

Diagnostics and imaging procedures

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JOINT TENDERNESS AND ULTRASOUND INFLAMMATION IN EARLY RHEUMATOID ARTHRITIS PATIENTS INCLUDED IN THE ARCTIC TRIAL

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Background: A tender joint count is part of most disease activity scores and remission criteria in rheumatoid arthritis (RA). A recent study found that tender joint count might not reflect inflammatory activity, assessed by ultrasound, in established RA (1).

Objectives: To explore if tender non-swollen joints is associated with sub-clinical inflammation, assessed by ultrasound, in DMARD-naïve early RA patients.

Methods: DMARD-naïve RA patients with <2 years symptom duration from first swollen joint and indication for DMARD treatment were included in the ARCTIC trial (2). For the current analyses we used data from the baseline examination, including a tender joint count assessed by Ritchie Articular Index and a 44-swollen joint count. The Ritchie Articular Index treat certain joints as a single unit (as the MCP-joints), and scoring of tenderness in joints and joint groups is graded 0-3. All patients underwent an ultrasound examination of 34 joints, with a semi-quantitative 0-3 score for power Doppler in each joint. An ultrasound atlas was available for reference (3). We predefined the wrist and the MCP 1-5 joints as joint areas of interest since they are commonly involved in RA and were assessed both clinically and by ultrasound. We selected only joints that were clinically non-swollen, and assessed the association between joint tenderness and ultrasound power Doppler signal by mixed logistic regression models with patient-specific intercept to adjust for within-patient dependencies. The analyses were repeated using generalized estimating equations for robustness. The frequency and odds ratio (OR) of ultrasound power Doppler activity (yes/no) in tender non-swollen wrists compared to non-tender non-swollen wrists were calculated. Similar analyses were performed for the MCP joints.

Results: A total of 222 patients with complete baseline data were included. 63% were female, median [SD] age 53.6 [41.2, 62.3], symptom duration 5.8 [2.9, 10.4] months, swollen joint count 9 [4, 15], joint tenderness 7 [4, 13] and power Doppler score 7 [3, 14]. Of 444 wrists, 268 were not swollen. The frequency of power Doppler signal >0 in tender non-swollen wrists were 50% (18/36), compared to 23% (53/232) in non-tender non-swollen wrists (p-value for comparison = 0.001). This corresponds to an OR of 4.32 (95% CI 1.47 to 12.65, p=0.008) for power Doppler signal if the wrist is tender but not swollen, compared to a non-tender non-swollen wrist. Similar results were found for the non-swollen MCP-joints (Table).

Table: The frequency and odds ratio (OR) of ultrasound power Doppler (PD) activity in Ritchie positive versus Ritchie negative non-swollen wrists and MCP joints.

	PD-signal positive if Ritchie positive	PD-signal positive if Ritchie negative	OR (CI)	p-value
Non-swollen wrist, n=268	18/36 (50%)	53/232 (23%)	4.32 (1.47 to 12.65)	0.008
Non-swollen MCP joints, n=165	15/35 (43%)	28/130 (22%)	4.84 (1.31 to 17.89)	0.02

Conclusion: Ultrasound power Doppler activity was more frequent in non-swollen wrists and non-swollen MCP joints if the joints had been scored as tender or painful by Ritchie Articular Index. Our findings indicate that in early RA patients, tenderness might reflect inflammation which is not detectable clinically.

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MRI-DETECTED DIGIT FLEXOR TENOSYNOVITIS IN BILATERAL PROXIMAL INTERPHALANGEAL JOINTS CONTRIBUTE TO JOINT TENDERNESS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Independent predictive value of ultrasonography-detected digit flexor tenosynovitis has been reported for rheumatoid arthritis (RA) development in patients with early arthritis, and it also was reported as an independent risk factor of flare in remission RA. However, proximal interphalangeal joints (PIPJs) were scarcely evaluated by MRI, nor recommended by RAMRIS so far.

Objectives: To explore the characteristics of MRI-detected inflammation in bilateral PIPJs in early RA patients and its clinical significance.

Methods: Early RA patients who fulfilled 2010 ACR/EULAR classification criteria with disease duration ≤1 year and DAS28-CRP ≥2.6 were recruited. New methodology of 3.0T whole-body MRI with contrast-enhanced imaging was used to scan bilateral hands simultaneously. MRI tenosynovitis, synovitis and osteitis were scored referring to the 2016 updated RAMRIS. Clinical data were collected.

