

The use of MRI in early inflammatory arthritis

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Evaluation of Magnetic Resonance Imaging–Detected Tenosynovitis in the Hand and Wrist in Early Arthritis

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Abstract

Objective

Magnetic resonance imaging (MRI) is a sensitive method to detect inflammation in rheumatoid arthritis (RA), visualizing synovitis, bone marrow edema, and tenosynovitis. The prevalence of MRI-detected tenosynovitis and its diagnostic value in early arthritis are unclear. This study was undertaken to identify the frequency of MRI-detectable tenosynovitis at the metacarpophalangeal (MCP) and wrist joints in early arthritis and the association of these with RA and the severity of RA.

Methods

A total of 178 patients with early arthritis underwent unilateral 1.5T extremity MRI at baseline. The MCP and wrist joints were scored using the Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system and Haavardsholm's tenosynovitis score. Sixty-nine patients fulfilled the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria for RA during the first year and were compared with the non-RA patients. Among the RA patients, comparisons were made with regard to anti–citrullinated protein antibody (ACPA) positivity and radiographic progression during year 1.

Results

Of all patients, 65% had MRI-detected tenosynovitis. RA patients had tenosynovitis more often than non-RA patients (75% versus 59%; P = 0.023). The flexor tendons at MCP5 and the extensor tendons at MCP2 and MCP4 and in extensor compartment I of the wrist were more frequently affected in RA patients than in other patients (odds ratios 2.8 [95% confidence interval (95% CI) 1.2–7.0], 9.1 [95% CI 1.9–42.8], 14.2 [95% CI 1.7–115.9], and 4.0 [95% CI 1.4–11.1], respectively). These associations were independent of local MRI synovitis. Specificities were all >82%. Within the group of RA patients, tenosynovitis scores were not associated with ACPA positivity or radiographic progression.

Conclusion

MRI-detected tenosynovitis is commonly seen in early arthritis. The flexor tendons at MCP5, the extensor tendons at MCP2 and MCP4, and the first extensor compartment of the wrist are more often affected in RA, independent of local synovitis.

Introduction

Magnetic resonance imaging (MRI) of hand, wrist, and foot joints is increasingly used in early arthritis and rheumatoid arthritis (RA), though mainly for research purposes. The advantage of MRI is its ability to sensitively depict both local inflammation and structural damage.^{1,2} For MRI of the hands and wrists, a validated scoring system (Rheumatoid Arthritis Magnetic Resonance Imaging Scoring [RAMRIS]) has been developed.³ Bone marrow edema, or osteitis, which cannot be detected by physical examination or ultrasound, is a potent predictor of future erosions in RA.^{4,5}

In addition to the RAMRIS method, which allows scoring of erosions, bone marrow edema, and synovitis in the metacarpophalangeal (MCP) and wrist joints, a separate tenosynovitis scoring method has been developed.⁶ Although this method allows the evaluation of the presence and extent of tenosynovitis in a standardized way, at present knowledge of the discriminative ability of MRI-detected tenosynovitis for RA in patients with early arthritis is still limited. This hampers the appreciation of tenosynovitis both for research purposes and potentially for the diagnostic process in daily clinical practice.

Tenosynovitis is defined as inflammation of the synovial lining of the tendon sheath, with or without synovial thickening; synovial fluid may be present. Inflammation around tendons without tendon sheaths is also observed, and its origin is less clear. Underlying joint synovitis potentially plays a role. The extensor tendons of the fingers and the flexor carpi ulnaris at the wrist lack a tendon sheath.⁷ The anatomy of all tendons around the wrist and MCP joints 2–5 is shown in detail in Figure 1. Tenosynovitis can be detected by physical examination, ultrasound, and MRI. Previous studies have shown that ultrasound and MRI have a higher sensitivity than physical examination.^{1,8}

Studies of MRI-detected tenosynovitis thus far have included relatively small numbers of patients, evaluated a selected patient group, or studied groups of extensor and flexor tendons instead of separate anatomically defined compartments.^{9–12} For instance, it was observed that RA patients more often had involvement of the group of extensor tendons than psoriatic arthritis patients,¹⁰ that tenosynovitis of the flexor tendons (analyzed as a group) was associated with RA development in undifferentiated arthritis,⁹ and that tenosynovitis of the flexor tendons of the second finger and the extensor carpi ulnaris was associated with progression to RA.¹¹ However, none of those studies performed detailed analyses in a large inception cohort of patients with early arthritis.

