RADAI-5 to monitor rheumatoid arthritis

B.F. Leeb[1,3], P.M. Haindl[2], H.P. Brezinschek[3], T. Nothnagl[1], B. Rintelen[1]

[1]2nd Department of Medicine, Center for Rheumatology Lower Austria, Karl Landsteiner Institute for Clinical Rheumatology, State Hospital Stockerau, Stockerau, Austria;
[2]State Hospital Korneuburg, Korneuburg, Austria;
[3]Department for Rheumatology and Immunology, Medical University of Graz, Graz, Austria.

Burkhard F. Leeb, MD, PhD
Pia M. Haindl, MD
Hans Peter Brezinschek, MD, PhD
Thomas Nothnagl, MD
Bernhard Rintelen, MD

Please address correspondence to:
Burkhard F. Leeb,
2nd Department of Medicine,
Center for Rheumatology Lower Austria,
Karl Landsteiner Institute for Clinical Rheumatology, State Hospital Stockerau,
Landstrasse 18,
A-2000 Stockerau, Austria.
E-mail: burkhard.leeb@stockerau.lknoe.at

ABSTRACT

Providing the physician with sufficient information about the disease course can be regarded as the most important requirement for any disease assessment tool besides easy applicability and time-sparing documentation. Applying the RADAI-5 in daily routine provides the patient's view at any time completing the questionnaire.

In a first study, the RADAI-5 resulted to be highly significantly correlated to the RADAI, and all composite indexes. Changes of the RADAI-5, the DAS28-ESR, and the CDAI were significantly correlated, indicating the instrument's sensitivity to change. A second study including 392 RA patients led to the establishment of thresholds for disease activity categories according to the RADAI-5, as follows: 0.0 up to 1.4 for a remission-like state, 1.6 up to 3.0 for mild disease activity, 3.2 up to 5.4 for moderate and from 5.6 up to 10.0 for high disease activity. In a third study, remission according to the RADAI-5 appeared to be highly specific for the ACR/EULAR criteria for remission

The RADAI-5 questionnaire constitutes an easily applicable tool for routine RA monitoring, providing physicians with reliable information about the disease course and sensitivity enough to sound the alarm should complications occur.

Providing the physician with sufficient information about the disease course and alerting in case of deterioration can be regarded the most important requirement for any disease assessment tool in clinical routine aside from easy applicability and time-sparing documentation. Composite indexes, such as the disease activity score (DAS), including a 44- or a 28-joint count (DAS28), have been successfully used, particularly in clinical trials, to express rheumatoid arthritis (RA) activity (1, 2). Acute phase reactants appeared to add little to those indexes, as revealed by item weighting analyses (3).

The treat-to-target approach is thought to result in a better outcome for the patients (4). It is one of this approach's overarching principles that RA therapy should be based on a shared decision between patient and rheumatologist (4). Applying the RADAI-5 in daily routine provides the patient's view at any time by completing the questionnaire.

Practising rheumatologists increasingly do not have enough time to perform joint counts at every patient visit or they think that they do not have (5). Thus, there is evidence, that most RA patient visits to rheumatologists do not include a formal joint count (5), which, however, is a prerequisite for the calculation of the respective indexes. Therefore, the burning question emerged whether joint counting is indispensably necessary for routine management of RA patients, or if applying a short and easy instrument providing reliable information also allows the realisation of daily routine care (6).

The Rheumatoid Arthritis Disease Activity Index (RADAI), combining four questions with patients' self-joint assessment showed high internal consistency as well as construct validity, and results in an absolute number. The calculation, however, appears to be rather complicated as question four (morning stiffness) and five (joint counts) are weighted by 6/10 and 48/10, respectively to produce a range from 0–10 (7). Considering the BASDAI (8), not including direct joint or spine assessment, and using a Likert format from 0 to 10, we considered the simplification of the original RADAI, and, in particular, we rethought omitting the joint-counts and the sophisticated item weighting of question four.

