE index is 6, which provides a sensitivity of 91% and a specificity of 40% for identifying women with low BMD[11].
2. Osteoporosis Risk Assessment Instrument (ORAI)[12]. This 3-item index was designed and validated in Canada and is based on age, weight, and current estrogen use. To calculate the ORAI score, 15 points are added for age ≥ 75 years, 9 points for age 65–74 years, 5 points for age 55–64 years, and 0 points for age ≤ 54 years; 9 points are added for body weight < 60 kg, 3 points for body weight 60–69 kg, and 0 points for body weight ≥ 70 kg; and 2 points are added for women who are not currently using estrogen. The threshold for the ORAI index is 9, which provides a sensitivity of 93%, a specificity of 46%, and a positive predictive value (+PV) of 35% for identifying women with low BMD[12].
3. Osteoporosis Self-Assessment Tool (OST)[13]. This index was designed to identify Asian women at increased risk for osteoporosis and it has been validated in white women from the United States, The Netherlands, and Belgium[13,14]. The OST is a 2-item index that includes age and weight as risk factors for osteoporosis. To calculate the OST, age is subtracted from weight (kg), and the result is multiplied by 0.2, and truncated to yield an integer[13]. The threshold for the OST is < 2, which provides a sensitivity of 86% and a specificity of 40% for identifying women with osteoporosis[14].
4. Age, Body Size, No Estrogen (ABONE), a 3-item index designed and validated in the United States for menopausal women, including age, weight, and estrogen use as risk factors for osteoporosis[15]. To calculate the ABONE index, 1 point is added for age ≥ 65 years; 1 point is added for body weight < 63.5 kg; and 1 point is added if the woman has never used oral contraceptives, and has not used estrogen therapy for at least 6 months[15,16]. The threshold for ABONE is ≥ 2, which provides a sensitivity of 56%, a specificity of 84%, and a +PV of 37% for identifying women with osteoporosis at the femoral neck[7].
5. Osteoporosis Index of Risk (OSIRIS). This 4-item index was designed and validated in Europe for postmenopausal women and includes age, body weight, current hormone replacement therapy, and history of low-impact fractures[17,18]. To calculate the OSIRIS, age is multiplied by –2 and weight (kg) by 2, and the results are truncated to yield an integer; 2 points are added if the woman is currently receiving estrogen therapy; and 2 points are added if the

woman has a history of low-impact fractures. The threshold for the OSIRIS is +1, which provides a sensitivity of 85%, a specificity of 39%, and a +PV of 42% for identifying women with osteoporosis[18].

6. Guidelines of the National Osteoporosis Foundation (NOF)[19]. These guidelines include 4 items, with 1 point added for each of these factors: age ≥ 65 years, personal history of minimal trauma fracture while > 40 years old, family history of fracture, and current cigarette smoking. The points are summed to calculate the NOF score. The threshold for the NOF index is ≥ 1, which provides a sensitivity of 94%, a specificity of 84%, and a +PV of 23% for identifying women with osteoporosis[7].

Specific indices. The following 2 specific indices were evaluated in the study:

1. The Amsterdam index. This index uses criteria for referring patients with RA for bone densitometry[20], which were validated by Nolla, *et al* in Spanish women with RA[21]. This specific index includes 3 items, with 1 point added for each of these factors: age > 50 years; high disease activity, defined as a mean CRP level > 20 mg/l or persistently increased ESR > 20 mm/h; and immobility, defined as a Health Assessment Questionnaire (HAQ) score ≥ 1.25, or a Steinbrocker score ≥ 3. The points are added together to calculate the Amsterdam score. The threshold for the Amsterdam index is ≥ 2, which provides a sensitivity of 86%, a specificity of 43%, and a +PV of 54% for identifying osteoporosis in postmenopausal women with RA[20].

2. The Modified Amsterdam (Mod Amsterdam) index, proposed in 2002 by a group of rheumatologists in Norway. The Mod Amsterdam criteria were validated in patients with RA[22]. This modified specific index includes 5 items, with 1 point added for each of these factors: age > 50 years; high disease activity, defined as mean CRP level > 20 mg/l or persistently increased ESR > 20 mm/h; immobility, defined as HAQ score ≥ 1.25 or a Steinbrocker score ≥ 3; weight < 60 kg; and use of corticosteroids (ever). The points are added together to calculate the Mod Amsterdam index. The threshold for the Mod Amsterdam index is ≥ 3, which provides a sensitivity of 82%, a specificity of 45%, and a +PV of 29% for identifying osteoporosis in women with RA[22].