The purpose of this study was to assess the prevalence of MRI-detected tenosynovitis at the level of the wrist and MCP joints using separate anatomic regions, to associate this with underlying synovitis, and to determine the discriminative ability of tenosynovitis for early RA in an unselected population of patients with early arthritis. Finally, we evaluated whether the presence of tenosynovitis is a feature associated with a severe course of RA.







Figure 1 Tendons and tendon sheaths (shown in blue) of the hand and wrist

A, Schematic illustration of the palmar side of the hand and wrist. The broken lines show the areas depicted in C and D. B, Schematic illustration of the dorsal side of the hand and wrist. C, Axial T1, postgadolinium, fat-saturated magnetic resonance image (MRI) at the level of the wrist without signs of inflammation. D, Axial T1, postgadolinium, fat-saturated MRI at the level of the metacarpophalangeal (MCP) joints without signs of inflammation. At the dorsum of the wrist 6 extensor compartments are defined under the extensor retinaculum and covered with a synovial sheath (numbered I–VI) containing the extensor pollicis brevis and abductor pollicis longus (II), extensor carpi radialis brevis and extensor indicus

proprius (IV), extensor digiti quinti proprius (V), and extensor carpi ulnaris (VI). However, moving distally, the tendons are connected to the bone by a complex ligamentous system; the extensor tendons at the level of the MCP joint have no synovium (arrows in D). On the palmar side, the 9 tendons in the carpal tunnel are covered by the synovium of the radial (3) and ulnar (2) bursa. The radial bursa contains the flexor pollicis longus tendon and extends to the thumb, and the ulnar bursa contains the 8 flexor tendons and extends distally to the fifth finger in the majority of cases. A connection between the ulnar and radial bursa is present in a majority of cases. A gap exists at the palm of the hand between the tenosynovium in the carpal tunnel and the second, third, and fourth fingers, which have a separate tenosynovial coverage that starts at the level of the metacarpal heads (arrowheads in D). Outside the carpal tunnel the flexor carpi ulnaris tendon (1) does not have a synovial sheath, but the flexor carpi radialis tendon (4) does (see refs. 7 and 20)^{7,20}.

Patients and methods

Patients

From August 2010 to April 2012, 350 patients were included in the Leiden Early Arthritis Clinic (EAC). MRI was performed at baseline in 179 patients, based on voluntary participation. One patient was excluded because no gadolinium (Gd) chelate contrast agent was administered. The EAC is a prospective populationbased inception cohort including patients with confirmed arthritis and symptom duration of <2 years. At baseline, the patients and rheumatologists completed questionnaires, joint counts were performed, serum samples were obtained, and hand and foot radiographs were obtained. The cohort has been described in detail previously.¹³ The diagnoses established after 1 year of followup were used in this study. RA was classified according to the American College of Rheumatology/ European League Against Rheumatism 2010 classification criteria ,¹⁴ and 69 of the 178 patients fulfilled the criteria. Written informed consent was obtained from all patients. The study was approved by the local medical ethics committee.

MRI scanning and scoring

MCP joints 2–5 and the wrist of the most painful side, or the dominant side in cases of equally severe symptoms on both sides, were scanned. MRI was performed using an MSK Extreme 1.5T extremity MRI system (GE) and a 100-mm coil.

The following sequences were acquired before contrast injection: T1-weighted fast spin-echo (FSE) sequence in the coronal plane (repetition time [TR]/echo time [TE] 650/17 msec, acquisition matrix 388 x 88, and echo train length [ETL] 2) and T2-weighted FSE sequence with frequency-selective fat saturation in the coronal plane (TR/TE 3,000/61.8 msec, acquisition matrix 300 x 224, and ETL 7). After intravenous injection of Gd chelate contrast agent (gadoteric acid; Guerbet) (standard dose of 0.1 mmole/kg), the following sequences were obtained: T1-weighted FSE sequence with frequency-selective fat saturation in the coronal plane (TR/TE 650/17 msec, acquisition matrix 364 x 224, and ETL 2) and T1-weighted FSE sequence with frequency-selective fat saturation in the axial plane (TR/TE 570/7 msec, acquisition matrix 320 x 192, and ETL 2). The field of view was 100 mm. Coronal sequences had 18 slices with a slice thickness of 2 mm and a slice gap of 0.2 mm. All axial sequences had a slice thickness of 3 mm and a slice gap of 0.3 mm, with 20 slices for the hand.

