Value of musculoskeletal ultrasonography in the diagnosis of peripheral enthesopathy in early spondyloarthropathy

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Objective
The aim of the study was to evaluate peripheral enthesopathy ultrasonography in early spondyloarthritis.

Patients and methods
A total of 50 patients were divided into two groups: group I included 30 patients who were diagnosed as spondyloarthropathy (SpA) and were divided into two subgroups – axial subgroup (19 patients) and peripheral subgroup (11 patients) – and group II included 20 patients diagnosed as rheumatoid arthritis. All patients were subjected to history taking, clinical examination and laboratory and radiological investigations: plain radiography and musculoskeletal ultrasonography.

Results
A significant difference was found between subgroups regarding clinical examination of plantar fascia, distal patellar ligament and proximal patellar ligament. We found a high significant difference between mean of Bath Ankylosing Spondylitis Metrology Index (BASMI) in axial (0.8 ± 0.6) and peripheral (0.09 ± 0.3) patients. A high significant difference was found between group I and group II regarding Madrid Sonographic Enthesitis Index (MASEI). In addition, a significant difference was found regarding the number of abnormal enthesis examined by ultrasonography. We found a highly significant difference between groups regarding structure, bursa, erosion, calcification and power Doppler scores (higher in group I); a significant difference was found between groups regarding distal patellar ligament thickness, calcification and power Doppler signal; proximal patellar ligament thickness, calcification and power Doppler and quadriceps tendon structure, thickness and power Doppler. We found significant difference between subgroups regarding structure score.

Conclusion
Enthesis are affected early in spondyloarthritis. MASEI score is a valuable tool for early diagnosis of SpA and can improve diagnostic accuracy of early SpA patients.

Keywords:
MUS muscloskeletal ultrasound, Enthesisyopathy, Spodyloarthropathy

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Introduction

Spondyloarthritis are a group of interrelated rheumatic conditions, including ankylosing spondylitis (AS), reactive arthritis (ReA), psoriatic arthritis (PsA), spondyloarthropathy (SpA) associated with inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), undifferentiated SpA and juvenile onset spondyloarthritis [1].

The SpA belongs to the most common rheumatic diseases, with a prevalence of 0.5–1.9%. The outcome is mainly influenced by the degree of disease activity over time and the loss of function and mobility, part of which is caused by inflammation, whereas the other part is due to destructive changes of the spine and of the peripheral joints. Male patients, who are slightly more frequently affected than female patients, have more radiographic progression [2].

Manifestations of SpA include inflammatory back pain with its characters, enthesitis, peripheral arthritis (asymmetric and/or predominantly in lower limbs), sacroiliitis detected clinically or radiologically, limited spinal mobility and chest expansion, strong correlation with HLA-B27 and extra-articular manifestations including psoriasis, IBD, urethritis, cervicitis and anterior uveitis [3]. Enthesis is defined as a site of insertion of a tendon, ligament, fascia or articular capsule into bone. Its involvement in any pathologic process, whether inflammatory, traumatic or degenerative, is referred to as enthesopathy, whereas the term 'enthesitis' is restricted to inflammation of the enthesis [4]. In tendinous or ligamentous attachment, two types of entheses have been described: fibrous and fibrocartilaginous (or chondroid). Fibrous entheses are characterized by pure dense fibrous tissue that links the tendon or ligament to the bone, whereas fibrocartilaginous entheses have a transitional zone of

fibrocartilage at the bone interface [5]. Most entheses are fibrocartilaginous: for example, those of the Achilles tendon, plantar fascia, quadriceps tendon and patellar tendon [6].

Peripheral enthesitis is observed in all SpA subtypes, including the undifferentiated forms. Several reports have pointed to enthesitis as a primary lesion in SpA, which may underlie all skeletal manifestations characteristic of these disorders, including synovitis. Peripheral enthesitis is usually revealed by clinical findings, which lack specificity, such as localized pain, tenderness and swelling and there are no definite clinical criteria for the diagnosis of this manifestation [7].