Patient's general health (GH) assessment appeared to be in significant relation to HAQ-scores, to patient's therapeutic attitude and even in significant relation to joint counts (9). In addition, GH assessment may also cover other disease aspects such as drug tolerabil-

ity, and, like the other individual components, it is known to significantly overlap within the DAS28 (9).

Therefore, we decided to substitute patient's joint self-assessment by patient's GH assessment in order to also include surrogate information about functionality, patient's therapeutic attitude, drug tolerability and other aspects. To further enhance applicability, the format of the original question 4 was also changed into a Likert-scale from 0–10 (6).

The RADAI-5 questionnaire

The RADAI-5 was established in German and comprises five items in a Likert format from 0 to 10 (6). 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 (see Fig. 1) (7).

In a first study, 169 rheumatoid arthritis (RA) outpatients completed the original RADAI and the RADAI-5. Simultaneously, the DAS28-ESR, the DAS28-CRP, the SDAI and the CDAI were applied. Internal consistency by Cronbach's alpha and the linear relationship of the different disease activity scales by Spearman's rho were calculated. In addition, convergent validity was determined; agreement analysis by applying kappa statistics was performed as well as the modified questionnaire's sensitivity to change was evaluated. Cronbach's alpha was the highest for the RADAI-5 (0.917) and the lowest for the DAS28-CRP (0.510). The RADAI-5 was highly significantly correlated to all other investigated in-

Fig. 1. The RADAI-5 Questionnaire: Σ Qu1+Qu2+Qu3+Qu4+Qu5)/5

Table I. Disease activity categories according to the RADAI-5 (6).

	Remission	mild	moderate	high
RADAI-5 value	0.0-1.4	1.6-3.0	3.2-5.4	5.6-10.0

struments. Agreement as expressed by Kappa between the RADAI-5 and all other scores except the RADAI was moderate. Changes of the RADAI-5, the DAS28-ESR, and the CDAI were significantly correlated, indicating the instrument's sensitivity to change (6).

Disease activity categories

A second study aimed at the establishment of thresholds for rheumatoid arthritis activity categories according to the RADAI-5 (10). To this end, 392 RA patients were categorised according to the DAS28, the CDAI and their satisfaction (PATSAT) with disease status. Patient assessments simultaneously meeting the identical DAS28, CDAI as well as PATSAT categories were taken

