

CONCISE REPORT

# Level of agreement of the 1987 ACR and 2010 ACR/EULAR rheumatoid arthritis classification criteria: an analysis based on ESPOIR cohort data

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## ABSTRACT

**Background** In 2010, new classification criteria for rheumatoid arthritis (RA) were developed.

**Objective** To assess agreement between 1987 American College of Rheumatology (ACR) and 2010 ACR/European League Against Rheumatism (EULAR) criteria and the potential source of discordance, based on ESPOIR cohort data.

**Methods** 813 early arthritis patients were included in ESPOIR between 2002 and 2005. Between-criteria agreement was based on the  $\kappa$  coefficient. Discordance was explored by logistic regression.

**Results** Data for 811 patients were available, with their main characteristics as follows: women 77%, swollen joint count 7.2, tender joint count 8.4, disease activity score in 28 joints 5.2, rheumatoid factor 46%, anticitrullinated protein antibody (ACPA) 39%, structural damage 22%. At baseline, 579 (71.4%) patients met the 1987 ACR criteria and 641 (79.0%) the 2010 criteria. Agreement at baseline was discordant for 168 patients: 115 satisfied the 2010 criteria and 53 the 1987 criteria. Concordance between the two sets was fair, with a  $\kappa$  coefficient of 0.45 and 0.42 at baseline and year 2, respectively. The main sources of discordance were the number and symmetry of joint involvement, as well as ACPA status.

**Conclusion** 2010 ACR/EULAR criteria identified more patients with RA than did 1987 criteria. The 2010 criteria failed to identify RA patients with symmetrical seronegative arthritis and limited joint involvement.

Diagnosis of rheumatoid arthritis (RA) might be difficult at the very early stages of the disease. Although not designed for diagnostic purposes, the 1987 American College of Rheumatology (ACR) classification criteria<sup>1</sup> might help to identify RA patients. However, at disease onset, the presentation might be incomplete. Moreover, the early initiation of disease-modifying antirheumatic drugs (DMARD) can prevent the realisation of the full RA picture.<sup>2</sup> Therefore, the 1987 ACR criteria do not work well in early-stage RA.<sup>3</sup> A new set of RA classification criteria was recently proposed jointly by the ACR and the European League Against Rheumatism (EULAR). These 2010 criteria aim to identify patients with RA at disease onset and their first visit to the rheumatologist. In these criteria, the experts in charge of their development defined a new paradigm for early RA, enabling the consideration of RA in patients with incomplete presentation.<sup>4</sup>

Therefore, it is interesting to investigate to what extent the 1987 ACR and 2010 ACR/EULAR criteria identify different patients and the source of potential disagreement between the two sets. Such an assessment requires data from an early arthritis cohort, such as the ESPOIR cohort.<sup>5</sup>

## PATIENTS AND METHODS

### ESPOIR cohort

The ESPOIR cohort included 813 patients with early arthritis from 14 rheumatology centres in France between 2002 and 2005.<sup>5 6</sup> Patients had to be 18–70 years old and have two or more swollen joints for over 6 weeks and less than 6 months. They should not have received DMARD or steroids for more than 2 weeks, and if these drugs were administered for a short duration, they should have been stopped for more than 2 weeks before inclusion. Patients with a definite diagnosis different from RA were excluded.

The ESPOIR research programme was approved by the ethics committee of Montpellier in July 2002, and all patients who participated in the study were asked to give written informed consent before entering the cohort.

### Data available

Data were available on patient demographics and medical history, date of symptom onset, main clinical and biological findings at inclusion and baseline presence of typical RA erosion on the hand and foot x-rays assessed by the local rheumatologist. Moreover, the opinion of the local rheumatologist was collected at baseline by the use of a 0–10 visual analogue scale (VAS) by which the rheumatologist in charge of the patient indicated the level of confidence in the diagnosis of RA between 0 (RA diagnosis unlikely) and 10 (RA diagnosis likely).<sup>5 6</sup>

The seven items of the 1987 ACR criteria<sup>1</sup> were recorded at baseline, as well as at 2 years (cumulative satisfaction), when they have been reported to be optimally sensitive and specific.<sup>3</sup> In addition, information required for the calculation of the 2010 ACR/EULAR criteria score<sup>4</sup> was available in the ESPOIR database.

