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Original article

High prevalence of ultrasonographic synovitis and enthesopathy in patients with psoriasis without psoriatic arthritis: a prospective case–control study

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Abstract

Objective. To investigate the presence of synovitis, tenosynovitis and enthesitis with power Doppler (PD) ultrasonography (US) in patients with psoriasis without musculoskeletal diseases as compared with controls with other skin diseases without musculoskeletal disorders.

Methods. A total of 162 patients with plaque psoriasis and 60 age-matched controls with other skin diseases, all without musculoskeletal diseases, were prospectively recruited at 14 centres. They underwent dermatological and rheumatological assessment and a blinded PDUS evaluation. Clinical assessment included demographics, comorbidities, severity of psoriasis, work and sport activities and musculoskeletal clinical examination. PDUS evaluation consisted of the detection of grey scale (GS) synovitis and synovial PD signal in 36 joints, GS tenosynovitis and tenosynovial PD signal at 22 sites, and GS enthesopathy and entheseal PD signal in 18 entheses.

Results. US synovitis and enthesopathy were significantly more frequent in psoriatic patients than in controls ($P = 0.024$ and 0.005, respectively). The percentage of joints with US synovitis was 3.2% in the psoriasis group and 1.3% in the control group ($P < 0.0005$). US enthesopathy was present in 11.6% of entheses in the psoriasis group and 5.3% of entheses in the control group ($P < 0.0005$). Entheseal PD signal was found in 10 (7.4%) psoriatic patients, whereas no controls showed this finding ($P = 0.05$). Among demographic and clinical data, having psoriasis was the only significant predictive variable of the presence of US synovitis [odds ratio (OR) 2.1; $P = 0.007$] and enthesopathy (OR 2.6; $P = 0.027$).

Conclusion. Psoriatic patients showed a significant prevalence of asymptomatic US synovitis and enthesopathy, which may indicate a subclinical musculoskeletal involvement.

Key words: Ultrasonography, Psoriasis, Synovitis, Enthesopathy, Enthesitis.

CLINICAL SCIENCE

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*See Appendix 1 for a list of the members of the Spanish Ecografia en artritis psoriásica (ECO-APs) group.

Introduction

Psoriasis is a common chronic immune-mediated skin disease that affects ~2% of the population [1, 2]. There is a variety of cutaneous manifestations of psoriasis, but the most frequent form is plaque psoriasis. PsA occurs in a variable, albeit considerable percentage of psoriatic patients that ranges from 10 to 30% depending on the studied population [3, 4]. PsA may be present in different clinical forms whose major features are synovitis and/or enthesitis. In most patients, psoriasis precedes the clinical onset of the joint inflammatory disease [5].

Both MRI and high-resolution ultrasound (US) have been widely shown to be more sensitive than clinical assessment in detecting joint synovitis [6–16] and enthesitis [7, 17–21] in inflammatory arthritis. MRI is not feasible for routine clinical practice because of its limited availability and high cost. However, there is a growing implementation of musculoskeletal US in rheumatological practice and research [22, 23]. The value of Doppler US for evaluating inflammatory activity in joints [24–28] and entheses [18] has also been demonstrated. In addition, this technique is non-invasive, relatively inexpensive, patient friendly and allows the scanning of all peripheral joints as many times as required.

Previous studies have reported the presence of subclinical signs of hand arthritis on MRI [29] or lower limb enthesseal abnormalities on US [30–32] in a higher percentage of psoriatic patients compared with controls. However, to the best of our knowledge, no study has comprehensively evaluated with Doppler US the prevalence of synovitis, tenosynovitis and enthesopathy in a large population of psoriatic patients without musculoskeletal involvement.

The present multicentre study was undertaken to investigate the presence of synovitis, tenosynovitis and enthesitis with power Doppler (PD) US in patients with psoriasis without symptoms of PsA or any other musculoskeletal disease as compared with controls with other skin diseases without musculoskeletal disorders.

Methods

Study population and patient flow chart

A total of 162 patients with plaque psoriasis and 60 age-matched controls with other skin diseases who consecutively attended the outpatient dermatology clinics at 14 Spanish centres were prospectively enrolled in the study. Psoriatic and control patients were recruited and assessed by a trained dermatologist at each centre. Inclusion criteria for psoriatic patients were the following: age $\geqslant$18 years; plaque psoriasis diagnosed by a dermatologist; no history of any inflammatory, microcrystalline, degenerative or infectious musculoskeletal disease; no history of polytraumatism; absence of past or present non-traumatic pain in any axial or peripheral musculoskeletal anatomic region; not having received any systemic therapy (i.e. MTX, ciclosporin or retinoids) in 8 weeks before the inclusion; not having received NSAIDs nor CSs in the 2 weeks before the study entry; never having received biological therapy; patient acceptance; and capability to participate in the study.

