

Ability of Foot Radiographs to Predict Rheumatoid Arthritis in Patients with Early Arthritis

VALÉRIE DEVAUCHELLE PENSEC, ALAIN SARAUX, JEAN M. BERTHELOT, SABINE ALAPETITE, SANDRINE JOUSSE, CATHERINE Le HENAFF, GÉRARD CHALES, JEAN B. THOREL, SYLVIE HOANG, ISABELLE NOUY-TROLLE, ANTOINE MARTIN, GILLES CHIOCCHIA, PIERRE YOUINOU, and PAUL Le GOFF

ABSTRACT. Objective. In a cohort of patients with early arthritis, to evaluate how well foot radiographs at study inclusion predicted a diagnosis of rheumatoid arthritis (RA) 2 years later.

Methods. A cohort of patients with arthritis of less than one year duration was evaluated in a multi-center study and followed for 30 ± 11 months. An observer blinded to patient data read all 149 hand and foot radiographs done at study inclusion, using item 7 of the 1987 American College of Rheumatology (ACR) criteria for RA and Sharp's method to score erosions and joint space narrowing.

Results. The kappa coefficient for the 1987 ACR item 7 was 0.52 for bony decalcification and 0.87 for erosions. Intra and interobserver correlation coefficients for Sharp's scores ranged from 0.90 to 0.98. Erosions at the feet were significantly associated with RA. The item 7 erosion component at the feet was more specific than the full item 7 (97.5% vs 94%; $p = 0.01$). Sharp's erosion score at the feet was not better than the erosion component of item 7 (sensitivity 18%; specificity 97.5%). Combined use of radiographs of the hands and feet improved the diagnostic performance of the item 7 erosion component; (sensitivity and specificity of item 7 erosions at the hands combined with the feet were 32.5% and 94.5%, respectively).

Conclusion. The "erosion" criterion at the feet had the best diagnostic performance and was significantly associated with a diagnosis of RA. Combining hand and foot radiographs improved diagnostic performance. (J Rheumatol 2004;31:66–70)

Key Indexing Terms:

RECENT ONSET ARTHRITIS
HAND RADIOGRAPHS

FOOT RADIOGRAPHS

RHEUMATOID ARTHRITIS
DIAGNOSIS

Rheumatoid arthritis (RA) is a chronic inflammatory disease in which joint destruction is a prominent feature. However, at an early stage, the diagnosis can be difficult, often requiring extensive diagnostic tests including radiographs. The 1987 American College of Rheumatology (ACR)

criteria¹ and numerous scoring methods such as Sharp's score² describe radiographic abnormalities commonly found in RA, such as erosions, bony decalcification, and joint space narrowing. However, the usefulness of these abnormalities for the early diagnosis of arthritis has not been investigated. Their specificity has not been satisfactorily investigated, since most studies used patients with well established inflammatory joint disease³.

The most widely used criteria set is the one developed by the ACR in 1987¹. These criteria are used routinely by clinicians for the diagnosis of arthritis. Item 7 consists of radiographic changes in the hands and wrists, but not the feet. Previously we showed⁴ that hand radiographs were of limited value for diagnosing early RA. Several authors⁵⁻⁸ have suggested that including foot radiographs may improve the sensitivity of radiographic criteria.

Here, we pursued the dual objective of determining whether radiographic features of the feet were significantly associated with RA in a cohort of patients with early inflammatory arthritis, and whether adding foot radiographs significantly improved the ability of the 1987 ACR item 7 and Sharp's score for the hands to predict whether early arthritis was due to RA.

From the Unit of Rheumatology and the Laboratory of Immunology, Hôpital de la Cavale Blanche, CHU Brest, Brest; Department of Rheumatology, Hôtel-Dieu, CHU Nantes, Nantes; and the Departments of Rheumatology of Rennes, Morlaix, Lorient, and Vannes, and the Department of Immunology, Institut Cochin Inserm U567 CNRS UMR 8104 IFR116, Paris, France.

Supported by the Brest Hospital Center and the 1995 Clinical Research Hospital Program (PHRC 1995).

