

# Ultrasonographic detection of subclinical enthesitis and synovitis: a possible stratification of psoriatic patients without clinical musculoskeletal involvement

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## Abstract

### Objective

To evaluate the prevalence of articular/extra-articular inflammatory lesions and structural damage on ultrasonography in patients suffering from psoriasis as well as to assess possible correlations between ultrasonographic elementary lesions and clinical features.

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### Methods

Psoriatic patients without musculoskeletal symptoms and healthy controls (HCs) were recruited. All patients received a blinded extended ultrasonographic examination of 42 joints, 12 entheses and 32 tendons. Active synovitis was defined by the presence of a grade  $\geq 2$  for grey scale (GS) and  $\geq 1$  for power Doppler (PD), while active enthesitis corresponded to enthesal hypoechogenicity in GS and enthesal PD signal ( $< 2$  mm from bone insertion).

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### Results

Forty psoriatic patients and 20 HCs were included. A total of 2516 joints and 712 entheses were scanned. Active synovitis was found in 11/40 (27.5%) psoriatic patients and 0/20 HCs ( $p=0.01$ ). Articular synovitis ( $GS \geq 2$ ) was more frequent in psoriasis than in HCs [34/40 (85.0%) and 11/20 (55.0%) respectively;  $p=0.024$ ]. Active enthesitis was found only in psoriatic patients, with a prevalence of 20.0% (8/40) ( $p=0.04$ ). No significant difference in the prevalence of tenosynovitis or paratenonitis was observed between psoriatic patients and HCs. In psoriasis cohort, age was correlated with the presence of active synovitis ( $p=0.03$ ), while male sex and a higher PASI score were independently correlated with the presence of active enthesitis ( $p=0.05$  and  $p=0.034$ , respectively).

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### Conclusion

Active enthesitis and synovitis could be useful to identify subclinical psoriatic arthritis. This might represent a relevant clinical step to better stratify patients with psoriasis.

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### Key words

psoriatic arthritis, enthesitis, psoriasis, ultrasonography, imaging

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## Introduction

Psoriasis (Pso) is an immune-mediated inflammatory skin disease affecting around 2% of Caucasian population. Growing evidence indicates that inflammation associated with Pso may also result in systemic consequences (*e.g.* arthritis, uveitis and metabolic syndrome), thereby justifying the concept of “psoriatic disease” (1). Psoriatic arthritis (PsA) is one of the most common clinical manifestations (1), with a prevalence of 6% to 42% among psoriatic patients (2). It is characterised by different possible musculoskeletal manifestations, such as peripheral arthritis, enthesitis, dactylitis and spondylitis (3). In most cases, skin lesions precede the onset of arthritis by several years, thus providing a unique opportunity to study a pool of patients suffering from psoriasis at risk of developing PsA (4). A possible preclinical stage of PsA has not been clearly defined so far, though several recent studies focused on the role of ultrasonography (US) to detect subclinical inflammatory lesions in Pso, especially lower limbs enthesitis (5). However, there is a lack of studies assessing synovial and soft tissue as well as prospective analyses (6). Indeed, there is only one US study investigating extra-entheseal structures (*e.g.* synovitis) in psoriatic patients which showed a significant increase in subclinical synovitis (without reporting the grade of synovitis) compared to healthy controls (HCs) (*i.e.* 50.7% in Pso versus 32.6% in HCs) (7). Additionally, imaging prospective studies showed that both symptoms related to arthralgia and subclinical synovitis and enthesitis independently influenced the risk of developing PsA in psoriatic patients (8, 9).

In our study, we carried out a cross-sectional extended clinical and US evaluation of Pso patients without musculoskeletal symptoms assessing enthesal and extra-entheseal sites (*i.e.* synovium, bursa and tendon) in order to stratify Pso patients based on US and identify possible correlations between US elementary lesions and clinical features.

