Concise report

Do we need to lower the cut point of the 2010 ACR/EULAR classification criteria for diagnosing rheumatoid arthritis?

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Abstract

Objective. In this study we aimed to evaluate the effect of lowering the cut point of the 2010 criteria to identify more patients with RA among early inflammatory arthritis patients.

Methods. We included early arthritis patients from the Rotterdam Early Arthritis Cohort with at least one joint with clinical synovitis and symptoms for < 1 year, with no other explanation for their symptoms. The demographic and clinical characteristics of each patient were recorded at baseline. Patients were classified as case or non-case at the 1-year follow-up by the definition used in the development of the 2010 criteria (MTX initiation). To assess the diagnostic performance of the 2010 criteria, the sensitivity and specificity at each cut point were determined.

Results. We included 557 patients in our analysis. At the 1-year follow-up, 253 patients (45%) were classified as case (MTX use). In the group of patients who scored 0–5 points (n=328), 98 patients (30%) were classified as case (MTX use). The sensitivity and specificity of the 2010 criteria using the cut point of 6 were 61% and 76%, respectively. With the cut point of 5, the sensitivity would increase to 76% and the specificity would decrease to 68%.

Conclusion. By lowering the cut point of the 2010 criteria from 6 to 5 points, we were able to identify 15% more RA patients at the cost of 8% more false-positive patients.

Key words: classification criteria, rheumatoid arthritis, diagnostic criteria.

Rheumatology key messages

• Lowering the cut point of the 2010 ACR/EULAR classification criteria identifies more RA patients.
• Lowering the cut point of the ACR/EULAR classification 2010 criteria is feasible in clinical practice for diagnosing RA.

Introduction

Recently, the 2010 ACR/EULAR classification criteria for RA were developed to facilitate research into earlier stages of the disease. The 2010 criteria also facilitate optimal use of the window of opportunity by starting disease-modifying drugs at an earlier time point [1]. The 2010 criteria assign the risk or probability of developing RA on a continuous score (from 0 to 10). A score of ≥6/10 is needed to classify a patient as having definite RA.

Some of the patients in whom arthritis persists over time do not fulfil the 2010 criteria (<6/10 points) at first...
consultation [2]. In unselected early arthritis cohorts, the proportion of missed persistent arthritis patients can increase to almost 40%, which is likely to reflect the case-load of daily practice [3]. As Krabben et al. [4] showed, neither ACPA nor the Leiden prediction rule are able to identify which individual patients will be missed by the 2010 criteria. Therefore, we need another way to identify patients whose arthritis will persist.

The developers of the 2010 criteria suggest that there is scope for using other cut points for different purposes [1]. In this study, we evaluated which cut point of the 2010 criteria would enable us to identify more early RA patients among early inflammatory arthritis patients at first consultation.

Methods
Patients
For the present study, we included early arthritis patients from the Rotterdam Early Arthritis Cohort (REACH) with at least one joint with clinical synovitis and symptoms for <1 year, with no other explanation for their symptoms. Patients were recruited via their general practitioner, or via the outpatient rheumatology clinic. Patients were included in REACH in the case of one or more swollen joints. Patients were excluded if their symptoms resulted from trauma or overuse, if their symptoms were present for over 12 months, or if they were younger than 16 years. For a detailed description of REACH, see Alves et al. [5].

Each patient was assigned a score from 0 to 10 points, using the four domains of the 2010 criteria: joint involvement; serology; acute-phase reactants; and symptom duration [1]. If results were not available for a domain, results were regarded as normal or negative, following the guidelines of the developers of the 2010 criteria [6]. The demographic and clinical characteristics of each patient were recorded at baseline, 6 months and 12 months.

Data collection included a detailed medical examination (swollen joint count (SJC), tender joint count (TJC)), laboratory variables (ACPA, RF, ESR), diagnosis and medication used.

Written informed consent was obtained from the participants in the REACH study, according to the Declaration of Helsinki. The REACH study was approved by the local medical ethics committee of Erasmus MC, University Medical Center Rotterdam, the Netherlands. This secondary analysis was covered by this ethical approval.

Case definition
Patients were classified as case (true-positive patients) or non-case after the 1-year follow-up by the definition used in the development of the 2010 criteria [1]. This definition includes the use of MTX after 1 year. If a patient had to stop MTX due to side-effects, and was assigned another DMARD, it was also considered a case. If no MTX was used and no other classifiable disease was present after the 1-year follow-up, the patient was regarded a non-case.

