# Sonographic evaluation of enthesopathy in rheumatoid arthritis patients

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**Background**
Rheumatoid arthritis (RA) is one of the most common autoimmune diseases. It affects mainly the synovial membranes of the small joints. However, it may also have extra-articular manifestations. Enthesopathy may occur as one of the extra-articular manifestations of RA and is not clinically detected. Ultrasound (US) is a relatively new tool for the detection of enthesopathy.
**Aim**
The aim of this study was to assess the presence and distribution of enthesopathy in RA patients using US.
**Patients and methods**
Twenty-nine consecutive patients with RA and 14 age-matched healthy controls were included in this study. All RA patients met the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA. Six entheses sites were evaluated using gray scale and Doppler US with a linear transducer and were scored using the Madrid Sonography Enthesitis Index (MASEI).
**Results**
US detected the presence of enthesopathy in patients with RA. There was a statistically significant difference in the enthesopathy score of plantar aponeurosis insertion and Achilles tendon insertion. The total enthesopathy score was statistically significant in patients with RA versus controls.
**Conclusion**
US entheseal abnormalities are present in a high percentage of RA patients. US enthesopathy is not associated with disease activity in RA patients.

**Keywords:**
enthesitis, enthesopathy, rheumatoid arthritis, ultrasonography

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## Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects mainly synovial membranes of small joints [1]. It is the most common cause of inflammatory arthritis [2]. The prevalence of RA is believed to range from 0.4 to 1.3% worldwide [3]. Although classified as an inflammatory arthritis, extra-articular involvement in RA is common [4].

Enthesopathy is associated with inflammation at the site of tendons or ligaments in the bone. It is a common feature of seronegative spondyloarthropathy [5]. However, clinical detection of enthesopathy is to some extent challenging because of low sensitivity and specificity of clinical testing [6].

Ultrasound (US) and MRI are tools for detecting the signs of inflammatory and chronic changes that may occur in the case of enthesopathy [7]. However, US seems to be better because of easy detection, low cost, and less technical adjustments [8].

There are limited data regarding US evaluation of enthesitis in RA. Thus, it is necessary to evaluate enthesopathy in RA by using US. The objective of this study was to find the prevalence of entheses involvement in RA patients by using US.

## Patients and methods

Twenty-nine consecutive RA patients were consecutively recruited from our outpatient clinic. The inclusion criteria were: patients of more than 18 years of age and those who met the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA [9]. We excluded patients who had diabetes, spondyloarthropathy, or other associated connective tissue disease, or any patient who had



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sport activity or received fluoroquinolone therapy during the previous 6 months or had clinically evident peripheral neuropathy of lower limbs. Fourteen healthy controls within the same age range that did not have any known musculoskeletal diseases were recruited from the hospital staff or visitors. The local ethics committee approved the study and informed consent was obtained from the patients and controls.

Educational level was grouped as illiterate, primary school, secondary school, intermediate diploma, high graduate, graduate, postgraduate, professional. Disease activity score 28 (DAS28) was used to assess RA disease activity in all patients [10].

All patients with RA and the healthy controls underwent an US examination by an experienced rheumatologist (5-years experience of musculoskeletal US) on EDAN U 2 US machine with linear transducer (8–13.4 MHz), manufactured by Edan healthcare company, Pingshan District, Shenzhen, China. The examiner was blind to the data of the patients and controls. Power Doppler settings were standardized with a pulse repetition frequency of 0.75–1.20 kHz and a power Doppler gain of 50–55 dB with a lower wall filter.

Six entheses sites (proximal plantar aponeurosis, distal Achilles tendon, distal and proximal patellar ligament insertion, distal quadriceps tendon, distal triceps tendon) were scanned bilaterally in axial and longitudinal planes as described by de Miguel [6]. The Madrid Sonography Enthesitis Index (MASEI) was used for entheses scoring [6]. In this scoring system, the following lesions were evaluated (all scorings and measurements were made during examination and images were stored): calcifications, erosions, bursitis, power Doppler signal in enthesis sites, and tendons/ligaments structure and thickness. Calcifications were scored as 0 if absent; 1 if a small calcification or ossification was present; 2 if there was clear presence of enthesophytes; or 3 if large calcifications and ossifications were present. Bursitis was scored as 0 if absent or 1 if well circumscribed, localized anechoic, or hypoechoic area was detected at the site of a bursa. Bony erosion was defined as a cortical breakage with a step-down bone contour defect (scored as 0 if absent and 3 if present). Power Doppler signal was scored as 0 if absent or 3 if present. Tendon/ligament structure was defined as pathological if there is loss of fibrillar pattern or hypoechoic aspect or fusiform thickening occurred (scored 0 or 1). Tendon and ligament thicknesses were measured at the point of maximal thickness on the bony insertion. Thicker tendons/ligaments were defined as (a thickness of>6.1 mm for quadriceps tendon, 5.29 mm for Achilles tendon, 4.4 mm for plantar aponeurosis, 4.3 mm for triceps tendon, and 4 mm for both proximal and distal patellar ligaments) [6].

