ORIGINAL ARTICLES

UDC: 616.517-06:616.7-073
DOI: https://doi.org/10.2298/VSP191014041D

Assessment of enthesitis in patients with psoriasis: relationships with clinical features, screening questionnaires results, and quality of life – An ultrasound study

Procena prisustva entezitisa kod bolesnika sa psorijazom: povezanost sa kliničkim karakteristikama, rezultatima *screening* upitnika i kvalitetom života – ehosonografska studija

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Abstract

Background/Aim. Often asymptomatic, enthesitis can be an integral feature of the wide clinical spectrum in psoriasis as well as an early sign of development of psoriatic arthritis (PsA). It may be difficult to clinically recognize enthesitis in patients with psoriasis or distinguish it from other causes of extraarticular pain. Ultrasound (US) expanding use with the development of accurate assessments through standardized US algorithms as the Glasgow Ultrasound Enthesis Scoring System (GUESS) and the Madrid Sonographic Enthesitis Index Scoring System (MASEI) scores made the US the dominant imaging technique in diagnosing enthesitis. The aims of this study were to establish the prevalence of US signs of enthesitis, compare it with screening questionnaires results, and estimate possible connections of US verified enthesitis with quality of life (QOL) of patients with psoriasis without PsA diagnosis. **Methods.** A cross-sectional study was performed on 67 patients with psoriasis who were without systemic therapy. The clinical presence of enthesitis was examined by an experienced rheumatologist, and systemic inflammation was estimated through serum level of C-reactive protein (CRP). The Psoriasis Area Severity Index (PASI) and Body Surface Area-Psoriasis (BSA-PsO) were calculated by a dermatologist. Visual analogue scale (VAS) for pain, screening questionnaires – the Toronto Psoriatic Arthritis Screening (ToPAS), Psoriasis Epidemiology Screening Tool (PEST), Psoriatic Arthritis Screening and Evaluation (PASE), Early Psoriatic Arthritis Screening Questionnaire (EARP), and Psoriasis and Arthrosis Screening Questionnaire (PASQ) – were filled by patients. GUESS and MASEI scores were determined by US. The QOL was estimated by the Dermatology Life Quality Index (DLQI). **Results.** The presence of clinical enthesitis was recorded in 8.7% of patients. According to US signs of enthesitis using GUESS and MASEI scores, only 7% and 2% of patients, respectively, had no sign of enthesitis. Duration of psoriasis and age of subjects were in a significant correlation with GUESS and MASEI scores, while systemic inflammation, VAS value, PASI, and BSA-PsO scores were not. GUESS and MASEI scores significantly correlated with scores of all screening questionnaires as well as with DLQI. **Conclusion.** US can detect subclinical enthesitis better than clinical examination and widely used screening questionnaires, even though the correlations between MASEI and/or GUESS scores and results of screening questionnaires were positive. US examination is important in the multidisciplinary approach in diagnosing and managing psoriasis.

Key words:
arthritis, psoriatic; psoriasis; surveys and questionnaires; tendons; ultrasonography; quality of life.

Apstrakt

Uvod/Cilj. Iako je često asimptomatski, entezitis može biti sastavni deo širokog spektra kliničke prezentacije psorijaze, ali i rani znak ispoljavanja psorijaznog artritisa (PsA). Obično je teško prepoznati prisustvo entezitisa kod bolesnika sa psorijazom, a posebno je teško razlikovati ga od drugih uzroka ekstraartikularnog bola. Ehosonografija

