

Development and Validation of the OMERACT Rheumatoid Arthritis Magnetic Resonance Tenosynovitis Scoring System in a Multireader Exercise

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ABSTRACT. Objective. To develop and validate a magnetic resonance imaging (MRI) tenosynovitis (TS) score for tendons at the wrist and metacarpophalangeal (MCP) joint levels in patients with rheumatoid arthritis (RA).

Methods. Axial T1-weighted precontrast and postcontrast fat-saturated MR image sets of the hands of 43 patients with RA initiating rituximab therapy were obtained at baseline and after 14, 26, 38, or 52 weeks. The MR images were scored twice by 4 readers. Nine tendon compartments of the wrist and 4 flexor tendon compartments at the MCP joints were assessed. Tenosynovitis was scored as follows: 0: No; 1: < 1.5 mm; 2: ≥ 1.5 mm but < 3 mm; 3: ≥ 3 mm peritendinous effusion and/or postcontrast enhancement. Intrareader and interreader intraclass correlation coefficients (ICC), smallest detectable change (SDC), percentage of exact and close agreement (PEA/PCA), and standardized response mean (SRM) were calculated.

Results. Intrareader and interreader ICC for status and change scores were very good (≥ 0.80) for total scores for all readers. Intrareader SDC was ≤ 3.0 and interreader SDC was < 2.0. The overall PEA/PCA intrareader and interreader agreements for change scores in all tendons were 73.8%/97.6% and 47.9%/85.0%, respectively. Average SRM was moderate for total scores and 60.5% of the patients had a tenosynovitis change score ≥ SDC.

Conclusion. The TS score showed high intrareader and interreader agreement for wrist and finger tendons, with moderate responsiveness, and the majority of the patients showed a change above the SDC. This scoring system may be included as a component of the RAMRIS. (J Rheumatol First Release May 1 2017; doi:10.3899/jrheum.161097)

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Tenosynovitis (TS) in the hand of patients with rheumatoid arthritis (RA) is a frequent and early occurring inflammatory feature that can cause tendon rupture and may be associated with subsequent bone erosion^{1,2,3,4,5}. Magnetic resonance imaging (MRI) provides excellent visualization of bone and soft tissues in the hand, including TS.

The Outcome Measures in Rheumatology (OMERACT) MRI in Arthritis Working Group developed an RA MRI score (RAMRIS) for synovitis, osteitis, bone erosion, and recently, for joint space narrowing^{6,7}. Adding TS to the RAMRIS may provide improved power to study and monitor the disease course of RA.

Haavardsholm, *et al* designed a TS score for the wrist that demonstrated good reliability and responsiveness^{8,9}. In addition, the Working Group has suggested and validated a TS score for the fingers as part of the psoriatic arthritis MRI score (PsAMRIS)^{10,11,12}. However, none of these scores covered the tendons at both wrist and metacarpophalangeal (MCP) joint level.

Our aim was to develop and validate an RA TS score for tendons at wrist and MCP joint levels. Here we present previously unpublished results that demonstrate the reliability of this novel score, enabling it to be included in the internationally renowned RAMRIS.

MATERIALS AND METHODS

Development of scoring system. In accordance with the processes in the OMERACT Handbook for technical tool development, previous MRI TS scores were identified through a thorough review of the literature by a fellow of the Working Group, which included rheumatologists, radiologists, methodologists, and industry representatives from 3 continents. The TS scores suggested by Haavardsholm, *et al* and the PsAMRIS appeared most thoroughly assessed methodologically and were tested in a pilot phase where the 2 TS scores were assessed at wrist and MCP joints by 2 readers at 2 timepoints^{8,9}. The methodology by Haavardsholm, *et al* seemed more applicable to the wrist area and was therefore chosen for subsequent intrareader and interreader agreement analyses in a pre-exercise with 80 hands at 2 timepoints (baseline/1-year followup), in which the exact thickness of TS was also measured. The results were presented and discussed at a subsequent meeting of the Working Group, and modifications were implemented based on tendon sheath thickness distributions (Supplementary Figure 1, available with the online version of this article). The group then proceeded to perform the multireader exercise below.

