Performance of Hand Radiographs in Predicting the Diagnosis in Patients with Early Arthritis

VALERIE DEVAUCHELLE-PENSEC, JEAN M. BERTHELOT, SANDRINE JOUSSE, ISABELLE SAMJEE, THIERRY JOSSEAUME, DANIELLE COLIN, GERARD CHALÉS, CATHERINE Le HENAFF, JEAN B. THOREL, SYLVIE HOANG, ANTOINE MARTIN, PIERRE YOUINOU, PAUL Le GOFF, and ALAIN SARAUX

ABSTRACT. ***Objective.*** To evaluate the ability of baseline hand radiographs to predict the diagnosis 2 years later in a cohort of patients with early arthritis.

Methods. A total of 258 patients with arthritis onset within the previous year were evaluated. At baseline, all patients underwent a standardized evaluation including laboratory tests and radiographs. Hand radiographs were read by a blinded observer who used a standardized procedure for detecting features of crystal deposition diseases and rheumatoid arthritis (RA). After 30 ± 11.3 months, the final diagnosis was established by a panel of rheumatologists. All radiographs were evaluated.

Results. Significant associations were found between radiographic features and a clinical diagnosis of RA, calcium pyrophosphate dihydrate (CPPD) arthritis, and hydroxyapatite arthritis. No radiographic abnormalities suggesting psoriatic arthritis or gout were seen. The sensitivities of hand radiographs for diagnosing CPPD or hydroxyapatite arthritis ranged from 80% to 100%. Baseline hand radiographs suggested the final diagnosis in 31/258 patients, including 21 (22.5%) of the 93 patients with RA, 10 of the 11 (91%) patients with CPPD or hydroxyapatite deposition disease, and none of the patients with other disorders. Sensitivity was 29%, specificity 86.5%, positive predictive value 61%, and negative predictive value 63%.

Conclusion. In our cohort of patients with recent arthritis, the overall performance of hand radiographs in predicting a diagnosis 2 years later was modest. However, they had an excellent diagnostic value for calcium deposition diseases. (First Release June 15, 2006; J Rheumatol 2006;33:1511–5)

Key Indexing Terms:
RECENT ARTHRITIS RHEUMATOID ARTHRITIS CRYSTAL DEPOSITION DISEASE
HAND RADIOGRAPHS DIAGNOSIS

Recent-onset arthritis can reveal many diseases, and investigations are often needed to establish the diagnosis. Although no guidelines exist, radiographs are usually part of the examination. Hand radiographs are widely available and easy to perform. They can reveal characteristic features of various forms of arthritis including rheumatoid arthritis (RA), psoriatic arthritis (PsA), and crystal deposition diseases (CDD). However, their diagnostic value has not been evaluated in a cohort of patients with recent-onset arthritis.

The diagnosis of early RA relies on a set of converging data from the physical examination, radiographs, and laboratory tests. Erosions often develop during the first 2 years and constitute a key argument in favor of RA[1], but they are often absent at an early stage of RA. However, hand radiographs in recent arthritis can also be useful to rule out other causes of arthritis. CDD produce characteristic radiographic features but can mimic RA[2]. The 3 main crystals responsible for CDD are monosodium urate (in gout), calcium pyrophosphate dihydrate (CPPD; usually chondrocalcinosis), and calcium phosphate (usually hydroxyapatite). Radiographs reveal typical calcific deposits in CPPD and hydroxyapatite deposition diseases. CPPD is the most common CDD, and can cause deposits not only in the tendons and ligaments, but also in the synovium and cartilage[3]. Chondrocalcinosis is a radiological feature of CPPD deposition disease in which linear and punctate calcifications are visible within the fibrocartilage and hyaline cartilage, frequently in a bilateral and symmetric distribution. Hydroxyapatite is a common cause of recurrent painful crystal deposition in periarticular soft tissues. The shoulders are most commonly affected, followed by the hands and wrists. The acute periarticular inflammation can replicate

From the Unit of Rheumatology, Cavale Blanche Hospital, CHU Brest, Brest, France.