V. Devauchelle Pensec, MD; A. Saraux, MD, PhD; S. Alapetite, MD; S. Jousse, MD; P. Youinou, MD, PhD; P. Le Goff, MD, Unit of Rheumatology and Laboratory of Immunology, Hôpital de la Cavale Blanche; J.M. Berthelot, MD, Department of Rheumatology, Hôtel-Dieu, CHU Nantes; G. Chales, MD, Department of Rheumatology, CHU Rennes; C. Le Henaff, MD, Department of Rheumatology, Morlaix; J.B. Thorel, MD, Department of Rheumatology, Lorient; S. Hoang, MD, Department of Rheumatology, CHR Vannes; I. Nouy-Trolle, MD, Department of Rheumatology, CHR Quimper; A. Martin, MD, Department of Rheumatology, CHR St. Brieuc; G. Chiochia, PhD, Institut Cochin INSERM U567 CNRS UMR 8104 IFR116, Paris.

Address reprint requests to Prof. A. Saraux, Unit of Rheumatology, Hôpital de la Cavale Blanche, BP 824, F29609 Brest cedex, France. E-mail: alain.saraux@univ-brest.fr

Submitted December 30, 2002; revision accepted June 9, 2003.

MATERIALS AND METHODS

Study population. The study included patients seen from 1995 to 1997 at 7 hospitals in Brittany, France, for arthritis of less than one year duration.

All the patients were referred to the study hospitals by general practitioners or rheumatologists. Inclusion criteria were as follows: age 16 years or older, swelling of at least one joint, absence of a previous diagnosis of any form of arthritis, and symptom duration of no more than one year. The study was approved by the institutional review board of the Brest University Hospital, and all the patients gave their written informed consent.

Study design. The study design has been described⁹. Briefly, the baseline assessment included a standardized interview; a general physical examination; laboratory tests [standard blood and urine measures; latex test and ELISA for IgM, IgG, and IgA rheumatoid factors; tests for antiperinuclear factor (APF), antikeratin antibody (AKA), anti-RA33 antibody, and antinuclear antibody; and HLA-DR phenotype determination]; and radiographs of the chest, pelvis, hands, and feet. Each patient was asked to undergo an evaluation every 6 months by an office-based rheumatologist. These evaluations were free of charge. The evaluations were stopped when the following occurred: (1) the office-based rheumatologist made a clinical diagnosis of a defined joint disease, and (2) the patient met published classification criteria for that joint disease (e.g., the 1987 ACR criteria for RA if the rheumatologist's diagnosis was RA). After the last visit, a panel of 5 rheumatologists determined whether the diagnosis was RA (RA group) or not (non-RA group). The diagnosis made by the panel after the last visit was used as the gold standard for evaluating the diagnostic efficacy of radiographs of the hands and feet.

Radiographic evaluation. Although 270 patients from 8 centers were included in our cohort and had radiographs of the hands and feet, only 4 of these 8 centers participated in the study of foot radiographs and sent duplicates of the radiographs to us. These radiographs were from 149 patients. The clinical presentation in these patients was similar to that in the remaining 121 patients (data not shown). In each patient, radiographs of hands and wrists and of both feet in posteroanterior view were obtained at the first visit by the patient's rheumatologist, who then sent them to the coordinating center (Brest). There, all 149 sets of radiographs were examined by one of us (VDP, who had no information about the patients) for typical erosions and/or unequivocal bony decalcification as described in item 7 of the 1987 ACR criteria and for determination of 1985 Sharp scores (erosions score, joint space narrowing score, and total score) at the hands¹⁰ and Sharp scores modified by Plant, *et al* at the feet¹¹.

Interobserver and intraobserver variabilities were assessed using 130 pairs of foot radiographs, with the interclass correlation coefficients. For the determination of intraobserver variation, the radiographs were read twice by a blinded observer (VDP) at an interval of 3 to 9 months. For interobserver variability, the radiographs were read by VDP and by another trained, blinded observer (SA).

Statistical analysis. Data were analyzed using the Statistical Package for the Social Sciences (SPSS 9.0). The kappa coefficient was used to quantify the reliability of categorical variables and the intra and interobserver correlation coefficients of quantitative variables. The sensitivity and specificity of each variable were determined. ROC curves¹² were plotted for qualitative variables. Data were analyzed using a chi-square test (or Fisher's exact test where appropriate) and the Mann-Whitney test. P values < 0.05 were considered significant.

