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# Modification of a sonographic enthesitis score to differentiate between psoriatic arthritis and young healthy volunteers

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**Objectives:** We aimed to describe sonographic structural and inflammatory changes in entheses of patients with recently diagnosed psoriatic arthritis (PsA), patients with established PsA, and young healthy volunteers, and to investigate whether the MADrid Sonographic Enthesitis Index (MASEI) enables us to distinguish these groups in an extreme comparison.

**Method:** New and established PsA patients and healthy volunteers (aged 20–30 years) were recruited. The triceps, quadriceps, patellar, Achilles and elbow extensor tendon insertion, and plantar fascia entheses were investigated sonographically for structural changes, erosions, calcifications, increased thickness, bursitis, and power Doppler (PD) signal according to the MASEI.

**Results:** The study included 25 new and 25 established PsA patients, and 25 healthy volunteers. Increased thickness and PD signal in knee entheses were common for patients and healthy volunteers, while changes at other locations predominantly occurred in patients only. PD was recoded (1, one spot; 1.5, two or three spots; 2, confluent signal; 3, severe confluent signal) and thickness of knee entheses excluded. This resulted in different modified MASEI scores between PsA patients and young healthy controls: median (interquartile range) modified MASEI of 13 (10–22.5) in new PsA, 13.5 (9.5–18) in established PsA, and 3 (1–8.5) in healthy volunteers ( $p = 0.002$ ).

**Conclusions:** Structural ultrasound changes and PD in entheses are common in both new and established PsA and healthy controls. MASEI score did not differentiate PsA patients from young healthy volunteers. After recoding of PD severity and excluding thickness of knee entheses, marked differences between PsA patients and healthy controls were observed.

Enthesitis is an entry criterion of the CIASSification criteria for Psoriatic ARthritis (CASPAR) criteria (1). It is an inflammation of tendon, ligament, or joint capsule insertion, with an estimated prevalence of 25–78% (2). The presentation is similar to other tendon complaints that are quite common in the healthy population (3). Therefore, general practitioners, dermatologists, and rheumatologists do not always recognize the presence of enthesitis or its association with psoriatic arthritis (PsA) (2).

In research, enthesitis is scored by counting the number of tender entheses. Tenderness does not occur in inflammatory enthesiopathy alone (4, 5). Other means may help to differentiate inflammatory from non-inflammatory enthesal tenderness. Ultrasound can be used to investigate multiple superficially located entheses. Abnormalities can

be quantified with a combined score, for example the MADrid Sonographic Enthesitis Index (MASEI) (6).

The main objective of this cross-sectional study was to investigate the frequency of ultrasound changes at the entheses of patients with recently diagnosed PsA, patients with established PsA, and young healthy volunteers (aged 20–30 years). In this extreme comparison, we aimed to describe sonographic signs of enthesitis in clearly diseased and clearly non-diseased entheses. The secondary objective was to investigate whether an enthesitis score (using the MASEI) was able to distinguish between the three groups. We chose a control group of young healthy volunteers because their tendons have matured but have had limited exposure to the other causes of enthesiopathy.

## Method

### Patients and setting

Three groups of participants were investigated: new PsA patients, established PsA patients and healthy volunteers

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(aged 20–30 years). Consecutive newly diagnosed and established patients were included in hospitals in the south-west of the Netherlands. Established disease was defined as having been diagnosed with PsA for at least 2 years. Those patients were included irrespective of disease activity. To reduce the impact of age on ultrasound readings and clinical evaluation, an age limit of 55 years was set in the established PsA group. Healthy 20–30-year-old volunteers were recruited via advertisement at the medical faculty and by word of mouth. Exclusion criteria for healthy volunteers were familiar hypercholesterolaemia, diabetes mellitus, and having any rheumatological disease. Participants were recruited from May 2015 to January 2016. Written informed consent was obtained from all participants according to the Declaration of Helsinki. The study was approved by the local medical research ethics committee of Erasmus MC, University Medical Center Rotterdam, the Netherlands (MEC-2012-549).

### Data collection

Ultrasound examination of the entheses was performed by a trained sonographer (KW) who was blinded to the clinical information. An Esaote MyLab60 with the Probe LA-435 (6–18 MHz; Doppler frequency of 8.3 MHz, pulse repetition frequency of 750 Hz, and a wall filter of 3) and Probe LA-523 (4–13 MHz; 6.3 MHz, 750 Hz, and a wall filter of 4) was used. A colour gain was set at the disappearance of colour noise in the bone underneath the enthesis. The six MASEI locations and the common extensor insertion at the lateral epicondyle of the elbow [increased thickness cut-off 4.2 mm (7)] were assessed bilaterally. Each ultrasound location was scored for calcifications, erosions, increased thickness, structure, power Doppler (PD) signal, and bursitis, in accordance with the MASEI (6).

