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Rheumatoid Arthritis Measures

Disease Activity Score (DAS), Disease Activity Score-28 (DAS28), Rapid Assessment of Disease Activity in Rheumatology (RADAR), and Rheumatoid Arthritis Disease Activity Index (RADAI)

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DISEASE ACTIVITY SCORE (DAS)

General Description

Purpose. The Disease Activity Score (DAS) combines single measures into an overall, continuous measure of rheumatoid arthritis (RA) disease activity (1,2). The use of a single index has advantages, because simultaneous interpretation of several measures of RA disease activity is difficult. It also has advantages for statistical analysis in studies. Because the DAS contains reduced joint counts, it is also feasible to use for monitoring of RA disease activity in daily clinical practice.

Content. The DAS includes the Ritchie Articular Index (RAI); a 44-joint swollen joint count, erythrocyte sedimentation rate (ESR), and a general health assessment on a visual analog scale (1,2).

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Versions. The DAS can be used with or without general health assessment. The DAS28 is analogous to the DAS but includes simplified 28-joint counts (3). A formula to transform DAS28 into DAS values is available (4). The DAS can also be calculated using C-reactive protein (CRP) instead of ESR (see www.das-score.nl).

Number of items in scale. The DAS has 4 items, or 3 when the general health assessment is omitted.

Subscales. None.

Populations. *Developmental/target.* Patients with rheumatoid arthritis.

Other uses. Not validated for other rheumatic disorders.

WHO ICF Components. Body function, Body structure, Impairment.

Administration

Method. Clinical assessment of joint counts and drawing a blood sample for ESR or CRP.

Training. Training is necessary for reliable assessment of joint counts.

Time to complete. Allow 5–8 minutes for joint counts. You should include an hour waiting time for the ESR result.

Equipment needed. Laboratory for ESR or CRP determination. For calculating the DAS, a programmed calculator or computer, or a computer with an internet connection is needed.

Availability/cost. The DAS is available free of charge, at http://www.das-score.nl.

Scoring

Responses. *Scale.* The RAI ranges from 0 to 78, the 44-joint swollen joint count ranges from 0 to 44 (44SJC). ESR may range from 0 to 150, General Health (GH) ranges from 0 to 100.

Score. The range of the DAS is 0–10.

Interpretation of scores. The level of disease activity can be interpreted as low (DAS ≤ 2.4), moderate (2.4 < DAS ≤ 3.7), or high (DAS >3.7) (5). A DAS <1.6 corresponds with being in remission according to the American Rheumatism Association (ARA) criteria (6).

A change of 1.2 (2 times the measurement error) in the DAS is considered a significant change (5), because changes that large are unlikely the result of random measurement error ($P \leq 0.05$). The European League Against Rheumatism (EULAR) response criteria classify patients as good, moderate, or non-responders, using the change in DAS and the level of DAS reached (5). For example, a patient must show a significant change as well as low disease activity to be classified as a good responder.

Method of scoring. The DAS is most easily calculated using a programmed calculator or a computer. Online and downloadable calculators are freely available at http://www.das-score.nl. The following formulas are used (1):

DAS-4 (four variables) = 0.53938 × sqrt(RAI) + 0.06465 × (44SJC) + 0.330 × ln(ESR) + 0.00722 × GH.

DAS-3 (three variables) = 0.53938 × sqrt(RAI) + 0.06465 × (44SJC) + 0.330 × ln(ESR) + 0.224.

Time to score. The calculation of the DAS takes 1 minute.

Training to score. None.

Training to interpret. None.

Norms available. Reference values are available, and are also useful for the interpretation of the disease activity scores from individual patients, see "interpretation of scores."

Psychometric Information

Reliability. *Test-retest.* Reproducibility of the DAS was determined by an interperiod correlation matrix of RA patients with ≥3 years followup. The measurement-remeasurement correlation was r = 0.80, and the measurement error was 0.6. A significant change in DAS for individual patients was defined as 2 times the measurement error (2 × 0.6) = 1.2 (2). Changes that large are unlikely the result of random measurement error ($P \leq 0.05$).

Validity. *Content.* The DAS includes measures from the "core set" of measures used to assess the efficacy of disease-modifying antirheumatic drugs. The DAS deliberately excludes measures of disability or joint damage (1).

Criterion. There is no real "gold standard" available to judge RA disease activity. Therefore, in the development of the DAS, physician judgement of low and high disease activity was used as external standard (1). In a validation study, the DAS showed larger power than other indices or single variables to discriminate low from high disease activity (7). The DAS showed a high predictive ability (pa = 0.93) in discriminating "active RA" from "partial or complete remission" in another study (8).

Concurrent. Of several composite indices, the DAS had the highest correlations with assessor's (r > 0.80) and patient's (r > 0.60) global assessment of disease activity (9). The DAS was well correlated (mean r = 0.61) with 12 other estimators of disease activity, whereas the composite indices all showed higher correlations than the single variables (7).

