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ORIGINAL ARTICLES

Detection of subclinical enthesitis by ultrasonography in patients with psoriasis and controls

Karamanlioglu DS[1], Ozkan FU[1], Arikan EEC[2], Pirdal BZ[3], Ozturk G[1], Aktas I[1]

ABSTRACT

Introduction: Psoriasis is a widespread chronic inflammatory skin disease; enthesitis is inflammation of the tendon, ligament, and joint capsule insertion, prevalent in patients with psoriatic arthritis.
Objectives: The aim of the study to evaluate the utility of the Madrid Sonography Enthesitis Index scoring system for accurate detection of subclinical enthesitis in patients with Psoriasis compared with healthy controls. Another objective was to assess increase in enthesis area and Psoriatic arthritis incidence, in a prospective 1-year follow-up.
Method: Patients aged ≥18 years who were diagnosed with Psoriasis, without musculoskeletal complaints, and who did not have any clinical sign and/or symptom of enthesitis and synovitis were included in the study. The patients and healthy controls were evaluated with ultrasonography. Ultrasonography evaluation consisted of the detection of gray-scale enthesitis and power Doppler signal in the enthesis areas. The Madrid Sonography Enthesitis Index scoring system was used to quantify the extent of the sonographic enthesis abnormalities.
Results: The mean MASEI score, structure, thickness, erosion, and calcification were significantly higher in the Psoriasis group than in the control group. The mean MASEI score, structure, erosion, and calcification measurements were significantly higher at the last examination when compared to the first examination. The triceps was the most commonly affected tendon in both groups.
Conclusion: Ultrasonography is an important tool for diagnosis and follow-up of subclinical enthesitis in patients with psoriasis. Regardless of disease duration and severity, patients should be screened using ultrasonography at yearly intervals.

Keywords: Madrid Sonography Enthesitis Index score; Psoriasis; Psoriatic Arthritis; Subclinical Enthesitis; Ultrasonography.

KEY MESSAGES

- The presence of enthesitis in patients with psoriasis is significantly higher than healthy controls.
- Ultrasound is a safe tool to detect the subclinical enthesitis in psoriatic patients even if they do not have symptoms

INTRODUCTION

Psoriasis (PsO) is a widespread chronic inflammatory skin disease with various clinical manifestations. Psoriatic arthritis (PsA), on the contrary, is a complex inflammatory musculoskeletal disease with different clinical features[1]. Most studies have reported the prevalence of PsA in patients with PsO as between 20% and 30%[1-4]. A recent study showed that the incidence of PsA was 8.5 per 100,000, with a prevalence of 181.8 per 100,000[5]. Clinical skin findings in PsO often precede the onset of arthritis by an average of 10 years; however, up to 10–15% of patients may develop arthritis before the occurrence of PsO[3].

Recently, it has been suggested that the period between the onset of PsO and development of PsA should be studied in three phases: preclinical, subclinical, and prodromal. Subclinical PsA is defined as PsO without symptoms of arthritis, but with synovial inflammation on imaging[6,7]. Most patients in the subclinical PsA phase remain asymptomatic and undiagnosed for a long time[6]. However, the damage caused by multiple inflammatory pathways persists until a debilitating form of arthritis develops[4,6].

The Classification Criteria for Psoriatic Arthritis, which was developed for PsA, includes enthesitis[8]. Recently, it has been argued that enthesitis is the primary lesion in most patients with PsA or spondyloarthritis[9].

[1] Physical Medicine and Rehabilitation Department, Fatih Sultan Mehmet Training and Research Hospital; [2] Dermatology Department, Bahçeşehir University Faculty of Medicine; [3] Republic of Turkey Ministry of Health, Istanbul Sultangazi District Health Directorate Ugur Mumcu

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Correspondence to: Duygu Silte Karamanlioglu
E-mail: drduygusilte@hotmail.com

Enthesitis is inflammation of a tendon, ligament, or joint capsule insertion[10]. Clinical studies have indicated that patients with PsA have a higher prevalence of enthesitis than expected[9]. The clinical evaluation of enthesitis in PsA is difficult because enthesitis is not usually accompanied by swelling[9].

Timely detection of subclinical PsA may enable clinicians to intervene early, delay or alleviate the onset of clinical symptoms, and even halt PsA progression[4,7]. Therefore, patients with PsO should be evaluated for subclinical PsA when suspected, regardless of the degree of skin lesions[11]. Enthesitis can also be detected during the preclinical period using ultrasonography (US). Studies have demonstrated the detection of subclinical enthesitis on US imaging, using various scoring systems, in patients with PsO without have clinical arthritis[12-18]. However, most studies have focused only on the present state of PsO enthesis in a single measurement, and few studies evaluated follow-up findings.

This study aimed to evaluate the utility of Madrid Sonography Enthesitis Index (MASEI) for detection of subclinical enthesitis in patients with PsO without musculoskeletal complaints, compared to healthy controls. Another objective was to assess increase in enthesis area and PsA incidence, and show a possible relationship with baseline findings in a prospective 1-year follow-up of patients with PsO. We also attempted to determine whether subclinical enthesitis could predict the development of PsA in patients with psoriasis.