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V. Devauchelle-Pensec, MD, Unit of Rheumatology, Hôpital de la Cavale Blanche, CHU Brest, and Unit of Immunology, Morvan Hospital, Brest; S. Jousse, MD; I. Samjee, Fellow; P. Le Goff, MD, PhD; A. Saraux, MD, PhD, Unit of Rheumatology, Hôpital de la Cavale Blanche, CHU Brest; J.M. Berthelot, MD, Department of Rheumatology, Hôtel-Dieu, CHU Nantes; T. Josseaume, Fellow; D. Colin, MD, Department of Radiology, Hôpital de la Cavale Blanche; G. Chales, MD, PhD, Department of Rheumatology, Rennes; C. Le Henaff, MD, Department of Internal Medicine, Morlaix; J.B. Thorel, MD, Department of Rheumatology, Lorient; S. Hoang, MD, Department of Rheumatology, Vannes; A. Martin, MD, Department of Rheumatology, St Brieuc; P. Youinou, MD, PhD, Unit of Immunology, Morvan Hospital, CHU Brest.

Address reprint requests to Dr. V. Devauchelle-Pensec, Unit of Rheumatology, Hôpital de la Cavale Blanche, BP 824, F29609 Brest cedex, France. E-mail: valerie.devauchelle-pensec@chu-brest.fr

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the clinical manifestations of RA. Monosodium urate crystal deposits are not visible on radiographs, but typical joint lesions can occur in patients with gout arthropathy.

Among the spondyloarthropathies (SpA), PsA can lead to destructive lesions of the fingers and toes whose distinctive radiographic appearance is readily differentiated from RA[4-8].

The diagnostic performance of each of these radiographic features has not been evaluated in a cohort of patients with recent-onset arthritis. The best definition of each feature should be determined, and sensitivity and specificity should be measured. We designed our study to determine (1) the diagnostic value of each of the radiographic features (including PsA and CDD) in a cohort of patients with recent-onset arthritis; and (2) the overall performance of hand radiographs for the diagnosis of recent-onset arthritis after a followup of 2 years.

MATERALS AND METHODS

Study population. The study has been described[9]. Patients evaluated from 1995 to 1997 in 7 hospitals in Brittany for arthritis ≤ 1 year duration were included. Posteroanterior radiographs of the hands and wrists ("hand radiographs") were taken twice a year using Fuji extremities film and sent to the coordinating study center (Brest Teaching Hospital, Brest). Baseline radiographs were available for 258 patients.

Patients were referred to the 7 study centers by general practitioners and rheumatologists who had been informed of the research project. Inclusion criteria were age ≥ 16 years, swelling of one or more joints, absence of previous diagnosis of a specific inflammatory joint disease, and symptom duration ≤ 1 year. The study was approved by the institutional review board of the Brest Teaching Hospital, and all patients gave their written informed consent.

Study design. Baseline assessment included a standardized interview; a rheumatological and general physical examination comprising more than 100 items, such as present and past medical history, family history (e.g., RA or SpA), joint examination, American College of Rheumatology (ACR) criteria, and extraarticular manifestations; laboratory tests [standard blood and urine measures; C-reactive protein; rheumatoid factors (RF) by the latex test (Fumouze, France)]; in-house ELISA for IgG, IgM, and IgA RF; anti-citrullinated antibody; antinuclear antibodies (ANA); HLA AB and DR tissue typing; and radiographs (chest, pelvis, hands, and feet). Each patient was asked to undergo an evaluation every 6 months by an office-based rheumatologist (OBR). Each 6-monthly evaluation included a standardized interview; a rheumatological and general physical examination; standard blood and urine tests; immunological tests; and radiographs of the hands and feet. Evaluations were stopped when the following occurred: (1) the OBR 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 OBR diagnosed RA). After the last visit, a panel of 5 rheumatologists determined whether the patient did or did not have RA, SpA, CPPD deposition disease, hydroxyapatite deposition disease, or gout. The diagnosis established by the panel after the last visit was considered more reliable than that of the OBR and was therefore used as the gold standard for classifying patients in the RA, SpA, and CDD groups and for evaluating the diagnostic performance of baseline hand radiographs.

Case ascertainment. The gold standard for diagnosis at the end of the study was established by the panel of 5 rheumatologists, using all the available data obtained during the followup until the last visit. As described in the study design patients were seen every 6 months and underwent physical examination and numerous standardized biological and radiographic evaluations. As hand and foot radiographs were also done every 6 months for 2 years, the panel of 5 rheumatologists used all of them and especially the last one for the diagnosis.

