The Disease Activity Score and the EULAR Response Criteria

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KEYWORDS

• Rheumatoid arthritis • Disease Activity Score
• EULAR • Response criteria

The Disease Activity Score (DAS), its modified version the DAS28, and the DAS-based European League Against Rheumatism (EULAR) response criteria are well-known measures of disease activity in rheumatoid arthritis (RA). The DAS and the DAS28 consist of a combination of the number of tender joints, the number of swollen joints, erythrocyte sedimentation rate (ESR), and a global assessment rating by the patient.[1–3] The EULAR response criteria are calculated with the DAS or the DAS28 using the individual change in disease activity and the level of disease activity reached to classify trial participants as good, moderate, or nonresponders.[4–7]

The DAS, DAS28, and the EULAR response criteria have been extensively validated.[8] Their use in RA clinical trials and for monitoring patients who have RA is still increasing. The DAS28 is included in the American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis as an outcome measure on which to base treatment decisions.[9] The DAS and DAS28 were used in several clinical trials that showed the beneficial effects of tight control for the treatment of RA.[10–12] For applying tight control principles in practice, and for interpreting results from clinical trials, the DAS used in RA are relevant for clinicians to know.

This article updates previous summaries[8,13] on the development and validation of the DAS, DAS28, and EULAR response criteria and their use in research and clinical practice.

THE DISEASE ACTIVITY SCORE

The DAS was originally developed as an index containing the Ritchie Articular Index (RAI, range, 0–78), a 44 swollen joint count (range, 0–44), ESR, and a patient global

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assessment on a visual analog scale (range, 0–100).[2,3] A specially programmed DAS calculator and a computer program that can be downloaded from the Internet are available to calculate the DAS (**Table 1**). The DAS has a continuous scale ranging from 0 to 10, and usually shows a Gaussian distribution in populations that have RA (**Fig. 1**). The level of disease activity can be interpreted as low (DAS $\leq$ 2.4), moderate (2.4<DAS $\leq$ 3.7), or high (DAS>3.7).[5] A DAS less than 1.6 corresponds with being in remission according to the American Rheumatism Association (ARA) criteria.[14] The DAS is reasonably well related to patient global assessment of disease activity (**Fig. 2**), despite the little weight that the patient-assessed global item received in the DAS formula. Therefore, the DAS also reflects patient-assessed disease activity.

Development of the Disease Activity Score

The DAS was developed using a large prospective study, in which decisions of rheumatologists to initiate or discontinue disease-modifying antirheumatic drug (DMARDs) treatment because of disease remission were equated with high and low disease activity, respectively.[1,2] High disease activity was characterized as either start of a DMARD or termination of DMARD treatment because of lack of effect. Low disease activity was characterized as either termination of DMARD treatment because of RA remission, not changing a DMARD for at least 1 year, or not starting DMARD treatment for at least 1 year. To develop the DAS, various statistical methods were used to identify the clinical and laboratory variables that explained most of the variation in rheumatologists' decisions on DMARD treatment, according to factor analysis, defining disease activity, discriminant analysis, regression analysis, and reproducibility.

Factor Analysis

A factor analysis was performed on the individual data, resulting in a five-factor model. The factors could be labeled as shown in **Box 1**.

Defining Disease Activity

The rheumatologists' decisions on initiating and terminating DMARDs were used as an external standard to define high and low disease activity. The clinical assessments were performed by specially trained research nurses, and the rheumatologists made all decisions concerning DMARDs independently of these assessments. The rheumatologists were not aware that their decisions were part of the investigation.

Discriminant Analysis

The factor values of the five factors were entered into a discriminant analysis, using assessments during defined high and low disease activity. Factors 3 and 5 were

Table 1
Computation of the disease activity score

Disease activity score (four variables) =
DAS–4 = 0.53938*$\sqrt{}$(Ritchie) + 0.06465*(swollen joints) + 0.330*ln(ESR) + 0.00722*(GH)
Disease activity score (three variables) =
DAS–3 = 0.53938*$\sqrt{}$(Ritchie) + 0.06465*(swollen joints) + 0.330*ln(ESR) + 0.224

Abbreviations: DAS, Disease Activity Score; ESR, erythrocyte sedimentation rate; GH, general health; Ritchie, Ritchie articular index; swollen joints, 44 swollen joint count.

Data from Van der Heijde DMFM, Van 't Hof MA, Van Riel PLCM, et al. Development of a Disease Activity Score based on judgment in clinical practice by rheumatologists. J Rheumatol 1993;20: 579–81.