The FRAX tool. This tool for evaluating fracture risk was developed by the WHO for women or men ages 40–90 years with or without BMD at the femoral neck, on the basis of the risks associated with selected clinical factors[23]. FRAX algorithms give the 10-year probability of hip fracture and major osteoporotic fracture (clinical spine, forearm, hip, or shoulder fracture). The clinical risk factors are age, sex, BMD, history of hip fracture in first-degree relatives, personal history of fragility fracture, RA, use of glucocorticoids (ever), other causes of secondary osteoporosis, current smoking, consumption of ≥ 3 units of alcohol/day, and (when available) BMD of the femoral neck[23,24]. FRAX calculation is available online at no charge at http://www.shef.ac.uk/FRAX. An algorithm was recently developed for Mexican individuals and it was used for our study[24].

BMD was measured (g/cm^2) by DEXA using a GE Lunar Prodigy densitometer (software V.8.8; GE Medical Systems) at the lumbar spine in the posterior-anterior projection (L1–L4) and the femoral neck. The coefficient of variation during the measurement of a standard phantom in our laboratory is 0.7%. The coefficient of variation was 2.4% at the lumbar spine and 1.6% at the femoral neck. All scans were performed by the same experienced technician, who was blinded to the osteoporosis indices of the patients. Each patient was classified into one of the following categories proposed by WHO: normal, defined as having a BMD within 1 SD of the BMD of a normal young adult (T score ≥ –1); osteopenia, defined as having a T score between –1 and –2.4 SD; and osteoporosis, defined as having a T score ≤ –2.5 SD. Patients with a T score ≤ –1.0 SD were considered to have low BMD.

Statistical analysis. The prevalence of low BMD was defined as the proportion of individuals with T scores ≤ –1.0 SD divided by the total number of patients evaluated (n = 191), and the prevalence of osteoporosis as the proportion of those with T score ≤ –2.5 SD. The performance of each risk index for identifying low BMD or osteoporosis in RA was evaluated using a Bayesian approach; sensitivity, specificity, +PV, and negative predictive value (–PV) were estimated. In our study, sensitivity was defined as the proportion of patients with low BMD or osteoporosis detected by each index; specificity was defined as the proportion of patients without low BMD or osteoporosis who were excluded by each index; +PV was defined as the proportion of patients who were identified by an index as having low BMD or osteoporosis according to the DEXA study; and –PV was defined as the proportion of patients who were excluded by an index and who did not have low BMD or osteoporosis according to the DEXA study; 95% CI were computed for each utility value. Positive likelihood ratio (+LR) was estimated as the number of times osteoporosis or low BMD was likely to occur in a patient with a positive result on a risk index. Pearson's correlation test (r) was used to evaluate the strength of association between the estimated 10-year absolute fracture risk identified by FRAX and the scores obtained for each risk index. All analyses were performed using SPSS V.8.0 and MedCalc V.10.4.3.0.

RESULTS

Of the 217 patients with RA who met inclusion criteria, 26 (12%) refused to participate. Thus, a total of 191 women (88%) were included. Table 1 shows the clinical characteristics of the participants: median age was 52 years, 124 patients (65%) were postmenopausal, and the median duration of RA was 11 years. Median joint count was 11 for tenderness and 5 for swelling (data not shown). The Steinbrocker functional class was III or IV in 27 patients (14%); 121 patients (63%) were receiving corticosteroids. According to the WHO criteria, 46 patients (24.1%) had osteoporosis and 73 patients

Table 1. Clinical characteristics of participants.

