Patient-Centered Rheumatoid Arthritis Disease Activity Assessment by a Modified RADAI

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ABSTRACT. ***Objective.*** To evaluate the psychometric properties and validity of a modified version of the Rheumatoid Arthritis Disease Activity Index (RADAI) without joint counts in order to facilitate rapid and easy RA activity assessment in daily routine.

Methods. One hundred sixty-nine outpatients with RA completed the original RADAI and the modified RADAI-5. Simultaneously, the Disease Activity Score-28-erythrocyte sedimentation rate (DAS28-ESR) and C-reactive protein (DAS28-CRP) and the Simplified Disease Activity Index (SDAI) and Clinical DAI (CDAI) were applied. Cronbach's alpha, as a measure for internal consistency, and Spearman's rho, to evaluate the linear relationship of the different disease activity scales, were calculated. Rho was determined for the RADAI-5 and the core set measures to assess convergent validity. For agreement analysis, kappa statistics were calculated. An attempt was made to estimate the modified questionnaire's sensitivity to change.

Results. Means for the RADAI and the RADAI-5 were 2.8 (range 0.0–9.12) and 3.07 (0–10), respectively. Other means were as follows: DAS28-ESR 3.51 (0.28–6.67), DAS28-CRP 3.19 (1.12–5.83), CDAI 11.53 (0.0–44.6), and SDAI 12.36 (0.1–44.9). Cronbach's alpha was highest for the RADAI-5 (0.917) and lowest for the DAS28-CRP (0.510). The RADAI-5 was highly significantly correlated (all $p < 0.0001$) to all other instruments. However, kappa was < 0.65 for the relation of the RADAI-5 and all other scores except the RADAI. Changes of the RADAI-5, DAS28-ESR, and CDAI were significantly correlated ($p < 0.001$).

Conclusion. The RADAI-5, refraining from joint counts, was shown to be capable of measuring RA activity. Reliability and convergent validity could be proven. (First Release May 15 2008; J Rheumatol 2008;35:1294–9)

Key Indexing Terms:
RHEUMATOID ARTHRITIS DISEASE ACTIVITY ASSESSMENT QUESTIONNAIRE

Providing the physician with sufficient information about the disease course and red flags in case of deterioration can be regarded as the most important requirement for any routine disease activity monitoring tool. Easy applicability and time-sparing documentation are other serious prerequisites.

Composite indexes, preferentially the Disease Activity Score (DAS), including a 44- or a 28-joint count (DAS28), have been successfully used, particularly in clinical trials, to express activity fluctuations of rheumatoid arthritis (RA)[1-4]. A numerical measure, as provided for example by the DAS28, and the respective disease activity categories, for example the EULAR response criteria[5], provide the opportunity to compare the disease status of patient groups and of individual patients[1,4]. Acute-phase reactants were shown to add little to those indexes, as revealed by item-weighting analyses[4].

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With respect to disease activity assessment, it seems that rheumatologists are focused on joints rather than on functional status and pain as important measures of disease activity[6,7]. Ironically, with respect to joint counts, however, there is evidence that most visits of most patients with RA to most rheumatologists do not include a formal quantitative joint count and that patient's self-joint assessment is as reliable as if performed by a physician[8,9]. Additionally, it is well established that a patient questionnaire score for functional status could be more informative than even a full joint count with respect to prognosis and monitoring[10]. Moreover, it was shown that 3 "patient-only" measures out of the American College of Rheumatology (ACR) response criteria, namely physical function, pain, and global status, were as reliable as the whole core set for describing RA activity changes and could constitute the basis for therapeutic decisions[11]. Just recently, an index of those 3 self-report scales on the ACR core dataset has been found to discriminate between active and placebo treatments in clinical trials as well as a DAS score[12].

