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ORIGINAL ARTICLE

Potential Classification Criteria for Rheumatoid Arthritis After Two Years: Results From a French Multicenter Cohort

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Objective. **To determine agreement among the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria, a diagnosis of rheumatoid arthritis (RA) by a rheumatologist, and other criteria previously used to classify arthritis.**

Methods. **We used a nationwide longitudinal prospective cohort of patients with recent-onset arthritis. After 2 years, the patients were classified as receiving disease-modifying antirheumatic drugs (DMARDs), having synovitis, having joint erosions typical of RA, having a rheumatologist diagnosis of RA with >50.0% certainty, having a no better alternative diagnosis with >50.0% certainty, and having a diagnosis of RA using the 1987 ACR criteria and the 2010 ACR/EULAR criteria. Agreement among these criteria was assessed based on Cohen's kappa coefficient, where ≥0.80 = excellent, 0.60–0.79 = good, 0.40–0.59 = moderate, and <0.40 = poor.**

Results. **Of the 692 evaluated patients, 544 (78.6%) had persistent arthritis (defined as synovitis, ongoing DMARD treatment, or both) after 2 years. Among these 544 patients, 496 (91.2%) were receiving DMARDs. Agreement among all criteria was poor (estimated κ = 0.09–0.43), except when including a rheumatologist diagnosis of RA with >50.0% certainty or a no better alternative diagnosis with >50.0% certainty (estimated κ = 0.69–0.81). The strongest associations with a rheumatologist diagnosis of RA with >50.0% certainty were the 2010 ACR/EULAR criteria and the combination of no better alternative diagnosis, persistent arthritis, 1987 ACR criteria, and positive anti–citrullinated protein antibody.**

Conclusion. **Rheumatologist diagnosis of RA with >50.0% certainty after 2 years agreed well with the 2010 ACR/EULAR criteria or a combination of items including no better alternative diagnosis, confirming high value as classification criteria after 2 years of followup.**

INTRODUCTION

The last few years have brought extraordinary insights into the immunologic mechanisms involved in rheumatoid arthritis (RA) and have witnessed the remarkable improvements in the treatment of this disease (1,2). In 2010, the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) issued new RA di-

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Significance & Innovations

- Two years after patients presented with arthritis, we found that the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria, a rheumatologist diagnosis of rheumatoid arthritis (RA), and a combination of items including a no better alternative diagnosis produced similar results, confirming the value of the 2010 ACR/EULAR as classification criteria.
- The presence of 1 or more joint erosions typical of RA may not consistently indicate RA.

agnostic criteria to identify patients with undifferentiated inflammatory synovitis who are at high risk for persistent or erosive RA. Patients fulfilling the 2010 ACR/EULAR criteria should receive disease-modifying antirheumatic drugs (DMARDs). The 2010 ACR/EULAR criteria were developed to identify patients with early arthritis at risk for RA, but they were published as classification criteria (3,4) and have not been validated in patients who have had RA for more than 2 years (4).

An important characteristic of the 2010 ACR/EULAR criteria not included in the 1987 ACR criteria (5) is an exclusion item, namely, the no better alternative (NBA) diagnosis (4). We previously demonstrated that this item explained much of the improvement in performance over previous criteria (6). The exclusion criterion may function merely as the opposite of a diagnosis of RA in patients having early arthritis with a potential for progressing to RA.

In previous studies, several criteria, but not validated classification criteria sets, were used to define RA after 2 years, including the degree of certainty of the physician diagnosis of RA (7), clinical synovitis, joint erosions, and DMARD treatment (8–10). A comparison of these criteria is needed to determine which are most reliable. In the present study, we aimed to evaluate the agreement between the 2010 ACR/EULAR criteria, a rheumatologist diagnosis of RA, and other criteria previously used to classify early arthritis. We also sought to identify the criterion or combination of criteria most closely associated with a rheumatologist diagnosis of RA in the ESPOIR (Étude et Suivi des Polyarthrites Indifférenciées Récentes [Study and Followup of Early Undifferentiated Polyarthritis]) cohort after 2 years of followup.

