Ability of Hand Radiographs to Predict a Further Diagnosis of Rheumatoid Arthritis in Patients with Early Arthritis

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ABSTRACT. ***Objective.*** To evaluate the ability of hand radiographs collected at study inclusion to predict a diagnosis of rheumatoid arthritis (RA) 2 years later, in a cohort of patients with early arthritis.

Methods. We evaluated 270 patients with arthritis of less than one year duration. At the first visit, all patients underwent a standardized evaluation including laboratory tests and radiographs. Followup was 30 ± 11.3 mo. The hand radiographs were read by observers blinded to patient data who looked for item 7 of the 1987 ACR criteria for RA and used Sharp's method to score erosions and joint space narrowing.

Results. The kappa coefficient for ACR item 7 was < 0.65 for bony decalcification and > 0.8 for erosions. Intra and interobserver correlation coefficients for Sharp score ranged from 0.90 to 0.95. The "erosion" component of ACR item 7 was more specific than the full item 7 (96% versus 87.5%; p = 0.02). Sharp erosion score was not better than the erosion component of item 7 (sensitivity 17%; specificity 96%).

Conclusion. Regardless of the criterion used, hand radiographs were of limited value to predict which patients would be considered as having RA 2 years later. Diagnostic performance was similar for the "erosions" component of the 1987 ACR item 7 and for Sharp erosion score. The full 1987 ACR item 7 (erosions or bony decalcification) performed less well. (J Rheumatol 2001;28:2603–7)

Key Indexing Terms:
RECENT ONSET ARTHRITIS
HAND RADIOGRAPH
RHEUMATOID ARTHRITIS
DIAGNOSIS

The diagnosis of early rheumatoid arthritis (RA) is difficult. It relies on a set of converging data from the physical examination, radiographs, and multiple laboratory tests. The value of investigations used in the diagnosis of recent onset arthritis has not been extensively evaluated.

RA is a chronic disease in which persistent inflammation leads to severe joint damage and disability. Radiographic abnormalities are included in several criteria sets for classifying RA [namely, the 1958 American Rheumatology Association (ARA) criteria, the 1961 Rome criteria, the 1966 New York criteria, and the 1987 American College of Rheumatology (ACR) revised criteria][1-4]. At present the most widely used criteria set is the one developed by the ACR in 1987, in which the radiographic criterion (item 7) is "changes typical of RA on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in, or most marked adjacent to, the involved joints (osteoarthritis changes alone do not qualify)." To determine the diagnostic value of item 7, one must conduct separate evaluations of the full item (erosions or bony decalcification) and of each of its 2 components. For each of these elements, the best definition must be determined, and sensitivity and specificity must be measured in a cohort of patients with recent onset arthritis.

The many scoring methods developed for RA range from Larsen's global patient score[5] to Sharp scores for erosions and joint space narrowing in a selected number of joints[6] and to the modification of Sharp score by van der Heijde[7]. Although these scores have been validated for monitoring radiographic progression in definite and recent onset RA[8-10], their diagnostic value has not been studied.

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We assessed the efficacy of the 1987 ACR item 7 and Sharp score for hands in determining whether early arthritis is due to RA.

MATERIALS AND METHODS

Study population. The study included 270 patients seen from 1995 to 1997 at 7 hospitals in Brittany, France, for arthritis of less than one year duration. Biannual radiographs of hand and wrist in posteroanterior view were made with Fuji extremities film and sent to the reference center at Brest. Two hundred fifty-eight radiographs of both hands and wrists taken at the first visit, (called "hand radiographs" in this article) were sent to the reference center and evaluated.

All patients were referred to the 7 study hospitals by general practitioners or rheumatologists who had been previously informed of this study. 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 not more than one year. The study was approved by the institutional review board of Brest University Hospital, and all patients gave written informed consent.

Study design. The baseline assessment included a standardized interview, a general physical examination and rheumatological examination, which included more than 100 variables for each patient such as complete medical history, family history (RA, spondyloarthropathy), joint examination, ACR criteria, and extraarticular manifestations. Patients also had laboratory tests (standard blood and urine measures; C-reactive protein, latex test and ELISA for IgM, IgG, and IgA rheumatoid factors (RF); tests for antiperinuclear factor, antikeratin antibody, antiRA33 antibody, antinuclear antibody (ANA); 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. Each included a standardized interview, a general examination, a rheumatological examination, standard blood and urine tests, immunological tests, and radiographs of the hands and feet. 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 reviewing the panel of clinical, biological, and radiological tests performed during the followup determined whether the diagnosis was RA (RA group) or not (non-RA group). As described[11], the diagnosis by the collegial group of rheumatologists after the last visit was considered to be more reliable than that of an isolated office based rheumatologist. Accordingly, the diagnosis of the panel of 5 rheumatologists at the last visit was taken as the gold standard for the classification of RA and for evaluating the diagnostic efficacy of radiographs of the hands.