### Statistics

The agreement between the two criteria was based on the  $\kappa$  statistic. To explore the source of disagreement between the two sets, patients were split into two groups: ‘concordant’ if their data satisfied both

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criteria sets, or 'discordant' if they satisfied only the 1987 or the 2010 criteria. Determinants of the 'discordant' status were first explored by the  $\chi^2$  test. For this step, data for all continuous

variables were dichotomised on the basis of laboratory norms for biological tests or the median for the other variables. Statistically significant variables ( $p \leq 0.15$ ) were included in a multivariate logistic regression, with statistical significance set at  $p < 0.05$ .

All statistical analyses involved use of SAS 8.2.

**Table 1** Main characteristics of the ESPOIR cohort patients at baseline

Characteristics	At baseline (n=811)
Age, years	48.1 $\pm$ 12.5
Female sex	624 (76.8%)
Swollen joint count*	7.2 $\pm$ 5.4
Tender joint count*	8.4 $\pm$ 7.0
ESR	29.4 $\pm$ 24.5
DAS28	5.2 $\pm$ 1.5
IgM RF positivity	372 (45.8%)
ACPA positivity	315 (38.8%)
Typical RA erosion on x-ray† (central reading)	178 (22.0%)
1987 ACR criteria	579 (71.4%)
2010 ACR/EULAR criteria	641 (79.0%)
Characteristics	At 2 years (n=692)
Any ongoing DMARD at the 2-year visit	502 (72.54%)
Methotrexate or equivalent‡	439 (87.5%)
Biological agent	76 (11%)
Fulfillment of the 1987 ACR criteria§	661 (87.2%)
Fulfillment of the 2010 ACR/EULAR criteria§	687 (88.2%)
RA as the preferred diagnosis for the rheumatologist¶	431 (62.4%)

Data are mean  $\pm$  SD or number (%).

\*All joint assessments were performed on 28 joints.

†Typical RA erosions are defined according to the 1987 ACR criteria, ie, 'Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localised in or most marked adjacent to the involved joints.'

‡Equivalent means sulfasalazine or leflunomide.

§Cumulative fulfillment at any visit from baseline to 2 years.

¶Diagnostic confidence in RA diagnosis of 7.5 or greater on a 0–10 visual analogue scale (consensus of the ESPOIR Scientific Committee).

ACPA, anticitrullinated protein antibody; ACR, American College of Rheumatology; DAS28, disease activity score in 28 joints; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; RA, rheumatoid arthritis; RF, rheumatoid factor.

## RESULTS

Complete data were available for 811 of the 813 early arthritis patients enrolled in the ESPOIR cohort. The main characteristics of patients are shown in table 1. At baseline, 579 (71.4%) patients satisfied the 1987 ACR criteria for RA and 641 (79.0%) the 2010 ACR/EULAR criteria; 526 patients satisfied both criteria and 168 patients were considered discordant, only 115 satisfying the 2010 criteria and 53 the 1987 criteria.

At 2 years, 82 patients initially ACR 1987 negative and 46 patients initially ACR 2010 negative became positive for each set, increasing the percentage of patients satisfying criteria from 71.4% to 87.2% for the 1987 set and from 79% to 88.2% for the 2010 set. Six hundred and eleven patients met both criteria and 89 were considered discordant: 51 satisfied only the 1987 criteria and 38 only the 2010 criteria. Concordance between the two sets was moderate to good: the  $\kappa$  coefficient was 0.45 (95% CI 0.38 to 0.52) at baseline and 0.42 (95% CI 0.33 to 0.51) at 2 years.

