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# Assessment of Widespread and Extraarticular Pain in Psoriatic Arthritis: A Case-control Study

Ennio Lubrano[1], Silvia Scriffignano[1], Romeo Morelli[1], and Fabio Massimo Perrotta[1]

*ABSTRACT.* ***Objective.*** A remarkable lack of detailed knowledge on pain areas in psoriatic arthritis (PsA) is present, and their clinical relevance is quite unknown. The main aim of the study was to explore pain areas in PsA, comparing them with those involved in patients with fibromyalgia (FM). In addition, a secondary aim was to investigate any possible association between pain areas and outcome measures in PsA.

***Methods.*** This was a case-control study on patients with PsA satisfying Classification Criteria for Psoriatic Arthritis criteria and patients with FM. In all patients with PsA and FM, a body chart filled in by the patient reporting pain areas in 80 body locations was performed. The Widespread Pain Index (WPI) was performed in all patients with PsA and FM. In all patients with PsA, an assessment of disease activity, treatment target, function, and impact of disease was carried out.

***Results.*** Fifty patients with PsA and 50 FM controls were evaluated. A significantly higher number of pain areas in the body chart and higher WPI scores were found in patients with FM when compared to patients with PsA. In PsA, the number of areas reported in the body chart significantly correlated with the Disease Activity Index for PsA, Health Assessment Questionnaire–Disability Index, and PsA Impact of Disease. Patients who showed a significantly high number of extraarticular pain areas involved were those who were not in remission/minimal disease activity, or who did not have a greater impact of disease or reduced function.

***Conclusion.*** The main results showed that widespread and extraarticular pain was present in patients with PsA, showing that this nonarticular pain had an impact on important disease domains. The present study could contribute to an important aspect of this challenging and multifaceted disease—namely, the assessment of widespread pain.

*Key Indexing Terms*: assessment, outcome measures, pain, psoriatic arthritis

Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by the association of arthritis and psoriasis, and by a variable clinical course.[1]

Despite the new treatment strategies that allow patients to achieve remission or low disease activity in almost all domains,[2,3,4] the assessment and management of chronic pain in patients with PsA still represent an unmet need, and residual pain can be observed.[5,6]

Pain in PsA is traditionally considered to be of peripheral nociceptive origin; however, pain hypersensitivity may persist after the control of inflammation and thus become a manifestation of maladaptive pathological changes in the central nervous system.[7,8] Data from the DANBIO register showed that > 20% of patients with inflammatory arthritis had neuropathic pain features.[9] Further, patients with PsA seem to have more neuropathic pain than other patients with spondyloarthritis (SpA).[9] However, there is a remarkable lack of detailed knowledge on pain areas in PsA, and their clinical relevance is quite unknown.

Identification of possible underlying pain mechanisms and a more detailed evaluation of pain areas in PsA may, therefore, be of great importance in the clinical decision-making process, helping in differential diagnosis with fibromyalgia (FM) and in the assessment of disease activity and quality of life. Moreover, the presence of concomitant FM in PsA may increase the burden of the disease.

The aim of this study was to explore, in more detail, the areas of pain in patients with PsA, comparing them with those in patients with FM. In addition, we aimed to investigate the possible association between the number and presence of specific pain areas and disease activity, treatment target, joint function, and impact of disease.

## METHODS

All adult patients with PsA satisfying the Classification Criteria for Psoriatic

[1]*E. Lubrano, MD, PhD, Associate Professor of Rheumatology, S. Scriffignano, MD, Specialist Registrar in Rheumatology, R. Morelli, MD, Clinical Research Fellow, F.M. Perrotta, MD, PhD, Lecturer in Physical Medicine and Rehabilitation, Dipartimento di Medicina e Scienze della Salute "Vincenzo Tiberio", Università degli Studi del Molise, Campobasso, Italy.*

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*Address correspondence to Dr. E. Lubrano, Head of Academic Rheumatology Unit and MoRhe Project, Dipartimento di Medicina e Scienze della Salute "Vincenzo Tiberio", Università degli Studi del Molise, Via Giovanni Paolo II, C/da Tappino, 86100 Campobasso, Italy. Email: enniolubrano@hotmail.com.*

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ARthritis (CASPAR)[10] criteria who attended our unit from September 1, 2019, to January 31, 2020, and who were on at least 6-month follow-up were considered potentially eligible for the study. Consecutive adult patients with FM satisfying the American College of Rheumatology (ACR) 2010 criteria[11] attending our unit in the same period were enrolled in the control group.

Exclusion criteria included the presence of diabetic neuropathy, episode of herpes zoster in the last 24 months, diagnosis of axonal or demyelinating neuropathy, and/or any musculoskeletal trauma in the previous 24 months. Moreover, patients with PsA who met the ACR 2010 criteria for FM were also excluded to limit jeopardization of the results.

