Identification of the Clinical Features Distinguishing Psoriatic Arthritis and Fibromyalgia

ANTONIO MARCHESONI, FABIOLA ATZENI, ANTONIO SPADARO, ENNIO LUBRANO, GIUSEPPE PROVENZANO, ALBERTO CAULI, IGNAZIO OLIVIERI, DANIELA MELCHIORRE, CARLO SALVARANI, RAFFAELE SCARPA, PIERCARLO SARZI-PUTTINI, MONICA MONTEPAONE, GIOVANNI PORRU, SALVATORE D'ANGELO, MARIAGRAZIA CATANOSO, LUISA COSTA, MARIA MANARA, VALENTINA VARISCO, LAURA ROTUNNO, ORAZIO DE LUCIA, and GABRIELE DE MARCO

ABSTRACT. ***Objective.*** To identify the clinical features that can help to distinguish between psoriatic arthritis (PsA) and fibromyalgia (FM).

Methods. Our cross-sectional study was carried out in 10 Italian rheumatology centers between January and September 2009, and enrolled all consecutive patients with PsA and FM who agreed to participate. Standard clinical and laboratory data for PsA and FM were collected from all patients. Records were made of somatic symptoms, response to nonsteroidal antiinflammatory drugs (NSAID), self-evaluated pain, general health, disability, and responses to the Fibromyalgia Impact Questionnaire. Data were statistically analyzed by univariate and multivariate analyses, and receiver-operating characteristic curves. The analysis concentrated on the clinical features shared by the 2 conditions.

Results. Two hundred sixty-six patients with PsA (mean age 51.7 yrs; disease duration 10.2 yrs) and 120 patients with FM (mean age 50.2 yrs; disease duration 5.6 yrs) were evaluated. Univariate analysis showed that patients with FM had higher mean tender point and enthesitis scores, more somatic symptoms, and responded less to NSAID. Multivariate analysis showed that the presence of ≥ 6 FM-associated symptoms and ≥ 8 tender points was the best predictor of FM.

Conclusion. The shared clinical features of PsA and FM that had the greatest discriminating power for FM were the number of FM-associated symptoms and tender point count. (First Release Jan 15 2012; J Rheumatol 2012;39:849–55; doi:10.3899/jrheum.110893)

Key Indexing Terms:
PSORIATIC ARTHRITIS FIBROMYALGIA PAIN ENTHESITIS

Fibromyalgia (FM) is a common cause of chronic widespread pain (CWP) and of rheumatologic consultations. Its prevalence in the adult general population is about 2% and differs considerably between men and women (about 0.5%

From the UOC Day Hospital Reumatologia, Istituto Ortopedico G. Pini, and the Unità di Reumatologia, Ospedale L. Sacco, Polo Universitario, Milan; Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma, Rome; the Academic Rheumatology Unit, Department of Health Sciences, University of Molise, Campobasso; UO Reumatologia, Azienda Ospedaliera "Ospedali Riuniti Villa Sofia – Cervello," Palermo; Department of Medical Sciences, University of Cagliari, Cagliari; Rheumatology Department of Lucania, San Carlo Hospital, Potenza, and Madonna delle Grazie Hospital, Matera; Department of Internal Medicine, Division of Rheumatology, University of Florence, Florence; Unità di Reumatologia, Arcispedale Santa Maria Nuova, Reggio Emilia; Rheumatology Research Unit, University Federico II, Naples, Italy; and the Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, London, UK.

A. Marchesoni, MD, UOC Day Hospital Reumatologia, Istituto Ortopedico G. Pini; F. Atzeni, MD, Unità di Reumatologia, Ospedale L. Sacco, Polo Universitario, and Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute; A. Spadaro, MD, Associate Professor of Rheumatology, Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma; E. Lubrano, MD, PhD, Associate Professor of Rheumatology, Academic Rheumatology Unit, Department of Health Sciences, University of Molise; G. Provenzano, MD, UO Reumatologia, Azienda Ospedaliera "Ospedali Riuniti Villa Sofia – Cervello"; A. Cauli, MD, Chair of Rheumatology, Department of Medical Sciences, University of Cagliari; I. Olivieri, MD, Rheumatology Department of Lucania, San Carlo Hospital and Madonna delle Grazie Hospital; D. Melchiorre, MD, Department of Internal Medicine, Division of Rheumatology, University of Florence; C. Salvarani, MD, Unità di Reumatologia, Arcispedale Santa Maria Nuova; R. Scarpa, MD, Associate Professor of Rheumatology, Rheumatology Research Unit, University Federico II; P. Sarzi-Puttini, MD, Unità di Reumatologia, Ospedale L. Sacco, Polo Universitario, and Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute; M. Montepaone, MD, Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma; G. Porru, MD, Chair of Rheumatology, Department of Medical Sciences, University of Cagliari; S. D'Angelo, MD, Rheumatology Department of Lucania, San Carlo Hospital and Madonna delle Grazie Hospital; M. Catanoso, MD, Unità di Reumatologia, Arcispedale Santa Maria Nuova; L. Costa, MD, Rheumatology Research Unit, University Federico II; M. Manara, MD, UOC Day Hospital Reumatologia, Istituto Ortopedico G. Pini; V. Varisco, MD, Unità di Reumatologia, Ospedale L. Sacco, Polo Universitario, and Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute; L. Rotunno, MD; O. De Lucia, MD; G. De Marco, MD, UOC Day Hospital Reumatologia, Istituto Ortopedico G. Pini.