The profile of the patients satisfying one or the other criteria differed substantially from those satisfying both criteria (table 2). Patients satisfying only the 1987 ACR criteria were more likely to have more swollen than tender joints, symmetrical joint involvement or morning stiffness, or to be negative for rheumatoid factor (RF) and anticitrullinated protein antibody (ACPA). However, patients meeting only the 2010 ACR/EULAR criteria were more likely to have a substantial number of tender joints (joint tenderness is considered equal to joint swelling), non-symmetrical joint involvement, or to be positive for RF or ACPA. As expected, discordant status was explained by

**Table 2** Baseline characteristics of patients depending on the satisfaction of the 1987 ACR or 2010 ACR/EULAR criteria, or both criteria

	Patients fulfilling			
	Both criteria (n=526)	Only 2010 criteria (n=115)	Only 1987 criteria (n=53)	None of the criteria (n=117)
Tender joints	10.4 $\pm$ 7.2	7.2 $\pm$ 6.2	3.8 $\pm$ 2.7	2.9 $\pm$ 2.4
1–3 Small joints	14 (2.7)	23 (20.0)	14 (26.4)	45 (38.5)
4–10 Involved small joints	91 (17.3)	31 (27.0)	38 (71.7)	55 (47)
$\geq 10$ Involved joints	421 (80.0)	61 (53.1)	1 (1.9)	0
Swollen joints	9.1 $\pm$ 5.5	3.9 $\pm$ 3.2	5.2 $\pm$ 2.6	2.6 $\pm$ 1.7
Arthritis of three or more joint areas	503 (95.6)	52 (45.2)	51 (96.2)	48 (41)
Symmetrical arthritis	486 (92.4)	42 (36.5)	52 (98.1)	41 (35)
Morning stiffness $\geq 60$ min	497 (94.5)	74 (64.4)	53 (100)	76 (65)
RF positivity	309 (58.7)	58 (50.4)	3 (5.7)	2 (1.7)
ACPA positivity	274 (52.1)	39 (33.9)	2 (3.8)	0
RA diagnosis confidence at inclusion on a 0–10 VAS	7.9 $\pm$ 1.8	5.0 $\pm$ 2.4	6.2 $\pm$ 2.1	3.9 $\pm$ 2
RA as the preferred diagnosis for the rheumatologist at baseline	344 (65.4)	20 (17.4)	15 (28.3)	3 (2.6)
RA diagnostic confidence at 2 years on a 0–10 VAS	8.1 $\pm$ 2.7	6.3 $\pm$ 3.6	6.4 $\pm$ 3.5	3.8 $\pm$ 3
RA as the preferred diagnosis for the rheumatologist at 2 years	346 (65.8)	48 (39.1)	22 (53.7)	15 (12.8)
% Patients receiving methotrexate at 6 months (ACR/EULAR recommendation)*	324 (65.6)	46 (44.2)	20 (41.7)	32 (29.1)
% Patients receiving any DMARD† at 6 months*	438 (88.7)	75 (72.1)	35 (72.9)	51 (46.4)

Data are mean  $\pm$  SD or number (%).

\*Data available for only 756 patients (481, 99, 46 and 105, respectively, in each category).

†Any DMARD: methotrexate, leflunomide, sulfasalazine or any biological agents.

ACPA, anticitrullinated protein antibody; ACR, American College of Rheumatology; DMARD, disease-modifying antirheumatic drug; EULAR, European League Against Rheumatism; RA, rheumatoid arthritis; RF, rheumatoid factor; VAS, visual analogue scale.

**Table 3** Determinants of discordant versus concordant status in terms of agreement with both the 1987 ACR and 2010 ACR/EULAR criteria by multivariate analysis

	Discordant (n=135) N (%)	Concordant (n=460) N (%)	OR (95% CI)
Absence of arthritis of three or more joint areas	54 (40.0)	18 (3.9)	36.32 (14.05 to 93.87)
Morning stiffness absent or <60 min	33 (24.4)	27 (5.9)	25.78 (9.48 to 70.14)
Less than 10 involved joints	82 (60.7)	89 (19.3)	22.16 (10.35 to 47.44)
Absence of symmetrical joint involvement	59 (43.7)	36 (7.8)	18.66 (8.01 to 43.46)
Absence of ACPA	101 (74.8)	212 (46.1)	11.31 (3.74 to 34.20)
Absence of IgM RF	84 (62.2)	184 (40.0)	7.83 (2.98 to 20.61)
Low level of confidence in RA diagnosis at baseline*	105 (77.8)	183 (39.8)	2.68 (1.32 to 5.46)
Low level of confidence in RA diagnosis at year 2*	94 (69.6)	208 (45.2)	2.25 (1.06 to 4.75)

\*Defined as ranking median or less on a 0–10 visual analogue scale.