Laboratory test methods. RF were measured using the latex test (Fumouze, France) and an in-house ELISA for IgG, IgM, and IgA RF. Antiperinuclear factor was assayed using indirect immunofluorescence[12]. Antikeratin antibody was detected using indirect immunofluorescence with a middle-third rat esophagus section as substrate. Titers of 1/10 were considered significant. AntiRA33 antibody was determined from freshly grown HeLa cells of a nuclear extract containing 7 to 10 mg/ml protein. ANA were detected using a standard immunofluorescence test on HEp-2 cells. Sera with ANA titer ≥ 1/20 were examined for antibodies against Sm, RNP, SSA, and SSB using an ENA profile microplate (EIA Kallestad, Sanofi-Pasteur, Minneapolis, MN, USA) and for antibodies against Jo1 and Scl70 using an ELISA kit (BMD, Marne la Vallée, France). HLA-AB tissue typing was performed using a standard microcytotoxicity test on B lymphocytes, and HLA-DR typing using a molecular biology method.

Radiographic evaluation. Two hundred fifty-eight radiographs of the hands and wrist were evaluable and were included in the analyses of diagnostic performance. All radiographs collected at the first visit were examined by one author (VDP, who had no information about the patients) and by the patient's office based rheumatologist for typical erosions and/or unequivocal bony decalcification as described in item 7 of the 1987 ACR criteria. The 1985 Sharp scores[13] for the hands (erosion score, joint space narrowing score, total score) were also determined by the blinded observer.

Interobserver and intraobserver variabilities were assessed using a panel of 130 pairs of these radiographs: for determination of intraobserver variation, the radiographs were read twice by the blinded observer (VDP) at an interval of 6 months; for determination of interobserver variation, the radiographs were read by the same blinded observer (VDP) and by another trained blinded observer.

The first set of radiographs for each patient were also used to compare the assessments of item 7 by the blinded observer (VDP) and the office based rheumatologist.

Receiver-operating characteristic (ROC) curves were plotted for all qualitative variables.

Statistical analysis. Data were recorded, then analyzed using the Statistical Package for the Social Sciences (SPSS 9.0).

Reliability. We determined the reliability of the radiographic abnormalities (erosion, juxtaarticular osteoporosis, joint space narrowing). The kappa coefficient was used to quantify the reliability of categorical variables[14], and the inter and intraobserver intraclass correlation coefficients to evaluate the reliability of quantitative variables.

Ability of the radiographs to predict RA. The sensitivity and specificity of each variable were determined. ROC curves[15] were plotted for qualitative variables.

Comparison of proportion and rank. Statistical association between radiographic criteria at inclusion and RA diagnosis at the final visit according to clinical and biological data at inclusion were evaluated 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 258 patients had a mean age of 49.5 ± 16.3 years at baseline. There were 176 women and 82 men. The mean synovitis count was 4.3 ± 6 and mean painful joint count was 8 ± 8.5 at baseline. Mean followup was 30 ± 11.3 months. Followup was less than one year in 13 patients (5%), 1–2 years in 17 (7%), 2–3 years in 92 (36%), 3–4 years in 81 (30%), and ≥ 4 years in 55 (20%). At the last visit, 93/258 patients (36%) were given a diagnosis of RA by the panel of 5 rheumatologists.

At baseline, 26% of patients had a positive ELISA for IgM RF and 22% a positive latex test; 31% tested positive for antiperinuclear factor, 15% for antikeratin antibodies, 20% for antiRA33 antibodies, and 43% for HLA-DR4.

Validity of the method

Radiograph assessment by the blinded observer. The intraobserver kappa coefficients for item 7 erosions was 0.88. Corresponding values for item 7 bony decalcification was 0.65.

For total Sharp score, the intra and interobserver correlation coefficients were both 0.98.

Radiograph assessment by office based rheumatologist. For comparison of assessments of the full item 7 by VDP (blinded) and patient's office based rheumatologist (unblinded), the intraobserver kappa coefficient was 0.29.

Radiographic findings at baseline

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

Diagnostic value of hand radiographs

Diagnostic value of item 7 of the 1987 ACR criteria. As compared to the full item 7, the erosions component was more specific (96% vs 87.5%; p = 0.02), but slightly less sensitive (17% vs 22.5%; p value nonsignificant).

