# How normal is the enthesis by ultrasound in healthy subjects?

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## Abstract

### Objective

*To explore the prevalence of the ultrasound (US) findings of enthesitis in a group of healthy subjects.*

### Methods

*US assessments of quadriceps, patellar and Achilles tendons, and plantar fascia entheses were performed by a rheumatologist on 82 healthy volunteers focusing on the US findings indicative of "active" inflammation according to the Outcome Measures in Rheumatology (OMERACT) definitions.*

### Results

*Eight hundred and twenty entheses were evaluated in 82 healthy subjects. One or more US findings of "active" inflammation were found in at least one enthesis in 30 out of 82 subjects (34.1%), in 69 out of 820 entheses (8.4%). Entheseal thickening, hypoechogenicity and PD signal were respectively found in at least one enthesis in 23 (28.0%), 11 (13.4%) and 8 (9.8%) out of 82 subjects. Among the 69 entheses showing US features of "active" inflammation, entheseal thickening, hypoechogenicity and PD signal were found as isolated in 61 entheses and in combination in the remaining 8 (entheseal thickening and hypoechogenicity).*

### Conclusion

*Our results show a relatively high prevalence of US findings of "active" inflammation at the lower limb entheses in a group of healthy subjects, thus questioning the discriminant power of the OMERACT definitions for the diagnosis of "active" enthesitis. A combination of grey-scale and PD findings at a specific threshold to be defined could improve both the reliability and clinical usefulness of US.*

**Key words**

ultrasound, enthesis, active inflammation, healthy subjects, diagnostic value

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## Introduction

Entheseal involvement is a recognied cardinal feature of spondyloarthritis (SpA) (1) but it may also be found in patients with other pathologic conditions, such as metabolic, degenerative, post-traumatic disorders and/or systemic diseases (2).

Over the years, ultrasound (US) has proven to be a promising imaging technique in the identification of entheseal pathology both in early and late stages (3, 4). The potential of US in the assessment of entheseal involvement has been evaluated especially in patients with SpA (5). Reduced echogenicity of enthesis, entheseal thickening, enthesophytes, calcifications, perientheseal bursitis, bone erosions and pre-insertional intra-tendinous power Doppler (PD) signal have been regarded as US features of enthesitis and/or enthesopathy (6, 7).

As highlighted by a recent systematic literature review on the US assessment of entheses, none of the US signs of enthesitis is specific for inflammation and therefore cannot be used to differentiate inflammatory from mechanical enthesitis (8).

Recently, the Outcome Measures in Rheumatology (OMERACT) US Group has proposed new definitions for the US elementary lesions of enthesitis in SpA (9). According to the OMERACT definitions, entheseal thickening, entheseal hypoechogenicity and PD signal should be regarded as US findings indicative of "active" inflammation, whereas calcifications, enthesophytes and bone erosions should be considered as US findings indicative of "structural damage" (9, 10).

Although an experts' agreement for US definition of enthesitis has been obtained, further investigation is still required to gather more data about the spectrum of entheseal US abnormalities in healthy subjects, especially as regards US findings indicative of "active" inflammation.

In the present study, we aimed to explore the prevalence and distribution of the US findings indicative of enthesitis at the main entheses of the lower limb in a group of healthy subjects, focusing on the US findings indicated as being the manifestation of "active" inflammation according to the OMERACT US working group definitions. We also analysed whether there was a correlation between the US findings and the clinical and demographic features.

## Methods

*Clinical examination*

Eighty-two healthy volunteers were enrolled. We recruited staff members of the Carlo Urbani Hospital (Jesi, Ancona, Italy) and visiting nursing and medical students from the Polytechnic University of Marche. Exclusion criteria were 1) clinical enthesitis at the time of the evaluation and/or episodes of entheseal pain in the preceding 12 weeks; 2) known history of metabolic disorders (*i.e.* dyslipidaemia, dysmetabolism and/or hyperuricaemia); 3) previous diagnosis of rheumatic disease, including microcrystal arthropathies (*i.e.* gout and/or calcium pyrophosphate deposition disease), connective tissue diseases, rheumatoid arthritis (RA) and SpA; 4) personal and/or family history for psoriasis and/or inflammatory bowel disease; 5) intense physical activity in the month preceding the evaluation; 6) previous surgical procedures (including joint injection) at knee and/or ankle level; 7) systemic corticosteroid and/or non-steroidal anti-inflammatory therapy in the four weeks preceding the evaluation.