Inclusion criteria for the control group were the following: age $\geqslant$18 years; presence of any skin disease not associated with musculoskeletal diseases diagnosed by a dermatologist (i.e. contact eczema, atopic dermatitis, nevus, actinic keratosis, lichen planus, prurigo, basal cell carcinoma and urticaria); no history of any inflammatory, microcrystalline, degenerative or infectious musculoskeletal disease; no history of polytraumatism; absence of past or present non-traumatic pain in any axial or peripheral musculoskeletal anatomic region; not having received any systemic therapy in the 8 weeks before the inclusion; not having received NSAIDs or CSs in the 2 weeks before study entry; never having received biological therapy; patient acceptance; and capability to participate in the study.

Recruited psoriatic and control patients were referred to an experienced rheumatologist at each centre who clinically evaluated them. Then the rheumatologists who performed the clinical assessment referred the psoriatic and control patients to 10 rheumatologists highly experienced in musculoskeletal US for having PDUS assessment at 10 centres. This was done in a predetermined fashion. Each rheumatologist ultrasonographer received the same proportion of psoriatic and control patients and a similar number of patients. These experts were unaware of the skin disease group (psoriasis or control group) and the dermatological and rheumatological findings. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee of Hospital Universitario Severo Ochoa. Written informed consent was obtained from all patients before study enrolment.

Dermatological assessment

The following data were recorded for each psoriatic and control patient at study enrolment: age, sex, disease duration, treatment received for the skin disease and history of comorbidities (i.e. hyperlipidaemia, hypertension, diabetes mellitus, ischaemic heart disease and obesity). In psoriatic patients, psoriatic nail involvement was also documented. Psoriasis severity was scored using the psoriasis area and severity index (PASI) and the body surface area (BSA) measurement [33].

Rheumatological assessment

Rheumatological evaluation included the following data: confirmation of absence of symptoms or history of any musculoskeletal disease or any disorder that may have musculoskeletal involvement; any drug received in the 8 weeks before inclusion; work and sport activities; and also history of bone fracture and joint surgery. Low, moderate or high musculoskeletal occupational demand was registered by the assessor. Sport activity, if present, was classified as low ($<$7 h/week) or high ($>$7 h/week). Sixty-eight peripheral joints were evaluated for tenderness, movement pain and range of motion. Also 66 joints were evaluated for swelling. The joint evaluation

also included assessment of tenderness or swelling of superficial periarticular tendons and entheses. Hands and feet were evaluated for dactylitis. Tenderness at 13 entheses [Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)] [34] was investigated. SI joints and spinal mobility were also assessed. Articular regions that had suffered from bone fracture or had undergone surgical procedures were excluded from the clinical examination. For each patient, RF (normal 0–15 IU/ml), CCP antibodies (normal 0–20 U), HLA-B27 antigen and serum markers of inflammation [CRP level (normal 0–10 mg/l) and ESR (normal 10–20 mm/h)] were obtained from laboratory tests at study entry.

PDUS assessment

Ten rheumatologists with 10–15 years of experience in musculoskeletal US performed a PDUS examination in psoriatic and control patients within 4 weeks of inclusion in the study. These experts had a similar background in musculoskeletal US, had conducted multiple consensus meetings and training sessions on joint and enthesis PDUS inflammatory findings, and had previously demonstrated reproducibility for detecting PDUS synovitis and enthesopathy [28, 35]. In addition, further standardization of scanning technique and identification of abnormalities were carried out among investigators before the study.

The PDUS assessment was blinded to the patients' skin disease and clinical findings. To reduce the possibility of bias, the patients were asked not to talk about their clinical data to the US examiner. We maximized the level of darkness in the examination room. Furthermore, we reminded the ultrasonographers from the outset about the importance of neither making physical contact nor looking at the patients. The only patient information that the rheumatologist ultrasonographers received from the clinical investigators was about the articular regions that had suffered from bone fractures or had undergone surgical procedures. These anatomic regions were excluded from the PDUS assessment.

For each patient, they carried out a systematic longitudinal and transverse multiplanar PDUS examination of 36 joints, 22 tendons/tendon compartments and 18 entheses with the same real-time scanner in all centres (Logiq 9; GE Medical Systems Ultrasound and Primary Care Diagnostics, LLC, Wauwatosa, WI, USA) using multifrequency linear array transducers (8–14 MHz). The following bilateral joints were investigated for the presence of grey scale (GS) synovitis and synovial PD signal: wrist joints (i.e. radiocarpal and midcarpal), MCP joints, PIP and DIP joints of the hands, knee and tibiotalar joint. We considered wrist synovitis or synovial PD signal positive if they were detected in either the radiocarpal or the midcarpal joints. Bilateral wrist extensor compartments (I–VI) and finger flexor tendons were evaluated for the presence of GS tenosynovitis and tenosynovial PD signal. We also considered the presence of wrist tenosynovitis or tenosynovial PD signal if any of the six extensor compartments showed the above abnormalities. The following bilateral entheses were assessed for the presence of GS enthesopathy and entheseal and perientheseal PD signal: proximal patellar tendon, distal patellar tendon, Achilles tendon, plantar fascia and deep flexor tendons of the fingers.