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(ES) je postala sastavni deo ispitivanja reumatoloških bolesnika, a u pogledu dijagnostike entezitisa suverena metoda, sa standardizovanim ES algoritmima kao što su *Glasgow Ultrasound Enthesis Scoring System* (GUESS) i *Madrid Sonographic Enthesitis Index Scoring System* (MASEI) skorovi. Ciljevi ove studije bili su da se ustanovi prevalenca ES znakova prisustva entezitisa, da se uporede ti rezultati sa razultatima *screening* upitnika i da se ispita moguća povezanost entezitisa dokazanog pomoću ES sa kvalitetom života kod bolesnika sa psorijazom, bez dijagnoze PsA. **Metode.** Sprovedena je studija preseka kod 67 bolesnika sa psorijazom koji nisu bili lečeni sistemskom terapijom. Prisustvo klinički manifestnog entezitisa utvrđivano je pregledom reumatologa, sistemska inflamacija je procenjivana na osnovu serumske kocentracije C-reaktivnog proteina (CRP). Indeksi *Psoriasis Area Severity Index* (PASI) i *Body Surface Area-Psoriasis* (BSA-PsO), kao mere zahvaćenosti kože, određivani su od strane dermatologa. Ispitanici su sami popunjavali vizuelnu analognu skalu (VAS) bola i *screening* upitnike za prisustvo PsA – *Toronto Psoriatic Arthritis Screening* (ToPAS), *Psoriasis Epidemiology Screening Tool* (PEST), *Psoriatic Arthritis Screening and Evaluation* (PASE), *Early Psoriatic Arthritis Screening Questionnaire* (EARP) i *Psoriasis and Arthrosis Screening Questionnaire* (PASQ). Skorovi GUESS i MASEI određivani su pomoću ES. Kvalitet života je procenjivan na osnovu *Dermatology Life Quality Index* (DLQI) upitnika. **Rezultati.** Kliničkim pregledom, entezitis je ustanovljen kod 8,7% ispitanika. Na osnovu ES ispitivanja preko GUESS i MASEI skorova, samo 7%, odnosno 2% ispitanika nije imalo znake entezitisa. Trajanje psorijaze i životno doba ispitanika bili su u značajnoj korelaciji sa vrednostima GUESS i MASEI skorova, dok sistemska inflamacija, vrednosti VAS, PASI i BSA-PsO skorova nisu pokazali značajnu povezanost. Skorovi GUESS i MASEI bili su u značajnoj korelaciji sa skorovima svih *screening* upitnika, kao i sa DLQI skorom. **Zaključak.** Primenom ES može se dokazati entezitis češće nego kliničkim pregledom ili pomoću *screening* upitnika, mada je postojala korelacija između MASEI i/ili GUESS skorova sa rezultatima *screening* upitnika. ES je značajna dijagnostička metoda u multidisciplinarnom pristupu dijagnostici i lečenju psorijaze.

Ključne reči:
artritis, psorijazni; psorijaza; ankete i upitnici; tetive; ultrasonografija; kvalitet života.

Introduction

In patients suffering from psoriasis (PsO), a chronic immune-mediated skin disease with a prevalence of 1%–3% in the general population, numerous comorbidities and other related conditions occur more frequently: psoriatic arthritis (PsA), inflammatory bowel disease, anxiety, non-alcoholic fatty liver disease, metabolic syndrome, cardiovascular diseases, and depression [1]. The prevalence of PsA has been estimated to be between 6% and 42% in PsO, and according to systematic review and meta-analysis of 266 observational and clinical studies examining 976,408 patients with PsO, it is 19.7% [2]. Arthritis presentation can vary from subtle manifestations to highly destructive forms. Joint and low back pain, stiffness, and swelling, as well as dactylitis, are the most common symptoms, and they are easily recognized by rheumatologists or dermatologists.

Enthesitis is included in the Classification Criteria for Psoriatic Arthritis (CASPAR) for diagnosing PsA as one of the hallmarks [3]. On the other hand, according to the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommendations for treatment of PsA, enthesitis is one of the domains that decides the modality of treatment [4]. Similar to other arthritis-related diseases, early treatment of PsA is expected to control joint damage, which usually occurs within the first 2 years of disease [2]. Unrecognized PsA characteristics, especially early signs like enthesitis, can delay the diagnosis of PsA [1]. Bagel and Schwartzman [5] reported that the average diagnostic delay of PsA in a combined population of patients with mild, moderate, and severe psoriasis is about 5 years. Even a 6-month delay in PsA diagnosis can adversely affect structural and functional long-term outcomes. It can be one of the reasons why systematic reviews and meta-analyses estimated an overall prevalence of undiagnosed PsA among PsO patients of 15.5% [6].

In diagnosing enthesitis in PsO, dermatologists and rheumatologists use clinical examination as the first step, by palpation of some entheses included in indices like Leeds Enthesitis Index (LEI) or Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC). It may be difficult to clinically recognize enthesitis in patients with PsO or distinguish it from other causes of extraarticular palpation pain in fibromyalgia, mechanical injury, or comorbid musculoskeletal condition.