In recent years, ultrasonography has proved to be a highly sensitive and noninvasive tool, especially in the assessment of tendon and joint involvement. Several studies have described the use of B-mode ultrasound to identify the features of lower limb enthesitis in SpA, revealing a high frequency of abnormal findings in asymptomatic entheses. More recently, power Doppler technology has allowed the visualization of abnormal vascularization and hyperaemia of soft tissues in inflammatory articular diseases. Doppler effect is a physical phenomenon in which the frequency of a wave that hits a moving body undergoes a variation that is directly related to the speed of the body itself [8].

Patients and methods

Patients

Our study was conducted at Minia University Hospital. All patients were recruited from rheumatology outpatient clinic during the period from February to October 2012. The study included 50 patients who were divided into two groups:

Group I

A total of 30 patients were diagnosed as axial or peripheral SpA (according to the ASAS classification criteria for axial [9] or peripheral [10] SpA, respectively). Then, patients divided into two subgroups as axial (subgroup Ia, 19 patients) and peripheral SpAs (subgroup Ib, 11 patients).

Group II

A total of 20 patients diagnosed as rheumatoid arthritis according to the 2010 ACR-EULAR classification criteria for rheumatoid arthritis [11] and disease duration less than 2 years (from onset of symptoms or appearance of first sign attributable to the disease) were classified as the control group.

Exclusion criteria

Exclusion criteria were disease duration more than 2 years or history of trauma or surgery to the knees, ankles or elbows.

Ethical considerations

The nature of the present study was explained to all patients. The laboratory and radiological procedures represent standard care and pose no ethical conflicts. Both written and verbal consent was obtained from all patients.

Methods

Patients were subjected to the following:

(1) History taking.
(2) Clinical examination.
    (a) General examination.
    (b) Musculoskeletal examination.

Examination of the joints

Examination of the back: (a) Cervical, dorsal and lumbar spine were examined for the assessment of spinal mobility by special tests (modified Schober's test, lateral spinal flexion test, tragus to wall test, cervical rotation test, intermalleolar distance test and chest expansion test) [12] and (b) sacroiliac joint was examined by the following tests: direct sacral pressure, side compression test, pelvic compression test, distraction [13], Gaenslen's test and Patrick's test [14].

Examination of the enthesis: Inferior and superior pole of the calcaneus and inferior and superior pole of the patella, tibial and olecranon tuberosity were examined.

    (c) Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) [12] were performed in group I patients only.
(3) Laboratory investigations: Erythrocyte sidemintation rate (ESR) was performed by the Westergren method, latex agglutination slide test was performed for qualitative and semiquantitative determination of C-reactive protein in nondiluted serum and rheumatoid factor was determined by the latex fixation test.
(4) Radiological investigations were performed in group I patients only.

Plain radiography was performed for sacroiliac joints (anteroposterior view) and cervical, dorsal and lumbar spines (lateral view). Grading of radiographic sacroiliitis was carried out [15].

Musculoskeletal ultrasonography, conventional grey-scale ultrasound and power Doppler examinations were carried out using Picus 4D, with a 7–12.5-MHz linear transducer.

(1) *Sites of examination*: The following enthesis were examined bilaterally according to the Madrid Sonographic Enthesitis Index (MASEI) [16]: inferior pole of the calcaneus, superior pole of the calcaneus, tibial tuberosity, inferior pole of the patella, superior pole of the patella and olecranon tuberosity.
(2) *Position and planes during examination*: Each tendon was scanned in both the longitudinal and transverse planes. Knee enthesis examination was performed with the patient in the supine position and the knee flexed at 70°. The Achilles tendon and the plantar aponeurosis were examined with the patient lying prone and the feet hanging over the edge of the examination table at 90° of flexion. The triceps insertion was examined with the arm flexed at 90° [16].
(3) Ultrasound evaluation of enthesis was performed for structure, thickness, erosions, calcifications, bursitis and power Doppler signal (according to MASEI) [16]. The total possible score on both sides (12 entheses) is 136.

Statistical analysis

Analysis of data was performed by personal computer using SPSS (version 16, Statistical Program for Social Science) as follows:

(1) *Descriptive statistics*: Description of quantitative variables was expressed as mean, SD and range. Description of qualitative variables was expressed as number (*n*) and percentage (%).
(2) *Group comparisons*: Comparisons were performed by the χ^2-test for qualitative variables. Student's *t*-test was used to compare two independent groups with respect to a quantitative variable.
(3) *Correlation*: Pearson's correlation coefficients (*r*) were calculated for detection of parametric correlations, whereas Spearman's correlation coefficients (*r*) were calculated for detection of nonparametric correlations between variables in one group.