Address correspondence to Dr. A. Marchesoni, UOC Day Hospital of Rheumatology, Istituto Ortopedico Gaetano Pini, Piazza A. Ferrari 1, 20122 Milan, Italy. E-mail: marchesoni@gpini.it

Accepted for publication October 25, 2011.

vs about 3.5%, respectively)[1,2]. According to the 1990 American College of Rheumatology (ACR) criteria[3], a diagnosis of FM requires the presence of CWP and tenderness in at least 11 out of 18 tender points when applying a pressure of 5 kg. A new set of criteria has recently been proposed by the ACR[4] that does not require a tender point examination but includes a subjective measure of the number of painful body regions and a somatic symptom severity scale. In association with CWP, typical features of FM are somatic symptoms such as fatigue, headache, irritable bowel syndrome, sleep disturbances, paresthesias, muscle weakness, bladder dysfunction, depression, anxiety, Raynaud's phenomenon (RP), and many others, and the constellation of symptoms is such that the disease is usually easily recognized by physicians. However, diagnostic difficulties may arise in cases of CWP due to conditions other than FM.

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disorder belonging to the heterogeneous group of spondyloarthropathies (SpA), and can affect up to 30% of patients with psoriasis[5]. It is a protean disease that involves the entheses, joints, tendons, and bones of both the peripheral and axial skeleton. Enthesitis can be very difficult to diagnose because its symptoms and signs may be aspecific and relatively indistinguishable from those of FM. Patients with primary FM and psoriasis or FM associated with PsA and those with psoriatic polyenthesitis may have almost identical clinical features and are at risk of misdiagnosis and management errors.

The aim of our study was to identify which clinical features recorded during a standard rheumatological evaluation might help to distinguish between PsA and FM.

MATERIALS AND METHODS

Study design. This cross-sectional study was carried out by 10 Italian tertiary rheumatology centers between January and September 2009: 7 of them specialized in PsA and enrolled only patients with PsA, 2 specialized in FM and enrolled only patients with FM, and 1 enrolled patients with either condition. All patients gave informed consent to participate in the study.

Inclusion and exclusion criteria and clinical evaluation. The inclusion criteria were a diagnosis of PsA or FM according to the ClASsification criteria for Psoriatic ARthritis study group[6] and the 1990 ACR criteria[3]. All consecutive adult patients aged ≥ 18 years attending the clinics for routine examinations during the 9-month study period who met the inclusion criteria were enrolled. They were all receiving current standard levels of care for PsA and FM, and none was involved in any interventional research protocol at the time. In addition, eligible patients with FM could not have a diagnosis or family history of PsA or psoriasis.

The study centers were provided with a paper or electronic case report form prepared by the coordinating center (the Department of Rheumatology, G. Pini Orthopedic Institute, Milan) for anonymous data collection. The case report form included a patient history, self-assessment questionnaires, and the findings of physical examinations and laboratory investigations. The history included the time since the onset of the first symptom, the family and personal history of psoriasis, the presence of inflammatory back pain as defined by Calin's criteria[7], the history of 9 FM-related conditions/symptoms apparently not due to other underlying conditions [fatigue, headache, irritable bowel syndrome, sleep disturbances, paresthesias, anxiety, depression, RP, and graded responsiveness (very good, good, slight, and none) to nonsteroidal antiinflammatory drugs (NSAID)]. The questionnaires were the Italian versions of the Disability Index of the Health Assessment Questionnaire (HAQ)[8], the Fibromyalgia Impact Questionnaire (FIQ)[9], and the Leeds Disability Questionnaire (LDQ)[10]. The patients were also asked to self-assess their pain and general health using a 100-mm visual analog scale (VAS). The examinations included routine anthropometry, swollen and tender 66/68 joint counts, the number of irreversibly damaged joints (defined as those with irreversible deformities and/or at least a 30% reduction in the normal range of movement due to anatomic changes), pressure on the sacroiliac joints to elicit pain, tender point counts, the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)[11], the number of digits with dactylitis, the Psoriasis Activity and Severity Index (PASI)[12] for skin involvement, and the number of nails with psoriatic changes. The pattern of articular involvement was established using the cumulative number of affected joints, meaning all the joints involved at the time of the study evaluation or documented by a competent examiner on a previous occasion. The required laboratory tests were the erythrocyte sedimentation rate (Westergren method; normal value < 15 mm/h) and C-reactive protein levels (normal value < 1 mg/dl). To reduce interobserver variability in the tender point and entheseal site examinations, a DVD was distributed to all the centers showing how to perform these examinations. We chose the MASES, rather than other more comprehensive enthesitis scores, because it was the instrument with which all of the investigators were most confident. However, the following entheseal sites were also examined: lateral and medial epicondyles, greater trochanters, quadriceps tendons, and plantar fascia insertions.