The following data were collected: age, gender, height, weight, sport activities, known history of entheseal pathology, such as Osgood-Schlatter disease, previous relevant trauma at knee and/or ankle level and previous episodes of enthesitis, which were defined as entheseal pain lasting more than 2 weeks with or without swelling of the enthesis. The body mass index (BMI) was also calculated.

A rheumatologist performed the musculoskeletal physical examination in all subjects in order to evaluate the presence of clinical enthesitis at the following entheses: the patellar insertion of the quadriceps tendon, the patellar insertion (proximal) of the patellar tendon, the tibial insertion (distal) of the patellar tendon, the calcaneal insertion of the Achilles tendon and of the plantar fascia. The clinical diagnosis of enthesitis was made if entheseal spontaneous pain

and/or entheseal pain generated by pressure and/or mobilisation and/or contraction against resistance was detected.

The present study was conducted according with local regulations. As regards healthy subjects, we have a program of constant updating of our clinical and US database that does not require a case-by-case approval from our Ethics Committee. All patients gave their informed consent for the anonymous analysis of the data.

*US examination*

The US examination was carried out by a rheumatologist with seven years of experience in musculoskeletal US (A.D.M.) using a My Lab Class C (Esaote SpA Genoa, Italy) equipped with a high frequency linear probe (6-18 MHz) and working at a Doppler frequency of 9.1 MHz. While the sono-grapher was aware he was scanning healthy subjects, he was blind to their clinical history (*i.e.* previous episodes of enthesitis) and current clinical data (*i.e.* exclusion criteria). According to the updated European League Against Rheumatism (EULAR) guidelines for US imaging in rheumatology (11), the knee entheses (patellar insertion of the quadriceps tendon, proximal and distal insertion of the patellar tendon) were examined with the patient in neutral position, lying supine on the examination bed. PD signal was assessed with extended lower limbs whereas echotexture abnormalities were investigated with the knees in semi-flexed position. The ankle entheses (calcaneal insertion of the Achilles tendon and of the plantar fascia) were evaluated with the patient lying in prone position with the feet hanging over the examination bed in neutral position.

All entheses were scanned bilaterally, in grey-scale (GS) and PD modality, both in longitudinal and transverse plans. According to the OMERACT definitions, the US elementary lesions indicative of enthesitis were identified as follows (9):

- entheseal thickening: increased thickness of the tendon/ligament insertion into the bone, as compared to the body of the tendon/ligament, with or without blurring of the tendon/ligament margins;
- hypoechogenicity: lack of the homogeneous fibrillar pattern with loss of the tightly packed echogenic lines after correcting for anisotropy;
- PD signal: Doppler activity approximately two millimetres near the bony cortex, localised at entheseal level, different from reflecting surface artifact or nutrition vessel signal;
- enthesophyte: a step up of bony prominence at the end of the normal bone contour, seen in two perpendicular planes, with or without acoustic shadow;
- calcification: a hyperechoic (bright) foci consistent with calcific deposits, with or without acoustic shadow, seen in two perpendicular planes, detected at the tendon insertion into the bone;
- bone erosion: a cortical breakage with a step down contour defect, seen in two perpendicular planes, at the insertion of the enthesis to the bone.

The PD signal was also evaluated according to a semiquantitative scale from 0 to 3, where: grade 0: absent, grade 1: mild, grade 2: moderate, and grade 3: severe (12, 13).

In each subject, a dichotomous score (0=absence, 1=presence) was calculated for US entheseal abnormalities indicative of "active" inflammation: entheseal thickening, hypoechogenicity, and PD signal. This score ranges from 0 to 1 for each enthesis and from 0 to 10 for each patient.

*Literature review: search strategy and studies selection*

A literature search was carried by PubMed database including articles from January 1st 1980 to May 1st 2018. The term search used were: (ultrasonography OR ultrasound OR US OR sonography OR sonographic) AND (enthesitis OR entheses OR enthesis OR enthesopathy OR entheseal). References of the included studies were taken into consideration for the analysis of further relevant data. Titles and abstracts were screened by two reviewers (E.C. and A.D.M.). If an abstract was selected by a reviewer, the full-text article was retrieved and subsequently screened for eligibility criteria prior selection for review. Only original articles that were written in English and that focused on the use of US for assessment of entheseal abnormalities in healthy subjects were included.