Positioning of patients followed the recommendations of the MASEI developers, but with the knee flexed at approximately 30° instead of 70° to improve PD signal

detection (8). The lateral epicondyle was examined in 90° elbow flexion. PD was scored with a semi-quantitative scoring system similar to the method used in arthritis (9): 0, absent; 1, one colour spot; 1.5, two colour spots; 2, confluent signal; and 3, severe signal (Supplementary Figure S1). Interrater agreement of rescoring was 93% and the weighted Cohen's kappa with linear weights was 0.92.

### Statistical methods

Simple descriptive techniques fitting the distribution were used to describe the study results and determine whether ultrasound data differed in the three groups, in STATA 14.0.

## Results

### Participants

In total, 75 participants were evaluated: 25 new PsA and 25 established PsA patients, and 25 young healthy volunteers. Median disease duration was 2.9 weeks in new PsA and 8.0 years in established PsA (Table 1). Median symptom duration of musculoskeletal complaints as reported by the new patients was 1.2 years [interquartile range (IQR) 0.6–3.1 years].

### Structural ultrasound findings

Calcifications were seen in all locations of entheses in patients, with the highest prevalence at the lateral epicondyle (entheses of new 56% vs established 28%), quadriceps tendon (68% vs 50%), and Achilles tendon (70% vs 56%) (Table 2 and Supplementary Table S1). In entheses of healthy volunteers, calcifications were seen far less frequently and they mainly occurred in the quadriceps tendon (30%). Increased thickness was seen at all locations in patient entheses, with the highest

Table 1. Characteristics of the participants in the three groups.

|  | New PsA<br>(n = 25) | Established PsA<br>(n = 25) | Healthy volunteers<br>(n = 25) |
|--|---------------------|-----------------------------|--------------------------------|
| Male, n (%)                            | 13 (52)             | 13 (52)                     | 12 (48)                        |
| Age (years), median (range)            | 52 (30–72)          | 44 (26–53)                  | 22 (20–26)                     |
| Time since PsA diagnosis, median (IQR) | 2.9 (0.7–5.3) weeks | 8.0 (5.0–11.0) years        |                                |
| Medication, n (%)                      |                     |                             |                                |
| DMARDs                                 | 4 (16)*             | 17 (68)                     |                                |
| Biologicals                            | 0 (0)               | 5 (20)                      |                                |
| Both DMARDs and biologicals            | 0 (0)               | 3 (12)                      |                                |
| LEI, median (IQR)                      | 1 (0–1)             | 1 (0–2)                     | 0 (0–0)                        |
| MASES, median (IQR)                    | 0 (0–4)             | 1 (1–3)                     | 0 (0–0)                        |

PsA, psoriatic arthritis; IQR, interquartile range; DMARD, disease-modifying anti-rheumatic drug; LEI, Leeds Enthesitis Index (range 0–6); MASES, Maastricht Ankylosing Spondylitis Enthesitis Score (range 0–13).

\*All DMARD use duration < 1 week.

Table 2. MAadrid Sonographic Enthesitis Index (MASEI) score per component per enthesitis location (n = 50 per group).

|                           | Structure |    |   | Thickness |    |    | Erosion |   |   | Calcification* |    |    | PD signal |    |    | Bursitis |   |   |
|---------------------------|-----------|----|---|-----------|----|----|---------|---|---|----------------|----|----|-----------|----|----|----------|---|---|
|                           | A         | B  | C | A         | B  | C  | A       | B | C | A              | B  | C  | A         | B  | C  | A        | B | C |
| Lateral epicondyle tendon |           | 4  |   | 80        | 74 | 20 |         |   |   | 56             | 28 | 8  | 36        | 34 |    |          |   |   |
| Triceps tendon            | 2         | 2  |   | 16        | 14 | 2  |         | 6 | 4 | 16             | 22 | 2  |           | 10 |    |          |   |   |
| Quadriceps tendon         | 2         | 8  | 2 | 66        | 56 | 50 |         |   | 2 | 68             | 50 | 30 | 28        | 30 | 34 |          |   |   |
| Proximal patella tendon   |           | 4  |   | 52        | 60 | 58 |         |   | 2 | 22             | 12 | 6  | 8         | 12 | 2  |          |   |   |
| Distal patella tendon     |           | 12 |   | 82        | 74 | 70 |         |   | 2 | 18             | 16 |    | 16        | 14 | 30 |          |   |   |
| Achilles tendon           |           |    |   | 8         | 26 |    | 4       | 8 | 4 | 70             | 56 | 8  | 8         | 10 | 2  | 8        | 6 |   |
| Plantar fascia            |           |    |   | 24        | 28 | 4  |         |   |   | 16             | 2  | 6  |           |    |    |          |   |   |

Data are shown as the number of abnormalities (%) per group.

PD, power Doppler; A, new psoriatic arthritis patients; B, established psoriatic arthritis patients; C, healthy volunteers.

\*Calcification is expressed as the number of tendons with a score > 0.

prevalence at the lateral epicondyle (entheses of new 80% vs established 74%) and at the knee entheses (prevalence range 52–82%). In healthy volunteers, only knee entheses had an increased thickness (range 50–70%).