Results: 1) Among 75 patients recruited, the median age was 49 years old (IQR: 38-59) with 71% female. The median disease duration was 7 months (IQR: 3-12) and the mean DAS28-CRP was 5.1 (IQR: 4.2-6.1). Forty-four patients (59%) were treatment-naïve who had never taken any DMARDs or glucocorticoids before recruitment. Both joint tenderness and swelling were present the most frequently in PIPJ2 and PIPJ3 (48% 61% and 43% 56%, respectively, Figure 1A). 2) MRI tenosynovitis, synovitis and osteitis were detected in 84%, 100% and 83% of the patients; and respectively in 21% 44%, 43% 56% and 5% 11% of various PIPJs. There were 12% 30%, 28% 40%, and 2% 8% of PIPJs without tender or swollen showing MRI tenosynovitis, synovitis and osteitis respectively. When non-dominant hands were used as self-control, the frequency of digit flexor tenosynovitis in dominant interphalangeal joint (IPJ) of thumb, PIPJ2 and PIPJ4 was 16% 18% higher than the non-dominant counterparts, indicating a potential impact of overuse on dominant tenosynovitis. 3) Tenosynovitis affects periarthral digit flexor tendon compartment and 65% 87% of tenosynovitis in PIPJs occurred together with synovitis in joint cavity and/or osteitis in subchondral bone. Among tender IPJ of thumb, 50% of them showed MRI synovitis together with digit flexor tenosynovitis, which was significantly more than those who showed MRI synovitis alone (21%, Chi-square test, p<0.017). Similar trend was found in tender PIPJ2 (45% vs. 26%, p<0.01). Generalized Estimating Equations with multivariate logistic regression showed not only MRI synovitis but also digit flexor tenosynovitis in bilateral PIPJs independently had more than twice probability of joint tenderness (both p<0.01, Figure 1B).

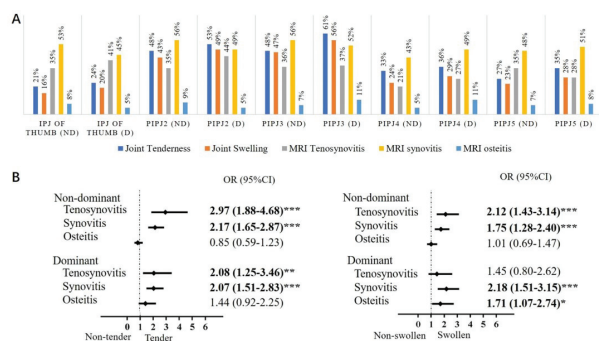


Figure 1 The prevalence and concordance between inflammation detected by MRI and physical examination in various proximal interphalangeal joints (PIPs) of early RA patients. **A:** The prevalence of joint tenderness, MRI tenosynovitis, synovitis and osteitis per PIP. **B:** Generalized Estimating Equations with multivariate logistic regression were used to show the contribution of MRI tenosynovitis, synovitis and osteitis to joint tenderness or swelling. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Conclusion: This preliminary study showed MRI-detected digit flexor tenosynovitis in bilateral PIPJs contributed to joint tenderness in early RA patients independently of synovitis which should not be ignored in clinical practice.

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U9: A NOVEL CLINICALLY ORIENTED ULTRASONOGRAPHIC SCALE FOR ASSESSING DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Musculoskeletal Ultrasonography (MSUS) is now a widely used tool for the monitoring of rheumatoid arthritis (RA). Although there are many proposed sets of composite scores, a fixed set of joints may not be an ideal tool to assess a disease like RA which affects many joints and tendons in different presentations.

Objectives: To assess the correlation of 3 proposed ultrasonographic composite scores with disease activity indices.

Methods: Three different composite scores were proposed by the first author, the first score (modified U8 score) which included bilateral wrists, 2nd MCP, 3rd MCP and knees which of the same set of joints proposed by Yoshimi et al 2015 with a modification of scoring of each joint according to EULAR/OMERACT combined score so the range of scores (0-24). The second score (U9) was the same of the modified U8 score plus scoring the most clinically affected joint or tendon (one joint or one tendon) so the range of score (0-27). The third proposed score (8+2) was the same of the modified U8 score plus scoring the 2 most clinically affected joint or tendon (one joint and one tendon or 2 joints or 2 tendons) so the range of score (0-30). All targeted joints were evaluated by grey-scale (GS) and power Doppler (PD) ultrasound using EULAR/OMERACT combined score (0-3). Targeted tendons were scored (0-3) by either -scale (GS) and power Doppler (PD) ultrasound and the highest score was used.

One hundred and fifty four RA patients diagnosed according to ACR/EULAR criteria were recruited for the present study. A total of 154 patients with RA were included. Disease activity was assessed by clinical disease activity indices (CDAI and DAS28 ESR). Functional status was assessed by health assessment questionnaire (HAQ).

Results: In the cross-sectional cohort with 154 patients, correlation between the modified (U8) score and clinical disease activity parameters (CDAI and DAS28) was significant but modest ($r=0.3$, $P=0.03$ and $r=0.4$, $P=0.01$) respectively. The same was true for the (U 8+2 score) ($r = 0.41$, $P = 0.0001$, $r=0.4$, $P=0.005$). The 8+1 (U9 score) gave the best positive correlation with CDAI and DAS28 ($r=0.7$, $P<0.001$, $r=0.6$, $P<0.001$) respectively.

HAQ was highly correlated with U9 score ($r=0.7$, $P<0.001$) and moderately correlated with U8+2 score ($r=0.3$, $P=0.05$) and not correlated with the modified 8 score.

Conclusion: The U9 score gave the best correlation with disease activity parameters. It is simple and applicable and gives a high degree of flexibility to the sonographer according to the clinical picture.

