Assessment of enthesis in patients with psoriatic arthritis and fibromyalgia using clinical examination and ultrasound

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Received on March 17, 2019; accepted in revised form on July 8, 2019.

Clin Exp Rheumatol 2020; 38 (Suppl. 123): S31-S39.

Key words: fibromyalgia, spondyloarthropathies, psoriatic arthritis, enthesitis, ultrasonography

Competing interests: none declared.

ABSTRACT

Objective. *The primary aim of this study was to compare the prevalence of clinical and particularly ultrasonographic signs of enthesitis in patients with psoriatic arthritis (PsA), fibromyalgia (FM), or both. The secondary aim was to assess the impact of FM on disease activity and clinimetric scores.*

Methods. *This single-centre, observational cross-sectional study involved 101 consenting patients: 39 with PsA (CASPAR criteria), 23 with FM (2016 criteria), and 39 with both. Standard PsA and FM clinical, laboratory and clinimetric data were recorded, and entheses were assessed using the Leeds Enthesitis Index (LEI) and the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES). All the patients underwent B mode (grey-scale) and Power Doppler (PD) ultrasonography bilaterally at the insertions of the quadriceps tendons, the proximal and distal patellar tendons, the Achilles tendons, and the plantar fascia insertions of the calcaneus, to evaluate the thickness of entheses, the hypoechogenicity, the presence of bony erosions, the enthesophytes, and the bursitis. The US findings were scored using the Glasgow Ultrasound Enthesitis Scoring System (GUESS). The data were statistically analysed using univariate and multivariate analyses, and receiver-operating characteristic (ROC) curves, concentrating on the shared clinical features of the two conditions.*

Results. *The mean age of the patients as a whole was 53.6±9.47 years. Females accounted for 64.1% of the PsA patients (disease duration 9.13 years), 95.6% of the FM patients (disease duration 5.09 years), and 92.3% of the patients with PsA-FM (disease duration 7.9 years). There were no between-group differences in the patients' body mass index (BMI). In accordance with the study inclusion criteria, none of the FM subjects had PsA or reported any personal or family history of psoriasis. The mean Psoriasis Area and Severity Index was 2.3±3.1 in the PsA group, and 1.2±2.45 in the PsA-FM group. Clinical evidence of enthesopathy was found in 43% of the patients with PsA, 51.3% of those with PsA-FM, and 50.8% of those with FM, while US entheseal abnormalities were detected in respectively 77%, 74% and 35%. The median Bath Ankylosing Spondylitis Disease Activity Index was significantly higher in the patients with PsA-FM than in those with PsA (7.7 [IQR 2.1] vs. 5.0 [IQR 3.8]; p<0.001), as was the median ESR-assessed Ankylosing Spondylitis Disease Activity Score (3.69 [IQR 1.00] vs. 2.82 [IQR 1.55; p=0.004), or CRP- assessed (median 3.27 [IQR 1.07] vs. 2.66 [IQR 1.26]; p=0.006).*

There was a correlation between GUESS scores and disease duration in the patients with PsA (rho=0.37; p=0.019, 95% CI 0.10-0.61) or PsA-FM (rho=0.38; p=0.016, 95% CI 0.10-0.61), but not in the FM group, and GUESS scores correlated with BMI (rho=0.2; p=0.05, 95% CI 0.00-0.37) and dyslipidaemia (rho=0.34; p=0.006, 95% CI 0.11-0.58) in all three groups.

Conclusion. *The use of a clinical examination and clinimetric scores alone may overestimate active enthesitis in FM patients. As US was more frequently positive in patients with PsA and PsA-FM than in those with FM, it may be useful in differentiating pain due to enthesitis from entheseal pain due to FM.*

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disorder belonging to the heterogeneous group of spondyloarthropathies (SpAs), which affect up to 30% of patients with psoriasis (1). However, there are no

genetic, laboratory or clinical biomarkers capable of identifying the patients with psoriasis who are likely to develop PsA (2). The ClASsification criteria for Psoriatic ARthritis (CASPAR) were developed in 2006 as a means of standardising the classification of PsA for clinical trials and observational studies and differentiating it from other forms of arthritis (3, 4) and, more recently, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) (5) has highlighted some widely accepted clinical domains specific to PsA that should be considered when treating patients, including peripheral arthritis, axial disease, dactylitis and, above all, enthesitis, which is a hallmark of PsA (6). An enthesis is the connective tissue between a tendon, ligament or joint capsule and its insertion into bone that facilitates joint motion, and may be fibrous or fibrocartilaginous depending on the type of tissue at the attachment site (7). The inflammatory entheseal changes associated with PsA almost always occur at sites of fibrocartilaginous attachments (8).

Evaluating PsA-related enthesitis is diagnostically and therapeutically essential, but may be very complex because of the wide range of signs and symptoms that partly overlap or co-exist with the clinical features of fibromyalgia (FM). The estimated general adult population prevalence of FM, one of the most frequent causes of chronic widespread pain (CWP) (9), is 2-3%, but this varies depending on the classification criteria used (10). The first diagnostic criteria for FM published by the American College of Rheumatology (ACR) in 1990 included a history of CWP for at least three months and pain upon digital palpation at >11/18 specific sites defined as tender points (TPs) (11). Most of the patients meeting the 1990 ACR criteria were female (a ratio of 9:1), probably because the pain threshold is lower in women. However, the new diagnostic criteria proposed in 2016, which are based on CWP and somatic symptoms and do not require a TP examination (12, 13), indicate a female-to-male ratio of 3:1, as in the case of other chronic painful conditions. The diagnosis of FM is mainly clinical because FM patients do not show any characteristic or consistent abnormalities in laboratory biomarkers.