Demographics and disease characteristics including sex, age, disease duration, level of education, pattern of articular manifestations, number of tender and swollen joints, enthesitis, and dactylitis were collected. Enthesitis was assessed using the Leeds Enthesitis Index,[12] and dactylitis as present/absent. Skin evaluation was performed using body surface area. The patient global assessment on a visual analog scale (VAS; 0–10 cm) was performed by all patients. Physician global assessment of disease activity on a VAS was also recorded.[13] Finally, C-reactive protein levels were collected within 1 month of clinical evaluation.

The Disease Activity Index for PsA (DAPSA) was calculated.[14] Minimal disease activity (MDA) was defined according to Coates, *et al*.[15] The patient acceptable symptom state (PASS) was also assessed.[16] The Health Assessment Questionnaire–Disability Index (HAQ-DI)[17] and the Psoriatic Arthritis Impact of Disease (PsAID) were evaluated as measures of function and impact of disease.[18] HAQ-DI ≤ 0.5 defined a good functional status, and PsAID ≤ 4 a low impact of disease.

The intensity of pain was assessed on a numeric rating scale (NRS; 0–10 cm). All patients with PsA and FM filled in an anterior and posterior body chart during the intake interview; this determined the presence of pain (yes = 1/no = 0) during the past week, in 80 body locations. The chart was reproduced according to Swinnen, *et al*.[19] Patients were asked to fill in the chart before the clinical examination and no provocative test for pain was used. Further, areas with a clear presence of tender/swollen joints or enthesitis were subsequently excluded from the analysis to ensure that the presence of pain was not due to the synovitis/enthesitis process.

Finally, the Widespread Pain Index (WPI) was performed in all patients with PsA and FM.[11] The WPI quantifies the extent of bodily pain on a 0–19 scale, by asking patients if they had pain or tenderness in 19 different body regions.

*Ethics.* The study protocol was in compliance with the Declaration of Helsinki and written consent was obtained from each participant. The study was approved by the institutional review board of the University of Molise (protocol no. 0001-09-2017).

*Statistical analysis.* The results were expressed as median (IQR) for nonparametric variables and as a mean (SD) for parametric ones. The prevalence of each body region and location was calculated for all patients. Pain areas between 2 diseases that were univariate were compared with chi-square test for frequencies. Further, Mann-Whitney *U* test was used to compare

*Table 1.* Demographic and clinical characteristics of patients with PsA and FM.

| | PsA, n = 50 | FM, n = 50 | *P* |
|---|---|---|---|
| Male sex, n (%) | 33 (66) | 3 (6) | < 0.001 |
| Age, yrs, mean (SD) | 56.7 (10.5) | 58.4 (11.4) | NS |
| Disease duration, yrs | 8 (5–10) | 8 (4–10) | NS |
| BMI, kg/m$^2$ | 27.7 (23.4–30.7) | 27.1 (23.1–30.2) | NS |
| Pain on NRS | 5 (0–10) | 8 (3–10) | < 0.001 |
| WPI | 3 (1–5.75) | 7 (1–20) | < 0.001 |
| VAS physician | 3.5 (1–5) | | |
| TJC | 3 (0–5) | | |
| SJC | 1 (0–2) | | |
| PtGA | 5 (2–6.75) | | |
| No. pain areas | 3 (1–7) | 8.5 (6–14) | < 0.001 |
| DAPSA | 14.15 (5–18.8) | | |
| MDA 5/7, n (%) | 22 (44) | | |
| HAQ-DI | 0.37 (0.125–0.725) | | |
| BSA% | 1 (0–3) | | |
| PsAID | 3 (1–4.8) | | |
| CRP, mg/dL | 0.25 (0.02–1.93) | | |
| PASS+, n (%) | 30 (60) | | |
| Treatment in the past 6 months, n (%) | | | |
| NSAID | 10 (20) | 8 (16) | NS |
| Analgesics (acetaminophen, codeine, tramadol) | 2 (4) | 15 (30) | < 0.001 |
| Muscle relaxants, antidepressants, anticonvulsants | 0 (0) | 27 (54) | < 0.001 |
| csDMARD | 8 (16) | 0 (0) | < 0.01 |
| bDMARD | 30 (60) | 0 (0) | < 0.001 |
| tsDMARD | 4 (8) | 0 (0) | NS |