Sensitivity and specificity of the full item 7 as evaluated by the blinded observer were 22.5% (21/93) and 87% (144/165), respectively. Corresponding figures for the office based rheumatologist were 23% (22/93) and 97.5% (161/165). This yielded a kappa coefficient of 0.29.

We evaluated the diagnostic value of hand radiographs in those patients with tenderness or swelling of one or more joints in one, 2, or 3 of the following areas: the proximal interphalangeal (PIP) joints, the metacarpophalangeal (MCP) joints, and the wrist (Table 2). This value was slightly higher than in the overall population.

Table 1. Ability of hand radiographs at study inclusion in patients with early arthritis to predict a diagnosis of RA 2 years later.

Radiographic Criteria	RA, n = 93	No RA, n = 165	p
Erosions, item 7 (%)	16 (17)	7 (4)	< 0.001
Bony decalcification	5 (5.5)	14 (8.5)	NS
Full item 7	21 (22.5)	21 (12.5)	NS
Joint space narrowing (Sharp)	3.6	1.45	< 0.001
Erosions (Sharp)	2.37	1.1	< 0.001
Total Sharp score	5.9	2.5	< 0.001

NS: not significant

Table 2. Ability of hand radiographs at study inclusion in patients with early arthritis to predict a diagnosis of RA 2 years later according to the number of swollen and/or tender areas (interphalangeal joints, metacarpophalangeal joints, and/or wrist) at the first visit.

ACR Criteria	Sensitivity (%)	Specificity (%)
Swollen joints = 0/3	2/22 (9)	88/91 (96.5)
Swollen joints = 1 or 2/3	8/51 (15.5)	58/61 (95)
Swollen joints = 3/3	6/20 (30)*	11/12 (91.5)
Tender joints = 0/3	3/18 (16.5)	73/74 (98.5)
Tender joints = 1 or 2/3	7/47 (15.5)	63/68 (92.5)
Tender joints = 3/3	6/30 (20)	21/22 (95.5)

* 3/3 versus 0/3; p < 0.04.

Sensitivity and specificity of the hand radiographs were not influenced by the presence of RF, antifilaggrin autoantibodies, or the HLA-DR4 type (Table 3). Sensitivity was higher in patients with than in those without antiRA33 antibodies.

Diagnostic value of Sharp scores in the hands. The mean total Sharp score at the hands was 5.9 ± 2.5. 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. For a sensitivity of 17% (Figure 1; cutoff, 4.5), erosions had a specificity of 96%.

DISCUSSION

Rheumatologists are acutely aware that the diagnosis of RA needs to be standardized. The earliest classification criteria for RA were based on physical signs[16]. Serological and radiographic findings were added later[17].

Radiographic change is a consequence of synovitis. Thus persistent synovitis predicts the development of erosions in RA. This implies that radiographic change does not occur "early" in the course of the disease and cannot be sensitive in early cases, although it may be specific.

Only 3 studies[18-20] have examined the diagnostic value of radiographs in recent onset inflammatory joint disease. Sensitivity of radiographic changes was nearly 20% and specificity about 90%. However, these studies did not compare different sets of radiographic criteria; neither did they evaluate statistical associations with RA. Moreover, the diagnosis was determined at study inclusion, although the diagnosis of RA is difficult to establish with confidence early in the disease. We investigated the diagnostic value of the 1987 ACR radiographic criterion in a large cohort of patients with recent onset arthritis whose diagnosis was determined by a panel of 5 rheumatologists after a followup of about 3 years.

Table 3. Ability of hand erosions at study inclusion in patients with early arthritis to predict a diagnosis of RA 2 years later according to immunological findings.

ACR Criteria	Sensitivity	Specificity
Latex 20 +	6/46 (13)	8/9 (89)
Latex 20–	10/47 (21.5)	147/153 (96)
IgM RF+	10/57 (17.5)	19/20 (95)
IgM RF+	6/30 (20)	130/136 (95.5)
APF +	4/46 (17.5)	31/33 (95)
APF–	8/42 (19)	117/121 (96.5)
AKA+	5/33 (15)	5/5 (100)
AKA–	9/52 (17.5)	141/147 (96)
RA33+	8/18 (44.5)*	33/34 (97)
RA33–	8/50 (16)	91/96 (95)
HLA = DR4 +	11/53 (20.5)	57/59 (96.5)
HLA = DR4 –	5/38 (13)	87/92 (94.5)

*p = 0.04. RF: rheumatoid factors, APF: antiperinuclear factor, AKA: antikeratin antibody, RA33: anti-RA33 antibody.

