Evaluation of a simplified version of the Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) comprising 5 joints (RAMRIS5)

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Abstract

Objective

The objective of this study was to evaluate a simplified version of the Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) reduced to five joints of the hand (RAMRIS5).

Methods

94 patients with rheumatoid arthritis (62 female; age 59±12 years, range 25–83 years; disease duration 60±90 months (median: 22 months, first quartile: 7 months, third quartile: 66 months) from the REMISSION PLUS study cohort who had complete files on C-reactive protein (CRP) levels and Disease Activity Score of 28 joints (DAS28) and complete MRI of the clinical dominant hand at baseline and after one year under anti-rheumatic therapy (follow-up time 12.5±1.1 months) in a dedicated extremity MRI scanner at 0.2T were included in this retrospective study.

Results

There was a strong correlation between RAMRIS5 and the RAMRIS sum-score for all patients ($r=0.87$, $p<0.001$) at baseline and follow-up ($r=0.87$, $p<0.001$). Among the subscores there was a significant correlation between RAMRIS5 and RAMRIS-MCP (baseline: $r=0.66$, $p<0.001$; follow-up: $r=0.74$, $p<0.001$) as well as between RAMRIS5 and RAMRIS-wrist (baseline: $r=0.72$, $p<0.001$, follow-up: $r=0.69$, $p<0.001$) at baseline and follow-up.

Conclusion

RAMRIS5, a modified shorter RAMRIS score based on five joints of the hand is a viable tool for semi-quantitative assessment of joint damage in RA. This abbreviated score might reduce the time needed for image analysis in MRI-controlled studies in RA and might facilitate the use of MRI in studies on therapy response assessment in RA.

Key words
rheumatoid arthritis, RAMRIS, RAMRIS5, magnetic resonance imaging

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Introduction

Rheumatoid arthritis (RA) is, next to gout and psoriatic arthritis, one of the most common inflammatory rheumatic diseases with a worldwide prevalence of 0.5–0.8% (1, 2).

Untreated RA leads to chronic joint inflammation causing pain and functional disability due to swelling and joint mutilation (2, 3). To achieve a better outcome an early diagnosis and therapy with anti-rheumatic drugs aiming at the induction of disease remission is required (1, 4).

Magnetic resonance imaging (MRI) is a useful tool in detecting changes relating to RA, due to its high sensitivity to soft-tissue inflammation and bone destruction (5). In 2003 the Outcome Measures in RA Clinical Trials (OMERACT) group with the RA MRI Score (RAMRIS) established a highly reliable sum-score based on the semi-quantitative rating of the severity of synovitis, bone marrow oedema and erosions in hand (metacarpophalangeal joints) and wrist joints (6). The RAMRIS system has been shown to be a sensitive tool for the evaluation of therapy response in RA patients (7, 8). Generally, the RAMRIS score and clinical and serological disease activity parameters show a similar tendency (9). But a recent more detailed analysis on the connection between the individual changes of RAMRIS levels and the change of the well-established disease activity score for 28 joints (DAS28) and C-reactive protein (CRP) levels on the other hand by Emery and colleagues indicated only a weak correlation (10). The authors of the study interpreted this lack of correlation as an effect of the superior sensitivity of MRI for inflammation compared to clinical assessment and serological parameters.

Semi-quantitative, structured evaluation of hand-MRI using the RAMRIS system is a widely accepted and validated parameter in MRI-controlled clinical trials in RA (9, 11, 12). The RAMRIS criteria propose a sum-score of 23 joint sites of the hand (metacarpophalangeal joints 2–5, carpo-metacarpophalangeal joints 1–5, intercarpal joints, radiocarpal and radioulnar joints), yielding the sum of individual joints subscore for synovitis (grade: 0–3), bone marrow oedema (BME; grade: 0-3) and erosions (grade: 0–10). Especially in clinical studies enrolling large numbers of patients receiving MRI on multiple time-points (*e.g.* before and after treatment) this evaluation is time consuming (13) and a resource saving short score may facilitate the use of MRI, provided it offers equal sensitivity to determine changes after therapy (diagnostic performance). The aim of this study was to assess an abbreviated RAMRIS measurement encompassing 5 frequently affected joint sites, the RAMRIS5 score.