Over the last 20 years, many studies carried out in order to clarify the aetiopathogenetic mechanisms of FM have shown that symptoms such as widespread musculoskeletal pain (9), chronic fatigue, sleep disorders, neurocognitive impairment and the presence of TPs (11) are common in patients with other painful rheumatic diseases, and recent studies have shown that they are related to an altered pain perception threshold (central sensitisation syndrome) accompanied by neuroendocrine and/or psycho-affective disorders in FM patients. Nevertheless, it may still be difficult to diagnose FM in patients with other conditions causing CWP.

Patients with PsA who complain of widespread extra-articular pain may also have polyenthesitis, FM, or both (14) Furthermore, patients with unknown psoriatic polyenthesitis may easily be erroneously diagnosed as having FM, thus leading to inappropriate patient management strategies that may allow disease progression and functional worsening, and consequently increase disability, mortality and socio-economic costs (15). Power Doppler Musculoskeletal ultrasonography (PDUS) may help in distinguishing the two disorders (16) as it has been shown that it is a reliable means of evaluating enthesitis, and can detect clinically asymptomatic enthesitis in psoriatic patients without PsA but recent studies have shown the potential role of musculoskeletal ultrasound (MSUS) in the evaluation of clinical and subclinical enthesitis also in other pathology (17-19).

Only a few published studies have so far evaluated the impact of FM on patients with PsA. The primary aim of this study was to determine the prevalence of entheseal involvement by means of a clinical examination and PDUS in patients with PsA, FM or both, and whether there are any particular aspects that can distinguish the two conditions. The secondary aim was to establish the extent of the impact of FM on disease activity, clinimetric scores, laboratory findings and US findings.

Materials and methods

This single-centre, observational cross-sectional involved a total of 101 sex- and body mass index [BMI]-matched consecutive adult patients with a definite diagnosis of PsA, FM or both according to the CASPAR (4), 1990 ACR, 2011 ACR and 2016 ACR FM criteria (11-13) who attended the Rheumatology Department of the University Hospital of Messina for routine examinations between January and June 2018.

The inclusion criteria were an age of ≥18 years and the administration of stable treatment (if any) during the four weeks preceding enrollment. The exclusion criteria were a BMI of >35 kg/m^2, previous knee and/or ankle surgery, procedural interventions on the examined structures (*e.g.* corticosteroid injections), a recent history of severe entheseal trauma, intense physical activity during the four weeks preceding the clinical evaluation, a previous diagnosis of crystal deposition arthropathy (gout and/or calcium pyrophosphate crystal deposition disease), a history of cancer or lymphoproliferaltive disease, uncontrolled diabetes or lower limb peripheral neuropathy, chronic leg ulcer, unstable ischaemic heart disease or congestive heart failure, active inflammatory bowel disease, recent stroke, neurological symptoms suggesting central nervous system demyelinating disease, and cognitive deficits. In addition, the patients with FM had to have no personal or family history of PsA or psoriasis. The paper case report forms prepared for anonymous data collection included patients' history (age, sex, BMI, disease duration, family and personal history of psoriasis, FM-related conditions/symptoms, the use of non-steroidal anti-inflammatory drugs [NSAIDs] and corticosteroids, and co-morbidities), self-assessment questionnaires, and the findings of physical examinations and laboratory investigations. All the patients taking NSAIDs were asked to stop doing so 24 hours before the clinical and US examinations.

All the patients gave their informed consent to participate in the study, which was conducted in accordance with the Declaration of Helsinki and local regulations. Local Ethics Com-

mittee approval was not required as the participants underwent the clinical and clinimetric examinations on the basis of routine hospital protocols.

Clinical assessment

All the patients underwent a thorough clinical examination including 66/68 swollen and tender joint counts, the Psoriasis Area and Severity Index (PASI) for skin involvement, tender point counts, and an evaluation of the following bilateral entheses: the patellar insertion of the quadriceps tendon, the proximal patellar insertion of the patellar tendon, the distal tibial insertion of the patellar tendon, the calcaneal insertions of the Achilles tendon and plantar fascia. Entheseal involvement was clinically measured using the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) modified for PsA (20) and the Leeds Enthesitis Index (LEI) (21).

A clinical diagnosis of enthesitis was made in the physical examination presence of spontaneous entheseal pain, entheseal pain generated by pressure and/or mobilisation and/or contraction against resistance, or local entheseal swelling. The decision to investigate lower limb entheses was based on their frequent involvement in rheumatic diseases (18), and because their anatomic location allows relatively easy assessment by means of US and physical examination (22).

The collected laboratory data were the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels, which were considered to be positive when they were above the laboratory reference ranges.

The pattern of articular involvement was established using the Disease Activity index for PSoriatic Arthritis (DAPSA) (23), which assesses peripheral joint disease activity. Disease activity in the PsA and PsA-FM patients was assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI) and the different versions of the Ankylosing Spondylitis Disease Activity Score (ASDAS: back pain, morning stiffness, patient global pain, pain/swelling of peripheral joints, plus ESR or CRP levels) in order to capture the subjective and objective aspects of PsA disease activity (24-26). Functional impairment and the quality of life of the FM patients were assessed using the Fibromyalgia Impact Questionnaire (FIQ) (27) and the Fibromyalgia Moldofsky Questionnaire (FMQ). Loss of function and the quality of life were evaluated in all three groups using the Short Form-36 (SF-36) (28). The patients were also asked to self-assess their pain and general health using a 100 mm visual analogue scale (VAS) and the Patient Global Assessment (PtGA) scale.