PDUS scanning method is described in supplementary table 1 (available as supplementary data at *Rheumatology* Online). PD imaging was performed by selecting a region of interest that included the bony margins, the synovial, tenosynovial or entheseal site, and a variable view of surrounding tissues. GS and PD machine settings were standardized among investigators before the study to optimize US scanning of superficial and deep anatomic areas. These settings were as follows: dynamic range of 72 dB, GS frequency of 12–14 MHz, Doppler frequency of 6.3–7.5 MHz, GS gain of 66 dB, colour gain of 41 dB, low-wall filters and pulse repetition frequency of 500–750 Hz. Flow was additionally demonstrated in two planes and confirmed by pulsed wave Doppler spectrum to exclude artefacts.

US synovitis, tenosynovitis and enthesopathy were identified according to the OMERACT definitions and published descriptions of US pathology [36, 37]. Synovitis was defined as the presence of abnormal hypoechoic (compared with subdermal fat) IA area, which may exhibit Doppler signal. Tenosynovitis was defined as hypoechoic or anechoic thickened tissue with or without fluid within the tendon sheath, which is seen in two perpendicular planes and which may exhibit Doppler signal. Enthesopathy was defined as abnormally hypoechoic (loss of normal fibrillar architecture) and/or thickened tendon or ligament at its bony attachment (may occasionally contain hyperechoic foci consistent with calcification), seen in two perpendicular planes, which may exhibit Doppler signal and/or bony changes including enthesophytes, erosions or irregularity. Enthesis thickening and hypoechogenicity were evaluated relative to the body of the tendon. When PD signal was detected at the cortical bone insertion, it was considered as entheseal. When PD signal was detected at the tendon body and/or adjacent bursitis, it was considered as perientheseal.

Statistical analysis

Statistical analysis was performed using SPSS, version 13.0 (SPSS, Chicago, IL, USA). Quantitative variables were presented as the mean (S.D.) and range. Categorical variables were presented as absolute frequencies and percentages. Comparisons between independent means were analysed using Student's *t*-test or Mann–Whitney test. Relationships between categorical variables were evaluated by chi-squared test or Fisher's exact test. Correlations between quantitative variables were analysed by Pearson's correlation coefficient. One-tailed test was used to study the relationship between group and PDUS findings. Two-tailed tests were used in the other analyses.

Multivariate logistic regression analysis was used to evaluate demographic and clinical data in predicting the presence of PDUS abnormalities. Three separated logistic regression models with synovitis, enthesopathy or any

PDUS abnormality, respectively, as dependent variables were fitted. Independent variables were the following: age, sex, musculoskeletal occupational demand, sport activity, hyperlipidaemia, hypertension, diabetes mellitus, ischaemic heart disease, obesity, tender joint count >0, swollen joint count >0, dactylitis >0, joint count for movement pain or restricted motion >0, MASES >0, positive SI joint manoeuvres, spinal movement pain or restricted motion, positive RF, CCP and HLA-B27, abnormal ESR and CCP, and the skin disease group (psoriasis or control group). Several methods for variable selection, enter, forward stepwise selection and backward stepwise elimination were used, with entry and removal criteria of 0.05 and 0.10 in stepwise methods. Mantel–Haenszel and Breslow statistics were applied to check independence and homogeneity between PDUS findings and groups (psoriasis and control). $P < 0.05$ was considered statistically significant.

Results

Demographics

Forty (26 psoriatic patients and 14 controls) people missed the PDUS visit. Complete clinical and PDUS data were obtained on 136 psoriatic patients (75 men and 61 women) and 46 controls (4 men and 42 women). There was no significant difference in psoriasis and control group distribution between the patients with complete data and patients who had missed the PDUS visit ($P = 0.239$). The mean (S.D.) age was 42.6 (15.7) years (range 18–79 years) for psoriatic patients and 39.9 (14.4) years (range 24–77 years) for controls ($P = 0.316$). The mean psoriasis duration was 13.4 (0.2) years (range 5–60 years).

Dermatological and rheumatological findings in psoriatic and control patients

The mean (S.D.) PASI score was 6.7 (5.9) (range 0–39.1), and the mean (S.D.) BSA involvement was 9.3% (11.3%) (range 0–74%). Fifty-three (38.9%) patients had psoriatic nail involvement. Table 1 displays clinical data and rheumatological findings in both psoriasis and control groups. Although the rheumatologists found some mild abnormalities on physical examination in a small number of asymptomatic psoriatic patients and controls (Table 1), they did not have criteria for PsA or other musculoskeletal disease and thus were not excluded from the study.

There were no significant differences between psoriatic and control patients in the following: prevalence of hypertension, diabetes mellitus, ischaemic heart disease and obesity, and also sport activity, bone fractures, joint surgery, tender joints, swollen joints, joints with movement pain or restricted motion, dactylitis, MASES, positive SI joint manoeuvres, spinal movement pain or restricted motion, positive RF, CCP and HLA-B27, abnormal ESR and CRP, and mean ESR and CRP. Sex distribution differed significantly between psoriatic patients and controls ($P < 0.0005$). The psoriasis group comprised a higher percentage of men (55.1%) than women (44.9%), whereas the control group had a higher percentage of women (91.3%) than men (8.7%). There were significantly more patients with hyperlipidaemia in the psoriasis group (19.9%) than in the control group (6.5%) ($P = 0.033$). The distribution of occupational musculoskeletal demand also differed significantly between psoriasis and control groups ($P < 0.0005$). The percentages of low and high demand (55.9 and 20.6%, respectively) were higher in the psoriasis group than in the control group (43.5 and 4.3%, respectively), whereas the percentage of moderate demand was higher in the controls (52.2%) than in the psoriatic patients (23.5%).