Several self-administered screening questionnaires have been developed and validated for identifying patients with PsA: Toronto Psoriatic Arthritis Screening (ToPAS) tool, Psoriasis Epidemiology Screening Tool (PEST), the Psoriatic Arthritis Screening and Evaluation (PASE), and the Early Psoriatic Arthritis Screening Questionnaire (EARP). Some of them (ToPAS, PEST, and EARP) have only questions about joint pain and swelling, especially fingers, wrists, elbows, hips, or dactylitis. These screening questionnaire tools can have limited usefulness in enthesitis diagnosis because of the heterogeneous nature of PsO and PsA. Some other musculoskeletal disorders might be identified as the cause of false-positive or false-negative results. On the other hand, according to the meta-analysis of Iragorri et al. [7], these questionnaires have a sensitivity of 0.65–0.85 and specificity of 0.73–0.87. It was calculated that 13%–35% of patients with PsA cannot be recognized early using these questionnaire tools. Enthesitis as unrecognized distinction PsA is considered important and may be crucial for early diagnosis and treatment of the disease and slow down its progression regarding the role of enthesitis in the pathogenesis of PsA [8]. These facts have contributed to an increase in the

importance of imaging techniques in recent years. Ultrasound (US) is considered more dominant to the diagnosis of enthesitis than magnetic resonance imaging (MRI) because it is cheaper and the assessment through standardized US algorithms is more accurate [9]. Several algorithms have been developed, including the most commonly used and exact Glasgow Ultrasound Enthesis Scoring System (GUESS) and the Madrid Sonographic Enthesitis Index Scoring System (MASEI) as the best standards in standardized enthesitis US assessment [10–12].

The impact of PsO on worse quality of life (QOL) has been well-documented in the clinical practice and literature and, in order to quantify it, numerous simple practical questionnaires for routine clinical use were made, among them, the Dermatology Life Quality Index (DLQI) as the most used, important, and reliable. It was developed by Finlay and Khan [13] in 1994 and Finlay et al. [14], and regarding some modifications of DLQI, a lot of analyses proved the reliability of DLQI.

Besides psoriatic plaques, itching, dandruff, peeling, bleeding, nail changes, other musculoskeletal involvement, as well as arthritis, dactylitis, and enthesitis lead to chronic pain and worsening movement and additionally deteriorate QOL in PsO.

The aims of this study were to establish the prevalence of US signs of enthesitis in patients with PsO without a diagnosis of PsA, to compare it with screening questionnaires results, and to estimate possible connections of US verified enthesitis in PsO patients on their QOL as an independent parameter.

Methods

Patients

This cross-sectional study included participants selected according to the following criteria: diagnosis of PsO without a diagnosis of PsA and volunteer participation. The study sample included 67 subjects with PsO who met the CASPAR classification criteria for the diagnosis (42 males, 25 females) with a mean age of 47.0 years. The mean disease evolution time was 14.9 years. Patients, who met the entry criteria, were informed and gave consent according to the ethical standards of the Helsinki Declaration of 1983 and ICH-GCP. Exclusion criteria included a diagnosis of PsA, osteoarthritis, fibromyalgia or mechanical injury, previous knee, ankle, or elbow surgery, a record of systemic conventional, targeted biologic therapy, or corticosteroid injection into any of the sites to be explored. The Military Medical Academy Ethics Committee approved this study on October 24, 2018. The clinical presence of enthesitis was examined by an experienced rheumatologist. Systemic inflammation was estimated through serum levels of C-reactive protein (CRP). The collection of demographic and case history data was performed by reviewing case notes and treatment records.

Psoriasis Area Severity Index (PASI) and Body Surface Area – Psoriasis (BSA-PsO) were calculated by a dermatologist.

Self-administered screening questionnaires and QOL determination

Visual Analogue Scale (VAS) for pain, ToPAS tool, PEST, PASE, EARP, and the Psoriasis and Arthritis Screening Questionnaire (PASQ) were filled by the patients themselves, and the results were calculated by a dermatologist. QOL was estimated by the Serbian version of the DLQI, also filled by patients. The DLQI consists of ten questions regarding the following topics: symptoms, humiliation, shopping and home care, clothes, social and recreation, sport, work or study, close relationships, gender, and treatment. Each question (scored from 0 to 3) estimates the influence of the skin disorders on the QOL during the previous 7 days. A possible score range is between 0 and 30.