The enthesis involvement was also evaluated by ultrasonography (US) in a subgroup of 30 patients with PsA and 30 patients with FM, all from the coordinating center. The power Doppler ultrasound (PDUS) investigation was performed by a rheumatologist with extensive experience in US, using a Logiq 5 machine (GE Medical Systems, Milwaukee, WI, USA) equipped with a broadband high-frequency (8–15 MHz) transducer, and adopting a standardized methodology[13]. The following entheseal sites were examined bilaterally: common extensor tendon at its insertion at the lateral humeral epicondyle, gluteus tendon at the insertion at the greater trochanter, quadriceps tendon at its insertion at the superior pole of the patella, patellar tendon at its proximal insertion at the inferior pole of the patella, patellar tendon at its distal insertion at the tibial tuberosity, and Achilles tendon and the plantar aponeurosis at their insertions at the calcaneus. According to the Outcome Measures in Rheumatology Clinical Trials definitions of enthesopathy, the following changes were registered[14]: tendon hypoechogenicity at its bony insertion, tendon thickening at its bony insertion, intratendinous calcifications, enthesiophytes, bony erosions, bony cortex irregularities, and presence of Doppler signal at the bony insertion.

The coordinating center collected the case report forms from all centers and confirmed the quality of data (asking for clarifications of any missing or doubtful data), created the final electronic database, cleaned the final data, and carried out the data analysis.

Statistical analysis. The descriptive statistics included the mean values and SD of the continuous variables, and the percentages and proportions of the categorical variables.

The univariate analyses were made using Student's t test, chi-squared test or Fisher's exact test, and Pearson's correlation test as appropriate. The multivariate logistic regression analysis yielded the OR and 95% CI for the risk of having FM rather than PsA for each variable.

As the primary study objective was to identify which of the clinical measures of PsA were more indicative of FM, only the FM-related features shared by both conditions were analyzed in greater detail. Accordingly, in the case of tender point counts, MASES scores, and the presence of somatic symptoms (the most critical continuous variables discriminating the 2 conditions), the most sensitive and specific cutoff points in favor of FM were sought using receiver-operating characteristic (ROC) curves. Similarly, the multivariate analysis considered only the clinical manifestations common to both conditions and most important for the differential diagnosis.

Because the patients with PsA belonging to the "enthesitis predominant" or oligoarticular subgroups and those without psoriasis could be the most difficult to distinguish from FM, we analyzed them separately.

Given the small number of cases, no statistical analysis was performed for the PDUS data.

For all the analyses, a p value of 0.05 was considered statistically significant. The data were analyzed using SPSS software for Windows (release 12.0, SPSS Inc., Chicago, IL, USA), version 17.0.

RESULTS

A total of 401 patients were enrolled but 9 patients with PsA were excluded because of missing data and 6 patients with FM because of the presence of dactylitis, a feature indicative of SpA. Of the remaining 386 patients, 266 had PsA (125 women and 141 men) and 120 had FM (114 women and 6 men); the women/men ratio was 0.89 for PsA and 19 for FM. Mean age at study entry was 51.7 years (SD 12.8) in the PsA group and 50.2 years (SD 10.7) in the FM group; the difference was not statistically significant. Mean disease duration was 10.2 years (SD 9.3) in the PsA group and 5.6 years (SD 4.5) in the FM group. The differences in gender ratios and disease duration were highly significant ($p < 0.001$) and inherent to the particular conditions. The mean body mass index (BMI) was 27.1 (SD 6.1) in patients with PsA and 24.4 (SD 3.6) in patients with FM ($p = 0.05$). Finally, the 30 patients with PsA (13 women, 17 men) and the 30 patients with FM (all women) of the PDUS cohort had comparable mean age (51.6 ± 12.2 and 51.2 ± 11.6 yrs, respectively) and BMI (25.2 ± 5.3 and 24.9 ± 3.7).