Ultrasonography

On the same day as the clinical examination, one of the study rheumatologists, who was blinded to the patients clinical and serological data, and had been trained in using ultrasonography to assess entheseal involvement in musculoskeletal disorders carried out a grey scale (GS) and power Doppler (PD) mode examination using a standardised method (29) and a MyLab Twice machine (Esaote, Florence, Italy) equipped with a 6–18 MHz linear probe working at a Doppler frequency of 9.1 MHz with a pulse repetition frequency (PRF) of 750 mHz. The US examination investigated the quadriceps, distal and proximal patellar, Achilles tendon, and proximal plantar aponeurosis entheseal insertions. The multi-planar US examinations of the quadriceps and patellar entheses were carried out with the patient in a supine position with lower limbs extended. The Achilles tendon and proximal plantar aponeurosis insertions were examined with the patient in a prone position with the feet hanging over the edge of the examination table at 90° of flexion (30).

US-detected pathological entheseal changes were identified on the basis of the definitions of enthesitis in spondyloarthritis proposed by the Outcome Measures in Rheumatology (OMERACT) Ultrasound Task Force (31, 32): tendon hypoechogenicity and/or thickening at its bony insertion, intratendinous calcifications, enthesophytes, bony erosions, bony cortex irregularities, and the presence of a Doppler signal <2 mm from the insertion. All the US findings indicative of enthesopathy were scored on the basis of the Glasgow Ultrasound Enthesitis Scoring System (GUESS) (18), and investigated in both the transverse and longitudinal views (from the proximal to the distal and from the medial to the lateral aspect of the enthesis). Entheseal thickness was measured at the point of maximal thickness 2 mm proximal to the bony insertion (normal values are 6.1 mm for the quadriceps tendon, 4 mm for proximal and distal insertion of the patellar, 5.29 mm for the Achilles tendon, and 4.4 mm for the plantar fascia); bursitis was defined as a well-circumscribed, localised anechoic or hypoechoic area at the site of an anatomical bursa that could be compressed by the transducer (33); bony erosions as cortical interruptions with a step-down contour defect; and enthesophytes as a step-up bony prominence at the end of a normal bone profile. One point was attributed to the presence of each pathological change, and the final score of 0-36 was the sum of the individual scores. The presence of power doppler signal was evaluated within 2 mm from the bony cortex of tendon insertion. Before starting the study, the investigators agreed on how to interpret the US findings.

Statistical analysis

The study data are given as median values and interquartile ranges (IQRs), or absolute values and relative frequencies (percentages). Between-group comparisons were made using the Kruskall-Wallis or chi-squared test; Dunnet's test was used for multiple comparisons. Spearman's rank correlation test with bootstrap confidence intervals was used to correlate the clinimetric scores, and the correlation coefficients were compared in accordance with Zou (34-36) using Bonferroni's correction; if necessary, the rank biserial correlation was also used. Given the nature of the composite indices, residual bootstrap regression was carried out using bias-corrected and accelerated (BCA) 95% confidence intervals and relative diagnostics (37, 38). The data were statistically analysed using two-tailed statistical tests, with a p.value of <0.05 being considered sta-

tistically significant. The analyses were made using R-cran software (39).

Results

One hundred and one patients who met the inclusion criteria were enrolled in the study: 39 with PsA (25 women and 14 men), 23 with FM (22 women and one man), and 39 with PsA and FM (36 women and three men). Table I shows their demographic and clinical characteristics. The prevalence of females was highly significant ($p<0.001$), and disease duration was significantly longer in the PsA than in the FM group ($p<0.05$), without a statistically significant difference between PsA and PsA-FM group (8 [IQR 7.5] *vs*. 6 [IQR 6]; $p=0.352$). There was no significant difference in BMI in the three groups (Table I). In line with the inclusion criteria, none of the FM patients had PsA or reported any personal or family history of psoriasis. Table II shows the questionnaire and composite scores.

As expected, median FIQ and FMQ scores were significantly high in the patients with FM and PsA-FM, without a statistically significant difference between them.

The median BASDAI was significantly higher in the patients with PsA-FM than in those with PsA (7.7 [IQR 2.1] *vs*. 5.0 [IQR 3.8]; $p<0.001$), as was the median ASDAS assessed using ESR (3.69 [IQR 1.00] *vs*. 2.82 [IQR 1.55]; $p=0.004$] or CRP (median 3.27 [IQR 1.07] *vs*. 2.66 [IQR 1.26]; $p=0.006$) (Table II.)

Figure 1 shows the plots of BASDAI, ASDAS-ESR and ASDAS-CRP values.