PATIENTS AND METHODS

Study population. The French Society of Rheumatology established a nationwide longitudinal prospective cohort (the ESPOIR cohort [11]) to enable investigations of the diagnosis, outcome markers, epidemiologic characteristics, pathogenesis, and medicoeconomics of early arthritis and RA. General practitioners and rheumatologists referred patients with early arthritis to hospitals participating in the ESPOIR cohort project. Patients were eligible for inclusion if they had a definitive or probable clinical diagnosis of RA or polyarthritis that was not better explained by another etiology. Patients were included if they were ages >18 years and <70 years, had swelling of at least 2 joints for 6 weeks with a symptom duration ≤6 months, and had no prior treatment with DMARDs or glucocorticoids; however, receiving glucocorticoids for ≤2 weeks at a mean dosage of ≤20 mg/day and with discontinuation for at least the past 2 weeks did not prevent study inclusion. The patients who were included were evaluated every 6 months for 2 years, then once a year for at least 10 years.

The study was approved by the Institutional Review Board of the Montpellier University Hospital, which was the coordinating center for this nationwide study. Before inclusion, all patients gave their written informed consent to participate in this prospective followup study.

Study design. The baseline assessment included a standardized interview; a general physical examination; laboratory tests (standard blood and urine variables; an enzyme-linked immunosorbent assay for IgM, IgG, and IgA rheumatoid factors; tests for anti–citrullinated protein antibodies [ACPAs] and antinuclear antibodies; and HLA–DR phenotype determination); and radiographs of the chest, pelvis, hands, and feet in the posteroanterior view and feet in the oblique view. Each patient was evaluated by an ESPOIR study rheumatologist every 6 months for 2 years and once per year thereafter. The certainties with which the rheumatologist diagnosed RA and established the absence of a better alternative diagnosis were evaluated on visual analog scales (range 0–100). The evaluations were free of charge. To determine which criteria the rheumatologists used to diagnose RA after 2 years, we classified patients on the basis of treatment with ≥1 DMARDs (methotrexate, sulfasalazine, leflunomide, gold, biologic agents, or >5 mg/day of prednisone), having synovitis (at least 1 joint with synovitis at month 24), having joint erosions typical of RA according to a blinded reader (GJT), having a rheumatologist diagnosis of RA with >50.0% certainty, having an NBA diagnosis with >50.0% certainty, and having a diagnosis of RA using the 1987 ACR criteria and the 2010 ACR/EULAR criteria. The 1987 ACR and 2010 ACR/EULAR criteria were considered present if noted at any time during ≥1 visits, except for the 2010 ACR/EULAR exclusion criterion (NBA diagnosis), which was evaluated only at the last visit.

Radiography. For each patient, a set of radiographs was obtained at baseline and again at every 6 months in each visit to the rheumatologist. The radiographs included posteroanterior views of the hands, wrists, and feet, as well as oblique views of the feet. The radiographs were sent to the coordinating center for independent interpretation by a rheumatologist (GJT) who had received no information about the patients. For each radiograph, the reader followed a standardized procedure to assess the number of joint erosions and severity of joint space narrowing scored according to the modified Sharp/van der Heijde method for posteroanterior views of the hands and feet (12,13). The

Table 1. Mean baseline and followup characteristics of patients in the ESPOIR cohort (n = 813)*

Characteristics	Patients with 2 years of followup (n = 692)	Patients with 2 years of followup and complete radiographs (n = 646)	Patients without 2 years of followup (n = 121)	*P*†
Female:male ratio	528:164	489:157	96:25	0.46
Age at onset, years	47.9 ± 12.2	47.8 ± 12.2	45.7 ± 14.2	0.12
Swollen joint count in 28 joints	7.5 ± 5.4	7.6 ± 5.4	5.2 ± 4.6	0.0001
Tender joint count in 28 joints	8.9 ± 7.1	8.9 ± 7.1	6.0 ± 6.2	0.0001
DAS28	5.2 ± 1.3	5.2 ± 1.3	4.7 ± 1.3	0.0001
Nodules, no./total (%)	14/692 (2)	14/646 (2)	3/121 (2.5)	0.75
ESR, mm/hour	11.8 ± 12.7	12.74 ± 11.1	16.8 ± 12.8	0.75
CRP level, mg/dl	20.8 ± 33.6	20.9 ± 33.9	16.9 ± 23.7	0.40
IgM-RF, no./total (%)	386/692 (55.8)	360/646 (55.7)	83/120 (69.2)	0.006
Joint erosion, no./total (%)	176/642 (27.4)	176/642 (27.4)	18/94 (19.1)	0.09