Ultrasound evaluation

The US was conducted by an experienced radiologist, using a Mindray, Resona 7 ultrasound system (Shenzhen Mindray Bio-Medical Electronics Co, China), with a 7–12 MHz linear array transducer, and the MASEI and GUESS indices were calculated.

The MASEI measurement and scoring implies examination of: 1) Inferior pole of the calcaneus: plantar aponeurosis enthesis – plantar aponeurosis structure (0 or 1), plantar aponeurosis thickness > 4.4 mm (0 or 1), inferior pole of calcaneus erosion (0 or 3), inferior pole of calcaneus enthesis calcification (0, 1, 2 or 3), plantar aponeurosis enthesis power Doppler (0 or 3); 2) Superior pole of the calcaneus: Achilles tendon enthesis – Achilles tendon structure (0 or 1), Achilles tendon thickness > 5.29 mm (0 or 1), retrocalcaneal bursitis (0 or 1), posterior pole of calcaneus erosion (0 or 3), posterior pole of calcaneus enthesis calcification (0, 1, 2 or 3), posterior pole of calcaneus power Doppler (0 or 3); 3) Tibial tuberosity: distal patellar ligament enthesis – patellar ligament structure (0 or 1), patellar ligament thickness 0.4 mm (0 or 1), infrapatellar bursitis (0 or 1), tibial tuberosity erosion (0 or 3), tibial tuberosity enthesis calcification (0, 1, 2 or 3), tibial tuberosity enthesis power Doppler (0 or 3); 4) Inferior pole of the patella: proximal patellar ligament enthesis – patellar ligament structure (0 or 1), patellar ligament thickness 0.4 mm (0 or 1), inferior pole of patella erosion (0 or 3), inferior pole of patella enthesis calcification (0, 1, 2 or 3), inferior pole of patella enthesis power Doppler (0 or 3); 5) Superior pole of the patella: quadriceps tendon enthesis: quadriceps tendon structure (0 or 1), quadriceps tendon thickness > 6.1 mm (0 or 1), superior pole of patella erosion (0 or 3), superior pole of patella enthesis calcification (0, 1, 2 or 3), superior pole of patella enthesis power Doppler (0 or 3); 6) Olecranon tuberosity: triceps tendon enthesis – triceps tendon structure (0 or 1), triceps tendon thickness 4.3 mm (0 or 1), olecranon erosion (0 or 3), olecranon enthesis calcification (0, 1, 2 or 3), olecranon enthesis power Doppler (0 or 3).

The total possible score on both sides (12 entheses) is 136. According to international statements, sensitivity of the MASEI is 83.3%, specificity 82.8%, positive predictive value 80.8%, negative predictive value 85.7%, positive likelihood

ratio (LR+) 4.87, negative likelihood ratio (LR-) 0.19. The MASEI score greater than 18 is considered as significant [11].

The GUESS measurement and scoring means examination of: 1) Superior pole of the patella (quadriceps tendon enthesis): quadriceps tendon thickness > 6.1 mm, suprapatellar bursitis, superior pole of patella erosion, superior pole of patella enthesophyte; 2) Inferior pole of the patella (proximal patellar ligament enthesis): patellar ligament thickness > 4 mm, inferior pole of patella erosion, inferior pole of patella enthesophyte; 3) Tibial tuberosity (distal patellar ligament enthesis): patellar ligament thickness > 4 mm, infrapatellar bursitis, tibial tuberosity erosion, tibial tuberosity enthesophyte; 4) Superior pole of the calcaneus (Achilles tendon enthesis): Achilles tendon thickness > 5.29 mm, retrocalcaneal bursitis, posterior pole of calcaneus erosion, posterior pole of calcaneus enthesophyte; 5) Inferior pole of the calcaneus (plantar aponeurosis enthesis): plantar aponeurosis thickness > 4.4 mm, inferior pole of calcaneus erosion, inferior pole of calcaneus enthesophyte; Each item scores one point. The total possible score on both lower limbs is 36 [10].

