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Concise Report

Use of rheumatoid arthritis impact of disease (RAID) in routine care; identification of DAS28 remission and unmet patient-reported outcomes

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Abstract

Objective. The aim was to assess how the patient-reported outcome RA impact of disease (RAID) relates to DAS28 categories in routine care, its utility in identifying patients in DAS28 remission (RDAS) or low disease activity (LDAS) and the burden of unmet patient-reported needs in those achieving RDAS/LDAS.

Methods. DAS28 and RAID scores were collected from patients with established RA attending for routine review. The relationship between RAID and DAS28 was assessed with univariate pairwise correlation and mixed-effects linear regression analyses. RAID <2 was defined as a patient-acceptable state.

Results. One hundred and ninety-eight patients were assessed, with 220 observations, using DAS28-CRP categories: 47.5% RDAS, 14.1% LDAS, 31.8% moderate DAS (MDAS) and 6.6% high DAS (HDAS). Both patient visual analog scale score and tender joint count exhibited a high statistical association with RAID using linear regression ($P < 0.0001$). The mean RAID score per DAS28-CRP category was RDAS 1.84, LDAS 4.78, MDAS 5.60 and HDAS 7.68, with a statistically significant increase in RAID per unit increase in DAS-CRP or DAS28-ESR on linear regression ($P < 0.001$). Of 66 patients with RAID <2, 64 (97%) were in RDAS and 65 (98.5%) in RDAS/LDAS. Of 134 patients in RDAS/LDAS, RAID was ≥ 2 in 69 (51.5%), with fatigue and sleep being the worst-scoring domains.

Conclusion. RAID functions well as a patient-reported outcome in routine care. Patients with RAID <2 have a high likelihood of being in RDAS/LDAS and, if pre-screened, could avoid a clinic visit. Analysis of RAID domains provides individualized targets for holistic care in RA management, with fatigue and sleep problems dominating unmet needs in those in RDAS/LDAS.

Key words: rheumatoid arthritis, disease activity score, RAID, patient-reported outcomes

CLINICAL SCIENCE

Introduction

Treat-to-target principles are widely recognized as the best strategy to achieve optimal disease outcomes in RA [1]. Two target outcomes are proposed within both ACR and EULAR guidelines [2, 3], and these have been endorsed by national bodies, such as the National Institute for Health and Care Excellence [4]. These targets, either remission or low disease activity, are based on the DAS28 composite score, which includes observer-, laboratory- and patient-reported assessments of disease activity.

Inflammation in RA has been linked clearly to joint damage and adverse cardiovascular outcomes, and in broad terms, new therapies and treatment strategies have been successful in suppressing both inflammation and its consequences [5, 6]. However, it has become increasingly clear that advances in RA management have

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Key messages

- RAID functions well in routine care and is closely associated with subjective components of DAS28.
- Patients with a RAID score <2 are highly likely to be in RDAS or LDAS.
- Fatigue and sleep are the worst-scoring domains in R/LDAS patients with a RAID >2.

had less impact on some patient-reported outcomes, such as fatigue, pain, depression, work performance and health-related quality of life [7–9].

Given the discordance in RA outcomes assessed by composite measures based on inflammation *vs* patient-reported outcomes, it is evident that to be truly holistic the management of RA in a treat-to-target context should include assessment of both aspects (inflammation and patient-reported outcome) in routine practice. DAS28 and SDAI provide assessments based on observer, patient and laboratory assessments. A variety of composite patient-reported outcomes is available to complement these, such as RA impact of disease (RAID), five item RA disease activity index (RADAI-5) and the Routine Assessment of Patient Index Data 3 (RAPID3). The RAID score is a patient-derived differentially weighted seven-item tool assessing pain, functional disability, fatigue, sleep, coping, physical and emotional well-being. It has been validated, is reliable, sensitive to change and EULAR adopted [10, 11]. It is well correlated with RADAI, patient global measures, SF36 physical and mental subscales, Euro Quality of Life 5 dimension index (EQ5D) and the DAS28 score [10, 12, 13]. On an individual patient level, a score <2 is deemed a patient-acceptable state [14, 15], and both absolute and relative minimally clinical important improvements are also defined [14].

