The use of MRI in early inflammatory arthritis

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Is the modified Disease Activity Score superior to the Disease Activity Score in early arthritis and rheumatoid arthritis? Comment on the article by Baker et al

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To the Editor:

We read with great interest the recent article by Baker et al, in which the authors describe the development of a modified Disease Activity Score (M-DAS) based on correlations with concurrent synovitis scores as measured by magnetic resonance imaging (MRI) in patients with rheumatoid arthritis (RA).[1] The original DAS was developed in the early 1990s based on the clinical findings of rheumatologists; it consists of the Ritchie Articular Index, the number of swollen joints, the erythrocyte sedimentation rate (ESR), and the patient's global assessment of disease activity measured on a visual analog scale (PtGA). Since then, the DAS has been modified and validated several times, including for use with the C-reactive protein level (DAS-CRP) instead of the ESR and for use with smaller joint counts (28-joint count DAS [DAS28]). In the recently developed M-DAS, tender joint count (TJC) and PtGA, the variables that are most subject to subjectivity, are no longer included, and the evaluator's global assessment (EvGA) is included. The M-DAS was developed using data from the GO-BEFORE study and validated using data from the GOFORWARD study (both RA clinical trials). Compared to the DAS28, correlations between MRI-detected synovitis and the M-DAS28 were superior, and the M-DAS28 was shown to be a more precise predictor of radiographic progression.[1] Similarly, modified versions of the Simplified Disease Activity Index (M-SDAI) and Clinical Disease Activity Index (M-CDAI) were derived.[1] These modified measures need to be evaluated in independent studies to determine their validity. We therefore compared the original and modified measures in a population-based inception cohort of patients with early arthritis, using MRI-detected inflammation (synovitis and bone marrow edema) and radiographic progression as outcomes.

Baseline MRI data and DAS28 scores of 127 patients with early arthritis, included in the Leiden Early Arthritis Cohort between 2010 and 2012, were available; of these patients, 91 had data on EvGA. The cohort and the details of the MRI protocol are described elsewhere.[2] Using the Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system, 2 readers scored MRIs for synovitis and bone marrow edema. The total synovitis and bone marrow edema scores of the metacarpophalangeal and wrist joint were calculated using the mean scores. Within-reader intraclass correlation coefficients (ICCs) for inflammation on MRI were 0.99 and 0.93 for the 2 readers, respectively; the between-reader ICC was 0.87 (2). Patients were followed up prospectively. Radiographs of the hands and feet of 87 patients were taken at baseline and after 1 year, and 1 reader chronologically scored the joints using the Sharp/van der Heijde scoring (SHS) method (withinreader ICC 0.86). Progression was defined as an increase in SHS of 1 (similar to the definition used by Baker et al). Sensitivity analyses defining progression as SHS of 3 were also performed. The following formulas were used: DAS28-CRP = 0.56 * sqrt(TJC28) +0.28 * sqrt(SJC28) +0.36*ln(CRP*10+1) + 0.14* PtGA+ 0.96 and m-DAS-CRP = 0.49*ln(CRP) + 0.15 * SJC28 + 0.22*EvGH, where SJC28 is the swollen joint count in 28 joints and ln(CRP) is the linear log-transformed CRP. When the CRP was 1 mg/dl, the linear log-transformed CRP was negative and was set to 0. The formulas used to calculate the CDAI and SDAI correspond to those used by Baker et al. Correlations between disease activity scores and MRI-detected inflammation were determined using the Pearson

correlation coefficient. Superiority of correlation coefficients (which were obtained in the same samples) was determined using the “corcor” command in Stata software. Areas under the curve (AUCs) were determined for the association with radiographic progression; differences in the AUC were compared using the “roccomp” Stata command.

Of the 127 patients with early arthritis, 58% were women and 28% were anti–citrullinated protein antibody (ACPA) positive. The mean age was 55.6 years, the median symptom duration at presentation was 13 weeks, the median SJC was 3, the median TJC was 4, the median ESR was 21.8 mm/hour, the median CRP level was 0.4 mg/dl, the median synovitis score on MRI was 3.5, and the median bone marrow edema score on MRI was 3.5. Radiographic progression (SHS 1) was present in 41% (SHS 3 in 17%). Fifty-one patients with early arthritis fulfilled the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria for RA;[3] these patients had a median SJC of 3, a median TJC of 4, a median CRP level of 0.8 mg/dl, and a median ESR of 25 mm/hour; 69% were ACPA positive, 46% had a SHS of 1, and 17% had a SHS of 3. Correlations of the original scores and the modified scores with MRI-evident synovitis are shown in Table 1. The correlation coefficients for the modified disease activity scores were slightly higher than those for the DAS28-CRP and DAS28- ESR (0.32 and 0.31 for the M–DAS-CRP and the DAS28- CRP, respectively, and 0.36 and 0.34 for the M–DAS-ESR and the DAS28-ESR, respectively); these differences were not statistically significant. For the correlation between bone marrow edema and the M-DAS28 and the DAS28, correlation coefficients were slightly higher for the M-DAS28 (Table 1), but were not significantly different. When comparing the M–DAS28-CRP and DAS28-CRP with radiographic progression (SHS 1) as the outcome, the AUCs were slightly higher for the M-DAS28 (0.54 versus 0.49, respectively). The same was true for the M–DAS28-ESR versus the DAS28-ESR (0.56 versus 0.50, respectively) (Table 1). These differences did not yield statistical significance either. When defining radiographic progression as SHS 3, similar results were obtained (data not shown). Analysis of the 51 patients who fulfilled the 2010 classification criteria for RA resulted in comparable findings; the M-DAS28 scores were not significantly better than the DAS28 scores (Table 1). When analyzing the M-CDAI and M-SDAI, no significant improvements were obtained compared to the original CDAI and SDAI (Table 1).