Statistical analysis

Using IBM SPSS Statistics version 19.0 (SPSS, Chicago, IL, USA), statistical analysis was performed. Categorical variables were presented as frequency. All continuous variables are presented as mean ± standard deviation (SD). The Shapiro-Wilk test was used to test the normality of data distribution. One-way ANOVA and *t*-test for dependent samples were used to investigate differences between groups for parametric variables and χ^2 test for nonparametric variables. The relation between variables was evaluated using the Pearson's coefficient correlation. Observations were considered significant if two-tailed *p* values were below 0.05.

Results

Demographic, clinical data, results of self-administered screening questionnaires, clinical and US enthesitis examination, and QOL questionnaires of the 57 patients with PsO are presented in Table 1.

According to our results, the presence of clinical enthesitis was recorded in 8.7% of the patients. According to US signs of enthesitis using the GUESS score, only 4 out of 57 patients with PsO without a diagnosis of PsA (7%) had no sign of enthesitis indicating high frequency of subclinical or clinical enthesitis in these subjects. The total possible score on both lower limbs is 36, and the average GUESS score was 13 in our sample.

According to the MASEI score, one subject had no sign of US verified enthesitis. The mean value of the MASEI score was high in our subjects (27). As the MASEI score has the cut off value ≥ 18, 75% of our patients with PsO and without a diagnosis of PsA had significant enthesitis with a score of 32.6.

Our analysis suggested that only the duration of PsO and age of subjects were in a significant correlation with the GUESS and MASEI scores, while systemic inflammation (estimated through CRP concentration), the VAS value, PASI, and BSA scores were not in correlation with US enthesitis scores (Table 2).

Table 1

Demographic, clinical data, self-administered screening questionnaires, quality of life (QOL) questionnaires, and ultrasound (US) enthesitis examination in patients with psoriasis (n = 57)

Parameter	Values
Age (years), mean ± SD (range)	47.0 ± 16.5 (14–82)
Male/female, n	42/25
Duration of disease (years), mean ± SD	14.9 ± 12.2 (1–54)
CRP (in referent level/increased), n (%)	59 (88)/8 (12)
PASI, mean ± SD (range)	11.3 ± 8.13 (0–42.6)
BSA-PsO, mean ± SD (range)	25.6 ± 13.4 (2–48)
VAS, mean ± SD (range)	1.1 ± 2.2 (0–7)
ToPAS, mean ± SD (range)	5.6 ± 2.1 (3–12)
PEST, mean ± SD (range)	1.1 ± 1.0 (0–4)
PASE, mean ± SD (range)	28.8 ± 13.5 (15–72)
EARP, mean ± SD (range)	1.8 ± 2.3 (0–9)
PASQ, mean ± SD (range)	2.2 ± 2.3 (0–8)
Presence of clinical enthesitis, n (%)	5 (8.7)
GUESS, mean ± SD (range)	13.0 ± 5.6 (0–22)
MASEI, mean ± SD (range)	27.0 ± 13.0 (0–57)
MASEI > 18 [n = 51 (75%)], mean ± SD (range)	32.6 ± 8.3 (18–57)
DLQI, mean ± SD (range)	10.1 ± 7.1 (0–30)

SD – standard deviation; CRP – C-reactive protein; PASI – Psoriasis Area Severity Index; BSA-PsO – Body Surface Area-Psoriasis; VAS – Visual Analogue Scale; TOPAS – Toronto Psoriatic Arthritis Screening; PEST – Psoriasis Epidemiology Screening Tool; PASE – Psoriatic Arthritis Screening and Evaluation; EARP – Early Psoriatic Arthritis Screening Questionnaire; PASQ – Psoriasis and Arthrosis Screening Questionnaire; GUESS – Glasgow Ultrasound Enthesitis Scoring System; MASEI – Madrid Sonographic Enthesitis Index Scoring System; DLQI – Dermatology Life Quality Index.