* Values are the mean ± SD unless otherwise indicated. ESPOIR = Étude et Suivi des Polyarthrites Indifférenciées Récentes (Study and Followup of Early Undifferentiated Polyarthritis); DAS28 = Disease Activity Score in 28 joints; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; IgM-RF = IgM rheumatoid factor.
† Patients with 2 years of followup versus patients without 2 years of followup.

location of each abnormality was recorded. Finally, the reader indicated whether patients had at least 1 joint erosion considered by the reader to be typical of RA (14) of the hands or feet.

Statistical analysis. First, we described the data by the presence or absence of persistent arthritis (synovitis, DMARD treatment, or both), the presence or absence of at least 1 joint erosion typical of RA, and the diagnosis established by the ESPOIR cohort rheumatologist. Second, we evaluated agreement, after 2 years of followup, among all definitions previously used to classify early arthritis (having a rheumatologist diagnosis of RA with >50.0% certainty, receiving DMARD treatment, having joint erosion[s] typical of RA, and having a diagnosis of RA using the 1987 ACR and 2010 ACR/EULAR criteria). Third, we used logistic regression to identify the criteria most strongly associated with a rheumatologist diagnosis of RA with >50.0% certainty after 2 years.

The data were analyzed using SPSS, version 15.0. The chi-square test (or Fisher's exact test, as appropriate) and Mann-Whitney test were used for the univariate analysis of criteria collected at the last visit and for a rheumatologist diagnosis of RA with >50.0% certainty. The variables associated with *P* values less than 0.1 by univariate analysis were entered in a multivariable regression model with forward selection. Cohen's kappa coefficient was determined to evaluate agreement among the criteria, where ≥0.80 = excellent, 0.60–0.79 = good, 0.40–0.59 = moderate, and <0.40 = poor (15). *P* values less than 0.05 were considered statistically significant.

RESULTS

Study group. The ESPOIR cohort included 813 patients, of which 624 (76.8%) were women. The mean time from symptom onset to the rheumatologist referral was 75 days. We evaluated 692 patients (85.1%) over 2 years of followup. Disease activity was higher in the subgroup evaluated over 2 years of followup than in the patients evaluated without 2 years of followup (Table 1). For 686 of the 692 patients, we obtained data on the degree of certainty of the rheumatologist diagnosis of RA, disease persistence, 1987 ACR criteria, and 2010 ACR/EULAR criteria. After 2 years, we had complete radiograph sets for 646 patients (79.5%).

Figure 1 shows the patient characteristics according to criteria classifying early arthritis after 2 years. The patients were classified into 8 groups according to disease persistence (groups A and B), definition of disease persistence if present (subgroups B1 [synovitis but no DMARDs], B2 [DMARDs but no synovitis], and B3 [both DMARDs and synovitis]), and joint erosions (at least one or none). Of the 692 patients with 2 years of data, 544 (78.6%) had persistent arthritis after 2 years, and most of these patients were receiving DMARDs (subgroups B2 and B3, n = 496 [91.2%]). Among the patients with persistent arthritis who were not receiving DMARDs (subgroup B1) and those with no persistent arthritis or DMARD treatment (group A), 24 (50.0%) of 48 and 48 (32.4%) of 148, respectively, met the rheumatologist diagnosis of RA with >50.0% certainty criterion.

Typical radiographic erosions were seen on 163 (25.0%) of 652 sets of the feet and 186 (28.4%) of 654 sets of the hands. Of 646 patients with complete sets, 179 (27.7%) had joint erosions typical of RA. The modified Sharp/van der Heijde score was ≥1 for 173 (26.5%) of 652 radiographs of the feet and 213 (32.6%) of 654 radiographs of the hands. Although having at least 1 joint erosion typical of RA was among the definitions of RA, 34 patients (17 in group A, 5 in group B1, 8 in group B2, and 4 in group B3) who had joint erosions did not have a rheumatologist diagnosis of RA with >50.0% certainty (the reported diagnoses were osteoarthritis, reflex sympathetic dystrophy, systemic lupus, Sjögren's syndrome, calcium pyrophosphate disease, undifferentiated arthritis, remitting seronegative symmetrical synovitis with pitting edema, fibromyalgia, and spondyloarthropathy).

