
Ultrasonography Enthesitis and Synovitis Screening in Psoriatic Patients: A Case Control Study

Soumaya Boussaid, Rania Ben Aissa, Sonia Rekik, Safa Rahmouni, Samia Jammali, Khaoula Zouaoui, Hela Sahli, Mohamed Elleuch

Mediterr J Rheumatol 2023;34(4):495-505



E-ISSN: 2529-198X



Ultrasonography Enthesitis and Synovitis Screening in Psoriatic Patients: A Case Control Study

Soumaya Boussaid^{1,2,3} , Rania Ben Aissa^{1,2}, Sonia Rekik^{1,2,3}, Safa Rahmouni^{1,2,3}, Samia Jammali^{1,2,3}, Khaoula Zouaoui^{1,2,3}, Hela Sahli^{1,2,3}, Mohamed Elleuch^{1,2}

¹Rheumatology Department, Rabta Hospital, Tunis, Tunisia, ²Faculty of Medicine of Tunis, University Tunis el Manar, Tunis, Tunisia, ³Research Unit LR 05 SP 01, La Rabta Hospital, Tunis, Tunisia

ABSTRACT

Background: The clinical screening of enthesitis and synovitis in patients with psoriasis lacks specificity and sensitivity during the preclinical phase. **Aims:** to assess US subclinical synovitis and enthesitis in psoriatic patients compared with healthy controls. **Methods:** A cross-sectional study on 40 psoriatic patients and 40 healthy sex- and age-matched controls. US examination of 18 joints was performed along with 22 enthesal sites on the upper and lower limbs. US subscores were established according to the US abnormalities: inflammatory score (tendon thickening, hypoechogenicity, bursitis, Doppler signal), damage score (calcification, enthesophytes, bone erosion) and total score (the sum of inflammatory and damage scores). **Results:** US synovitis were more frequent in psoriatic patients (0.68%) than in controls (0.29%), but the difference was not significant. Patients with psoriasis had more US enthesitis (92,5%) compared to controls (40%)($p < 0.001$). The total number of enthesitis was higher in the psoriatic group (20.90%) compared to controls (4,78%)($p < 0.001$). There were more US abnormalities in the psoriatic group compared to controls for calcaneal tendon enthesitis($p < 0.001$), distal patellar tendon enthesitis($p < 0.001$) and deep flexor tendons of the finger enthesitis($p < 0.001$). Compared to controls, psoriatic patients had a significantly higher inflammatory score (Mean \pm SD) (2.85 \pm 3.34 versus 0.58 \pm 1.17), damage score (3 \pm 2.57 versus 0.60 \pm 1.41), and total score (5.85 \pm 5.20 versus 1.18 \pm 2.07) ($p < 0.001$ each). Patients with scalp psoriasis had more US enthesitis ($p = 0.020$). **Conclusion:** Our results indicate that US enthesitis and synovitis are more frequent in patients with psoriasis. Prospective studies with larger sample size are needed to define the contribution of US in predicting the clinical onset of PsA.

Mediterr J Rheumatol 2023;34(4):495-505

<https://doi.org/10.31138/mjr.180923.ues>

Article Submitted: 09 Aug 2022; Article Accepted: 16 Aug 2022; Available Online: 18 Sep 2023

Corresponding Author:

Soumaya Boussaid
Assistant Professor
University Hospital Assistant,
Rheumatology Department
La Rabta Hospital 1007, Tunis, Tunisia
Tel.: +216 97 32 87 91
E-Mail: soumayaboussaid@hotmail.com

Keywords: psoriasis, psoriatic arthritis, ultrasonography

HIGHLIGHTS

- Ultrasound enthesitis and synovitis are more frequent in patients with psoriasis.
- Patients with scalp psoriasis had

- more ultrasound enthesitis.
- There are more ultrasound abnormalities in the enthesitis of the fingers deep flexor tendon in patients with psoriasis.

INTRODUCTION

Psoriasis is a common chronic inflammatory skin disease affecting between 0.5 and 11.43% of the general population.¹ Among psoriasis patients, up to 30% may develop Psoriatic arthritis (PsA).² PsA could evolve into a destructive and disabling form,³ and its clinical aspects include skin, nails, enthesitis, and joint involvement.⁴ Psoriasis precedes most often rheumatic manifestations by 7 to 12 years.⁵ The progression of inflammation from integument components to the synovial tissue and enthesitis during this interval is an opportunity to screen for subclinical lesions related to the development of PsA.⁶ The classification criteria for Psoriatic Arthritis (CASPAR)⁷ are based on clinical, biological, and radiographic criteria. It is the most used classification for PsA diagnosis, but its sensitivity in the detection of early PsA remains limited.⁷⁻⁹ Enthesitis is one of the major features of PsA. Clinical screening of enthesitis and synovitis remains difficult due to the proximity of the various joint structures that could be affected (known as the synovio-entheseal complex).¹⁰⁻¹² Several clinical scores were developed for the evaluation of enthesitis in PsA but are still insufficient to detect enthesitis in comparison with imaging techniques.¹³ Standard radiography, ultrasound (US), and magnetic resonance imaging (MRI) are used for different stages of PsA evolution. Several studies in psoriasis patients without clinical articular manifestations suggest the role of US in screening for synovitis and/or enthesitis at a subclinical stage long before developing PsA.^{12,14,15} US detects more subclinical enthesitis (74%) than clinical examination (46%) and standard radiographs (26%).¹⁶ We conducted this study aiming to evaluate the prevalence of subclinical enthesitis and synovitis in psoriatic patients free from clinical arthritis or enthesitis compared with controls. Our second end point was to study the possible relationships of US findings with psoriasis characteristics such as phenotype, disease duration, severity, and current treatment.

METHODS

Study design

We conducted a monocentre case-control study between August 2020 and March 2021. The study was approved by the local Ethics Committee of the Hospital (approval CEBM.EPS.HR/30/2021). All participants signed an informed consent form.

Study population

The study was conducted on patients with a diagnosis of psoriasis confirmed after clinical examination by a dermatologist and referred by the dermatology department. They were compared with 40 controls (without any inflammatory rheumatism or inflammatory pathology that can affect the entheses), sex and age-matched recruited from hospital workers and their relatives. The inclusion

criteria were: age > 18 years and patients with psoriasis. The exclusion criteria were as follows: any history of inflammatory rheumatic, or crystal arthritis, fulfillment of the PsA CASPAR criteria, recent trauma, orthopedic surgery, amputation, or corticosteroid injection of the examined structures, or any biologic disease-modifying antirheumatic drugs (DMARDs) for psoriasis in the previous 3 months before the beginning of the study.