In an increasingly over-populated and time-constrained health-care service, a particular attraction of RAID is its simplicity, with applicability to patient completion at home and submission electronically, potentially avoiding the need for a face-to-face consultation. We have therefore assessed the utility of RAID in routine care as a tool to identify patients in DAS28 remission (RDAS) or low disease activity (LDAS) and to reveal the burden of unmet patient needs in those achieving RDAS/LDAS.

Methods

Patients attending for routine RA review at St George's University Hospitals NHS Foundation Trust were assessed by a rheumatologist, nurse practitioner or physician assistant. Data collected at each clinic visit included the DAS28 score, acute phase reactants and the RAID questionnaire. All data were collected as standard routine care practice. Patients gave verbal consent to pooled retrospective data analysis.

The RAID score was calculated using the online EULAR toolkit [11]. Each of the seven individual domains of the RAID is scored on a 10-item numerical rating scale, with zero being a good or low activity score and 10 a high or severe activity score. In the absence of guidance, we arbitrarily classified the numerical rating scale results into one of three equivalent-sized ranges (mild: 0–2; moderate: 3–6; severe: 7–10) to give an overall idea of which domains scored particularly poorly or well.

The DAS28-ESR thresholds for remission (<2.6), low (2.6–3.2), moderate (3.3–5.1) and high (>5.1) disease activity were used, whereas for DAS28-CRP adjusted thresholds were adopted, remission (<2.4), low (2.4–2.9), moderate (2.91–4.6) and high (>4.6) disease activity, respectively [16].

Seropositive status was defined as testing positive for either RF or ACPA, or both. Only those who tested negative for both RF and ACPA were defined as seronegative.

The relationship between RAID scores with both DAS28-CRP and DAS28-ESR and their subcomponents was initially explored descriptively by comparing mean scores and univariate pairwise correlation analysis. The swollen joint count and tender joint count scores were square-root transformed, whereas the ESR and CRP were logarithmically transformed to match their form used in the DAS28 formulation. The relationship between each subcomponent of the DAS28 and the RAID score was explored using mixed-effects linear regression. Mixed-effects regression allows multiple observations per patient to be modelled, accounting for the likely correlation attributable to non-independence within these observations. The model included all subcomponents of the DAS28 and controlled for important confounders, including age, sex and seropositive status. The analyses were conducted separately for the DAS28-CRP and DAS28-ESR. All analyses were conducted using Stata v.15.

Results

One hundred and ninety-eight patients with established RA were assessed, contributing 220 observations. The sample was 80.8% female, mean age 59.0 years, 72.2% RF positive and 77.8% ACPA positive. Our of all the patients, 84.8% tested positive for either RF or ACPA (or both) and were defined as seropositive RA. Patients were on a range of therapies, including conventional synthetic DMARDs and biologic DMARDs, managed according to standard care.

DAS28-CRP was available for all 198 patients. The number in RDAS at first observation was 94 (47.5%),

LDAS 28 (14.1%), MDAS 63 (31.8%) and HDAS 13 (6.6%). The distribution per DAS28-ESR category was similar, with RDAS 46.7%, LDAS 16.8%, MDAS 29.4% and HDAS 7.1%.

The RAID scores were recorded 218 times from 196 patients, with a mean of 3.87 (S.D. 2.55), range 0–9.64. Patients reported no difficulties in understanding or completing the questions, taking <5 min. Only two questionnaires (1%) had missing data. The requirement to complete the RAID questionnaire during the consultation caused no delays to the normal conduct and running of the clinics.

Fig. 1 shows the relationship between RAID scores and DAS28-CRP, Spearman correlation 0.78. RAID scores were also correlated strongly with DAS28-ESR ($r = 0.75$) and patient global visual analog scale ($r = 0.83$), but less well with the square-root of tender joint count ($r = 0.55$), square-root of swollen joint count ($r = 0.39$), log ESR ($r = 0.38$) and log CRP ($r = 0.30$).