Image selection. MR image sets were selected from a study¹³ in which patients with active RA (disease activity score > 3.2, rheumatoid factor-and/or anticyclic citrullinated peptide-positive, ≥ 1 previous disease-modifying antirheumatic drug) were treated with 2–3 doses of 1000 mg rituximab at baseline. MRI of the dominant hand was performed on a Siemens 1.5 Tesla MRI unit using a dedicated hand coil. Axial T1-weighted fat-saturated precontrast and postcontrast gradient echo MR image sets (slice thickness 0.45 mm, repetition time 30 ms, echo time 6.8 ms, field of view 150 mm) were obtained at baseline (n = 43) and after 14 (n = 5), 26 (n = 8), 38 (n = 15), or 52 (n = 15) weeks.

Scoring of images. Four readers (DG, FG, MØ, PB) with previous experience in MRI-assessment of TS participated in the exercise. The readers performed a calibration session the evening before the exercise. Forty-three paired MR image sets were blinded for patient data but not for chronology¹⁴, and were read twice on identical 23-inch screens over 2 days with reanonymizing and rerandomizing between the 2 reads.

Reader rules and scoring system. At the wrist, 6 extensor tendon compartments and 3 flexor tendon compartments were assessed between the radioulnar joint and the hook of hamate. At the level of the second to the fifth MCP joints, flexor tendons were assessed in an area from 1 cm proximal to 1 cm distal to each joint (Figure 1A).

TS was defined as peritendinous effusion and/or postcontrast enhancement of the tendon sheath seen on axial sequences over ≥ 3 consecutive slices. The maximum width of the effusion and/or enhancing tendon sheath was measured perpendicularly to the tendon, and the TS score was graded as follows: 0: No; 1: < 1.5 mm; 2: ≥ 1.5 mm but < 3 mm; 3: ≥ 3 mm peritendinous effusion and/or postcontrast enhancement (Figure 1A). Tendon sheaths of crossing tendons were measured proximally to the crossing point, and tendon bundles within a common tendon sheath were assessed as 1 unit (Figure 1B-C). Supplementary Figure 2 (available with the online version of this article) shows examples of TS.

Statistical analysis. Descriptive statistics and the Wilcoxon signed-rank test were used to assess changes in score over time.

Intrareader and interreader agreement were assessed using single and average measure intraclass correlation coefficient (smICC/avmICC), respectively. The smallest detectable change (SDC) was calculated for intrareader and interreader change scores¹⁵ and was also expressed as the percentage of maximum observed change (%MOC). The percentage of exact agreement (PEA, scores equal) and the percentages of close agreement (PCA, scores ≤ 1 different) between the 2 reads and the 4 readers were calculated for intrareader and interreader agreement, respectively.

Responsiveness was assessed by the standardized response mean (SRM). Ability to show change was also assessed by the percentage of patients with change score \geq SDC.

RESULTS

Baseline and followup characteristics of the patients are presented in Supplementary Table 1 (available with the online version of this article). Median (range) change in total TS score was -1.0 (-1.0 to -2.5 ; $p < 0.01$).

Intrareader smICC for baseline scores were very good for all measures in all readers, except for MCP scores in 1 reader (smICC 0.79). Intrareader smICC for change scores were good to very good for all measures. All readers demonstrated very good intrareader smICC for total scores. Baseline/change interreader avmICC were > 0.90 (i.e., very good) for all measures. Median (range) intrareader SDC was 2.8 (2.1–3.0) for total scores. Interreader SDC for scores averaged over 4 readers were < 2.0 for wrist, MCP (< 1.0), and total scores. The percentage of patients with a total change score \geq SDC was 39.5% to 54.7% for intrareader SDC. For interreader SDC, this percentage was 60.5%. The %MOC was below 20% for intrareader and interreader total scores (Table 1).