To determine the sample size, we were based on a rate of synovitis and enthesitis in psoriatic patients of 3.2% and 11.6%, respectively,¹⁷ an error of 5%, and an accuracy of 7%. Thus, the number of subjects needed for a descriptive study would be 25 for synovitis and 40 for enthesitis. We selected 40 patients during the study period. Selection criteria are shown in **Figure 1**.

Clinical evaluation and assessment

For each patient, we assessed: demographic characteristics, body mass index (BMI), current treatment for psoriasis, and sports activity within the last 2 weeks. We used the Arabic version of IPAQ-SF¹⁸ for all participants. We examined the joints using the 66/68 joint count for swelling (S_{JN}) and tenderness (T_{JC}).¹⁹ For the enthesitis examination, we used two scores: the Leeds Enthesitis Index (LEI) and the Spondyloarthritis Research Consortium of Canada (SPARCC).^{20,21} Patients and

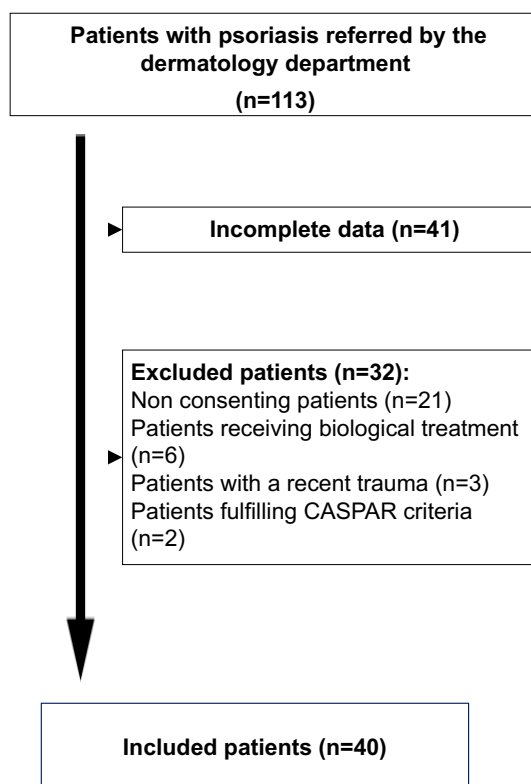


Figure 1. Flowchart of patient inclusion

controls were examined by a rheumatologist blinded to the US data.

The severity of psoriasis was assessed by a dermatologist who scored the Body Surface Area (BSA) (severe > 10%, 3% < moderate < 10%, < 3% mild), the psoriasis area severity index (PASI) score,²² and the Nail Psoriasis Severity Index (NAPSI)²³ if a psoriasis nail involvement was documented.

Laboratory Measurement of C-reactive protein (CRP) was done using the enzyme-linked immunosorbent assay (ELISA) technique, which was considered positive if > 6 mg/l. The clinical and biological assessment was evaluated on the same day of the US examination.

US protocol and acquisition

US examinations were performed at the Rheumatology Department of the Rabta Hospital using a Mylab Gamma (Esoate) equipped with a 6- to 18-MHz broadband linear transducer by an expert US rheumatologist in musculoskeletal US imaging blinded of the clinical assessment findings. Grayscale (GSUS) and power Doppler (PDUS) at i) joints (bilateral wrist, metacarpophalangeal (MCP), proximal interphalangeal [PIP]), and ii) entheses sites (deep digital flexor entheses (from 2nd to 5th finger), lateral epicondyles, triceps tendon insertion into the olecranon tuberosity, proximal, and distal patellar tendons, calcaneal tendon, and plantar fascia) were performed.

Each joint was scanned in transverse and longitudinal planes. GSUS synovitis was defined as the presence of an abnormal hypoechoic intra-articular area with synovial effusion and/or synovial thickening, which may exhibit PDUS signals.

Enthesitis was defined according to the OMERACT when we found: abnormal hypoechoic tendon insertion, enthesal thickness of the tendon, bursitis, calcification, enthesophytes, bone erosion, or PDUS signals found within 2 mm of the bony cortex.²⁴ The Madrid Sonographic Enthesitis Index (MASEI) score was used as a reference to the normal value of thickness of the lower limb and triceps insertion entheses,²⁵ for the common extensor tendon insertion on the lateral epicondyle, the cutoff established by Lee et al. was used.²⁶

US findings interpretation

US findings interpretations for both GSUS and PDUS synovitis were graded on a qualitative scale (0= absence, 1=presence).

Subscores for the US entheses examination were elaborated:

- The damage score has been defined for structural abnormalities (calcification, enthesophytes, bone erosion)
- The inflammatory score has been defined for inflammatory abnormalities (tendon thickening, entheses hypoechoic, bursitis, PDUS signals within 2 mm of the bony cortex).

- The total score was obtained by summing the damage and inflammatory score values.

Power Doppler settings were standardized with a Doppler frequency of 8–10 MHz and a pulse repetition frequency of 750 Hz. The color gain was adjusted just lower to the level that causes the appearance of noise artifacts

Data analysis

The descriptive study included calculation of means±standard deviation(SD), (minimum and maximum) and medians (interquartile range [IQR]) for quantitative variables with normal and nonnormal distribution, respectively; and absolute frequencies and percentages for categorical variables. Student's t-test or Mann-Whitney test were used to compare independent means (eg, US scores, SJC, TJC, BMI, SPARCC, LEI) of psoriasis and control groups. Relationships between categorical variables were evaluated by chi-squared test. One-way analysis of variance (ANOVA) was used to compare quantitative data of three groups or more (eg, psoriasis clinical form, current treatment, sports activity). Correlations between quantitative variables (eg, disease duration and total score) were analysed using Spearman's rank correlation coefficient. The study data were entered and analysed using Statistical Package for Social Sciences (SPSS) version 22 software. Throughout the statistical study, the significance level (p) was set at 0.05.

RESULTS

Clinical and US findings

A total of 40 patients with psoriasis and 40 sex- and age-matched controls were enrolled. The characteristics of the study population are shown in **Table 1**. Patients and controls were similar regarding their mean age, sex distribution, BMI, sports activity, and clinical findings (SJC, TJC, LEI, and SPARCC).