RESULTS

The 149 patients had a mean age of 50.2 ± 15.9 years at baseline. There were 102 (68.5%) women and 47 (31.5%) men. The mean disease duration at the first visit was 0–2 months for 43% (64/149) of the patients, 3–5 months for 25.5% (38/149), 6–8 months for 12% (18/149), and 9–11 months for 19.5% (29/149). At baseline, 26 patients had

joint symptoms in the feet, consisting of joint pain (26/149, 17.5%) with or without synovitis (10/26, 38%). Laboratory tests showed that 23% had IgM rheumatoid factor (RF) by ELISA and 21.5% a positive latex test; 21.5% tested positive for APF, 16% for AKA, 23% for anti-RA33 antibodies, and 47% for HLA-DR4. Mean followup was 31 ± 11 months.

The panel of 5 rheumatologists assigned 37% of the patients (55/149) to the RA group at the end of followup.

Validity of the method: Radiograph assessment by the blinded observer. The intraobserver kappa coefficients for item 7 at the feet were 0.87 for erosions, 0.52 for bony decalcification, and 0.72 for the full item (VDP vs VDP).

The interobserver kappa coefficients for item 7 at the feet were 0.80 for erosions, 0.55 for bony decalcification, and 0.70 for the full item (VDP versus SA).

For total Sharp score at the feet, the intraobserver correlation coefficient was 0.98 and the interobserver correlation coefficient 0.90.

Radiographic findings at baseline. We looked for statistical associations between various changes on radiographs of the feet (Table 1). Sharp scores (erosion score, joint space narrowing score, and total score) were significantly associated with RA. Item 7 erosions alone or in combination with bony decalcification (full item 7) were significantly associated with RA, whereas bony decalcification alone was not.

Diagnostic value of the radiographs

Diagnostic value of foot radiographs. Sensitivity and specificity were 18% (10/55) and 97.5% (92/94), respectively, for item 7 erosions (Table 2). For the full item 7, sensitivity was higher (12/55, 22%), but specificity was lower (88/94, 94%).

The sensitivity and specificity of Sharp scores at the feet using various cutoffs for erosions, joint space narrowing, and the total score are shown in Figure 2. For a sensitivity of 22% (Figure 2, cutoff = 1), erosions had a specificity of 96%.

Diagnostic value of foot radiographs in patients with polyarticular disease. We also evaluated the diagnostic value of erosions on foot radiographs in the patients with polyarticular synovitis (> 4 joints with synovitis in any

Table 1. Statistical associations between radiographic changes at the feet in a cohort of patients with early arthritis and RA 2 years later.

Radiographic Criteria	RA, n = 55 (%)	No RA, n = 94 (%)	p
Erosions (item 7)	10 (18)	2 (2)	< 0.01
Bony decalcification (item 7)	2 (3.5)	4 (4)	NS
Full item 7	12 (22)	6 (6)	< 0.02
Joint space narrowing (Sharp)	1.5	1	< 0.04
Erosions (Sharp)	0.8	0.1	< 0.002
Total Sharp score	2.3	1.2	< 0.004

NS: nonsignificant.

Table 2. Value of radiographic erosions at the hands and/or feet for predicting a diagnosis of RA 2 years later (item 7 of the 1987 ACR criteria for hands, feet, and both).

Erosions	Sensitivity (%)	Specificity (%)
Hands	10/55 (18)	91/94 (96.5)
Feet	10/55 (18)	92/94 (97.5)
Hands and/or feet	18/55 (32.5)	89/94 (94.5)

joints) at baseline. There were 76 (51%) patients in this subgroup. For item 7 erosions, sensitivity and specificity were 9% (7/76) and 96% (70/73), respectively. For the full item 7, sensitivity was higher (11/76, 14.5%), but specificity was lower (66/74, 89%).

Diagnostic value of foot radiographs in patients with metatarsophalangeal (MTP) pain and/or synovitis. The diagnostic value of foot radiographs (ACR erosions) was not better in patients with MTP pain (3/26 vs 7/123; $p = 0.3$) or MTP synovitis (1/26 vs 9/123; $p = 0.66$).