Studies not reporting data on prevalence and distribution of US entheseal abnormalities, not evaluating entheses of the lower limb and including paediatric patients were excluded. Any disagreement in the selection process was resolved by consensus. The same reviewers (E.C. and A.D.M.) extracted the following data from each article: authors and year of publication, population included (*i.e.* RA, SpA), number of healthy subjects, number and type of entheses evaluated, US score/definition for enthesitis, and US settings adopted (both in GS and PD modality), prevalence and distribution of entheseal abnormalities.

*Statistical analysis*

The results are expressed as mean ± standard deviation (SD) for quantitative variables and as number and/or percentage for qualitative variables. The prevalence of each US pathological findings is reported using the 95% confidence interval (95%CI). The Mann-Whitney test was used for the quantitative variables whereas the Chi-square test was used for qualitative variables.

The associations between the US scores (*i.e.* entheseal thicknening, hypoechogenicity and PD signal) and clinical variables (*i.e.* age, sex, physical activity and BMI) were explored.

The Point-biserial correlation was used to evaluate the association between the US findings and the qualitative variables (sex and physical activity), whereas the Spearman's rank correlation was used to correlate the US findings and the quantitative variables (age and BMI).

Two tailed *p*-values less than 0.05 were considered significant. Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) software (v. 24.0 for Mac, Chicago, Illinois, USA).

## Results

*Clinical and US results*

A total of 820 entheses in 82 healthy subjects were evaluated. The mean±SD age was 44.0±14.8 years, the female/

**Table I.** Prevalence and distribution of entheseal US abnormalities, according to the OMERACT definitions, in healthy subjects

| US abnormalities | Entheses of the lower limbs | | | | | | |
|---|---|---|---|---|---|---|---|
| | Subjects | Quadriceps tendon | Proximal patellar tendon | Distal patellar tendon | Achilles tendon | Plantar fascia | SUM |
| Entheseal thickening | 28.0% (19.5%-38.6%) | 6.3% (3.4%-11.1%) | 3.8% (1.7%-7.9%) | 6.3% (3.4%-11.1%) | 8.1% (4.8%-13.4%) | 4.4% 2.1%-8.8%) | 28.8% (22.3%-36.2%) |
| Hypoechogenicity | 13.4% (7.7%-22.4%) | 2.5% (1.0%-6.3%) | 0.6% (0.1%-3.5%) | 1.9% (0.6%-5.4%) | 5.0% (1.4%-7.1%) | 2.5% (1.0%-6.3%) | 12.5% (8.2%-18.5%) |
| PD signal =1 | 8.5% (4.2%-16.6%) | 1.9% (0.6%-5.4%) | 0.6% (0.1%-3.5%) | 2.5% (1.0%-6.3%) | 1.3% (0.3%-4.4%) | 0% (0%-2.3%) | 6.3% (6.3%-15.6%) |
| PD signal >1 | 1.2% (0.2%-6.6%) | 0.6% (0.1%-3.5%) | 0% (0%-2.3%) | 0% (0%-2.3%) | 0% (0%-2.3%) | 0% (0%-2.3%) | 0.6% (0.1%-3.5%) |
| Enthesophyte | 24.4% (16.4%-34.7%) | 8.8% (5.3%-14.2%) | 1.3% (0.3%-4.4%) | 1.3% (0.3%-4.4%) | 8.8% (5.3%-14.2%) | 2.5% (1.0%-6.3%) | 22.5% (16.7%-29.6%) |
| Bone erosion | 6.1% (2.6%-13.5%) | 0% (0%-2.3%) | 1.9% (0.6%-5.4%) | 0.6% (0.1%-3.5%) | 0% (0%-2.3%) | 0.6% (0.1%-3.5%) | 3.1% (1.4%-7.1%) |
| Calcification | 28.0% (19.5%-38.6%) | 6.9% (3.9%-11.9%) | 1.9% (0.6%-5.4%) | 7.5% (4.3%-12.7%) | 6.3% (3.4%-11.1%) | 3.8% (1.7%-7.9%) | 26.3% (20.1%-33.6%) |
| SUM | / | 26.9% (20.6%-34.2%) | 10.0% (6.3%-15.6%) | 20.0% (14.5%-26.9%) | 29.4% (22.9%-36.9%) | 13.8% (9.3%-19.9%) | / |

Percentages under the subheading "Subjects" refer to the total number of healthy subjects assessed (n=82). Percentages under the heading "Entheses of the lower limbs" refer to the total amount of entheseal pathological findings (n=160).
Values in brackets are the 95%CI of the prevalence of each US abnormalities.
95%CI: 95% confidence interval; OMERACT: Outcome Measures in Rheumatology; PD: power Doppler; US: ultrasound.