Thirty-one patients reported fractures involving different bones. In four of them, fractures involved articular regions included in the study. Surgical procedures consisted of hallux valgus correction in three patients, disc herniation intervention in three patients, shoulder luxation correction in one patient, knee meniscectomy in one patient, knee ligament surgical repair in one patient and wrist extensor tendon repair in one patient.

PDUS findings in psoriatic and control patients

With PDUS, we evaluated in total 6181 joint areas, 3275 entheses and 2183 flexor/extensor tendon regions. Seven joints, one extensor tendon region (I–VI wrist compartments) and one enthesis were excluded from the PDUS assessment because of previous fracture or surgery involving the articular region. One hundred and five (77.2%) psoriatic patients showed PDUS abnormalities, while 26 (56.5%) controls showed PDUS abnormalities ($P = 0.007$). There was a significantly higher percentage of psoriatic patients who showed joint synovitis and enthesopathy than controls ($P = 0.024$ and 0.005, respectively) (Table 2).

In patients with the above abnormalities, the mean number of joints with synovitis and mean number of entheses with enthesopathy per patient were also significantly higher in psoriatic patients [2.3 (1.5) (range 1–7) for synovitis; 3.4 (2.3) (range 1–13) for enthesopathy] than in controls [1.3 (0.6) (range 1–3) for synovitis, $P = 0.015$; 2.4 (2.4) (range 1–11) for enthesopathy, $P = 0.025$]. Forty-nine (36%) psoriatic patients showed both synovitis and enthesopathy, whereas only 7 (15.2%) controls showed both abnormalities ($P = 0.009$).

Entheseal PD signal was found in 10 (7.4%) psoriatic patients and perientheseal PD signal in 10 (7.4%) psoriatic patients, whereas none of the controls showed these findings ($P = 0.05$) (Table 2). Five psoriatic patients showed both entheseal and perientheseal PD signals, five showed only entheseal PD signal and five showed only perientheseal PD signal. There were no significant differences in the presence of synovial PD signal, tenosynovitis and tenosynovial PD signal between psoriatic and control patients (Table 2).

In the psoriasis group, we found a significantly higher percentage of sites that showed synovitis ($P < 0.0005$), enthesopathy ($P < 0.0005$), entheseal PD signal ($P = 0.013$) and perientheseal PD signal ($P = 0.002$) than in the control group (Table 2). There were no significant differences in the percentage of sites with synovial PD

Table 1 Clinical data and rheumatological findings in psoriatic and control patients

Clinical data	Psoriasis group ($n = 136$)	Control group ($n = 46$)	*P*-values
Sex, *n* (%)			
Men	75 (55.1)	4 (8.7)	
Women	61 (44.9)	42 (91.3)	<0.0005
Hyperlipidaemia, *n* (%)	27 (19.9)	3 (6.5)	0.033
Hypertension, *n* (%)	20 (14.7)	4 (8.7)	0.448
Diabetes mellitus, *n* (%)	7 (5.1)	1 (2.2)	0.681
Ischaemic heart disease, *n* (%)	4 (2.9)	0 (0)	0.573
Obesity, *n* (%)	11 (8.1)	4 (8.7)	0.759
Occupational demand, *n* (%)			
Low	76 (55.9)	20 (43.5)	
Moderate	32 (23.5)	24 (52.2)	<0.0005
High	28 (20.6)	2 (4.3)	
Sport activity, *n* (%)			
No	85 (62.5)	31 (67.4)	0.686
Low	40 (29.4)	13 (28.3)	
High	11 (8.1)	2 (4.3)	
Bone fractures, *n* (%)	25 (18.4)	6 (13)	0.635
Joint surgery, *n* (%)	8 (5.9)	2 (4.3)	1.000
TJC > 0, *n* (%)	20 (14.7)	6 (13.0)	1.000
TJC, mean (S.D.) (range)	0.31 (0.99) (0–9)	0.62 (2.03) (0–10)	0.318
SJC > 0, *n* (%)	4 (2.9)	3 (6.5)	0.370
SJC, mean (S.D.) (range)	0.05 (0.31) (0–2)	0.09 (0.36) (0–2)	0.509
JC for MP/RM > 0, *n* (%)	14 (10.3)	6 (13.0)	0.593
JC for MP/RM, mean (S.D.) (range)	0.14 (0.45) (0–2)	0.42 (1.44) (0–8)	0.206
Dactylitis > 0	0 (0)	2 (4.3)	0.064
MASES > 0, *n* (%)	8 (5.9)	4 (8.7)	0.491
MASES, mean (S.D.) (range)	0.11 (0.42) (0–9)	0.25 (1.01) (0–10)	0.383
Positive SI joint manoeuvres, *n* (%)	2 (1.5)	0 (0)	1.000
Cervical MP/RM, *n* (%)	17 (12.5)	4 (8.7)	0.424
Lumbar MP/RM, *n* (%)	21 (15.4)	8 (17.4)	0.841
Positive RF, *n* (%)	4 (2.9)	0 (0)	0.575
Positive CCP, *n* (%)	3 (2.2)	0 (0)	0.575
Positive HLA-B27, *n* (%)	8 (5.9)	0 (0)	0.202
Abnormal ESR, *n* (%)	23 (16.9)	7 (15.2)	1.000
Abnormal CRP, *n* (%)	16 (11.8)	2 (4.3)	0.247
ESR, mean (S.D.) (range), mm/h	12.6 (10.8) (1–49)	11.7 (10.2) (1–39)	0.673
CRP, mean (S.D.) (range), mg/l	1.6 (2.3) (0–15)	1.3 (2.1) (0–11.6)	0.569

