The Journal of Rheumatology 2021;48:214–21
doi.10.3899/jrheum.190857
First Release December 1 2020

The Journal of Rheumatology

The Pattern of Musculoskeletal Complaints in Patients With Suspected Psoriatic Arthritis and Their Correlation With Physical Examination and Ultrasound

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ABSTRACT. ***Objective.*** To describe the pattern of musculoskeletal (MSK) symptoms and their correlation with clinical and sonographic findings among psoriasis patients with suspected psoriatic arthritis (PsA).

Methods. Patients with psoriasis and no prior diagnosis of PsA were referred for assessment of their MSK complaints. The study included the following steps: (1) assessment by an advanced practice physiotherapist, (2) targeted MSK ultrasound, and (3) assessment by a rheumatologist. In addition, patients were asked to complete questionnaires about the nature and duration of their MSK symptoms and to mark the location of their painful joints on a homunculus. Each patient was classified by a rheumatologist as "Not PsA," "Possible PsA," or "PsA". MSK symptoms and patient-reported outcomes (PRO) were compared between patients with PsA and Possible/Not PsA. Agreement between modalities was assessed using κ statistics.

Results. Two hundred three patients with psoriasis and MK symptoms were enrolled (8.8% PsA, 23.6% Possible PsA). Patients classified as PsA had worse scores on the PsA Impact of Disease (P = 0.004) and Functional Assessment of Chronic Illness Therapy–Fatigue scale (P = 0.02). There was no difference between the 2 groups in the presence, distribution, and duration of MSK symptoms. Analysis of agreement in physical examination between modalities revealed the strongest agreement between the rheumatologist and physiotherapist (κ = 0.28). The lowest levels of agreement were found between ultrasound and patient (κ = 0.08) and physiotherapist and ultrasound (κ = 0.08).

Conclusion. The results of this study suggest that the intensity, rather than the type, duration, or distribution of MSK symptoms, is associated with PsA among patients with psoriasis.

Key Indexing Terms: psoriasis, psoriatic arthritis, ultrasound, diagnostic tools

Psoriasis is an immune mediated skin disease affecting 1–3% of the general population[1]. Up to one-third of patients with psoriasis develop psoriatic arthritis (PsA), which causes pain, stiffness, and swelling in the joints and can lead to severe joint damage and loss of function in the first few years of the disease[2]. In the majority of patients, psoriasis precedes the diagnosis of PsA[3]. Earlier diagnosis of PsA is associated with improved long-term outcomes, including reduced damage to the joints and better quality of life (QOL) for patients[4]. Unfortunately, PsA often goes undiagnosed in patients with psoriasis for a significant period of time. A metaanalysis reported a prevalence of 15.5% of psoriasis patients with previously undiagnosed PsA[5]. A previous study showed that nearly one-third of patients with PsA remain without a diagnosis for more than 2 years after they first experience symptoms[6]. Some of the delays can be attributed to the lag time between the initial primary care visit for MSK complaints to the referral to rheumatology[6]. However, rheumatologists also face challenges related to early diagnosis of PsA among psoriasis patients presenting with MSK symptoms. Our group has shown that in a longitudinal cohort of patients with psoriasis, a significant proportion of those who ultimately developed PsA experienced MSK symptoms several years prior to PsA diagnosis, without having distinct findings suggestive of PsA on physical examination[7]. Unlike other rheumatic diseases, PsA lacks an objective, reliable biomarker that could assist the clinician in diagnosing the disease at early phases when findings on physical examination are often very subtle. The frequent coexistence of osteoarthritis (OA) and other common noninflammatory MSK conditions further complicates the assessment of psoriasis patients with MSK symptoms.

S. Sarabia was supported by a summer studentship award from the National Psoriasis Foundation. L. Eder is supported by a Young Investigator Award from the Arthritis Society. The Early Arthritis Clinic was supported by unrestricted educational grants from UCB, Celgene, Novartis, and Janssen.

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Accepted for publication May 1, 2020.

MSK ultrasound (US) is playing an increasingly important role in optimizing clinical assessment of patients with rheumatic conditions, and substantially improves therapeutic and diagnostic capabilities. US is a reliable modality in detecting a wide range of MSK inflammatory lesions in PsA[8,9,10]. It correlates well with MRI findings and was found to be more reliable than physical examination in the assessment of MSK abnormalities[11]. In addition, US is an affordable and accessible tool that is widely used in rheumatology practice. Recent advances in US technology hold promise to introduce highly mobile devices that could potentially be used in nonrheumatology settings (e.g., dermatology, primary care), increasing access to this technology. This highlights the potential use of US as a point-of-care tool for optimizing early diagnosis of PsA at early stages of their disease.