In conclusion, we observed that the differences between the correlation coefficients for the M-DAS28 and the DAS28 were marginal and not statistically significant in demonstrating correlation with MRI measurements of inflammation. With regard to radiographic progression, we observed increases in the AUC of 0.05. This indicates that among random pairs of patients with and without radiographic progression, the M-DAS28 was higher than the DAS28 in 5% of pairs of patients with radiographic progression. These increases were not statistically significant, and whether they are clinically relevant is questionable, as the absolute AUCs were rather low. Our population of patients with early arthritis and early RA had less severe disease than the patients with longstanding RA studied by Baker et al, who had a mean SJC28 of 9.3 and TJC28 of 13.8.[1] Based on the present data, we cannot prove that the M-DAS28 is superior to the DAS28. More studies on this subject in other patient populations are needed.

Table 1 Associations of modified and original DAS, SDAI, and CDAI scores with MRI-detected synovitis and bone marrow edema, as well as radiographic progression (ΔSHS≥1) during 1 year of followup*

	MRI-detected synovitis		MRI-detected BME		radiographic progression	
	Correlation coefficient	p	Correlation coefficient	p	OR (95% CI)	AUC (95% CI)
Early Arthritis						
DAS-CRP						
M-DAS28-CRP	0.32	<0.01	0.34	<0.01	1.17 (0.65-2.10)	0.54 (0.38-0.69)
DAS28-CRP	0.31	<0.01	0.26	<0.01	0.98 (0.66-1.45)	0.49 (0.37-0.62)
DAS-ESR						
M-DAS28-ESR	0.36	<0.01	0.34	<0.01	1.17 (0.71-1.93)	0.56 (0.41-0.72)
DAS28-ESR	0.34	<0.01	0.29	<0.01	0.98 (0.72-1.34)	0.50 (0.38-0.62)
SDAI						
M-SDAI	0.34	<0.01	0.33	<0.01	1.03 (0.94-1.13)	0.53 (0.37-0.68)
SDAI	0.34	<0.01	0.33	<0.01	1.01 (0.95-1.06)	0.51 (0.34-0.69)
CDAI						
M-CDAI	0.25	0.02	0.31	<0.01	1.02 (0.92-1.12)	0.53 (0.38-0.68)
CDAI	0.28	0.01	0.30	<0.01	1.00 (0.94-1.06)	0.49 (0.32-0.66)
Subgroup of RA						
DAS-CRP						
M-DAS28-CRP	0.43	0.01	0.40	0.02	1.16 (0.58-2.33)	0.58 (0.35-0.81)
DAS28-CRP	0.41	<0.01	0.25	0.08	1.15 (0.67-1.95)	0.57 (0.39-0.74)
DAS-ESR						
M-DAS28-ESR	0.40	0.02	0.37	0.03	1.17 (0.62-2.21)	0.59 (0.36-0.82)
DAS28-ESR	0.46	<0.01	0.30	0.03	1.02 (0.64-1.63)	0.55 (0.36-0.73)
SDAI						
M-SDAI	0.42	0.01	0.37	0.03	1.03 (0.93-1.15)	0.61 (0.38-0.84)
SDAI	0.33	0.09	0.31	0.11	1.02 (0.95-1.10)	0.63 (0.37-0.88)
CDAI						
M-CDAI	0.29	0.09	0.36	0.04	0.99 (0.88-1.12)	0.53 (0.30-0.76)
CDAI	0.21	0.27	0.25	0.19	1.00 (0.92-1.09)	0.56 (0.30-0.82)

* There was no significant difference between the correlation coefficients for the modified scores and the original scores. Similarly, differences in the area under the curve (AUC) for the modified scores and original scores were not statistically significant. MRI = magnetic resonance imaging; SHS = Sharp/van der Heijde score; OR = odds ratio; 95% CI = 95% confidence interval; M–DAS28-CRP = modified Disease Activity Score in 28 joints using the C-reactive protein level; M–DAS28-ESR = modified DAS28 using the erythrocyte sedimentation rate; M-SDAI = modified Simplified Disease Activity Index; M-CDAI = modified Clinical Disease Activity Index; RA = rheumatoid arthritis.

References

1 Baker JF et al. *Arthritis Rheumatol* 2014;66:794–802.
2 Krabben A et al. *Ann Rheum Dis* 2013;74:506–12.
3 Aletaha D et al. *Arthritis Rheum* 2010;62:2569–81.