ACPA, anticitrullinated protein antibody; ACR, American College of Rheumatology; EULAR, European League Against Rheumatism; RA, rheumatoid arthritis; RF, rheumatoid factor.

only a few items diverging between the 1987 and the 2010 criteria, mainly a low number of swollen joints, lack of significant morning stiffness or symmetry in joint involvement, and the absence of autoantibodies, a higher impact with the absence of anticyclic citrullinated peptide antibodies (Table 3). Moreover, discordant status was associated with more doubtful or atypical presentations for which the clinicians reported a lower level of confidence. Neither rheumatoid nodules nor typical RA erosions were associated with the discordant status.

## DISCUSSION

The present study brings additional information to improve the understanding of the extent to which the 1987 ACR and the 2010 ACR/EULAR criteria for RA can identify the same patients with early arthritis. Our results cannot be considered a validation of the 2010 criteria because the ESPOIR data have been used—among other cohort data—in the initial data-driven phase of the construction of the 2010 criteria.<sup>4</sup> During this phase, the data for several early arthritis cohorts were used to identify and select the items that optimally revealed patients with ‘probable RA’, defined by a proxy: initiation of methotrexate within a couple of months after symptom onset, as now widely recommended,<sup>7–9</sup> based on extensive scientific evidence.<sup>2 10–12</sup> The first data-driven phase was then followed by an expert-based phase involving clinical vignettes to switch from the predictors of methotrexate initiation to predictors of RA diagnosis, regardless of the initiation of a specific DMARD.<sup>4 13</sup> Therefore, our results were not tautological and could bring additional information on the new set properties.

The 2010 ACR/EULAR criteria identified more ‘RA’ patients in ESPOIR than did the 1987 ACR criteria—79% versus 71.4%, which is consistent with recently published studies.<sup>14–16</sup> This finding was expected because the 2010 criteria included more items, such as tender not just swollen joints, biological markers of inflammation or ACPA. Moreover, they allowed for considering a diagnosis of RA in patients with only one swollen joint (although with a low probability). The higher detection ability of the new set was desirable because several studies demonstrated that the 1987 criteria were likely to ‘miss’ RA at a very early phase of the disease,<sup>3 4</sup> and that the recommended early DMARD initiation could potentially stop the development of RA and thus the completion of at least four items of the 1987 criteria.<sup>2</sup>

Determining whether this detection ability is accurate is a complex issue and the ESPOIR cohort is probably not the correct population to answer this question. The cohort inclusion criteria were designed to recruit patients likely to have RA, thus limiting the number of patients with other diagnoses. Moreover, no centralised diagnosis ascertainment was performed in ESPOIR and only the local rheumatologist’s opinion—diagnostic confidence VAS—was available as a surrogate marker, which is questionable.<sup>17 18</sup> The level of diagnostic confidence was higher in ‘concordant’ patients. In the ‘discordant’ population, the confidence level was higher in patients satisfying only the 1987 criteria than in those only meeting the 2010 criteria. ‘Although the 1987 ACR criteria are not diagnostic criteria, they reinforce the rheumatologist opinion in making RA diagnosis and thus constitute an important contribution in the rheumatologist opinion as well as his/her level of confidence in RA diagnosis. With regards to this, the new criteria are able to identify patients less “typical” at baseline.’

As expected, the characteristics of joint involvement were significant sources of discordance between the two criteria sets, as the 2010 set disentangled it in small or medium to large joints with different cut-off values, based on both swollen and tender joints. Besides, after extensive discussion, morning stiffness and symmetry were finally rejected.<sup>4</sup> From our results, these decisions have a substantial impact on patient classification. In addition, as previously reported, ACPA was important for RA diagnosis<sup>4 19</sup> and the weight of ACPA in the 2010 set is now similar to that of RF.

In conclusion, with the use of the 2010 ACR/EULAR criteria, more patients were identified as having RA than with the use of the 1987 ACR criteria. However, the 2010 criteria may miss patients with symmetrical seronegative arthritis that would be considered as RA according to the 1987 criteria. This highlights the unavoidable and persistent risk of patient misclassification.<sup>20</sup>

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**Patient consent** Obtained.

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