The median MASES was significantly higher in the patients with FM or PsA-FM than in those with PsA ($p<0.001$), but the difference between the FM *vs*. PsA-FM groups was not statistically significant (6 [IQR 2] *vs*. 7 [IQR 3]; $p=0.737$). The median LEI was significantly higher in the patients with FM or PsA-FM ($p<0.001$), with no statistically significant difference between these two groups (4 [IQR 4] *vs*. 4 [IQR 2]; $p=0.658$). The median GUESS score was significantly higher in the patients with PsA than in those with FM (9 [IQR 7.5] *vs*. 3 [IQR 2]; $p<0.001$), and significantly higher in the patients with PsA-FM group than in those with FM (8 [IQR 4.5] *vs*. 3 [IQR 2]; $p<0.001$). There was no statistically significant difference between the patients with PsA and those with PsA-FM (9 [IQR 7.5] *vs*. 8 [IQR 4.5]; $p<0.112$) (Table II).

Figure 2 shows the plots of GUESS scores, MASES and the LEI.

No statistically significant Spearman correlation coefficient (rho) was found between GUESS scores and MASES in

Table I. Demographic and clinical characteristics of the study population.

Variables	FM (n=23)	PsA-FM (n=39)	PsA (n=39)	*p*-value
Median age (IQR)	49 (20)	53 (10)	56 (9)	0.135
Females, n (%)	22 (95.7)	36 (92.3)	25 (64.1)	<0.001
Median BMI, kg/m^2 (IQR)	28.12 (6.38)	28.58 (4.48)	28.58 (6.75)	0.536
Median disease duration, years (IQR)	4.0 (6.5)	6.0 (6.0)	8.0 (7.5)	0.018
Median ESR, mm/h (IQR)	10.0 (8.5)	12.0 (15.0)	14.0 (14.5)	0.095
Median CRP level, mg/L (IQR)	2.0 (2.5)	3.0 (4.3)	3.3 (3.8)	0.181
Median TJ count (IQR)	4.0 (5.0)	6.0 (6.0)	4.0 (6.0)	0.033
Median SJ count (IQR)	0.0 (0.0)	0.0 (3.5)	0.0 (2.0)	0.001
Median VAS score (IQR)	8.0 (2.0)	8.0 (1.0)	6.0 (2.5)	<0.001
Median PGA score (IQR)	7.0 (2.0)	7.0 (2.0)	5.0 (3)	<0.001
Psoriasis, n (%)	-	15 (38.4%)	17 (43.5%)	0.21
Medications				
NSAIDs, n (%)	-	19 (48.7%)	16 (41%)	0.47
Corticosteroids, n (%)	-	2 (5%)	1 (2%)	0.74
csDMARDs, n (%)	-	20 (51.3%)	24 (61.5%)	0.83
bDMARDs, n (%)	-	31 (79%)	30 (77%)	0.08
FM therapy, n (%)	21 (95.4%)	36 (92%)	-	0.23

FM: fibromyalgia; PsA: psoriatic arthritis; IQR: inter-quartile range; BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; PGA: patient global assessment; TJ: tender joint; SJ: swollen joint; NSAIDs: non-steroidal anti-inflammatory drugs; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDS: biological disease-modifying anti-rheumatic drugs.

Table II. Questionnaire and composite scores.

Variables	FM (n=23)	PsA-FM (n=39)	PsA (n=39)	*p*-value
Median BASDAI (IQR)	-	7.7 (2.1)	5.0 (3.8)	<0.001
Median BASFI (IQR)	-	5.4 (3.6)	3.2 (3.4)	<0.001
Median BASMI (IQR)	-	0.0 (2.0)	0.0 (2.0)	NS
Median ASDAS-ESR (IQR)	-	3.69 (1.00)	2.82 (1.55)	0.004
Median ASDAS-CRP (IQR)	-	3.27 (1.07)	2.66 (1.26)	0.006
Median FIQ (IQR)	77.08 (20.05)	72.74 (15.80)	-	NS
Median FMQ (IQR)	12.0 (4.0)	12.0 (5.5)	-	NS
Median LEI (IQR)	4.0 (4.0)	4.0 (2.0)	2.0 (2.0)	<0.001
Median MASES (IQR)	6.0 (2.0)	7.0 (3.0)	2.0 (2.0)	<0.001
Median GUESS (IQR)	3.0 (2.0)	8.0 (4.5)	9.0 (7.5)	<0.001

FM: fibromyalgia; PsA: psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; IQR: inter-quartile range; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; FIQ: Fibromyalgia Impact Questionnaire; FMQ: Fibromyalgia Moldofsky Questionnaire; LEI: Leeds Enthesitis Index; MASES: MaastrichAnkylosing Spondylitis Enthesitis Score; GUESS: Glasgow Ultrasound Enthesitis Scoring System. NS: not statistically significant.

Table III. Spearman's correlations (rho) between GUESS, MASES and LEI scores.

GUESS/MASES	Spearman (rho)	*p*-value	95% CI	
APs	0.19	0.254	-0.17	0.52
APs-FM	0.04	0.799	-0.32	0.39
FM	-0.04	0.859	-0.48	0.42
GUESS/LEI				
APs	0.18	0.266	-0.13	0.46
APs-FM	0.36	0.023	0.04	0.63
FM	0.16	0.471	-0.3	0.54