Some exclusively patient self-assessment questionnaires, such as the modified Health Assessment Questionnaire (M-HAQ) and its derivatives, the Rheumatoid Arthritis Disease Activity Index (RADAI) or the Rapid Assessment of Disease

Activity in Rheumatology questionnaire (RADAR), have been proposed for RA activity monitoring[6,13,14]. As an example for the feasibility and effectiveness of patient-centered disease activity assessment over the last 25 years the HAQ and derivatives such as the MD-(multidimensional) HAQ have been found to be useful to monitor patients in usual care[15]. In addition, the questionnaires were found to be an excellent predictor of most severe longterm outcomes of RA[16].

Regarding RA outcome measures, there is currently a trend to develop either patient-reported outcomes (PRO) or physician-reported outcomes. Concerning the latter, the goal is to improve the assessment of inflammation, in particular synovitis, by using ultrasonography and/or magnetic resonance imaging in addition to the physical examination, which obviously surpasses the possibilities in daily routine[17,18].

Practicing rheumatologists increasingly appear to agree that information from patient self-report can be valuable in assessing and monitoring patients, perhaps even as effective as joint counts and other physician-generated data. However, in daily routine there is always a battle between the need for documentation and the time necessary for it. Thus a short and easy instrument providing reliable information about disease activity and providing an alert in case of deterioration could improve and standardize daily routine care significantly. In addition, rheumatologists should provide nonrheumatologist physicians who are frequently involved in RA patient care with a quantitative measure to assess and monitor individual patients with RA.

Both the RADAI, combining 4 questions with patient's self-joint assessment, and its 4-item version (omitting the joint list) were shown to provide high internal consistency and construct validity as an instrument for RA activity monitoring. They also result in an absolute number[13,19]. The calculation, however, appears to be rather complicated as questions 4 (morning stiffness) and 5 (joint counts) are weighted by 6/10 and 48/10, respectively, to produce a range from 0 to 10[13]. Considering the Bath Ankylosing Spondylitis Disease Activity Index[20], not including direct joint or spine assessment, and using a Likert format from 0 to 10, we considered a simplification of the original RADAI, particularly omitting the joint counts and the sophisticated item-weighting of question 4.

We had previously found, in a different RA population[21], that patient's general health assessment was significantly related to HAQ scores and to patient's therapeutic attitude and there was a slightly significant relation to the joint counts. General health assessment may also cover other disease aspects such as drug tolerance, and, as with the other individual components, can significantly overlap within the DAS28[22]. Therefore, we substituted the joint counts, which are covered by 2 other questions, with patient's general health assessment in order to also include surrogate information about functionality, patient's therapeutic attitude, drug tolerance, and other aspects. To enhance applicability, the format of the original question 4 was also changed into a Likert scale from 0 to 10. The final result is easy to calculate by addition, followed by a division by 5.

We performed an observational investigation in our outpatient clinic of this modified RADAI, denoted RADAI-5, to determine its value for monitoring daily routine RA disease activity.

MATERIALS AND METHODS

Questionnaire. The RADAI-5 was established in German and comprises 5 items in a Likert format from 0 to 10. The respective questions are "How active was your arthritis the last six months?" (0 = completely inactive to 10 = extremely active), "How active is your arthritis today with respect to joint tenderness and swelling?" (0 = completely inactive to 10 = extremely active), "How severe is your arthritis pain today?" (0 = no pain to 10 = unbearable pain), "How would you describe your general health today? (0 = very good to 10 = very bad), and "Did you experience joint (hand) stiffness on awaking yesterday morning? If yes, how long was this stiffness?" (0 = no stiffness to 10 = stiffness the whole day). In contrast, to the rather complicated formula of the original RADAI, the result can be easily calculated: (Q1 + Q2 + Q3 + Q4 + Q5)/5.

The single questions target different disease aspects. Question 1 relates to the individual RA course, which is essential for the patient's actual satisfaction with disease status[6]. Question 2 covers joint involvement, while question 3 interrogates for pain, which is of crucial importance for the patient and as a determinant of functionality[23]. While the first 3 questions can be regarded as indispensable, discussion may arise with respect to the last 2 questions. Question 4, for patient's general health, and question 5, for stiffness, may be regarded as of less importance. However, in our opinion they also cover important aspects of RA activity.