Characteristics	N = 191
Age, yrs, median (range)	52 (21–79)
Menopausal, n (%)	124 (65)
Weight, kg, median (range)	66 (36-115)
Oral contraceptives use, n (%)	85 (45)
Duration of RA, yrs, median (range)	11 (1–40)
DAS28 score, median (range)	4 (0–7)
Global functional status III-IV, n (%)	27 (14)
HAQ-DI score, median (range)	0.69 (0–2.7)
ESR, mm/h, median (range)	30 (6–116)
CRP, mg/l, median (range)	19 (1–159)
Medications*, n (%)	
Glucocorticoid	121 (63)
Methotrexate	141 (74)
Sulfasalazine	81 (42)
Chloroquine	72 (38)
Anti-TNF agents	12 (6)
Bone mineral density (BMD) by WHO classification, n (%)	
Normal BMD	72 (38)
Osteopenia	73 (38)
Osteoporosis	46 (24)
FRAX: 10-year probability of fracture**, n (%)	Major osteoporotic fractures
< 10%	147 (82)
10-20%	26 (14)
> 20%	7 (4)

* Patients' other medications: azathioprine, 26 (4%); penicillamine, 11 (6%); etanercept, 9 (5%); infliximab, 3 (2%); rituximab, 1 (< 1%). ** FRAX was computed for 180 patients; the 11 remaining patients were excluded because of their age (< 40 yrs). major osteoporotic fractures include spine, forearm, hip, or shoulder. DAS28: Disease Activity Score of 28 joints; HAQ-DI: Health Assessment Questionnaire-Disability Index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; TNF: tumor necrosis factor; FRAX: WHO fracture risk assessment tool.

(38.2%) had osteopenia; 63 patients (33%) had osteopenia and 21 (11%) had osteoporosis in the femoral neck, whereas 67 patients (35%) had osteopenia and 40 (21%) had osteoporosis in the lumbar spine. Thirty-three (18%) patients had a FRAX 10-year probability ≥ 10% of major osteoporotic fracture, and 6 patients (4%) had a 10-year probability of hip fracture ≥ 10%.

Table 2 shows selected clinical risk factors for low BMD in participants. Over half the patients (106; 55%) were 40–54 years old; 58 patients (30%) weighed < 60 kg; 102 patients (53%) had no history of estrogen therapy; and only 17 patients (9%) were currently receiving estrogens. With respect to risk factors for low BMD related to the severity of RA, most patients (136; 71%) had a CRP > 20 mg/l or ESR > 20 mm/h at the time of the study and 31 (16%) had a HAQ-DI score ≥ 1.25, or a Steinbrocker class ≥ 3.

Table 3 lists the sensitivity, specificity, +PV, –PV, and likelihood ratios of the generic and specific risk indices for diagnosing low BMD (< –1.0 SD). Among the generic indices, SCORE had the highest sensitivity (94%), followed by ORAI (59%). OSIRIS had the highest specificity (94%) for diagnosing low BMD, followed by OST (90%). OSIRIS also had the highest +PV (92%), followed by OST (88%). On the other hand, SCORE had the highest –PV (80%), followed by ORAI (51%). For the specific indices, the Mod Amsterdam index had higher sensitivity (56%), while the original Amsterdam index had higher specificity (79%).

Table 4 shows the sensitivity, specificity, predictive values, and likelihood ratios of the generic and specific risk indices for diagnosing osteoporosis (T score ≤ –2.5 SD). SCORE had the highest sensitivity (96%), followed by ORAI (76%). OSIRIS and ORAI had the highest specificities (87% and 82%, respectively). OSIRIS had the highest +PV (60%), followed by OST (54%); SCORE had the highest –PV (94%), followed by OST (89%) and ORAI (89%). Of the specific indices, the Mod Amsterdam had higher sensitivity (62%) and the original Amsterdam had higher specificity (68%).

Table 5 shows the correlations between the 10-year probability of hip or major osteoporotic fractures estimated by FRAX and the scores obtained using the risk indices for osteoporosis. Although statistical correlations ($p < 0.001$) were observed between the FRAX results and the scores of all the indexes, these correlations were "moderate" for most of the indices and lowest for the NOF, Amsterdam, and Mod Amsterdam.

Table 2. Prevalence of risk factors for low bone mineral density.

Characteristic	n (%)
Females	191 (100)
Age, yrs	
< 40	11 (6)
40-54	106 (55)
55-64	49 (26)
65-74	24 (12)
≥ 75	1 (1)
Weight, kg	
< 60	58 (30)
60-69	59 (31)
≥ 70	74 (39)
Estrogen therapy	
Never used	102 (53)
Current user	17 (9)
Family history of fractures	6 (3)
Personal history of low-trauma fractures*	6 (3)
Current smoker	19 (10)
Alcohol consumption 3 or more units/day	4 (3)
CRP level > 20 mg/l or ESR > 20	136 (71)
HAQ-DI ≥ 1.25 or Steinbrocker ≥ 3	31 (16)
Glucocorticoids	121 (63)

* Personal history of low-trauma fractures: 3 with vertebral fractures and 3 with forearm fractures. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HAQ-DI: Health Assessment Questionnaire-Disability Index.