**Table II.** US findings of "active" inflammation detected as isolated or combined with other abnormalities of enthesitis/enthesopathy.

| US findings of "active" inflammation | Number of US abnormalities | | Isolated | | Combined with the other US abnormalities | | |
|---|---|---|---|---|---|---|---|
| Entheseal thickening | 46 | 5.6% | 23 | 50% | | 23 | 50% |
| | | | | | Hypoechogenicity | 8 | |
| | | | | | PD signal | 0 | |
| | | | | | Enthesophyte | 15 | |
| | | | | | Calcification | 12 | |
| | | | | | Bone erosion | 0 | |
| Hypoechogenicity | 20 | 2.4% | 3 | 15.0% | | 17 | 85.0% |
| | | | | | Entheseal thickening | 8 | |
| | | | | | PD signal | 0 | |
| | | | | | Enthesophyte | 2 | |
| | | | | | Calcification | 11 | |
| | | | | | Bone erosion | 2 | |
| PD signal | 11 | 1.3% | 6 | 54.5% | | 5 | 45.5% |
| | | | | | Entheseal thickening | 0 | |
| | | | | | Hypoechogenicity | 0 | |
| | | | | | Enthesophyte | 3 | |
| | | | | | Calcification | 2 | |
| | | | | | Bone erosion | 0 | |

Percentages in the column under the heading "Number of US abnormalities" refer to the total amount of entheses assessed (n=820). Percentages in the columns under the heading "Isolated" and "Combined with the other US abnormalities" are in relation with the total number of each US elementary lesion (entheseal thickening: n=46, hypoechogenicity: n=20, PD signal: n=11).
PD: power Doppler, US: ultrasound.

male ratio was 49/33. The mean±SD BMI was: 23.2±2.8 kg/m$^2$.

Regular physical activity (twice or more in a week) was reported by 27 out of 82 subjects (32.9%). Six entheses (four plantar fascia and two Achilles tendons), in five participants, were reported as previously involved in the medical history. No subject reported a previous diagnosis of Osgood-Schlatter disease or previous relevant trauma at knee and/or ankle level.

The prevalence and distribution of the US elementary abnormalities indicative of enthesitis, according to the OMERACT US group definitions of enthesitis in SpA, at the lower limb entheses in our group of healthy subjects, are reported in Table I.

One or more US findings indicative of "active" inflammation were found in at least one enthesis in 30 out of 82 healthy subjects (34.0%) and in 69 out of 820 entheses (8.4%). PD grades >1 were found in only one enthesis (0.12%) in one subject.

The prevalence of entheseal thickening was significantly higher than the prevalence of hypoechogenicity and PD signal both at patient ($p$=0.02 and $p$=0.002, respectively) and at entheseal level ($p$=0.001 and $p$<0.001, respectively).

Table II shows whether the US lesions indicative of "active" inflammation were found as isolated findings or combined with the other US abnormalities indicative of enthesitis and/or enthesopathy.

In the 69 entheses with US findings indicative of "active" inflammation, entheseal thickening, hypoechogenicity and PD signal were found as isolated in 61 entheses (38 increased thickening, 12 hypoechogenicity, 11 PD signal) and

combined in the remaining 8 (entheseal thickening and hypoechogenicity).

Six entheses (4 plantar fascia and 2 Achilles tendon) were reported as previously involved in the subject's medical history. In 3 of these entheses, the US exam revealed the following abnormalities: an entheseal thickening, at plantar fascia level, as isolated finding; entheseal thickening, hypoechogenicity and calcifications in 1 plantar fascia; entheseal thickening and hypoechogenicity in 1 one Achilles tendon. In the remaining 3 entheses, no US abnormalities were detected.