Statistical analysis
Discriminative performance of the 2010 criteria in relation to the case definition was determined by calculating the receiver operating characteristic (ROC) curve. The sensitivity and specificity were calculated for each cut point (0–10 points). To obtain information on other potential clinical characteristics that could help improve the diagnostic performance, we tested differences between cases and non-cases among the patients with <6/10 points, using the independent t test or Wilcoxon-Mann–Whitney test, depending on the distribution of the data. Frequencies were compared using a χ² test. Analyses were done using STATA 12.0.

Results
In REACH, we identified 726 early arthritis patients. At baseline, we excluded 169 patients with another classifiable disease, such as gout, psoriatic arthritis or systemic diseases. Consequently, in 557 patients, the 2010 criteria could be applied, of which 328 patients (69%) obtained a score from 0 to 5.

Sensitivity and specificity 2010 criteria
The ROC curve was calculated for the 2010 criteria in relation to MTX use in the total study population (0–10 points; n = 557) (Fig. 1). The area under the ROC curve (AUC) was 0.79 (S.E. 0.02). From this curve, the sensitivity and specificity for each score were determined.

The sensitivity and specificity of the 2010 criteria using the cut point of 6 were 61% and 76%, respectively. With the cut point of 5, the sensitivity increased to 76% and the specificity decreased to 68%. Among patients with 5 points (n = 59), 22 patients (37%) would be false-positively classified as RA. After the 1-year follow-up, the diagnosis of these false-positive patients was osteoarthritis (n = 2) or remitting oligoarthritis/polyarthritis (n = 20).

Patients with 0–5 points
Of the patients with 0–5 points (n = 328), 98 patients (30%) used MTX (case) after the 1-year follow-up. The distribution of cases and non-cases over the 2010 score can be described as patients with a higher score on the 2010 criteria showing a higher frequency of MTX use after 1 year.

The characteristics of patients with MTX (case; n = 98) were compared with those of patients who did not use MTX (non-case; n = 230) (Table 1). Patients who used MTX tended to have more tender and swollen joints and higher ESR values, but showed no differences on the other characteristics such as RF and ACPA positivity.

Discussion
By lowering the cut point of the 2010 criteria from 6 to 5 points, we were able to identify 15% more RA patients at a cost of 8% more false-positive patients. If these reclassified patients had started DMARD therapy after the first consultation, two-thirds of the patients would have received optimal treatment earlier, while the other
one-third of the patients might not have needed this treatment, as their symptoms were not related to the presence of RA. Each rheumatologist has to weigh the benefit of early treatment in true-positive RA patients against the harm of treatment in oligoarthritis/polyarthritis and osteoarthritis patients, i.e. the false-positive patients. Balancing the benefit and harm of treatment depends on the safety profile of the DMARDs and the quality of life lost if true-positive patients are left untreated [7]. In general, the safety profile of the various DMARDs is regarded as acceptable in the treatment of RA [8], but it is not clear whether this also holds for arthritis patients who score 5 points. Treatment in arthritis patients with 5 points seems beneficial [9], but none of these studies have evaluated the potentially negative effect of treatment in false-positive patients. In terms of quality of life, Geuskens et al. [10] found no difference in health-related quality of life between RA patients and non-RA patients, which might imply that treatment in arthritis patients with 5 points will improve their quality of life. Data is lacking on the presence of the off-days mentioned by patients, which affects worker productivity due to the side effects of medication.

The characteristics of the patients with 0–5 points (n = 328) differed little between those with and those...
without MTX. Although SJCs and TJCds differed, the differences were not strong enough to be used as an additional diagnostic criterion (data not shown). This is in accordance with the findings of Krabben et al. [4]. To reduce overtreatment in false-positive patients and to be more certain which patients could start early DMARD treatment, it might be beneficial to add other (imaging) biomarkers that could distinguish true-positive patients from false-positive patients at an earlier stage [11–13]. Nevertheless, lowering the cut point from 6 to 5 points would be a more feasible way to identify more persistent arthritis patients. This study showed that two-thirds of the patients with 5 points were already being treated with MTX after the 1-year follow-up, which could indicate that our results reflected daily clinical practice.

Our study has certain strengths and limitations. The REACH dataset was one of the early arthritis cohorts included in the pooled analysis to develop the new criteria for RA [1, 14]. The cut point of 6 was chosen using the AUC of three cohorts, including REACH. When we removed those patients (n = 184) from our analysis, the results were similar (data not shown). However, external validation of our results in another early arthritis cohort is recommended. Especially, larger cohorts could advance our work and could give more insight into other variables. The strength of our study includes the selection of patients, which was not biased towards RA. In REACH, no limits were set regarding the minimal number of swollen joints required, and the sample represents patients in an early phase of their disease (median duration of symptoms was 3 months).

In conclusion, by lowering the cut point of the 2010 criteria, we identified more RA patients in whom early treatment could have been initiated. This could have led to better patient outcomes.

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References