In total, 436 (84.7%) of 515 patients with persistent arthritis (and radiographs) after 2 years (group B) and 224 (91.4%) of 245 patients with both persistent arthritis and

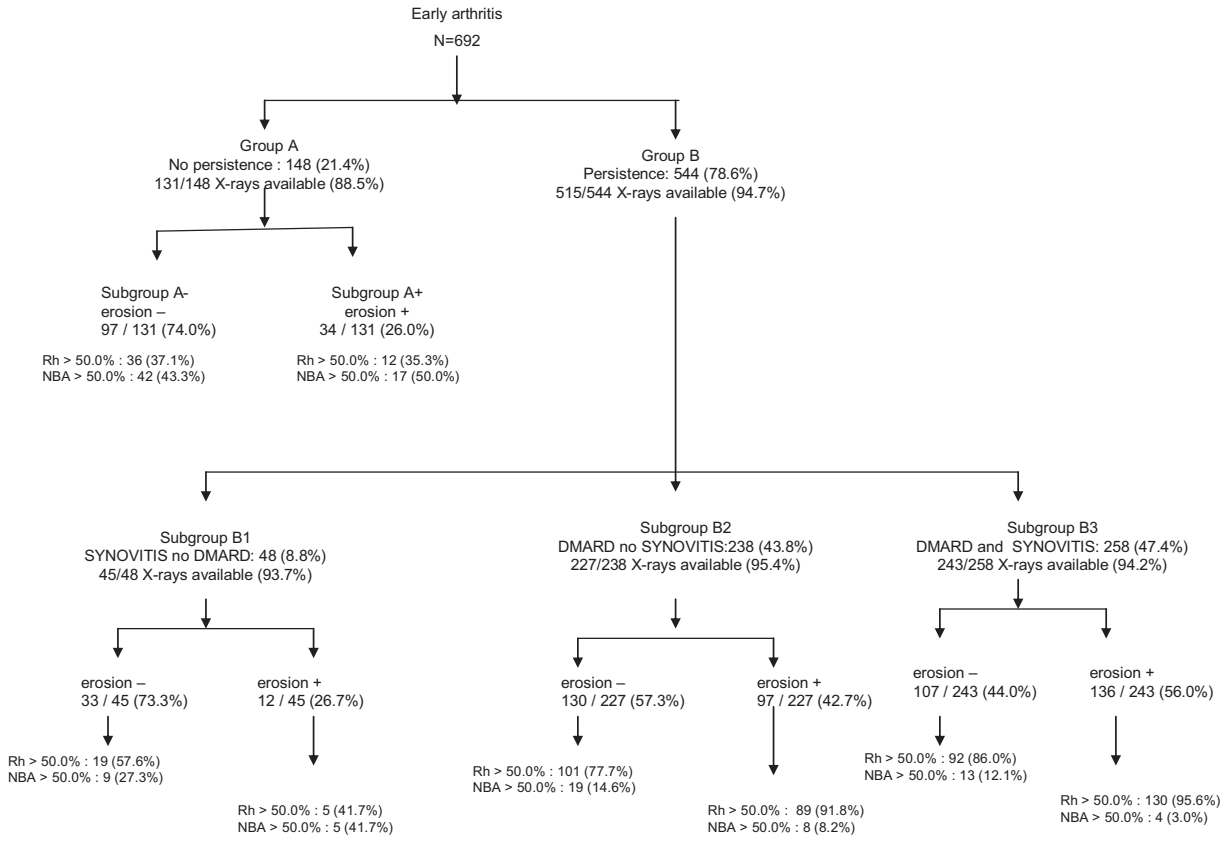

Figure 1. Patient characteristics according to the criteria for classifying early arthritis after 2 years of followup. Erosion = at least 1 joint erosion typical of rheumatoid arthritis (RA); Rh = rheumatologist diagnosis of RA (the certainty of the RA diagnosis was determined using a visual analog scale [VAS]); NBA = no better alternative diagnosis (the certainty of diagnoses other than RA was determined using a VAS); DMARDs = treatment with disease-modifying antirheumatic drugs.