as the references to establish the thresholds for the respective RADAI-5-categories by calculating the 3rd quartile of the corresponding RADAI-5 values. Seven hundred and fifty-eight assessments (2 assessments median/patient) could be finally obtained. Calculating the 3rd quartile, the RADAI-5 thresholds were as follows: 0.0 up to 1.4 for a remission-like state, 1.6 up to 3.0 for mild disease activity, 3.2 up to 5.4 for moderate, and from 5.6 up to 10.0 for high disease activity (Table I). Categorisation according to the RADAI-5 showed a normal distribution. Auxiliary, tender and swollen joint counts as well as physician's global assessment and ESR proved to be highly significantly different within the different
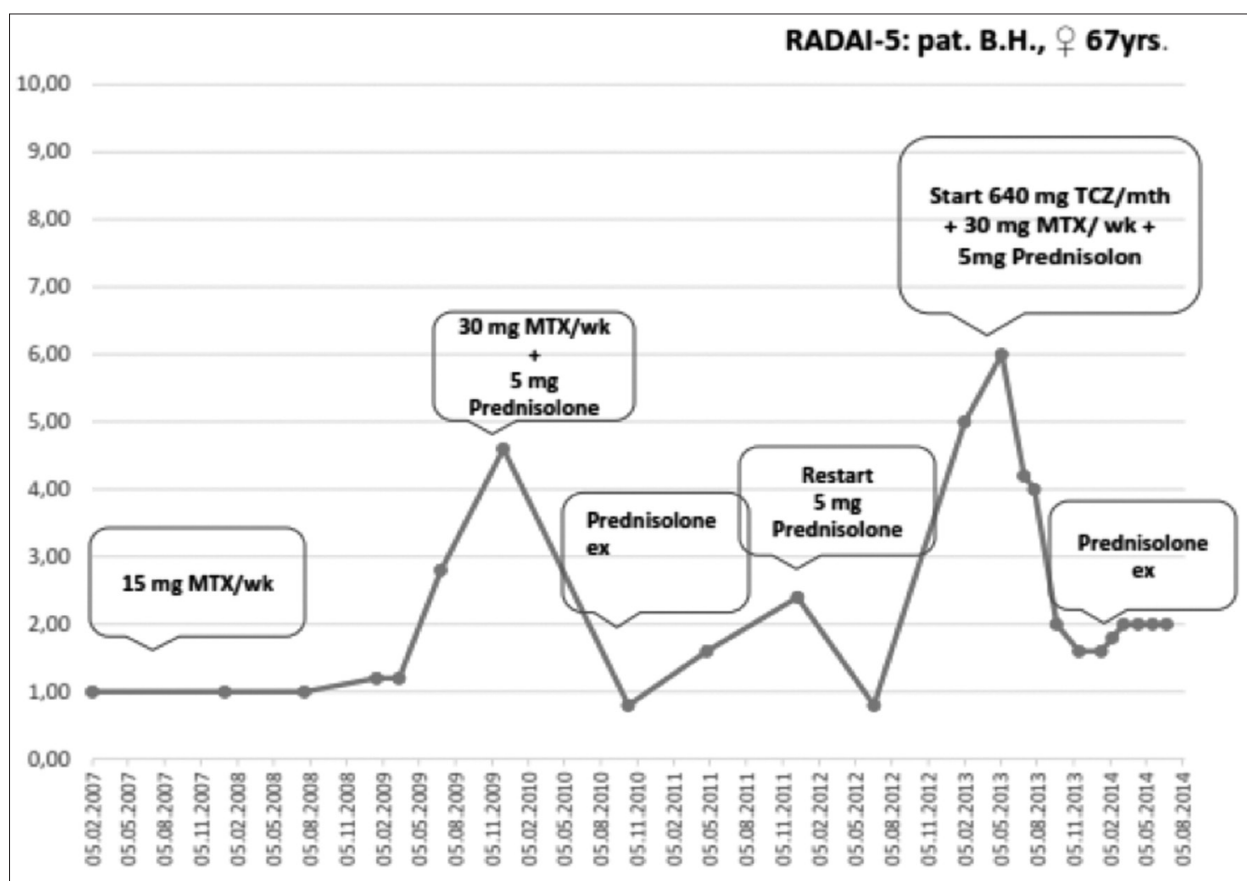
Fig. 2. A female patient's disease course since Febraury 2007, and the respective therapeutic changes according to the RADAI-5

RADAI-5 categories according to the Kruskal Wallis test ($p<0.001$) (10).

As as it had been anticipated that the RADAI-5 and the RAPID-3 (Routine Assessment of Patient Index Data 3) (11), would perform similarly in some aspects such as time to score, distinguishing active from control treatments in clinical trials, and monitoring patients in clinical care (12) it stood to reason to directly compare both questionnaires with established composite indexes in daily routine (13). 128 RA out-patients were invited to complete the RADAI-5 and the RAPID3. Simultaneously, the DAS28-ESR, and the CDAI were calculated. Cronbach's alpha as a measure for reliability was calculated, factorial analysis was performed and, for agreement analysis, Kendall's Tau was calculated. Time to score the questionnaires was 25 sec. Cronbach's alpha for the RADAI-5 was 0.906 and 0.871 for the RAPID3, respectively; however, it amounted to only 0.165 for the DAS28-ESR and 0.210 for the CDAI, respectively. Factorial analysis revealed that both questionnaires and the DAS28-ESR, but not the CDAI appeared to be mono-dimensional in this cohort. Agreement between the RADAI-5 and the RAPID3 appeared to be moderate as was found for the DAS28-ESR and the CDAI, while it was considerably lower between the questionnaires and the composite indexes, respectively (13).