## Methods

### Study population

This is a cross-sectional study including psoriatic patients without clinical

musculoskeletal involvement and gender- and age-matched randomly selected HCs. Pso patients were referred to the Rheumatology Institute of the University Hospital of Udine (Italy) by dermatologists of the same Hospital and by primary healthcare physicians. Inclusion criteria for Pso patients were: (I) age >18 years; (II) cutaneous and/or nail psoriasis diagnosed by a dermatologist; (III) lack of fulfilment of CASPAR criteria; and (IV) absence of present/past signs/symptoms of arthritis, dactylitis, enthesitis or inflammatory back pain (evaluated by a rheumatologist with expertise in assessment of PsA). Exclusion criteria were: (I) the use of cDMARDs, steroid therapy (oral and intra articular) and NSAIDs during the previous three months from enrolment; and (II) previous or current use of retinoids, bDMARDs or small molecules (*e.g.* JAK inhibitors or PDE4i).

### Rheumatological assessment

For each patient, we recorded demographic data, including age, sex, body mass index (BMI), smoking history, alcohol intake and comorbidities (obesity, diabetes type II, hypertension, metabolic syndrome, fatty liver disease, inflammatory bowel disease, uveitis, depression, neoplastic disease, cardiovascular disease). Articular and enthesal examination, including joint count (66/68 joints) and tenderness at 13 entheses (Maastricht Ankylosing Spondylitis Enthesitis Score) plus quadriceps patellar insertion, proximal and distal patellar insertion, plantar fascia and common extensor tendon insertion, was performed by a rheumatologist with significant expertise in PsA. Articular regions that had suffered from bone fractures or had undergone surgical procedures were excluded from the clinical examination. A mild joint tenderness, which is commonly detected also in HCs, was not an exclusion criterion. Possible previous manifestations consistent with PsA were excluded by an accurate medical history. Each patient completed a Numerical Rating Scale (NRS) questionnaire for musculoskeletal pain, a health assessment questionnaire (HAQ) to document physical function and a Bath Ankylosing Spondylitis Disease Activ-

Competing interests: none declared.

ity Index (BASDAI) for disease activity assessment. The study procedures were performed in accordance with the standards of the Helsinki Declaration and an informed consensus was signed by all participants.

#### *Dermatological assessment*

Dermatological assessment was performed by a Dermatologist of the Dermatologic Institute of the University Hospital of Udine. Psoriasis subtype, nail involvement, age at disease onset and previous medications for cutaneous or nail psoriasis were recorded. Severity of psoriasis and nail involvement were scored according to the Psoriasis Area and Severity Index (PASI) and Nail Psoriasis Severity Index (NAPSI), respectively.

#### *Ultrasonography*

US assessment was performed by rheumatologists (FZ, AZ) with significant clinical and US experience in the early detection of PsA, using an ESAOTE MyLab ClassC equipped with a linear probe at 6–18 MHz. US grey-scale (GS) imaging parameters were optimised for maximal image resolution and power Doppler (PD) settings were standardised at the following values: 750 Hz for pulse repetition frequency for synovial hypertrophy and 500 Hz for entheses evaluation, 3 for wall filter, 4 for persistence and colour gain between 50–55%. The US exam was blinded to the patient's clinical findings and skin disease and was performed in a darkened room. Each patient was asked not to undress but only to discover, from time to time, the anatomic site to be studied. Moreover, sonographer was asked to focus only on the examination site not talking with the patient about clinical and dermatological condition to reduce possible biases. Synovitis was evaluated by including its two components (*i.e.* joint effusion and synovial hypertrophy) according to OMERACT definition (10) and it was scored from 0 to 3 (11, 12). Active synovitis was considered to be present if both grey scale inhomogeneity (GS  $\geq 2$ ) and intra articular Power Doppler (PD) signal ( $\geq 1$ , score 0–3) were detected. According to OMERACT definition, the following enthe-