Diagnosing PsA has been proven challenging due to the clinical heterogeneity, the lack of reliable objective biomarker, and the often-subtle clinical findings. There is limited information about the constellation of MSK symptoms experienced by patients with early PsA. The aims of the study were to describe the pattern of MSK symptoms and their correlation with findings on physical examination and US, among patients with psoriasis presenting to a rapid access clinic for suspected PsA.

MATERIALS AND METHODS

Setting and study population. This cross-sectional study evaluated patients with psoriasis who were experiencing MSK complaints and did not have a prior diagnosis of PsA. Prior to enrollment, potential participants were asked if they had been previously diagnosed as PsA, and their electronic medical records (EMR) were reviewed to help exclude those with a prior PsA diagnosis. Participants were recruited from the dermatology clinics, and the Phototherapy Education and Research Centre (PERC) and Family Medicine clinics at Women's College Hospital in Toronto, Ontario, Canada. The dermatology and phototherapy clinics serve as a tertiary referral center for dermatologists from the Greater Toronto Area. Patient recruitment for this study consisted of both self-referral and direct referral systems. In the province of Ontario, people require a referral from a physician to access rheumatology care; this practice may lead to delays in the diagnosis of PsA[6]. The direct referral system refers to the conventional route of patients who were referred to rheumatology by a physician, typically by their family physician or dermatologist. In this study, the self-referral system allowed patients without such referral to access rheumatology care. Several methods were used to enroll patients through the self-referral system. The first was by direct mail invitation: Patients with a diagnosis of psoriasis who had visited one of the participating clinics between February 2015 and December 2017 were identified through EMR. They were contacted by a mailed invitation to participate in the study. Patients were asked to respond by mail or through an online form and to identify if (1) they were currently experiencing back, joint, or tendon complaints, and (2) if they were willing to participate in the study. Those who answered yes to both questions were invited to participate. Additional methods used for self-referral included posters and flyers in dermatology and family medicine clinics that contained information about the early signs and symptoms of PsA and invited patients who were interested in being evaluated to contact the clinic. In the conventional direct referral system, participating dermatologists and family physicians could directly refer patients who have psoriasis and were experiencing MSK symptoms. The study was approved by the Women's College Hospital Ethics Board and all patients gave their informed consent (REB#2016-0043).

Data collected. All patients were assessed in a rapid access clinic for PsA at Women's College Hospital to determine whether they have PsA[12]. The assessment included the following 3 steps: (1) assessment by an advanced practice physiotherapist; (2) targeted MSK US; and (3) assessment by a rheumatologist. Examinations by the rheumatologist and physiotherapist were performed independently of each other and without knowledge of US results. They included taking the medical history and performing a MSK examination of 68 and 66 joints for tenderness and swelling, respectively. Additionally, enthesitis was assessed according to the Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis index[13], and the presence and number of dactylitic digits were recorded. In addition, the extent of psoriasis was assessed by Psoriasis Area and Severity Index (PASI), and the presence of psoriatic nail lesions was recorded. The advanced practice physiotherapist (CF) had 10 years of experience working with rheumatic patients. She was also specifically trained to perform the MSK and skin assessments required for this study. The rheumatologist (DJ), who had over 20 years of experience particularly in evaluating patients with PsA, classified each patient at the end of the visit to one of the following 3 categories: (1) PsA; (2) Not PsA; and (3) Possible PsA. The last category included patients in which the diagnosis was suspected based on typical inflammatory MSK symptoms (e.g., prolonged morning stiffness, inflammatory back pain, reported joint swelling), but could not be confirmed after completing the physical examination and reviewing the results of the laboratory tests and radiographs. Patients were asked to complete questionnaires about the nature and duration of their MSK symptoms. They were also asked to mark the location of their painful joints on a homunculus. PRO were also collected using the following questionnaires: level of pain [visual analog scale (VAS) 0–10], Dermatology Life Quality Index (DLQI), Functional Assessment of Chronic Illness Therapy Fatigue scale (FACIT-F), Health Assessment Questionnaire (HAQ), Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, and the patient global assessment of arthritis (VAS 0–10). Finally, erythrocyte sedimentation rate (ESR) and C-reactive protein were tested.