In order to determine the diagnosis value of hand radiographs, the initial radiographs were read by one author (VDP), who had no information about the patients. The panel of 5 rheumatologists was unaware of the conclusion of the reader.

Radiographic evaluation. Baseline hand radiographs were available for 258 patients. They were evaluated by each patient's OBR, then sent to the coordinating center, where they were read by one author (VDP), the observer, who had no information about the patients. A standardized evaluation procedure was used to record the site and number of the following abnormalities: typical erosions and/or unequivocal bony decalcification as described in item 7 of the 1987 ACR criteria; crystal deposits with their number and location, and whether CPPD or hydroxyapatite deposition disease was diagnosed; typical features of gouty arthritis; and typical features of osteoperiostitis affecting one or more distal phalanges and distal interphalangeal joints as described by Fournié, *et al*[5], or the radiological criteria of Avila, *et al*[4] (destruction of the distal interphalangeal joint and bony proliferation at the base of the distal phalanx) for PsA. Finally, the observer recorded whether the radiographs provided a diagnosis.

Radiographic assessment. We evaluated the reliability of radiographic abnormalities, using the kappa coefficient for categorical variables and the intra- and interobserver correlation coefficients for quantitative variables. Intra- and interobserver variability for erosions, bony decalcification, joint space narrowing, and chondrocalcinosis were assessed using 130 hand radiographs. Because few radiographs showed evidence of chondrocalcinosis, we also determined intra- and interobserver variability using 50 radiographs of both hands and both knees from 50 patients with chondrocalcinosis who were not part of the study cohort. Intraobserver variability was determined by having one observer (VDP) evaluate the same radiographs twice, 3 months apart. Interobserver variability was evaluated by asking 2 blinded observers (including VDP) to read the same radiographs. Intraobserver kappa coefficients were 0.88 for item 7 erosions and 0.65 for item 7 bony decalcification. Intraobserver kappa coefficients were 0.87 and 0.42 for these 2 features, respectively, as described[10]. For crystal deposits, intraobserver kappa coefficients were 0.89, 0.86, and 0.91 for all sites, the triangular cartilage at the distal radioulnar joint, and the knee, respectively. Corresponding interobserver kappa coefficients were 0.83, 0.78, and 0.71, respectively.

Statistical analysis. Data were analyzed using the Statistical Package for the Social Sciences (SPSS 9.0). Statistical associations between baseline radiograph findings and clinical diagnosis of RA, CPPD deposition disease, hydroxyapatite deposition disease, gout, or PsA at the last visit were evaluated using a chi-square test (or Fisher's exact test where appropriate). P values < 0.05 were considered significant. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each baseline radiographic variable in predicting the final diagnosis were determined. The intra- and interobserver correlation coefficients were used to evaluate the reliability of quantitative variables.

RESULTS

The 258 patients had a mean age of 49.5 ± 16.3 years at baseline. There were 176 women and 82 men. At baseline, the mean synovitis count was 4.3 ± 6 and the mean painful joint count 8 ± 8.5. At the hands and wrists, symptoms consisted of tenderness in one or more joints in 64% (163/255) of patients and/or in swelling of one or more joints in 56.5% (144/255) of patients. Mean followup was 30 ± 11.3 months. Mean disease duration at baseline was 0–2 months in 124 (48%) patients, 3–5 months in 65 (25%) patients, 6–8 months in 30 (11%) patients, and 9–11 months in 39 (15%) patients. The mean number of joints with arthritis between symptom onset and the baseline visit was 8.5 ± 8. At baseline, 44 (17%) patients had monoarthritis and 214 (83%) had oligo- or polyarthritis; 26%

of patients had a positive ELISA for IgM RF, 22% had a positive latex test, 20% a positive anti-RA33 test, and 43% a positive HLA-DR4 test.

At the end of followup, 93 (36%) patients were given a diagnosis of RA by the panel of rheumatologists. In addition, 50 (19.3%) patients had PsA or another SpA and 13 (5%) had a CDD (CPPD deposition disease, n = 6; hydroxyapatite deposition disease, n = 5; gout, n = 2). In 33 (12.8%) patients, the diagnosis remained unknown. Sixty-nine patients had another different diagnosis. As described[9], the final diagnosis of the panel was based on a set of converging data including clinical examination, radiological abnormalities, and biological tests.