seal elementary lesions were recorded: hypoechogenicity, increased thickness, enthesophytes, erosions and PD activity  $< 2$  mm from enthesis (13). Active enthesitis was defined as the presence of PD signal within 2 mm from bony attachment and GS-hypoechogenicity. Tenosynovitis was defined, in accordance to OMERACT definition, as GS hypoechoic or anechoic thickened tissue with or without fluid within the tendon sheath, which is seen in two perpendicular planes (score 0–3) (14), while paratenonitis was defined as GS hypoechoic swelling surrounding the extensor digitorum tendon, associated with subcutaneous edema (score 0–1) (15). We used the terms “active tenosynovitis” and “active paratenonitis” to identify the presence of both tendon GS inhomogeneities and PD signal. In the evaluation of structural damage we considered the presence of osteoproliferation [defined as cortical protrusion of the bony surface (score 0–1) (16, 17)] and/or erosions [defined as intrarticular interruption of the cortical contour of bone seen in two perpendicular planes (score 0–1) (18)]. Target joints, tendons and entheses were selected according to the protocol of the recently started UP-STREAM study on PsA sponsored by Italian Society of Rheumatology (19, 20). For each patient, a longitudinal and transverse PDUS examination of 42 joints (Metacarpophalangeal (MCP), proximal (PIP) and distal (DIP) interphalangeal joints, wrists, knees, metatarsophalangeal (MTP) joints), 12 entheses (Achilles, quadriceps, proximal and distal patellar, plantar aponeurosis and common extensor tendon entheses), retrocalcaneal bursa and 32 tendons (extensor digitorum tendons, flexor digitorum tendons and extensor tendon compartments of the wrist) was performed. Articular regions that had suffered from bone fractures or had undergone surgical procedures were excluded from US assessment.

#### *Statistical analysis*

Quantitative variables were presented as means with standard deviations (SD), medians and interquartile range. Categorical variables were presented as absolute frequencies and percentages.

Comparisons between independent means were analysed using Wilcoxon Mann Whitney test, while accurate Fisher test for categorical variables was used to evaluate differences between groups. Interobserver reliability was studied by calculating kappa statistics (21).

## **Results**

### *Demographic and clinical features of population*

Demographic and clinical features of 40 Pso patients and 20 HCs are showed in Table I. There was no significant difference in gender, age, BMI, smoking exposure and comorbidities distribution between the Pso group and HCs, while HCs had a significantly higher prevalence of alcohol consumption. A mild joint tenderness was recorded in 10/40 (25%) Pso patients and 1/20 (5%) HCs ( $p=0.08$ ). Among Pso patients, 37/40 (92.5%) were affected by psoriasis vulgaris, while 30/40 (75%) presented nail involvement, with a mean ( $\pm$ SD) PASI score of  $3.5 \pm 2.6$  and a mean ( $\pm$ SD) NAPSI score of  $8.7 \pm 8.0$ , respectively. Two patients were previously treated with cyclosporine and corticosteroids for cutaneous psoriasis 3 and 10 years before the enrolment, respectively.

### *US assessment*

The inter-observer agreement between the 2 sonographers, considering all the studied elementary lesions, was 0.82.

### *Synovitis*

US was performed in a total of 2516 joints; 4 articular sites were excluded from evaluation due to previous surgery or bone fractures. Considering all the studied joints, the prevalence of articular synovitis was statistically higher in Pso than HCs ( $p=0.0001$ ) (Table II). When evaluating joint involvement for each subject, psoriatic cohort showed a significantly higher prevalence of active synovitis (GS  $\geq 2$  and PD  $\geq 1$ ), with a figure of 27.5% (11/40) vs. 0.0% (0/20) in HCs ( $p=0.01$ ). Such a finding was also observed when excluding MTP joints [8/40 (20.0%) in Pso vs. 0/20 (0.0%) in HCs;  $p=0.04$ ]. On the other hand, no difference was found between the two groups when considering mild articular