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ASSESSING SYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS BY ULTRASOUND – AN AGREEMENT STUDY EXPLORING THE MOST ACTIVE SIDE

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Background: Though ultrasound examination of all RA patients - if offered a very tight clinical control - may not be necessary for obtaining clinical remission (1,2), there are still patients where ultrasound may have a role in monitoring disease activity. Scoring synovitis unilaterally will by far reduce the examination time, however, no consensus exists on how to choose the side to be examined and if one side per se is always the most inflamed side.

Objectives: To assess ultrasound (US) inflammation and sensitivity to change in hands, aiming to identify if the right hand, the dominant hand, or the hand with more clinically swollen joints (SwJ) is per se the most inflamed and more sensitive to change, and hence the preferred side for unilateral scoring of synovitis by US in rheumatoid arthritis (RA) patients.

Methods: This is an agreement study exploring the impact on US scoring methods in a longitudinal study of early RA (ARCTIC trial, n=230) and established RA (ULRABIT trial, n=212) patients initiating conventional and biological Disease Modifying Anti-Rheumatic Drugs, respectively. Tender and swollen joint count for 28 joints (TJC28 and SJC28) and C-reactive protein (CRP mg/L) were obtained. Using the hands as model, bilateral MCP 1-5, PIP 2+3 and wrists were evaluated by US using a 0-3 scoring system for grey-scale (GS) and power Doppler (PD) US according to the atlas by Hammer et al. (3) GS sum score, PD sum score and global synovitis score (GLOESS) were calculated for each hand (0-30). According to our prespecified protocol a reasonable equivalence margin in this study (agreement between groups) was defined to correspond to a 95% Confidence Interval around the observed paired mean difference: -2.99 to +2.99.

Table						
Ultrasound inflammatory activity in the dominant hand versus non-dominant hand, in the hand with clinically more swollen joint versus less swollen joints and the right versus left hand using different ultrasound composite scores						
Baseline			Change values from baseline to 3 months			
GS sum score (0-30)	Doppler sum score (0-30)	GLOESS (0-30)	Δ GS sum score (0-30)	Δ Doppler sum score (0-30)	Δ GLOESS (0-30)	
Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	
*Dominant Hand (n=232)						
Dominant	7.70 (7.09 to 8.40)	4.81 (4.26 to 5.35)	5.07 (3.39 to 6.75)	-3.11 (-3.65 to -2.57)	-2.57 (-3.10 to -2.04)	0.40 (-0.99 to 2.82)
Non-Dominant	7.08 (6.41 to 7.72)	4.22 (3.68 to 4.76)	7.28 (6.60 to 7.96)	-3.12 (-3.66 to -2.58)	-2.35 (-2.88 to -1.82)	-0.29 (-0.87 to 2.71)
Difference	-0.69 (-1.61 to 0.24)	-0.58 (-1.35 to 0.20)	-0.79 (-1.76 to 0.18)	0.005 (-0.76 to 0.75)	0.22 (-0.52 to 0.96)	0.11 (-0.70 to 0.92)
P-value	0.13	0.14	0.11	0.99	0.57	0.79
*Clinical Hand (swollen joints) (n=314)						
Worst Clinical (lowest SJC)	5.51 (7.57 to 9.16)	5.37 (4.83 to 5.91)	8.83 (8.16 to 9.50)	-3.79 (-4.32 to -3.25)	-3.05 (-3.57 to -2.52)	-4.06 (-4.63 to -3.49)
Least Clinical (highest SJC)	6.30 (5.65 to 6.94)	3.66 (3.13 to 4.20)	6.52 (5.85 to 7.19)	-2.43 (-2.96 to -1.92)	-1.87 (-2.40 to -1.35)	-2.64 (-3.21 to -2.06)
Difference	-0.78 (-1.52 to -0.10)	-1.70 (-2.47 to -0.94)	-2.31 (-3.26 to -1.36)	1.34 (0.60 to 2.08)	1.17 (0.44 to 1.91)	1.43 (0.63 to 2.22)
P-value	<0.001	<0.001	<0.001	0.0004	0.002	0.0005
*Hand side (n=437)						
Right side	7.70 (7.12 to 8.44)	4.82 (4.28 to 5.37)	8.12 (7.44 to 8.80)	-3.19 (-3.73 to -2.65)	-2.64 (-3.17 to -2.11)	-3.49 (-4.07 to -2.91)
Left side	7.08 (6.37 to 7.68)	4.21 (3.6 to 4.76)	7.23 (6.55 to 7.91)	-3.05 (-3.59 to -2.51)	-2.38 (-2.81 to -1.93)	-3.21 (-3.78 to -2.63)
Difference	-0.75 (-1.60 to -0.10)	-0.61 (-1.36 to -0.16)	-0.89 (-1.85 to -0.06)	0.14 (-0.61 to 0.89)	0.26 (-0.38 to 1.10)	0.28 (-0.32 to 1.09)
P-value	0.11	0.12	0.07	0.71	0.34	0.49

*Analysed using a factor for the specific analysis, and trial (ARCTIC and ULRABIT, respectively) as a fixed effect, and the patient-ID was applied as a random effect