Synovitis was scored at MCP joints 2–5 separately and, according to the RAMRIS method, in 3 regions of the wrist: the distal radioulnar joint, the radiocarpal joint,

and the intercarpal and carpometacarpal joints.¹⁵ Tenosynovitis was scored as described by Haavardsholm et al,⁶ on a scale of 0–3, where 0 = normal, 1 = <2 mm peritendinous effusion or synovial proliferation with enhancement, 2 = >2 and <5 mm peritendinous effusion or synovial proliferation with enhancement, and 3 = >5 mm peritendinous effusion or synovial proliferation with enhancement. Examples of MR images without inflammation are shown in Figure 1. Examples of scores 1 and 2 are available from the author upon request. Enhancement of tissue surrounding tendons without a tenosynovial sheath (the extensor tendons at the MCP joints and the tendon of the flexor carpi ulnaris) was scored following the same method. In the analyses we used the term tenosynovitis for both. A total of 18 tenosynovitis locations were scored in each patient: 10 at the wrist, including 6 extensor compartments and 4 regions on the volar side (the flexor digitorum profundus and flexor digitorum superficialis, the flexor pollicis longus, the flexor carpi ulnaris, and the flexor carpi radialis), and 8 locations at MCP joints 2–5 (paired flexor tendons and extensor tendons of the fingers) (Figure 1).

The MRIs were independently scored by 2 readers who were blinded with regard to the clinical data. The within reader intraclass correlation coefficients (ICCs) for the total RAMRIS score were 0.98 and 0.83; the between-reader ICC was 0.82. When scores were dichotomized as indicating the presence or absence of synovitis or tenosynovitis, a joint or tendon was scored positive for the presence of synovitis or tendons (e.g., all MCPs or wrist) were considered positive when at least 1 of the locations evaluated in the group was scored as having synovitis or tenosynovitis present. When sensitivity analyses were performed, tenosynovitis was considered present when both readers assigned a score of at least 2 to the location.

Conventional radiography and scoring

Radiographs of the hands and feet of RA patients were scored according to the Sharp/van der Heijde (SHS) method¹⁶ by a trained reader (within-reader ICC 0.91). Baseline radiographs were available for all 69 patients with RA, and radiographs obtained after 1 year were available for 56 (81%) of the patients. The progression in total SHS score (erosion and narrowing score) in the hands and feet over 1 year was used in the analyses.

Statistical analysis

Tenosynovitis and synovitis scores that could not be determined on MRI due to insufficient image quality, mostly due to inhomogeneous fat suppression or movement artifacts, were imputed with the median value for that feature across all locations within the same patient. For synovitis, 12 (0.5%) of 2,492 joints could not be scored, and for tenosynovitis, 49 (0.8%) of 6,408 locations could not be scored. To compare proportions, Pearson's chi-square test or Fisher's exact test, when appropriate, was used. Univariable and multivariable logistic regression analyses were used to analyze the associations between tenosynovitis, synovitis, and RA. In multivariable logistic regression all covariates were entered simultaneously. Spearman's rank correlation and the Mann-Whitney U test were used for analysis of the non– normally distributed total tenosynovitis score. IBM SPSS for Windows, version 20.0 was used. P values less than 0.05 were considered significant.

Results

Frequency of tenosynovitis in early arthritis

Baseline characteristics of the patients are presented in Table 1. In total, 3,204 separate anatomic locations were assessed for tenosynovitis in 178 patients. Tenosynovitis in at least 1 location was present in 65% of all of the patients with early arthritis. Figure 2 shows the frequency of tenosynovitis per location. The tendon of the extensor carpi ulnaris was most frequently affected (34% of all patients with early arthritis).