Baseline radiographic findings (Table 1). We looked for statistical associations between various initial hand radiograph abnormalities described by the observer and the final diagnosis at the end of followup by the panel of rheumatologists. Erosions typical of RA were significantly associated with a final diagnosis of RA. Radiographic evidence of hydroxyapatite or CPPD deposition disease was strongly associated with a final diagnosis of the corresponding disease ($p < 0.0001$). Of the 5 cases of gout, none was detected on the baseline hand radiographs. Osteoperiostitis was not detected in our cohort. Consequently, we focused our study on the diagnostic performance of item 7 erosions for RA and of evidence suggesting hydroxyapatite or CPPD deposition.

Diagnostic value of hand radiographs (Table 1). The panel gave a diagnosis of CPPD deposition disease in 6 (2.3%) patients. Among them, 5 had chondrocalcinosis on baseline hand radiographs examined by the observer. The sensitivity and specificity of chondrocalcinosis on baseline radiographs were 83% (5/6) and 100% (253/253), respectively.

Calcium phosphate deposits were noted at baseline in 49 patients, of whom only 5 (10%) were given a diagnosis of hydroxyapatite deposition disease by the observer who evaluated the baseline radiographs. Table 2 gives the number of deposits in each of the 49 patients and shows that only patients with ≥ 6 deposits were given a diagnosis of hydroxyapatite deposition disease. The sensitivity and specificity of ≥ 6 deposits were both 100% (5/5 for sensitivity, 253/253 for specificity) for the diagnosis of hydroxyapatite deposition disease.

Table 2. Number of crystal deposits visible on baseline hand radiographs in patients who were or were not given a diagnosis of hydroxyapatite deposition disease based on the radiographs.

No. of Deposits per Patient	Diagnosis of Hydroxyapatite Deposition Disesae	
	Yes	No
1	0	21
2	0	16
3	0	3
4	0	2
5	0	2
6	1	0
7	1	0
9	2	0
10	1	0
Total	5	44

Only 3 diagnoses were predicted by baseline hand radiographs, namely, RA, CPPD deposition disease, and hydroxyapatite deposition disease. Hand radiographs were unable to predict gout or PsA.

Hand radiogaphs were able to predict RA with a sensitivity of 22.5% (21/93) and a specificity of 87.5%, a NPV of 66% (144/216) and a PPV of 50% (21/42).

Overall, baseline hand radiographs predicted the diagnosis (Table 3) made 2 years later in 31 of the 258 patients, with 30% sensitivity (31/108) and 85% specificity (119/140). The NPV was 60% (119/206) and PPV was 57.7% (21/52).

DISCUSSION

We evaluated the performance of hand radiographs in predicting a diagnosis 2 years later in a large cohort of patients with recent-onset arthritis. Hand radiographs at inclusion were read by a blinded observer (VDP), who had no information about the patients' data. The gold standard was the diagnosis of a panel of 5 rheumatologists. They made the diagnosis at the end of the followup, using all data (clinical, biological, and radiological) concerning each patient. They used in particular the last radiographs for their diagnosis. Hence the diagnostic value of initial radiographs can be determined without major bias. As previously reported the diagnosis of the panel was

Table 1. Associations between criteria on baseline hand radiographs and the final diagnosis of the panel of rheumatologist 2 years later.

Diagnosis of the Observer on Initial Radiographs	Diagnosis After 2 Years: Diagnosis Considered Present 2 Years Later by the Panel	Diagnosis After 2 Years: Diagnosis Considered Absent 2 Years Later by the Panel	p
Radiographic features of RA (%)	21/93 (22.5)	188/167 (87.3)	0.039
Radiographic features of hydroxyapatite deposition disease (%)	5/5 (100)	253/253 (100)	< 0.0001
Radiographic features of chondrocalcinosis deposition disease	5/6 (83.3)	252/252 (100)	< 0.0001

Table 3. Performance of baseline hand radiographs in predicting the diagnosis established 2 years later.