Values are median (IQR) unless otherwise indicated. bDMARD: biologic DMARD; BSA: body surface area; CRP: C-reactive protein; csDMARD: conventional synthetic DMARD; DAPSA: Disease Activity Index for Psoriatic Arthritis; DMARD: disease-modifying antirheumatic drug; FM: fibromyalgia; HAQ-DI: Health Assessment Questionnaire–Disability Index; MDA: minimal disease activity; NSAID: nonsteroidal antiinflammatory drug; PASS: patient acceptable symptoms state; PsAID: Psoriatic Arthritis Impact of Disease; tsDMARD: targeted synthetic DMARD; NRS: numeric rating scale; NS: not significant; PsA: psoriatic arthritis; PtGA: patient global assessment; SJC: swollen joint count; TJC: tender joint count; VAS: visual analog scale; WPI: Widespread Pain Index.

the number of pain areas and the WPI between the 2 groups. Correlation between the number of pain areas and clinical indices was assessed with Spearman rho. The 1-way ANOVA was applied and a multiple comparison between the 4 DAPSA groups was performed using the Bonferroni correction. *P* values < 0.05 were considered significant.

## RESULTS

During the study period, 50 patients with PsA and 50 controls with FM who met the inclusion and exclusion criteria were evaluated. The main demographic and clinical characteristics of patients are summarized in Table 1. No more than 5 minutes were spent to fill in the body chart, showing how quick and feasible this instrument was.

As expected, a significantly higher number of pain areas in the body chart and higher WPI were found in patients with FM when compared to patients with PsA (Table 1). Interestingly, only 5 patients with PsA (10%) did not report any pain areas as well as no pain on NRS. Figure 1 illustrates the pain locations, displayed as prevalence in patients with PsA and FM. In particular, in patients with PsA, pain was mainly localized at the level of the hands, knees, and feet. However, pain was also present in other extraarticular areas. When evaluating the pain areas in the FM control group, the locations were, to a certain extent, similar to those in PsA cases, but more frequent. A full comparison of all pain regions for PsA and FM based on WPI are reported in the Supplementary Table 1 (available from the authors on request).

In patients with PsA, the number of painful areas assessed with the body chart significantly correlated with DAPSA, HAQ-DI, and PsAID (rho 0.69, 0.38, and 0.48, respectively; $P < 0.01$). We observed similar results for WPI (rho 0.59, 0.40, and 0.49, respectively; $P < 0.01$). Further, we found statistically significant differences in the median number of pain areas between patients in DAPSA remission, DAPSA low disease activity, DAPSA moderate disease activity, and DAPSA high disease activity (see Table 2).

Finally, patients who were not in remission/MDA nor had a greater impact of disease or reduced function showed a significantly high number of extraarticular pain areas involved (Table 2).

## DISCUSSION

To our knowledge, this is the first study to detail the topography of pain in PsA and to relate these findings to key clinical outcomes. The main results showed that widespread and extraarticular pain were present in our patients and seem to have an impact on important disease domains.

Amplification of nervous system signaling may lead to a complex perception of the painful stimulus, potentially steering