Figure 1. Scoring sheet for the TS score. At the wrist, 6 extensor tendon compartments and 3 flexor tendon compartments are assessed, and at the level of the second to the fifth metacarpophalangeal (MCP) joints, the flexor tendons are assessed. The range of the scores is 0-27, 0-12, and 0-39 for the tendons at the wrist, MCP joints, and total score, respectively (A). Measuring the common tendon sheath perpendicularly from an individual tendon (B) will result in overestimation of the thickness of the tendon sheath. Therefore, the tendons within a common tendon sheath are assessed as 1 unit (C), illustrated by the dashed lines. The enhancing tendon sheath is measured perpendicularly to the unit at the thickest point. FCR: flexor carpi radialis; FPL: flexor pollicis longus.

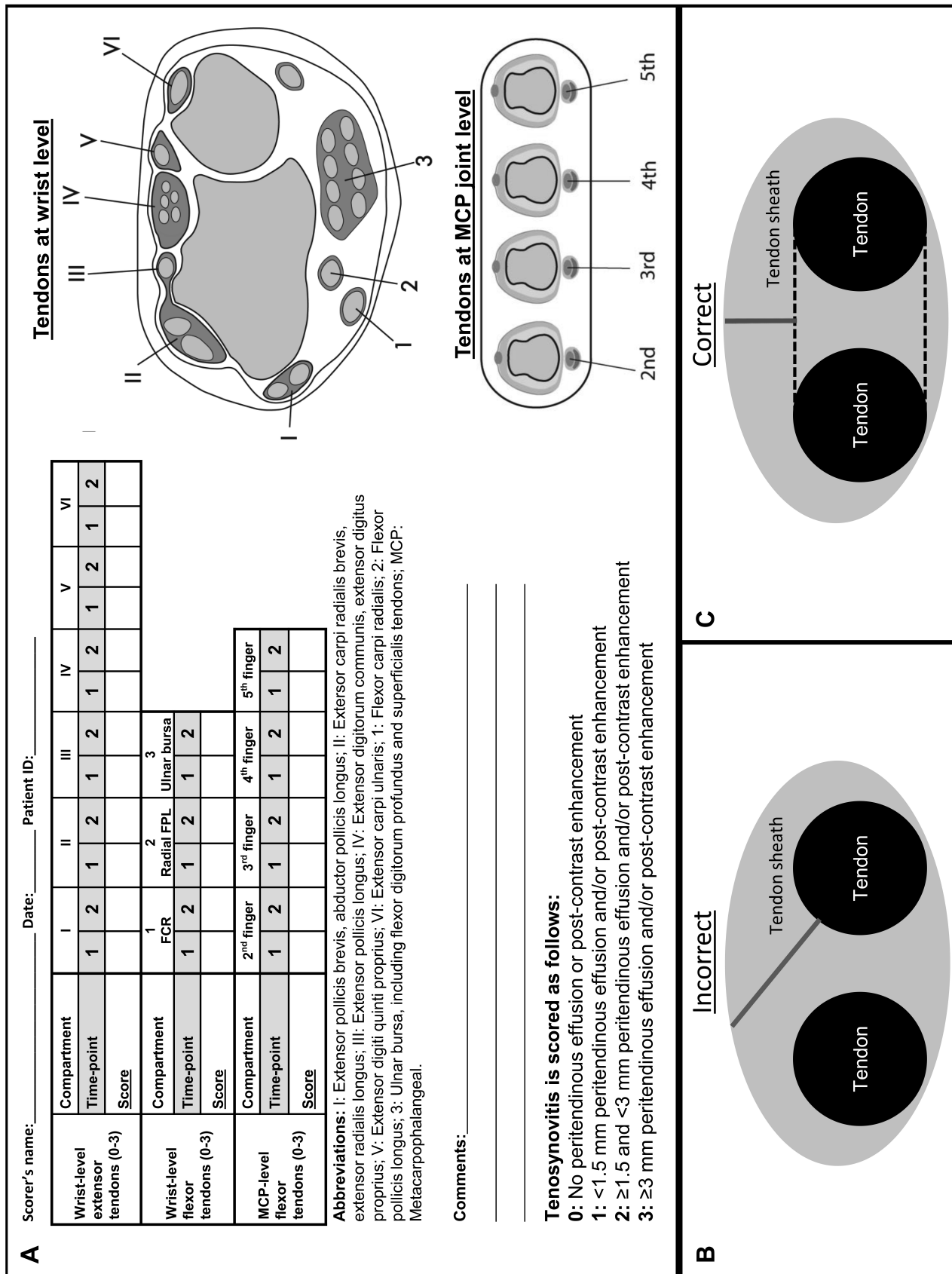


Figure 1.