MATERIALS AND METHODS

Thirty-one volunteer patients who were diagnosed with PsO without musculoskeletal complaints and thirty gender, age, body mass index (BMI)-matched healthy controls (HCs) were included in the study. All participants underwent dermatological assessment by a dermatologist, musculoskeletal examination by a physiatrist, and blinded ultrasound evaluation by another physiatrist.

Patients aged ≥18 years who were diagnosed with PsO by a dermatologist, without musculoskeletal complaints, and who did not have any clinical sign and/or symptom of enthesitis, arthritis and synovitis were included in the study. HCs were aged ≥ 18 years without PsO or musculoskeletal complaints, and had no clinical sign and/or symptom of arthritis, enthesitis, or synovitis. Patients with history of gout, arthritis, peripheral neurological disease, trauma, or intensive sports activity in the last 2 weeks, and those who had received any systemic therapy, such as disease-modifying anti-rheumatic drugs, non-steroidal anti-inflammatory drugs, corticosteroids, immunosuppressants, retinoids, or biological agents, within the previous 3 months were excluded. Pregnant or breastfeeding patients were also excluded from the study.

Age, BMI, duration of disease, smoking history, alcohol intake, comorbidities (type 2 diabetes, hypertension, and cardiovascular disease), and the drugs used were assessed in all patients. The severity of PsA with Psoriasis Area Severity Index (PASI) score[19]. and nail involvement with Nail Psoriasis Severity Index (NAPSI) score were evaluated by a dermatologist[20]. The presence of swollen and/or tender joints was investigated with detailed history and physical examination, and patients with arthritis were excluded from the study. Patients and HCs were evaluated by the Spondyloarthritis Research Consortium of Canada (SPARCC), and enthesis points with tenderness were determined and recorded for each participant[21]. US was performed on selected enthesis areas in both groups. The evaluation consisted of detection of grayscale enthesitis and power Doppler signals in the enthesis areas. MASEI scoring system was used to quantify the extent of sonographic enthesis abnormalities[22]. This study was performed in line with the principles of the Declaration of Helsinki. Informed consent was obtained from all the participants, and approval was granted by the Ethics Committee of Fatih Sultan Mehmet Research and Training Hospital (FSMEAH-KAEK 2019/74; clinical trial number: NCT04209894).

Ultrasound evaluation

US was performed by two physiatrists using a LOGIQ 5 US device (GE Healthcare) with a 10–15 MHz probe. Power Doppler settings were standardized with pulse repetition frequency of 750 Hz, colour mode frequency of 9.1 MHz, and low-wall filters. The researchers who conducted the US were blinded to the groups of participants. The imaging was performed in a dark room. Each patient was asked not to undress completely but only to expose the anatomical region of interest at the time of examination. In addition, to reduce potential bias, the physiatrist was asked to focus only on the examination area, without talking to the patients about their clinical and dermatological statuses. The same examination and US were performed again 1 year later in the PsO patient group. Each US scan took approximately 20 minutes. At second evaluation of PsO patients, the patients were questioned about weight gain, physical activity changes and trauma. The plantar fascia (at its insertion into the calcaneus), Achilles tendon, distal patellar tendon, proximal patellar tendon, quadriceps tendon, and triceps tendon (at its insertion into the olecranon prominence) were scanned bilaterally using MASEI scoring system. Each tendon was scanned and evaluated in both longitudinal and transverse planes. The patients were in the supine position for evaluation of the patellar and quadriceps entheses. The knee was

maintained at approximately 70° flexion during the assessment. To evaluate Achilles tendon and plantar fascia entheses, the patients were placed in the prone position with their feet at the end of the examination table. Triceps tendon enthesis was evaluated by flexing the elbow at 90°. Grayscale US findings that indicate enthesopathy include thickness of the enthesis and structural changes in the tendon insertion, calcifications, and erosions in the tendon insertion. Thickness of the enthesis was measured at the insertion of the deeper tendon edge into the bone along the longitudinal axis. Vascularization was evaluated at the cortical bone insertion. Calcifications were evaluated at the area of the enthesis insertion and scored as 0 if absent, or a 1 if a small calcification or ossification with an irregularity of enthesis cortical bone profile was seen. Calcifications were given a score of 2 if there was clear presence of enthesophytes, or if medium-sized calcifications or ossification were seen. Lastly, they were classified as a 3 if large calcifications or ossifications were present. Bony erosion was described as a cortical breakage with a stepdown bone contour defect in both longitudinal and transverse axes. According to the MASEI scoring system, ≥18 points are considered positive for spondylarthritis[22]. (Figure 1).