Results

Patients of both groups showed no significant differences regarding age, sex and disease duration.

Table 1 shows the comparison between laboratory and radiological data of all groups.

Table 2 shows MASEI score, frequency of enthesitis and elementary lesions score by ultrasonography in groups I and II. There was statistically high significant difference between groups regarding MASEI score (higher in group I; $P = 0.001$) and number of abnormal enthesis examined by ultrasonography ($P = 0.04$). We found a statistically high significant difference between groups regarding structure ($P = 0.03$), bursa ($P = 0.001$), erosion ($P = 0.008$), calcification ($P = 0.001$) and power Doppler signal ($P = 0.001$) scores (higher in group I).

Table 3 shows comparison between activity indices in both subgroups. We found a statistically high significant difference between axial and peripheral patients with respect to BASMI ($P = 0.001$), whereas there was no statistically significant difference with respect to previous other variables.

Table 4 shows ultrasonographic findings of distal and proximal patellar ligaments and quadriceps tendon, plantar fascia and Achilles tendon in groups I and II. As a result of previous findings, a statistically significant difference was found between groups regarding distal patellar ligament thickness ($P = 0.02$), calcification ($P = 0.003$) and power Doppler signal ($P = 0.01$); proximal patellar ligament thickness ($P = 0.01$), calcification ($P = 0.002$) and power Doppler signal ($P = 0.003$); and quadriceps tendon structure ($P = 0.02$), thickness ($P = 0.001$) and power Doppler signal ($P = 0.01$).

Table 5 shows correlations between MASEI score and different variables in subgroup Ia and Ib. There was a

Table 1 Comparison between laboratory and radiological data of all groups

Laboloatory and radiological findings	Group I (SpA) (*n* = 30)	Group II (RA) (*n* = 20)	χ^2/t	*P*-value
ESR (first hour) (mean ± SD)	27.1 ± 11.4	57.9 ± 20.6	−6.763	0.001**
CRP positivity [*n* (%)]	14 (46.7)	15 (75)	3.95	0.04*
CRP titre (mean ± SD)	16 ± 19.25	27.6 ± 20.6	−2.028	0.04*
Rheumatoid factor [*n* (%)]	0 (0)	15 (75)	32.14	0.001**
HLA-B27 [*n* (%)]	16 (53.3)	NA	NA	NA
Suspicious radiological sacroiliitis [*n* (%)]	6 (20)	NA	NA	NA
Positive active sacroiliitis by MRI [*n* (%)]	20 (66.7)	NA	NA	NA

The values are calculated by χ^2-test and Student's *t*-test. CRP, C-reactive protein; RA, rheumatoid arthritis; SpA, spondyloarthropathy.
*Significant *P*-value > 0.05. **Highly significant *P*-value > 0.01.

Table 2 MASEI score, frequency of enthesitis and elementary lesions score by ultrasonography in groups I and II

Ultasonographic findings and scores	Group I (SpA) (n = 30)	Group II (RA) (n = 20)	t	P-value
MASEI score				
Range	20–38	6–22		
Mean ± SD	27.8 ± 5.4	12.2 ± 4.3	10.85	0.001**
Male				
Range	20–38	6–22		
Mean ± SD	26.8 ± 5.6	13.1 ± 4.1		
Female				
Range	22–36	8–22	–1.12'' 0.764'''	0.2'' 0.4'''
Mean ± SD	29.1 ± 5.04	11.6 ± 4.6		
Abnormal enthesis by ultrasonography (number of abnormal enthesis/total enthesis examined)	239/360 (66.3%)	80/240 (33.3%)	1.22	0.04*
Structure score (mean ± SD)	4.6 ± 1.9	3.5 ± 1.3	2.804	0.03*
Thickness score (mean ± SD)	1.3 ± 1.1	1.6 ± 1.2	–0.840	0.4
Bursa score (mean ± SD)	2.2 ± 1	0.9 ± 0.7	6.102	0.001**
Erosion score (mean ± SD)	2.5 ± 2.5	0.7 ± 1.6	5.133	0.008**
Calcification score (mean ± SD)	7 ± 2.19	3.4 ± 1.7	2.750	0.001**
Power Doppler score (mean ± SD)	10 ± 2	0.6 ± 0.5	8.861	0.001**

MASEI, Madrid Sonographic Enthesitis Index; RA, rheumatoid arthritis; SpA, spondyloarthropathy, *Statistically significant. **Highly statistically significant. ***Very highly statistically significant.