Diagnostic value of foot radiographs in patients with a strong suspicion of RA. We evaluated the diagnostic value of foot erosions in the subgroup of patients with a strong suspi-

cion of RA. Previously, we had found that neither the office-based rheumatologist's opinion nor the ACR criteria at baseline was reliable for identifying those patients who had a diagnosis of RA within the next 2 years⁹. A diagnosis of RA by the office-based rheumatologist at the first visit had high sensitivity (93%; 91/98) but low specificity (60%; 104/172) for RA 2 years later⁹. Similarly, in the present study, the diagnostic value of foot radiographs was not better when a diagnosis of RA was suspected at baseline (8/91 vs 2/58 for the erosion criterion alone; $p = 0.3$).

Diagnostic value of hand radiographs

Diagnostic value of item 7 of the 1987 ACR criteria. Compared to the full item 7, the erosions component was more specific (96.5% vs 87.5%; $p = 0.01$), but slightly less sensitive (18% vs 22.5%; p nonsignificant).

Diagnostic value of Sharp scores at the hands. The sensitivity and specificity of Sharp score with various cutoff values for erosions, joint space narrowing, and the total score are depicted as ROC curves in Figure 1. The ROC curves for erosions showed the best specificity.

Diagnostic value of the combination of hand and foot radio-

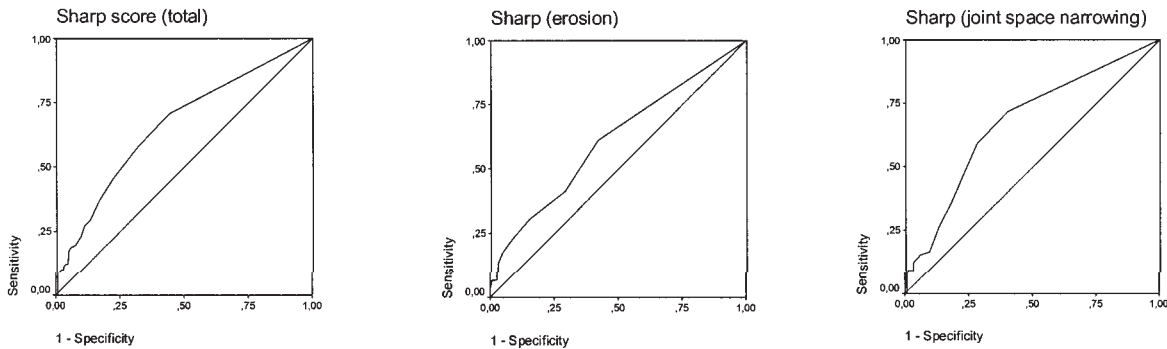


Figure 1. ROC curves of Sharp scores at the hands.

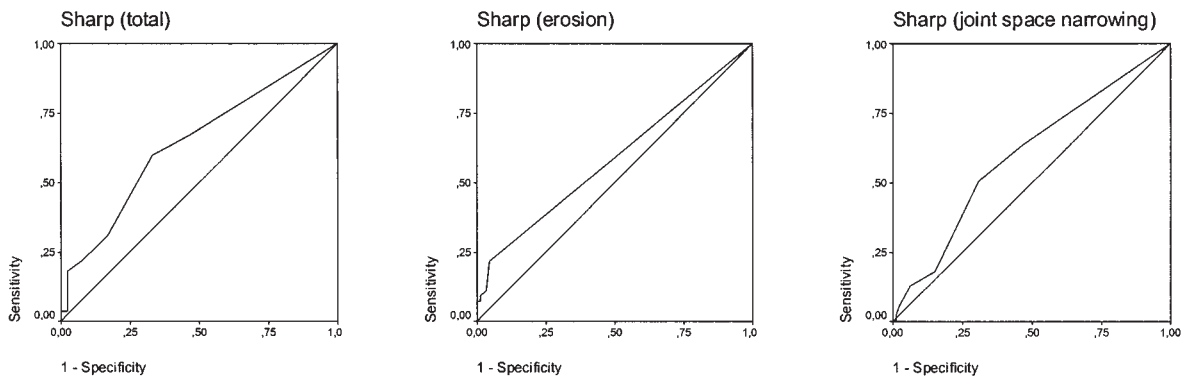


Figure 2. ROC curves of Sharp scores at the feet.

graphs. Sensitivity and specificity of item 7 erosions at the hands and/or feet were 32.5% and 94.5%, respectively (Table 2). Combining Sharp scores at the hands and feet was not better for the diagnosis than item 7 erosions (Figure 3). For a sensitivity of 28% (Figure 3, cutoff = 3.5), erosions had a specificity of 90%.