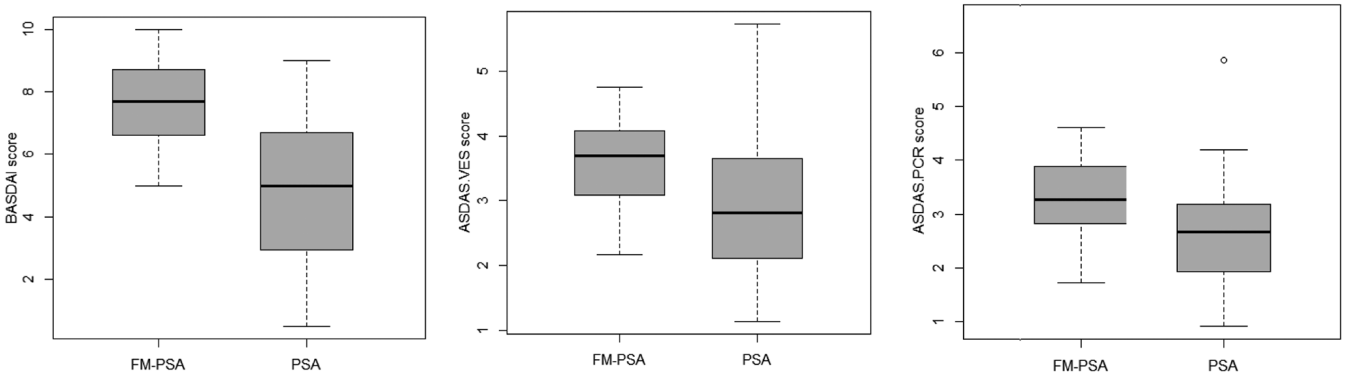

Fig. 1. Plots of BASDAI, ASDAS-ESR and ASDAS-CRP values.
The boxes show median values (horizontal line), and the 25th and 75th percentiles; the whiskers represent the 5th and 95th percentiles.

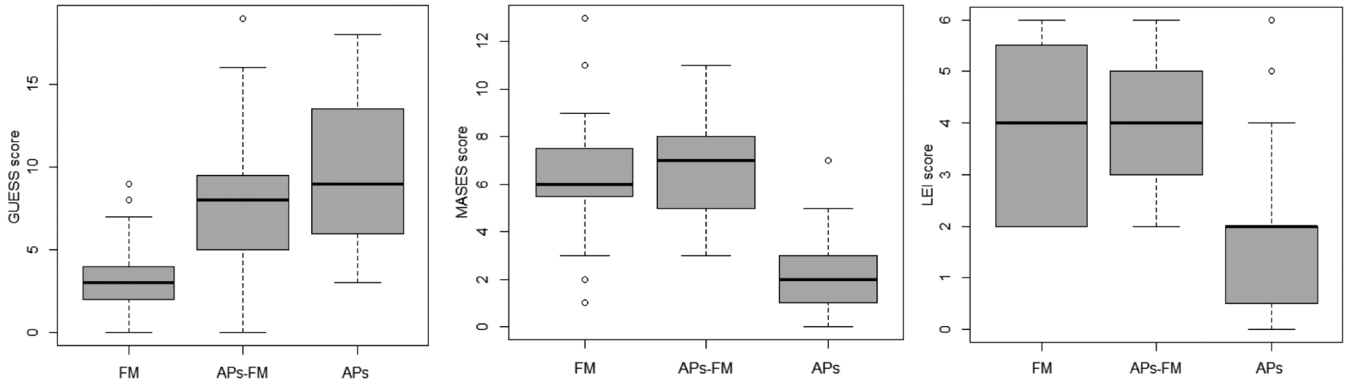

Fig. 2. Plots of GUESS scores, MASES and the LEI.
The boxes show median values (horizontal line), and the 25th and 75th percentiles; the whiskers represent the 5th and 95th percentiles.

any of the groups, but there was a weak correlation between GUESS and LEI scores in the PsA-FM group (rho=0.36; *p*=0.023, 95% CI 0.04-0.63) (Table III). There was no linear relationship between GUESS scores and MASES or the LEI in any group (Fig. 3).

There was a statistically significant correlation between GUESS scores and disease duration in the PsA group (rho=0.37; *p*=0.019, 95% CI 0.10–0.61) and PsA-FM group (rho=0.38; *p*=0.016, 95% CI 0.10–0.61), but not in the FM group (rho=0.07; *p*=0.761, 95% CI -0.30 - 0.43). GUESS scores correlated with the BMI (rho=0.2; *p*=0.05, 95% CI 0.00–0.37) and dyslipidaemia (rho=0.34; *p*=0.006, 95% CI 0.11–0.58) in all the groups (Fig. 4).

A total of 390 entheseal sites in the 39 patients with PsA, 390 in the 39 patients with FM-PsA, and 230 in the FM patients were examined clinically and by means of US. There was clinical evidence of enthesopathy in 43% of the patients with PsA, 51.3% of those with PsA-FM, and 50.8% of those with FM, and there were US-detected entheseal abnormalities in respectively 77%, 74% and 35% (Table IV).

Signs of enthesopathy in most of the entheseal sites were more frequent among the PsA and PsA+FM patients. The entheseal sites with the highest number of US signs of enthesopathy were the insertion of the Achilles tendon (7.2% in FM group *vs*. 27.4% in PsA and PsA+FM groups *p*=0.000), followed by the insertions of quadriceps tendon (8.7% in FM group *vs*. 27.3% in PsA and PsA+FM groups, *p*=0.000) and the proximal patellar tendon (9.1% in FM group *vs*. 17.2% in PsA and PsA+FM groups, *p*=0.03). No bone erosions were detected in the FM patients, but there were erosions in 25/780 entheses (3%) of the patients with PsA.