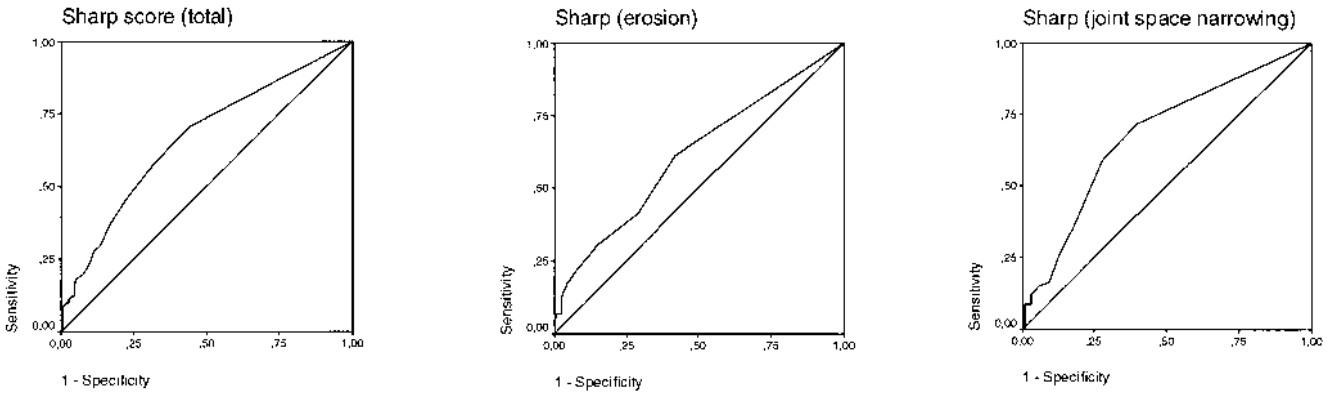

Figure 1. Receiver-operating characteristic curves for the ability of the Sharp score for hands in predicting at first visit which patients would have a diagnosis of RA at the last visit.

First, we evaluated the diagnostic value of item 7 of the 1987 ACR criteria, that is, presence of erosions and/or bony decalcification. In the hands, erosions were significantly associated with RA, whereas bony decalcification alone or in combination with erosions was not.

Substantial interobserver variation occurred for bony decalcification. Although Larsen[21] stated that bony decalcification was specific for RA, this abnormality may be of limited usefulness because its assessment varies according to the radiographic technique[22]. Fletcher, *et al*[23] and Thould, *et al*[24] found bony decalcification in 5% of patients with definite RA and considered this abnormality nonspecific for RA. In contrast, Brook, *et al*[25] reported that bony decalcification was present in 28% of patients with RA of less than one year duration. In a recent study, Rau *et al*[26] developed a new scoring method for RA based on the recommendations of a panel. Neither soft tissue swelling nor bony decalcification are included in their score.

In our study, erosions were associated with RA. Interobserver variation for item 7 erosions was high (kappa = 0.88). It has been suggested that erosions should be used to evaluate radiographic damage in RA[27,28]. Recently, van der Heijde, *et al*[29] reported that the presence of erosions was as sensitive for the diagnosis of RA as the full item 7. However, the diagnostic value of item 7 erosions was low in our cohort.

We determined the best cutoff for erosions scored using Sharp's method. In our study, the ROC curves of Sharp scores suggested that erosions offered the best diagnostic performance characteristics. However, the diagnostic value of the Sharp erosion score was not significantly different from that of item 7 erosions. We also found that Sharp joint space narrowing score and Sharp erosions score had similar diagnostic values, and that combining these 2 scores did not produce any noticeable improvement.

In our study, the diagnostic value of hand radiographs was slightly better in patients with hand synovitis (tenderness and/or swelling) than in those without. In contrast, diagnostic value was not influenced by the presence of a positive ELISA for IgM RF, a positive latex test, antikeratin antibodies, antiperinuclear factor, or the HLA-DR4 phenotype. Sensitivity was significantly better in the patients with antiRA33 antibody. We studied only the radiographs obtained at baseline; and consequently, our results do not provide any information on prognostic factors in RA[30-35].

In conclusion, regardless of the criterion used, hand radiographs in early arthritis were of limited value to predict at the first visit which patients would receive a diagnosis of RA at the last visit, 2 years later.

Bony decalcification was of no diagnostic assistance. Presence of erosions was the best diagnostic indicator and showed little intra and interobserver variation. Combining hand radiographs with clinical or laboratory findings did not benefit the diagnosis.

Only hand radiographs are taken into account in item 7 of the 1987 ACR criteria, but the absence of foot radiographs in these criteria has been heavily criticized, especially in Europe. Studies suggest that sensitivity improved after addition of radiographs of the feet[36-39]. Thus, we plan to study the efficacy of both Sharp score for the feet and combination of hand and foot radiographs in determining whether early arthritis is due to RA in our population.

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