Statistical analyses were performed using the statistical package for the social sciences (SPSS 20.0; IBM, Armonk, New York, USA). Descriptive statistics were used to compute the mean and SD for continuous variables and proportion for categorical variables. Student's *t*-test and Mann–Whitney *U*-test were used to compare patient and control groups. $\chi^2$ or Fisher's exact test was used to compare the difference between proportions. The relationship between parameters was analyzed using Pearson's and Spearman's correlation coefficients. Test results with *P* value less than 0.05 were considered statistically significant.

## Results

The study population included 29 RA patients and 14 healthy controls. We scanned 348 enthesis sites in patients with RA and 168 in healthy controls. The RA patients included 22 (75.9%) women and seven

**Table 1 Comparison of Madrid Sonographic Enthesitis Index scores and tendon or ligament thickness**

| | Rheumatoid arthritis (*n*=58) | Control (*n*=28) | *P* |
|---|---|---|---|
| Plantar aponeurosis thickness (mm) | 3.6±0.71 | 3.6 ±0.87 | 0.364 |
| Achilles tendon thickness (mm) | 4.8±0.72 | 4.5±061 | 0.406 |
| Distal patellar ligament thickness (mm) | 3.9±0.81 | 3.7 ±0.73 | 0.719 |
| Proximal patellar ligament thickness (mm) | 4±0.64 | 3.8 ±0.71 | 0.872 |
| Quadriceps tendon thickness (mm) | 5.7±1.1 | 6.2 ±0.68 | 0.141 |
| Triceps tendon thickness (mm) | 4.2±0.74 | 4.1 ±0.66 | 0.307 |
| MASEI proximal plantar aponeurosis insertion | 0–8 | 0–3 | 0.005 |
| MASEI Achilles tendon insertion | 0–5 | 0–1 | 0.009 |
| MASEI distal patellar ligament insertion | 0–5 | 0–4 | 0.412 |
| MASEI proximal patellar ligament insertion | 0–7 | 0–5 | 0.08 |
| MASEI quadriceps tendon insertion | 0–5 | 0–1 | 0.700 |
| MASEI distal triceps tendon insertion | 0–6 | 0–1 | 0.651 |
| MASEI total score | 0–23 | 0–5 | <0.000 |

MASEI, Madrid Sonography Enthesitis Index.

**Table 2 Presence of abnormalities suggesting enthesopathy**

| | Rheumatoid arthritis [*n* (%)] | Control [*n* (%)] | *P* |
|---|---|---|---|
| At least one thicker tendon/ligament | 44 (75.9) | 19 (76.9) | 0.432 |
| At least one structural change | 36 (62.1) | 8 (28.6) | 0.004 |
| At least one erosion | 13 (22.4) | 2 (7.1) | 0.08 |
| At least one bursitis | 6 (10.3) | 1 (3.6) | 0.282 |
| At least one calcification | 14 (24.2) | 3 (10.7) | 0.143 |
| At least one PD signal | 18 (31) | 0 | 0.001 |

(24.1%) men, while the healthy controls included 13 (92.9%) women and only one (7.1%) male (*P*=0.077). The mean age of patients with RA and healthy controls was 43.06±15.19 and 40.14±14.85 years, respectively (*P*=0.156). For the RA group, the range of RA duration was 1– 29 years, the disease activity score 28 (DAS28-ESR) was 3.6±1.6. Twenty (69%) of RA patients were using methotrexate, while only 13 (44.8%) were receiving antimalarial drugs. Only three (10.3%) patients were on low-dose steroids. Two (6.9%) were receiving azathioprine. Only one (3.4%) was on biological therapy in the form of weekly subcutaneous dose of 50 mg etanercept.

There were no statistically significant difference in the thickness of tendons or ligaments between RA patients and the control group.

MASEI scores of plantar aponeurosis and Achilles tendon were higher in patients with RA compared with those in the control group. However, there was no statistically significant difference in MASEI scores of distal and proximal patellar tendon, quadriceps tendon insertion, nor distal triceps tendon insertion. However, MASEI total score was higher in patients with RA than the control group (Table 1). Table 2 represents the presence of abnormalities suggestive of enthesopathy .The distribution of the enthesopathy sites at six locations are represented in Table 3. Figure 1 shows the relationship between the enthesitis score and DAS28. Figure 2 shows the sonographic findings at plantar aponeurosis in patients with RA.