Table 2

Pearson's correlation coefficients between clinical characteristics and ultrasound (US) scores in patients with psoriasis (n = 57)

Parameter	GUESS score		MASEI score	
	r	*p*	r	*p*
Age (years)	0.10	ns	0.37	< 0.05
Duration of disease (years)	0.48	< 0.05	0.43	< 0.05
CRP: in referent level/increased	0.08	ns	0.11	ns
PASI	-0.25	ns	-0.16	ns
BSA	-0.15	ns	-0.13	ns
VAS	0.11	ns	0.08	ns

For abbreviations see under Table 1.

All investigated subjects filled the PsA screening questionnaires. Results are presented in Table 3.

When we analyzed paired results of screening questionnaires with US enthesitis scores, both scores (GUESS and MASEI) significantly correlated with scores of all screening questionnaires. The GUESS score was the most correlated with the PASE score, followed by the EARP, PASQ, ToPAS, and in the less manner with the PEST score. In the case of the MASEI score, the best correlation was achieved with the EARP score, followed by the PEST, PASQ, PASE, and finally ToPAS score (Table 4).

We also estimated the effects of US verified enthesitis on QOL, by investigating the relationship between the GUESS and MASEI scores with DLQI scores. In this study, the average DLQI in the patients with PsO was 10.1 ± 7.1.

With the aim to escape confounding effects, we included correlations of age, duration of disease, VAS, CRP concentrations, the PASI, and BSA on DLQI (Table 5). Model

Table 3

Results of psoriatic arthritis (PsA) screening questionnaires filled by patients with psoriasis and without the diagnosis of PsA (n = 57)

Questionnaire	Questions (n)	Cut-off score	Subjects with positive questionnaire results n (%)
ToPAS	12	8	9 (15.7)
PEST	5	3	67 (10.5)
PASE	15	47	10 (17.5)
EARP	10	3	20 (35.0)
PASQ	10	7	6 (10.5)

For abbreviations see under Table 1.

Table 4

Pearson's correlation coefficients between screening questionnaire results and ultrasound (US) scores in patients with psoriasis (n = 57)

Questionnaire	GUESS score		MASEI score	
	r	*p*	r	*p*
ToPAS	0.36	< 0.05	0.33	< 0.05
PEST	0.26	ns	0.36	< 0.05
PASE	0.37	< 0.05	0.37	< 0.05
EARP	0.40	< 0.05	0.42	< 0.05
PASQ	0.35	< 0.05	0.39	< 0.05

For abbreviations see under Table 1.

Table 5

Pearson's correlation coefficients between age, duration of the disease, CRP value and PASI, BSA-PsO, VAS, GUESS and MASEI scores with DLQI score in patients with psoriasis (n = 57)

Parameter	DLQI score	
	r	*p*
Age	-0.01	ns
Duration of disease	-0.07	ns
CRP (in referent level/increased)	0.11	ns
PASI score	0.38	< 0.05
BSA-PsO score	0.35	< 0.05
VAS score	0.41	< 0.05
GUESS score	0.74	< 0.05
MASEI score	0.59	< 0.05
MASEI score < 18	0.65	< 0.05
MASEI score > 18	0.37	< 0.05

For abbreviations see under Table 1.

of linear regression analysis was performed to avoid false results and to confirm the potential relationship between the GUESS and MASEI scores with DLQI scores. It showed that US results are independently connected with the DLQI scores ($R^2 = 0.13$, $^{®} = 4.383$; $p < 0.05$).

Discussion

Enthesitis is part of the CASPAR criteria for PsA and the target for PsA treatment as one of the domains in GRAPPA recommendations. Patients with PsO independently of PsA have a higher prevalence and more severe enthesitis compared to healthy controls [15].

Clinical examination has low sensitivity and specificity, detecting generally swelling and tenderness, and limitations which include a risk of missing clinical or subclinical enthesitis and mimicking other conditions. Polachek et al. [16], using only clinical examination in patients with PsO, identified 15% of subjects with enthesitis as part of possible undiagnosed PsA[16]. In our sample, only 5/57 (8.7%) psoriatic patients with enthesitis were identified by clinical examination (Table 1). Ranza et al. [17] demonstrated a higher frequency (30%) in a cross-sectional study similar to a population-based study from Olmstead County (23%) [18] or Lehtinen et al. [19] (15%). A similar prevalence like in our study was observed in Iceland population-based study (8%) [20].