**Table I.** Demographic and clinical data at baseline.

| Baseline data                         | Pso group<br>(n=40) | Control group<br>(n=20) | p-value |
|---------------------------------------|---------------------|-------------------------|---------|
| Sex, n. (%)                           |                     |                         |         |
| Men                                   | 17 (42.5)           | 8 (40)                  | 1.000   |
| Women                                 | 23 (57.5)           | 12 (60)                 |         |
| Age, mean ( $\pm$ SD)                 | 51 ( $\pm$ 16)      | 47 ( $\pm$ 16)          | 0.290   |
| BMI, mean ( $\pm$ SD)                 | 25 ( $\pm$ 4.1)     | 24 ( $\pm$ 4.3)         | 0.098   |
| Family history of PsA, n. (%)         | 10 (25.6)           | 1 (5)                   | 0.079   |
| Smoke history                         |                     |                         |         |
| never, n. (%)                         | 23 (57.5)           | 10 (50)                 | 0.699   |
| former, n. (%)                        | 5 (12.5)            | 4 (20)                  |         |
| active, n. (%)                        | 12 (30)             | 6 (30)                  |         |
| Alcohol intake                        |                     |                         |         |
| never, n. (%)                         | 22 (55)             | 3 (15)                  | 0.005   |
| less than monthly, n. (%)             | 7 (17.5)            | 4 (20)                  |         |
| one or more times per week, n. (%)    | 10 (25)             | 13 (65)                 |         |
| daily (< 1/2 lt), n. (%)              | 1 (2.5)             | 0 (0)                   |         |
| daily (> 1/2 lt), n. (%)              | 0 (0)               | 0 (0)                   |         |
| Comorbidities                         |                     |                         |         |
| Obesity, n. (%)                       | 4 (10)              | 1 (5)                   | 0.656   |
| Type II Diabetes Mellitus, n. (%)     | 3 (7.5)             | 2 (10)                  | 1.000   |
| Hypertension, n. (%)                  | 6 (15)              | 5 (25)                  | 0.481   |
| Metabolic syndrome, n. (%)            | 4 (10)              | 4 (20)                  | 0.422   |
| Fatty liver disease, n. (%)           | 4 (10)              | 1 (5)                   | 0.656   |
| Inflammatory bowel disease, n. (%)    | 1 (2.5)             | 0 (0)                   | 1.000   |
| Uveitis, n. (%)                       | 2 (5)               | 0 (0)                   | 0.548   |
| Depression, n. (%)                    | 2 (5)               | 0 (0)                   | 0.548   |
| History of cancer, n. (%)             | 2 (5)               | 0 (0)                   | 0.548   |
| Ischaemic heart disease, n. (%)       | 3 (7.5)             | 1 (5)                   | 1.000   |
| Clinimetrics                          |                     |                         |         |
| Tender joints                         |                     |                         |         |
| 1, n. (%)                             | 7 (17.5)            | 0 (0)                   | 0.060   |
| > 1, n. (%)                           | 3 (7.5)             | 1 (5)                   |         |
| Tender entheses, n. (%)               | 3 (7.5)             | 0 (0)                   | 0.544   |
| NRS pain, mean ( $\pm$ SD)            | 2 ( $\pm$ 2.4)      | 2 ( $\pm$ 2.4)          | 0.685   |
| BASDAI, mean ( $\pm$ SD)              | 2 ( $\pm$ 2.2)      | 1 ( $\pm$ 1.8)          | 0.483   |
| HAQ, mean ( $\pm$ SD)                 | 0 ( $\pm$ 0.3)      | 0 ( $\pm$ 0.2)          | 0.599   |
| Psoriasis history                     |                     |                         |         |
| Type of psoriasis                     |                     |                         |         |
| Vulgaris, n. (%)                      | 37 (92.5)           |                         |         |
| Pustular, n. (%)                      | 1 (2.5)             |                         |         |
| Erythrodermic, n. (%)                 | 0                   |                         |         |
| Guttate, n. (%)                       | 1 (2.5)             |                         |         |
| Nail, n. (%)                          | 30 (75)             |                         |         |
| Inverse, n. (%)                       | 1 (2.5)             |                         |         |
| Psoriasis onset, yrs mean ( $\pm$ SD) | 21 ( $\pm$ 23)      |                         |         |
| Baseline PASI, mean ( $\pm$ SD)       | 3.5 ( $\pm$ 2.6)    |                         |         |
| Baseline NAPSI, mean ( $\pm$ SD)      | 8.7 ( $\pm$ 8.0)    |                         |         |