DISCUSSION

RA is the most common inflammatory joint disease and requires early treatment aimed at minimizing joint damage. Destruction of peripheral joints seen on plain radiographs is an important criterion for the early diagnosis of RA¹³. We previously found that hand radiographs had limited diagnostic value for RA in a cohort of patients with early arthritis⁴. Foot radiographs can reveal the joint damage characteristic of RA, and several studies have found that erosions occurred first at the feet⁵⁻⁷. We investigated the value of foot radiographs for predicting a diagnosis of RA 2 years later. Only 3 studies¹⁴⁻¹⁶ have evaluated the diagnostic value of radiographs in early arthritis. However, these studies were usually restricted to a specific diagnostic group and used inadequate classification criteria for the initial diagnosis. In our study, we investigated the diagnostic value of foot radiographs in a cohort of patients with recent onset of inflammatory arthritis. The final diagnosis was made by a panel of 5 rheumatologists, after a followup of about 2 years.

We first investigated statistical associations of bony decalcification and erosions with RA. As described in our study of hand radiographs⁴, bony decalcification at the feet was not associated with RA. Moreover, substantial interobserver and intraobserver variations occurred for bony decalcification. We agree with others^{17,18} that this abnormality may be of limited usefulness and specificity for RA. By contrast, erosions at the feet were significantly associated with RA. However, the diagnostic value of item 7 erosions was low in our cohort, with a sensitivity of only 18%, but a high specificity, of 97.5%.

In our study, patients were seen early in the disease course. Most were seen during the first 6 months of the

arthritis. The mean disease duration at the first visit was 0–6 months for 68.5% (102/149) of the patients, and 7–12 months for 31.5% (47/149). This short time between the first symptoms and the baseline evaluation may explain the low sensitivity of radiographic criteria in our study. However, it reflects the challenges raised by recent-onset arthritis in everyday clinical practice that were the focus of this study.

We determined the best cutoff for erosions scored using Sharp's method without van der Heijde's modification¹⁹. This modification is widely used and can be applied to foot radiographs²⁰⁻²². However, the physicians who read the radiographs in our study were trained in the use of Sharp's score. We evaluated 100 sets of hand and foot radiographs using Sharp's score with and without van der Heijde's modification and found no significant difference in reliability (data not shown). The ROC curves suggested that the Sharp erosion score at the feet offered the best diagnostic performance characteristics. Sensitivity was low, in keeping with earlier evidence that foot damage does not occur very early in RA, but specificity was high. For example, on our ROC curve, with a cutoff of 1, sensitivity was 22% and specificity was 96%.

We found that combining hand and foot radiographs improved sensitivity to 28% (cutoff = 3.5), with a specificity of 90%. In several studies, the feet were found to be the first site of development of radiographic erosions. However, these studies were conducted either in patients with longstanding RA or in small numbers of patients^{6,7,23-27}. Priolo, *et al*⁶ reported that sensitivity of radiographic erosions increased from 57% to 68% when radiographs of the hands and feet were used in combination. Similarly, in a study by Paimela, *et al*⁷, sensitivity improved from 12% to 35% after addition of foot radiographs to hand radiographs.