Table 3 Comparison between activity indices in subgroups

Activity indices	Subgroup Ia (axial SpA) (n = 19)	Subgroup Ib (peripheral SpA) (n = 11)	t	P-value
BASDAI (mean ± SD)	2.1 ± 0.7	1.6 ± 0.4	1.66	0.1
BASMI (mean ± SD)	0.8 ± 0.6	0.09 ± 0.3	0.26	0.001**
BASFI (mean ± SD)	2.4 ± 0.6	2.3 ± 0.5	3.88	0.7
Chest expansion (mean ± SD)	6.1 ± 0.4	6.3 ± 0.3	–1.34	0.1
MASES (mean ± SD)	0.6 ± 1.2	1.3 ± 1.6	1.3	0.2

The values are calculated by Student's t-test. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; SpA, spondyloarthropathy. **Highly significant P-value > 0.01.

Table 4 Comparison between ultrasonographic findings of distal patellar ligament, proximal patellar ligament and quadriceps tendon in groups I and II

Ultrasonographic findings	Group I (SpA) (n = 30) [n (%)]	Group II (RA) (n = 20) [n (%)]	χ^2	P-value
Distal patellar ligament				
Structure	16 (53.3)	11 (55)	0.013	0.5
Thickness	17 (56.7)	5 (25)	4.884	0.02*
Infrapatellar bursa	13 (43.3)	7 (35)	0.347	0.3
Calcification	22 (73.3)	6 (30)	9.145	0.003**
Erosion	4 (13.3)	2 (10)	0.126	0.5
Power Doppler	16 (53.3)	4 (20)	5.556	0.01*
Proximal patellar ligament				
Structure	16 (53.3)	10 (50)	0.053	0.5
Thickness	18 (60)	5 (25)	5.918	0.01*
Calcification	4 (13.3)	5 (25)	9.73	0.002**
Erosion	21 (70)	2 (10)	0.126	0.5
Power Doppler	17 (56.7)	3 (15)	8.681	0.003**
Quadriceps tendon				
Structure	20 (66.7)	7 (35)	4.844	0.02*
Thickness	21 (70)	4 (20)	12	0.001**
Erosion	4 (13.3)	0 (0)	2.257	0.1
Calcification	17 (56.7)	7 (35)	2.899	0.1
Power Doppler	13 (43.3)	2 (10)	6.349	0.01*

The values are calculated by χ^2-test. RA, rheumatoid arthritis; SpA, spondyloarthropathy. *Significant P-value > 0.05. **Highly significant P-value > 0.01.

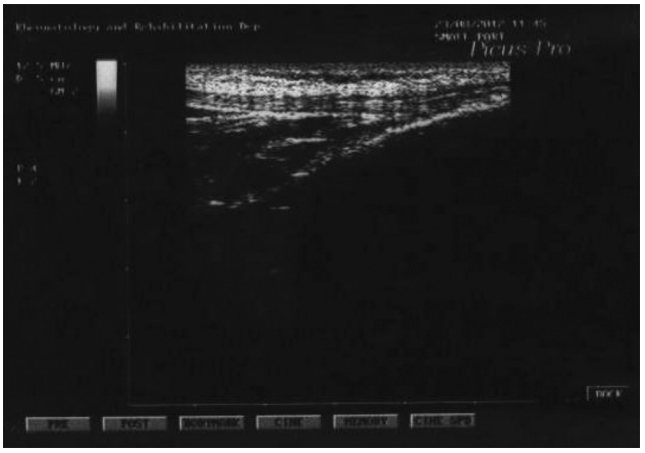
significant correlation found between MASEI score and BASDAI (P = 0.001) and BASFI (P = 0.01) in subgroup Ib (Figs. 1 and 2).