US assessment. All the US assessments were performed by a single rheumatologist (LE), who has 8 years of experience in MSK US. MyLab Twice scanner (Esaote) equipped with a 6–18 MHz linear transducer (Esaote) was the US device. Power Doppler (PD) settings were standardized with a Doppler frequency of 8.3–10 MHz. A targeted MSK examination of the peripheral joints was performed, in addition to a standardized assessment of 14 entheses. To determine which peripheral joints to assess, the patients were first assessed by the advanced practice physiotherapist, who identified tender and/or swollen joints for a targeted MSK US assessment. The sonographer scanned these clinically affected joints as well as their contralateral side, and was blinded to the affected side. The peripheral joints were assessed for the presence of the following lesions: (1) synovitis: defined as synovial hypertrophy in greyscale (GS) and intraarticular PD[14]; (2) peritenonitis: defined as peritendon swelling (GS) and positive peritendinous PD in the extensor tendons in the hands and feet[15,16]; and (c) tenosynovitis: synovial inflammation in tendons with tendon sheet (GS and PD)[17]. In addition, enthesitis was assessed in the following 7 entheseal sites bilaterally: quadriceps tendons insertions to the patella, patellar tendons insertions to the patella and tibial tuberosity, Achilles tendons and plantar fascia insertions into the calcaneus, triceps tendon insertions to the olecranon process, and common extensor tendon insertion to the lateral epicondyle. The presence of GS and PD entheseal lesions were assessed according to the Outcomes in Rheumatology (OMERACT) definition[18]. We considered the presence of both GS and PD abnormalities in the joint, peritendon, or tendon sheath an indication of sonographic synovitis, peritenonitis, and tenosynovitis, respectively. The presence of hypoechogenicity and/or entheseal thickening in GS lesions and at least grade 2 PD was considered as enthesitis. Active MSK inflammation was defined as any evidence of sonographic synovitis, enthesitis, tenosynovitis, or peritenonitis as outlined above.

Statistical analysis. Descriptive statistics included median (IQR) or mean for continuous variables (depending on the variable distribution) and frequencies (%) for categorical variables. Wilcoxon rank tests and chi-square tests were used to compare variables between patients who were classified as

having PsA and those with Possible/Not PsA. A 2-sided P value of < 0.05 was considered statistically significant. Due to the exploratory nature of the study, we considered both uncorrected and Bonferroni-corrected P values.

The level of agreement in joint/enthesis assessment between the 4 modalities was evaluated using the following statistics: κ statistics and its 95% CI, and the proportion of positive and negative agreement. Since κ is highly dependent on the prevalence of the assessed condition, we also reported the prevalence adjusted and bias adjusted kappa (PABAK)[19]. Compared with κ, PABAK reflects the ideal situation (assuming 50% prevalence) and ignores the variation of prevalence. Reporting both measures of agreement (κ and PABAK) allows interpretation and comparison with other populations where the prevalence is considerably different.

RESULTS

Patient enrollment. A total of 765 patients with a diagnosis of psoriasis in their EMR were identified (97.2% from dermatology) and invited to participate in the study by mail invitation. Of these, 288 patients responded (260 of them had current MSK symptoms). A total of 203 patients participated in the study, of which 135 (66.5%) resulted from self-referrals and 68 (33.5%) resulted from direct physician referrals. Of the 135 patients resulting from self-referrals, 113 (83.7%) were identified through dermatology records, and 22 (16.3%) through family medicine records. Of the 68 direct physician referrals, 66 (97.1%) were referred by dermatologists and 2 (2.9%) by family physicians.

Comparison of patient characteristics by disease status. A total of 18 (8.8%) patients were classified by the rheumatologist as having PsA, 48 (23.6%) as Possible PsA, and the remaining 137 (67.4%) as Not PsA. The MSK symptoms of the last group were attributed mostly to noninflammatory rheumatic conditions, such as OA and nonspecific back pain. Patient characteristics by disease status are presented in Table 1. There were no significant differences in patient demographics, family history of psoriatic disease, and duration of psoriasis between patients with PsA and those with Possible/Not PsA (combined into 1 group for the analysis). Patients who were classified as having PsA were more likely to use systemic nonbiologic ($P = 0.02$) and biologic medications for psoriasis ($P = 0.006$), in particular the interleukin 12/23 inhibitor ustekinumab ($P = 0.009$). Additionally, those who were classified as having PsA had more severe psoriasis with higher PASI scores ($P = 0.02$) and were more likely to have psoriatic nail lesions ($P = 0.02$), in particular nail pitting ($P = 0.008$). As expected, patients who were classified as having PsA had higher tender and swollen joint counts; however, there was no difference in the number of tender entheses between the groups.

Table 1. Characteristics of the study population by disease status.