	All (n=178)	RA (n=69)†	non-RA (n=109)‡
Age, mean (SD) years	54.2 (15.2)	54.5 (15.5)	53.9 (15.1)
Sex, no. (%) female	98 (55.1)	43 (62.3)	55 (50.5)
Symptom duration at first visit, weeks	17.8 (8.2-35.0)	19.7 (8.5-25.6)	17.1 (7.9-41.5)
Swollen joint count (66 joints)	3.0 (2.0-5.0)	5.0 (2.0-10.0)	2.5 (1.0-4.3)
ESR level above reference value, no. (%)	71 (39.9)	35 (50.7)	36 (33.0)
CRP level above reference value, no. (%)	56 (31.5)	31 (44.9)	25 (22.9)
ACPA above reference value, no. (%)	45 (25.3)	42 (60.9)	3 (2.9)
Baseline SHS	2 (0-5)	2 (0-4)	2 (0-6)

Table 1 Baseline characteristics of the patients with early arthritis*

* Except where indicated otherwise, values are the median (interquartile range). ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; ACPA = anti–citrullinated protein antibody; SHS = Sharp/ van der Heijde score.

† Fulfilled the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria for rheumatoid arthritis (RA) during the first year.

‡ Of the patients without RA, 54 had undifferentiated arthritis, 13 had osteoarthritis, 12 had psoriatic arthritis, 4 had spondyloarthritis with peripheral arthritis, 4 had gout, and 22 had other diagnoses.

Association between tenosynovitis and RA

Subsequently, we studied the 69 patients with RA. In 75% of the RA patients, at least 1 location was scored positive for tenosynovitis, which was higher than the prevalence of tenosynovitis in patients with other arthritides (59%) (P = 0.023). Similar comparisons were performed for tenosynovitis at the MCP joints (54% in RA patients versus 36% in non-RA patients; P = 0.019) and the wrist (55% in RA patients versus 47% in non-RA patients; P = 0.282). Figure 2 also shows the frequency of tenosynovitis per anatomic location within the wrist and MCP joints for patients with RA and those with other diagnoses. RA patients had significantly more inflammation at the flexor tendons at MCP5, with an odds ratio (OR) of 2.8 (95% confidence interval [95% CI] 1.2–7.0), and at the extensor tendons at MCP2 (OR 9.1 [95% CI 1.9–42.8]) and MCP4 (OR 14.2 [95% CI 1.7–115.9]) and in wrist compartment I (OR 4.0 [95% CI 1.4–11.1]), wrist compartment II (OR 2.6 [95% CI 1.0–6.4]), and wrist compartment IV (OR 2.2 [95% CI 1.1–4.5]) (Table 2).





Table 2 Diagnostic	s value	of tenosyı	novitis for RA	at locations th	at were more	significantly	affected in RA	than in other a	arthritides*	
Location	RA %	non-RA %	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)	OR (95% CI)	٩
Flexor mcp 5	20.3	8.3	20% (14%-26%)	92% (88%-96%)	61% (54%-68%)	65% (57%-72%)	2.46 (1.13-5.37)	0.87 (0.76-0.99)	2.83 (1.15-6.95)	0.020
Extensor mcp 2	14.5	1.8	14% (9%-20%)	98% (96%-100%)	83% (78%-89%)	64% (57%-71%)	7.9 (1.78-34.98)	0.87 (0.79-0.96)	9.07 (1.92-42.77)	0.002
Extensor mcp 4	11.6	0.9	12% (7%-16%)	99% (98%-100%)	89% (84%-94%)	64% (57%-71%)	12.64 (1.62-98.85)	0.89 (0.82-0.97)	14.16 (1.73-115.95)	0.002
Wrist extensor compartment I	18.8	5.5	19% (13%-25%)	94% (91%-98%)	68% (62%-75%)	65% (58%-72%)	3.42 (1.37-8.58)	0.86 (0.76-0.97)	3.99 (1.44-11.06)	0.005
Wrist extensor compartment II	18.8	8.3	19% (13%-25%)	92% (88%-96%)	59% (52%-66%)	64% (57%-71%)	2.28 (1.03-5.05)	0.88 (0.78-1)	2.58 (1.04-6.41)	0.037
Wrist extensor compartment. IV	33.3	18.3	33% (26%-40%)	82% (76%-87%)	53% (46%-61%)	66% (59%-73%)	1.82 (1.08-3.05)	0.82 (0.68-0.99)	2.23 (1.11-4.47)	0.023
* RA = rheumatoid odds ratio.	arthritis;	95% Cl =	95% confidenc	e interval; PPV	<pre>' = positive pre</pre>	dictive value; 1	VPV = negative	predictive value	e; LR =likelihood	atio; OR =

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The total numbers of patients affected per location were 23 for flexor metacarpophalangeal (MCP) joint 5, 12 for extensor MCP2, 9 for extensor MCP4, 19 for wrist extensor compartment I, 22 for wrist extensor compartment II, and 4 for wrist extensor compartment IV.