Discussion

The SpAs are a group of interrelated inflammatory arthritis that share multiple clinical features as well as common genetic predisposing factors. The group includes AS, ReA, PsA, SpA associated with IBD (Crohn's disease or ulcerative colitis) and undifferentiated SpA [1].

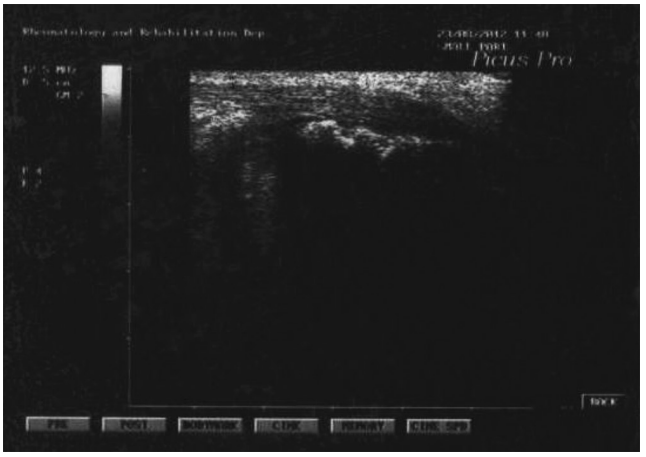
Enthesitis is a distinctive feature of SpA. It is observed in all SpA subtypes. Several reports have pointed to enthesitis as a primary lesion in SpA, which may underlie all skeletal manifestations characteristic of these disorders, including synovitis [17]. There are interesting previous data suggesting that B-mode ultrasound combined with Doppler ultrasound allowed for the detection of peripheral enthesitis in a majority of spondyloarthritis patients, thereby differentiating them from control populations; this finding could be very useful for the diagnosis of spondyloarthritis [16–18].

Figure 1



Left distal patellar ligament of 28-year-old axial spondyloarthropathic woman showing abnormal structure and calcification (star).

Figure 2



Right Achilles tendon of 25-year-old peripheral spondyloarthropathic man showing multiple erosions (white arrow), abnormal structure and retrocalcaneal bursitis (green arrow).

Table 5 Correlations between MASEI score and different variables in subgroup Ia and Ib

Clinical and laboratory parameters in subgroups	MASEI score			
	Subgroup Ia		Subgroup Ib	
	r	*P*-value	*r*	*P*-value
Age of the patient	−0.049	0.8	−0.460	0.1
Disease duration	0.241	0.3	0.033	0.9
ESR (first hour)	0.261	0.2	0.06	0.88
CRP titre	0.194	0.4	−0.211	0.5
BASDAI	0.7	0.1	0.8	0.001**
BASMI	0.1	0.8	0.2	0.5
BASFI	0.6	0.2	0.7	0.01*
MASES	0.2	0.3	0.3	0.2

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C-reactive protein; MASEI, Madrid Sonographic Enthesitis Index; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score. *Significant *P* value < 0.05. **Highly significant *P* value < 0.01.

Our study goes one step further to describe the assessment of peripheral enthesopathy by ultrasonography in early spondyloarthritis patients.

Our study found that the number of abnormal entheses by clinical examination in early spondyloarthritis patients was 52 per 360 (14%) examined entheses, whereas the number found by ultrasonographic examination was 239 per 360 (66.3%) examined entheses. This shows that sonography is very important to assess enthesis better than clinical examination.

In agreement with our results, Balint *et al.* [19] studied 35 SpA patients (27 AS, seven PsA and one ReA) and underwent clinical and ultrasonographic examination of five lower limb entheseal sites bilaterally according to the Glasgow Ultrasound Enthesitis Scoring System (GUESS). They reported that the number of abnormal entheses by clinical examination was 75 per 348 (22%) entheses examined, whereas the number found by ultrasonographic examination was 155 per 348 (56%) entheses examined. In addition, D'Agostino *et al.* [17] studied 164 SpA patients according to the Amor and ESSG criteria and 64 control patients (34 with mechanical back pain and 30 with rheumatoid arthritis). They underwent careful clinical examination in only 34 SpA patients. They found that clinical examination was abnormal in 88 per 612 (14.4%) entheses examined, whereas ultrasonographic examination was abnormal in 220 per 612 (36%) entheses examined, which is in agreement with our results. In our study, we found that number of abnormal entheses by ultrasonography was 239 per 360 (66.3%) entheses examined in early spondyloarthritis patients, whereas the number was 80 per 240 (33.3%) entheses in rheumatoid control patients.