	All, N = 203	Not PsA, N = 137	Possible PsA, N = 48	PsA, N = 18	PsA vs Possible/ Not PsA, *P*
Age, yrs, mean (SD)	52 (22.2)	54.5 (21.9)	45.2 (25.1)	53.5 (16.6)	0.75
Sex, female	133 (65.5)	93 (67.9)	31 (64.6)	9 (50)	0.19
Psoriasis duration, yrs, mean (SD)	11.9 (24)	10.5 (25)	18.8 (14.9)	11.7 (10)	0.24
Use of systemic nonbiologic medications for psoriasis	7 (3.5)	0	4 (8.3)	3 (16.7)	**0.02**
Methotrexate	2 (1)	0	1 (2.1)	1 (5.5)	0.17
Apremilast	5 (2.45)	0	3 (6.25)	2 (11.1)	0.06
Use of biologics	22 (10.8)	9 (6.7)	7 (14.6)	6 (33)	**0.006**
TNFi	8 (3.9)	3 (2.2)	3 (6.25)	2 (11.1)	0.15
IL-12/IL-23 inhibitor	11 (5.4)	5 (3.7)	2 (4.17)	4 (22.2)	**0.009**
IL-17 inhibitor	2 (1)	1 (0.7)	1 (2.1)	0	–
Family history of PsA	15 (7.4)	10 (7.3)	4 (8.3)	1 (5.6)	> 0.99
Family history of psoriasis	107 (52.7)	70 (50.1)	29 (60.4)	8 (44.4)	0.47
BMI, kg/m^2, mean (SD)	27.8 (7.5)	27.6 (7.6)	28.2 (7.4)	27.8 (7.5)	0.81
Fibromyalgia	4 (2)	2 (1.5)	2 (1)	0 (0)	> 0.99
Nail psoriasis	79 (39.1)	47 (34.6)	20 (41.7)	12 (66.7)	**0.02**
Pitting	52 (25.9)	29 (21.3)	13 (27.7)	10 (55.6)	**0.008**
Onycholysis	34 (16.9)	22 (16.2)	7 (14.9)	5 (27.8)	0.20
PASI score, mean (SD)	2.4 (3.8)	2.2 (3.1)	2.4 (5.4)	5.8 (10.9)	**0.004**
Severe psoriasis (PASI > 10)	35 (17.2)	18 (13.1)	10 (20.8)	7 (38.9)	**0.02**
Tender joint count, median (IQR)	1 (4)	1 (3)	1 (3.5)	3 (5)	**0.05**
Swollen joint count, median (IQR)	1 (0.9)	0 (1)	0 (0)	1 (6)	**0.005**
Enthesitis count, median (IQR)	1 (1.5)	0 (2)	1 (2)	0.5 (2)	0.96
CRP, mg/dL, mean (SD)	1.9 (3)	1.6 (3)	1.3 (2.9)	2.4 (6.9)	**0.04**
ESR, mm/h, mean (SD)	11 (12)	11.5 (11.5)	10 (11.5)	17.5 (23.5)	0.13
MASEI, median (IQR)	8 (12)	8 (11)	7 (13)	11.5 (8)	0.14
MASEI-Doppler, median (IQR)	1 (3)	1 (3)	0.5 (3)	2.5 (4)	0.06
US MSK inflammation in ≥ 1 site	120 (59.1)	75 (54.7)	29 (60.4)	16 (88.9)	**0.01**
US MSK inflammation in ≥ 2 sites	57 (28.1)	34 (24.8)	11 (22.9)	12 (66.7)	**0.0004**

Values in bold are statistically significant. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IL: interleukin; MASEI: Madrid Sonographic Enthesitis Index; MSK: musculoskeletal; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; TNFi: tumor necrosis factor inhibitor; US: ultrasound.

The majority of the study participants had at least 1 site with active MSK inflammation by US (59.1%), and the prevalence of 1 and 2 sites with US MSK inflammation was higher in patients who were classified as PsA ($P \leq 0.01$ for both); however, there was no difference in the total sonographic enthesitis score.

Pattern of MSK symptoms by disease status. In general, there was no difference between the 2 groups in the presence, distribution, and duration of MSK pain, including in features that are considered to be typical of PsA, such as prolonged morning stiffness and inflammatory back pain (Table 2). The primary differences between the 2 groups appeared to be related to the intensity of MSK and skin-related symptoms and their effect on domains like physical function, QOL, and fatigue. Patients classified as PsA had worse scores on PsAID ($P = 0.004$), DLQI ($P = 0.002$), FACIT-F ($P = 0.02$), 36-item Short-Form health survey mental component summary score ($P = 0.02$), and HAQ ($P = 0.06$). No difference was found in SF-36 physical component summary and pain scores between the groups. After correction for multiple testing, only DLQI remained statistically significant. When patients who were classified as PsA and Possible PsA were combined and compared with those classified as Not PsA, the differences were less significant (data not shown).