Material and methods

Patients

Ethics committee vote; trial num. 3226. After institutional review board approval, the datasets of 94 RA patients [62 female; age 59±12 years, range 25-83 years; disease duration 60±90 months (median: 22 months, first quartile: 7 months, third quartile: 66 months, range 3 weeks - 44 years)] from the REMISSION PLUS study cohort (14) recruited from a single centre were retrospectively included in this study. All patients fulfilled the 2010 American College of Rheumatology/European League Against Rheumatism Rheumatoid arthritis classification criteria (15, 16). Baseline and follow-up MRI scans were acquired of the clinically dominant hand and wrist. Follow-up MRI was performed approximately 12 months (12.5±3.5 months) after the baseline scan. The DAS 28 (CRP included) was documented at both examination dates by an experienced rheumatologist (16). All patients received disease-modifying anti-rheumatic drugs (DMARD), either methotrexate/15 mg (oral)/weekly or sulfasalazine (2000mg/d)). Concomitant prednisolone was allowed up to a dose of ≤10 mg/d.

MR imaging

MR imaging of the clinically dominant hand and wrist was performed using an open, extremity MR-System with a fieldstrength of 0.2T (Esaote, C-Scan, Genova Italy). The system provides the most available comfort for patients with RA, resulting in a higher subjective acceptability of MRI examina-

tions (17). The imaging protocol met the OMERACT recommendations (6, 18) and included pre- and post-contrast (intravenous injection of a standard dose of 0.2 ml/kg bodyweight of Gadolinium-based MRI contrast material, Dotarem®) T1-weighted images with a maximum slice thickness of 3 mm in at least two orthogonal planes and coronal fat-supressed short tau inversion recovery (STIR) sequences.

In detail, we used the following sequences:

1. Coronal Short tau inversion recovery (STIR) sequence with a Field of view (FoV) of 180* 180 mm, matrix size 192* 152, slice thickness 3 mm, Time to repetition (TR) 2420 ms, Time to excitation (TE) 26 ms, Time to inversion (TI) 85 ms).
2. Coronal 3 dimensional T1-weighed gradient echo sequence with a FoV of 180* 180* 60 mm, matrix size 192* 192* 40, slice thickness 1 mm, TR 50 ms, TE 16 ms prior and after intravenous injection of contrast material. The 3 dimensional T1-weighed gradient echo sequence was additionally reconstructed in sagittal and axial planes.

The field of view contained the metacarpophalangeal joints, the carpometacarpal joints, carpal joints, radiocarpal and radioulnar joints. The overall image acquisition time was 18 minutes. MR images were analysed by two experienced radiologists, who have been trained for RAMRIS scoring.

Image analysis (Fig. 1)

MR images were read in consensus by two radiologists trained in RAMRIS-Scoring. Images were evaluated for synovitis (grade: 0–3), bone marrow oedema (BME; grade: 0–3) and erosions (grade: 0–10) according to the RAMRIS guidelines (5, 19) (Fig. 2). In MCP joints the distal and proximal joint portions were analysed separately for presence of BME and erosions. BME and erosions were also detected in the bases of metacarpal bones 1–5, intercarpal bones, distal radius and ulna. For the evaluation of synovitis MCP, carpometacarpal, intercarpal, radiocarpal and radioulnar joints of the clinically dominant hand and wrist were analysed.

Table I. Spearman rho correlation analysis at baseline and at follow-up measurement for C-reactive protein (CRP), Disease Activity Score 28 (DAS28), $RAMRIS_{MCP}$, $RAMRIS_{wrist}$, RAMRIS and RAMRIS 5.

	CRP	DAS28	RAMRIS wrist	RAMRISMCP	RAMRIS	RAMRIS5
			Baseline			
CRP	1.00	0.43	0.32	0.11	0.29	0.21
DAS28	0.43	1.00	0.21	0.14	0.20	0.17
$RAMRIS_{wrist}$	0.32	0.21	1.00	0.26	0.90	0.72
$RAMRIS_{MCP}$	0.11	0.14	0.26	1.00	0.61	0.66
RAMRIS	0.29	0.20	0.90	0.61	1.00	0.87
RAMRIS5	0.21	0.17	0.72	0.66	0.87	1.00
			Follow-up			
CRP	1.00	0.22	0.14	-0.02	0.10	0.03
DAS28	0.22	1.00	0.25	0.27	0.32	0.31
$RAMRIS_{wrist}$	0.14	0.25	1.00	0.29	0.91	0.69
$RAMRIS_{MCP}$	-0.02	0.27	0.29	1.00	0.61	0.74
RAMRIS	0.10	0.32	0.91	0.61	1.00	0.87
RAMRIS5	0.03	0.31	0.69	0.74	0.87	1.00