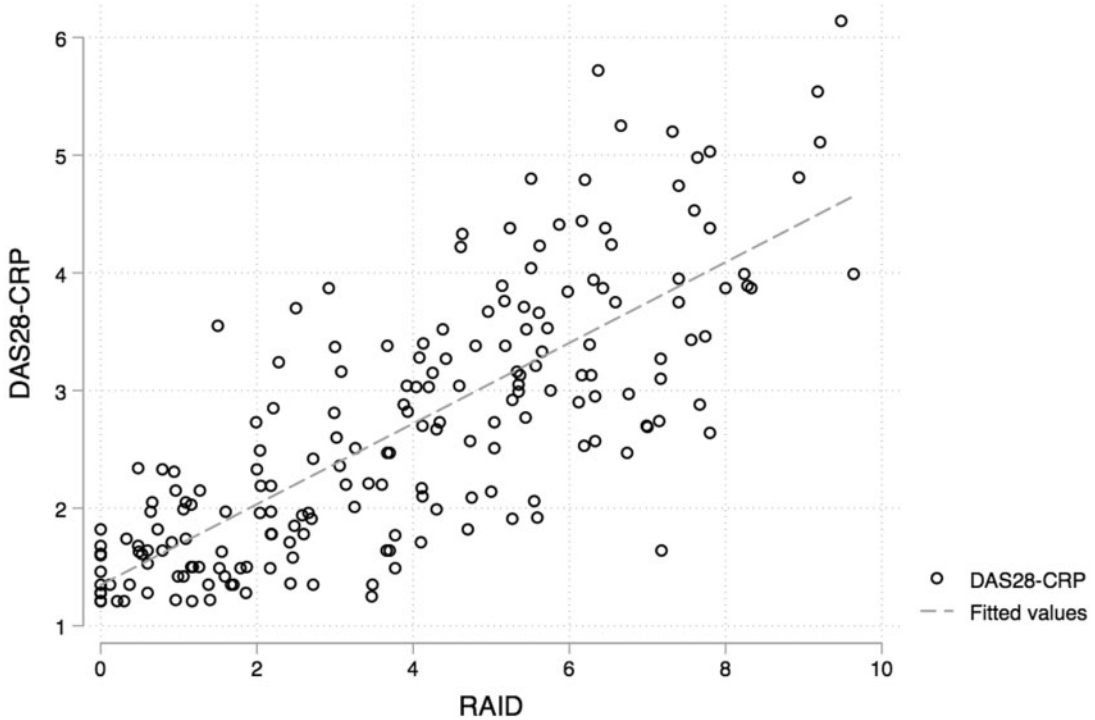
Using multiple mixed-effects linear regression, both the patient global visual analog scale and the square-root of tender joint count exhibited a highly statistically significant association with RAID scores ($P < 0.01$), whereby high tender joint count and patient global assessment were associated with increased scores on the RAID. Standardized coefficients indicate that the patient global visual analog scale had the largest association at 0.65, followed by tender joint count at 0.23. Additionally, the log CRP indicated statistical significance at $P = 0.048$, although the level and comparative effect were small relative to the tender joint count and patient global assessment, with a standardized coefficient of 0.08. The results are provided in Supplementary Table S1, available at *Rheumatology Advances in Practice* online.