synovitis (at least one joint with GS $\geq$ 1), even if non-active (*i.e.* independently of PD positivity or negativity) [40/40 (100.0%) in Pso *vs.* 19/20 (95.0%) in HCs;  $p=0.33$ ). However, the number of involved joints was significantly higher in Pso than in HCs (7.5 $\pm$ 4.0 *vs.* 3.9 $\pm$ 2.5 joints per patient respectively;  $p=0.001$ ). Notably, prevalence was significantly higher in Pso than HCs when considering moderate-severe articular synovitis (GS  $\geq$ 2) [34/4 (85.0%) *vs.* 11/20 (55.0%) respectively;  $p=0.024$ ],

still with more affected joints in the former than in the latter (3.15 $\pm$ 2.63 *vs.* 1.1 $\pm$ 1.33, respectively;  $p=0.001$ ).

#### Enthesitis and bursitis

US was performed in a total of 712 enthesal sites; 8 sites were excluded from assessment due to previous bone surgery or fractures. The prevalence of active enthesitis was significantly higher in Pso (Table III). Considering enthesal involvement per patient, active enthesitis was exclusively found

in Pso patients, with a prevalence of 20.0% (8/40) ( $p=0.04$ ). GS hypoechogenicity (GS=1) was more frequent in Pso (20/40, 50.0%) than HCs (5/20, 25.0%), ( $p=0.09$ ). Conversely, PD signal distribution (within 2 mm from the cortical bone), without enthesal GS alterations, was similar in Pso and HCs (11/40, 27.5% *vs.* 4/20, 20% respectively;  $p=0.75$ ). In addition, Pso patients had a higher mean enthesal thicknesses than HCs, although the only enthesal site reaching statistically difference was proximal patellar enthesitis ( $p=0.03$ ) (Table IV). No patient displayed US signs of bursitis, both in cases and controls.

#### Peri-tendinitis and tenosynovitis

Two out of 40 (5.0%) Pso patients and 0/20 HCs showed peritendinitis on MCP joints, but in both patients this was detected only in GS. US abnormalities of flexor tendons or extensor tendon compartments of the wrist were never detected in both psoriatic patients and HCs.