Prior published studies demonstrated the joints mostly affected in RA: MCP 2 and 3 in the hand and distal ulna, radius, capitate, lunate, triquetrum, scaphoid, pisiform in the wrist (20-23). Additionally we took our MRI experience in joint involvement in RA into account (14, 24) and developed a new, abbreviated score. The RAMRIS5 score included the following joints of the clinically dominant hand and wrist: MCP 2 and 3 (to evaluate synovitis, erosions and bone marrow oedema); capitate bone, triquetral bone and distal ulna (to evaluate erosions and bone marrow oedema). Synovitis of the capitate bone, triquetral bone and distal ulna was assessed as a composite wrist synovitis score comprising the intercarpal and radiocarpal joints.

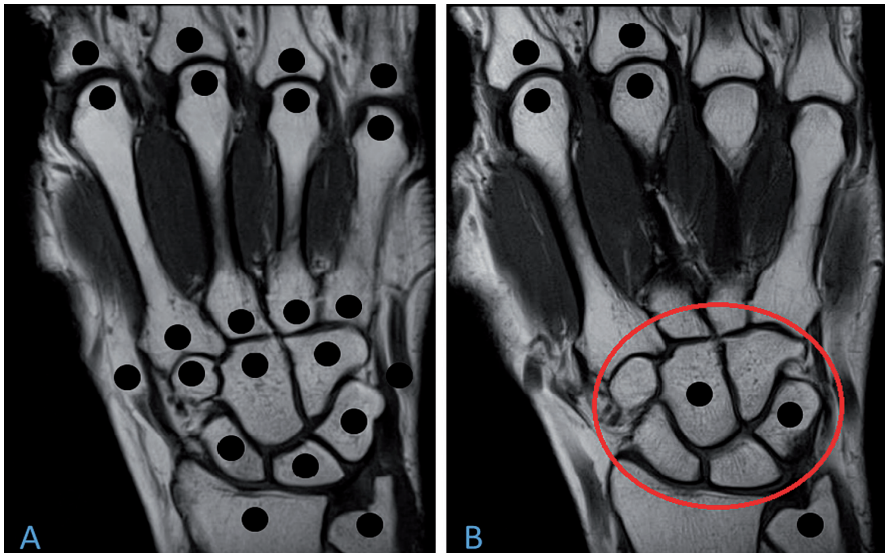

Fig. 1. Picture A and B show 3T MRI of the right hand. The black dots in picture A visualise areas analysed in the clinically dominant hand with RAMRIS for erosions, oedema and synovitis. For erosions 23 areas were evaluated including wrist (distal radius, distal ulna, carpal bones, metacarpal bases) and second to fifth MCP joints (metacarpal heads, phalangeal bases) with a scale from 0–10. For osteoedema the same 23 areas were evaluated as those for erosions with a scale from 0–3. For synovitis distal radioulnar joint, radiocarpal joint, intercarpal joints and second to fifth MCP joints were analysed with a scale from 0–3. Picture B shows joint sites analysed in RAMRIS5 in regard with erosions, oedema and synovitis. For erosions 5 areas were evaluated including MCP 2 and 3, carpitate bone, triquetral bone and distal ulna. We evaluated the same 5 areas for osteoedema. For synovitis we analysed MCP 2 and 3, as well as intercarpal and radiocarpal joint as one common space (red ellipse). The scale was identical in RAMRIS and RAMRIS5.