The sensitivity of these features for RA was low (generally <20%), indicating that although RA patients had tenosynovitis at these locations more frequently than patients with other arthritides, the majority of RA patients did not have tenosynovitis at these specific locations. The specificity, however, was high (generally >90%), indicating that tenosynovitis at these locations rarely occurred in patients with early arthritis without RA (Table 2). Furthermore, the positive likelihood ratios for inflammation at the extensors at MCP2 and MCP4 were relatively high (7.9 and 12.64, respectively) (Table 2).

Association between synovitis and tenosynovitis

Next, since synovitis was often present in joints next to tendons showing tenosynovitis (range 70–100%) (data are available from the author upon request), we examined if the associations observed were all driven by the association between synovitis and RA or whether the associations of tenosynovitis with RA were independent of the presence of local synovitis. Four locations of tenosynovitis were associated with RA independent of the presence of local synovitis. Four locations of tenosynovitis were associated with RA independent of the presence of local synovitis: the flexor tendons at MCP5 (OR 4.2 [95% CI 1.4–12.9]), the extensor tendons at MCP2 (OR 9.4 [95% CI 1.9–45.8]) and MCP4 (OR20.1 [95% CI 2.2–186.0]), and extensor compartment I of the wrist (OR 3.7 [95% CI 1.3–10.4]) (Table 3). The extensor tendons at the MCP joints lack a tenosynovium, which makes them different from the other tendons studied. Interestingly, in the patients with early arthritis

Location	-	OR	95%CI	р
MCP 5				
	Flexor	4.22	(1.38-12.85)	0.01
	Synovitis	0.52	(0.19-1.42)	0.20
MCP 2				
	Extensor	9.38	(1.92-45.81)	0.01
	Synovitis	0.93	(0.48-1.81)	0.84
MCP 4				
	Extensor	20.08	(2.17-185.95)	0.01
	Synovitis	0.60	(0.22-1.62)	0.32
Wrist†				
	Extensor comp. I	3.69	(1.3-10.42)	0.01
	Synovitis	1.29	(0.67-2.46)	0.45
	Extensor comp. II	2.32	(0.89-6.03)	0.08
	Synovitis	1.27	(0.66-2.47)	0.48
	Extensor comp. IV	2.08	(0.97-4.45)	0.06
	Synovitis	1.17	(0.58-2.33)	0.66

Table 3 Association of tenosynovitis with RA adjusted for local synovitis*

* Data were analyzed by multivariable logistic regression for an association with fulfilling the American College of Rheumatology/ European League Against Rheumatism 2010 classification criteria for rheumatoid arthritis (RA) during the first year. Analyses were performed per location. OR = odds ratio; 95% CI = 95% confidence interval; MCP5 = metacarpophalangeal joint 5.

† Local synovitis of the wrist is defined as synovitis in at least 1 of the following joints: the distal radioulnar joint, the radiocarpal joint, or the intercarpal and carpometacarpal joints. without RA, extensor tendon involvement at the MCP joints always coexisted with local synovitis, while isolated extensor tendon involvement at MCP2, MCP3, and MCP4 was seen in 11–25% of the RA patients (Table 4). Inflammation was seen in the absence of local synovitis in the flexor tendons at the MCP joints, which have a tenosynovium, in up to 31% and 33% of RA patients and non-RA patients, respectively (Table 4). Three areas in the wrist were scored for synovitis and each tendon (group) was scored as a whole, hampering adequate assessment of the relationship between synovitis and tenosynovitis. Nonetheless, tenosynovitis without any synovitis in the wrist was uncommon (range 0–12%) (data are available from the author upon request).