PD signal was more frequent in patients with PsA or PsA+FM at the insertion of quadriceps tendon (3% in FM group *vs*. 5% in PsA and PsA+FM groups *p*=0.01), at the proximal patellar tendon (0.9% in FM group *vs*. 3.33% in PsA and PsA+FM groups *p*=0.05), at the Achilles tendon (2.6% in FM group *vs*. 5.9% in PsA and PsA+FM groups *p*=0.05) and at plantar aponeurosis (0.4% in FM group *vs*. 1.41% in PsA and PsA+FM groups p=0.04). Table V shows the distribution of entheseal involvement.

PD signal was positive: in 23 (59%) PsA+FM patients and in 16 (41%) PsA patients at the insertion of quadriceps tendon, in 15 (38%) PsA+FM patients and in 11 (28%) PsA patients at the insertions of proximal patellar tendon, in 4 (10%) PsA+FM patients and in 5 (12%) PsA patients at the insertions of the distal patellar tendon, in 20 (51%) PsA+FM patients and in 26 (66%) PsA patients at the Achilles tendon, in 4 (10%) PsA+FM patients and in 7 (18%) PsA patients at plantar aponeurosis.

Discussion

Our study showed higher clinical evidence of enthesopathy in FM patients

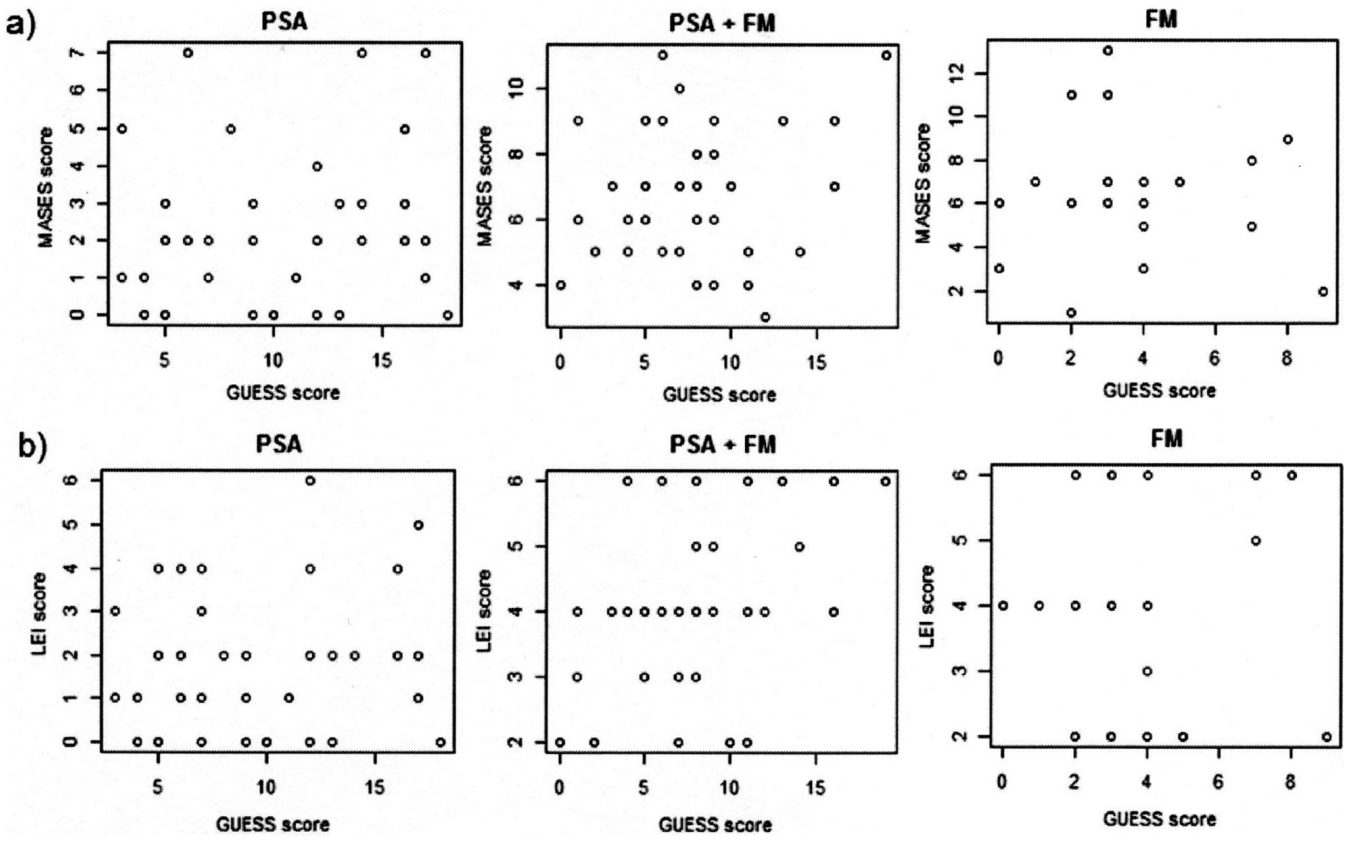

Fig. 3. Comparison of correlation coefficients.
a) GUESS and MASES scores: PsA *vs*. PsA-FM (p=0.518, CI -0.30 0.58); FM *vs*. PSA+FM (p=0.774, CI% -0.59 0.45), FM *vs*. PsA (p=0.404, CI -0.71 0.31).
b) GUESS and the LEI scores: PsA *vs*. PsA+FM (p=0.408, CI -0.59 0.23); FM *vs*. PsA+FM (p=0.439, CI -070 0.29); FM *vs*. PsA (p=0.941, CI -0.54 0.48).