The mean disease duration was 16.86±16.04 years [1-57], the mean PASI score was 10.48±10.43 [0-44]. Clinical forms of psoriasis were: plaque psoriasis in 90% of cases, guttate psoriasis in 5% of cases, and pustular psoriasis in 5% of cases. Nail involvement was found in 14 patients (35%) and scalp psoriasis in 15 (37.5%). The mean NAPSI score was 6.08±8.85 [4-22]. The BSA indicated severe psoriasis in 17 patients (42.5%), moderate in 19 (47.5%), and mild in four patients (10%). Patients had a statistically significant higher CRP level than controls, but the value was low in both groups (median value 2.05 mg/l [0.07-7] versus 1mg/l [0-2.95], p= 0.037).

At inclusion, 24 (60%) patients were receiving topical steroids, 14 (35%) were receiving methotrexate (MTX) (mean dose 14.33±2.58mg/week [10-20] and mean duration 40.41±12.74 months [0.16-336]), four patients were receiving aciclovir and six were on phototherapy.

Among the 1040 scanned joints in each group, subclinical synovitis was found in seven joints in psoriasis

Table 1. Demographic, clinical data, and rheumatological findings in psoriasis group and controls.

Parameters	Unit/category	Psoriasis group (n=40)	Control group (n=40)	P-value*
Age	Years	51.9±15.90	52.3±14.83	0.905
Sex	Female	16 (40)	16 (40)	1
	Male	24 (60)	24 (60)	
Smokers	Yes	14 (35)	7 (17.5)	0.077
BMI	Kg /m ²	27.14±5.55	27.21±4.78	0.506
Diabetes mellitus	Yes	6 (15)	8 (20)	0.562
Hypertension	Yes	13 (32.5)	7 (17.5)	0.124
Hyperlipidaemia	Yes	9 (22.5)	5 (12.5)	0.245
Physical activity	Inactive	8 (20)	26 (65)	0.175
	Minimally Active	22 (55)	10 (25)	
	Active	10 (25)	4 (10)	
TJC	>0	10 (25)	14 (35)	0.702
TJC		0 (0-1)	0 (0-1)	0.390
SJC >0	>0	2 (5)	1 (2.5)	0.816
SJC		0 (0-0)	0 (0-0)	0.320
LEI		0 (0-2)	1 (0-2)	0.804
SPARCC		1 (0-4)	2 (0-4)	0.872
CRP	mg/l	2.05 (0.07-7)	1 (0-2.95)	0.037

BMI: Body Mass Index; TJC: Tender joint count; SJC: swollen joint count; LEI: Leeds Enthesitis Index; SPRACC: Spondyloarthritis Research Consortium of Canada; CRP: C-reactive protein.

Quantitative data were mean±SD or median (IQR). Categorical data were number (%).

* p-values <0.05 (Student's t-test or Mann-Whitney test or chi-squared test).

patients (0.68%) (2 wrists, 5 MCP) and 3 joints in controls (0.29%) (3 MCP) ($p=0.420$) (**Table 2**). No PDUS signal was found in the psoriasis group, whereas one MCP in controls showed power Doppler activity.

Almost 880 entheses had been scanned in each group. In psoriasis patients, the US showed at least one sign of enthesitis in 184 enthesal sites (20.90%) (**Table 2**). The calcaneal enthesitis was the one with the highest number of enthesitis signs (47.5%), followed by distal patellar enthesitis (41.25%), lateral epicondyle enthesitis (32.5%), plantar aponeurosis enthesitis (28.75%), the proximal patellar enthesitis (25%), and the deep digital flexor enthesitis (5.94%) (**Table 2**).

The most frequent elementary lesion was enthesal thickening ($n=70/880$), followed by enthesophytes ($n=60/880$), bone erosion ($n=54/880$), enthesitis hypoechogenicity ($n=21/880$), and enthesitis calcification ($n=10/880$) respectively. Different ultrasonographic pathological findings in our patients are illustrated in **Figure 2**.

In the control population, the US found at least one sign of enthesitis in 42 of the 880 (4.78%) enthesal sites ($P<0.001$). In this group, the enthesal site with the

highest number of US signs of enthesitis was the calcaneal enthesitis (10/80) (12.5%) and the lateral epicondyle enthesitis (10/80) (12.5%).

The mean inflammatory score, damage score, and total score values were significantly higher in patients rather than in controls ($P < 0.001$ each) (**Table 2**).

Correlation between US findings, clinical features, and disease characteristics of psoriasis patients

The age was fairly correlated with: the number of US enthesitis per patient ($r=0.523$, $p=0.001$), the inflammatory score, damage score, and total score ($r=0.399$, $p=0.011$; $r=0.442$, $p=0.004$; $r=0.475$, $p=0.002$ respectively).

No statistically significant association was found between US enthesitis findings (number of enthesitis per patient, scores) and psoriasis duration, PASI, NAPS, BMI, and sports activities. The BSA was correlated with the inflammatory score, but with no statistical significance ($p=0.067$). Scalp psoriasis was correlated with a higher number of US enthesitis per patient ($p=0.020$).

A statistically significant correlation was found between the number of US enthesitis per patient, and LEI and