Disease characteristics by the presence of sonographic MSK inflammation. Considering the presence of US MSK inflammation as an outcome of interest (regardless of the clinical diagnosis of PsA), we compared the same disease characteristics between patients with and without US inflammation (Table 3). Patients with US MSK inflammation were older ($P < 0.0001$), reported more morning stiffness ($P = 0.02$) and physical dysfunction (by HAQ, $P = 0.02$), and had higher tender and swollen joint counts ($P < 0.01$ for both) and higher PASI scores ($P = 0.04$). After correction for multiple testing, age and swollen joint count remained statistically significant. Overall, there was no significant difference between the groups in the presence and intensity of the remaining MSK symptoms and PRO.

Agreement between joint assessment modalities. The distributions of affected (tender or swollen) joints and entheses as reported by each of the assessors are shown in Figure 1. Of note, joints and the adjacent entheseal sites were considered together, since patients were unable to distinguish between them. In general, the larger joints (knees, ankles, elbows, and shoulders), as well as the wrists and proximal interphalangeal joints in the hands, were most commonly affected in all modalities. Significant discrepancies were found with respect to the detection of affected joints at the joint level between the different assessors. Overall, patients reported the highest level of affected joints in most sites, followed by US. The physiotherapist and rheumatologist assessment resulted in the lowest number of affected sites, with the rheumatologist reporting a slightly lower number of sites. Analysis of agreement between modalities in regards to evaluation of hand, foot, ankle, knee, elbow, and shoulder joints (50 joints total) for tenderness or swelling (Table 4) revealed the strongest agreement between the rheumatologist and physiotherapist ($\kappa = 0.28$, PABAK 0.87), followed by physiotherapist and patient ($\kappa = 0.18$, PABAK 0.65). A similar level of agreement was found between rheumatologist and US ($\kappa = 0.11$, PABAK 0.71), and rheumatologist and patient ($\kappa = 0.12$, PABAK 0.68). The lowest levels of agreement were found between US and patient ($\kappa = 0.08$, PABAK 0.39), and physiotherapist and US ($\kappa = 0.08$, PABAK 0.46). Overall, the majority of disagreement was related

Table 2. Musculoskeletal (MSK) symptoms and patient- reported outcomes by disease status.

	All, N = 203	Not PsA, N = 137	Possible PsA, N = 48	PsA, N = 18	PsA vs Possible/ Not PsA, *P*
Prolonged MSK pain (> 2 yrs)	111 (56.1)	73 (54.9)	27 (57.5)	11 (61.1)	0.80
Duration of joint pain, yrs, mean (SD)	3.5 (8.5)	3.6 (9)	3 (1.5)	3.6 (8.2)	0.80
Duration of back pain, yrs, mean (SD)	6.9 (14.6)	6.1 (14.7)	8.6 (12.4)	12.5 (11)	0.31
Presence of morning stiffness	152 (77.2)	102 (77.2)	36 (76.6)	14 (77.8)	> 0.99
Duration of joint stiffness > 1 h	32 (15.7)	19 (13.9)	8 (16.7)	5 (27.8)	0.17
Duration of back stiffness > 1 h	35 (17.2)	25 (18.3)	8 (16.7)	2 (11.1)	0.74
Peripheral joint pain	183 (90.2)	121 (88.3)	45 (93.8)	17 (94.4)	> 0.99
Heel pain	76 (37.4)	46 (33.6)	24 (50)	6 (33.3)	0.80
Axial pain	168 (82.8)	114 (83.2)	41 (85.4)	13 (72.2)	0.21
Back stiffness	114 (56.2)	71 (51.8)	4 (70.8)	9 (50)	0.62
Inflammatory back pain	54 (26.6)	31 (22.6)	19 (39.6)	4 (22.2)	0.79
PsAID score, mean (SD)	2.5 (4.3)	2.2 (3.6)	2.6 (5)	5.3 (3.2)	0.004
FACIT-F, mean (SD)	38 (16)	40 (14)	38 (17)	30 (9.5)	0.02
SF-36 PCS, mean (SD)	43.5 (16.5)	43 (17.8)	45.4 (12.5)	46.3 (15)	0.77
SF-36 MCS, mean (SD)	46.7 (18)	47.9 (17)	45.1 (20.4)	40.7 (13.3)	0.02
DLQI, mean (SD)	4 (8)	4 (7.5)	6 (11)	9.5 (14)	**0.002**
Pain score (0–10), mean (SD)	3 (4)	3 (4)	4 (3)	5.5 (4)	0.16
HAQ, mean (SD)	0.25 (0.63)	0.13 (0.63)	0.25 (0.62)	0.50 (0.50)	0.06

Values are expressed in n (%) unless otherwise specified. Values in bold show statistical significance after correction for multiple testing ($P < 0.003$). DLQI: Dermatology Life Quality Index; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue scale; HAQ: Health Assessment Questionnaire; MCS: mental component summary score; PCS: physical component summary score; PsA: psoriatic arthritis; PsAID: Psoriatic Arthritis Impact of Disease; SF: 36-item Short Form health survey.