at least 1 joint erosion typical of RA had a rheumatologist diagnosis of RA with >50.0% certainty. For the patients without persistent arthritis, 35.3% (12/34) and 37.1% (36/97) of those with and without at least 1 joint erosion typical of RA, respectively, had a rheumatologist diagnosis of RA with >50.0% certainty. Of the 12 patients with persistent arthritis and at least 1 joint erosion typical of RA who were not receiving DMARDs, 9 were taking hydroxychloroquine (not classified as a DMARD in our study) and 5 were diagnosed with a condition other than RA (undifferentiated arthritis in 4 patients and chondrocalcinosis in 1). The 17 patients without persistent arthritis but with at least 1 joint erosion typical of RA who were not receiving DMARDs had a diagnosis other than RA (3 had spondyloarthritides, 2 Sjögren's syndrome, 6 osteoarthritis, 1 reflex sympathetic osteodystrophy, 1 remitting seronegative symmetrical synovitis with pitting edema, 1 fibromyalgia, and 3 undifferentiated arthritis).

Agreement among definitions after 2 years. We compared a rheumatologist diagnosis of RA with >50.0% certainty to other definitions of RA on the basis of classification criteria, persistent arthritis, and degree of certainty of NBA. We noted marked disagreement among a rheumatologist diagnosis of RA with >50.0% certainty, the 1987 ACR criteria, and persistent arthritis. In total, 7 patients met the rheumatologist diagnosis of RA with >50.0% certainty criterion; 32 met the rheumatologist diagnosis of RA with >50.0% certainty and persistent arthritis criteria; 45 met the rheumatologist diagnosis of RA with >50.0% certainty and 1987 ACR criteria; 429 met the rheumatologist diagnosis of RA with >50.0% certainty, persistent arthritis, and 1987 ACR criteria; 28 met the persistent arthritis criterion; 53 met the persistent arthritis and ACR 1987 criteria; 46 met the 1987 ACR criteria; and 46 met none of the criteria. The kappa coefficients shown in Table 2 confirm the low level of agreement. A rheumatologist diagnosis of RA with >50.0% certainty agreed fairly well with persistent disease (κ = 0.46 [95% confidence interval 0.38, 0.54]) but agreed poorly with the 1987 ACR and 2010 ACR/EULAR criteria at any visit and the joint erosion criterion. Agreement was best between an NBA diagnosis with >50.0% certainty and the 2010 ACR/EULAR criteria at the last visit (κ = 0.81 [95% confidence interval 0.78, 0.84]). The good agreement between an NBA diagnosis with >50.0% certainty and a rheumatologist diagnosis of RA with >50.0% certainty (κ = 0.69 [95% confidence interval 0.63, 0.76]) may explain this result.

Comparison of patients with and without RA. To determine the combination of criteria most strongly associated with a diagnosis of RA, we separated the patients into 2 groups on the basis of whether the rheumatologist diagnosis of RA with >50.0% certainty criterion was met and

Table 2. Agreement among all definitions of RA*

	1987 ACR criteria	Rheumatologist diagnosis of RA with >50.0% certainty	No better alternative diagnosis with >50.0% certainty	Persistent disease†	Joint erosion
ACR/EULAR 2010					
Present at any time‡	0.43 (0.39, 0.47)	0.38 (0.34, 0.42)	0.32 (0.27, 0.37)	0.32 (0.27, 0.37)	0.09 (0.02, 0.11)
Present at last visit§	0.39 (0.35, 0.43)	0.71 (0.68, 0.74)	0.81 (0.78, 0.84)	0.38 (0.34, 0.42)	0.16 (0.13, 0.19)
1987 ACR criteria		0.40 (0.32, 0.48)	0.32 (0.23, 0.41)	0.28 (0.20, 0.37)	0.09 (0.06, 0.12)
Rheumatologist diagnosis of RA with >50.0% certainty			0.69 (0.63, 0.76)	0.46 (0.38, 0.54)	0.16 (0.13, 0.20)
No better alternative diagnosis with >50.0% certainty				0.35 (0.26, 0.43)	0.02 (−0.02, 0.07)
Persistent disease†					0.13 (0.10, 0.16)