Statistical analysis

Power analysis was performed using the G*Power program. When effect size d=0.879 and standard deviation=6.5 were considered for the MASEI score (based on a previously conducted study by Ebstein et al.[23]), for power=0.80 and α=0.05, the minimum sample size required was 22. Data were analyzed using IBM SPSS Statistics 21 software (SPSS IBM, Turkey). Normal distribution of the data was determined using Shapiro–Wilk test histogram plots. Continuous data were presented as means, standard deviations, and medians (25^{th}–75^{th} percentile), whereas categorical data were presented as frequencies and percentages. Mann–Whitney U test was used to compare continuous data between the PsO and HC groups, as the groups were not normally distributed, and chi-square and Fisher's exact tests were performed for comparison of categorical data. Wilcoxon test was used to compare continuous variables of the first and last measurements in the PsO group, and McNemar test was used for categorical data. Quade's analysis of variance was performed to identify the significant variables in the first and last measurements of MASEI scores. All tests were bilateral, and statistical significance was set at $p < 0.05$.

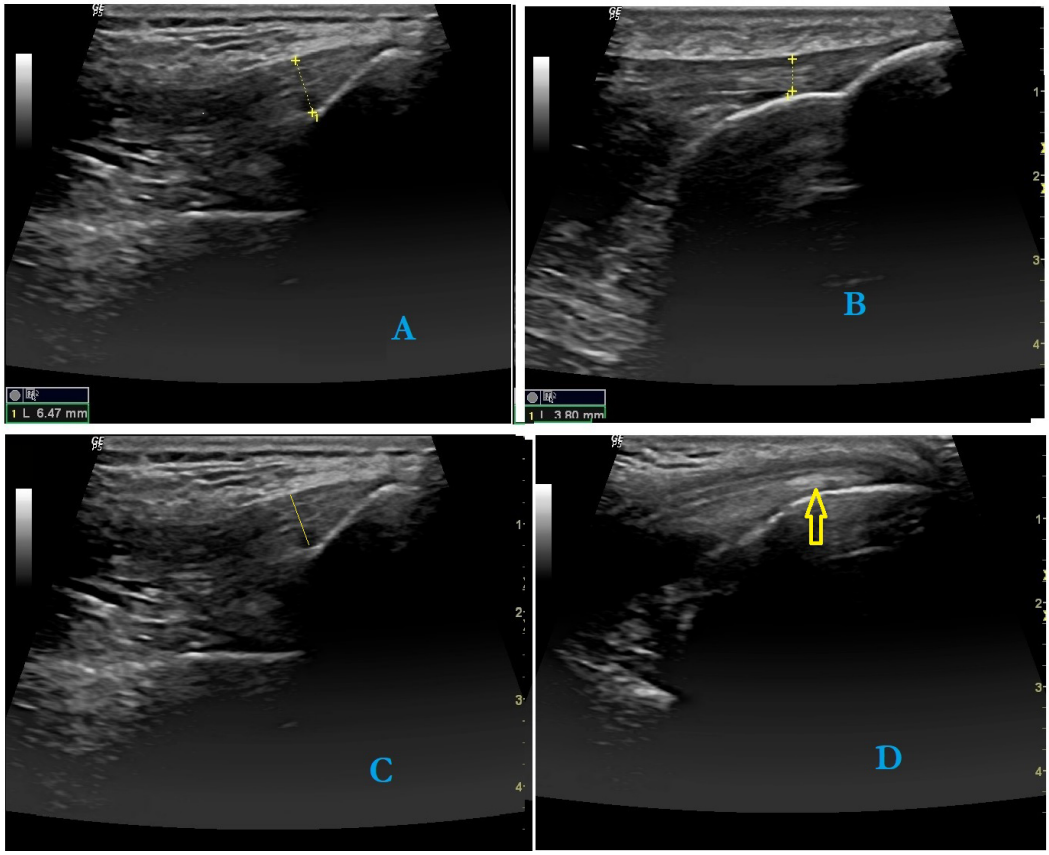

Figure 1. Ultrasonographic findings. A) Quadriceps tendon, measurement of tendon thickness; B) Distal patellar tendon measurement of tendon thickness; C) Thickening of quadriceps tendon and loss of fibrillar pattern in the same side; D) Calcification of triceps tendon in longitudinal plane.