TJC: tender joint count; SJC: swollen joint count; JC: joint count; MP/RM: movement pain or restricted motion.

signal, tenosynovits and tenosynovial PD signal between psoriasis and control groups (Table 2).

Table 3 shows the distribution of PDUS findings in psoriatic patients and controls at the studied sites. The knee was the most frequently involved joint for synovitis in both psoriatic patients [64 (23.5%) knees] and controls [9 (9.8%) knees]. Enthesopathy and PD signal were most frequently found in the Achilles tendon in both psoriatic [114 (41.9%) tendons for enthesopathy; 8 (2.9%) tendons for entheseal PD signal; and 11 (4%) tendons for peri-entheseal PD signal] and control patients [17 (18.5%) tendons]. Synovitis was present in a significantly higher percentage of MCP ($P = 0.034$), PIP of the hands ($P = 0.036$) and knee joints ($P = 0.002$) in psoriatic patients than in controls (Table 3). Enthesopathy was found in a significantly higher percentage of proximal patellar tendon ($P < 0.0005$), distal patellar tendon ($P = 0.008$), Achilles tendon ($P < 0.0005$) and plantar fascia ($P = 0.005$) entheses in psoriatic patients than in control patients (Table 3). Representative US images of pathological findings in psoriatic patients are shown in Fig. 1. After excluding the patients with hyperlipidaemia from the analysis, there was a significantly higher percentage of psoriatic patients who showed joint synovitis [58 (54.7%) patients] and enthesopathy [66 (62.3%) patients] than controls [8 (22.6%) patients for synovitis, $P = 0.008$; and 11 (37.9%) patients for enthesopathy, $P = 0.017$]. After considering only patients with low and moderate occupational musculoskeletal demand, there was a significantly higher percentage of psoriatic patients who showed joint synovitis [52 (49.1%) patients] and enthesopathy [65 (61.3%) patients] than controls [13 (30.2%) patients for synovitis, $P = 0.027$; and 17 (39.5%) patients for enthesopathy, $P = 0.013$]. We performed a Mantel–Haenszel

TABLE 2 Prevalence of PDUS findings in psoriatic and control patients and at evaluated sites in psoriatic and control patients

Group	Synovitis	Synovial PD signal	Enthesopathy	Entheseal PD signal	Perientheseal PD signal	Tenosynovitis	Tenosynovial PD signal
Patients in psoriasis group, *n* (%)	69 (50.7)	13 (9.6)	85 (62.5)	10 (7.4)	10 (7.4)	5 (3.7)	1 (0.7)
Patients in control group, *n* (%)	15 (32.6)	3 (6.5)	18 (39.1)	0 (0)	0 (0)	1 (2.2)	0 (0)
P-values	0.024	0.529	0.005	0.050	0.050	0.526	0.747
Sites in psoriasis group, *n* (%)	147 (3.2)	18 (0.4)	285 (11.6)	15 (0.6)	21 (0.9)	5 (0.3)	1 (0.1)
Sites in control group, *n* (%)	21 (1.3)	3 (0.2)	44 (5.3)	0 (0)	0 (0)	1 (0.2)	0 (0)
P-values	<0.0005	0.183	<0.0005	0.013	0.002	0.529	0.747

TABLE 3 Distribution of PDUS findings in psoriatic patients and controls at the studied sites

