The American College of Rheumatology/European League Against Rheumatism Criteria for the classification of rheumatoid arthritis: a game changer

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Over the last several years the two preeminent professional societies representing rheumatology, the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR), have been discussing increasing their collaboration in areas of interest to rheumatologists worldwide. These discussions resulted in a letter of agreement in 2008 on the framework whereby the two organisations would work together to develop disease classification criteria as well as recommendations for conducting of clinical trials. To enhance communication between the two organisations, ACR representatives now sit on the EULAR Standing Committee for Clinical Affairs and the EULAR Standing Committee of Epidemiology, and EULAR representatives now sit on the ACR Criteria Subcommittee and Quality of Care Committee.

The first result of this effort was the joint publication, in *Annals of the Rheumatic Diseases* and *Arthritis Care & Research*, of the recommendations on reporting disease activity in clinical trials of patients with rheumatoid arthritis (RA).1 2 This document was important in that it delineated the minimal standards necessary for clinical trials evaluating new therapeutics in RA. Several collaborative projects are under way on RA, and also on gout, scleroderma, myositis and vasculitis. The positive aspects of developing a consensus among the dominant voices in world of rheumatology are self-evident.

The recent initiative to revise the ACR classification criteria for RA3 is the most significant cooperation so far. For the past 2 years rheumatologists on both sides of the Atlantic have been working on this project, and the fruits of their work are now published in this journal.

The last classification criteria were published in 1987,4 and are widely regarded as unsatisfactory for the diagnosis of RA (for which they were not designed). The need for the new classification criteria has been made more urgent by the understanding that, at presentation, RA may be an evolving disease, the final phenotype of which can be altered by interventions. From work in European clinics evaluating patients presenting with early undifferentiated arthritis, it was clear that the discriminant ability of the previous RA classification criteria was insufficient to distinguish those patients destined eventually to develop RA from those who would have a limited course or whose condition would evolve into other forms of inflammatory arthritis.5 Additionally, the developing science regarding the importance of antibodies to citrullinated proteins in RA6 occurred subsequent to the last classification criteria, and it was clear that inclusion of this testing in updated criteria was critical. Over the last two decades, early intervention to prevent functional decline has become accepted as the standard of care. The ideal therapeutic intervention would be undertaken at an early stage before the development of the final phenotype, described by the previous classification criteria, producing a positive impact on disease progression in the majority of patients.

The joint working group, realising the deficiencies of the previous criteria, set out with several major goals. These included identifying, among patients with newly presenting undifferentiated arthritis, a subset with a high risk of chronicity and erosive damage, and ensuring that the new criteria could be used as a basis for initiating disease-modifying antirheumatic drug therapy. A comprehensive programme was developed and conducted in three phases. In Phase 1, utilising a data-driven approach based on three cohorts of patients with early arthritis, the working group identified factors that were associated with the subsequent decision by physicians to initiate methotrexate therapy, and their relative weights. Phase 2 was consensus driven, with a science-based approach informed by data from Phase 1. Phase 3 was the derivation from the previous two phases: the final classification criteria set. The final criteria set was validated with three cohorts not used in Phase 1. The criteria are thus a mix of pragmatic expert opinion and a science-driven approach.

As noted by the working group, utilisation of these criteria ‘redefines the current paradigm of RA’. The 1987 classification criteria were useful in discriminating patients with RA from those with other inflammatory arthritides, but have not been helpful in identifying patients who would potentially benefit from early intervention. The new criteria differ from the previous criteria in that the presence of synovitis in at least one joint is required, with no alternative diagnosis to explain the synovitis. Symmetric disease involvement is not required, nor is the presence of structural joint damage or rheumatoid nodules, both reflective of longstanding, established disease. A scoring system evaluating four categories—joint involvement, serology, acute-phase response and duration of symptoms—has been developed. Using this new scoring system, 87–97% of patients in three early arthritis cohorts in whom methotrexate treatment was begun within 12 months from symptom onset met the new classification criteria for ‘definite RA’. Importantly, the domains assessed have face validity, as was predicted several years ago.7 The new criteria provide a more rigorous scientific basis for this approach.

We believe these new classification criteria will be rapidly adopted in daily practice, and we look forward to their implementation in clinical trials. Certainly this will accelerate the use of more aggressive treatment for patients and, as the authors note, additional studies in different clinical settings need to be conducted to determine their applicability. How these criteria might impact...
patient selection for clinical trials will be
of great interest.

Change can be difficult for a genera-
tion of rheumatologists used to classify-
ing RA with the old criteria. Concerns
over the absence of erosion in the scor-
ing system, as well as the absence of the
necessity of symmetric joint involve-
ment, will be raised. The working group
does acknowledge that the presence
of erosions typical of RA would justify
classification of a patient as having RA,
but also raises the question of what is
meant by significant erosive disease and
what evidence of erosions should be con-
sidered acceptable as signifying ‘typical
of RA’. Symmetric joint disease was not
found to provide additional independent
weight to the criteria. Additional con-
cerns exist regarding the utility of these
classification criteria for the primary care
physician who must determine synovitis
by examination and then exclude other
possible diagnoses that might explain the
synovitis. The authors correctly point
out that the criteria are not to be used as
a tool for referral of patients with inflam-
matory arthritis to the rheumatologist,
and there are several ongoing efforts in
progress to provide primary care prac-
titioners with the tools to recognise
patients who need rapid, early referral.

It might be predicted that classic phar-
aceutical studies of ‘early’ active RA
will be unchanged, since the vast major-
ity of these patients with a high disease
activity score and frequent radiological
erosions have an advanced phenotype.
The exciting new area will be patients
previously labelled as having undiffer-
entiated arthritis, with one to two swol-
len joints and anticitrullinated protein
antibody positivity, who may well score
sufficiently to be labelled as having RA.
This should encourage studies of the
disease at this crucial stage of evolution.

For these patients, the issue of defining
synovitis and, as noted above, a ‘typical’
erosion will need to be evaluated, and
the current subjective clinical diagnosis
may need refinement using objective and
more sensitive imaging modalities, such
as MRI and ultrasound.

We applaud the efforts of all involved
in the development of the new RA clas-
cification criteria. Prior to publication,
the manuscript was critically reviewed not
only by the journal editors and review-
ers, but also by leadership of both the
ACR and EULAR, including the boards
of directors and committee members.
That input was important in the eventual
publication of this straightforward and
well-written document. The acceptance
of the evolving nature of RA is a step-
change conceptually. We look forward
to the identification of future biomark-
ers that will again result in another call
to modify the RA classification criteria.
When that occurs, improvement in the
quality of life of our patients will surely
follow.

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