TABLE I. Comparison of demographic data

Category		PsO (31)	HC (30)	p
Sex				
Female	*n (%)*	15 (48.4)	19 (63.3)	0.240[1]
Male	*n (%)*	16 (51.6)	11 (36.7)	
Age	*Mean ± std. deviation*	39.5 ± 13.5	36.3 ± 7.4	0.323[2]
	Median (25-75. percentile)	41 (26-51)	35.5 (29-43.3)	
BMI	*Mean ± std. deviation*	26.9 ± 4	26.2 ± 4.3	0.159[2]
	Median (25-75. percentile)	27.7 (25-29.7)	25.5 (22.2-28)	
Type 2 DM	*n (%)*	1 (3.2)	0 (0)	1.00[3]
HT	*n (%)*	6 (19.4)	1 (3.3)	0.104[3]
CAD	*n (%)*	0 (0)	0 (0)	-
Smoking	*n (%)*			
Never	*n (%)*	7 (22.6)	23 (76.7)	
Previous smoking	*n (%)*	19 (61.3)	7 (23.3)	**<0.001**[3]
Active	*n (%)*	5 (16.1)	0 (0)	
Alcohol intake	*n (%)*			
Never	*n (%)*	16 (52.6)	16 (53.3)	
Less than monthly	*n (%)*	1 (3.2)	12 (40)	**<0.001**[1]
More than monthly	*n (%)*	14 (45.2)	1 (3.3)	
Family history				
1. Degree relative PsO+	*n (%)*	7 (22.6)		
1. Degree relative PsA +	*n (%)*			
PsO-	*n (%)*	19 (61.3)		
2. Degree relative PsO +	*n (%)*	5 (16.1)		
Psoriasis onset area	*n (%)*			
Extremity	*n (%)*	19 (61.3)		
Scalp	*n (%)*	9 (29)		
Trunk	*n (%)*	1 (3.2)		
Nail	*n (%)*	2 (6.5)		
RF +	*n (%)*	0 (0)		
ANA +	*n (%)*	4 (12.9)		
HLA B27 +	*n (%)*	3 (9.6)		
Anti-CCP	*n (%)*	(0)		
Duration of disease	*Mean ± std. deviation*	8.5 ± 8.8		
	Median (25-75. percentile)	5 (1-13)		
Development of PsA	*n (%)*	4 (15.4)		

[1]Chi square test. [2]Mann Whitney U test. [3] Fisher's exact test. ANA:anti nuclear antibody, BMI: Body mass index; CAD: Coronary artery disease, CCP: cyclic citrullinated peptide, HC: healthy control, HLA: Human leukocyte Antigen HT: Hypertension, DM: diabetes mellitus, PsO: Psoriasis, PsA: psoriatic arthritis, RF: rheumatoid factor.

RESULTS

We included 31 PsO and 30 HCs. There were no differences in age, sex, or mean BMI between the two groups (p=0.240, p=0.323, and p=0.159, respectively). In the patient group, the cases were most frequently housewives, while most of healthy controls were health care workers such as physiotherapists, medical doctors and medical secretaries The mean disease duration in the PsO group was 8.5 ± 8.8 years. PsA developed in 15.4% (n=4) of the patients in the PsO group during follow-up. Participant demographics reported in Table I.

When age, BMI, sex, smoking, alcohol use, family history, and PASI, MASEI, and NAPSI at first measurement were compared between patients who developed PsA and those who did not, no significant differences were observed (p>0.05).

In the PsO group, there was no significant associ-

TABLE II. Examination of the difference of the last and first measurements of MASEI in the PsO group and the first measurement according to the variables

	MASEI first Median (25-75. ercentile)	p	MASEI last-first difference Median (25-75. percentile)	p
Sex				
Female	6 (4-13)	0.202	6 (3-6)	0.443
Male	10.5 (4.5-15.8)		9 (4-12)	
Smoking				
Never	6 (3-13)	0.124[3]	6 (4.3-7.5)	0.268[3]
Previous smoking	14 (10-21)		4 (4-13)	
Active	7 (4-13)		6 (2-7)	
Alcohol intake				
Never	7 (4-13.5)	0.343[2]	6 (4-10.3)	0.587[2]
Less than monthly	-		-	
More than monthly	10 (4-13.8)		4 (2.3-12.8)	
Occupation				
Housewife	5.5 (4-7.8)	0.255	6 (2-6)	0.930[2]
Employed	12 (4-15)		5 (4-12)	
D Vitamin				
<20	7 (4-16)	0.813[3]	4.9 (3.3-11.3)	0.751[3]
20-29	6 (3-14)		8.5 (0.8-11.8)	
≥30	8 (2-14)		8 (6-10)	
RF				
+	–		–	
–	7 (4-14)		6 (4-11)	
ANA				
+	9.5 (4.5-13)	0.976[2]	4.5 (3-6)	0.529[2]
–	7 (4-15)		6 (4-11.5)	
HLA B27				
+	7 (4.5-7)	0.314[2]	4 (2.5-5)	0.242[2]
–	8.5 (4-14.5)		6 (4-12)	
CCP				
+	–		–	
–	7 (4-14)		6 (4-11)	

[1]Chi square test. [2]Mann Whitney U test. [3] Fisher's exact test. BMI Body mass index; CAD Coronary artery disease, CCP cyclic citrullinated peptide, HC healthy control, HT Hypertension, DM diabetes mellitus, PsO Psoriasis, PsA psoriatic arthritis, RF rheumatoid factor

ation between the first MASEI measurement and sex, vitamin D level, ANA, HLA B27 positivity, occupation, smoking, or alcohol use. Furthermore, there were no significant associations between the results of the first and last (follow-up) MASEI measurements and sex, vitamin D level, ANA, HLA B27 positivity, occupation, smoking, or alcohol use ($p>0.05$) (Table II). The PsO group showed no significant correlation between the first MASEI measurement and age, BMI, disease duration, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, and PASI and NAPSI scores. There was also no significant correlation between the difference in the first and last MASEI measurements in the PsO group and age, BMI, disease duration, ESR, CRP levels, or PASI and NAPSI scores.