Our study suggests that, when seeking to discriminate between patients with early inflammatory joint disease who will and those who will not be diagnosed with RA 2 years later, sensitivity and specificity are better when radiographs of the feet are used also instead of radiographs of the hands alone. However, only hand radiographs are taken into account in item 7 of the 1987 ACR criteria. Although

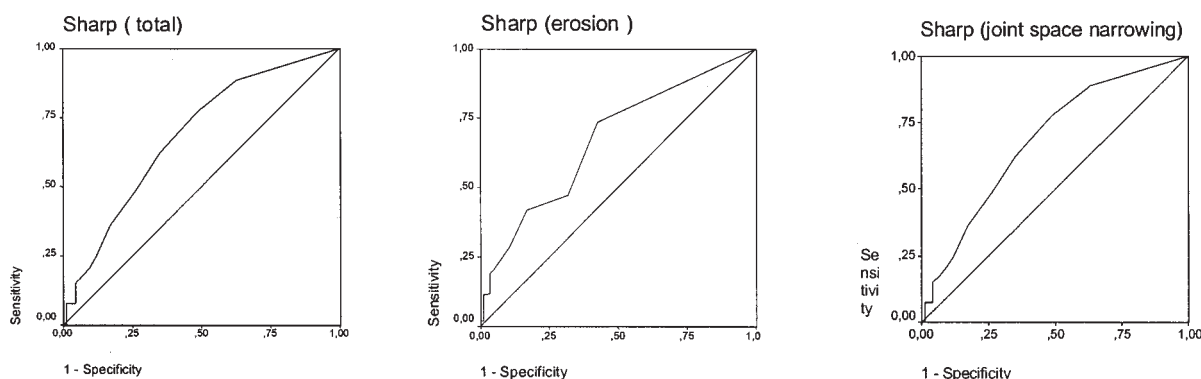


Figure 3. ROC curves of Sharp scores for the feet and the hand.

obtaining radiographs of the feet involves additional exposure of the patient to radiation and additional cost, the improvement in sensitivity may decrease the need for taking radiographs later on.

Thus the presence of erosions at the feet was a better radiological diagnostic measure than erosions at the hands and wrists. Foot erosions were significantly associated with RA 2 years later and showed little intraobserver and interobserver variation. Similar to hand radiographs alone, foot radiographs alone were of limited value for discriminating between patients with early arthritis who would and would not have RA 2 years later. Combining hand and foot radiographs provided better sensitivity and specificity than hand radiographs alone as in the 1987 ACR criteria, but the sensitivity was nevertheless too low to make hand and foot radiographs useful when used alone for the clinical diagnosis in cohorts of patients with recent-onset arthritis.

ACKNOWLEDGMENT

We are grateful to the following rheumatologists for referring patients to us: E. Blat, P. Busson, A. Castagné, J-P. Caumon, P. Chicault, V. Desmas, J-P. Elie, X. Filliol, C. Gauthier, J. Glemarec, J-Y. Grolleau, M.N. Guillermit, R. Guyader, M. Hamidou, P. Herrou, G. Lavel, F. Le Jean, R. Lemaître, M.C. Lheveder, A. Martin, Y. Maugars, J. Olivry, C. Paturel, N. Paugam, A. Prost, D. Rault, B. Ribeyrol, A. Rossard, D. Rodet, P. Vilon, and P. Voisin. We thank Dr. O. Meyer, Paris, for his help with antiRA33 detection.