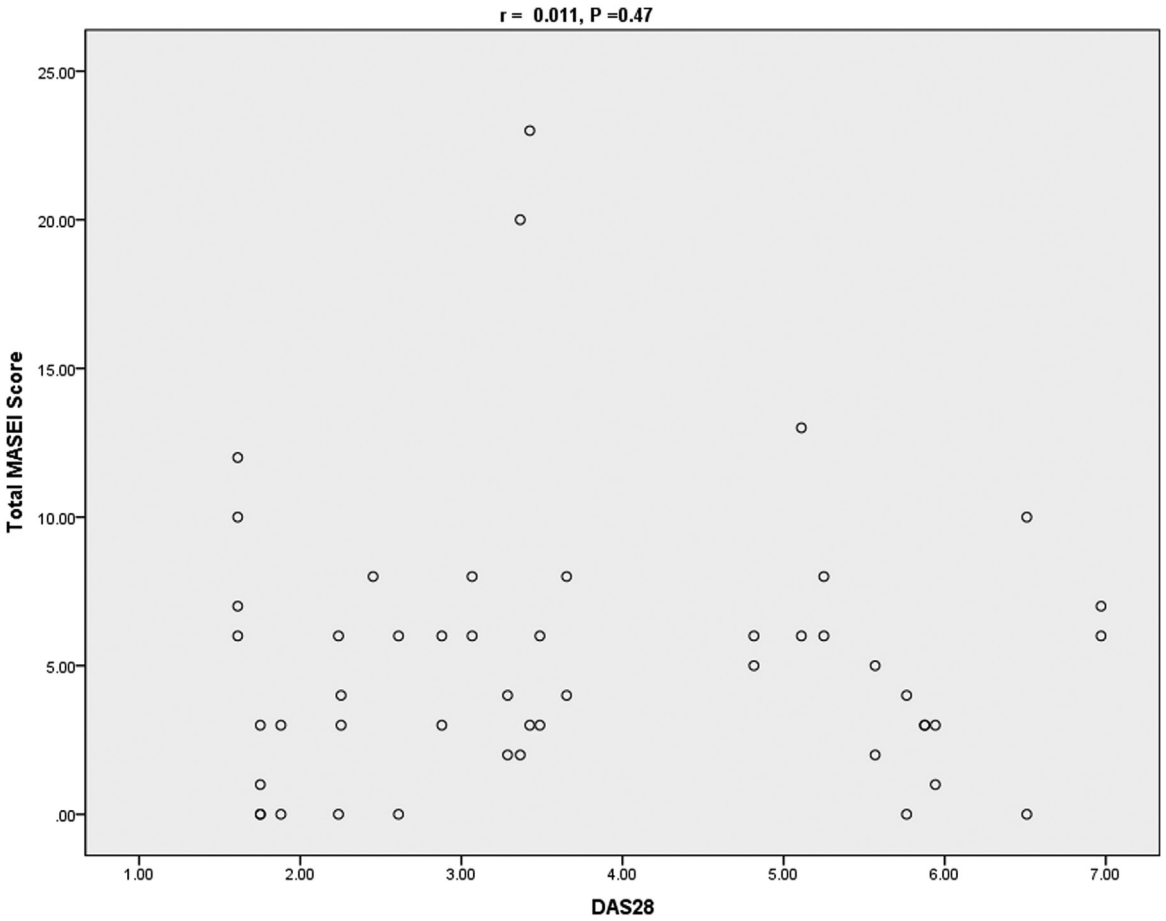
## Discussion

RA is the most common inflammatory arthritis. It affects about 1% of the general population [11]. Synovitis is the most prominent clinical abnormality in RA. Extra-articular components like bursae or tendon sheaths can also be affected in patients with RA. There are a wide variety of clinical manifestations that occur in patients with RA which may be