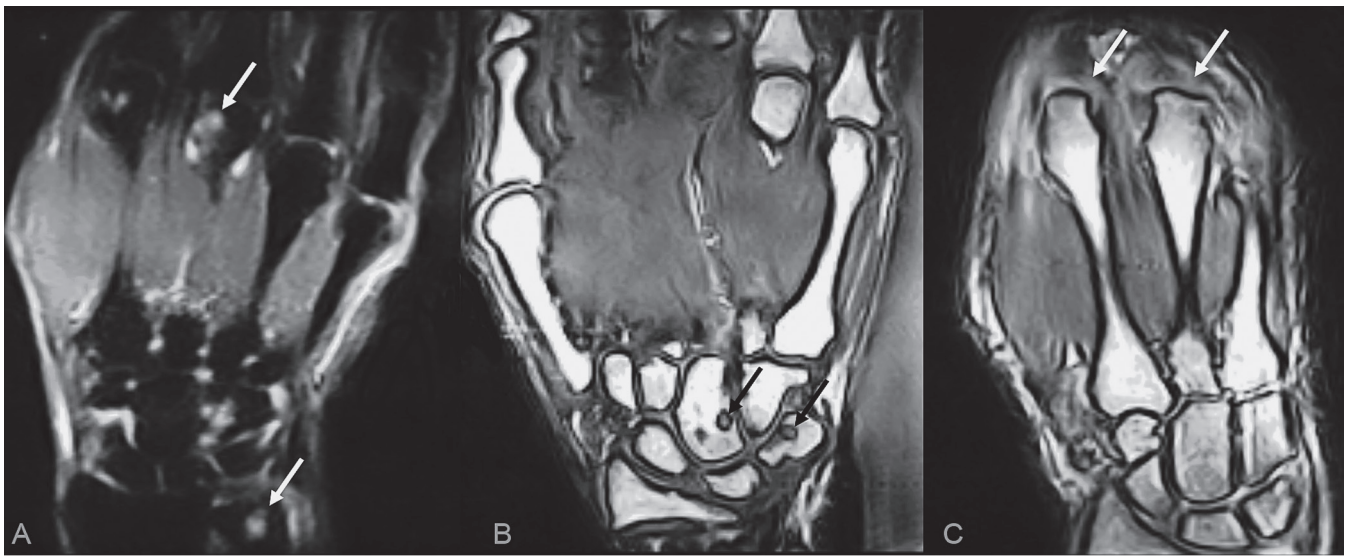

Fig. 2. A-C show typical MR imaging findings in RA. Picture **A** demonstrates a coronal STIR with bone marrow oedema in the distal ulna and in the caput of metacarpal 3 (white arrow). Coronal plane shows erosions in capitate and triquetral bone in the T1-weighted sequence (black arrows in **B**). Picture **C** presents a coronal plane after contrast agent application. There is a strong enhancement of the synovitis MCP 2 and 3 (white arrow), additionally synovitis can be seen in intercarpal and radiocarpal joints.

RAMRIS subscores were assessed for MCP joints and wrist by calculating the sumscores of inflammatory findings of the corresponding joints.

All statistical analyses were performed using the software R, version 2.11.1 (The R Foundation for Statistical Computing). For correlation analyses Spearman's rank correlation coefficient was used. A p-value <0.05 was chosen to demonstrate statistical significance.

Results

Correlation of RAMRIS, RAMRIS subscores and clinical parameters of disease activity

There was a weak correlation between RAMRIS and CRP levels (r=0.29, p<0.01) at baseline and follow-up (r=0.10, p=0.34) as well as between RAMRIS and DAS28 (baseline: r=0.20, p=0.05, follow-up: r=0.32, p<0.01). At baseline and follow-up there was a good correlation between the subscores of $RAMRIS_{MCP}$ (baseline: r=0.61, p<0.001; follow-up: r=0.61, p<0.001) and $RAMRIS_{wrist}$ (baseline: r=0.90, p<0.001; follow-up: r=0.91, p<0.001) with RAMRIS.

Correlation of RAMRIS5 and clinical parameters of disease activity (Fig. 3-5)

The correlation between RAMRIS5 and CRP was weak at baseline (r=0.21, p<0.05) and follow-up (r=0.03, p=0.76). Moreover, there was a poor correlation between RAMRIS5 and DAS28 at baseline (r=0.17, p=0.11) and follow- up (r=0.31, p<0.01).

Correlation of RAMRIS5, RAMRIS and RAMRIS subscores

There was a strong correlation between RAMRIS5 and RAMRIS (r=0.87, p<0.001) at baseline and follow-up (r=0.87, p<0.001). There was also a good correlation between RAMRIS5 and the subscores $RAMRIS_{MCP}$ and $RAMRIS_{wrist}$ at baseline (r_{MCP} = 0.66, r_{wrist} = 0.72, each p<0.001) and follow-up (r_{MCP} = 0.74, r_{wrist} = 0.69, each p<0.001).