Table 1 shows the clinical characteristics of the study population. Following the protocol, none of the FM subjects had PsA or reported any personal or family history of psoriasis. The mean PASI of the patients with PsA was only 2.2 (SD 3.1), indicating good control of the skin disease. It is worth noting that 41 patients with PsA (15.4%) had arthritis without psoriasis. The predominant pattern of articular involvement in the PsA group was polyarthritis (150 patients, 56.8%), followed by oligoarthritis (67, 25.4%), axial involvement (30, 11.4%), and enthesitis (17, 6.4%). Subgroup classification data were missing for 2 patients. Although almost 57% of the patients with PsA were in the polyarthritis subset, the mean number of swollen joints was only 1.8 (SD 3.5). This discrepancy probably appeared because virtually all these patients were taking disease-modifying drugs and about 30% of them were taking tumor necrosis factor-α (TNF-α) blockers.

A number of the significant clinical differences between the 2 groups (Table 1) were expected and due to the intrinsic type of each disease, but some were not. The proportion of patients with inflammatory back pain and tenderness in the sacroiliac joints upon examination was similar in the 2 groups (about 35%–40%), whereas the mean MASES was significantly higher in the patients with FM. One hundred sixteen patients with PsA (43.6%) reported a "good" or "very good" response to NSAID therapy, against only 13 of the patients with FM (3.1%; $p < 0.001$).

Table 1. Clinical characteristics of the study population (n = 386). Data are n (%) unless otherwise specified.

Characteristics	PsA, 266 Patients	FM, 120 Patients	p
PsA			
Psoriasis	207 (77.8)	0 (0)	< 0.001
Personal history of psoriasis	225 (85.6)	0 (0)	< 0.001
Family history of psoriasis	124 (46.6)	0 (0)	< 0.001
Tender joint count, mean (SD)	5.0 (6.9)	0.1 (0.9)	< 0.001
Swollen joint count, mean (SD)	1.8 (3.5)	0.0 (0.0)	< 0.001
Damaged joint count, mean (SD)	1.2 (3.3)	0.0 (0.0)	< 0.001
MASES, mean (SD)	1.9 (2.4)	4.2 (3.8)	< 0.001
Dactylitis	101 (38.0)	0 (0)	< 0.001
Inflammatory back pain	115 (43.2)	43 (35.8)	0.17
Tenderness in sacroiliac joints	96 (36.1)	45 (37.5)	0.79
Good or very good response to NSAID	116 (43.6)	13 (10.8)	< 0.001
Anti-TNF-α therapy	89 (33.5)	0 (0)	< 0.001
FM			
Extraarticular pain	107 (40.2)	84 (70)	< 0.001
Tender point count, mean (SD)	3.5 (3.9)	12.3 (3.9)	< 0.001
Fatigue	175 (65.8)	120 (100)	< 0.001
Headache	73 (27.4)	98 (81.7)	< 0.001
Irritable bowel syndrome	56 (21.1)	100 (83.3)	< 0.001
Sleep disturbances	94 (35.3)	110 (94.0)	< 0.001
Paresthesias	94 (35.3)	102 (85.0)	< 0.001
Stiffness	139 (52.3)	107 (89.2)	< 0.001
Depression	65 (24.4)	80 (66.7)	< 0.001
Anxiety	124 (46.6)	93 (77.5)	< 0.001
Raynaud phenomenon	13 (4.9)	68 (56.7)	< 0.001

PsA: psoriatic arthritis; FM: fibromyalgia; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; NSAID: nonsteroidal antiinflammatory drugs; TNF: tumor necrosis factor-α.

About 40% of the patients with PsA complained of extraarticular pain, but only 6.9% had at least 11 tender points upon examination. All the somatic manifestations were significantly much more frequent in the patients with FM, but as many as about 66% of the patients with PsA complained of fatigue.

As the MASES scores correlated closely with the tender point counts ($r = 0.688$, $p < 0.001$), we investigated whether any of the MASES sites were significantly more frequently involved in 1 condition than the other. Univariate analysis showed that all the sites were significantly more frequently involved in FM, but only the seventh rib and the anterior superior iliac spine remained significantly associated with FM in the multivariate analysis ($p < 0.001$).

The PDUS evaluation showed inflammatory changes (tendon hypoechogenicity, bony erosions, and PD signal in the enthesis) in 21 (70%) patients with PsA but also in 7 (21.3%) patients with FM. Bony erosions were the only findings absolutely specific for PsA, but they were seen in only 6 patients (20%). Ten entheseal sites per patient were examined both clinically and by PDUS. This comparison

yielded very different results in the 2 conditions. Of the 300 sites examined in patients with PsA, 25 were clinically positive and PDUS-negative, 39 clinically negative and PDUS-positive, and 18 positive by both methods. In patients with FM, 112 sites were clinically positive and PDUS-negative, 8 clinically negative and PDUS-positive, and only 4 were positive by both methods. Interestingly, in these patients epicondyles and greater trochanters were the sites of almost all the clinical entheseal involvement; only 4 Achilles tendons, 5 quadriceps tendons, and no plantar fascia insertions were positive on examination.