Table 1. Intrareader and interreader agreement of the TS score.

		Wrist		MCP Flexor Tendons		Total Score	
		Baseline	Change	Baseline	Change	Baseline	Change
Intrareader ICC and SDC, Reader 1	smICC (95% CI)	0.91 (0.82–0.95)	0.82 (0.69–0.90)	0.89 (0.80–0.94)	0.81 (0.68–0.89)	0.90 (0.82–0.95)	0.88 (0.79–0.93)
	SDC (% patients ≥ SDC) [%MOC]		1.8 (54.7) [18.9]		1.1 (22.1) [15.5]		2.1 (39.5) [13.5]
Intrareader ICC and SDC, Reader 2	smICC (95% CI)	0.93 (0.87–0.96)	0.80 (0.67–0.89)	0.88 (0.79–0.93)	0.83 (0.71–0.90)	0.94 (0.90–0.97)	0.83 (0.70–0.90)
	SDC (% patients ≥ SDC) [%MOC]		2.0 (57.0) [18.2]		1.2 (23.3) [10.6]		2.7 (40.7) [13.3]
Intrareader ICC and SDC, Reader 3	smICC (95% CI)	0.84 (0.72–0.91)	0.76 (0.59–0.86)	0.79 (0.65–0.88)	0.68 (0.48–0.81)	0.87 (0.77–0.93)	0.84 (0.73–0.91)
	SDC (% patients ≥ SDC) [%MOC]		2.9 (48.8) [22.8]		1.8 (44.2) [23.8]		3.0 (54.7) [15.8]
Intrareader ICC and SDC, Reader 4	smICC (95% CI)	0.94 (0.89–0.97)	0.64 (0.42–0.79)	0.92 (0.85–0.96)	0.87 (0.78–0.93)	0.95 (0.91–0.97)	0.80 (0.67–0.88)
	SDC (% patients ≥ SDC) [%MOC]		2.3 (37.2) [29.7]		1.1 (44.2) [13.5]		2.7 (50.0) [18.1]
Intrareader PEA and PCA, %, average	PEA	76.7	75.4	73.4	70.3	75.7	73.8
	PCA	98.3	97.4	99.4	98.0	98.6	97.6
Interreader ICC and SDC	avmICC (95% CI)	0.94 (0.87–0.97)	0.91 (0.86–0.95)	0.96 (0.93–0.98)	0.94 (0.91–0.97)	0.96 (0.90–0.98)	0.94 (0.90–0.96)
	SDC (% patients ≥ SDC) [%MOC]		1.7 (49.4) [17.1]		0.9 (50.6) [10.2]		1.8 (60.5) [10.2]
Interreader PEA and PCA, %	PEA	42.5	50.3	41.0	42.4	42.0	47.9
	PCA	81.1	84.0	86.9	87.2	82.9	85.0

An intraclass correlation (ICC) ≥ 0.50 was considered good and an ICC ≥ 0.80 was considered very good. The smallest detectable change (SDC) was calculated for the change scores and expresses the lowest amount of change that can be considered as true change and not measurement error. The percentage of exact agreement (PEA) was defined as the percentage of individual tendons having an exact agreement between the 2 reads for intrareader agreement and between the 4 readers for interreader agreement. The percentage of close agreement (PCA) was defined as the percentage of tendons with agreement differing ≤ 1 . PEA and PCA are presented as the average percentages for total scores. TS: tenosynovitis; MCP: metacarpophalangeal; %MOC: percentage of maximum observed change; smICC: single measure ICC; avmICC: average measure ICC.

