Evaluation of Selected Rheumatoid Arthritis Activity Scores for Office-based Assessment

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ABSTRACT. ***Objective.*** Patient-reported measures can quickly provide assessments of rheumatoid arthritis (RA) disease activity in the office setting and do not require a laboratory test or physician examination. The goal of our study was to establish the validity of patient-reported indices compared to the C-reactive protein-based Disease Activity Score (DAS28-CRP4).

Methods. Baseline and 1-year followup DAS28-CRP4 data were obtained from 740 RA subjects and were compared to indices (MDHAQ, CDAI, RAPID, RADAI, GAS) according to cyclic citrullinated peptide (CCP) status and change at 1 year. Pairwise correlations were calculated for each index.

Results. Among 740 subjects, mean age 57 years, disease duration 14 years, the CDAI (r = 0.84, Δ r = 0.80) and RAPID (r = 0.71, Δ r = 0.70) had the highest correlation with the DAS28-CRP4 scores at baseline and 1 year. These correlations were not influenced by CCP status, disease-modifying antirheumatic drug use, biologic use, or by disease duration.

Conclusion. In RA, the CDAI and RAPID correlated well with the DAS28-CRP4. They may both be practical and informative in the care of patients in the office setting. (First Release September 1 2010; J Rheumatol 2010;37:12; 2466–8; doi:3899/jrheum.091349)

Key Indexing Terms:
RHEUMATOID ARTHRITIS DISEASE ACTIVITY SCORE 28
ARTHRITIS ACTIVITY SCORES

The Disease Activity Score 28 (DAS28) is the established method for calculating disease activity in rheumatoid arthritis (RA). It correlates well with American College of Rheumatology (ACR) response criteria and is a clinically valid measuring tool[1,2]. However, using the C-reactive protein-based DAS28 (DAS28-CRP4) requires difficult calculations and a waiting period for laboratory test results, making it inconvenient for an office setting[3]. Inflammatory markers are validated as an indicator of disease activity. However, data show that inflammatory markers have little effect on the overall score of composite indices[2].

Researchers have been developing disease activity indices for use in a clinic setting that would require minimal calculations and would not require laboratory test results. Five of these indices are the Multi-Dimensional Health Assessment Questionnaire (MDHAQ)[4], Clinical Disease Activity Index (CDAI)[5], Routine Assessment of Patient Index Data (RAPID5)[6], Rheumatoid Arthritis Disease Activity Index (RADAI)[7], and Global Arthritis Score (GAS)[8]. The aim of this study was to examine the correlation of these 5 indices with the DAS28-CRP4.

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MATERIALS AND METHODS

Study population. BRASS (Brigham Rheumatoid Arthritis Sequential Study) is a single-center prospective observational cohort study of RA patients receiving care at the Brigham and Women's Hospital, Boston, Massachusetts, USA. Baseline assessment of patients includes demographic and clinical information, assessment of functional status, disease activity, comorbidity, laboratory testing, and hand radiographs. Physical examination includes joint examination and assessment of pain and disease activity by both rheumatologist and patient, which is collected yearly[9]. Samples of blood for immunophenotyping, including C-reactive protein (CRP), cytokines, chemokines, rheumatoid factor (RF), anticyclic citrullinated peptide (anti-CCP) as well as blood specimens for DNA/RNA testing were collected and stored at baseline and yearly. We exclude patients with a history of systemic lupus erythematosus or juvenile RA.

Our analysis is limited to subjects with data at both baseline and 1 year (n = 740) and whose DAS28-CRP4 scores were calculated at baseline and followup. For our study the MDHAQ, RADAI, CDAI, RAPID5, and GAS scores were also calculated for each patient at baseline and 1 year. Each index is described in Table 1. The study was approved by the Partners Institutional Review Board.

Statistical analysis. We assessed the validity of each score (MDHAQ, RADAI, CDAI, RAPID5, GAS) by calculating the pairwise correlation of each with the DAS28-CRP4 score at baseline, and from baseline to 1 year, with the change in DAS scores (Δ DAS28-CRP4) over the same timeline. The same analysis was done comparing cyclic citrullinated peptide (CCP) status, disease modifying antirheumatic drug (DMARD) use, biologic use, and disease duration to determine if any of these disease indices would correlate well within subgroups of patients with RA. Correlations were calculated using Spearman's correlation coefficient[10].

Table 1. Description of disease indices.

