RBR

2010 ACR-EULAR classification criteria for rheumatoid arthritis

With the recognition that early treatment achieves better outcomes in patients with rheumatoid arthritis (RA), increasing emphasis has been placed on the need to identify RA earlier. Early arthritis clinics (EACs) have been designed to enable rheumatologists to assess patients with potential RA earlier, using markers of inflammation, serology, and imaging assessments to complement the clinical assessment in making the diagnosis. Although designed for purposes of disease classification, the 1987 ACR RA criteria are often used to aid diagnosis. They also frequently form the basis for the entry criteria for inclusion into many therapeutic intervention studies. The criteria however have their limitations and have been shown not to perform as well in early disease.[1] A significant proportion of patients not meeting the classification criteria may therefore be labelled as undifferentiated arthritis (UA). Although some will have a spontaneously remitting course, others with a progressive, erosive phenotype will require early intervention.[2] Rheumatologists need to be able to identify those patients with a persistent, progressive course early to ensure timely initiation of therapy.

To address this, a joint working group from the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) has recently developed a new approach to classifying RA at an earlier stage in the disease continuum.[3] The classification system aims to identify, among patients with newly presenting inflammatory arthritis (IA), factors that best discriminated those who are at high risk for persistent and/or erosive disease *versus* those who are not and, in so doing, identify those who would warrant early initiation of therapy.

For the classification criteria to be applied two mandatory requirements must be met (table1). First, there must be clinical evidence of currently active synovitis (i.e. swelling) in at least one joint. All joints, except those typically involved in osteoarthritis (distal interphalangeal (DIP) joints, the first metatarsophalangeal (MTP) joint, and the first carpometacarpal (CMC) joint), are assessed for this. Second there is a requirement for clinician judgment, in that the criteria may only be applied where other possible causes for the synovitis (e.g. systemic lupus erythematosus, and gout) have been excluded. A scoring system, based on measures which are used in clinical practice, is then applied and the disease classified as RA if a total score of 6 or more (out of 10) from the individual scores in four domains is achieved. The domains are number and site of involved joints (score range 0-5), serological abnormality (score range 0-3), elevated acute phase response (score range 0-1) and symptom duration (2 levels; range 0-1) (Table 1). An important difference from the 1987 ACR RA classification criteria is that once definite clinical synovitis has been confirmed, both tender and swollen joints can be included to determine the score for number and type of joints involved. A symmetric distribution is also not necessary but is likely accounted for within the score given for joint involvement – greater joint involvement being associated with a greater likelihood of symmetry. Unlike the 1987 criteria, the presence of nodules and typical changes on X-rays, which both reflect long-standing disease, are not included this scoring system. Anti-cyclic peptide antibody (ACPA) status which has been shown to be one of the strongest predictor of evolution to RA in cohorts of patients with UA is now included in the criteria.[4]

Although the focus of the criteria is to classify patients with early disease, it is recognized that patients may present at a later stage of the disease. To maintain a single classification system for RA and to include this group of patients, two caveats to the criteria have been included. Patients with erosions typical for RA with a history compatible with prior fulfillment of the 2010 ACR EULAR RA criteria are classified as RA. Similarly patients with long-standing disease, both active and inactive (on or off treatment), who have previously satisfied these classification criteria based on retrospectively available data are also classified as RA.

Patients with very early disease may not fulfill the new criteria at initial assessment and may need to be reviewed and the criteria reapplied. As the disease evolves the criteria may be fulfilled over time. The introduction of a scoring system in the classification criteria also provides the notion of risk gradient

Correspondence to: Ricardo Fuller. Av. Brigadeiro Luiz Antonio, 2.466, conjs. 93-94. São Paulo, SP, Brazil. CEP 01402-000.

Table 1

Target population (who should be tested?)	
Patient with at least 1 swollen joint with definite clinical synovitis (swelling).* Synovitis is not better explained by another disease. *Differential diagnoses differ in patients with different presentations but may include conditions such as systemic lupus erythematosus, psoriatic arthritis and gout. If unclear about the relevant differentials, an expert rheumatologist should be consulted.	
Classification criteria for RA (Score-based algorithm: add score of categories A-D) A score of ≥ 6/10 is needed for a definite classification of a patient with RA.	
Joint involvement[A]	
1 large[B] joint	0
2-10 large joints	1
1-3 small[C] joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
>10 joints[D] (at least one small joint)	5
Serology[E] (at least one test result is needed for classification)	
Negative RF **and** negative ACPA	0
Low positive RF **or** low positive ACPA	2
High positive RF **or** high positive ACPA	3
ACUTE PHASE REACTANTS[F] (at least one test result is needed for classification)	
Normal CRP **and** normal ESR	0
Abnormal CRP **or** abnormal ESR	1
Duration of symptoms[G]	
< 6 weeks	0
≥ 6 weeks	1