The mean value of the US scores of entheseal thickening, hypoechogenicity and PD signal was 0.6±1.1, 0.2±0.8 and 0.1±0.5, respectively.

There was a positive correlation between the US score of entheseal thickening and age (R=0.256, $p$=0.02) and BMI (R=0.225, $p$=0.045). No significant association was found between the US scores of hypoechogenicity and PD signal and the demographic and clinical data which had been taken into account.

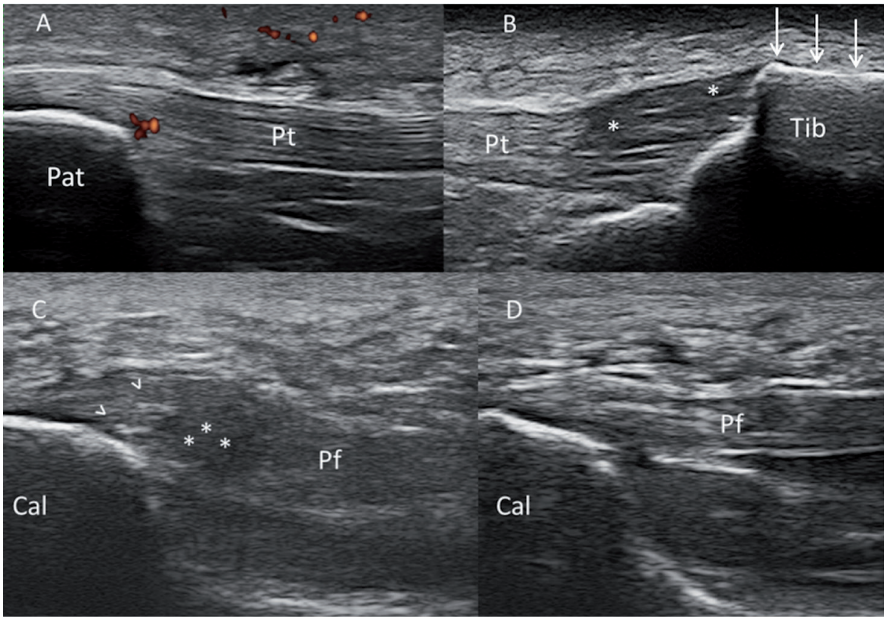


**Fig. 1.** Examples of US findings indicating entheseal "active" inflammation at lower limb entheses in healthy subjects.
**A**: the longitudinal scan of the proximal insertion of the patellar tendon shows a grade 1 PD signal at the enthesis (red spots). **B**: the longitudinal scan of the distal insertion of the patellar tendon reveals a thickened enthesis, a large hypoechoic area (asterisks) and an enthesophyte (white arrows).
**C**-**D**: The side-by-side comparison of a plantar fascia shows an entheseal thickening with loss of the homogenous fibrillar pattern (asterisks) and calcifications (arrowheads) at the right side (**C**). This plantar fascia was reported as previously involved in the subject's medical history.
Pat: patella, Pt: patellar tendon; Tib: tibia, Cal: calcaneal bone; Pf: plantar fascia.

*Literature search and study characteristics*

The initial search strategy yielded 1244 articles for screening which was reduced to 15 articles after application of filters and screening of titles and abstracts. The main characteristics of these studies are reported in Tables III and IV. In all these studies, healthy subjects were included as controls.

## Discussion

This study focused on the evaluation of the US findings indicative of entheseal "active" inflammation (*i.e.* entheseal thickening, hypoechogenicity and PD signal) according to the OMERACT definitions.

The main results can be summarised as follows:

- the prevalence of the US findings considered as indicative of entheseal "active" inflammation was relatively low in relation to the total number of entheses (8.4%), but remarkable at subject-level (34.0%), especially as regards entheseal thickening and, to a lesser extent, hypoechogenicity;
- the prevalence of PD signal was lower if compared to entheseal thickening and hypoechogenicity both at subject and entheseal level. It should be noted that PD grades >1 were found in only 1 enthesis in a single healthy subject;
- entheseal thickening, hypoechogenicity, and also PD signal, were mostly found in combination with US findings indicative of "structural damage", such as enthesophytes and calcifications;
- entheseal thickening and hypoechogenicity were found in combination in 8 out of 69 cases. No association between PD signal and entheseal thickening or hypoechogenicity was detected;
- there was a significant correlation between the US score of entheseal thickening and age and BMI.