PDUS findings	Sites in psoriasis group, *n* (%)	Sites in control group, *n* (%)	*P*-values
Wrist synovitis	28 (10.3)	7 (7.6)	0.281
Wrist synovial PD signal	8 (3)	2 (2.2)	0.512
MCP synovitis	27 (2)	3 (0.7)	0.034
MCP synovial PD signal	3 (0.2)	0 (0)	0.417
PIP synovitis	17 (1.3)	1 (0.2)	0.036
PIP synovial PD signal	1 (0.1)	0 (0)	0.747
DIP synovitis	8 (0.7)	1 (0.3)	0.293
DIP synovial PD signal	0 (0)	0 (0)	NA
Knee synovitis	64 (23.5)	9 (9.8)	0.002
Knee synovial PD signal	6 (2.2)	1 (1.1)	0.436
TT synovitis	3 (1.1)	0 (0)	0.416
TT synovial PD signal	0 (0)	0 (0)	NA
PPT enthesopathy	41 (15.1)	2 (2.2)	<0.0005
PPT entheseal PD signal	2 (0.7)	0 (0)	0.561
PPT perientheseal PD signal	2 (0.7)	0 (0)	0.558
DPT enthesopathy	46 (16.9)	6 (6.5)	0.008
DPT entheseal PD signal	3 (1.1)	0 (0)	0.415
DPT perientheseal PD signal	4 (1.5)	0 (0)	0.310
ACHT enthesopathy	114 (41.9)	17 (18.5)	<0.0005
ACHT entheseal PD signal	8 (2.9)	0 (0)	0.097
ACHT perientheseal PD signal	11 (4)	0 (0)	0.038
PF enthesopathy	52 (19.1)	7 (7.6)	0.005
PF entheseal PD signal	1 (0.4)	0 (0)	0.747
PF perientheseal PD signal	3 (1.1)	0 (0)	0.416
DFT enthesopathy	32 (2.4)	12 (2.6)	0.436
DFT entheseal PD signal	1 (0.1)	0 (0)	0.749
DFT perientheseal PD signal	1 (0.1)	0 (0)	0.747
ET tenosynovitis	1 (0.4)	0 (0)	0.747
ET tenosynovial PD signal	1 (0.4)	0 (0)	0.747
FFT tenosynovitis	4 (0.3)	1 (0.2)	0.629
FFT tenosynovial PD signal	0 (0)	0 (0)	NA

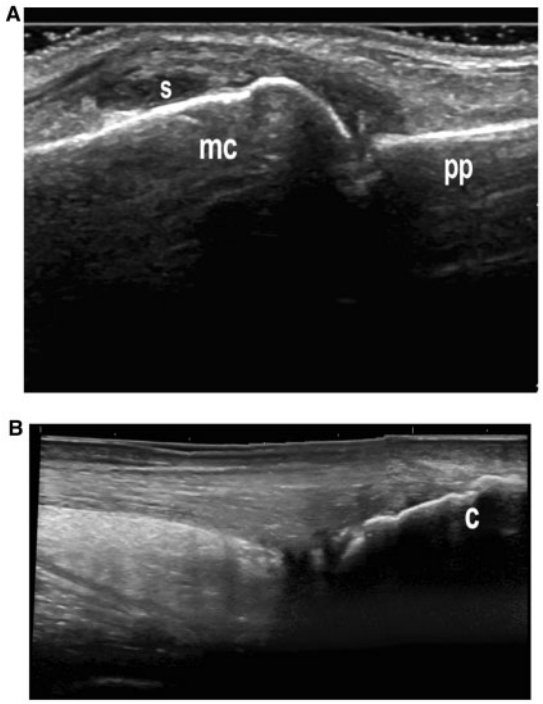
TT: tibiotalar; PPT: proximal patellar tendon; DPT: distal patellar tendon; ACHT: Achilles tendon; PF: plantar fascia; DFT: deep flexor tendon of the fingers; ET: extensor tendon compartments at the wrist; FFT: finger flexor tendons; NA: not applicable.

independence test and a Breslow homogeneity test to control for the effect of sex distribution between psoriasis and control groups. There was still a significant association between the presence of synovitis and enthesopathy and the psoriasis group ($P = 0.048$ and 0.028, respectively). There was no significant association between psoriatic nail involvement and PDUS findings in either the DIP joints of the hands or the deep flexor tendons of the fingers ($P > 0.05$).

Comparison between psoriatic patients with and without PDUS abnormalities

We analysed the demographic and clinical data in patients with and without PDUS findings. There were no significant

FIG. 1 (**A**) Longitudinal ultrasonographic image of the dorsal aspect of an MCP joint that shows synovitis (s). (**B**) Longitudinal ultrasonographic image of the Achilles tendon enthesis at the superior pole of the calcaneous (c). The enthesis shows abnormal thickening, hypoechogenicity and bone proliferation. mc: metacarpal bone; pp: proximal phalanx.



differences in either the mean PASI score or the mean BSA involvement between psoriatic patients who had synovitis ($P = 0.792$ and $P = 0.490$, respectively), synovial PD signal ($P = 0.412$ and 0.437, respectively), enthesopathy ($P = 0.991$ and 0.639, respectively), intra-entheseal PD signal ($P = 0.302$ and 0.328, respectively), perientheseal PD signal ($P = 0.731$ and 0.742, respectively) or tenosynovial PD signal ($P = 0.731$ and 0.742, respectively) and those who did not have these PDUS findings. Patients with tenosynovitis (five patients) had a mean PASI score [12.08 (6.04)] significantly higher than patients without tenosynovitis [6.38 (5.96)] ($P = 0.029$). However, patients with tenosynovitis showed a similar BSA involvement [12.8 (6.83)] to patients without tenosynovitis [9.40 (12.27)] ($P = 0.08$).

There were no significant differences between psoriatic patients with and without PDUS joint synovitis in the following: age, sex distribution, disease duration, PASI score, BSA involvement, occupational musculoskeletal demand, sport activity, tender joints, swollen joints, joints with movement pain or restricted motion, MASES, positive SI joint manoeuvres, spinal movement pain or restricted motion, positive RF, CCP and HLA-B27, and mean ESR and CRP (Table 4).