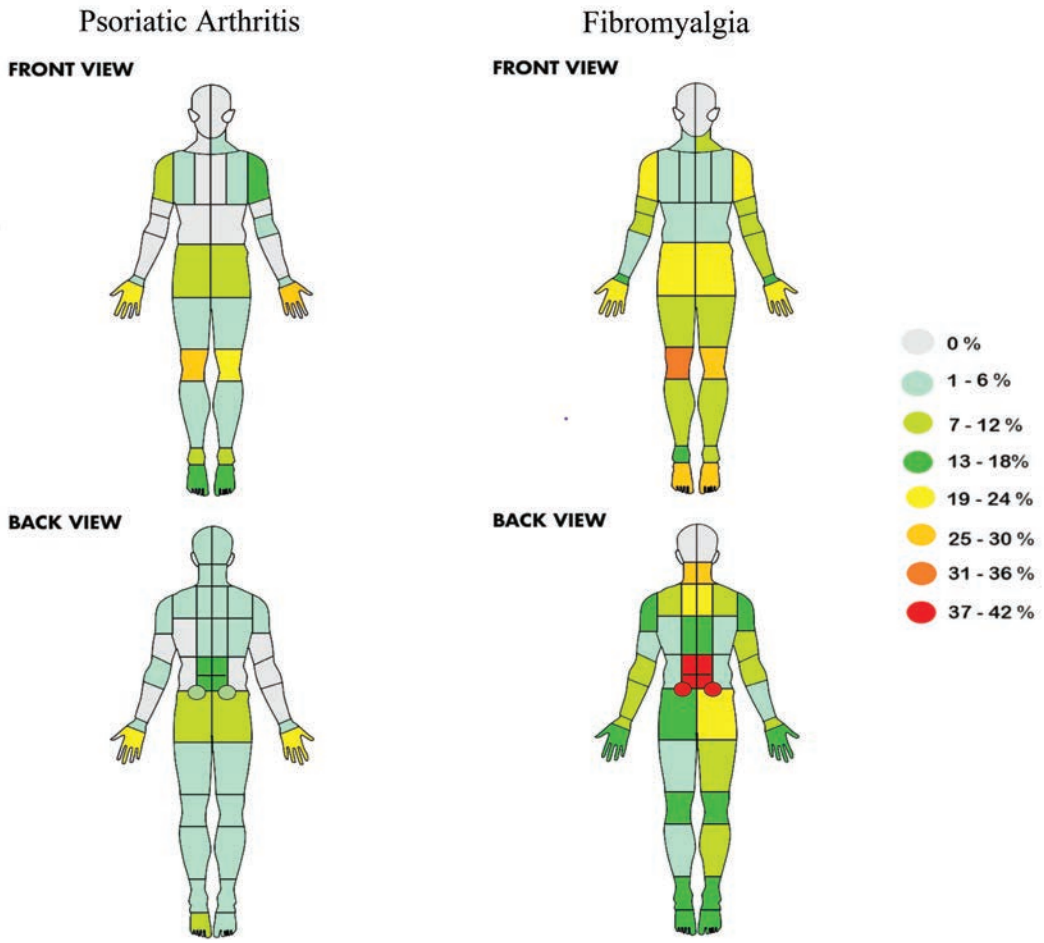


*Figure 1.* Graphic illustrating pain locations, displayed as prevalence in patients with psoriatic arthritis and fibromyalgia controls.

*Table 2.* Difference in the number of pain areas based on patients with PsA who had different patterns of the disease and on patients who did or did not achieve key clinical outcomes.

| No. of Pain Areas, Median (IQR) | | *P* |
|---|---|---|
| HAQ-DI ≤ 0.5, n = 31 | HAQ-DI > 0.5, n = 19 | |
| 2 (1–4) | 6 (2.5–7.5) | 0.03 |
| PsAID ≤ 4, n = 33 | PsAID > 4, n = 17 | |
| 2 (1–4) | 7 (2–10) | 0.03 |
| VAS pain ≤ 20, n = 15 | VAS pain > 20, n = 35 | |
| 1 (0–1.5) | 4 (2.5–7.5) | < 0.001 |
| PASS yes, n = 30 | PASS no, n = 20 | |
| 2 (1–3.75) | 5.5 (3.75–8.5) | 0.03 |
| BSA ≤ 3, n = 44 | BSA > 3, n = 6 | |
| 3 (1.75–7) | 2.5 (1–4) | 0.51 |
| MDA yes, n = 22 | MDA no, n = 28 | |
| 1.5 (1–2.75) | 4.5 (2.75–7.25) | < 0.001 |
| DAPSA ≤ 14, n = 24 | DAPSA > 14, n = 26 | |
| 1 (1–2.25) | 5.5 (3.25–7.75) | < 0.001 |

BSA: body surface area; DAPSA: Disease Activity score for Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire–Disability Index; MDA: minimal disease activity; PASS: patient acceptable symptoms state; PsA: psoriatic arthritis; PsAID: Psoriatic Arthritis Impact of Disease; VAS: visual analog scale.

the clinician and the patient to an overestimation/underestimation of disease activity. Clinically, these pain mechanisms may translate to widespread pain, a feature seen in approximately 2–34% of patients with SpA that resemble those seen in patients with FM.[19] Our results are in line with studies that found dissonance between the outcomes reported by doctors and patients.[20]

In our study, although the number of areas involved were significantly lower with respect to FM, we found approximately 20–35% of patients with PsA also experienced pain in some specific body areas. This latter result is difficult to explain based only on the body chart and further studies are needed. In fact, the presence of subclinical synovitis or enthesitis, potentially influencing the pain perception, could not be excluded. The present study also showed that widespread pain was more frequent in PsA patients with the following characteristics: high disease activity, no achievement of MDA, higher HAQ-DI, higher PsAID, and no PASS. All these results could be in keeping with an association between the presence of widespread pain and poor outcome.

Our study had strengths and limitations. The use of a body chart has allowed a more detailed assessment of pain in PsA, showing that it is a quick and feasible instrument to adopt in clinical practice. As a potential limitation, a possible bias is linked to sex differences. This could affect the results because of the different pain expression between the 2 sexes.[21] Further, we did not systematically assess the presence of comorbidities such as depression, which may influence the pain perception.

In conclusion, the present study contributes to an important aspect of this multifaceted disease, which is the assessment of widespread pain in a more detailed fashion. This assessment should be considered by treating physicians, as a more detailed pain evaluation may be useful for the management of PsA, with personalized treatment strategies that go beyond synthetic and biologic disease-modifying antirheumatic drugs.

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