Editorial

# The Mean Overall Index-RA: A New Disease Activity Measure in Rheumatoid Arthritis

The last decade has seen major advances in the care of patients with rheumatoid arthritis (RA). New therapeutics are available that significantly reduce disease activity, improve physical function, and reduce the damage to joints that, over time, can lead to disability. Further, studies such as the BeST study, the TICORA study, and others have convincingly demonstrated that systematic application of defined treatment strategies in the clinic setting can reduce disease activity to low levels in large proportions of patients[1-4]. Critical to accomplishing these important advances has been the development and refinement of measurement tools to accurately assess disease activity in clinical trials and in the clinic.

Unlike other diseases, for which activity can be monitored using a single measure, there is no single variable that can be used as a gold standard in RA. Instead, disease activity is monitored using a combination of distinct measures. Currently used disease activity measures incorporate some or all of the 7 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) core set measures. This core set includes 3 physician-assessed measures (tender and swollen joint counts, physician global), 3 patient-assessed measures (pain, physical function, patient global), and a laboratory measure (acute-phase reactant erythrocyte sedimentation rate or C-reactive protein, CRP).

In general, measures that assess disease activity come in 2 varieties: those that measure disease activity per se at a given moment in time, e.g., the Disease Activity Score (DAS) or DAS28[5], and those that measure improvement in disease activity compared to some specified baseline, e.g., the ACR20 criteria[6], the recently described ACR-hybrid[7], and EULAR response criteria[5]. Each of these measures has undergone extensive validation, and all are widely accepted as outcome measures in clinical trials. One of the most widely used disease activity scores is the DAS, which uses a mathematical formula that combines values for a subset of the core set measures (tender and swollen joint counts, patient global, and acute-phase reactant) to generate a continuous score that correlates with physician judgment of high or low disease activity. However, there is still a place for other disease activity measures since the DAS may not be the optimal disease activity measure in all settings. It is, for example, not straightforward to calculate. The Simplified Disease Activity Index[8] (SDAI) and Clinical Disease Activity Index[9] (CDAI) were developed to make the process of scoring easier by simple numerical summing of a subset of the core set components (the tender and swollen joint counts, physician and patient global assessments with and without CRP for the SDAI and CDAI, respectively). Finally, other disease activity measures have been developed that allow rapid scoring by relying on patient assessments and omitting formal physician-measured joint counts (RAPID3 and PDAS[10,11]).

In this issue of *The Journal*, Mäkinen, *et al* propose a novel measure of disease activity — the Mean Overall Index for Rheumatoid Arthritis (MOI-RA)[12]. The MOI-RA utilizes all 7 core set measures. Each core set measure is standardized to a 0–100 scale, and the total score is a mean of the values of all 7 components. The authors assess the validity of the MOI-RA using data from the Finnish Rheumatoid Arthritis Combination Therapy Trial (FIN-RACo)[13]. The MOI-RA contains the appropriate domains relevant to disease activity based on the fact that it includes all the core set measures. To assess criterion validity the authors demonstrate that scores on the MOI-RA correlate with other well established disease activity measures. The authors also provide evidence for responsiveness and sensitivity to change.

Given the large number of well accepted disease activity measures it is reasonable to ask whether the MOI-RA has potential advantages over other instruments. The authors argue that unlike other disease activity measures the MOI-RA includes contributions from all 7 core set measures,

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while other instruments include a subset of these. This is a potential advantage since physical disability, as measured by the HAQ, has been shown to have only a limited correlation with other core set components. However, the authors did not demonstrate that MOI-RA better reflects disease activity based on the core set measures than other disease activity measures. Another potential advantage of the MOI-RA that the authors demonstrate in the clinical trial setting is that values for the measure are stable with respect to missing values for up to 3 of the 7 components. In addition, the authors argue that the MOI-RA has the advantage of standardizing the components to generate the score rather than adding together components that are measured using different scales. While this is a potential advantage, it remains to future research to determine whether standardizing the components improves the performance of the MOI-RA compared to other instruments.

How then are clinicians and clinical researchers to decide which disease activity measure to use in a given setting? One important consideration in choosing a measurement instrument is fitness for use. That is, the properties of an instrument should be well suited for their intended use in a given setting. Thus, for example, in the clinical trial setting, the ACR20 is well suited for distinguishing efficacious drugs in a placebo-controlled trial. In contrast, a continuous measure such as the ACR-hybrid or the DAS28 may be a more sensitive endpoint to compare 2 known, effective products that are similar in efficacy to one another. Other considerations apply in the clinic setting, where busy clinicians may not routinely perform formal joint counts. In the clinic, it is possible that one of the simplified disease activity scores may prove adequate for assessing responses to new agents and assuring that patients attain the low disease activity state that is the target of therapy.

Choosing sensitive and valid measures of disease activity is essential both in clinical trials and in the clinic. Clinical trials typically collect comprehensive measurements of the key measures of disease activity and response to therapy. Given the proliferation of available disease activity measures it will be important to develop guidelines for reporting results of clinical trials so key domains are reported using instruments that have undergone appropriate validation. In the clinic, disease activity measurement is equally important. Several studies have shown excellent outcomes when clinicians adjust DMARD therapy with a goal of obtaining a low disease activity state or remission. These studies suggest that following disease activity in a quantitative manner can assure the maximum benefits to patients of the potent new therapies in the rheumatologist's armamentarium.

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