* Values are the kappa coefficient (95% confidence interval). The definitions of rheumatoid arthritis (RA) were the 1987 American College of Rheumatology (ACR) criteria, 2010 ACR/European League Against Rheumatism (EULAR) criteria, rheumatologist diagnosis of RA or no better alternative diagnosis with >50.0% certainty, persistent synovitis, and ≥1 joint erosions.
† Defined as having synovitis, receiving disease-modifying antirheumatic drug therapy, or both.
‡ 2010 ACR/EULAR criteria were present if noted at any time during followup.
§ 2010 ACR/EULAR criteria were present if noted at any time during followup, except the exclusion criterion (no better alternative diagnosis), which was considered present only if it was met at the last visit.

then evaluated the associations with all other criteria (Table 3).

A logistic regression analysis including all criteria associated with the reference standard (a rheumatologist diagnosis of RA with >50.0% certainty) showed that the best combination for identifying patients with RA was an NBA diagnosis with >50.0% certainty, persistent disease, positive tests for rheumatoid factors and ACPAs, symmetric arthritis, and at least 1 joint erosion typical of RA. When we added the 1987 ACR criteria to the model, an NBA diagnosis with >50.0% certainty, persistent disease, and positive ACPA test remained in the model (Table 4). Therefore, the best combination for identifying patients with RA was an NBA diagnosis with >50.0% certainty, persistent disease, and presence of the 1987 ACR criteria plus positive ACPA test or the presence of the 2010 ACR/EULAR criteria.

We were thus able to classify the patients into 4 groups:

Table 3. Definitions of RA for patients whose rheumatologist diagnosed RA with >50.0% or ≤50.0% certainty*

	>50.0% certainty, no./total (%)	≤50.0% certainty, no./total (%)	*P*
Synovitis	261/513 (50.9)	45/177 (25.4)	0.0001
DMARDs	434/513 (84.6)	62/178 (34.8)	0.0001
Persistent disease (synovitis and/or DMARDs)	461/513 (89.9)	83/178 (46.6)	0.0001
No other better diagnosis with >50.0% certainty	501/513 (97.7)	116/178 (65.2)	0.0001
1987 ACR criteria	474/513 (92.4)	99/173 (57.2)	0.0001
Criterion 1	326/513 (63.5)	75/178 (42.1)	0.0001
Criterion 2	264/513 (51.5)	43/178 (24.2)	0.0001
Criterion 3	345/513 (67.3)	64/178 (36)	0.0001
Criterion 4	285/513 (55.6)	44/178 (24.7)	0.0001
Criterion 5	22/513 (4.3)	2/178 (1.1)	0.0001
Criterion 6	285/513 (55.6)	12/177 (6.8)	0.0001
Criterion 7	236/484 (48.8)	43/162 (26.5)	0.0001
2010 ACR/EULAR at any time†	487/513 (94.9)	111/177 (62.7)	0.0001
2010 ACR/EULAR with the exclusion criterion present at the last visit‡	477/513 (93.0)	39/177 (22.0)	0.0001
ACPAs	275/506 (54.3)	22/177 (12.4)	0.0001

* All patients had complete radiograph sets, but clinical or biologic items were occasionally missing, thus explaining why the total is not 691 patients (513 >50.0% certainty and 178 ≤50.0% certainty). Criteria 7 (radiographic evaluation by the rheumatologist in each center) and ACPA test were not always completed because a centralized evaluation was also done. RA = rheumatoid arthritis; DMARDs = disease-modifying antirheumatic drugs (methotrexate, sulfasalazine, leflunomide, gold, biologic agents, or >5 mg/day of prednisone); ACR = American College of Rheumatology; EULAR = European League Against Rheumatism; ACPAs = anti–citrullinated protein antibodies.
† 2010 ACR/EULAR criteria were present if noted at any time during followup.
‡ 2010 ACR/EULAR criteria were present if noted at any time during followup, except the exclusion criterion (no better alternative diagnosis), which was considered present only if met at the last visit.