When the measurements of the PsO and HC groups were compared, the mean MASEI score, plantar fascia, Achilles tendon, distal patellar tendon, proximal patellar tendon, quadriceps tendon, triceps tendon, structure, thickness, erosion, and calcification in the PsO group were significantly higher than those in the HC group (all p values <0.05). There were no significant differences in the mean Doppler activity, frequency of retrocalcaneal bursitis, and vitamin D levels between

TABLE III. First US scanning comparison of Pso and HC groups

		PsO (31)	HC (30)	p
MASEI scores	Mean ± std. deviation	9.84 ± 7	2.73 ± 2.21	<0.001[1]
	Median (25-75. percentile)	7 (4-14)	2 (1-3.3)	
MASEI ≥18	n (%)	11 (35)	0 (0)	-
Plantar fascia	Mean ± std. deviation	0.65 ± 1.45	0.1 ± 0.4	0.043[1]
	Median (25-75. percentile)	0 (0-2)	0 (0-0)	
Achilles tendon	Mean ± std. deviation	1 ± 1.48	0.03 ± 0.18	<0.001[1]
	Median (25-75. percentile)	0 (0-2)	0 (0-0)	
Distal Patellar tendon	Mean ± std. deviation	1.38 ± 2.12	0.17 ± 0.53	0.002[1]
	Median (25-75. percentile)	0 (0-2)	0 (0-0)	
Proximal patellar tendon	Mean ± std. deviation	1.48 ± 2.01	0.27 ± 0.45	<0.001[1]
	Median (25-75. percentile)	1 (0-2)	0 (0-1)	
Quadriceps tendon	Mean ± std. deviation	2.48 ± 2.99	0.3 ± 0.75	<0.001[1]
	Median (25-75. percentile)	2 (0-3)	0 (0-0)	
Triceps tendon	Mean ± std. deviation	2.81 ± 2.04	1.87 ± 1.96	0.031[1]
	Median (25-75. percentile)	2 (1-4)	2 (0.8-2)	
Structural abnormalities	Mean ± std. deviation	1.97 ± 2.55	0.37 ±0.72	0.007[1]
	Median (25-75. percentile)	1 (0-4)	0 (0-0.25)	
The thickness of enthesis	Mean ± std. deviation	3.48 ± 2.26	1.6 ± 0.89	<0.001[1]
	Median (25-75. percentile)	3 (2-4)	2 (1-2)	
Erosions	Mean ± std. deviation	0.58 ± 0.99	0 ± 0	0.001[1]
	Median (25-75. percentile)	0 (0-1)	0 (0-0)	
Calcification	Mean ± std. deviation	0.97 ±1.05	0.23 ± 0.5	0.001[1]
	Median (25-75. percentile)	0 (0-1)	0 (0-0)	
Doppler activity	Mean ± std. deviation	0.32 ± 0.75	0.17 ± 0.53	0.314[1]
	Median (25-75. percentile)	0 (0-0)	0 (0-0)	
Retrocalcaneal Bursitis	Mean ± std. deviation	0.06 ± 0.36	0 ±0	0.325[1]
	Median (25-75. percentile)	0 (0-0)	0 (0-0)	
	Median (25-75. percentile)	15.7 (9.1-21)	16.1 (10.7-22.2)	

[1] Mann Whitney U test. MASEI MAdrid Sonographic Enthesitis Index, HC Healthy control; PsO: Psoriasis

the two groups (p>0.05) (Table III).

When the first and last examinations of the PsO group were conducted, the mean values of MASEI score, plantar fascia, Achilles tendon, distal patellar tendon, proximal patellar tendon, quadriceps tendon, triceps tendon, structure, erosion, and calcification in the last examination were significantly higher than those in the first examination (all p values <0.05). We also found that the rates of MASEI positivity ≥18 at the first and last examinations did not differ significantly with the mean PASI, NAPSI-hand, NAPSI-foot, SPARCC, thickness, Doppler activity, and presence of retrocalcaneal bursitis (all p values >0.05) (Table IV).

We found that the triceps, quadriceps, proximal patellar tendon, distal patellar tendon, Achilles tendon, and plantar fascia, in descending order of frequency, were affected in patients with PsO. The incidence of enthesitis was significantly higher in the triceps tendon than in the distal patellar tendon, Achilles tendon, and plantar fascia, but it was not significantly different from that in the proximal patellar or quadriceps tendon (p<0.001). The triceps, proximal patellar tendon, quadriceps, distal patellar tendon, plantar fascia, and Achilles tendon, in descending order of frequency, were affected in the HC group. The incidence of enthesitis was significantly higher in the triceps tendon than in the other tendons (p<0.001). The incidence of thickness was significantly higher than that of other lesions in the PsO group, while the incidence of retrocalcaneal bursitis was significantly lower than that of other lesions (p<0.001). In both the PsO and HC groups, the incidence of thickness was significantly higher than that of other lesions (p<0.001) (Table V).