Examples of US findings regarded as indicative of "active" inflammation, according to the OMERACT definitions, at the lower limb entheses in healthy subjects are shown in Figure 1.

Some studies have already demonstrated the presence of US findings indicative of enthesitis and/or enthesopathy at the lower limb enthesis of healthy subjects, all including a lower number of examined subjects (Table III), showing a considerable variability in the prevalence of US findings indicative of "active" inflammation (Table IV). At entheseal level, the prevalence of entheseal thickening, hypoechogenicity and PD signal ranged from 0.0% to 37.5%, from 0.0 to 7.5%, and from 0.0% to 13.6%, respectively. PD signal at the enthesis was absent in most cases.

A wide variability in the score for US enthesitis and for the definition of its elementary lesions, as well as heterogeneity in type of entheses evaluated and both US equipment and setting used, was found among these studies (Table IV).

To the best of our knowledge, this is the first study that aimed to explore the spectrum of the US abnormalities at the entheses of the lower limb, as well as their correlation with the clinical and demographic features, in a cohort of healthy subjects.

Our decision to investigate the five main entheses of the lower limb was based on their common involvement in rheumatic diseases (20, 28-32). Moreover,

**Table III.** Main general characteristics of the US studies.

| Authors | Year of publication | Population of interest | Number of healthy subjects | Examined entheses | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Quadriceps tendon | Proximal patellar tendon | Distal patellar tendon | Achilles tendon | Plantar fascia | Other entheseal sites evaluated |
| D'Agostino *et al*. (14) | 2003 | uSpA, PsA, IBD, ReA, AS | 34 | Y | Y | Y | Y | Y | Y |
| Genc *et al*. (15) | 2005 | RA, AS | 20 | Y | Y | Y | Y | Y | Y |
| Alcalde *et al*. (16) | 2007 | AS | 10 | Y | Y | Y | Y | Y | N |
| Genc *et al*. (17) | 2007 | RA, AS | 18 | Y | Y | Y | Y | Y | N |
| Gisondi *et al*. (18) | 2008 | Pso | 30 | Y | Y | Y | Y | Y | N |
| Gutierrez *et al*. (19) | 2011 | Dia | 33 | Y | Y | Y | Y | Y | N |
| Gutierrez *et al*. (20) | 2011 | Pso | 45 | Y | Y | Y | Y | Y | N |
| Ruta *et al*. (21) | 2011 | SpA | 30 | Y | Y | Y | Y | Y | N |
| Feydy *et al*. (22) | 2012 | SpA | 24 | N | N | N | Y | Y | N |
| Freeston *et al*. (13) | 2012 | PsA | 10 | N | N | Y | Y | Y | Y |
| Jousse-Joulin *et al*. (23) | 2013 | pSS | 9 | Y | Y | Y | N | N | Y |
| Aydin *et al*. (24) | 2013 | Pso, PsA | 23 | Y | Y | Y | Y | Y | N |
| Kilic *et al*. (25) | 2015 | SSc | 41 | Y | Y | Y | Y | Y | Y |
| Di Matteo *et al*. (26) | 2018 | SLE, PsA | 50 | Y | Y | Y | Y | Y | N |
| Wervers *et al*. (27) | 2018 | PsA | 25 | Y | Y | Y | Y | Y | Y |

From each study, only US data on the main entheses of the lower limb (patellar insertion of the quadriceps tendon, proximal and distal insertions of the patellar tendon, calcaneal insertion of plantar fascia and Achilles tendon) are reported.
AS: ankylosing spondylitis; Dia: dialysed patients; IBD: inflammatory bowel disease; N: no; PsA: psoriatic arthritis; Pso: psoriasis; pSS: primary Sjögren's syndrome; RA: rheumatoid arthritis; ReA: reactive arthritis; SLE: systemic lupus erythematosus; SpA: spondyloarthritis; SSc: systemic sclerosis; uSpA: undifferentiated spondyloarthritis. Y: yes.