When the Outcome Measures in Rheumatology (OMERACT) team has defined criteria for US visualized enthesitis: hypoechogenicity, increased tendon penetration thickness, enthesophytes, calcifications, erosions, and Doppler activity, numerous US scores were developed but the GUESS and MASEI scores approved as much reliable and they are most widely used in different clinical trials [21]. They are also applicable for patients with skin PsO alone [22]. When we used the GUESS score, the average value in our subjects was 13 of maximal 36, and 98.2% of them had US signs of enthesitis on at least one point of interest. In literature, by using the GUESS score, signs of enthesitis were found in 90–95.5% of patients with PsO depending on US mode [23, 24]. In the same ULISSE trial, US assessment results were similar in patients with PsA and PsO and significantly higher than in the healthy controls or fibromyalgia population [23]. It was also shown in other studies that the GUESS score was much higher in the patients with PsO without joint and entheseal symptoms compared to age-matched healthy controls. In the study by Gisondi et al. [15], the mean GUESS score was significantly higher in patients with PsO (n = 30) compared with healthy subjects (n = 30): 7.9 vs. 2.9, respectively, while Pistone et al. [22] found a significantly higher the GUESS score in 59 patients with PsO in comparison to 59 patients with other dermopathies.

Using a US MASEI score with a cut-off value of more than 18, we found in the same sample 75% of patients with enthesitis with an average value of 32.6 (maximal score being 36). Eder et al. [25] compared total MASEI score in patients with PsA (n = 50), psoriatic patients (n = 66) and healthy controls (n = 60) [25]. Total MASEI scores were higher in patients with PsA than in those with PsO, with both being higher than in healthy control ($p < 0.0001$, among all groups). The sensitivity of a MASEI score ≥ 18 to correctly classify patients as having PsA was 90% among patients with psoriatic diseases. The specificity was 89% when compared to patients with psoriatic disease (PsA and PsO) [21]. The study of Hamdy et al. [26] included 50 patients with PsO and 20 age- and sex-matched healthy controls. Similar to our results, enthesitis was detected by US in 37 patients (74%) with PsO and 3 (15%) healthy controls with median MASEI scores of 27.8 and 4.3, respectively. In the study by Van der Ven et al. [27], in 542 primary care PsO patients, which were US evaluated, 36% had the MASEI score greater than 18, but some typical structural changes were observed in 95% of PsO patients. On the contrary to our study, 97% of them were treated with systemic therapy (biologics or immunomodulatory drugs).

According to some opinions, US enthesitis scores can predict the development of PsA. Tinazzi et al. [28] performed longitudinal evaluation using repeat ultrasound assessment through the GUESS score in a cohort of 30 cases of PsO for 3.5 years. At follow-up, 23% fulfilled CASPAR criteria, and in the logistic regression analysis, baseline higher values of GUESS score were found to be an independent predictor of the development of PsA. The association between the baseline GUESS score and the development of PsA was strong. In the study by El Miedany et al. [29], 126 psoriatic patients were prospectively evaluated by US at 0, 6, and 12 months for enthesitis, and increased probability for structural progression development in the presence of enthesitis was observed (OR = 3.50). Therefore, they concluded that the presence of enthesitis and higher GUESS score at baseline are predictors of progressive, early PsA [29].

According to our results, the age of a patient and duration of PsO have a significant influence on the presence of enthesitis detected by US, while systemic inflammation (measured as CRP level), pain, body mass index, PASI, and BSA-PsO have no impact on the presence of enthesitis (Table 2). In the study of Eder et al. [25], MASEI enthesopathic changes correlated moderately with age but also with BMI. Gisondi et al. [15] reported the same manner of significant correlation between the GUESS score and aging, as well as BMI. Like in our study, Macıa-Villa and De Miguel [21] did not observe the correlation between th MASEI score and BMI.

Macıa-Villa and De Miguel [21] in the systematic review of the literature concluded that in most studies, the MASEI score did not correlate with CRP levels, except in the study of Falcao et al. [30], which is in concordance with our results.