The mean age was significantly higher in psoriatic patients who showed PDUS enthesopathy [46.7 (15.5) years] than in psoriatic patients without this finding [35.8 (13.8) years] ($P < 0.0005$) (Table 4). There were no significant differences between psoriatic patients with and without PDUS enthesopathy in the other demographic, dermatological, rheumatological and laboratory data (Table 4).

Predictor factors of PDUS abnormalities in psoriatic patients

Independent of the method used for variable selection in the logistic regression analysis, having psoriasis was the only significant predictive variable for the presence of synovitis [odds ratio (OR) 2.13; 95% CI 1.06, 4.29; $P = 0.035$], enthesopathy (OR 2.59; 95% CI 1.31, 5.15; $P = 0.007$) and PDUS abnormalities (OR 2.36; 95% CI 1.16, 4.81; $P = 0.018$). No other regressor variable showed predictive value for synovitis, enthesopathy or any PDUS abnormality. The same results were obtained with forward and backward procedures.

Discussion

Chronic inflammation in psoriatic skin and PsA joints and entheses shares common cellular and vascular immunopathological features (i.e. characteristic lymphocyte infiltrate and angiogenesis) [38]. Over the past decade, there has been an increasing number of studies on the validity of US with Doppler technique in the evaluation of synovitis [15, 24–28] and enthesitis [39, 40] in inflammatory arthritis. As in RA, musculoskeletal US is playing an increasingly important role in the assessment of PsA because of its capability to detect subclinical synovitis [7, 12–14] and enthesitis [7, 17–19].

To the best of our knowledge, this is the first study that has comprehensively evaluated PDUS involvement of joints, tendons and entheses using agreed definitions for US pathology in a large population of psoriatic patients without musculoskeletal diseases. We recorded and analysed a considerable amount of demographic and clinical data that could have an effect on the presence of PDUS abnormalities. Using PDUS, we assessed those joints, tendons and entheses frequently involved in PsA according to previously published studies [7, 12, 14, 18, 41–43]. We excluded the palmar aspect of the finger joints and the MTP joints from the PDUS evaluation because, although they are very sensitive to US imaging in arthritis, a high frequency of synovitis has also been reported at these locations in normal subjects [13, 44]. We used agreed definitions for pathology in order to assess PDUS abnormalities at each examined site more reliably.

We found PDUS synovitis and enthesopathy in a high percentage of psoriatic patients and psoriatic sites. The prevalence of asymptomatic PDUS synovitis and enthesopathy was significantly higher in psoriatic patients than in controls. In addition, there was a significantly higher percentage of psoriatic patients who showed both the abnormalities than controls. Above all, it was significant that among the demographic and clinical variables, the only predictor factor of the presence of the above findings

TABLE 4 Demographic, rheumatological and dermatological data in psoriatic patients with and without US synovitis and enthesopathy

Clinical data	Psoriasis patients			Psoriasis patients		
	With US synovitis ($n = 69$)	Without US synovitis ($n = 67$)	*P*-values	With US enthesopathy ($n = 85$)	Without US enthesopathy ($n = 51$)	*P*-values
Age, mean (S.D.), years	44.20 (16.52)	40.95 (14.84)	0.229	46.7 (15.5)	35.8 (13.8)	<0.0005
Sex, *n* (%)			0.380			0.277
Men	41 (59.4)	34 (50.7)		50 (58.8)	25 (49)	
Women	28 (40.6)	33 (49.3)		35 (41.2)	26 (51)	
Disease duration, mean (S.D.), years	13.2 (11.7)	12.4 (11.1)	0.926	13.9 (11.5)	11.6 (11.2)	0.475
PASI score, mean (S.D.)	6.5 (6.9)	6.8 (5.1)	0.792	6.6 (5.8)	6.6 (6.5)	0.991
BSA, mean (S.D.), %	8.5 (10.7)	9.9 (12.3)	0.49	8.8 (10.6)	9.8 (13)	0.639
Occupational demand, *n* (%)			0.449			0.596
Low	35 (50.7)	41 (61.2)		46 (54.1)	30 (58.8)	
Moderate	19 (27.5)	13 (19.4)		20 (23.5)	12 (23.5)	
High	15 (21.7)	13 (19.4)		19 (22.3)	9 (17.6)	
Sport activity, *n* (%)			0.904			0.664
No	44 (63.8)	41 (61.2)		55 (64.7)	30 (58.8)	
Low	19 (27.5)	21 (31.3)		23 (27.1)	17 (33.3)	
High	6 (8.7)	5 (7.5)		7 (8.2)	4 (7.8)	
TJC > 0, *n* (%)	11 (15.9)	9 (13.4)	0.809	14 (16.5)	6 (11.8)	0.618
SJC > 0, *n* (%)	1 (1.4)	3 (4.5)	0.619	3 (3.5)	1 (2)	1
JC for MP/RM > 0, *n* (%)	8 (11.6)	6 (9)	0.779	10 (11.8)	4 (7.8)	0.568
MASES > 0, *n* (%)	5 (7.2)	3 (4.5)	0.717	7 (8.2)	1 (2)	0.140
Positive SI joint manoeuvres, *n* (%)	1 (1.4)	1 (1.5)	1	1 (1.2)	1 (2)	1
Cervical MP/RM, *n* (%)	10 (14.5)	7 (10.4)	0.208	9 (10.6)	8 (15.7)	0.472
Lumbar MP/RM, *n* (%)	12 (17.4)	9 (13.4)	0.427	14 (16.5)	7 (13.7)	0.441
Positive RF, *n* (%)	3 (4.3)	1 (1.5)	0.324	4 (4.7)	0 (0)	0.297
Positive CCP, *n* (%)	3 (4.3)	0 (0)	0.245	3 (3.5)	0 (0)	0.292
Positive HLA-B27, *n* (%)	3 (4.3)	5 (7.5)	0.716	5 (5.9)	3 (5.9)	1
ESR, mean (S.D.), mm/h	13.1 (11.2)	12.3 (10.5)	0.696	13.2 (12.1)	11.8 (8.2)	0.470
CRP, mean (S.D.), mg/l	1.4 (1.9)	1.9 (2.7)	0.335	1.6 (2.6)	1.7 (1.9)	0.802