The mean RAID score per DAS28-CRP disease activity category was RDAS 1.84 (S.D. 1.55), LDAS 4.78 (S.D. 1.73), MDAS 5.60 (S.D. 1.63) and HDAS 7.68 (S.D. 1.29) (see Supplementary Fig. S1, available at *Rheumatology Advances in Practice* online). When modelled using mixed-effects linear regression, whilst controlling for age, sex and seropositivity, there was a statistically significant increase in RAID scores for each one unit increase in DAS28-CRP score ($\beta = 1.76$; 95% CI: 1.59, 1.94, $P < 0.001$). Likewise, when DAS28-ESR was modelled in a mixed-effects linear regression, controlling for age, sex and seropositivity, there was a statistically significant increase in RAID scores for each one unit increase in DAS28-ESR ($\beta = 1.43$; 95% CI: 1.28, 1.58, $P < 0.001$), with mean RAID score per DAS28-ESR disease activity category, RDAS 2.14 (S.D. 1.93), LDAS 4.16 (S.D. 1.96), MDAS 5.52 (S.D. 1.62) and HDAS 7.52 (S.D. 1.59).

Of 66 patients with RAID <2 (patient-acceptable state), DAS28-CRP was <2.4 in 64 (97%) and ≤2.9 in 65 (98.5%); likewise, DAS28-ESR was < 2.6 in 61 (92.4%) and ≤3.2 in 65 (98.5%).

Of 105 patients with DAS28-CRP <2.4 (remission), RAID was ≥2 in 41 (39%), and of 134 patients with DAS28-CRP ≤2.9 (remission and low disease activity) RAID was ≥2 in 69 (51.5%). Fig. 2 shows the proportion

Fig 1 The relationship between DAS28-CRP and RA impact of disease scores



RAID: RA impact of disease.

of patients with DAS28-CRP $\leq$2.9 and RAID $\geq$2 scoring mild (0–2), moderate (3–6) and severe (7–10) for each domain of the RAID questionnaire. The domains with the largest proportion of these patients scoring in the severe range were fatigue 35.6%, sleep 33.3% and emotional well-being 28.9%. None of the seven domains scored uniformly well, the best being functional disability and coping, where 35.6 and 33.3% of patients, respectively, scored 0–2 on these domains.

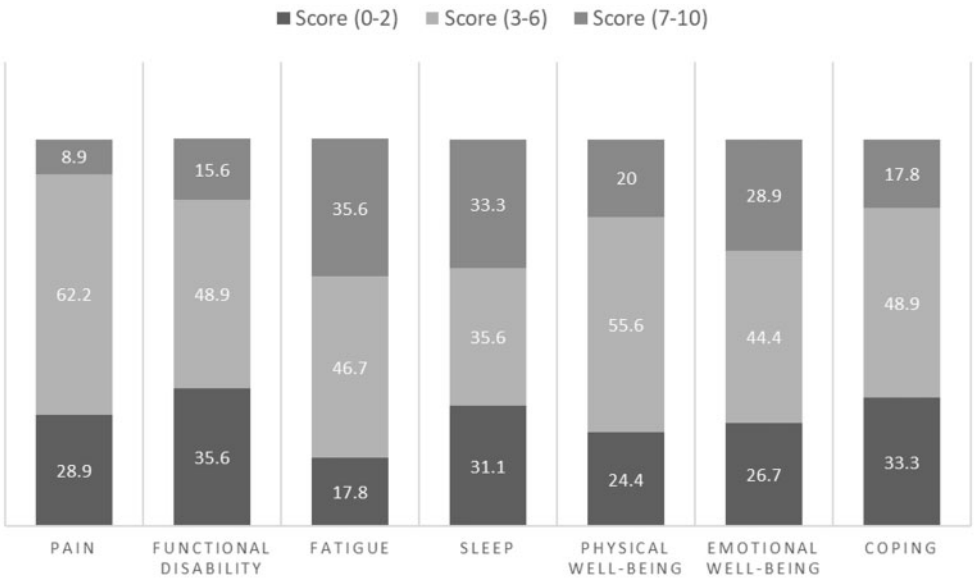
Discussion

This is the first report of the utility of the RAID patient-reported outcome measure in a routine care setting in UK practice. The score is well correlated with the total DAS28-CRP or DAS28-ESR score and with patient global assessment and tender joint count, but not with swollen joint count, CRP or ESR, as found by others [10, 12] and in keeping with this being a patient-derived outcome, rather than a measure of inflammation. Significant differences in RAID scores between patients in RDAS, LDAS, MDAS and HDAS categories, whether using DAS28-CRP or DAS28-ESR, confirm previous reports that there are significant differences in patient-reported outcomes between these categories, including remission and low disease activity in early RA [17, 18]. Our findings in a mixed population of patients with established RA under routine review add support to remission being a preferable goal compared with low disease activity in treat-to-target terms.