DISCUSSION

Our findings show that in Mexican Mestizo women with RA, SCORE was the risk index with the highest sensitivity for diagnosing osteoporosis. Three indices, OSIRIS, ORAI, and OST, had similarly high specificities and +PV for diagnosing osteoporosis. The Amsterdam index, a specific index[20], and the modified version of it[22], showed no added value compared with the generic indices in terms of substantially greater sensitivity, specificity, or +PV.

Low bone mass is a frequent complication of RA; thus, BMD measurement is required for patients with a reasonable suspicion of osteopenia or osteoporosis because of the increased risk for fractures[2,5,25]. However, it may be impractical to perform BMD measurement on every patient with RA because of economic costs. This is even more relevant in developing countries because of waiting lists (for tests and followup) and lack of DEXA equipment in rural areas. When resources are limited, informed decisions must be made about which patients to refer for BMD measurement. Indices to predict low BMD or osteoporosis should be based on individual risk factors that have both high sensitivity and high +PV. In this setting, high sensitivity is preferred at the expense of specificity for detecting early preclinical disease; a false-positive label by one of these indices carries the additional cost of bone density testing to confirm diagnosis, with no major deleterious health effects. In the context of postmenopausal women, multiple generic risk indices have been designed for identifying patients with high probability of osteopenia or osteoporosis. Geusens and colleagues reported the performance of 4 generic risk indices for identifying low BMD at the femoral neck or lumbar spine in postmenopausal patients[26]. In that study, the sensitivities of SCORE, OST, and ORAI and a risk index derived from the Study of Osteoporotic Fractures were compared, and the authors obtained results similar to ours in terms of sensitivity and specificity. The study by Geusens, *et al* differed from ours in that 82% of the patients

Table 3. Comparison of utility values of the risk indices for the diagnosis of low bone mineral density (T score ≤ –1.0 SD).

Index	Sensitivity, % (95% CI)	Specificity, % (95% CI)	+PV, % (95% CI)	–PV, % (95% CI)	+LR (95% CI)	–LR (95% CI)
SCORE	94 (88–98)	39 (28–51)	72 (64–79)	80 (63–92)	1.54 (1.27–1.88)	0.15 (0.07–0.33)
ORAI	59 (49–68)	72 (60–82)	78 (68–86)	51 (41–62)	2.12 (1.42–3.16)	0.57 (0.44–0.74)
OST	44 (35–53)	90 (81–96)	88 (77–95)	49 (40–58)	4.49 (2.16–9.35)	0.62 (0.52–0.74)
ABONE	48 (39–57)	74 (62–83)	75 (64–84)	49 (39–56)	1.82 (1.18–2.79)	0.71 (0.57–0.88)
OSIRIS	37 (28–46)	94 (88–98)	92 (80–98)	48 (40–57)	8.68 (2.50–17.75)	0.67 (0.58–0.77)
NOF	53 (44–62)	59 (49–70)	68 (57–77)	43 (33–53)	1.27 (0.92–1.75)	0.81 (0.61–1.08)
AMS	50 (40–59)	79 (68–88)	78 (69–88)	49 (39–58)	2.38 (1.46–3.87)	0.64 (0.51–0.79)
Mod AMS	56 (46–66)	70 (58–81)	75 (64–84)	50 (39–61)	1.90 (1.25–2.87)	0.62 (0.47–0.81)

+PV: positive predictive value, –PV: negative predictive value, +LR: positive liklihood ratio, –LR: negative liklihood ratio; SCORE: Simple Calculated Osteoporosis Risk Estimation; ORAI: Osteoporosis Risk Assessment Instrument; OST: osteoporosis Self-Assessment Tool; ABONE: Age, Body Size, No Estrogen; OSIRIS: Osteoporosis Index of Risk; NOF: Guidelines of the US National Osteoporosis Foundation; AMS: Amsterdam (original); Mod AMS: modified Amsterdam.

Table 4. Comparison of utility values of the risk indices for the diagnosis of osteoporosis (T score ≤ –2.5 SD).