Construct. The DAS was well correlated with disability as measured with the Health Assessment Questionnaire (HAQ) (7,10), this correlation remained fairly constant (r = 0.51–0.68) throughout 12 years of disease duration (10). An increase in the DAS over time was associated with an increase in disability over the same period (11). Joint damage may be looked at as the result of the activity of the RA disease process over time. The mean DAS (7), and increase and fluctuations in the DAS (12) were well related to increase in joint damage over the same time period.

The DAS-based EULAR response criteria are generally evaluated for their performance in RCTs or the association with disability and joint damage. It was shown that the EULAR response criteria performed as well as (4,13) or better (5,14) than the modified American College of Rheumatology (ACR) or WHO/ILAR response criteria in discriminating the stronger treatment from control treatment in RCTs. No differences were found between ACR and EULAR criteria when using full or reduced joint counts (15). Good responders according to the EULAR criteria showed significantly more improvement in pain ($P < 0.001$) and disability ($P < 0.001$) than moderate and non-responders. Joint damage progressed in moderate ($P = 0.005$) and non-responders ($P = 0.01$) but not in good responders ($P = 0.94$) (16). Other studies also showed that the EULAR response criteria are clearly related to change in disability (4) and progression of joint damage (4,5,14) and perform as well as or better than the ACR response criteria.

Responsiveness to change. In a trial comparing sulfasalazine with a combination of methotrexate, sulfasalazine, and prednisolone, all composite indices were more responsive than single core set measures. The ACR20% criteria were most responsive; the Standardized Response Mean (mean change divided by SD change) of the DAS was about half as large (13).

Comments and Critique

The DAS, DAS28, and the EULAR response criteria are extensively validated and are finding increasing use in RA clinical trials and for monitoring individual RA patients. In the literature, there are several formulas available for calculation of the DAS, which may cause confusion (17). Values of the DAS and DAS28 are not directly comparable, but a transformation formula has to be used.

The DAS can be used as a guide in the suppression of RA disease activity with disease-modifying antirheumatic drugs. However, it must be noticed that even firm suppression of disease activity may not be sufficient to totally stop the progression of joint damage. Furthermore, even when the DAS is a useful guide for treatment decisions, it does not replace careful patient examination and inquiry.

A disadvantage of the DAS in practice is the need for a blood sample and joint counts by a trained health-care provider. Self-assessment of RA disease activity by the patient may be less laborious for the physician. However, patient assessed disease activity may proxy but not automatically replace the DAS (18).

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DISEASE ACTIVITY SCORE-28 (DAS28)

General Description

Purpose. The Disease Activity Score-28 (DAS28) combines single measures into an overall, continuous measure of rheumatoid arthritis (RA) disease activity (1–3). The use of a single index has advantages because simultaneous interpretation of several measures of RA disease activity is difficult. It also has advantages for statistical analysis in studies. Since the DAS28 contains reduced joint counts, the DAS28 is also feasible to use for monitoring of RA disease activity in daily clinical practice.

Content. The DAS28 includes a 28 tender joint count, a 28 swollen joint count, erythrocyte sedimentation rate, and a general health assessment on a visual analog scale (2,3).

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Versions. The DAS28 can be used with or without general health assessment. The DAS28 is analogous to the DAS but includes 28-joint counts. A formula to transform DAS28 into DAS values is available (4). The DAS28 can also be calculated using C-reactive protein (CRP) instead of ESR (see http://www.das-score.nl).

Number of items in total scale. The DAS28 has 4 items, or 3 when the general health assessment is omitted.

Subscales. None.

Populations. *Developmental/target.* Patients with rheumatoid arthritis.

Other uses. Not validated for other rheumatic disorders.

WHO ICF Components. Body function, Body structure, Impairment.

Administration

Method. Clinical assessment of joint counts and drawing a blood sample for ESR or CRP.

Training. Training is necessary for reliable assessment of joint counts.

Time to complete. Allow 3–5 minutes for 28 joint counts. You should include an hour waiting time for ESR result.

Equipment needed. Laboratory for ESR or CRP determination. To calculate the DAS28, a programmed calculator or computer, or a computer with an internet connection is needed.

Availability/cost. The DAS is available free of charge, at http://www.das-score.nl.

Scoring

Responses. *Scale.* The 28 tender joint count (28TJC) and 28 swollen joint count (28SJC) both range from 0 to 28. ESR may range from 0 to 150, General Health (GH) ranges from 0 to 100.

Score. The range of the DAS28 is 0–9.4.