Index	DAS28-CRP4 (0–10)	RADAI (0–10)	CDAI (0–76)	RAPID5 (0–10)	GAS (0–62)
MDHAQ (0–10)				X	X
Patient pain (VAS, 0–10)		X		X	X
Morning stiffness (0–6)		X			
Patient global assessment (VAS, 0–10)		X	X	X	
Physician global assessment (VAS, 0–10)	X		X	X	
No. tender joints (0–28)	X	X	X		
No. swollen joints (0–28)	X	X	X		
Self-reported joint count (RADAI) (0–10)				X	X
CRP or ESR	X				

MDHAQ: Multi-Dimensional Health Assessment Questionnaire; DAS28-CRP4: C-reactive protein-based DAS28; RADAI: Rheumatoid Arthritis Disease Activity Index; CDAI: Clinical Disease Activity Index; RAPID5: Routine Assessment of Patient Index Data; GAS: Global Arthritis Score; VAS: visual analog scale; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

RESULTS

Of the 740 patients who completed baseline and 1-year visits, 614 were female (83%), their mean (SD) age was 57 (13.7) years, and mean disease duration was 14.3 (12.3) years. At baseline, mean (SD) DAS28-CRP4 was 4.1 (1.5) and median score for the MDHAQ was 0.5 (range 0.0–2.5). There were 63.8% RF-positive and 66.1% CCP-positive patients. Baseline medication data are shown in Table 2.

Table 3 shows correlations between the composite activity scores at baseline and correlations between the change in composite activity scores between 0 and 12 months. The most favorable correlations with the DAS28-CRP4 at baseline were the CDAI (r = 0.84) and RAPID5 (r = 0.71). The MDHAQ (r = 0.51), RADAI (r = 0.48), and GAS (r = 0.54) did not correlate as well with the DAS28-CRP4. The ΔCDAI (r = 0.80) and ΔRAPID5 (r = 0.70) also correlated well with the Δ DAS28-CRP4. The Δ MDHAQ (r = 0.39), Δ RADAI (r = 0.50), and Δ GAS (r = 0.49) were not as strongly correlated with the ΔDAS28-CRP4. Also, CDAI and RAPID5 correlated well with each other at baseline (r = 0.94) and with change over 1 year (r = 0.92). The correlation coefficients for all correlation analyses had a p value < 0.0001.

Table 2. Baseline demographics (n = 740).

Characteristic	
Female, n (%)	614 (83.0)
Age, mean yrs (SD)	57.06 (13.7)
Disease duration, mean yrs (SD)	14.25 (12.3)
MDHAQ, median	0.5 (0.0–2.5)
DAS28-CRP4, mean (SD)	4.05 (1.5)
Rheumatoid factor-positive, n (%)	464 (63.8)
Cyclic citrullinated peptide-positive, n (%)	479 (66.1)
Medication, n (%)	
None	24 (3.2)
Narcotic	73 (9.9)
Nonsteroidal antiinflammatory drug	383 (51.8)
Corticosteroid	233 (31.5)
Plaquenil	129 (17.4)
Sulfasalazine	50 (6.8)
Leflunomide	76 (10.3)
MTX without anti-TNF	225 (30.4)
MTX with anti-TNF	126 (17.0)
Anti-TNF without MTX	151 (20.4)
Anti-TNF	335 (34.86)
Biologic	335 (34.86)
Disease modifying antirheumatic drug	655 (68.16)

MDHAQ: Multi-Dimensional Health Assessment Questionnaire; DAS28-CRP4: C-reactive protein-based DAS28; TNF: tumor necrosis factor; MTX: methotrexate.

Table 3. Cross-sectional and longitudinal correlation of DAS28-CRP4 with MDHAQ, RADAI, CDAI, RAPID5, and GAS*.

	Baseline Activity Score*				
DAS28-CRP4	**0.51**	**0.48**	**0.84**	**0.71**	**0.54**
0.39	MDHAQ	**0.60**	**0.64**	**0.73**	**0.85**
0.51	0.49	RADAI	**0.70**	**0.76**	**0.82**
0.80	0.50	0.63	CDAI	**0.94**	**0.73**
0.70	0.62	0.66	0.92	RAPID5	**0.82**
0.50	0.76	0.71	0.62	0.71	GAS
Change in Activity Score Over 1 Year†					

* Values shown in bold type. † Values shown in regular type. DAS28-CRP4: C-reactive protein-based DAS28; MDHAQ: Multi-Dimensional Health Assessment Questionnaire; RADAI: Rheumatoid Arthritis Disease Activity Index; CDAI: Clinical Disease Activity Index; RAPID5: Routine Assessment of Patient Index Data; GAS Global Arthritis Score.