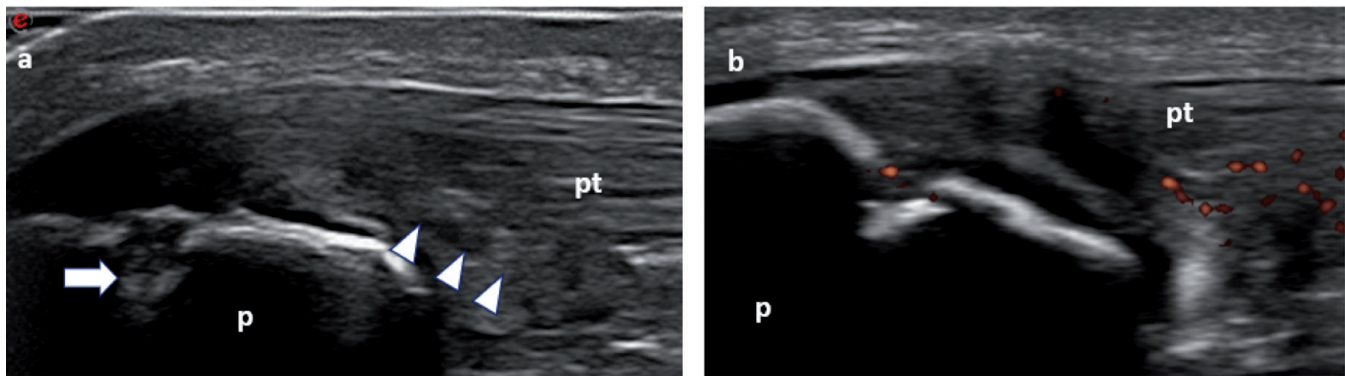
#### Structural damage

Bone erosions were detected only in the Pso group, both in joints (2/40 patients; 2.5%) and enthesal sites (2/40 patients; 2.5%), with involvement of II MCP and II PIP for joints and Achilles tendon and proximal insertion of patellar tendon for entheses. When considering all the evaluated joints, we found a significantly higher prevalence of osteoproliferation in Pso ( $p=0.006$ ), but, when considering the joint involvement per patient, no differences were noticed compared to HCs (Table V).

#### Correlation between US active synovitis and clinical features of psoriatic patients

In the Pso group, the age was the only variable significantly correlated with the presence of active synovitis, with older patients having a greater prevalence of subclinical joint involvement ( $p=0.03$ ). No association was seen with gender, BMI, smoke and alcohol exposure, comorbidities, psoriasis extent and severity, psoriatic nail disease severity, NRS pain, HAQ and BASDAI score (Table VI).





**Fig. 1.** Active enthesitis. Longitudinal scan of the patellar tendon (pt) and proximal insertion on patella (p) in B-mode (a) and Doppler mode (b). Enthesal erosion (white arrow) and enthesal hypoechoogenicity (white arrowheads).

**Table II.** Prevalence of GS inhomogeneities, PD signal and active synovitis in Pso and HC.

| US lesion                               | Joints          |              | p-value |
|---|-----------------|--------------|---------|
|   | Pso (n=1676)    | HC (n=840)   |         |
| GS $\geq$ 1, joint n. (%)               | 299/1676 (17.8) | 78/840 (9.3) | 0.0001  |
| GS $\geq$ 2, joint n. (%)               | 126/1676 (7.5)  | 22/840 (2.6) | 0.0001  |
| GS=3, joint n. (%)                      | 16/1676 (0.9)   | 3/840 (0.4)  | 0.142   |
| PD $\geq$ 1, joint n. (%)               | 78/1676 (4.6)   | 25/840 (3.0) | 0.054   |
| PD $\geq$ 2, joint n. (%)               | 21/1676 (1.3)   | 4/840 (0.5)  | 0.086   |
| PD=3, joint n. (%)                      | 2/1676 (0.12)   | 0            | 0.555   |
| GS $\geq$ 2 + PD $\geq$ 1, joint n. (%) | 22/1676 (1.3)   | 0            | 0.0002  |

**Table III.** Distribution of enthesal GS inhomogeneities, PD signal and active enthesitis in Pso and HC.

| US lesion                   | Entheses     |              | p-value |
|-----------------------------|--------------|--------------|---------|
|                             | Pso (n=472)  | HC (n=240)   |         |
| GS=1, entheses n. (%)       | 38/472 (8)   | 13/240 (5.4) | 0.221   |
| PD=1, entheses n. (%)       | 17/472 (3.6) | 7/240 (2.9)  | 0.827   |
| G=1 + PD=1, entheses n. (%) | 10/472 (2.1) | 0            | 0.019   |