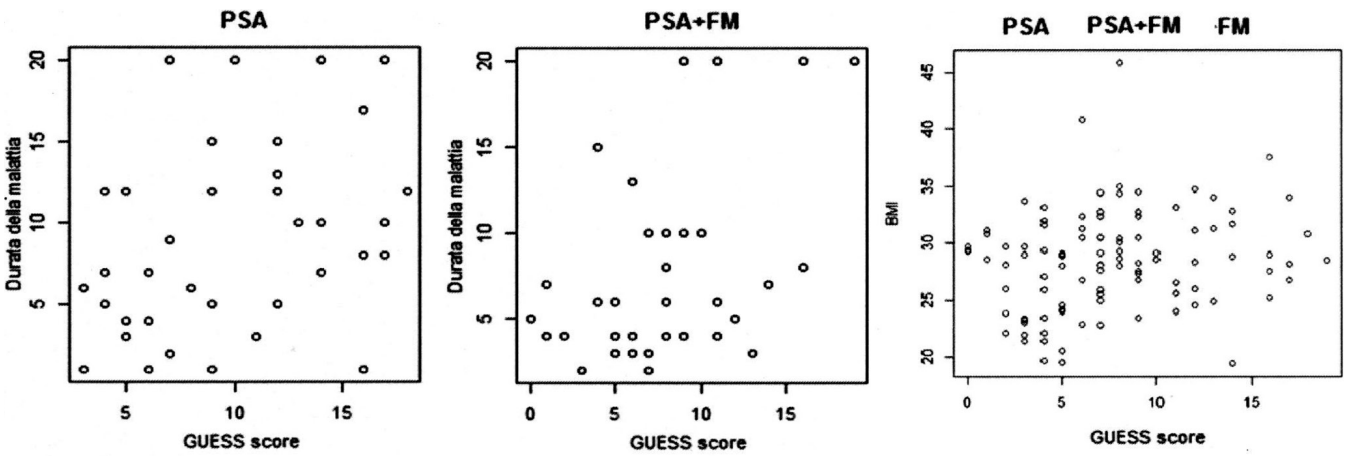

Fig. 4. Correlations between guess scores and disease duration and BMI.

compared to PsA and o PsA-FM while higher US entheseal abnormalities were detected in PsA-FM and PsA patients than in these with FM suggesting a role of US in differentiating pain due to enthesitis from entheseal pain due to FM. Furthermore, we reported a significant higher BASDAI in the patients with PsA-FM than in those with PsA suggesting an impact of FM disease activity. FM frequently co-exists with rheumatic diseases, and has also been found concomitantly with PsA. The estimated prevalence of FM in patients with axial PsA is 17.2% (95% CI 15.1–19.9); its prevalence among women is 34.2% (95% CI 31.9–36.4) as against 6.1% among males (95% CI 5.0–7.6) (41). Evaluating disease activity in PsA patients is essential, but it is also complex because of the wide range of signs and symptoms that partly overlap or co-exist with those of other diseases (8, 14, 40, 42). Co-existing FM is related to worse scores on all tested measures in patients with PsA: Brikman *et al*. found that the Composite Psoriatic Disease Activity Index (CPDAI) and DAPSA scores were significantly higher in patients with PsA and FM than in

Table IV. Ultrasonographic and clinical entheseal findings.

	US*	Clinical tender points (patients number)	*p*	US*	Clinical tender points	*p*	US*	Clinical tender points	*p*
	FM			FM-PSA			PSA		
Quadriceps tendons	15/46 (33%)	30/46 (65%)	0.0002	67/78 (86%)	57/78 (73%)	0.04	68/78 (87%)	49/78 (63%)	0.0004
Patellar tendons (proximal)	18/46 (39%)	34/46 (73%)	0.001	55/78 (70.5%)	44/78 (56.4%)	NS	61/78 (78%)	29/78 (37%)	0.000
Patellar tendons (distal)	24/46 (52%)	26/46 (56%)	NS	54/78 (70%)	40/78 (51.3%)	0.02	55/78 (70.5%)	21/78 (27%)	0.000
Achilles tendons	15/46 (33%)	22/46 (47.8%)	NS	73/78 93%)	43/78 (55%)	0.000	75/78 (95%)	45/78 (57.6%)	0.000
Plantar aponeuroses	9/46 (19.5%)	5/46 (10.8%)	NS	40/78 (51%)	16/78 (20.5%)	0.001	50/78 (64%)	23/78 (29.5%)	0.001
Total scores	81/230 (35%)	117/230 (50.8%)	0.0007	289/390 (74%)	200/390 (51.3%)	0.000	301/390 (77%)	167/390 (43%)	0.000

Clinical findings: PsA (390 sites), PsA-FM (390 sites), FM (230 sites). FM: fibromyalgia; PsA: psoriatic arthritis; NS: not statistically significant.
*US findings: thickened tendons, bursitis, bone erosion, enthesophytes, PD signal.

Table V. Distribution of morphostructural changes.