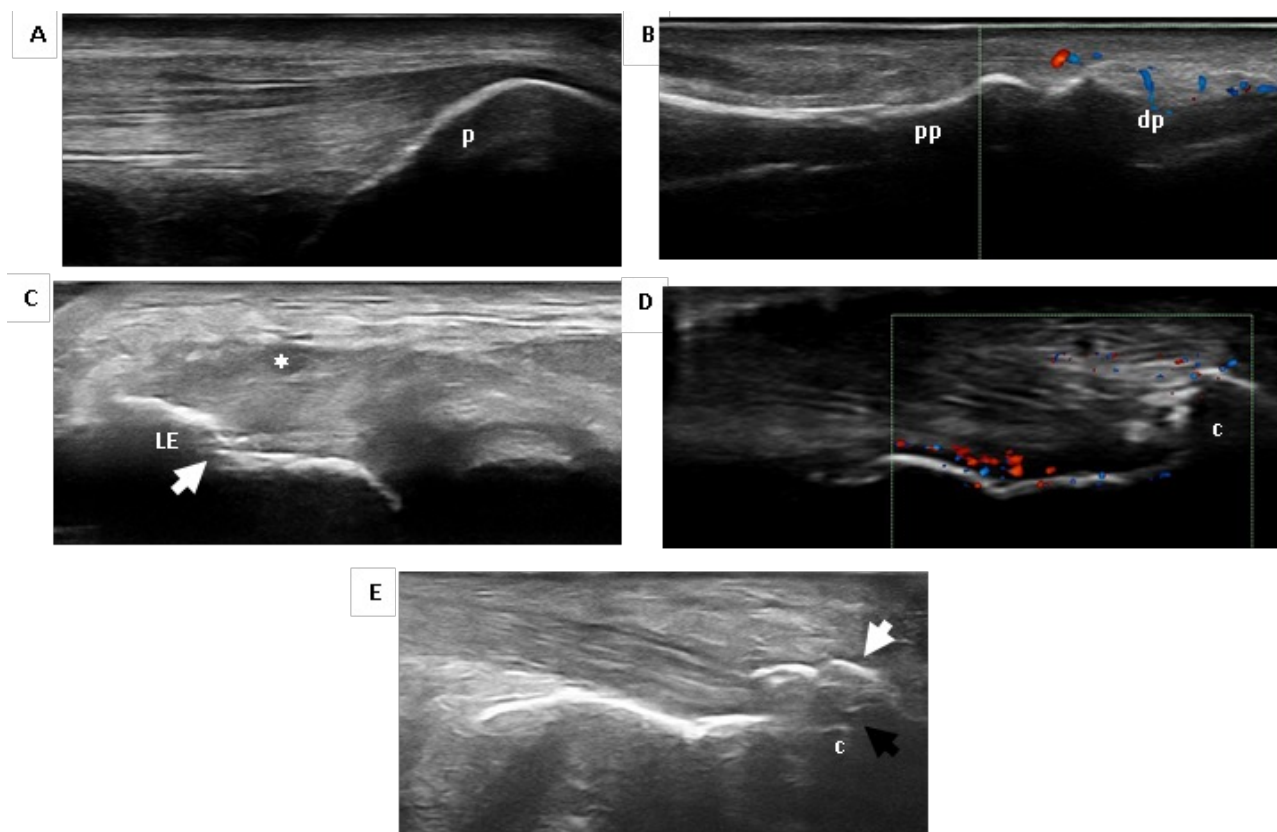


Figure 2. (A) Longitudinal ultrasonographic image of the quadriceps tendon shows a normal aspect of the enthesis. (B) Longitudinal ultrasonographic image of the deep flexor tendon of the 3rd finger shows power Doppler signal. (C) Longitudinal ultrasonographic image of the common extensor tendon insertion shows bone erosions (white arrow) abnormal thickening and hypoechogenicity (asterisk). (D) Longitudinal ultrasonographic image of the calcaneal tendon shows power Doppler signal. (E) Longitudinal ultrasonographic image of the calcaneal tendon shows enthesophyte (white arrow) and bone erosion (black arrow). p: patella ; md: medial phalange; dp: distal phalange; LE: lateral epicondyle; c: calcaneus.

SPARCC scores ($r=0.317$; $p=0.046$, $r=0.424$; $p=0.006$, respectively). The SPARCC score was more correlated than LEI with inflammatory score, damage score, and total score (**Table 3**). Both LEI and SPARCC were correlated with the PDUS findings ($r=0.470$; $p=0.001$, $r=0.437$; $p=0.002$, respectively) (**Table 3**).

Dealing with the influence of current treatment for psoriasis, there was no significant difference between the US scores of patients receiving MTX and those receiving other treatments (topical steroids, systemic retinoids). However, the dose of MTX was inversely correlated with the damage score ($r=-0.445$, $p=0.169$), unlike the total duration of MTX intake, which was not correlated with the different US scores.

DISCUSSION

Enthesitis is one of the hallmarks of Spondyloarthritis (SpA) including PsA.¹⁵ The high-resolution US combined with the Doppler technique has been studied over the

past two decades to show its validity in revealing subclinical synovitis and enthesitis in inflammatory arthritis.^{27,28} In this study, we aimed to detect subclinical synovitis and enthesitis using the GSUS and PDUS scores in psoriasis patients compared with controls. We blindly investigated almost all relevant joints and entheses. We also studied the deep flexor tendon enthesis of the fingers which is rarely scanned in this context, and this is the major strength of our study. Our findings showed that US enthesitis and synovitis are more frequent in patients with psoriasis.

The US role in the detection of enthesitis has been demonstrated in patients with SpA first by D'Agostino.²⁹ Lately, several US scores have been established for the assessment of US enthesitis in patients with PsA, interesting lower limb (GUESS),³⁰ or both lower and upper limbs (MASEI).²⁵ Currently, the GRAPPA has initiated a workgroup in order to develop a diagnostic US tool for enthesitis: the DUET.³¹

Table 2. Distribution of US findings in psoriatic patients and controls.

Studied structures/US score	Psoriasis group	Controls	P-value*
Presence of US synovitis			
Total synovitis			
Per patient	7/40 (17.5)	3/40 (7.5)	0.487
Per joint	7/1040 (0.68)	3/1040 (0.29)	0.420
Wrist synovitis			
GSUS	2 (5)	0 (0)	0.156
PDUS	0 (0)	0 (0)	NA
MCP synovitis			
GSUS	5 (12.5)	3 (7.5)	0.462
PDUS	0 (0)	1 (2.5)	0.320
IPP synovitis			
GSUS	0 (0)	0 (0)	NA
PSUS	0 (0)	0 (0)	NA
Presence of US enthesitis			
Per patient	37/40 (92.5)	16/40 (40)	<0.001
Per enthesial site	184/880 (20.90)	42/880 (4.78)	<0.001
Abnormal entheses			
Deep digital flexor	19/320 (5.94)	1/320 (1.25)	< 0.001
Common tensor tendon	26/80 (32.5)	10/80 (12.5)	0.011
Brachial triceps	8/80 (10)	3/80 (3.75)	0.145
Quadriceps	17/80 (21.25)	6/80 (7.5)	0.040
Proximal patellar tendon	20/80 (25)	3/80 (3.75)	0.001
Distal patellar tendon	33/80 (41.25)	4/80 (5)	<0.001
Calcaneal tendon	38/80 (47.5)	10/80 (12.5)	<0.001
Plantar fascia	23/80 (28.75)	7/80 (8.75)	0.007
US scores			
Inflammatory score	2.85 ±3.34	0.58 ±1.17	< 0.001
Damage score	3 ±2.57	0.60 ±1.41	< 0.001
Total score	5.85 ±5.20	1.18 ±2.07	< 0.001

US: ultrasonography, MCP: metacarpophalangeal, GSUS: Grayscale, PDUS: power Doppler, IPP: proximal interphalangeal, NA: not applicable.

Quantitative data were mean ±SD. Categorical data were number (%).

* p-values <0.05 (Student's t-test or chi-squared test).