TABLE IV. Comparison of the first and last examination measurements of the PsO group

		First examination (31)	Last examination (26)	p
MASEI scores	Mean ± std. deviation	9.84 ± 7	16.3 ± 9.3	**<0.001**[1]
	Median (25-75. percentile)	7 (4-14)	16 (8-24)	
MASEI ≥18	n (%)	11 (35)	5 (16.1)	0.070[2]
Plantar fascia	Mean ± std. deviation	0.65 ± 1.45	1.58 ± 2.25	**0.008**[1]
	Median (25-75. percentile)	0 (0-2)	1 (0-3)	
Achilles tendon	Mean ± std. deviation	1 ± 1.48	2.08 ± 1.62	**0.001**[1]
	Median (25-75. percentile)	0 (0-2)	2 (1-3)	
Distal Patellar tendon	Mean ± std. deviation	1.38 ± 2.12	2.19 ± 2.47	**0.005**[1]
	Median (25-75. percentile)	0 (0-2)	1.5 (0-4)	
Proximal patellar tendon	Mean ± std. deviation	1.48 ± 2.01	2.42 ± 2.42	**0.002**[1]
	Median (25-75. percentile)	1 (0-2)	2 (0-4)	
Quadriceps tendon	Mean ± std. deviation	2.48 ± 2.99	3.88 ± 2.64	**0.005**[1]
	Median (25-75. percentile)	2 (0-3)	3.5 (2-6)	
Triceps tendon	Mean ± std. deviation	2.81 ± 2.04	4.12 ± 2.27	**<0.001**[1]
	Median (25-75. percentile)	2 (1-4)	4 (2-6)	
PASI	Mean ± std. deviation	5.51 ± 3.9	4.83 ± 5.1	0.426[1]
	Median (25-75. percentile)	4.5 (2.5-8.2)	3.3 (0.5-7.3)	
NAPSI- hand	Mean ± std. deviation	7.13 ± 10.3	6.24 ± 7.93	0.943[1]
	Median (25-75. percentile)	3.5 (0-12)	3.75 (0-9.3)	
NAPSI-foot	Mean ± std. deviation	6.14 ± 11.76	6.85 ± 7.09	0.115[1]
	Median (25-75. percentile)	1.3 (0-7)	5 (0-15.2)	
Sparc	Mean ± std. deviation	0.07 ± 0.35	0.22 ± 0.85	0.317[1]
	Median (25-75. percentile)	0 (0-0)	0 (0-0)	
Structural abnormalities	Mean ± std. deviation	1.97 ± 2.55	3.48 ± 2.26	**0.001**[1]
	Median (25-75. percentile)	1 (0-4)	3 (2-4)	
The thickness of enthesis	Mean ± std. deviation	3.48 ± 2.26	3.58 ± 2.4	0.554[1]
	Median (25-75. percentile)	3 (2-4)	3 (2-5)	
Erosion	Mean ± std. deviation	0.58 ± 0.99	0.96 ± 1.28	**0.024**[1]
	Median (25-75. percentile)	0 (0-1)	0 (0-2)	
Calcification	Mean ± std. deviation	0.97 ± 1.05	3.73 ± 2.81	**<0.001**[1]
	Median (25-75. percentile)	1 (0-1)	4 (1-5)	
Doppler activity	Mean ± std. deviation	0.32 ± 0.75	0.19 ± 0.63	0.234[1]
	Median (25-75. percentile)	0 (0-0)	0 (0-0)	
Retrocalcaneal Bursitis	Mean ± std. deviation	0.06 ± 0.36	0.15 ± 0.46	0.157[1]
	Median (25-75. percentile)	0 (0-0)	0 (0-0)	

[1]Wilcoxon test, 2McNemar test. MASEI MAdrid Sonographic Enthesitis Index, NAPSI Nail Psoriasis Severity Index, PASI Psoriasis Area and Severity Index.

DISCUSSION

Enthesitis is the clinical manifestation of an inflammatory disorder. It can also arise from trauma, mechanical overuse, or metabolic conditions. The poor inter-observer reliability in clinical identification of enthesitis and lack of precision in its diagnosis justify the need for alternative imaging modalities, such as magnetic resonance imaging and US. US has many practical advantages over magnetic resonance imaging, such as low cost, ease of access to multiple anatomical sites, and higher sensitivity and specificity for peripheral entheses lesions[24,25]. We evaluated the role of US in the diagnosis of subclinical enthesitis in patients with PsO, factors affecting enthesitis, and progression of enthesitis in patients with PsO at 1-year follow-up, using MASEI scoring.