Course of clinical and imaging parameters under therapy

Under therapy DAS28 and CRP decreased from 4.87±2.94 (baseline score) to 2.88±2.18 (follow-up) and from 16.63±22.56 to 9.08±15.48, respectively. Baseline RAMRIS score was 37.65±31.06 and decreased to 25.22±17.90 in follow-up measurement (percentage change: 33.01%). Baseline RAMRIS5 score was 14.91±10.77 and decreased to 11.00±7.38 in follow-up measurement (percentage change: 26.22%).

RAMRIS5 and RAMRIS time comparative analysis

One radiologist tested the time which

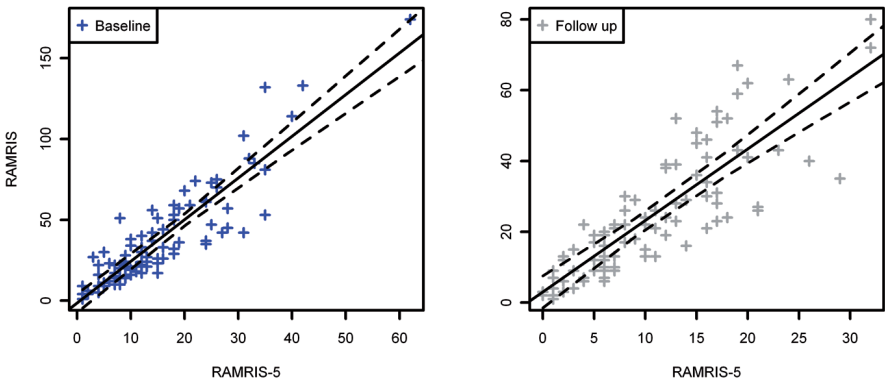

Fig. 3. Correlation of RAMRIS and RAMRIS5 at baseline and follow-up measurement. There was a significant and strong correlation between RAMRIS and RAMRIS 5 at baseline and follow-up measurement.

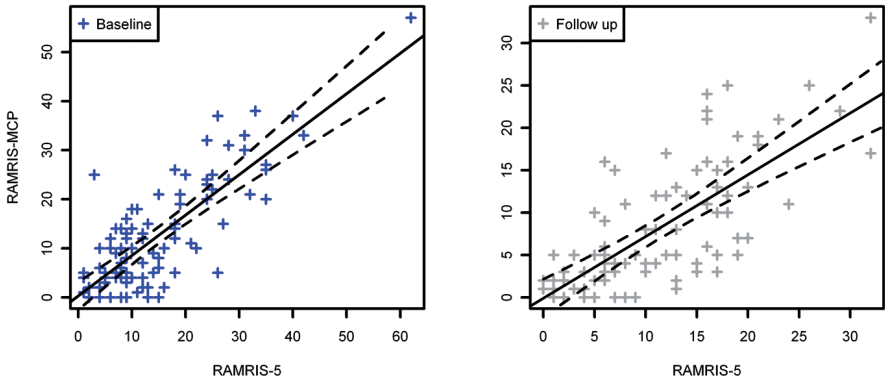

Fig. 4. Correlation of $RAMRIS_{MCP}$ subscore and RAMRIS5. The graphic shows a good correlation between $RAMRIS_{MCP}$ subscore and RAMRIS5.

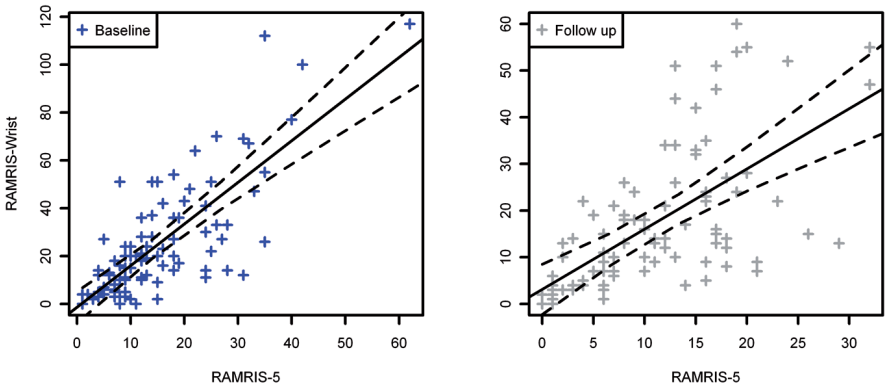

Fig. 5. Correlation of $RAMRIS_{WRIST}$ subscore and RAMRIS 5. The graphic shows a good correlation between $RAMRIS_{WRIST}$ subscore and RAMRIS5.

was used for both scoring methods. The examination time varied with the number of lesions present and ranged from 28 to 55 seconds (39.4±9.00) when using RAMRIS5 and from 242 to 312 seconds (278.8±20.31; p=0.001) when using RAMRIS. Under therapy the time period for RAMRIS5 was 30 to 53 seconds (38.3±8.63) and for RAMRIS 240 to 315 seconds (277.8±21.00; p=0.001).