Table 3. Comparison of patient characteristics by ultrasound (US) inflammation (at least 1 joint or entheseal site with positive Doppler).

	US Inflammation		
	Negative, N = 83	Positive, N = 120	*P*
Age, yrs, mean (SD)	45 (14)	54.8 (13)	**< 0.0001**
Sex, female	25 (30.1)	45 (37.5)	0.28
Prolonged MSK pain (> 2 yrs)	43 (52.4)	68 (58.6)	0.39
Use of nonbiologic medications for psoriasis	4 (4.8)	3 (2.5)	0.37
Use of biologic medications	9 (10.8)	13 (10.8)	0.99
Severe psoriasis (PASI > 10)	15 (18.1)	20 (16.7)	0.79
Duration of joint pain, yrs, mean (SD)	6.5 (8.3)	6.9 (8.3)	0.75
Duration of back pain, yrs, mean (SD)	10.2 (10.9)	10.9 (10.5)	0.73
Morning stiffness	43 (51.8)	81 (67.5)	0.02
Duration morning stiffness > 1 h	12 (14.5)	20 (16.7)	0.67
Duration back stiffness > 1 h	15 (18.1)	20 (16.7)	0.79
Peripheral joint pain	74 (89.2)	109 (90.8)	0.69
Heel pain	35 (42.2)	41 (34.2)	0.25
Axial pain	69 (83.1)	99 (82.5)	0.91
Back stiffness	41 (49.4)	73 (60.8)	0.11
Inflammatory back pain	24 (28.9)	30 (25)	0.53
BMI, kg/m^2, mean (SD)	29.6 (7.1)	29 (6.1)	0.55
Nail psoriasis	30 (36.6)	49 (40.8)	0.54
Pitting	21 (25.6)	31 (26.1)	0.94
Onycholysis	9 (11)	25 (21)	0.06
PASI score, mean (SD)	3 (3.1)	4.4 (6.4)	0.04
Tender joint count, median (IQR)	1.9 (2.5)	3.3 (4.1)	0.003
Swollen joint count, median (IQR)	0.3 (0.8)	1.3 (2.3)	**< 0.0001**
Clinical enthesitis count, median (IQR)	1.5 (2.4)	1.6 (2.2)	0.83
Fibromyalgia	1 (1.2)	3 (2.5)	0.52
CRP, mg/dL, mean (SD)	3.8 (4.3)	4 (8.6)	0.85
ESR, mm/h, mean (SD)	13.4 (9.4)	12.9 (9.4)	0.70
PsAID score, mean (SD)	3.5 (3.3)	3.4 (2.7)	0.83
FACIT-F score, mean (SD)	35.4 (11.3)	35.6 (11.2)	0.91
SF-36 PCS, mean (SD)	44.6 (10.5)	42.9 (9.9)	0.28
SF-36 MCS, mean (SD)	43.2 (10.9)	44.4 (10.8)	0.47
DLQI, mean (SD)	6.6 (6.3)	6.7 (6.5)	0.87
Pain score (0–10), mean (SD)	3.5 (2.3)	4.2 (2.5)	0.32
HAQ, mean (SD)	0.3 (0.4)	0.4 (0.4)	0.02

Values in bold are statistically significant after correction for multiple testing ($P < 0.0014$). CRP: C-reactive protein; DLQI: Dermatology Life Quality Index; ESR: erythrocyte sedimentation rate; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue scale; HAQ: Health Assessment Questionnaire; MCS: mental component summary score; MSK: musculoskeletal; PASI: Psoriasis Area and Severity Index; PCS: physical component summary score; PsAID: Psoriatic Arthritis Impact of Disease; SF: 36-item Short Form health survey.

to the positive findings (positive agreement range: 16–31%), whereas there was a general agreement with respect to normal joints (negative agreement 81–97%).

DISCUSSION

In this study, we described the pattern of MSK symptoms in patients with psoriasis who are suspected to have PsA. We found that while there were some differences in psoriasis characteristics between those who were diagnosed as having PsA and the remaining patients, the distinction between the groups based on the presence and duration of symptoms was challenging to make. However, patients with PsA tended to score worse in several PRO evaluating QOL, physical function, and fatigue compared to the remaining psoriasis patients with MSK symptoms not explained by PsA. These findings, in conjunction with the low agreement between diagnostic modalities, highlight the challenges entailed with early detection of PsA among patients with psoriasis and the need for additional objective biomarkers that can potentially assist the clinician in establishing the diagnosis.