D'Agostino *et al.* [17] agree with our study, as they found that the number of abnormal entheses by sonography was 1131 per 2952 (32%) entheses examined in SpA patients, whereas it was 132 per 1152 (11%) entheses examined in controls. D'Agostino *et al.* [20] studied 118 patients (51 early SpA, 48 non-SpA and, 19 unclassified patients). They found that 88 of the 118 patients (75%), who underwent ultrasonographic examination of enthesis, had at least one abnormal enthesis. It was significantly greater in SpA than in non-SpA patients ($P > 0.01$), which is in agreement with our results.

Our study demonstrated a statistically significant difference between early SpA and rheumatoid arthritis patients with respect to affection of enthesis around the knee (proximal and distal patellar ligament and quadriceps tendon entheses) and Achilles tendon (being more affected in the early SpA group).

D'Agostino *et al.* [20] agree with our study with respect to Achilles tendon affection. They found that it was significantly higher in SpA patients than in non-SpA patients ($P = 0.01$). In addition, D'Agostino *et al.* [17] found that the most commonly affected enthesis in SpA patients are knee enthesis and Achilles tendon, which is in agreement with our results. In addition, we found that mean MASEI score was highly statistically significant in SpA patients than in rheumatoid control patients ($P = 0.001$). It was 27.8 ± 5.4 in SpA patients, whereas it was 12.2 ± 4.3 in controls.

In agreement with our results, De Miguel *et al.* [21] found that the MASEI score was 23.36 ± 11.4 in SpA patients, whereas it was 12.26 ± 6.85 in controls, with statistically significant difference between both groups ($P = 0.001$). In addition, a study by Tatiana *et al.* [22] found that the mean MASEI score was 26.17 ± 13.68 in SpA patients, whereas it was 13.3 ± 7.97 in controls, with statistically significant difference between them ($P > 0.001$).

MASEI score in our results was 27.5 ± 5.4 in axial SpA patients and 28.1 ± 5.7 in peripheral SpA patients, with no statistically significant difference between both subgroups. De Miguel *et al.* [21] agree with our study, as they found that the MASEI score was 23.44 ± 12.18 in axial SpA patients and 23.23 ± 10.23 in peripheral SpA patients, with no statistically significant difference between them.

Our results revealed that no statistically significant difference was found between male and female SpA patients with respect to MASEI score. De Miguel *et al.* [21] and Tatiana *et al.* [22] do not agree with our study, as they found a higher MASEI score in SpA men than in SpA women, with statistically significant difference between them ($P > 0.01$ and $P > 0.07$, respectively); the discrepancy in results is likely to depend on differences in the duration of disease.

In addition, when we estimated elementary lesions score as a part of MASEI score, we found a statistically significant difference between early SpA and rheumatoid arthritis patients (higher in SpA patients). They included power Doppler ($P = 0.001$), calcification ($P = 0.001$), erosion ($P = 0.008$), bursa ($P = 0.001$) and structure ($P = 0.03$) scores, whereas there was no statistically significant difference with respect to thickness score.

De Miguel *et al.* [21] demonstrated a statistically significant difference between SpA patients and controls with respect to calcification, erosion and power Doppler scores, whereas there was no statistically significant difference with respect to thickness score, which is in agreement with our study. However, they do not agree with our study with respect to structure and bursa scores, which were not statistically significant different between both groups. D'Agostino *et al.* [20] showed a statistically significant difference between SpA and non-SpA patients with respect to the number of enthesis with power Doppler signal positivity ($P > 0.001$), which is in agreement with our results.

In accordance with our result, a study by Balint *et al.* [19] found no significant correlation between GUESS and acute phase reactants.

Acknowledgements

Conflicts of interest

None declared.

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