Interpretation of scores. The level of RA disease activity can be interpreted as low (DAS28 $\leq$3.2), moderate (3.2 < DAS28 $\leq$5.1), or as high disease activity (DAS28 >5.1) (4). A DAS28 <2.6 corresponds with being in remission according to the ARA criteria. A change of 1.2 (2 times the measurement error) in DAS28 is considered a meaningful change (5) because changes that large are unlikely to be the result of random measurement error ($P \leq 0.05$). The EULAR response criteria classify patients as good, moderate, or non-responders, using the change in DAS28 and the level of DAS28 reached (4). For example, a patient must show a significant change as well as low disease activity to be classified as a good responder.

Method of scoring. The DAS28 is most easily calculated using a programmed calculator or a computer. Online and downloadable calculators are free available at www.das-score.nl. The following formulas are used (2):

DAS28-4 (four variables) = 0.56 × sqrt(28TJC) + 0.28 × sqrt(28SJC) + 0.70 × ln(ESR) + 0.014 × GH.

DAS28-3 (three variables) = (0.56 × sqrt(28TJC) + 0.28 × sqrt(28SJC) + 0.70 × ln(ESR)) × 1.08 + 0.16.

The transformation formula to calculate the DAS28 from the DAS is DAS28 = (1.072 × DAS) + 0.94, (5).

Time to score. The calculation of the DAS28 takes 1 minute.

Training to score. None.

Training to interpret. None.

Norms available. Reference values are available, and are also useful for the interpretation of the disease activity scores from individual patients, see "interpretation of scores."

Psychometric Information

Reliability. *Test-retest.* Reproducibility of the DAS was determined by an interperiod correlation matrix of RA patients with ≥3 years followup. The measurement-remeasurement correlation was r = 0.80, and the measurement error was 0.6. A significant change in DAS or DAS28 for individual patients was defined as 2 times the measurement error (2 × 0.6) = 1.2 (4,5). Changes that large are unlikely the result of random measurement error ($P \leq 0.05$).

Validity. *Content.* The DAS28 includes measures from the "core set" of measures used to assess the efficacy of disease-modifying antirheumatic drugs. The DAS28 deliberately excludes measures of disability or joint damage.

Criterion. There is no real "gold standard" available to judge RA disease activity. Therefore, in the development of the DAS28, physician judgement of low and high disease activity was used as external standard (2). The DAS28 showed a high predictive ability (pa = 0.88) in detecting a flare of RA disease activity (6).

Concurrent. Of several composite indices, the DAS28 had the highest correlations with assessor's (r > 0.80) and patient's (r > 0.60) global assessment of disease activity (7). The DAS28 correlated well (r > 0.94) with the original DAS (2).

Construct. Cross-sectionally, the DAS28 was well correlated (r = 0.49 and r = −0.46) with disability as measured with the Health Assessment Questionnaire (HAQ) or the Short Form-36 Physical Functioning scale (8). Joint damage may be looked at as the result of the activity of the RA disease process over time. As expected, the DAS28 was not strongly correlated (r < 0.20) with joint damage, in the cross-sectional sample (8). The time integrated DAS28 (2) was well related to increase in joint damage over the same time period.

It was shown that the DAS-based EULAR response criteria performed as well as (4,9) or better (5,10) than the modified ACR or WHO/ILAR response criteria in discriminating the stronger treatment from control treatment in RCTs. No differences were found between ACR and EULAR criteria when using full or reduced joint counts' (11). It was shown that the EULAR response criteria using the DAS28 were clearly related to change in disability and progression of joint damage (11) and perform as well as or better than the ACR response criteria.

Responsiveness to change. In a trial where flares of disease activity occurred, the standardized effect size (SES: difference of within-group changes divided by the pooled SD of change) of the DAS28 was 1.56, which was higher than its components (SES < 1.18) or the HAQ (SES = 1.16), but lower than patient assessed pain (SES = 1.67) (6).

Comments and Critique

The DAS, DAS28, and the EULAR response criteria are extensively validated and are finding increasing use in RA clinical trials and for the monitoring of individual RA patients.

In the literature, there are several formulas available for calculation of the DAS28 and the DAS, which may cause confusion (12,13). Values of the DAS28 and DAS are not directly comparable, but a transformation formula has to be used.

The joint counts of the DAS28 do not include the feet, which joints may be among the first involved in early RA. Nevertheless, the performance of the DAS28 and the DAS is comparable in early RA.

The DAS28 can be used as a guide in the suppression of RA disease activity with disease-modifying antirheumatic drugs. However, it must be noticed that even firm suppression of disease activity may not be sufficient to totally stop the progression of joint damage. Furthermore, even when the DAS28 is a useful guide for treatment decisions, it does not replace careful patient examination and inquiry.

A practical advantage of the DAS28 is that reduced joint counts are used, but a blood sample still has to be analyzed. Self-assessment of RA disease activity by the patient may be less laborious for the physician. However, patient assessed disease activity may proxy but not automatically replace the DAS28 (13).

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