Given its efficacy in PsA, TNF-α therapy may have been a confounder in 33% of the patients with PsA. However, because extraarticular pain was similarly frequent regardless of whether the patients were taking this therapy (44.9%) or not (39.6%), its effect on the clinical findings could have been limited.

Table 2 shows the laboratory findings and the mean results of the questionnaires and VAS. As expected, inflammatory indices were significantly higher in the patients with PsA. The mean FIQ values were significantly higher in the patients with FM, whereas the mean values of the 2 disability indices (HAQ and LDQ) were similar in the 2 groups.

Because all of the somatic symptoms were significantly more frequent in the patients with FM, we used logistic regression analysis to establish which symptoms were independently predictive of FM. The results showed that sleep disturbances, irritable bowel syndrome, RP, and headache had the strongest OR for FM (Table 3), whereas fatigue, stiffness, depression, and anxiety did not discriminate between PsA and FM.

The ROC curves (Figure 1) showed that the most sensitive and specific predictors of a diagnosis of FM were the presence of at least 6 somatic symptoms (Figure 1A, sensitivity 93% and specificity 82%), at least 8 tender points (Figure 1B, sensitivity 93% and specificity 82%), and a MASES score ≥ 3 (Figure 1C, sensitivity 68% and specificity 72%). The number of patients satisfying the cutoff values derived from the ROC analysis of each variable was obviously much higher in the FM group. However, 17.6% of patients with PsA had at least 8 tender points (as against 92.7% of patients with FM), 14.1% had at least 6 FM-related symptoms (92.7% of patients with FM), and 28.2% had a MASES score ≥ 3 (67.7% of patients with FM).

Table 2. Laboratory and questionnaire results. Data are mean (SD) unless otherwsie specified.

Variables	PsA, 266 Patients	FM, 120 Patients	p
ESR, mm/h	19.2 (15.8)	11.3 (6.8)	< 0.001
CRP, mg/dl	1.5 (2.7)	0.3 (0.4)	< 0.001
ESR > 15 mm/h, n (%)	118 (45.4)	27 (23.3)	< 0.001
CRP > 1 mg/dl, n (%)	90 (35.0)	4 (3.5)	< 0.001
VAS pain score	38.3 (24.1)	58.1 (21.3)	< 0.001
HAQ score	0.7 (0.6)	0.7 (0.5)	0.92
VAS general health score	55.4 (22.7)	58.7 (19.3)	0.14
FIQ score	32.9 (21.0)	57.9 (20.0)	< 0.001
LDQ score	0.9 (2.7)	1.7 (3.3)	0.43

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; VAS: visual analog scale; HAQ: Health Assessment Questionnaire; FIQ: Fibromyalgia Impact Questionnaire; LDQ: Leeds Disability Questionnaire.

Table 3. Logistic regression of somatic symptoms (yes/no) indicating a risk of fibromyalgia.

Symptoms	OR (95% CI)	p
Extraarticular pain	3.4 (1.3–9.1)	0.01
Fatigue	1.2 (0.4–2.2)	0.67
Headache	4.7 (1.9–11.7)	0.001
Irritable bowel syndrome	9.8 (3.9–24.4)	< 0.001
Sleep disturbances	6.9 (2.1–22.5)	0.001
Paresthesias	3.0 (1.1–8.0)	0.02
Stiffness	2.3 (0.8–7.0)	0.13
Depression	0.7 (0.3–1.9)	0.56
Anxiety	0.5 (0.2–1.6)	0.28
Raynaud phenomenon	8.3 (3.0–22.7)	< 0.001

The logistic regression model, which included all the variables that were common to the 2 conditions and most relevant to their differential diagnosis, showed that the number of somatic symptoms and the number of tender points were independent predictors of FM (Table 4). Using the cutoff values identified by the ROC analysis, the same model yielded an OR of 14.73 (95% CI 3.61–60.09) for ≥ 6 somatic symptoms and 30.55 (95% CI 5.04–185.39) for ≥ 8 tender points.

Finally, the analysis of the 17 patients of the "enthesitis predominant" subgroup, the 67 with oligoarthritis, and the 41 without psoriasis did not yield significant differences with the PsA group as a whole, with the exception of "extraarticular pain," which was more frequent in the enthesitis subgroup (60% vs 40.2% in the whole PsA group).