	Quadriceps tendon			Patellar tendons (proximal)			Patellar tendons (distal)			Achilles tendons			Plantar aponeurosis		
	FM	PSA FM-PSA	*p*	FM	PSA FM-PSA	*p*	FM	PSA FM-PSA	*p*	FM	PSA FM-PSA	*p*	FM	PSA FM-PSA	*p*
Thickening	8 (3.5%)	72 (9.2%)	0.004	18 (7.8%)	81 (10.4%)	NS	24 (10.4%)	99 (12.7%)	NS	6 (2.6%)	63 (8%)	0,0001	4 (1.7%)	50 (6.4%)	0,004
Bursitis	4 (1.7%)	26 (3.33%)	NS	N/A	N/A	///	1 (0.4%)	7 (0.9%)	NS	0	13 (1.66%)	0,04	N/A	N/A	///
Bone erosions	0	12 (1.5%)	///	0	1 (0.1%)	///	0	6 (0.8%)	///	0	6 (0.77%)	///	0	0	///
Enthesophytes	5 (2.2%)	64 (8.2%)	0,001	1 (0.4%)	26 (3.33%)	0,01	1 (0.4%)	14 (1.8%)	NS	6 (2.6%)	86 (11%)	0,0001	7 (3%)	64 (8.2%)	0,007
PD signal	3 (1.3%)	39 (5%)	0,01	2 (0.9%)	26 (3.33%)	0,05	1 (0.4%)	9 (1.15%)	NS	6 (2.6%)	46 (5.9%)	0,05	1 (0.4%)	11 (1.41%)	0,04
Total	20 (8.7%)	213 (27.3%)	0,000	21 (9.1%)	134 (17.2%)	0,03	27 (11.7%)	129 (16.5%)	NS	18 (7.2%)	214 (27.4%)	0,000	12 (5.2%)	130 (16.6%)	0,0001

PsA (390 sites) + PsA-FM (390 sites), FM (230 sites).
FM: fibromyalgia; PsA: psoriatic arthritis; NS: not statistically significant; ///: unmeasurable chi-squared test.

patients with PsA alone (respectively, 9.23±1.92 *vs*. 4.25±3.14, $p<0.001$, and 27.53±19.23 *vs*. 12.82±12.71, $p=0.003$) (43). Our data are in line with the previous study consequently evaluation PsA disease activity is very important in clinical practice as it aids the choice of treatment with biological agents and the identification of refractory patients. The accumulating evidence indicating an association between FM and PsA raises the question of how to differentiate the clinical features of the two conditions: for example, it is often difficult to determine whether the tenderness detected during a clinical examination is due to entheseal involvement or FM. Furthermore, the presence of FM can complicate the evaluation of PsA: the main cause of diagnostic confusion in the 1990 ACR criteria (44) is due to the overlap of PsA-related enthesitis with the tender points of FM and, although the alternative 2010 ACR diagnostic criteria for FM (45) are based on patient self-assessment without a tender point count, some authors consider them as confusing as those of 1990 (8,14). In an attempt to approach the essence of enthesitis, it has been suggested that PsA and FM can be differentiated by means of PDUS (46), but this is not available to everyone in everyday clinical practice,

and has the drawbacks that it is operator dependent and there is no standardised approach to studying entheses (47). Our findings show that US imaging is a valid means of detecting signs of enthesopathy that can distinguish PsA and FM patients, particularly when the clinical features of the two conditions overlap and may lead clinician to underestimate the symptoms or formulate a misdiagnosis (48-49). Buskila *et al*. found ten painful sites in about 24% PsA patients, and the mean dolorimetric thresholds of tenderness at six fibrotic sites were 3.97+1.99 in patients with rheumatoid arthritis (RA) and 5.95+2.28 in patients with PsA (p<0.0001) (40). In a recent study of 266 patients with PsA and 120 with FM, Marchesoni *et al*. (16) found that the clinical features making it possible to distinguish the two diseases were somatic symptoms and the number of tender points. A cut-off point of ≥3 involved sites had the greatest discriminating power in the patients with PsA, who were the only patients with bony erosions, and PDUS signs of plantar fascia enthesopathy and Achilles tendon inflammation were highly specific for PsA. FM patients often also feel pain and tenderness at non-specific sites, which reflects a reduction in the pain threshold (16); otherwise, concomitant peripheral and/or axial articular inflammatory involvement would clearly suggest PsA (14). Furthermore, a PDUS examination of 30 PsA and 30 FM patients has shown that PDUS can differentiate the two diseases on the basis of the number and distribution of the affected joints. Our findings confirm previously published data, but our study is different in terms of its population, considering the PSA associated with FM. They also demonstrate that a clinical evaluation alone does not seem to provide an accurate estimate of entheseal involvement as it could lead to an overestimate of the disease activity assessed by means of the BASDAI and ASDAS in patients with PsA-FM. Physicians should bear our findings in mind when managing patients with these diseases in order to avoid both over- and under-treatment.

Furthermore, MSUS with PDUS seems to be a crucial means of avoiding inappropriate switching or swapping biological DMARDs on the basis of incorrectly assessed disease activity, and therefore can help to reduce the related costs. One limitation of this study is the small study population but, to the best of our knowledge, this is the first study comparing three cohorts of patients. Another limitation is that restricting the study to lower limb entheses may have led to an underestimate of the prevalence of enthesitis in FM patients.

However, in conclusion we demonstrated that the use of a clinical examination and clinimetric scores alone may overestimate active enthesitis in FM patients. As grayscale US and PDUS was more frequently positive in patients with PsA and PsA-FM than in those with FM, it may be useful in differentiating pain due to enthesitis from entheseal pain due to FM, although further studies are necessary to confirm our data.

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