[A]Joint involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis. Distal interphalangeal joints (DIPs), 1st carpo-metacarpal (CMC) joint, and 1st metatarso-phalangeal (MTP) joint are *excluded from assessment*. Categories of joint distribution are classified according to the location and number of the involved joints, with placement into the highest category possible based on the pattern of joint involvement.

[B]Large joints refer to shoulders, elbows, hips, knees and ankles.

[C]Small joints refer to the wrists, metacarpo-phalangeal (MCP) joints, proximal interphalangeal (PIP) joints, thumb interphalangeal (IP) joints and metatarsophalangeal (MTP).

[D]In this category, at least 1 of the involved joints must be a small joint ; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g. temperomandibular, acromioclavicular and sternoclavicular joints).

ENegative refers to international unit (IU) values that are £ upper limit of normal ULN for the lab and assay. Low titre refers to IU values that are > ULN but £ 3X ULN for lab and assay. High titre positive: > 3X ULN for lab and assay. Where RF is only available as positive or negative, a positive results should be scored as 'low positive' for RF.

FNormal /abnormal is determined by local laboratory standards (*Other causes for elevated acute phase reactants should be excluded*).

[G]Duration of symptoms refers to patient self-report of the duration of signsor symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.

RF = rheumatoid factor; ACPA = anti-citrullinated protein/ peptide antibodies; ULN = upper limit of normal; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein.

for the development of persistent disease - one may consider reassessing patients with a higher score more frequently.

Several cohorts have been used to assess the performance of the new criteria. Preliminary findings have shown that they perform well in identifying persistent arthritis when applied to patients with inflammatory arthritis (IA). In one group of patients with IA the new criteria indentified more than twice the number of patients that the 1987 ACR RA criteria.[5] Analysis of data from an early arthritis cohort found an area under the curve (95% CI) of 0.72 (0.64-0.79) to predict persistent arthritis and 0.63 (0.50-0.76) for fulfilment of the 1987 ACR RA criteria.[6] Finding from another group[7] were similar – UA patients with a score of ≥ 6 at baseline had a 0.74 probability of developing persistent arthritis at 2 years. Use of the new criteria in clinical practice may therefore help to improve early identification of patients with RA. Reclassification of these patients who would otherwise have been termed UA in the past to RA may in turn enable physicians to initiate DMARD therapy with greater confidence, thereby avoiding unwanted delays in starting treatment and accelerating to more aggressive therapy where required.

Several studies of drug intervention in patients previously defined as UA have been undertaken.[8,9] Many however used different definitions for UA so that study outcomes are not always directly comparable and applying these in clinical practice not always easy. It is likely that these cohorts included patients with early RA who did not fulfil the 1987 ACR classification criteria. Use of the new criteria in the design of future clinical trials may help to standardise the classification of early RA and allow better evaluation of early therapy. Treating earlier may in turn halt the progression to the phenotype fulfilling the 1987 ACR RA criteria. The use of the scoring system may also allow the possibility of investigating different treatment strategies at different cut-offs. A more aggressive approach, for example, could be tested in patients with a higher score.

The 2010 ACR EULAR classification criteria therefore provide a further step towards improving the identification and thereby the outcomes for patients with RA. Validation in different cohorts and clinical settings is needed to assess their performance and evaluate their ease of use in daily practice. As the field of rheumatology continues to evolve, the discovery of new biomarkers and may further enhance the diagnosis and management of RA.

Edith Villeneuve

Section of Musculoskeletal Disease, Leeds Institute of Molecular Medicine, University of Leeds

Jackie Nam

Section of Musculoskeletal Disease, Leeds Institute of Molecular Medicine, University of Leeds
NIHR Leeds Musculoskeletal Biomedical Research Unit,
Leeds Teaching Hospitals Trust, Leeds, UK

Paul Emery

Section of Musculoskeletal Disease, Leeds Institute of Molecular Medicine, University of Leeds
NIHR Leeds Musculoskeletal Biomedical Research Unit,
Leeds Teaching Hospitals Trust, Leeds, UK

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