TJC: tender joint count; SJC: swollen joint count; JC: joint count; MP/RM: movement pain or restricted motion.

was having psoriasis. Interestingly, entheseal PD signal was only found in psoriatic patients. The presence of PD signal at entheses has not been found in healthy controls [45] and has been shown to be specific for peripheral enthesitis in spondyloarthritis [18].

Our results were in accordance with those of previous studies that assessed either joint or entheseal imaging abnormalities in smaller populations of psoriatic patients without musculoskeletal involvement [19, 29–32]. Offidani *et al*. [29] evaluated with MRI the hand joints of 25 psoriatic patients and 12 healthy controls. Sixty-eight per cent of the psoriatic patients showed capsular distension and/or joint effusion, while only one control showed any joint abnormality. Özçakar *et al*. [30] reported a significantly higher mean thickness of the Achilles tendon measured by US in 30 psoriatic patients than in 20 healthy controls. De Filippis *et al*. [19] described that 6 (25%) of 24 patients with psoriasis showed asymptomatic US abnormalities in hand entheses and tendons. Gisondi *et al.* [31] studied US entheseal abnormalities in the lower limbs of 30 psoriatic patients without articular involvement and 30 controls. In the latter study, entheseal structure and thickness, the presence of bony erosions, enthesophytes and bursitis were assessed using the Glasgow Ultrasound Enthesitis Scoring System (GUESS), which was described by Balint *et al*. [17]. Gisondi *et al*. [31] found a significantly higher mean GUESS score in psoriatic patients as compared with controls. Gutierrez *et al*. [32] found significantly more US signs of enthesopathy and higher GUESS score in the lower limbs of 45 psoriatic patients as compared with 45 healthy controls. In agreement with our findings, these latter authors detected entheseal PD signal only in psoriatic patients in a similar percentage (0.9%). The percentages of entheses with at least one US sign of enthesopathy in psoriatic patients (32.9%) and controls (8.4%) were higher than in our population. Different definitions of enthesopathy were possibly the reason for this discrepancy.

Consistent with the findings of previous studies [29, 31, 32], we did not find an association between most PDUS abnormalities and psoriasis severity, psoriasis duration or psoriatic nail involvement. Only the presence of

tenosynovitis was associated with a higher PASI score. Due to the small number of patients with tenosynovitis, this finding should be considered with caution. In accordance with Gisondi *et al*. [31], the presence of enthesopathy was associated with a higher age in psoriatic patients.

Some limitations in our study should be noted. Although psoriatic plaques could have interfered with the blinding of the PDUS examinations, we made every effort to minimize the possibility of bias in the study results. Psoriatic patients and controls were not matched for sex distribution. However, after correcting for this factor, there was still a significant association between the presence of US synovitis and enthesopathy and having psoriasis. In addition, in the logistic regression analysis, sex distribution did not have predictive value for the presence of the above PDUS abnormalities.

As previously reported [46], the prevalence of hyperlipidaemia was higher in our psoriatic population than in controls. Entheseal abnormalities, mainly tendon thickening, have been reported in hypercholesterolaemic patients [47]. However, further analyses excluded this factor as a predictor of PDUS enthesopathy in our study.

Although we did not assess inter-observer reliability, the ultrasonographer investigators had an extensive common training in muskuloskeletal US focused on joint and entheseal PDUS abnormal findings. They had demonstrated good inter-observer reliability for assessing synovitis and enthesopathy in previous studies [28, 35]. In addition, we used a dichotomous scoring system in order to reduce inter-observer variability.

In conclusion, our results suggest that psoriasis is associated with a relevant prevalence of asymptomatic PDUS synovitis and enthesopathy. Future longitudinal studies should consider whether these PDUS findings have predictive value in developing PsA.

Rheumatology key messages

- Psoriatic patients showed a significantly higher prevalence of asymptomatic ultrasonographic synovitis and enthesopathy than controls.
- A subclinical musculoskeletal involvement may exist in psoriatic patients.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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Appendix 1

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