Location	All	RA	non-RA
Flexors			
Flexors MCP 2	73.3	68.8	78.6
Flexors MCP 3	82.1	81.3	82.6
Flexors MCP 4	84.2	100.0	76.9
Flexors MCP 5	69.6	71.4	66.7
Extensors			
Extensors MCP 2	83.3	80.0	100.0
Extensors MCP 3	96.0	88.9	100.0
Extensors MCP 4	77.8	75.0	100.0
Extensors MCP 5	100.0	100.0	100.0

Table 4 Frequency of local MRI-detected synovitis at locations with MRI-detected tenosynovitis at the MCP joints $\!\!\!\!\!\!^*$

* Values are the percent. MRI = magnetic resonance imaging; MCP =metacarpophalangeal; RA = rheumatoid arthritis.

Association between tenosynovitis and features of RA severity

Last, we studied whether MRI-detected tenosynovitis within the group of RA patients is a feature of more severe disease, reflected by anti– citrullinated protein antibody (ACPA) positivity and radiographic progression in the first year. Tenosynovitis scores at baseline were studied. The total tenosynovitis score did not differ significantly between ACPA-positive and ACPA-negative RA patients (median 3 and 3, respectively; P = 0.52). The mean progression in total SHS, the combination of the erosion and narrowing scores in both the hands and feet, over 1 year was 1. There was no correlation between the total tenosynovitis score and progression of the total SHS during the first year (Spearman's p = 0.081; P = 0.55). Because of the low level of radiographic progression, it was not possible to compare tenosynovitis with structural damage at specific locations. For instance, only 2 patients had radiographic progression at the ulna of the extensor carpi ulnaris was associated with local structural damage.

Sensitivity analysis

In the analyses described above, tenosynovitis was considered to be present in cases in which both readers assigned a score of at least 1. We also performed analyses in which tenosynovitis at a specific location was considered to be present

in cases in which both readers assigned a score of 2 or higher.

Given this more stringent cutoff, the prevalence of tenosynovitis at any location was 8.4% in the total group of patients with early arthritis, 6% in patients with arthritides other than RA, and 13% in patients with RA (P = 0.078). The locations with the highest frequency of tenosynovitis scored >2 were the tendon of the extensor carpi ulnaris at the level of the wrist joints and the flexor tendons of the second finger at the level of the MCP joints. Using this more stringent cutoff, the frequency of tenosynovitis at individual locations was too low to perform further analyses.

Discussion

This study aimed to explore MRI-detected tenosynovitis at the wrist and MCP joints in early arthritis. We observed that MRI-detected tenosynovitis was present in 65% of all patients with early arthritis and that the flexor tendons at MCP5 and the extensor tendons at MCP2 and MCP4 and in the first extensor compartment of the wrist were more frequently affected in RA than in other arthritides; these locations were independent of the presence of local synovitis.

A strength of this study is that it was performed in a large inception cohort of patients with early arthritis, implying that the test characteristics observed may be generalizable to the diagnostic process in patients with early arthritis in daily practice. Other advantages are that tendons were not only assessed at the level of the wrist, but also at the level of the MCP joints, that analyses were done for all tendons, and that the number of patients in this study was larger than that in previous MRI studies.^{9,11,12,17}

Interestingly, in our study, inflammation of the extensor tendons at the level of the MCP joints was only seen in combination with local synovitis in patients with early arthritis with diagnoses other than RA. The presence of synovitis in an MCP joint might affect the overlying, closely related extensor tendons due to continuous inflammation. The fact that there is no tendon sheath demarcating and protecting the finger extensor tendon might explain the high correlation between synovitis and extensor tendon involvement. In an ultrasound and MRI study, inflammation at the extensor tendon sheath, the flexor carpi ulnaris tendon, was never scored positive in any of the patients with early arthritis in this study. Its relatively separate location with its insertion at the pisiform might be an explanation for this. In contrast to the finding in arthritides other than RA, in patients with RA, inflammation of the extensor tendons at the MCP joints also occurred in isolation, without underlying synovitis of these joints. This suggests a direct effect of RA, which is not related to the synovium or tenosynovium.

Notably, this study evaluated MRI-detected tenosynovitis and not clinically detectable tenosynovitis; the latter variable was not recorded. Since the large majority of the MRI-detected tenosynovitis lesions had a score of 1, we anticipate that the large majority of these tenosynovitis lesions were not clinically detectable.