REFERENCES

1. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988;31:315-24.
2. Sharp JT, Lidsky MD, Collins LC, et al. Methods of scoring the progression of radiologic changes in rheumatoid arthritis. *Arthritis Rheum* 1971;14:706-20.
3. Berthelot JM, Saraux A, Maugars Y, Prost A, Le Goff P. The nosology-taxonomy of recent-onset arthritis: The experience of early-arthritis clinics. *Semin Arthritis Rheum* 2001;30:354-65.
4. Devauchelle Pensec V, Saraux A, et al. Ability of hand radiographs to predict a further diagnosis of rheumatoid arthritis in patients with early arthritis. *J Rheumatol* 2001;28:2603-7.
5. Isomaki H, Kaarela K, Martio J. Are hand radiographs the most suitable for the diagnosis of rheumatoid arthritis? *Arthritis Rheum* 1988;31:1452-3.
6. Priolo F, Bacarini L, Cammisia M, Cesare A, Ferrara R, Della Casa-Alberighi O. Radiographic changes in the feet of patients with early rheumatoid arthritis. *J Rheumatol* 1997;24:2113-8.
7. Paimela L. The radiographic criterion in the 1987 revised criteria for rheumatoid arthritis. Reassessment in a prospective study of early disease. *Arthritis Rheum* 1992;35:255-8.
8. Okubo S, Lehtinen K, Isomaki H. Sensitivity of radiographic changes of hand and foot joints as a diagnostic criterion in patients with rheumatoid arthritis. *Scand J Rheumatol* 1992;21:145-7.
9. Saraux A, Berthelot JM, Chales G, et al. Ability of the American College of Rheumatology 1987 criteria to predict rheumatoid arthritis in patients with early arthritis and classification of these patients two years later. *Arthritis Rheum* 2001;44:2485-91.
10. Sharp JT, Young DY, Bluhm GB, et al. How many joints in the hands and wrists should be included in a score of radiologic abnormalities used to assess rheumatoid arthritis? *Arthritis Rheum* 1985;28:1326-35.
11. Plant MJ, Saklatvala J, Borg AA, Jones PW, Dawes PT. Measurement and prediction of radiological progression in early rheumatoid arthritis. *J Rheumatol* 1994;21:1808-13.
12. Metz LE. Basic principles of ROC analysis. *Semin Nucl Med* 1978;8:283-98.
13. Fex E, Jonsson K, Johnson U, Eberhardt K. Development of radiographic damage during the first 5-6 yr of rheumatoid arthritis. A prospective follow-up study of a Swedish cohort. *Br J Rheumatol* 1996;35:1106-15.
14. Mau W, Raspe HH, Mersjann H. Early arthritides: Nosography, nosology and diagnostic criteria. *Scand J Rheumatol* 1989;79:3-12.
15. Nissila M, Isomaki H, Kaarela K, Kiviniemi P, Martio J, Sarna S. Prognosis of inflammatory joint diseases: a three year follow-up study. *Scand J Rheumatol* 1983;12:33-8.
16. Van der Horst-Bruinsma IE, Speyer I, Visser H, Breedveld FC, Hazes JM. Diagnosis and course of early-onset arthritis: results of a special early arthritis clinic compared to routine patient care. *Br J Rheumatol* 1998;37:1084-8.
17. Thould AK, Simon G. Assessment of radiological changes in the hands and in the feet in rheumatoid arthritis. *Ann Rheum Dis* 1966;25:220-8.
18. Rau R, Wassenberg S, Herborn G, Stucki G, Gebler A. A new method of scoring radiographic change in rheumatoid arthritis. *J Rheumatol* 1998;25:2094-107.
19. Van der Heijde DM, van Leeuwen MA, van Riel PL, et al. Biannual radiographic assessments of hands and feet in a three-year prospective follow-up of patients with early rheumatoid arthritis. *Arthritis Rheum* 1992;35:26-34.
20. Drossaers-Bakker KW, Ames E, Zwinderman AH, Breedveld FC, Hazes JM. A comparison of three radiologic scoring systems for the long-term assessment of rheumatoid arthritis. *Arthritis Rheum* 2000;43:1465-72.
21. Swinkels HL, Laan RF, van't Hof MA, van der Heijde DM, de Vries N, van Riel PL. Modified Sharp method: factors influencing reproducibility and variability. *Semin Arthritis Rheum* 2001;31:176-90.
22. Bruynesteyn K, van der Heijde D, Boers M, et al. Determination of the minimal clinically important difference in rheumatoid arthritis joint damage of the Sharp/van der Heijde and Larsen/Scott scoring methods by clinical experts and comparison with the smallest detectable difference. *Arthritis Rheum* 2002;46:913-20.
23. Thould AK, Simon G. Assessment of radiological changes in the hands and in the feet in rheumatoid arthritis. *Ann Rheum Dis* 1966;25:220-8.
24. Heikkila S, Isomaki H. Long-term outcome of rheumatoid arthritis has improved. *Scand J Rheumatol* 1994;23:13-5.
25. Mottonen TT. Prediction of erosiveness and rate of development of new erosions in early rheumatoid arthritis. *Ann Rheum Dis* 1988;47:648-53.
26. Van der Heide A, Remme CA, Hofman DK, Jacobs JW, Bijlsma JW. Prediction of progression of radiologic damage in newly diagnosed rheumatoid arthritis. *Arthritis Rheum* 1995;38:1466-74.
27. Young MA, van der Heijde DM. Can we predict aggressive disease? *Baillieres Clin Rheumatol* 1997;11:27-37.