Patients. All patients gave their informed consent to be enrolled into this observational study according to the Declaration of Helsinki. The study design was approved by the local ethics committee. One hundred sixty-nine outpatients with RA, all meeting the 1987 American Rheumatism Association classification criteria[24], were enrolled consecutively (Table 1). They were asked to complete the RADAI-5 questionnaire and the original RADAI[13] before their assessment, in the waiting area. For the purpose of this study, the German version was downloaded from the website of the German Society of Rheumatology[25]. If necessary, a short instruction was given by a nurse, but afterwards patients completed the questionnaire on their own. The RADAI was calculated as prescribed[13]. In addition, the following were recorded: tender and swollen joint counts (TJC, SJC) out of the 28-joint count[1], ESR (mm/h), patient's general health assessment [visu-

Table 1. Patients' demographic data (n = 169).

Characteristic	Mean (range)
F/M	135/34
RF-positive, %	50
Caucasian, %	100
Age, yrs	57 (19–78)
RA duration, yrs	7.2 (0.2–46.0)
RADAI	2.80 (0.0–9.12)
RADAI-5	3.07 (0.0–10.0)
DAS28–ESR	3.51 (0.28–6.67)
DAS28–CRP	3.19 (1.21–5.83)
CDAI	11.53 (0.0–44.6)
SDAI	12.36 (0.1–44.9)

RADAI: Rheumatoid Arthritis Disease Activity Index, DAS28–ESR: Disease Activity Score-28 erythrocyte sedimentation rate, CRP: C-reactive protein, CDAI/SDAI: clinical/simplified DAI.

al analog scale (VAS) 0–100 mm; wording: none to extreme; GHVAS], physician's global assessment of disease activity (VAS 0–100 mm; wording: no activity to maximum activity; PhGA), and CRP.

Joint assessments were performed by 3 experienced physicians. Consensus meetings concerning joint assessment are part of the routine quality control program at regular intervals in order to avoid high internal variations among the physicians. For the purpose of this study, however, no formal agreement analysis between the physicians was performed. As all core set variables were assessed, the DAS28-ESR, the DAS28-CRP, the SDAI, and CDAI were calculated accordingly[1-4].

One hundred seventeen of these patients were followed a second time within 3 months. All of them completed the RADAI-5, and the composite indexes were calculated as at the first assessment in order to estimate the tool's sensitivity to change (for demographic data see Table 1). Fifty-two patients not attending the outpatient clinic within this time period after their first assessment were excluded. Retrospective data checks revealed that on average, these patient groups experienced the same course of disease.

One hundred sixty patients were treated with disease modifying antirheumatic drugs (DMARD), namely methotrexate, sulfasalazine, leflunomide, antimalarials, tumor necrosis factor-α blockers, including infliximab, etanercept and adalimumab, as well as rituximab, and anakinra; 105 patients (62%) were taking corticosteroids (mean 3.3 mg prednisolone/day, range 1.25–25 mg) and all patients received nonsteroidal antirheumatic drugs on demand.

Statistical analysis. Statistical evaluation was carried out using SPSS for Windows 11.0. For internal consistency assessment, alpha was calculated[26]. Because an alpha value of even 0.70 indicates that the standard error of measurement will be more than half (0.55) a standard deviation, higher values were regarded as necessary for individual assessments[27].

In addition, factor analysis by principal component analysis was performed to reveal the structure and item loading of the new questionnaire. To assess the linear relationship between the different disease activity indexes on the group level, Spearman rank-correlation was applied[28], as it also was to double-check convergent validity by relating the RADAI-5 values to ESR and CRP values as well as SJC, TJC, and physician's global assessment of RA activity. Kappa statistics were applied to assess individual agreement between the 6 disease activity scales investigated. Cohen's kappa measures the agreement between the evaluations of 2 raters when both are rating the same object[29]. A value of 1 indicates perfect agreement; a value of 0 indicates agreement is not better than chance. Kappa values > 0.60 are commonly regarded as indicating a substantial relationship[29,30]. To estimate sensitivity to change, the differences between the first and the second assessment of the RADAI-5, the DAS28-ESR, and the CDAI were calculated, and subsequently the Spearman rank-correlations as well as kappa statistics were applied.