Index	Sensitivity, % (95% CI)	Specificity, % (95% CI)	+PV, % (95% CI)	–PV, % (95% CI)	+LR (95% CI)	–LR (95% CI)
SCORE	96 (85–99)	23 (16–30)	28 (21–36)	94 (81–99)	1.24 (1.11–1.38)	0.19 (0.05–0.77)
ORAI	76 (61–87)	82 (54–70)	39 (29–50)	89 (81–94)	2.0 (1.54–2.61)	0.39 (0.23–0.66)
OST	70 (54–82)	81 (74–87)	54 (41–67)	89 (89–94)	3.74 (2.53–5.52)	0.37 (0.24–0.58)
ABONE	65 (50–79)	69 (60–76)	40 (29–51)	88 (78–92)	2.08 (1.49–2.83)	0.51 (0.34–0.77)
OSIRIS	63 (48–79)	87 (80–92)	60 (45–74)	88 (82–93)	4.81 (3.00–7.73)	0.43 (0.29–0.62)
NOF	65 (49–79)	58 (49–65)	32 (23–43)	84 (75–90)	1.50 (1.13–1.99)	0.62 (0.40–0.94)
AMS	59 (43–73)	68 (59–75)	36 (26–48)	84 (76–90)	1.81 (1.29–2.54)	0.61 (0.43–0.88)
Mod AMS	62 (46–76)	59 (50–68)	34 (23–45)	82 (73–89)	1.52 (1.10–2.08)	0.64 (0.43–0.97)

+PV: positive predictive value, –PV: negative predictive value, +LR: positive liklihood ratio, –LR: negative liklihood ratio; SCORE: Simple Calculated Osteoporosis Risk Estimation; ORAI: Osteoporosis Risk Assessment Instrument; OST: osteoporosis Self-Assessment Tool; ABONE: Age, Body Size, No Estrogen; OSIRIS: Osteoporosis Index of Risk; NOF: Guidelines of the US National Osteoporosis Foundation; AMS: Amsterdam (original); Mod AMS: modified Amsterdam.

Table 5. Correlation between FRAX results regarding the 10-year probability of fracture and the scores of the risk indices for osteoporosis. In the analysis, r was obtained using the Pearson's correlation coefficient.

	FRAX, Hip Fracture		FRAX, Major Osteoporotic Fracture	
Index	r	p	r	p
Score	0.47	< 0.001	0.57	< 0.001
ORAI	0.49	< 0.001	0.56	< 0.001
OST	–0.48	< 0.001	–0.55	< 0.001
ABONE	0.44	< 0.001	0.44	< 0.001
OSIRIS	–0.50	< 0.001	–0.57	< 0.001
NOF	0.30	< 0.001	0.34	< 0.001
AMS	0.26	< 0.001	0.37	< 0.001
Mod AMS	0.34	< 0.001	0.43	< 0.001

FRAX: World Health Organization fracture risk assessment tool; SCORE: Simple Calculated Osteoporosis Risk Estimation; ORAI: Osteoporosis Risk Assessment Instrument; OST: Osteoporosis Self-Assessment Tool; ABONE: Age, Body Size, No Estrogen; OSIRIS: Osteoporosis Index of Risk; NOF: Guidelines of the US National Osteoporosis Foundation; AMS: Amsterdam (original); Mod AMS: modified Amsterdam.

were white and only 5% had RA. One study from 6 different countries[27] investigated the performance of a modified version of OST for Latin American women (OsteoRisk), using a cutoff of ≤ 1 versus > 1. According to their results the OsteoRisk for Latin American postmenopausal women had a sensitivity of 92% and a specificity of 44%[27]. As could be expected, the change in the cutoff for OsteoRisk that differs from the original OST (< 2) increased its sensitivity and inversely, decreased its specificity. The analysis of our data using this cutoff in our patients with RA resulted in an increase in sensitivity (82% with OsteoRisk vs 70% with OST) and a decrease in specificity (67% with OsteoRisk vs 81% with OST). Thus, we considered that for patients with RA the change in threshold for OsteoRisk did not improve its overall performance.