In 2011, The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) defined remission in rheumatoid arthritis for clinical trials (14). Given that also in daily routine, remission constitutes the ultimate treatment-goal, a study in a daily routine setting was performed to assess whether the RADAI-5 remission criterion meets ACR/EULAR remission definitions (16). Seven hundred and five patient assessments were included. In the case of RADAI-5, remission sensitivity was 78%, specificity 86%, the PPV was 45% and NPV 96% also for indicating remission according to the Boolean based-definition, while the values were 60%, 92%, 66%, and 90%, respectively also for indicating remission according to the SDAI-based definition. In case of remission according to the SDAI-based ACR/EULAR definition sensitivity was 52%, specificity 100%, PPV 98% and NPV 87% also indicating remission according to the Boolean definition, while according to the Boolean definition the values were 98%, 87%, 52% and 100%, respectively. Kappa statistics show fair to good agreement for all three definitions.

Nearly twice as many assessments could be classified as being in remission using the SDAI-based or the RADAI-5 definitions when compared to the Boolean-based definition. Remission according to the RADAI-5 is also highly specific for both ACR/EULAR criteria (15).

Concluding remarks

The RADAI-5 provides the advantage that the primary target of all therapeutic interventions is given the key role in activity assessment. Moreover, inter-

physician variations in assessing joints or global disease activity are avoided.

Of course, neither the application of any questionnaire nor index can be a substitute for careful clinical patient examination (13). As individualised treatment strategies become increasingly important, patient-related outcome tools may provide essential advantages in identifying patients requiring particular attention. Applying the RADAI-5 can be regarded a substantial step forward in this respect as this instrument is capable of expressing a wide range of the patient's perspective of the disease process.

Only stable low RADAI-5 values are indicators for an uncomplicated disease course as it is the case with other instruments. Significant changes, though, have to be assessed with respect to the changes of the single items and possibly coexisting or newly occurring diseases (16). Translating the RADAI-5 derived disease activity categories into current routine care, the clinical remission like state corresponds to a green flag, the mild disease activity category to a yellow one, and moderate as well as high activity agrees with a red flag situation, which should be clarified as soon as possible – meaning reconsidering patient's management and taking action. A remission like state and above all a stable remission according to the RADAI-5 definitely mean something different than remission according to the DAS28 or CDAI, as question one includes the factor time; therefore a result meeting the RADAI-5 remission like state cannot be expected after a short time period.

In all the studies, positive support could be found for the arguments that the RADAI-5 comprises questions targeting patient's pain perception and global health estimate, which can be seen as surrogates for functionality. (17). The RADAI-5 has been designed specifically for busy clinical settings (12), with attention not only to validity and reliability, but also to feasibility and acceptability.

Self-report questionnaires, such as the RADAI-5, have been shown to be capable of substituting physician-derived disease activity scores, which were developed primarily for research purposes (18). All the results of our studies support the idea behind the development of the RADAI-5, namely to be as parsimonious as well as reliable as possible in daily routine monitoring of RA patients, which should not be confused with the special circumstances of clinical trials.

The RADAI-5 allows better participation in the care of RA patients, especially by non-specialists such as primary care physicians, without having been trained in formal joint counts. In this respect, it might also be of interest for the assessment that a patient not satisfying the RADAI-5 remission criteria has a high likelihood of not satisfying the ACR/EULAR remission criteria. These results could enforce the use of the RADAI-5 as a patient self-reported disease activity parameter in clinical trials and particularly in daily clinical routine.

No single measure can serve as a *gold standard* in the diagnosis and assessment of individual patients with most rheumatic diseases (11). The RADAI-5 questionnaire constitutes one easily applicable option for routine RA monitoring, which enables physicians to get reliable information about the disease course and is sensitive enough to sound the alarm if deteriorations occur.

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