Diagnosis Made After 2 Years by a Panel of Rheumatologists	Diagnosis Predicted at Baseline Based on Hand Radiographs			
	Sensitivity, %	Specificity, %	PPV, %	NPV, %
RA, chondrocalcinosis, or hydroxyapatite deposition disease	29 (31/108)	85 (119/140)	60 (31/52)	57.7 (119/206)

PPV: positive predictive value, NPV: negative predictive value.

often different from the initial diagnosis. We had found[10] that hand radiographs performed only moderately well for predicting RA at an early stage. This is in accord with reports that specific radiographic manifestations of RA appeared later. However, hand radiographs in recent arthritis can be useful also to rule out other causes of arthritis. Therefore, we designed our study to determine the overall performance of hand radiographs in predicting the cause of early arthritis. We developed a standardized procedure for interpreting the baseline radiographs; we defined radiographic features indicating RA, PsA, CPPD deposition disease, hydroxyapatite deposition disease, and gout.

We first assessed the ability of hand radiographs to predict RA, PsA, chondrocalcinosis, hydroxyapatitis, and gout. We demonstrated that hand radiographs were able to predict RA, hydroxyapatitis, and chondrocalcinosis. Radiographic abnormalities were significantly associated with the clinical diagnosis of the panel of 5 experts. Baseline hand radiographs failed to predict gout and PsA.

Gout was the final diagnosis in 5 patients. Gout crystals are not visible on radiographs, and the typical radiographic signs of gouty arthritis[11] develop only 5 to 10 years after symptom onset[12]. However, radiographic features of gouty arthritis have been reported in symptom-free patients[13]. In early gout, mild soft tissue swelling about the joint may be the only abnormality. In our study, the final diagnosis of gout was based on knee synovitis with identification of typical monosodium urate crystals.

Similarly, PsA was not predicted by the baseline hand radiographs. Again, the most likely explanation is the short disease duration at study inclusion. Psoriatic osteoperiostitis on hand radiographs srongly suggests PsA. This abnormality was described at the great toe by Avila, *et al*[4] and by Resnick, *et al*[7]. Whereas other SpA rarely target the hands and wrists, the distal interphalangeal joint constitutes a typical site of involvement in PsA, as shown by Fournié, *et al*[5]. Osteoperiostitis of the distal interphalangeal joints develops gradually over the first 5 years of the disease. In our cohort only 4 patients were given a diagnosis of PsA, based on typical skin lesions associated with distal inflammatory arthritis of the hand. None of these patients had radiological destructive lesions at baseline.

In our cohort, we observed that baseline hand radiographs had high sensitivity and specificity for predicting the diagnosis of CPPD or hydroxyapatite deposition disease. To our knowledge, this is the first study that evaluated the prevalence of CDD in a cohort of patients with recent-onset arthritis. The prevalence of CDD in the general population is difficult to determine because many patients are free of symptoms. Chondrocalcinosis becomes increasingly common with advancing age. In prospective studies, CDD was found in 2% to 30% of individuals older than 60 years[14-18] and in 50% of patients aged 80 to 89 years[19]. In symptomatic forms, the most common pattern is acute pseudogout, with self-limited attacks most commonly involving the knee[20]. The prevalence of hand and wrist involvement has ranged across studies from 27% to 94%[8,17,21,22]. Concomitant RA and CPPD deposition disease has been reported[23].

Intraarticular hydroxyapatite crystals have been described in association with erosive arthritis, particularly in rapidly destructive forms. It is unclear whether the crystals are the initial pathogenic factor or whether they are the consequences of joint destruction.

The diagnosis of hydroxyapatitis is based on a set of converging data[24], and identification of crystals on radiographs or in synovial fluid is crucial. The prevalence of this deposition disease increases with age. In our cohort, crystals of hydroxyapatitis were reported by the reader on hand radiographs in 16% of the population, but a diagnosis of hydroxyapatite deposition disease was given by the reader in only 12% (5/41) of patients. Due to the high prevalence of hydroxyapatitis, the diagnosis was considered relevant by the reader when the number of deposits was higher than 5.

We then determined the global performance of initial hand radiographs to predict a diagnosis of arthritis after 2 years' followup. Radiographs were able to predict the diagnosis for 22.5% (21/93) of patients with RA, 100% (5/5) of patients with hydroxyapatitis, and 83.3% (5/6) of patients with chondrocalcinosis disease. Baseline hand radiographs in our cohort of 258 patients with recent-onset arthritis had 29% sensitivity and 85% specificity for predicting the diagnosis established 2 years later, when only RA, CPPD deposition disease, and hydroxyapatite deposition disease were taken into account.

Hand radiographs can help to confirm the diagnosis of early RA and to eliminate other diagnoses, until diagnostic criteria for early RA are developed.

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