The overall PEA/PCA intrareader and interreader agreements for change scores in all tendons were 73.8%/97.6% and 47.9%/85.0%, respectively (Table 1). PEA/PCA for individual tendons are presented in Supplementary Table 2 (available with the online version of this article). The interreader PEA/PCA for pairs of 2 readers were 72.4%/99.6% (baseline) and 73.3%/98.8% (change) for the best matched pair and 64.3%/98.3% (baseline) and 67.5%/97.0% (change) for the average pair when all tendons were considered.

The average SRM for total scores was moderate (Table 2). Overall, there were no differences in ICC, %MOC, PEA/PCA, and SRM between tendon sheaths at wrist versus MCP joint levels.

Table 2. Responsiveness of the TS score.

	Change Wrist	Change MCP	Change Total
Reader 1	0.36	0.44	0.42
Reader 2	0.44	0.42	0.48
Reader 3	0.44	0.54	0.54
Reader 4	0.52	0.47	0.54
Average	0.44	0.47	0.50

Standardized response mean (SRM) for individual readers, expressed as the mean change divided by the SD of the change scores. SRM interpretation: trivial < 0.20 ; small 0.20–0.49; moderate 0.50–0.79; good ≥ 0.80 .

DISCUSSION

This longitudinal multireader exercise of patients with active RA showed that the TS score had high intrareader and interreader agreement and moderate responsiveness. The results were similar at wrist and MCP joint level.

Intrareader and interreader ICC were very good, both for total baseline and change scores, indicating that the TS score is reliable and can monitor change over time.

The average intrareader PEA was high and the PCA was close to 100%. Interreader PEA was acceptable considering the increased difficulty of 4 assessors needing to reach exact agreement, as compared to 2 assessors. Because most clinical trials have 2 assessors, we also analyzed the PEA/PCA for paired readers, and found the average percentages close to the intrareader agreements and the percentages of the best paired assessors in line with the intrareader agreements.

The interreader SDC was ≤ 2.0 and the %MOC $< 11\%$. Although the average SRM was only 0.50 (moderate), $> 60\%$ of the patients showed a change \geq SDC. Variable treatment regimens (related to different timing of infusions) and different timing of followup MRI may have affected the responsiveness but would not be expected to alter the intrareader and interreader agreement. Future studies should assess the responsiveness in early RA cohorts and in placebo-controlled studies, where responsiveness can be compared between groups.

This TS score was developed as a modification from the score by Haavardsholm, *et al* after assessing this and the PsAMRIS TS score in a pilot phase^{8,9,10,11}. A key modification of the methodology by Haavardsholm, *et al* was to narrow the intervals of tendon sheath thickness within each increment to potentially increase the ability to detect change. As proven by this exercise, the reliability of the current TS score remained high. The responsiveness was not increased compared to the results reported by Haavardsholm, *et al*⁹, but because therapies in the 2 cohorts were different, the results are not fully comparable. Other advances, compared to the score by Haavardsholm, *et al*, included clarifications on how to score tendon sheaths of crossing tendons and common tendon sheaths of tendon bundles (Figure 1B-C).

Other MRI TS scores have previously been used. Several have not assessed reliability and responsiveness^{1,16} or have scored TS qualitatively as absent/present^{2,4,17,18,19,20,21,22}. Regarding the monitoring of change, qualitative scores may have less power to detect changes in TS. Semiquantitative TS scores have been suggested by McQueen, *et al*²³ and Schirmer, *et al*²⁴, but did not assess the performance in longitudinal settings nor the intrareader and interreader agreement. Lisbona, *et al*²⁵ suggested a TS score for the hand (based on incomplete and complete halos of enhancing tendon sheath) that showed high intrareader and interreader ICC, but small SRM.

This TS score was developed as a potential addendum to the existing RAMRIS^{6,26}. Therefore, we strived to design the score so that it covered the tendons at the joint regions included in the RAMRIS core set. Because TS is scored on the same MRI sequences and projections as synovitis, these pathologies may be scored simultaneously and therefore the addition of TS score will add only a small amount of time to assessing a hand when using the RAMRIS method. Based on this and the reliability and responsiveness data, we conclude that this TS score fulfills the OMERACT filter criteria concerning truth, discrimination, and feasibility²⁷ and may be included as a component of the RAMRIS for assessing TS of the hand in RA clinical trials.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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