RESULTS

Values for the disease activity indexes are given as means (range). At the first assessment the means for the RADAI and the RADAI-5 were 2.8 (0.0–9.12) and 3.1 (0–10), respectively. The mean DAS28-ESR for all 169 patients was 3.51 (0.28–6.67), mean DAS28-CRP was 3.19 (1.12–5.83), mean CDAI 11.53 (0.0–44.6), and the mean SDAI 12.36 (0.1–44.9) (Table 1).

The mean RADAI-5 in 117 patients at the second assessment was 3.09 (0.0–9.53), mean DAS28-ESR 3.35 (0.49–6.84), mean DAS28-CRP 3.05 (1.21–6.67), mean CDAI 10.27 (0.0–39.0), and the mean SDAI was 11.19 (0.1–47.8). All disease activity indexes indicate moderate disease activity, on average, for the entire patient population[1-4].

Internal consistency testing of all scales was performed by calculating alpha; the respective results are given in Table 2. Both RADAI scales, with the RADAI-5 performing better, easily surpassed a value of 0.7, commonly regarded as the limit for substantial reliability, while an alpha > 0.7 could be shown only for the CDAI, but not for the SDAI, DAS28-ESR, or DAS28-CRP. Factor analysis by principal component analysis revealed the RADAI-5 to be a one-dimensional instrument. Item loading (from 0.701 to 0.951) indicated that all items contribute significantly to the aggregate score.

After internal consistency of the new instrument was proved, the linear relationship between the established and validated disease activity indexes and the RADAI-5 was evaluated by Spearman rank-correlation. The RADAI-5 appeared in a nearly perfect linear relationship with its mother instrument, the original RADAI (rho = 0.995), but was also highly significantly correlated with all the other established disease activity indexes (Table 3). As the RADAI-5 was proven to be in a substantial linear relationship with the 4 most popular RA disease activity scales, the assumption of external validity would have been justified. Nevertheless, the relationship between the RADAI-5 — not including any joint count — and SJC, TJC, ESR, CRP, as well as physician's assessment of disease activity, was considered of great importance to estimate convergent validity. TJC, SJC, and physician's global assessment were found to be closely statistically significantly correlated to the RADAI-5 (rho = 0.747, $p < 0.001$ for TJC; rho = 0.598, $p < 0.001$ for SJC; rho = 0.603, $p < 0.001$ for physician assessment), while no significant relationship was found with the ESR and CRP values.

Aside from the linear relationship of 2 instruments on a group level, kappa as a more individual measure is of particular interest when comparing disease activity assessment tools. As expected, almost perfect agreement was found

Table 2. Cronbach's alpha of the RADAI-5 and the comparator scores. For definitions see Table 1.

Disease Activity Index	Alpha
RADAI-5	0.917
RADAI	0.895
DAS28-ESR	0.553
DAS28-CRP	0.510
CDAI	0.758
SDAI	0.689

Table 3. Correlations between the RADAI-5 and the comparator scores.

Spearman's rho	RADAI-5	p
RADAI	0.995	< 0.001
DAS28-ESR	0.638	< 0.001
DAS28-CRP	0.719	< 0.001
CDAI	0.740	< 0.001
SDAI	0.735	< 0.001

between the RADAI-5 and the original RADAI (kappa = 0.882), while only fair, although statistically significant, agreement was seen between the RADAI-5 and the DAS28-ESR, DAS28-CRP, SDAI, and CDAI (kappa 0.290, 0.337, 0.385, 0.369, respectively). Of note, kappa for the relationship between SDAI and CDAI, the latter developed from the former, was almost perfect (0.826), while the respective kappa for both DAS28 scales was 0.598, indicating only moderate agreement between them[30].