Table 4. Multiple logistic regression with forward selection to identify factors associated with a rheumatologist diagnosis of rheumatoid arthritis made with >50.0% certainty*

	Mean coefficient (SEM)	*P*	Odds ratio
No other diagnosis with >50.0% certainty, 1 = yes and 0 = no	4.0 (3.6, 4.4)	< 0.0001	52.4
Persistent disease, 1 = yes and 0 = no	1.6 (1.3, 2)	< 0.0001	5.1
1987 ACR criteria, 1 = present and 0 = absent	1.6 (1.2, 1.9)	< 0.0001	4.9
ACPA positivity, 1 = yes and 0 = no	1.4 (1.0, 1.7)	< 0.0001	4

* Variables with $P < 0.10$ by single variable model analysis were entered into the model. ACR = American College of Rheumatology; ACPA = anti–citrullinated protein antibody.

definitive RA (NBA diagnosis with >50.0% certainty, persistent disease, 1987 ACR criteria, and positive ACPA test), confirmed RA (NBA diagnosis with >50.0% certainty plus 2 of the other 3 criteria), doubtful RA (absence of the NBA diagnosis with >50.0% certainty criterion but presence of the other 3 criteria or presence of the NBA diagnosis with >50.0% certainty criterion and one of the other 3 criteria), and no RA (absence of the NBA diagnosis with >50.0% certainty criterion and presence of 1 or 2 of the other 3 criteria or presence of the NBA diagnosis with >50.0% certainty criterion and absence of the other 3 criteria) (Table 5). The agreement with a rheumatologist diagnosis of RA with >50.0% certainty was good (definitive or confirmed and doubtful or no RA versus a rheumatologist diagnosis of RA with >50.0% certainty present or absent [κ = 0.68 (95% confidence interval 0.65, 0.71)]).

DISCUSSION

A definitive diagnosis of RA remains difficult. Use of the 2010 ACR/EULAR criteria allows an earlier diagnosis of RA, but may lead to a mistaken diagnosis of RA in patients with self-limiting disease (16–19). We aimed to determine which RA definition assessed after 2 years of followup in patients with early arthritis (ESPOIR cohort) was most strongly associated with our reference standard for diagnosing RA, namely, the rheumatologist diagnosis of RA with >50.0% certainty criterion. Among patients meeting the rheumatologist diagnosis of RA with >50.0% certainty criterion after 2 years, 10.0% had also received another diagnosis after 2 years of followup, as determined by the rheumatologists. Most patients with a rheumatologist diagnosis of RA with >50.0% certainty had persistent synovitis or received DMARDs, and most met the 1987 ACR criteria. Adding the 2010 ACR/EULAR exclusion criterion (NBA) to the rheumatologist diagnosis of RA with >50.0% criterion certainty improved the level of agreement with a combination of items from validated criteria sets. The best combination of criteria for identifying patients who had a rheumatologist diagnosis of RA with >50.0% certainty was an NBA diagnosis with >50.0% certainty, persistent clinical disease, and presence of the 1987 ACR criteria plus a positive ACPA test or presence of the 2010 ACR/EULAR criteria. Thus, the best classification of RA patients seems to require the opinion of a rheumatologist about the

Table 5. Classification of patients as having definitive RA, confirmed RA, doubtful RA, or no RA according to the presence or absence of 4 criteria*

	Definitive RA (n = 254)†	Confirmed RA (n = 205)‡	Doubtful RA (n = 138)§	No RA (n = 81)¶
Synovitis	140 (55.1)	110 (53.7)	39 (28.3)	12 (14.8)
DMARDs	254 (100)	178 (86.8)	53 (38.4)	12 (14.8)
Persistent disease	254 (100)	194 (94.6)	68 (49.3)	19 (23.5)
Other diagnosis with >50.0% certainty	0	0	43 (31.2)	81 (100)
1987 ACR criteria	254 (100)	193 (94.1)	86 (62.3)	32 (39.5)
2010 ACR/EULAR criteria#	249 (98.0)	191 (93.2)	70 (50.7)	0
Positive ACPA test	254 (100)	23 (11.2)	15 (10.9)	4 (4.9)
Joint erosion	139 (54.7)	82 (40.0)	31 (22.5)	23 (28.4)
Diagnosis of RA with >50.0% certainty	249 (98.0)	188 (91.7)	65 (47.1)	4 (4.9)
Diagnosis of RA with >75.0% certainty	233 (94.1)	149 (72.7)	34 (24.6)	0