DISCUSSION

The main aim of our study was to identify the clinical features that can help to distinguish between PsA and FM. Although oligopolyarthritis is the most common articular manifestation in PsA, extraarticular pain is frequent and its origin may be difficult to establish because it may be caused by enthesitis (a common feature of PsA) but also by FM. The prevalence of FM among patients with PsA is unknown, although 1 study[15] found tenderness in 10 or more fibrositic sites in 24% of patients with PsA as compared to 57% of patients with rheumatoid arthritis. In the absence of objective signs of inflammation at entheseal sites, it may be difficult to distinguish enthesitic and fibromyalgic pain clinically. The symptom overlap between the 2 conditions may lead to even more difficulty in patients with undiagnosed PsA characterized by enthesitis alone. Only about 6% of the patients with PsA in our study population presented this dis-

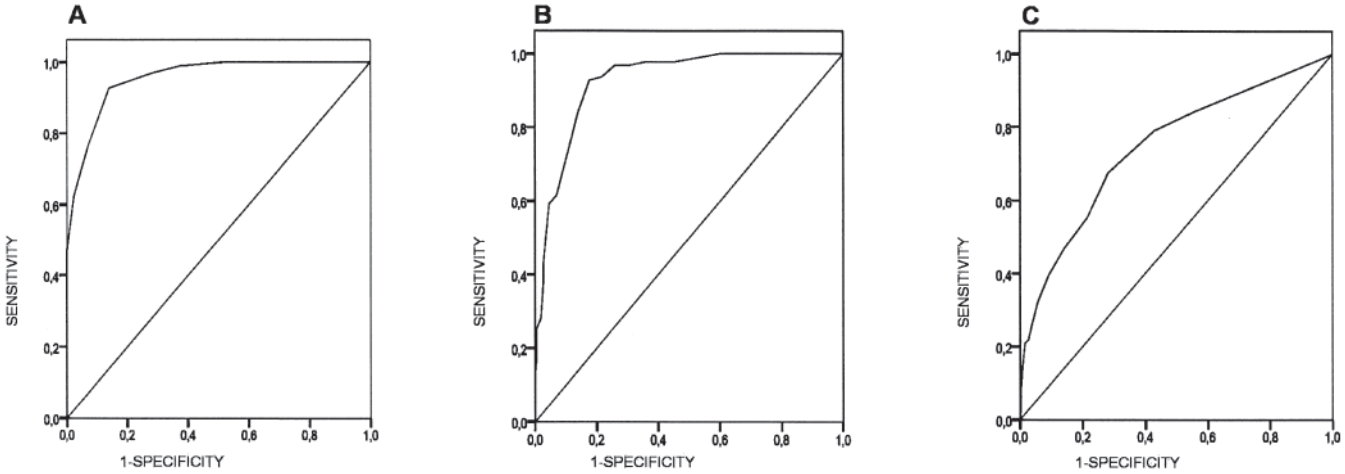

Figure 1. Receiver-operating characteristic curves of sensitivity and specificity of somatic symptoms, tender point count, and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES; fibromyalgia vs psoriatic arthritis). A. Somatic symptoms, area under the curve (AUC) 0.95, 95% CI 0.93–0.97, p < 0.001. B. Tender point count, AUC 0.92, 95% CI 0.9–0.95, p < 0.001. C. MASES, AUC 0.74, 95% CI 0.68–0.8, p < 0.001.

Table 4. Multivariate logistic regression including the main variables possibly associated with fibromyalgia, and shared by fibromyalgia and psoriatic arthritis.

Variables	OR (95% CI)	p
Female sex	0.23 (0.02–2.54)	0.23
FIQ score	0.98 (0.94–1.02)	0.26
VAS pain score	0.99 (0.95–1.02)	0.51
Somatic symptoms	3.25 (1.96–5.38)	0.001
MASES	0.78 (0.63–0.98)	0.03
Tender points	1.63 (1.31–2.03)	0.001
No response to NSAID	1.99 (0.40–9.87)	0.39

VAS: visual analog scale; FIQ: Fibromyalgia Impact Questionnaire; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; NSAID: nonsteroidal antiinflammatory drug.

ease pattern. The analysis of these patients, as well as those with oligoarthritis and those without psoriasis, yielded results similar to those of the whole PsA population. With the limitation of the low number of patients, this finding might indicate that "enthesitis predominant" is a definite PsA subgroup, distinguishable from FM.

Our results suggest that the presence of ≥ 6 somatic manifestations and ≥ 8 tender points indicates the greatest probability of having FM. RP, sleep disturbances, irritable bowel syndrome, and headache were the somatic disturbances with the highest individual odds ratio for FM, whereas fatigue, stiffness, anxiety, and depression were not significantly associated with FM in multivariate analysis. In particular, fatigue (a typical symptom of FM) was also present in the majority of patients with PsA (about 66%), a finding that is consistent with previous data[16].