**Table 3 Distribution of enthesopathy between groups**

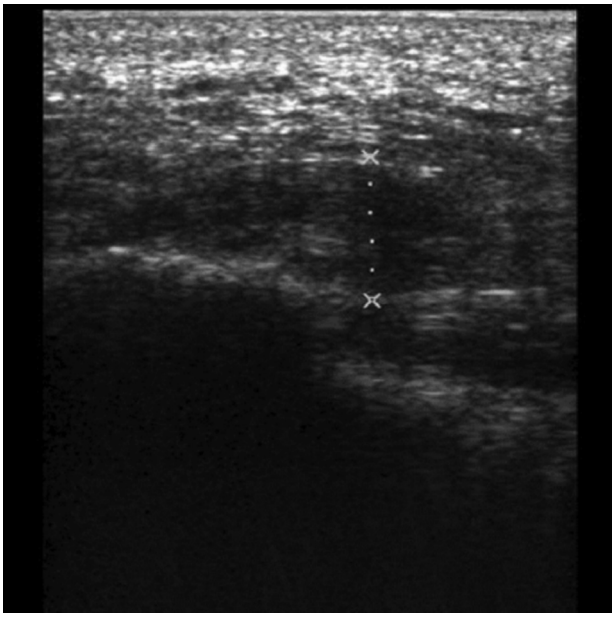
| | Plantar aponeurosis enthesis [*n* (%)] | | Achilles tendon enthesis [*n* (%)] | | Distal patellar ligament enthesis [*n* (%)] | | Proximal patellar ligament enthesis [*n* (%)] | | Quadriceps tendon enthesis [*n* (%)] | | Triceps tendon enthesis [*n* (%)] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Rheumatoid arthritis | Control | Rheumatoid arthritis | Control | Rheumatoid arthritis | Control | Rheumatoid arthritis | Control | Rheumatoid arthritis | Control | Rheumatoid arthritis | Control |
| Tendon/ligament structure pathology | 19 (32.8) | 2 (7.1) | 3 (5.2) | 0 | 13 (22.4) | 4 (14.3) | 17 (29.3) | 1 (3.6) | 9 (15.5) | 0 | 5 (8.9) | 1 (3.6) |
| Thicker tendon/ligament | 9 (15.5) | 2 (7.1) | 15 (25.9) | 1 (3.6) | 18 (31) | 6 (21.4) | 16 (27.6) | 7 (25) | 16 (27.6) | 14 (50) | 13 (22.4) | 8 (28.9) |
| Erosions | 2 (3.4) | 0 | 2 (3.4) | 0 | 2 (3.4) | 1 (3.6) | 3 (5.1) | 1 (3.6) | 3 (5.2) | 0 | 2 (3.4) | 0 |
| Enthesis calcification | 7 (12) | 1 (3.6) | 0 | 0 | 3 (5.1) | 1 (3.6) | 2 (3.4) | 1 (3.6) | 2 (3.4) | 0 | 1 (1.7) | 0 |
| Enthesis PD signal | 6 (10.3) | 0 | 2 (3.4) | 0 | 4 (6.9) | 0 | 9 (15.5) | 0 | 2 (3.4) | 0 | 3 (5.2) | 0 |
| Bursitis | | | 4 (6.9) | 1 (3.6) | 2 (3.4) | 0 | | | | | | |

**Figure 1**




Correlation between total scores of Madrid Sonographic Enthesitis Index (MASEI) and Disease Activity Score (DAS28) in patients with rheumatoid arthritis ($r = 0.011$, $P = 0.47$).

**Figure 2**



Sonographic findings at plantar aponeurosis in patients with rheumatoid arthritis.

subclinical [12] like entheseal abnormalities. However, there are only few studies about enthesopathy in patients with RA.

Enthesopathy has been regarded as the primary lesion in SpA [6]. Since clinical examination and conventional radiology are not sensitive nor specific for entheseal assessment, US becomes a valuable tool in detecting any signs of enthesopathy [13]. US gives a detailed information about active and chronic lesions affecting the entheses [14]. Two sonographic enthesitis indices have been described: GUESS [15] and MASEI [6]. We prefer MASEI as it evaluates the upper limb also.

In this study, gray scale and power Doppler US were used to evaluate six enthesis sites. There was no significant difference in the ligament or tendon thickness between patients with RA compared with those in the control group. MASEI score of proximal plantar aponeurosis insertion was significantly higher in patients with RA. In a study done by Genc *et al.*

[11], enthesophytes observed in plantar aponeurosis enthesis were not found more often in RA patients than healthy controls.

MASEI score of Achilles tendon insertion was significantly higher in patients with RA in comparison with the control group. Also, total MASEI score was significantly higher in RA patients.

With US evaluation of entheses: there was at least one structural change affecting ligaments or tendons in 62.1% RA patients in comparison to healthy controls. There was at least one PD signal at the entheses in 31% patients with RA. There was no significant correlation between the MASEI total score and DAS28.

MRI and US can be used for the evaluation of enthesopathy. However, MRI shows many disadvantages as it is expensive, with no dynamic studies or simultaneous examination of enthuses as US [16].

In addition to the relatively small number of patients, our study has some other limitations. There was no group including spondyloarthropathy patients as a comparative group. In addition, the cross-sectional design of the study was better to be longitudinal which would allow evaluation of the predictors and long-term outcome of enthesopathy in RA patients.

## Conclusion

US entheseal abnormalities are present in a high percentage of RA patients. US enthesopathy is not associated with disease activity in RA patients. We think that further studies are required to validate our results in RA.

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**Conflicts of interest**
There are no conflicts of interest.

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