Similar to other studies, we found that the mean

TABLE V. Comparison of the incidence of enthesitis location and features in the PsO and HC groups within the group and between the groups

Categories	PsO (31) n (%)	HC (30) n (%)	p
Plantar fascia	8 (25.8)	2 (36.7)	0.081[2]
Achilles tendon	13 (41.9)	1 (3.3)	**<0.001**[1]
Distal Patellar tendon	14 (45.2)	3 (10)	**0.002**[1]
Proximal patellar tendon	20 (64.5)	8 (26.7)	**0.005**[1]
Quadriceps tendon	22 (71)	5 (16.7)	**<0.001**[1]
Triceps tendon	29 (93.5)	25 (76.7)	0.081[2]
p*	**<0.001**[1]	**<0.001**[1]	
Structural abnormalities	17 (54.8)	8 (26.7)	**0.025**[1]
Enthesis thickening	31 (100)	26 (86.7)	0.053[2]
Erosion	10 (32.3)	0 (0)	**0.001**[2]
Calcification	19 (61.3)	6 (20)	**0.001**[1]
Doppler activity	6 (19.4)	3 (10)	0.473[2]
Retrocalcaneal Bursitis	1 (3.2)	0 (0)	1.00[2]
p**	**<0.001**[1]	**<0.001**[1]	

[1] Chi square test, [2] Fisher's exact test. HC Healthy control, PsO Psoriasis, P* - The incidence of enthesitis was significantly higher in the triceps tendon than in the other tendons (p<0.001). P** - In both the PsO and HC groups, the incidence of thickness was significantly higher than that of other lesions.

MASEI score was significantly higher in patients with PsO than in HCs[13-15,26]. We did not find any correlation between the mean MASEI score and the duration or severity of PsO, BMI, or age. These observations are supported by those of several other studies[13,16,17,27]. In a study by Gisondi *et al.*, enthesis score evaluated using the Glasgow Ultrasound Enthesitis Scoring System (GUESS) was found to be directly related to age and BMI in both patients with PsO and controls; however, similar to our finding, the score was not correlated with PASI value, disease duration, and severity[13]. Chen *et al.* concluded that PsO severity, age, and BMI were independent risk factors for the development of synovoenthesitis. They also reported no difference in the severity of skin lesions between the sub-PsA and clinical PsA phases[6]. Zuliani *et al.* observed more widespread enthesis inflammation on US in patients with high PASI score, confirming the close relationship between the skin and entheses in patients with PsO[14]. Huang *et al.,* reported a modest correlation between GUESS and Brown University Nail Enthesis Scale scores in the PsA group[28]. In contrast, Graceffa *et al.* reported a correlation between enthesis thickness and BMI[29]. Furthermore, Moshrif *et al.* concluded that a positive correlation exists between enthesitis and age, disease duration, BMI, and hyperuricemia[29]. We did not find any correlation between sex and MASEI score. While the results of the study by Moshrif[30] were the same as those of our study, Zuliani found a high rate of active enthesitis among males, which was attributed to occupational overload[14]. No statistically significant differences in MASEI score was found between PsO patients with nail involvement and those without nail involvement in our study. These results are consistent with those of several other studies[14-17]. However, Ash *et al.,* who found significantly higher enthesopathy scores in patients with nail disease than in those without, concluded that nail involvement frequently underlies systemic subclinical enthesopathy[31]. Likewise, El Miedany *et al.* reported that structural joint damage or extensor tendon enthesopathy and nail changes were associated[32]. These studies support the suggestion that clinical evidence of nail involvement may be related with enthesopathy in PsO patients. Increased enthesis scores and/or enthesis thickness are more common in patients with PsA than in those with PsO[26,28]. These results in existing literature highlight the necessity for more extensive, long-term research on age, BMI, disease duration and severity, with more participants.

In our study, the incidence of increased thickness in the PsO and HC groups was significantly higher than that of other lesions. In addition to the literature that supports widespread involvement of the lower extremity enthesis regions[6,15,27,30] we concluded that the triceps tendon can also be involved early in the course of the disease, and its thickness measured at that stage is as valuable as that of the proximal patellar and quadriceps tendons. Graceffa *et al.* reported that the thicknesses of the lateral and medial enthesis areas of the elbow, superior pole of the patellar tendon, and tibial insertion

of the patellar tendon were significantly higher in patients with PsO than in HCs[29]. Graceffa *et al.* showed also the thickness of the triceps tendon in PsA patients higher than PsO patients and HCs but they did not find any significant differences between PsO patients and HCs[29]. Zuliani *et al.* reported that enthesitis is mostly observed in the proximal patellar tendon, and the most common lesion is increase in enthesis thickness[14]. On the contrary, Vyas *et al.* reported that the Achilles tendon was the most affected area among participants, and the most common elementary lesion detected was loss of a fibrillar pattern[17]. Huang et al. reported that the distal patellar and Achilles tendons were significantly thicker in PsA than in PsO[28]. Involved enthesis areas were determined as Achilles, distal patellar, proximal patellar, quadriceps, and plantar aponeurosis entheses, in descending order of frequency, in the study by Moshrif *et. al.*[30] Based on these studies; it is difficult to determine the most commonly affected tendon in patients with PsO. Our results may be due to the excessive use of the upper extremity in both the patient group (mostly housewives) and the healthy controls (mostly health care workers). Even if we think that it is due to repetitive movements, triceps thickness was found to be higher in the PsO patients than in HCs. Hence, the triceps tendon, which is easily accessible, should also be scanned with US to detect and follow up subclinical enthesopathy in these patients. Although we do not yet have scientific evidence in patients with subclinical enthesitis, we may recommend daily life activities specific to areas where enthesitis is detected. We may suggest to avoid of repetitive traumas, and customized exercise programs.