There are few data describing the complexity of symptoms that PsA patients experience in the early stage of their disease. Unfortunately, many of the symptoms that characterize the prediagnosis phase of PsA are nonspecific, thus making diagnosis difficult. Our group described a prediagnosis period that is characterized by nonspecific MSK symptoms in patients with psoriasis who ultimately developed PsA[7]. This study found that the intensity of symptoms, as opposed to simply their presence or absence, is also important in predicting who is ultimately going

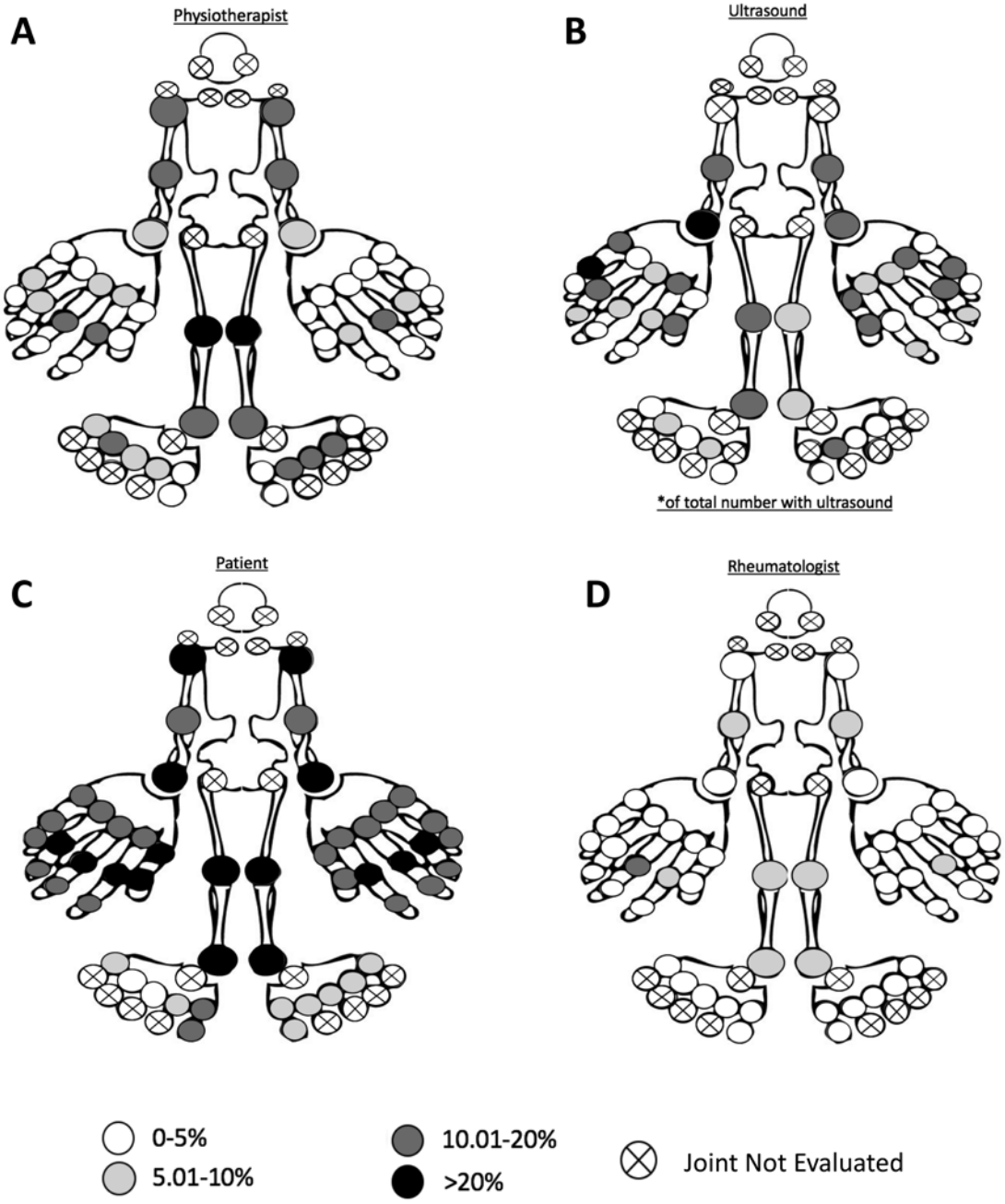

Figure 1. Proportion of joints with swelling or tenderness as reported by each modality: (A) physiotherapist; (B) ultrasound (of the joints scanned); C: patient; and (D) rheumatologist.

to develop PsA[7]. Our findings in the present study support this by showing that although there was no difference in the presence, distribution, or duration of symptoms, patients who were diagnosed as having PsA had higher levels of symptoms, which may be associated with a clinical onset of the disease. Alternatively, physicians may be more inclined to diagnose a disease in patients who have a higher degree of symptoms. The fact that these symptoms are not entirely specific to PsA highlights the need for additional diagnostic tools such as imaging or laboratory markers.