Table 3. Correlations of number of US enthesitis per patient and US scores and abnormalities with LEI and SPARCC.

	LEI		SPARCC	
	r	p	r	p
US enthesitis per patient	0.317	0.046	0.424	0.006
US scores				
Inflammatory score	0.239	0.138	0.407	0.009
Damage score	0.293	0.066	0.356	0.024
Total score	0.298	0.061	0.435	0.005
US abnormality				
Hypoechogenicity	0.194	0.115	0.357	0.015
Tendon-thickening	0.256	0.055	0.394	0.006
Enthesophytes	0.388	0.007	0.410	0.004
Bone erosion	0.071	0.331	0.184	0.127
Calcification	0.076	0.321	0.051	0.378
PDUS signal	0.470	0.001	0.437	0.002

LEI: Leeds Enthesitis Index, SPARCC: Spondyloarthritis Research Consortium of Canada, US: ultrasonography, PDUS: power Doppler.

"Pearson r": ^a"fair" if it was between 0.30-0.50; and ^b"weak or no association" if it was < 0.30.

Our results were in accordance with those of previous studies that assessed enthesial US abnormalities in larger populations of psoriatic patients without musculoskeletal involvement [16;31-35]. According to the US score, the studies were interested in the enthesitis of the lower limb or both lower and upper limbs. In our study, we assessed the enthesitis of both the lower and upper limbs. Most studies had concluded that subclinical US enthesitis was more frequent in patients with psoriasis compared to controls by using different US scores (**Table 4**). The prevalence of US enthesitis in our patients (20.9% among the examined entheses) was in agreement with that of the literature (from 2.5% up to 67.8% within the examined entheses)^{17,36-38} (**Table 5**). This discrepancy in prevalence could be due to the different total number of entheses examined in each study. In fact, there is no consensus and some enthesial sites seem to have abnormalities in both PsA and psoriasis patients with no musculoskeletal symptoms.³⁹

We studied the enthesial sites that are often studied in the literature: lateral epicondyles, triceps tendon insertion into the olecranon tuberosity, proximal, and distal patellar tendons, calcaneal tendon, and plantar fascia. We added the deep flexor tendon of the finger enthesitis, which is rarely studied by US to screen for enthesitis in psoriatic patients.

Table 4. Comparison between US enthesitis findings in the literature according to different scores.

Study, yetar ^{ref}	Study populations Cases/ Controls (Size)	Scanned entheses	US scores	p
Gisoni et al. 2007 ³¹	Psoriasis (30) Other dermatosis (30)	QT,PPT,DP,CT, PPF	.GUESS score ^a . Case :7.9± 0.6 . Controls :2.9± 0.3	<0.0001
Eder et al. 2014 ³²	Psoriasis (66) Healthy controls (60)	TT QT PPT,DPT CT, PPF	.Modified MASEI score .Inflammatory score ^b .Case:2 (4) .Controls: 1(2)	0.002
			.Damage score ^b .Case:4 (6) .Controls: 0.023 (6)	0.1
			.Total score ^b .Case:6 (8) . Controls : 3.5 (7.5)	0.02
Hamdy et al. 2015 ¹⁶	Psoriasis with rheumatic manifestations without fulfilling CAPSAR criteria (50) Healthy controls (20)	TT QT PPT,DPT CT, PPF	.MASEI score ^a .Case:27.8±5.4 .Controls : 12.2±4.3	0.001
Günaydin et al. 2020 ³³	Psoriasis (30) Healthy controls (30)	SST CET, CFT GT QT, PPT CT, PPF	.SPARCC US score ^a .Case:4.7 ± 3.5 .Controls : 2.9 ± 2.3	0.04
Vyas et al. 2020 ³⁵	Psoriasis (50) Healthy controls (50)	TT,QT, PPT,DPT, CT, PPF	.MASEI score ^a .Case:12.72±7.55 .Controls : 5.14±4.69	0.000001
Our study, 2021	Psoriasis (40) Healthy controls (40)	DDF,CET, TT, QT, PPT,DPT, CT, PPF	.Inflammatory score ^a .Case:2.85 ±3.34 .Controls :0.58 ±1.17	<0.001
			.Damage score ^a . Case: 3 ±2.57 . Control: 0.60 ±1.41	<0.001
			.Total score ^a .Case:5.85 ±5.20 .Controls : 1.18 ±2.07	<0.001

US : ultrasonography, QT: quadriceps tendon, PPT: proximal patellar tendon, DPT: distal patellar tendon, CT: calcaneal tendon, PPF: proximal plantar fascia, TT: triceps tendon, SST: supraspinatus tendon , CET: common extensor tendon , CFT: common flexor tendon , GT: great trochanter, DDF: deep digital flexor.

^a: (mean± SD), ^b: (median(IQR))

Naredo et al. had studied this enthesitis in 136 patients with psoriasis and 46 healthy sex- and age-matched controls, but did not find a significant difference compared to controls (p=0.436).¹⁷ Our findings showed a statistically higher enthesitis rate at this site compared to controls (19/320 (5.94%) versus 1/320 (1.25%), p< 0.001).

The age of our patients was correlated with a higher number of US enthesitis in the psoriasis group (p=0.001).

All US scores (inflammatory, damage, total) increased with age (p=0.011; p=0.004; p=0.002, respectively). Inconsistent with our results, Gisoni et al. and Eder et al. found a positive correlation between the age and the US scores (GUESS and MASEI).^{31,32} Bakirci et al., however, confirmed this correlation in healthy subjects.⁴⁰

The patient gender was not correlated with the number of US enthesitis nor with the different US scores in both

Table 5. Comparison between US enthesitis prevalences in the literature according to the scanned entheses.