We found a significant correlation of the MASEI and GUESS scores with the duration of the disease but not with the PASI and BSA_Pso scores. In the study of Gisondi et al. [15], in 30 subjects with PsO, the GUESS score was not correlated either with the duration or severity of the disease according to the PASI and BSA-PsO. In the other analysis of Girolomoni and Gisondi [32], the association between the GUESS score and PASI score was found, but a significant correlation with the disease duration, age, and BMI was not. In the ULISSE study, in 51 patients with PsO, the GUESS

score significantly correlated with the disease duration [15], like in our study, but also with BMI. According to Polachek et al. [16], more pain was associated with US signs of enthesitis, which is not in agreement with our results. Rezvani et al. [33] also found a positive correlation between enthesitis and pain. We can conclude that connections of enthesitis with different variables of PsO are not still clear.

Screening questionnaires (PEST, PASE, ToPAS, PASQ, and EARP) can be used to help during the examination of early identification of signs and symptoms of PsA, although their usefulness is partially limited because of the incapacity to differentiate structural changes, missing subclinical and manifesting enthesitis, especially in patients with central sensitization and/or pain amplification, depression, and comorbid musculoskeletal conditions independent of PsA. Most of these questionnaires, except for the EARP and PEST, have no question about enthesitis, thus their sensitivity and specificity are from 0.66 to 0.85 and from 0.76 to 0.83, respectively. Recent developed Simple Psoriatic Arthritis Screening (SiPAS) questionnaire between five, have one question about pain in heels with sensitivity and specificity of 0.79 and 0.87, respectively [34]. Regarding our results, both US scores (GUESS and MASEI) were in a significant correlation with all screening questionnaires (Table 4). The MASEI score, especially, has a good correlation with EARP and PEST scores (containing question about possible enthesitis) and the GUESS score with PASE (the most detailed) and EARP scores. We confirmed their relative usefulness in detecting subclinical or manifesting enthesitis in PsO.

In this study, the average DLQI in the patients with PsO was 10.1 ± 7.1. It is worse than the mean DLQI (5.9 ± 5.9) from the cross-sectional study of Langenbruch et al. [35] on 1,243 participants with PsO. Among our patients, 63% had a DLQI score in the range from 0 to 1, PsO had no effect on the patient's QOL. The low effect (DLQI 2–5) reported 16% of examinees, moderate effect (DLQI 6–10) 9%, very large or extremely large effect (DLQI 11–20 or 21–30) 10% and 2%, respectively. In the previously mentioned study [35], 21.3% of subjects had DLQI > 10. For example, Finlay and Khan [13] in 52 subjects with PsO reported a DLQI score of 8.9 ± 6.3, higher than in 100 healthy volunteers (0.5 ± 1.1), matched for age and major comorbidities; availability was confirmed using the test-retest method, which is in accordance with our results. In many studies [35, 36], a significant direct correlation between the PASI and the DLQI score was detected, which was also found in our study.

Our study is the first one that showed that a strong correlation between US verified subclinical enthesitis and QOL exists, i.e. between the MASEI and GUESS scores, and on the other hand, the DLQI score in the patients with PsO ($r = 0.59$, $p < 0.001$; $r = 0.74$, $p < 0.001$, respectively). In the available literature, we were unable to find studies that correlated the MASEI and GUESS scores with DLQI in patients with psoriasis. Pain and limitation of movements can be some of the reasons. Moreover, Rezvani et al. [33] found a positive correlation between enthesitis and low QOL in subjects with spondyloarthritis, which was explained by higher pain scores. An analysis of data from the Corrona registry showed that QOL in PsA is significantly worse in patients with enthesitis compared to those without enthesitis, including functional status, patient-reported pain, fatigue, sleep disturbance, working abilities, and experience of overall impairment [6].

Conclusion

US can detect subclinical enthesitis in patients with psoriasis as a component of a wide spectrum of its clinical picture or possible early sign of subsequent development of PsA, better than widely used screening questionnaires, although the correlations between MASEI and/or GUESS scores and results of screening questionnaires were positive. It is widely available and can be used repeatedly. Enthesitis verified by US and other imaging techniques may provide better insight into the effect of psoriasis on their QOL as one of the key outcomes in the comprehensive care of these patients. US examination is important in the multidisciplinary approach in the diagnosis and management of patients with psoriasis.

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Received on October 14, 2019
Revised on March 31, 2020
Accepted on April 9, 2020
Online First April, 2020