Although the presence of ≥ 8 tender points and ≥ 6 FM-related symptoms was strongly predictive of FM, they were recorded respectively in about 14% and 18% of our patients with PsA. These may have been patients with secondary FM, but the collected data did not allow this distinction. However, only about 7% of the patients with PsA reached the cutoff point of 11 positive tender points considered diagnostic of FM by the 1990 ACR criteria[3].

It has been observed that patients with FM respond poorly to NSAID, and this has been used as a means of differentiating FM and spondyloarthritic-enthesitic patients[17]. However, as many as about 66% of our patients with PsA did not respond well to NSAID, and lack of response to NSAID was not independently associated with FM in the multivariate analysis. Therefore, the discriminating usefulness of this measure by itself seems to be limited.

Our findings showed that tender points and entheseal sites overlapped so much that median MASES values were significantly higher in the patients with FM. The involvement of 3 or more entheseal sites proved to be the most sensitive and specific cutoff point for a diagnosis of FM, but significance was lost in the multivariate analysis, and about 30% of our patients with PsA had involvement of 3 or more entheseal sites. Together, these data suggest that tenderness at entheseal sites by itself is not at all useful in distinguishing between the 2 conditions. We did not investigate swelling at these sites, which should be quite specific, but probably poorly sensitive, for inflammation. Because the PDUS study, which was performed in a small cohort of patients (30 PsA and 30 FM), evaluated the main entheses of the limbs, of the sites included in the MASES, only the Achilles tendons were investigated by this imaging technique. In contrast to the clinical findings, the PDUS evaluation showed that inflammatory changes in the entheseal sites were much more frequent in patients with PsA than in patients with FM. However, as these changes were also found in about 21% of the patients with FM, they were not highly specific for PsA.

The relatively low concordance rate between clinical and PDUS enthesitis in the patients with PsA was an intriguing finding. Of the 82 sites involved according to at least 1 of the 2 methods, only 18 (22%) were positive at both. This result raises the issue of the definition of enthesitis. In our study it was defined as tenderness upon application of pressure at enthesis enough to blanch the examining nail. Using this method, 43 sites were positive in the PDUS cohort, but the 39 sites with inflammatory changes on PDUS were clinically silent. This finding suggests that enthesitis could often be asymptomatic, but it also indicates that a more reliable definition of enthesitis is needed. Finally, in the patients in the PDUS cohort who had FM, on clinical examination some entheses (epicondyles and greater trochanters) were involved in a high percentage of cases, whereas other entheses (quadriceps tendon, Achilles tendons, plantar fascia insertion) showed almost no involvement. This finding suggests that methods more comprehensive than MASES could be more useful to distinguish patients with PsA from patients with FM. However, in the whole study population Achilles tendon entheses were not significantly more involved in patients with PsA, due to the infrequent involvement of this tendon in these patients (low sensitivity).

The mean self-assessed pain and FIQ scores were higher in the patients with FM, but their odds ratios were not significant in the multivariate analysis. The mean values of the 2 disability indices (HAQ and LDQ) and the patients' evaluation of general health were similar in the 2 groups and therefore do not distinguish the 2 conditions. Inflammatory back pain and tenderness in the sacroiliac joints were similarly frequent in the 2 groups; however, it is worth mentioning that sacroiliac joint examinations are not consistently capable of identifying inflammatory involvement[18]. Finally, inflammatory joint involvement and abnormal acute-phase reactant values were absent or very rare in the patients with FM, but as they are intrinsic characteristics of PsA, they cannot be used to identify which patients with known PsA also have FM.

To our knowledge, this is the first study investigating how to differentiate patients with FM from patients with PsA. However, it is interesting to note that a small cohort study of only 33 patients[17] with extraarticular pain found that the significant differences in the clinical characteristics of SpA and FM were similar to those we found between PsA and FM.

Our findings seem to indicate that somatic symptoms and tender point counts could be used in clinical practice to determine whether patients with PsA have associated FM when they complain of extraarticular pain. In this situation, the likelihood of having FM is proportional to the number of positive features, and is very high in the case of ≥ 8 tender points and ≥ 6 FM-related symptoms. These findings may also be extended to help diagnose patients with psoriasis or undifferentiated SpA with extraarticular pain, but this possibility needs to be evaluated by specifically oriented studies.

Our study has some limitations. The PsA group included patients with any PsA clinical pattern, not only those who had polyenthesitis; the extent to which our findings apply to these patients needs to be evaluated further. Because mean disease duration in the PsA group was quite long, the results can be considered valid only for patients with longstanding disease; patients with early PsA might be different. Tender point evaluations are highly examiner-dependent and subject to considerable interobserver variability. We tried to minimize this by providing a DVD showing how to do the tender point count, but we did not check the way the examination was actually conducted; however, as this was a multicenter study, the large number of examiners may have compensated for the variability. Finally, because about one-third of the patients with PsA were taking anti-TNF therapy, all the inflammatory features of these patients, including enthesitis and joint swelling, were profoundly modified. Obviously the results of our study were biased by this, but in a way consistent with what happens in daily practice.