Study, year ^{ref}	Study populations Cases/Controls (size)	Scanned entheses	US enthesitis n (%)		P
			Cases	Controls	
Naredo et al. 2011¹⁷	Psoriasis (162) Healthy controls (60)	DDF PPT,DPT CT, PPF	285/2457 (11.6)	44/818 (5.3)	<0.0005
Gutierrez et al. 2011³⁶	Psoriasis (45) Healthy controls (45)	QT PPT,DPT CT, PPF	148/450 (32.9)	38/450 (8.4)	<0.0001
Freeston et al. 2012³⁷	Early PsA (42) Healthy controls (10)	CET DPT CT, PPF	24/296 (8.1)	9/78 (11.5)	NP
Hamdy et al. 2015¹⁶	Psoriasis with rheumatic manifestations without fulfilling CAPSAR criteria (50) Healthy controls (20)	TT QT PPT,DPT CT, PPF	407/600 (67.8)	20/240 (8.3)	0.004
Elnady et al. 2019³⁸	Psoarthritis (109) Healthy controls (90)	CET, CFT PPT,DPT CT, PPF	22/872 (2.5)	7/720(0.97)	0.01
Our study 2021	Psoarthritis (40) Healthy controls (40)	DDF CET, TT QT PPT,DPT CT, PPF	184/880 (20.90)	42/880 (4.78)	<0.001

US: ultrasonography; DDF: deep digital flexor; PPT: proximal patellar tendon; DPT: distal patellar tendon; CT: calcaneal tendon; PPF: proximal plantar fascia; QT: quadriceps tendon; TT: triceps tendon; CET: common extensor tendon; CFT: common flexor tendon; NP: not precised.

psoriasis and control groups, which was confirmed by Hamdy et al. in a follow-up case-control US study using MASEI score.¹⁶ However, male sex was a risk factor for the development of enthesitis ($p = 0.003$) in a study of healthy participants.⁴⁰

The duration of psoriasis in our study ranged from one year to 57 years and it was not correlated with the number of US enthesitis nor to different US scores. In a literature review, which focused on the predictive factors of PsA, the duration of psoriasis was not correlated with a higher incidence of PsA,⁴¹ unlike Wilson et al.,⁴² who confirmed that the cumulative incidence of PsA increased with the disease duration.

Three psoriasis phenotypes were found among our population: plaque psoriasis (90%), guttate psoriasis (5%), and pustular psoriasis (5%). Several authors advanced the hypothesis of a psoriasis risk phenotype for the development of PsA such as nail and scalp involvement.^{6,41-42} This is consistent with our results. In fact, a greater number of US enthesitis were found in patients with scalp involvement ($p=0.020$), but no association was observed for the other psoriasis phenotypes.

Savage et al. in their literature review advanced the absence of a link between the severity of psoriasis (PASI) and the likelihood of developing PsA.⁶ That was confirmed in later studies.^{16,33,43} Wilson et al. contrarily, showed that severe psoriasis were a predictive factor of developing PsA.⁴⁴ Actually, it has been shown that synovium and skin lesions in PsA express the proinflammatory cytokine tumor necrosis factor α (TNF α); therefore, the larger affected skin area of psoriasis may result in increased systemic levels of TNF α and therefore in developing PsA.^{45,46}

Mechanical stress, such as overweight and physical activity, could be risk factors and induce structural changes (enthesophyte, calcification, erosion) of the entheses, especially in the lower limbs.^{31,32,40,47} According to enthesal sites, different findings are reported. In the study of Gisondi et al. investigating the lower limb and using the GUESS score, the authors identified a link between BMI and US enthesitis.³¹ However, Eder et al. by studying both upper and lower limbs using the MASEI score, did not observe a significant difference between US findings of patients (psoriasis patients and healthy controls) and BMI

over than 30. Whereas, that was found in patients with a BMI less than 30.³² In our population, we did not observe associations between US enthesitis and BMI or physical activity intensity. However, for US scores, sedentary patients (inactive) had higher inflammation score values compared to minimally active or active patients ($p=0.055$). Studies results are controversial about the link between physical activity and US enthesitis abnormalities, some authors support this notion,³⁵ while others confirm that regular physical activity could improve US outcomes.⁴⁸ In our study, we sought the influence of disease-modifying treatment on US enthesitis abnormalities. A higher dose of MTX reduced the damage score, but not significantly ($r=-0.445$, $p=0.169$). Few studies have investigated the influence of MTX intake on the structural and inflammatory changes of enthesitis. Acquacalda et al. provided US monitoring of the enthesitis of two groups of patients (psoriasis, PsA) treated with methotrexate alone or in combination with biologic drugs.⁴⁹ An improvement in the US abnormalities of the enthesitis was noted for the psoriasis group after six months of treatment ($p=0.021$), however, there was no significant improvement for the PsA group ($p=0.164$). These results suggest the role of systemic disease-modifying treatments for psoriasis on the subclinical evolution of enthesitis and, by analogy, the evolution towards a possible PsA in the absence of treatment or its optimisation.⁴⁹

Our study has some limitations: first, the sample size of our study was the major limitation and does not allow us to generalise our results. Second, axial joint and enthesitis involvement, which are commonly seen with PsA, were not included in this study since it cannot be properly imaged by US. Third, although the US examination was carried out by an expert; ultrasonography remains an operator-dependent examination. Finally, more than a third of patients were on MTX which could alter US findings, but we noted no significant difference between the US scores of patients receiving (MTX) and those receiving other treatments. The results should be interpreted with caution. A follow-up of psoriatic patients with US abnormalities should be conducted in order to detect eventually early features of the disease and to establish the incidence of PsA and other risk factors.

CONCLUSION

In conclusion, our results suggest that psoriasis is associated with a higher prevalence of asymptomatic US synovitis and enthesitis. Future longitudinal studies with larger sample sizes should consider whether US findings in asymptomatic psoriasis patients have predictive value in developing PsA. US could be used as a screening tool to detect early PsA, especially in patients with scalp involvement and a positive SPARCC score. Such patients should be referred to a rheumatologist in an early stage, seeking a better outcome.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

FUNDING STATEMENT

The authors declared that no fundings were involved in supporting this work.

AVAILABILITY OF DATA AND MATERIAL

All data underlying the results are available as part of the article and no additional source data are required. All data are available in our rheumatology department and could be consulted at any time.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the ethical committee of la Rabta Hospital; we have obtained oral patient's consent before inclusion in this study (which was approved by the ethic committee CEBM.EPS.HR30/2021)

CONSENT FOR PUBLICATION

We have obtained patient's consent for publication before inclusion in this study.