* Values are the number (percentage). The 4 criteria were no better alternative diagnosis with >50.0% certainty (criterion 1), persistent disease (criterion 2), 1987 ACR criteria (criterion 3), and positive ACPA test (criterion 4). RA = rheumatoid arthritis; DMARDs = disease-modifying antirheumatic drugs (methotrexate, sulfasalazine, leflunomide, gold, biologic agents, or >5 mg/day of prednisone); ACR = American College of Rheumatology; EULAR = European League Against Rheumatism; ACPA = anti–citrullinated protein antibody.
† Defined as criteria 1, 2, 3, and 4 present.
‡ Defined as criterion 1 present, and 2 or 3 of criteria 2, 3, and 4 present.
§ Defined as criterion 1 absent and criteria 2, 3, and 4 present, or criterion 1 present and one of criteria 2, 3, and 4 present.
¶ Defined as criterion 1 absent and 1 or 2 among criteria 2, 3, and 4 present, or criterion 1 present and criteria 2, 3, and 4 absent.
# Other diagnosis at last visit.

presence of RA and the absence of a better alternative diagnosis.

The strengths of our study are the high quality of the data available in the ESPOIR cohort (the procedures were set up to avoid losing patients to followup as much as possible; each center was evaluated by an external observer who verified the data of 139 randomized patients [intraclass correlation coefficient 0.99]), the high numbers of data (clinical and biologic variables were recorded and quality of life questionnaires [including a medicoeconomic questionnaire] were performed at each visit), the large number of patients, and the centralized radiograph reading procedure. The limitations are the lack of a validated reference standard for diagnosing RA (although the 2010 ACR/EULAR criteria might be considered the reference standard) and the large number of rheumatologists involved in the study because the interobserver agreement regarding the certainty regarding the diagnosis of RA was not evaluated.

Only a small proportion of patients were not included in the analysis after 2 years of followup (14.9%). Disease activity was lower in the group of patients without 2 years of followup than in the group with 2 years of followup. Therefore, the proportion of patients included in the doubtful RA or no RA groups should be slightly higher than the result we observed in our study.

A recent study showed that a high percentage of non-RA patients received DMARDs (18). After 2 years in our study, 78.6% of patients had persistent arthritis and most of these patients (91.2%) were receiving DMARDs. However, among the patients with or without persistent arthritis who were not receiving DMARDs, a non-negligible percentage met the rheumatologist diagnosis of RA with >50.0% certainty criterion. This finding indicates that the evaluation of clinical criteria by rheumatologists, such as physical findings, immunologic markers, and joint erosions typical of RA, may improve diagnostic accuracy compared with the classification criteria sets. Interestingly, the rheumatologists considered some patients who met the 2010 ACR/EULAR criteria at some point during followup as not having RA after 2 years because of the presence of a better alternative diagnosis.

In conclusion, 2 years after patients presented with arthritis, the 2010 ACR/EULAR criteria, a rheumatologist diagnosis of RA, and a combination of items including an NBA produced similar results. These 3 methods may offer the greatest accuracy for diagnosing RA. The 2010 ACR/EULAR criteria may be the best reference standard because these criteria have been the focus of the most extensive validation studies and include an exclusion criterion (NBA) that plays a crucial role in its better performance than that of other criteria. As far as we are aware, this is the first study to assess the value of the 2010 ACR/EULAR classification criteria after a 2-year followup in a cohort of patients with early arthritis. The classification into 4 groups (definitive RA, confirmed RA, doubtful RA, and no RA) may be useful for studies requiring groups of patients in whom RA has been convincingly determined or ruled out. According to our findings, the presence of 1 or more joint erosions typical of RA may not consistently indicate RA. However, the assessment of joint erosions typical of RA is partly subjective because no validated definition for this criterion is currently available.

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All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Saraux had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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