It may be difficult to distinguish polyenthesitis and FM in patients with PsA and extraarticular pain, but our findings show that some of the clinical data that can be collected easily during a standard rheumatological visit can provide a differential diagnosis. These findings should be tested in a control population of patients with PsA. PDUS and/or magnetic resonance imaging of the entheses might provide further data on this topic[19,20].

REFERENCES

1. Wolfe F, Ross K, Anderson J, Russell IJ, Herbert L. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum 1995;38:19-28.
2. Salaffi F, De Angelis R, Grassi W. Prevalence of musculoskeletal conditions in an Italian population sample: Results of a regional community-based study. I. The MAPPING study. Clin Exp Rheumatol 2005;23:819-28.
3. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. Arthritis Rheum 1990;33:160-72.
4. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res 2010;62:600-10.
5. Salvarani C, Lo Scocco G, Macchioni P, Cremonesi T, Rossi F, Mantovani W, et al. Prevalence of psoriatic arthritis in Italian psoriatic patients. J Rheumatol 1995;22:1499-503.
6. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H, et al. Classification criteria for psoriatic arthritis. Development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
7. Calin A, Porta J, Fries JF, Schurman DJ. Clinical history as a screening test for ankylosing spondylitis. JAMA 1977;237:2613-4.
8. Ranza R, Marchesoni A, Calori G, Bianchi G, Braga M, Canazza S, et al. The Italian version of the functional disability index of the Health Assessment Questionnaire. A reliable instrument for multicenter studies in rheumatoid arthritis. Clin Exp Rheumatol 1993;11:123-8.
9. Sarzi Puttini P, Atzeni F, Fiorini T, Panni B, Randisi G, Turiel M, et

al. Validation of an Italian version of the Fibromyalgia Impact Questionnaire (FIQ-I). Clin Exp Rheumatol 2003;21:459-64.
10. Lubrano E, Sarzi Puttini P, Parsons WJ, D'Angelo S, Cimmino MA, Serino F, et al. Validity and reliability of an Italian version of the revised Leeds Disability Questionnaire for patients with ankylosing spondylitis. Rheumatology 2005;44:666-9.
11. Heuft-Dorenbosch L, Spoorenberg S, van Tubergen A, Landewé R, Dougados M, Mielants H, et al. Assessment of enthesitis in ankylosing spondylitis. Ann Rheum Dis 2003;62:127-32.
12. Fredriksson T, Petterson U. Severe psoriasis — oral therapy with a new retinoid. Dermatologica 1978;157:238-44.
13. Riente L, Delle Sedie A, Filippucci E, Iagnocco A, Grassi W, Valesini G, et al. Ultrasound imaging for the rheumatologist IX. Ultrasound imaging in spondyloarthritis. Clin Exp Rheumatol 2007;25:349-53.
14. Wakefield RJ, D'Agostino MA, Iagnocco A, Filippucci E, Backhaus M, Scheel AK, et al. The OMERACT Ultrasound Group: Status of current activities and research directions. J Rheumatol 2007;34:848-51.
15. Buskila D, Langevitz P, Gladman DD, Urowitz S, Smythe HA. Patients with rheumatoid arthritis are more tender than those with psoriatic arthritis. J Rheumatol 1992;19:1115-9.
16. Husted JA, Tom BD, Schentag CT, Farewell VT, Gladman DD. Occurrence and correlates of fatigue in psoriatic arthritis. Ann Rheum Dis 2009;68:1553-8.
17. Godfrin B, Zabraniecki L, Lamboley V, Bertrand-Latour F, Sans N, Fournié B. Spondyloarthropathy with entheseal pain. A prospective study in 33 patients. Joint Bone Spine 2004;71:557-62.
18. Spadaro A, Iagnocco A, Baccano G, Ceccarelli F, Sabatini E, Valesini G. Sonographic-detected joint effusion compared with physical examination in the assessment of sacroiliac joints in spondyloarthritis. Ann Rheum Dis 2009;68:1559-63.
19. D'Agostino MA, Said-Nahal R, Hacquard-Bouder C, Brasseur JL, Dougados M, Breban M. Assessment of peripheral enthesitis in the spondyloarthropathies by ultrasonography combined with power Doppler: A cross-sectional study. Arthritis Rheum 2003;48:523-33.
20. Eshed I, Bollow M, McGonagle DG, Tan AL, Althoff CE, Asbach PE, et al. MRI of enthesitis of the appendicular skeleton in spondyloarthritis. Ann Rheum Dis 2007;66:1553-9.