**Table IV.** Mean enthesal thickness in Pso and HC

| Enthesis                            | Mean thickness  |                 | p-value |
|-------------------------------------|-----------------|-----------------|---------|
|                                     | Pso (n=472)     | HC (n=240)      |         |
| Achilles, mm ( $\pm$ SD)            | 4.28 $\pm$ 0.72 | 4.00 $\pm$ 0.6  | 0.1     |
| Quadriceps, mm ( $\pm$ SD)          | 6.02 $\pm$ 0.96 | 5.63 $\pm$ 0.93 | 0.134   |
| Proximal patellar, mm ( $\pm$ SD)   | 4.16 $\pm$ 0.58 | 3.71 $\pm$ 0.82 | 0.012   |
| Distal patellar, mm ( $\pm$ SD)     | 4.23 $\pm$ 0.82 | 4.09 $\pm$ 0.74 | 0.649   |
| Plantar aponeurosis, mm ( $\pm$ SD) | 3.46 $\pm$ 0.66 | 3.28 $\pm$ 0.95 | 0.363   |

#### Correlation between US enthesitis and the clinical features of psoriatic patients

A higher prevalence of active enthesitis among male Pso patients was observed ( $p=0.05$ ). Moreover, Pso patients with active enthesitis had a higher PASI score ( $4.5 \pm 1.41$ ) than patients without active enthesitis ( $3.23 \pm 2.84$ ;  $p=0.034$ ). Active enthesitis was not related with age, BMI, smoking and alcohol exposure, family history of PsA, comor-

bidity and nail disease severity (Table VI). Regarding baseline clinimetric features, Pso patients with enthesitis showed higher NRS general pain scores than Pso patients without enthesitis ( $3.36 \pm 2.86$  vs.  $1.26 \pm 2.0$ , respectively;  $p=0.15$ ), while HAQ and BASDAI scores were similar in the two groups.

#### Possible definition of subclinical PsA

If US criteria for active synovitis and/or active enthesitis (which were never

observed in HCs in this study) are used to define subclinical arthritis (*i.e.* without clinical signs of arthritis on physical examination), 40% of Pso patients showed a subclinical PsA.

#### Discussion

The importance of early diagnosis and treatment is well established in chronic arthritis (22), while the detection, follow-up and treatment of the preclinical phases of arthritis are poorly studied and might represent a significant advance in the future. In such a scenario, musculoskeletal ultrasonography could play a relevant role due to its sensitivity to detect synovitis and enthesitis (22–24). Recently, *Oddie* highlighted that psoriasis is the ideal disease to identify risk factors of progression because the risk pool group to develop arthritis is well-known (*i.e.* patients suffering from Pso) (25). Most of the previous US studies on Pso focused on enthesitis, while less is known about subclinical involvement of joint and tendinous synovia. Similarly to previous MRI studies (9), in this cross-sectional study we found that nearly one third (27.5%) of Pso patients without clinical features of arthritis had a subclinical active synovitis and 20% had a subclinical active enthesitis. Of note, synovitis was herein defined not only in terms of presence *versus* absence, as previously done, but also by grading GS and PD synovitis. In this way, the detection of higher degrees of synovitis increased the specificity of US. Interestingly, a moderate-severe synovitis (GS $\geq$ 2) with PD activity was observed only in Pso. Such a finding was also confirmed when excluding