AUTHORS' CONTRIBUTIONS

Dr S B: Conceptualisation, Writing- original draft, Supervision, Validation,
Dr R B A: Data curation, Writing - original draft,
Dr S R: Supervision, Validation
Dr K Z: Supervision, Validation
Dr S R: Supervision, Validation
Dr S Je: Writing- original draft
Dr K Z: Supervision, Validation
Dr S H: Supervision, Validation
Dr M E: Supervision, Validation

REFERENCES

1. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. *J Eur Acad Dermatol Venereol JEADV* 2017;31:205–12. <https://doi.org/10.1111/jdv.13854>.
2. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis. *N Engl J Med* 2017;376:957–70. <https://doi.org/10.1056/nejmra1505557>.
3. Kane D, Stafford L, Bresnihan B, Fitzgerald O. A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience. *Rheumatol Oxf Engl* 2003;42:1460–8. <https://doi.org/10.1093/rheumatology/keg384>.
4. Greb JE, Goldminz AM, Elder JT, Lebwohl MG, Gladman DD, Wu JJ, et al. Psoriasis. *Nat Rev Dis Primer* 2016;2:1–17. <https://doi.org/10.1038/nrdp.2016.82>.
5. Kim WB, Jerome D, Yeung J. Diagnostic et prise en charge du psoriasis. *Can Fam Physician* 2017;63:e210–8.
6. Savage L, Tinazzi I, Zabotti A, Laws PM, Wittmann M, mcgonagle D. Defining Pre-Clinical Psoriatic Arthritis in an Integrated Dermato-Rheumatology Environment. *J Clin Med* 2020;9:3262. <https://doi.org/10.3390/jcm9103262>.
7. 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. <https://doi.org/10.1002/art.21972>.
8. Raychaudhuri SP, Wilken R, Sukhov AC, Raychaudhuri SK,

- Maverakis E. Management of psoriatic arthritis: Early diagnosis, monitoring of disease severity and cutting edge therapies. *J Autoimmun* 2017;76:21–37. <https://doi.org/10.1016/j.jaut.2016.10.009>.
9. Coates LC, Conaghan PG, Emery P, Green MJ, Ibrahim G, MacIver H, et al. Sensitivity and specificity of the Classification of Psoriatic Arthritis criteria in early psoriatic arthritis. *Arthritis Rheum* 2012;64:3150–5. <https://doi.org/10.1002/art.34536>.
 10. mcgonagle D, Aydin SZ, Tan AL. The Synovio-entheseal Complex and Its Role in Tendon and Capsular Associated Inflammation. *J Rheumatol Suppl* 2012;89:11–4. <https://doi.org/10.3899/jrheum.120233>.
 11. Lekpa FK, Claudepierre P. Les enthésites. *Rev Rhum* 2017;84:A21–8. [https://doi.org/10.1016/S1169-8330\(17\)30326-5](https://doi.org/10.1016/S1169-8330(17)30326-5).
 12. Tinazzi I, mcgonagle D, Biasi D, Confente S, Caimmi C, Girolomoni G, et al. Preliminary Evidence That Subclinical Enthesopathy May Predict Psoriatic Arthritis in Patients with Psoriasis. *J Rheumatol* 2011;38:2691–2. <https://doi.org/10.3899/jrheum.110505>.
 13. Kristensen S, Christensen JH, Schmidt EB, Olesen JL, Johansen MB, Arvesen KB, et al. Assessment of enthesitis in patients with psoriatic arthritis using clinical examination and ultrasound. *Muscles Ligaments Tendons J* 2016;6:241–7. <https://doi.org/10.11138/mltj.2016.6.2.241>.
 14. D'Agostino M-A. Enthesitis detection by ultrasound: where are we now? *Clin Exp Rheumatol* 2018;36 Suppl 114:127–30.
 15. Oğuz ID, Gül Ü, Koparal SS, Deren T, Külcü Çakmak S, Bodur H, et al. Investigation of Enthesopathy with Ultrasonography and Comparison with Skin Findings in Asymptomatic Psoriatic Patients. *Dermatol Basel Switz* 2016;232:312–8. <https://doi.org/10.1159/000444218>.
 16. Hamdy M, Omar G, Elshereef RR, Ellaban AS, Amin M. Early detection of spondyloarthropathy in patients with psoriasis by using the ultrasonography and magnetic resonance image. *Eur J Rheumatol* 2015;2:10–5. <https://doi.org/10.5152/eurjrheumatol.2015.0075>.
 17. Naredo E, Möller I, de Miguel E, Battle-Gualda E, Acebes C, Brito E, et al. High prevalence of ultrasonographic synovitis and enthesopathy in patients with psoriasis without psoriatic arthritis: a prospective case–control study. *Rheumatology* 2011;50:1838–48.
 18. Al-Hazzaa HM. Health-enhancing physical activity among Saudi adults using the International Physical Activity Questionnaire (IPAQ). *Public Health Nutr* 2007;10:59–64.
 19. Gladman DD, Mease PJ, Strand V, Healy P, Helliwell PS, Fitzgerald O, et al. Consensus on a core set of domains for psoriatic arthritis. *J Rheumatol*. 2007;34(5):1167-70.
 20. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures and development of an instrument specific to psoriatic arthritis. *Arthritis Rheum* 2008;59:686-91.
 21. Maksymowych WP, Mallon C, Morrow S, Shojania K, Olszynski WP, Wong RL, et al. Development and validation of the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index. *Ann Rheum Dis* 2009;68:948-53.
 22. Puzenat E, Bronsard V, Prey S, Gourraud PA, Aractingi S, Bagot M, et al. What are the best outcome measures for assessing plaque psoriasis severity? A systematic review of the literature. *J Eur Acad Dermatol Venereol* 2010;24 Suppl 2:10-6.
 23. Rich P, Scher RK. Nail psoriasis severity index: a useful tool for evaluation of nail psoriasis. *J Am Acad Dermatol* 2003;49(2):206-12.
 24. Tom S, Zhong Y, Cook R, Aydin SZ, Kaeley G, Eder L. Development of a preliminary ultrasonographic enthesitis score in psoriatic arthritis — GRAPPA ultrasound working group. *J Rheumatol* 2019;46(4):384-90.
 25. De Miguel E, Cobo T, Muñoz Fernández S, Naredo E, Usón J, Acebes JC, et al. Validity of enthesitis ultrasound assessment in spondyloarthropathy. *Ann Rheum Dis* 2009;68(2):169-74.
 26. Lee MH, Cha JG, Jin W, Kim BS, Park JS, Lee HK, et al. Utility of sonographic measurement of the common tensor tendon in patients with lateral epicondylitis. *Am J Roentgenol* 2011;196(6):1363-7.
 27. Filer A, de Pablo P, Allen G, Nightingale P, Jordan A, Jobanputra P, et al. Utility of ultrasound joint counts in the prediction of rheumatoid arthritis in patients with very early synovitis. *Ann Rheum Dis* 2011;70:500–7. <https://doi.org/10.1136/ard.2010.131573>.
 28. Plaza M, Nowakowska-Plaza A, Pracoń G, Sudol-Szopińska I. Role of ultrasonography in the diagnosis of rheumatic diseases in light of ACR/EULAR guidelines. *J Ultrason* 2016;16:55–64. <https://doi.org/10.15557/jou.2016.0006>.
 29. D'Agostino M-A, Said-Nahal R, Hacquard-Bouder C, Brasseur J-L, Dougados M, Breban M. Assessment of peripheral enthesitis in the spondylarthropathies by ultrasonography combined with power Doppler: A cross-sectional study. *Arthritis Rheum* 2003;48:523–33. <https://doi.org/10.1002/art.10812>.
 30. Balint PV, Kane D, Wilson H, McInnes IB, Sturrock RD. Ultrasonography of enthesal insertions in the lower limb in spondyloarthropathy. *Ann Rheum Dis* 2002;61:905–10. <https://doi.org/10.1136/ard.61.10.905>.
 31. Eder L, Kaeley GS, Aydin SZ. Development and Validation of a Sonographic Enthesitis Instrument in Psoriatic Arthritis: The GRAPPA Diagnostic Ultrasound Enthesitis Tool (DUET) Project. *J Rheumatol Suppl* 2020;96:50–2. <https://doi.org/10.3899/jrheum.200128>.
 32. Gisondi P, Tinazzi I, El-Dalati G, Gallo M, Biasi D, Barbara LM, et al. Lower limb enthesopathy in patients with psoriasis without clinical signs of arthropathy: a hospital-based case-control study. *Ann Rheum Dis* 2008;67:26–30. <https://doi.org/10.1136/ard.2007.075101>.
 33. Eder L, Jayakar J, Thavaneswaran A, Haddad A, Chandran V, Salonen D, et al. Is the Madrid Sonographic Enthesitis Index Useful for Differentiating Psoriatic Arthritis from Psoriasis Alone and Healthy Controls? *J Rheumatol* 2014;jrheum.130949. <https://doi.org/10.3899/jrheum.130949>.
 34. Günaydin EB, Aladağ P, Tecer D, Yenice IS, Adışen E, Göğüş FN. Ultrasonographic evaluation of subclinical enthesitis in patients with psoriasis. *Int J Rheum Dis* 2020;23:744–52. <https://doi.org/10.1111/1756-185X.13835>.
 35. Vyas K, Jain SK, Mittal A, Kumar R, Saxena S, Malviya S. Sonographic evaluation of subclinical enthesopathy in patients of chronic plaque psoriasis. *Indian Dermatol Online J* 2020;11(4):580-5.
 36. Gutierrez M, Filippucci E, De Angelis R, Salaffi F, Filosa G, Ruta S, et al. Subclinical enthesal involvement in patients with psoriasis: an ultrasound study. *Semin Arthritis Rheum* 2011;40(5):407-12.
 37. Freeston JE, Coates LC, Helliwell PS, Hensor EA, Wakefield RJ, Emery P, et al. Is there subclinical enthesitis in early psoriatic arthritis? A clinical comparison with power doppler ultrasound. *Arthritis Care Res* 2012;64(10):1617-21.
 38. Elhady B, El Shaarawy NK, Dawoud NM, Elkhoully T, Desouky DS, ElShafey EN, et al. Subclinical synovitis and enthesitis in psoriasis patients and controls by ultrasonography in Saudi Arabia; incidence of psoriatic arthritis during two years. *Clin Rheumatol* 2019;38(6):1627-35.
 39. Tang Y, Cheng S, Yang Y, Xiang X, Wang L, Zhang L, Qiu L. Ultrasound assessment in psoriatic arthritis (PsA) and psoriasis vulgaris (non-PsA): which sites are most commonly involved and what features are more important in PsA? *Quant Imaging Med Surg* 2020;10(1):86-95.
 40. Bakirci S, Solmaz D, Stephenson W, Eder L, Roth J, Aydin SZ. Enthesal Changes in Response to Age, Body Mass Index, and Physical Activity: An Ultrasound Study in Healthy People. *J Rheumatol* 2020;47:968–72. <https://doi.org/10.3899/jrheum.190540>.
 41. Rouzaud M, Sevrain M, Villani AP, Barnette T, Paul C, Richard M-A, et al. Is there a psoriasis skin phenotype associated with psoriatic arthritis? Systematic literature review. *J Eur Acad Dermatol Venereol JEADV* 2014;28 Suppl 5:17–26. <https://doi.org/10.1111/jdv.12562>.
 42. Wilson FC, Icen M, Crowson CS, McEvoy MT, Gabriel SE, Kremers HM. Incidence and Clinical Predictors of Psoriatic Arthritis in Patients With Psoriasis: A Population-Based Study. *Arthritis*