US has proven to be successful in detecting a variety of inflammatory lesions in PsA[9,10]. Therefore, it can potentially be used to improve the detection of MSK inflammation, especially in situations where the findings on physical examination are ambiguous or confounded by factors such as OA or obesity. We have generally found that over half of the patients had at least 1 joint site with sonographic inflammation and over a quarter had at least 2 sites. However, the majority of these patients were not diagnosed as having PsA by the rheumatologist even though they all had MSK symptoms. This is also reflected by the general poor agreement observed between the different

Table 4. Agreement between methods of joint/enthesis assessment (tender or swollen joints on physical examination and the presence of positive Doppler on ultrasound).

Method 1	Method 2	κ (95% CI)	% of Positive Agreement	% of Negative Agreement	PABAK
Rheumatologist	Physiotherapist	0.28 (0.21–0.35)	0.31	0.97	0.87
Rheumatologist	Ultrasound	0.11 (0.05–0.17)	0.18	0.92	0.71
Rheumatologist	Patient	0.12 (0.09–0.15)	0.16	0.91	0.68
Physiotherapist	Patient	0.18 (0.15–0.22)	0.26	0.90	0.65
Physiotherapist	Ultrasound	0.08 (0.03–0.12)	0.21	0.84	0.46
Patient	Ultrasound	0.08 (0.04–0.12)	0.21	0.81	0.39

PABAK: prevalence-adjusted and bias-adjusted kappa.

modalities used for physical examination in our study. US has shown to be potentially useful in detecting subclinical MSK inflammation in patients with psoriasis without PsA[20,21,22,23,24]. Importantly, emerging data suggest that subclinical sonographic synovitis and enthesitis predicted future development of PsA in psoriasis patients without arthritis at the time of assessment[25,26]. In conjunction with our data on the lack of agreement between US and clinical assessment, the potential usefulness of US in detecting PsA at an early stage is further highlighted.

The potential additional information provided by US raises several questions surrounding how PsA should be diagnosed and which patients should be on a treatment plan. The ClASsification for Psoriatic ARthritis classification criteria can be used for diagnosing PsA. They apply to any patient with inflammatory articular disease, including inflammatory arthritis, enthesitis, or spondylitis, and use a point system to identify those with PsA[27]. It is unclear what means should be used to determine the presence of MSK inflammation. Should any patient with psoriasis, MSK symptoms, and inflammation in the joints, as detected by US, be diagnosed with PsA? Should psoriasis patients with subclinical enthesitis or synovitis as detected by US, but no MSK symptoms, undergo treatment? These are important questions that must be answered if US is going to be used in the diagnostic process of PsA.

There are several limitations associated with this study. First, MSK US was performed only on joints identified by the physiotherapist as being symptomatic, along with the contralateral joints. This limited our ability to detect subclinical enthesitis and synovitis in joints that were not evaluated by US, especially given the discrepancies between physiotherapist and rheumatologist. In addition, the cross-sectional nature of the study limits our ability to determine if patients with subclinical enthesitis or synovitis will go on to clinical PsA as determined by a rheumatologist. However, other studies showed that sonographic MSK inflammation can predict future diagnosis of PsA in similar populations[25]. Finally, this is a single-center study, where the majority of the patients came from dermatology clinics; this may limit the generalizability of the results due to the tendency for more severe psoriasis.

In conclusion, in this study we described the complex pattern of MSK symptoms in patients with suspected PsA. We found that the intensity, rather than the type, duration, or distribution of symptoms was associated with PsA. In addition, the correlation between joint examination modalities was relatively low. This study begins to explore the potential for MSK US to provide additional information to the clinical assessment and aid in diagnosing patients with PsA at earlier stages. Further research is required to define the role of MSK US in early diagnosis of PsA.

ACKNOWLEDGMENT

We wish to acknowledge the contribution of Drs. Noah Ivers and Carol Kitai from the Department of Family Medicine at Women's College Hospital and the team at the Phototherapy Education and Research Centre at Women's College Hospital in patient recruitment.

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