Subgroup analyses of patients by CCP status, DMARD use, biologic use, and by disease duration (excluding subjects with less than 2 years disease duration) were completed to see if these correlations remained constant. For each subgroup analyzed, the CDAI continued to have the most favorable correlation with the DAS28-CRP4 (r = 0.82–0.85; Δ r = 0.74–0.83) followed by the RAPID5 (r = 0.68–0.74; Δ r = 0.61–0.70) at baseline and change over 1 year. The correlation coefficients for all correlation analyses had p values < 0.0001.

DISCUSSION

Our analysis showed that the CDAI and RAPID5 scores correlated well with the DAS28-CRP4 scores at baseline and Δ

CDAI and ΔRAPID5 scores also correlated well with the ΔDAS28-CRP4 scores. Comparing subgroups of RA patients did not significantly affect correlations with the DAS28-CRP4 at baseline or change over 1 year. The CDAI and RAPID5 correlated most favorably with the DAS28-CRP4 and may be considered desirable alternatives.

Other studies show similar correlations between these disease activity indices and the DAS28. A study of RAPID5 found a higher correlation with the DAS28 than our study (r = 0.64–0.67)[6]. A study of CDAI compared to the DAS28 at baseline and 1-year followup found a similar significant correlation to DAS28 (r = 0.87–0.90)[5]. In a study of test-retest, the RAPID3 and CDAI were shown to be reliable, with a smallest detectable difference (SDD) of 0.90 and 0.89, respectively. The same study also calculated the correlation coefficient between the indices and DAS28 and found RAPID3 (r = 0.62) and CDAI (r = 0.88) to correlate well, confirming our own results[12].

While it would be useful to compare all 5 disease indices to the ACR20 or ACRn, which is often used in clinical practice, these disease activity measures are not appropriate to use in a cross-sectional study. DAS28-CRP4 was the most inclusive disease index that could be used with this cross-sectional study design and other studies note that it correlates well with the ACR response criteria[1,2]. One limitation to our analysis is that the CDAI correlated well with the DAS28-CRP4 compared to the other indices because it contains 3 of the same measurements (physician global assessment, tender joints, and swollen joints). The aim of our study was to assess if laboratory tests were a necessary component in assessing disease activity of RA patients or if using disease activity indices without acute-phase reactants is a viable option in patient care. Both the CDAI and the RAPID do not require laboratory testing to calculate, and both correlated well to the DAS28-CRP4.

Although our study shows that CDAI and RAPID5 scores correlated well with the DAS28-CRP4, this does not mean that they can replace it in clinical trials. However, for office practices or clinical research these instruments may be of value for improving patient care. Because of its reliance on time-consuming laboratory results, DAS28-CRP4 can take a few days to calculate, while CDAI and RAPID5 scores can be calculated in less than 1 minute[8,13]. Future studies should include assessment of the agreement between quartiles of each score, comparisons with ACR response criteria and radiographic change, and sensitivity to change of scores in response to treatment in clinical trials.

DAS28-CRP4 is widely used in clinical studies but is cumbersome in the office setting. The purpose of office-based disease activity measures like the CDAI and RAPID5 is to provide physicians with easy to use tools to assess RA activity, independent of laboratory tests; these measures are valuable additions to patient care. Additionally, if they are found to correlate well with DAS scores, they would decrease costs associated with laboratory testing. Our analysis suggests that less complex disease activity measures such as CDAI and RAPID5 correlated moderately well with the DAS28-CRP4 score and may be reasonable alternatives. However, further validation of these disease activity indices is necessary before they can replace DAS28-CRP4 scores in clinical trials.

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Correction

Evaluation of Selected Rheumatoid Arthritis Activity Scores for Office-based Assessment

Sullivan MB, Iannaccone C, Cui J, Lu B, Batra K, Weinblatt M, Shadick NA. Evaluation of selected rheumatoid arthritis activity scores for office-based assessment. J Rheumatol 2010;37:2466-8. In the abstract under Results, "CDAI ($r = 0.74$, $\Delta r = 0.64$)" should read "CDAI ($r = 0.84$, $\Delta r = 0.80$)"; and "RAPID ($r = 0.62$, $\Delta r = 0.57$)" should read "RAPID ($r = 0.71$, $\Delta r = 0.70$)". We regret the error.

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