- Rheum 2009;61:233–9. <https://doi.org/10.1002/art.24172>.
43. Bandinelli F, Prignano F, Bonciani D, Bartoli F, Collaku L, Candelieri A, et al. Ultrasound detects occult enthesal involvement in early psoriatic arthritis independently of clinical features and psoriasis severity. *Clin Exp Rheumatol* 2013;31:219–24.
44. Wilson FC, Icen M, Crowson CS, McEvoy MT, Gabriel SE, Kremers HM. Incidence and clinical predictors of psoriatic arthritis in patients with psoriasis: a population-based study. *Arthritis Rheum* 2009 Feb 15;61(2):233–9. doi:10.1002/art.24172
45. Anandarajah AP, Ritchlin CT. Pathogenesis of psoriatic arthritis. *Curr Opin Rheumatol* 2004;16:338 – 43.
46. Hueber AJ, McInnes IB. Immune regulation in psoriasis and psoriatic arthritis: recent developments. *Immunol Lett* 2007;114:59–65.
47. Wervers K, Herrings I, Luime JJ, Tchetverikov I, Gerards AH, Hazes JMW, et al. Association of Physical Activity and Medication with Enthesitis on Ultrasound in Psoriatic Arthritis. *J Rheumatol* 2019;46:1290–4. <https://doi.org/10.3899/jrheum.180782>.
48. Méric J-C, Grandgeorge Y, Lotito G, Pham T. Walking Before an Ultrasound Assessment Increases the Enthesis Score Significantly. *J Rheumatol* 2011;38:961–961. <https://doi.org/10.3899/jrheum.101059>.
49. Acquacalda E, Albert C, Montaudie H, Fontas E, Danre A, Roux CH, et al. Ultrasound study of entheses in psoriasis patients with or without musculoskeletal symptoms: A prospective study. *Joint Bone Spine* 2015;82:267–71. <https://doi.org/10.1016/j.jbspin.2015.01.016>.