#### Inflammatory ultrasound findings

The majority of patients and half of the healthy volunteers had a PD signal present in at least one enthesitis (Table 3). A PD score of 2 or more in at least one enthesitis was present in 52% of new and 44% of established PsA patients and in 28% of healthy volunteers. The lateral epicondyle and the quadriceps tendon were affected in one-third of the entheses in patients (Table 2). In healthy volunteers, one-third of the quadriceps entheses and distal patellar entheses showed a PD signal.

#### MASEI

The median MASEI score with the lateral epicondyle added was 18 (IQR 15–31) in new with PsA, 22 (IQR

15–27) in established PsA, and 10 (IQR 5–15) in healthy volunteers ( $p = 0.002$ ). As described before, the main contributors to the MASEI scores in healthy volunteers were increased thickness and PD signal in knee entheses. After we excluded knee enthesal thickness and used the new PD scores, the IQRs were no longer overlapping. The scores of the modified MASEI were 13 (IQR 10–22.5), 13.5 (IQR 9.5–18), and 3 (IQR 1–8.5,  $p = 0.002$ ) (Table 3).

#### Discussion

Sonographic changes in the entheses were observed in young, healthy volunteers, patients with recently diagnosed PsA, and patients with established PsA. Increased thickness and a subtle positive PD signal in knee entheses were common in healthy volunteers and patients, while abnormalities at other locations predominantly occurred in patients. After we excluded patellar tendon enthesitis thickness and applied a new method of scoring PD, the modified MASEI was able to distinguish between PsA patients and healthy controls. Furthermore,

Table 3. Outcome of the MAadrid Sonographic Enthesitis Index (MASEI) scoring system and different adjustments to the MASEI scoring system in the three participant groups.

|                               | New PsA<br>(n = 25) | Established PsA<br>(n = 25) | Healthy volunteers<br>(n = 25) |
|-------------------------------|---------------------|-----------------------------|--------------------------------|
| Ultrasound examination        |                     |                             |                                |
| MASEI*                        | 15 (11–25)          | 16 (11–26)                  | 10 (5–13)                      |
| PD                            |                     |                             |                                |
| PD in any enthesitis          | 76%                 | 96%                         | 56%                            |
| PD $\geq 2$ in any enthesitis | 52%                 | 44%                         | 28%                            |
| $\geq 3$ entheses with PD     | 20%                 | 32%                         | 24%                            |
| Amendments (stepwise)         |                     |                             |                                |
| + Lateral epicondyle          | 18 (15–31)          | 22 (15–27)                  | 10 (5–15)                      |
| – Quadriceps thickness        | 13 (11–28)          | 17 (12–23)                  | 5 (2–12)                       |
| Amending PD score†            | 13 (10–22.5)        | 13.5 (9.5–18)               | 3 (1–8.5)                      |

Data are shown as median (interquartile range) or percentage of participants.

PsA, psoriatic arthritis; PD, power Doppler signal.

\*Range 0–136. †Using new scoring system to award points for PD: 1a was given 1 point and 1b 1.5 points.

we showed that ultrasound abnormalities are already very common in early PsA.

The extreme contrast we expected between young healthy volunteers and PsA was not reflected in the MASEI score. We chose to compare PsA patients and clearly non-diseased young subjects, expecting a big contrast owing to differences in disease status and age. Tendon thickness reference values explained part of the overlap, especially in the case of the knee entheses. The reference values originate from an ultrasound study of human cadaveric limbs aged 67–87 years (10) and probably underestimate enthesis thickness. Small spots of PD signal in healthy volunteers further diminished the expected extreme contrast. Our findings seem to suggest that a single spot of PD is not of value in identifying active enthesal inflammation and that at least a confluent signal is necessary. Furthermore, the patellar tendon is susceptible to showing hypervascularity after acute physical stress. A study performing PD examination on runners showed hypervascularity in the patellar tendon directly after a marathon (11).

Our results raise questions and challenges for the future. First, our controls were not age matched. Therefore, the differences between controls and patients cannot solely be ascribed to enthesal inflammation due to PsA. The effect of ageing is likely to play a role as well, which is also reflected in higher scores in the slightly older new PsA group. The effect of factors such as obesity, physical exercise, age, and gender could not be analysed, as the subgroups would be too small to analyse. Secondly, compared to other studies in early PsA, we found slightly higher scores on PD, possibly due to differences in study design and the machines used (12, 13).

## Conclusion

Ultrasound structural changes and inflammation in the enthesis were common in both new and established PsA patients, and in the knees of healthy young adults, using the MASEI score. Excluding knee entheses thickness and refinement of PD signal scores provided

discrimination of PsA from healthy young volunteers in terms of enthesis pathology.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article.

**Supplementary Figure S1.** Recoding of PD score within 2 mm of the cortex.

**Supplementary Table S1.** Calcification scores per individual using the MASEI scoring system.

**Supplementary Table S2.** PD scores using the new scoring system per individual.

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