The mean differences (ranges) for the disease activity scores between the first and second assessment in the remaining 117 patients were as follows: ΔRADAI-5 0.16 (–5.73 to 6.33), ΔDAS28-ESR –0.28 (–3.12 to 3.96), and ΔCDAI –1.85 (–25.0 to 22.7). Changes at the group level were all insignificant, despite highly significant changes in individual patients, as indicated by the ranges. Spearman's rho for the linear relationship between ΔRADAI-5 and ΔDAS28-ESR was 0.589 and for ΔCDAI 0.569 (both $p < 0.001$). Kappa for the relationship between ΔRADAI-5 and ΔDAS28-ESR was 0.295, and for ΔRADAI-5 and ΔCDAI it was 0.269 (both moderate). As kappa for the relationship between ΔDAS28-ESR and ΔCDAI was 0.538, the relationship between the changes of the 3 disease activity scores on the individual level can be regarded as fair[30].

Considerations about shortening the questionnaire

In order to be as parsimonious as possible we also considered other simplifications of the original RADAI. As the 4-item version of the original RADAI (omitting the joint counts, but retaining the complicated calculation of question 4) was also shown to be valid to express RA activity[19], we calculated alpha for the simplified 4-item version (omitting patient's general health, question 4, in the same Likert format as the other 3). Alpha for this version was found to be 0.873. This version's correlations to the other disease activity indexes were slightly weaker than those of the RADAI-5, but still statistically significant ($p < 0.01$), as were the respective correlations to the single core set variables. Omission of question 1 (targeting the disease course) had resulted in an insignificant reduction of alpha to 0.902; however, there was consensus that the individual course of the disease provides important information[23] and should therefore remain within the questionnaire.

DISCUSSION

The main objective of this study was to assess whether a modified version of the RADAI, the RADAI-5, could be used as a completely patient-administered tool for daily RA monitoring, not only for rheumatologists, but also and perhaps primarily for nonrheumatologists. The RADAI-5 should enable physicians to get reliable information about the disease course, and on the other hand should be sensitive enough to give the alarm if deteriorations occur. Thus this study was performed within a routine outpatient clinical setting.

In the current discussion about physician or patient-reported outcome measures, the original RADAI, including patient's self-assessment of joints[13], can be regarded as a hybrid — a tool assessed by patients comprising domains that are selected by physicians. The RADAI provides the advantage that the primary target of all therapeutic interventions is given the key role in activity assessment[13]. Moreover, interphysician variations in assessing joints or global disease activity are avoided. Of course measurement of patient symptoms alone has the shortcoming that symptom levels are differently valued and expressed between patients. However, physical function on a HAQ, the patient-reported outcome used most widely, is the measure that is most significant in identifying and predicting work disability, explaining costs, and predicting mortality in RA, much more effectively than the other core dataset measures[31].

Feasibility and acceptability to physicians and patients can be regarded an important requirement of any assessment tool. If most visits of most RA patients to most rheumatologists do not include a formal quantitative joint count, how could we expect nonrheumatologists, e.g., general practitioners, to do so[8].

Reliability, as a measure of the extent to which a variable or set of variables is consistent in what it is intended to measure, is another serious prerequisite. These considerations formed the basis for our omission of joint counts and the simplification of the question format, and also for the inclusion of patient's general health assessment and in support of question 1 (disease history).

The newly adapted RADAI-5 was investigated for its psychometric properties and for its comparability with established disease activity scales. The RADAI-5 performed identically to the original RADAI, with considerably higher values for Cronbach's alpha than the comparator instruments. Alpha, however, is also a measure of redundancy[27]. The combination of 5 symptom questions with the same scaling and similar anchoring on the same questionnaire form, in contrast to different scaling in the original scale, does not induce what is called framework bias, given the minor differences between the RADAI-5 and the original RADAI.

As alpha for all the other indexes was found to be substantially lower, one might consider whether acute-phase reactants and/or joint counts contribute to the low internal consistency of activity scales for RA or other diseases[4]. Changes in symptoms may indeed reflect underlying change in synovitis, as shown in randomized controlled trials, but the level of symptoms is not always in close agreement with level of synovitis[32]. The RADAI-5 proved to be significantly correlated to established RA activity assessment tools on the group level. Kappa values, however, indicate only about 60% agreement of the RADAI-5 and the DAS28 scales, as well as the SDAI/CDAI. This also holds true for the agreement between the DAS28 scales and the SDAI/CDAI; even the agreement between the two DAS28 scales was found to be fairly weak. So the

RADAI-5 could offer a perspective for a more individualized patient monitoring[7].