Discussion

The development of new therapeutic strategies for rheumatoid arthritis, aiming at the early suppression of the disease activity using DMARDs and biologicals promoted the use of MRI for the sensitive detection and monitoring of joint inflammation (25-28).

The Outcome Measures in Rheumatology Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Imaging Score is the current standard for the structured, semi-quantitative assessment of joint alterations in rheumatoid arthritis (6). Since RAMRIS scoring is time-consuming, even after training, we evaluated an abbreviated scoring system, the RAMRIS5, comprising 5 instead of 23 joint sites. We found that the RAMRIS5 was strongly correlated to the standard RAMRIS at baseline and one year after anti-rheumatic therapy (DMARD). Additionally, RAMRIS5 and RAMRIS both showed similar tendencies under anti-rheumatic therapy and were both concordant with the clinical parameters (DAS28 or CRP) that demonstrated therapy response. RAMRIS5 showed a significant reduction of scoring time. Thus RAMRIS5 is a time and resource saving alternative for semi-quantitative scoring of inflammatory joint pathologies of the hand and their change in follow-up patients.

In contrast to the SAMIS (13), another simplification of the RAMRIS, we did not reduce the number of steps on the scales for BME, erosions and synovitis that have to be applied to all RAMRIS joint sites, in order to prevent the necessity of a new training of the readers, who are already familiar and well trained on the original scoring system. Instead, following examples of well-established ultrasound scoring systems in RA (29-31), we simplified the test by reducing the number of joint sites that have to be evaluated to five of the most frequently affected in RA. Backhaus et al. examined five joints in the hand and wrist: wrist, MCP 2 and 3, proximal interphalangeal joint (PIP) 2 and 3. In contrast to Backhaus we evaluated erosions, synovitis and bone marrow oedema according to the original RAMRIS criteria. The ultrasound scoring system cannot detect bone marrow oedema depends on technical factors. Instead, the scoring system take synovitis, tenosynovitis and bone marrow oedema into account (29).

Sharp *et al*. had previously reported that an abbreviated scoring system, using a combination of 17 joints to score erosions and 18 to score joint space narrowing, more accurately reflects the dimension of abnormalities than does the original scheme including more bones (32). Compared to the score of Sharp et al. our modified RAMRIS preserves the original RAMRIS criteria and encompassed the scoring of erosions, bone marrow oedema and synovitis. Since the latter are the dominant MRI pathologies found in RA we consider the preservation of the original RAMRIS criteria an advantage of the RAMRIS5. To save additional time for imaging and image evaluation, departing from the original RAMRIS recommendations, we only imaged and scored the clinically dominant hand. However, we do not consider this approach a relevant drawback of our study, since Ejbjerg *et al*. had previously demonstrated that there was no significant difference with respect to the detection of progressive joint destruction in rheumatoid arthritis between unilateral and bilateral MR imaging of the wrist and MCP joints (33).

Our study has limitations. We did not evaluate the inter- and intra-reader reliability of the RAMRIS5. Since the RAMRIS scoring system has a previously described high inter- and intra-reader reliability (34, 35) and due to the fact that both readers of this study were well experienced and trained for RAMRIS scoring, we consider this a minor

limitation. Additionally, the evaluation of the correlation between the RAMRIS5 and the RAMRIS when applied by readers with different levels of experience would have been desirable to establish the objective reliability of the abbreviated score. Further longitudinal studies with larger patient cohorts are needed to support our results and to answer the question if RAMRIS5 and RAMRIS lead to identical definitions of disease activity, therapeutic decisions and remission.

In conclusion, the shortened MR imaging scoring method RAMRIS5, is closely correlated with the RAMRIS for baseline and follow-up measurements. Thus RAMRIS5 can be used as a time and resource saving alternative for semi-quantitative description of inflammatory joint changes and therapy monitoring in RA.

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