This study has several limitations. Although it is the largest study to date of

MRI-detected tenosynovitis, it was not large enough to make comparisons for diagnoses other than RA, such as psoriatic arthritis or spondyloarthritis. A second limitation is that there was little radiographic damage progression. This could be due to the short followup period, but it is likely that treatment effects occurred as well. Larger longitudinal studies are required to validate our findings and explore the prognostic value of MRI-detected tenosynovitis in more detail. A high prevalence of tenosynovitis of the extensor carpi ulnaris tendon and the flexor tendons of digits 2 and 3 was found in our patients. The inclusion of a control group could have given more insight into the prevalence of tenosynovitis secondary to overuse.

Finally, it should be considered that the MRI scanning and the scoring method used are sensitive and that most lesions had the lowest positive MRI score of 1. To prevent false-positive scores, tenosynovitis was only considered to be present in cases in which both readers assigned a score of at least 1. Discordant scores were regarded as negative. When scores of >2 were defined as positive, the prevalence of tenosynovitis was considerably lower.

MRI is increasingly used instead of radiographs as an outcome measure in randomized clinical trials. The advantage of MRI is its sensitivity to measure inflammation and structural damage, which might increase the power to find differences between treatment groups. Tenosynovitis is increasingly assessed in trials.¹⁸ Although the predictive value of bone marrow edema and synovitis for future radiologic joint destruction is known, the prognostic value of tenosynovitis in this respect is unknown. In a cross-sectional analysis, we did not find higher tenosynovitis scores in ACPA-positive RA patients, a group that is characterized by more severe joint destruction. In addition, we found no correlation between the severity of tenosynovitis and radiographic progression during the first year of the disease. As mentioned above, larger studies with longer followup are needed to determine the prognostic value of tenosynovitis. However, since the presence of radiographic progression during the first year is strongly associated with long-term radiologic progression, the present data suggest that MRI-detected tenosynovitis is less relevant with regard to the long-term disease outcome than are bone marrow edema and synovitis.¹⁹ The question remains whether evaluating MRI-detected tenosynovitis is of value in clinical practice. We observed that tenosynovitis at several locations is associated with RA independently of the presence of local MRI-detectable synovitis. Further studies are needed to evaluate the value of MRI-detected local inflammation in determining the prognosis of patients with early undifferentiated arthritis.

In conclusion, when considering the tendons and tenosynovial sheaths of the hand and wrist in early arthritis, we observed that any sign of inflammation was frequently present in early arthritis and in particular in RA. Locations with a high specificity for RA are the tendons of the flexors at MCP5, the extensors at MCP2 and MCP4, and the first extensor compartment of the wrist.

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References

- 1 Colebatch AN et al. Ann Rheum Dis Published Online First: 21 March 2013.
- 2 Group AC of RRACTTFI et al. *Arthritis Rheum* 2013;65:2513–2523.
- 3 Østergaard M et al. J Rheumatol 2003;30:1385-6.
- 4 Haavardsholm EA et al. Ann Rheum Dis 2008;67:794–800.
- 5 Hetland ML et al. Ann Rheum Dis 2009;68:384–90.
- 6 Haavardsholm EA et al. Ann Rheum Dis 2007;66:1216–20.
- 7 Doyle JR. Lippincott Williams & Wilkins 2003.
- 8 Krabben A et al. Ann Rheum Dis 2013;74:506–12.
- 9 Eshed I et al. *Rheumatology* 2009;48:887–91.
- 10 Narváez J et al. Semin Arthritis Rheum Published Online First: 15 May 2012.
- 11 Navalho M et al. *Radiology* 2012;264:823–33.
- 12 Boutry N et al. J Rheumatol 2003;30:671–9.
- 13 de Rooy DPC et al. *Rheumatology* 2011;50:93–100.
- 14 Aletaha D et al. Arthritis Rheum 2010;62:2569–81.
- 15 Østergaard M et al. Ann Rheum Dis 2005;64 Suppl 1:i3-7.
- 16 Heijde DVD et al. The Lancet 1989;333:1036-8.
- 17 Wakefield RJ et al. Arthritis Care Res 2007;57:1158–1164.
- 18 Axelsen MB et al. Ann Rheum Dis Published Online First: 10 January 2014.
- 19 Lindqvist E et al. Ann Rheum Dis 2003;62:611–6.
- 20 Scheldrup EW. Surg Gynecol Obstet 1951;93:16–22.