RA activity assessment without joint counts would provide the advantage of not overlooking activity by applying certain counting models, such as the 28-joint count, excluding the foot joints[1]. This is of course of less importance on a group level; however, it may cause problems with respect to individual patient care. The RADAI-5 includes 2 questions that cover all joints as a whole, and thereby makes a place for individual weighting of impairment; this is not the case with the composite indexes, which weight, for example, the fifth metacarpal joint identically to the knee joint. In that respect the RADAI-5 was found to be highly significantly correlated to tender and swollen joint counts and physician's global assessment of disease activity[10]. This can be regarded as proof for convergent validity, and also as a possibility to overcome the difficulties with certain joint counts in daily routine care. Moreover, one may conclude that joint counts are not indispensable for routine RA activity measurement[33,34].

All the 4 comparator indexes are of proven validity, and 2 of them, the DAS28-ESR and the SDAI, have been shown to be in agreement with patients' attitudes, except the perception of improvement and deterioration of the disease[21,35-38]. The RADAI-5, and also the simplified 4-item version, could be demonstrated to be in substantial linear relationship with all those scales on a group level. Therefore, an attempt was made to estimate the sensitivity to change of the RADAI-5 by correlating its changes to those of the DAS28-ESR and the CDAI.

Of course an assessment tool's sensitivity to change can only be formally evaluated after a recognized efficient therapy at a fixed interval of time using a specific statistical method. As this was a noninterventional study performed in clinical routine, no standardized therapeutic intervention and no fixed interval could be provided and no statistically significant changes of RA activity between the 2 timepoints of assessment could be observed on the group level. However, some highly significant disease activity changes in individual patients occurred. RADAI-5 changes at the group level were in close agreement with the changes of the DAS28-ESR and the CDAI, suggesting that the scale could indeed provide sensitivity to identify RA activity changes accordingly. On the individual level, however, all 3 instruments seemed to be rather different in expressing RA activity changes. The sensitivity to change of the RADAI-5 remains to be proven during a standardized intervention and applying conventional statistical methods such as the standardized response mean or the effect size. This should be performed in a treatment-naive RA population and at the initiation of a new treatment after previous ones have failed.

Our results give additional evidence that a "gold standard" for disease activity monitoring in RA remains undefined[39]. No questionnaire or index can substitute for careful clinical patient examination[40]. As individualized treatment becomes increasingly important, patient-related outcome tools could provide substantial advantages in identifying patients requiring particular attention.

The limitations to these observations include that the study was performed in a single center within a relatively small region; second, the study population, although representative for the center's entire RA patient population, in general had mild to moderate level disease. Third, increased self-efficacy as a member of a study population constitutes a factor possibly influencing a patient's self-assessment[41]. Fourth, as with the other instruments, coexisting fibromyalgia, present in about 15% of patients with RA at least once during the disease course, could have exerted an influence on the RADAI-5[42]. However, as with the other instruments, only stable low RADAI-5 values can be regarded as indicators of an uncomplicated disease course. Significant changes, however, must be assessed with respect to the changes of the single items and possibly coexisting or newly occurring diseases[42]. To be comprehensive and parsimonious in this respect we finally retained questions targeting disease history and patient's global health on the 5-item score.

In our observational study we demonstrate that the RADAI-5, refraining from joint counts, is capable of measuring RA activity. Reliability and convergent validity of this modified RADAI were proven. Compared to the original RADAI and the 4-item version (omitting joint count) the adapted questionnaire proved to be highly reliable and valid[13,43]. The RADAI-5 questionnaire could be an option for routine RA monitoring that enables physicians to get reliable information about the disease course that is sensitive enough to give the alarm if deterioration occurs.

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