**Table IV.** Prevalence of the US findings indicating enthesitis/enthesopathy, US score/definition for enthesitis and US settings used.

| Authors | US score/ definition for enthesitis | US settings (GS/PD frequency in MHz) | Number of entheses | US findings at entheseal level | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Entheseal thickening | Hypoechoge-nicity | PD signal | Enthesophyte | Entheseal calcification | Bone erosion |
| D'Agostino *et al*. (14) | D'Agostino | 13 / NR | 340 | NR | NR | 0.0% | NR | NR | NR |
| Genc *et al*. (15) | GUESS | 7.5 / NR | 200 | 37.5% | 7.5% | NR | 12.5% | NR | 5.0% |
| Alcalde *et al*.. (16) | SEI | 7.5 /NR | 100 | 0.0% | 0.0% | NR | NR | 0.0% | 0.0% |
| Genc *et al*. (17) | GUESS | 7.5 /NR | 180 | 27.8% | 8.3% | NR | 8.3% | NR | 2.8% |
| Gisondi *et al*. (18) | GUESS | 10–15 / NR | 300 | 9.0% | NR | NR | 26.3% | NR | 0.0% |
| Gutierrez *et al*. (19) | GUESS | 6-18 / 9.1-11.1 | 330 | 4.5% | NR | NR | 10.3% | NR | 1.2% |
| Gutierrez *et al*. (20) | GUESS | 6-18 / 9.1-11.1 | 450 | 4.0% | NR | NR | 4.2% | NR | 0.0% |
| Ruta *et al*. (21) | GUESS | 6-18 / 8.3-12.5 | 300 | 0.0% | 0.0% | 0.0% | 0.0% | NR | 0.0% |
| Feydy *et al*. (22) | NR | 7-15 / NR | 96 | 3.1% | 7.3% | 2.1% | 22.9% | 2.1% | 1.0% |
| Freeston *et al*. (13) | OMERACT | 5-15 / NR | 60 | 0.0% | 0.0% | 0.0% | 21.7% | 3.3% | 3.3% |
| Jousse-Joulin *et al*. (23) | NR | 5-13 / NR | 54 | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Aydin *et al*. (24) | GUESS | 6-15 / 9.1 | 230 | 30.0% | 12.6% | 0.0% | 39.1% | 9.6% | 0.4% |
| Kilic *et al*. (25) | MASEI | 7-12 / NR | 410 | 2.4% | 2.9% | 0.0% | NR | 5.6% | 0.0% |
| Di Matteo *et al*. (26) | OMERACT | 6-18 / 9.1 | 500 | 6.8% | 3.6% | 0.4% | 4.6% | 6.2% | 0.8% |
| Wervers *et al*. (27) | MASEI | 4-18 / 6.3-8.3 | 250 | 36.4% | 0.4% | 13.6% | 0.0% | 10.0% | 2.0% |

GS: grey-scale; GUESS: Glasgow Ultrasound Enthesitis Scoring System; MASEI: MAdrid Sonography Enthesitis Index; NR: not reported; OMERACT: Outcome Measure in Rheumatology; PD: power Doppler; SEI: Sonographic Entheseal Index; US: ultrasound.

such entheses are superficial anatomic structures that allow relatively easy assessment with both US and physical examination.

The results of our study prompt the following observations: 1) PD signal may represent the most reliable US biomarker of "active" inflammation at the enthesis because it was the US finding with the lowest prevalence in our cohort of healthy subjects; 2) combining the US elementary features of "active" inflammation (*i.e*. PD signal ≥1 + entheseal thickening and/or hypoechogenicity) as well as considering as pathological only PD grades >1 may increase the diagnostic accuracy of the US findings in detecting "active" enthesitis; 3) in subjects with hypoechogenicity and, mostly, entheseal thickening, isolated or in combination, without intra and/or peri-lesional Doppler signal, previous episodes of enthesitis and/or the presence of pathologic conditions that may determine structural damage at the enthesis, as a consequence of a local disorders or chronic process, should be taken into account.

The main limitation of the study is represented by the lack of an across-operator reproducibility analysis of the US examinations, as they were performed by a single sonographer in a single

centre. Further investigations including patients with SpA, such as psoriatic arthritis and ankylosing spondylitis, are needed to explore the diagnostic accuracy of the proposed cut-off of "active" enthesitis.

## Conclusions

Our results show a relatively high prevalence of US findings of "active" inflammation at the lower limb entheses in a group of healthy subjects, thus questioning the discriminant power of the OMERACT definitions for the diagnosis of "active" enthesitis. A combination of grey-scale and PD findings at a specific threshold to be defined could improve both the reliability and clinical usefulness of US.

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