A very practical utility of RAID in routine care is apparent from the fact that virtually all patients with a RAID $<$2, defined as a patient-acceptable state [14, 15], were also either in RDAS or in LDAS. As such, if the RAID score is $<$2 it may be assumed confidently that the patient has also achieved a DAS28 treat-to-target goal. If developed as a tool for use at home, for example via a telephone app, the RAID could function as a triage tool, potentially avoiding the need for a face-to-face disease activity assessment in the clinic. This would be an innovative advance in an over-populated and resource-limited health-care system, where priority is better given to those RA patients with unsuppressed disease activity, requiring active changes in treatment.

In contrast, where the RAID is $>$2 the range of DAS28 scores is very wide (see Fig. 1), and inferences cannot be made. Of particular note is the fact that 51.5% of all patients who have achieved the DAS28 CRP treat-to-target LDAS or RDAS outcome ($\leq$2.9) have a RAID score $\geq$2, in an unacceptable patient range. This represents a high proportion of LDAS and RDAS patients with unmet needs and indicates that there is much scope for investigation and improved intervention strategies for these patients who have achieved seemingly good DAS28 outcomes. The RAID has additional utility in this regard, because scrutiny of the seven domains identifies those areas with particularly poor scores, enabling focused interventions, such as cognitive behavioural techniques. We found fatigue and sleep to be the most frequent high-scoring domains in patients in DAS28-CRP RDAS/LDAS but with a RAID $\geq$2. Fatigue is widely described to be a persisting long-term symptom in RA patients, including those in remission defined by DAS [7, 9, 19, 20], and our data are consistent with this. However, many patients scored poorly on all of the seven domains, indicating the need for a widespread package of care for truly holistic management. The high proportion

Fig. 2 Patients with DAS28-CRP $\leq$ 2.9 (LDAS and RDAS) and RAID score $\geq$ 2 ($n = 69$)



Distribution (percentage) scoring each RAID domain: mild (0–2), moderate (3–6) or severe (7–10). LDAS: low DAS; RAID: RA impact of disease; RDAS: remission.

of patients with a RAID score in the unacceptable range (≥2), yet in LDAS or RDAS, argues for a dual treat-to-target strategy incorporating both an inflammation-derived target and a patient-reported outcome target to be holistic. This is in keeping with the conclusions of Ferreira *et al.* [21], who advocate a three-component composite score (swollen joint count, tender joint count and CRP) as the target for immunosuppressive therapy and a separate disease impact target based on an expanded analysis of the patient global score, such as RAID. Our findings confirm that the RAID does function well as a treat-to-target patient-reported outcome, aiming for a score <2. The strength of our findings is that they demonstrate the utility of RAID in a real-world routine care setting. Nonetheless, the data are preliminary, because they are from only one centre, and they should be replicated in other settings and in larger numbers.

In summary, we have found the RAID questionnaire to be simple and easy to incorporate into the routine care setting for patients with RA. The finding that >97% of all patients with a score in the patient-acceptable range <2 are also in the DAS28-CRP categories of LDAS or RDAS provides potential time-saving utility by avoiding face-to-face disease activity assessments for these patients. Conversely, RAID reveals a high burden of unmet needs in patients in RDAS/LDAS, with >50% scoring ≥2. Scrutiny of the seven domains assessed provides individualized opportunities for improved RA management, especially for fatigue and sleep problems. For truly holistic care, there should be two treat-to-target goals, one based on an inflammation-derived measure and one on a patient-reported outcome. The RAID performs well as a patient-reported outcome in routine care.

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Supplementary data

Supplementary data are available at *Rheumatology Advances in Practice* online.

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