There is currently limited information about the performance of specific indices for identifying patients with RA who are at risk for low BMD. In 2001, Nolla, *et al*[21] validated the Amsterdam index originally proposed by Lems and Dijkmans[20] for identifying patients with RA who should be evaluated by bone mineral densitometry. According to that evaluation[21], performed in Spanish women, the Amsterdam index had good sensitivity (86%), but a low +PV for detecting patients at risk for osteoporosis. Subsequently, Haugeberg, *et al*[22] evaluated the Mod Amsterdam index that included 2 addi-

tional criteria, weight and use of corticosteroids. They found that the Mod Amsterdam index had slightly greater sensitivity for detecting women with osteoporosis than the original Amsterdam index. In contrast, our findings showed that the 2 specific indices did not add sensitivity or +PV compared with results obtained using the generic indices. Our findings are similar to those from a study of Australian postmenopausal women with RA[7], in which the SCORE showed high sensitivity but low specificity. Nevertheless, our study differed from the Australian study because we found poorest sensitivity of the specific indices (AMS and Mod AMS) compared with the generic indices. There were 2 major differences between the Australian study and our results. First, densitometry of the lumbar spine was not performed in the Australian study; therefore, it is likely that the prevalence of low BMD and osteoporosis may have been underestimated, which would have affected their PV. Further, only 51% of the Australian patients agreed to participate in the study compared to 88% in our study; this is one of the strengths of our study. Race may also explain the differences in the results of the 2 studies. In the Australian study, 98% of the sample was white[7], whereas our study is the first to our knowledge to evaluate the utility of these osteoporosis risk indices in Latin American women. Also, this is the first study to report correlations between the scores of these generic and specific indices designed for detecting patients at risk for low BMD or osteoporosis and the results of the 10-year probability of hip or major fractures according to FRAX. FRAX uses the following clinical risk factors: age, sex, BMD, history of hip fracture in first-degree relatives, personal history of fragility fracture, presence of RA, use of glucocorticoids (ever), other causes of secondary osteoporosis, current smoking, consumption of 3 or more units of alcohol/day, and (when available) BMD of the femoral neck[23,24]. Some of these risk factors for fractures are also identified and included in the indices we assessed. We therefore wanted to assess the association of the tested indices with FRAX, since it has been shown that it correlates with fractures. Interestingly, the correlations of the indices with FRAX were only fair to moderate, which also suggests that the performance of current indices may not be as adequate as desired.

Our study has limitations that are inherent to its cross-sectional design. It is important to note that we evaluated the performance of osteoporosis risk indices only at a specific point in time, and we did not evaluate the use of these indices to predict development of osteoporosis, which must be addressed in future studies.

A relevant aspect of our study is that in our patients specific indices had worse performance compared with the results obtained by others[7,21,22], specifically poor sensitivity and specificity. Unlike the predictive values of a diagnostic test, which depend on the prevalence of disease in the sample evaluated, sensitivity and specificity are assumed to be constant. However, this is not always the case, and technical or methodological factors may affect the results of a test. The sensitivity of the Amsterdam index ranged from 59% in our study to 100% in the results from Brand, *et al*[7], a difference that is statistically significant since the 95% CI do not overlap. In their original study, Nolla, *et al* reported a sensitivity of 86%[21], and Haugeberg, *et al* reported 73%[22]. This difference in results could be explained by spectrum bias or spectrum effects, which can occur when the patient case-mix varies across studies. Conceivably, the characteristics of patients with RA in these studies could have varied, changing the performance of the test. Brand, *et al*[7], who reported the highest sensitivity and poorest specificity of the Amsterdam and Mod Amsterdam for diagnosing osteoporosis, studied only white patients over 50 years of age with low disease activity, mostly with long disease duration and substantial impairment of functional status. In contrast, we included patients with a broader spectrum of disease, with both active and inactive disease and better functional status, with more than half the patients receiving steroids. Most important, all patients in our study were Mexican Mestizos. Because this ethnic group has not been evaluated in any previous studies of specific osteoporosis risk indices for RA, information was available to allow comparisons about the performance of these indices in this ethnic group.

In Mexican Mestizo women, the RA-specific indices currently available did not perform well. Prospective cohort studies should be performed to identify or add items that increase the sensitivity of specific indices to detect low BMD or osteoporosis. Generic indices, particularly the SCORE index, may help physicians decide which patients with RA to refer for bone densitometry. New RA-specific indices should be developed to further increase the utility and efficiency of screening patients with RA who are at risk for low BMD or osteoporosis.

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