There was no significant difference in mean Doppler activity and retrocalcaneal bursitis between the two groups. Similar to our finding, Zuliani *et al.* reported no difference in power Doppler activity alone between the two groups[14]. They emphasized that the grading of power Doppler activity should be studied in the future. The Doppler activity may not be determined particularly in the very early stages of the disease[29]. We think that we were would not able to obtain Doppler activity because we included cases without complaints or sensitivity in the enthesitis area in the present study.

Tinazzi *et al.* reported that 23% of patients with subclinical PsO transitioned to the PsA phase within a mean of 13 months. This rate was 15.4% at 1-year follow up. Polyarticular involvement was detected in two patients, oligoarticular involvement in five, and plantar fasciitis and Achilles tendinitis in three. The GUESS scores did not change significantly during the follow-up period. The baseline GUESS scores of patients with PsO who developed PsA or osteoarthritis were significantly higher than those of patients who remained symptom-free after 3.5 years of follow up, but no statistical difference was found between the GUESS scores of patients with PsO who developed PsA and those who did not. The researchers determined that the basal thickness of the quadriceps tendon was an independent indicator of PsA development[33]. In our study, sacroiliitis was detected in one patient, polyarticular involvement in one patient, and oligoarticular involvement in two patients. We did not find any significant differences in age, sex, BMI, MASEI score, NAPSI score, PASI, smoking, alcohol use, or family history between patients who developed PsA and those who did not. Furthermore, we could not identify any independent indicator of PsA development. In our study, the initial enthesitis scores and CRP values of the four patients diagnosed with PsA were not significantly higher than those of patients who did not develop PSA. In contrast, Elnady *et al.* found that patients diagnosed with PsA had higher initial subclinical enthesitis, synovitis, and CRP levels[15]. In our study, at the 1-year follow up, the MASEI score and average structure, erosion, and calcification measurements in each tendon were significantly higher than those obtained at the first examination in the PsO group. This increase was not related to ESR, CRP, vitamin D levels, PASI or NAPSI score, disease duration, ANA, HLA B27 positivity, occupation, smoking, or alcohol consumption. Hence, this result leads to the conclusion that the risk of inflammation in the enthesis area in patients with PsO increases independently of these variables, and even if the patients do not have any complaints or symptoms, they require annual follow-up US scans.

Eder *et al.* divided MASEI score into two subgroups: MASEI inflammatory (entheseal thickening, structural changes, bursitis, and vascularization) and MASEI damage (calcifications, enthesophytes, and erosions) scores. In this study, the highest MASEI damage score was recorded among patients with PsA, while no difference was found between patients with PsO and HCs. This finding is considered to have low specificity[26]. We concluded that chronic changes such as erosion and calcification are more common in patients with PsO than in HCs, although such observations are generally not reported in the literature[6,17,26]. A review found that evaluation of chronic changes, such as the presence of erosions, was more likely to reveal the underlying inflammatory pathology[24]. Similarly, in the present study significantly higher chronic changes in the enthesis areas of patients with PsO was determined, but can this be explained by chronic inflammation in PsO or mechanical factors? This should be further investigated in the future.

While many studies have investigated and emphasized enthesis of the lower extremities, our study

showed that triceps thickness is also an important parameter in demonstrating enthesis in this patient group. The significance of acute changes, such as thickness and structural changes, was demonstrated in our study, although we also observed that chronic changes were more common in patients with PsO than in HCs. The importance of early diagnosis and treatment of PsA is well-established[4,7]; however, the detection, follow up, and treatment of patients with PsO in the preclinical phase have rarely been studied. There is no consensus regarding the frequency of screening Sub-PsA patients. Haroon et al suggested that a 6-month delay from symptom onset to the first visit with a rheumatologist contributed to worse radiographic damage and worse long-term physical function.[34] We could not reach definitive information about how often these patients should be followed up from the results of our study. Nevertheless, musculoskeletal US may play an important role in the follow up of patients with PsO in the future because of advantages such as cost-effectiveness, ease of access, and sensitivity for detection and follow-up of enthesitis. The limited number of patients in our study renders it difficult to comment on variables that affect enthesopathy and the development of PsA in patients with PsO. The strength of our study is that, unlike many previous studies on enthesis in PsO that were cross-sectional, the patients in our study were followed up for 1 year.

CONCLUSION

In conclusion, US is an important tool for diagnosis and follow-up of subclinical entheses in patients with PsO. Although we do not have clinical evidence, we may advise daily life activities specific to these enthesis areas. We may suggest avoiding repetitive trauma, and customized exercise programs for patients with subclinical enthesitis. Regardless of disease duration and severity, patients should be screened using US at regular intervals. There is no definitive information about how often these patients should be followed. However, these regular screenings prevent delay in the diagnosis of PsA, thus, increase the chance of early treatment and minimizing the risk of comorbidity.

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