**Table V.** Prevalence of joint and enthesal osteostructural damage in Pso and HC.

| US lesions (joints)                  | Pso (n=40)          | HC (n=20)         | p-value         |
|--------------------------------------|---------------------|-------------------|-----------------|
| Bone erosions, n. patients (%)       | 2 (5)               | 0                 | 0.548           |
| Osteoproliferation, n. patients (%)  | 33 (82.5)           | 14 (70)           | 0.326           |
| Osteoproliferation, mean ( $\pm$ SD) | 7.15 ( $\pm$ 7.16)  | 5.4 ( $\pm$ 5.47) | 0.390           |
|                                      | <b>Pso (n=1676)</b> | <b>HC (n=840)</b> | <b>p-values</b> |
| Osteoproliferation, joints n. (%)    | 286 (17.1)          | 108 (12.9)        | 0.006           |
| US lesions (entheses)                | Pso (n=40)          | HC (n=20)         | p-values        |
| Erosions, n. patients (%)            | 2/40 (5)            | 0                 | 0.548           |
| Osteoproliferation, n. patients (%)  | 36 (90)             | 16 (80)           | 0.145           |
| Osteoproliferation, mean ( $\pm$ SD) | 3.72 ( $\pm$ 2.46)  | 3.2 ( $\pm$ 2.71) | 0.389           |
|                                      | <b>Pso (n=472)</b>  | <b>HC (n=240)</b> | <b>p-values</b> |
| Osteoproliferation, entheses n. (%)  | 149 (31.6)          | 64 (26.7)         | 0.194           |

MTP joints from the evaluation, which commonly show US signs of joint inflammation also in HCs (26).

Moving to the enthesis, this study showed that only the combination of GS hypoechogenicity and enthesal PD activity was significantly associated with Pso compared to HCs. On the other hand, the sole presence of hypoechogenicity or PD activity  $<2$  mm near the body cortex did not differ significantly between the two groups. Although the enthesal PD signal within 2 mm of bone insertion has been established as elementary component of enthesitis (13), we did not observe any relevant difference in enthesal PD signal alone in Pso *versus* HCs. This discrepancy could be partly explained by the set-

tings of the machine as we set a lower PRF having a higher sensitivity for low flows (*i.e.* 500 Hz) to evaluate entheses. In addition, the development of a grading score also for the PD findings would be relevant in the future. Overall, the detection of US features being more specific for Pso (*i.e.* synovitis with GS $\geq$ 2 and active synovitis and enthesitis) may be helpful to detect a subclinical PsA in Pso patients without clinical symptoms and signs of PsA; this was found in about more than one third of patients with Pso. Conversely, tenosynovitis, bursitis and peritendinitis, which are other common PsA features, were rarely found in Pso cohort by US. Whether the presence of these additional US findings may better de-

fine subclinical PsA or they may just represent a following step in the progression towards PsA still remains an open question.

Notably, we found that patient's age was the only clinical variable significantly correlated with the presence of active synovitis in psoriatic subjects, with older patients having a higher prevalence of subclinical joint involvement. Moreover, males showed a higher prevalence of active enthesitis, likely due to the different occupational musculoskeletal demand and higher exposition to microdamage. Finally, we observed a more common enthesal inflammation on US assessment in patients with higher PASI score, thus confirming the close relationship between skin and entheses in psoriatic patient. On the other hand, no correlation between clinimetrics health and disability assessment questionnaires and US musculoskeletal inflammation was found.

The main strong point of this study is the exhaustive assessment of joint, entheses, bursae and tendons in well clinically characterised Pso patients while the principal limitation is the small sample size. So far, the clinical impact of this result is still limited. Prospective clinical and US evaluation – which goes beyond our purposes – with the objective of identifying possible US predic-

**Table VI.** Correlation between US active synovitis and entesitis and the clinical features of psoriatic patients.

| Variable                           | Active synovitis (n=11) | Not active synovitis (n=29) | p-value | Active enthesitis (n=8) | Not active enthesitis (n=22) | p-value |
|------------------------------------|-------------------------|-----------------------------|---------|-------------------------|------------------------------|---------|
| Age, mean $\pm$ SD                 | 60 (11)                 | 48 (16)                     | 0.03    | 56 (12)                 | 50 (17)                      | 0.361   |
| Gender, women n. (%)               | 5 (45.4)                | 18 (62.1)                   | 0.477   | 2 (25)                  | 21 (65.6)                    | 0.053   |
| BMI, mean $\pm$ SD                 | 27.24 (3.53)            | 24.75 (4.14)                | 0.079   | 26.35 (3.6)             | 25.2 (4.23)                  | 0.37    |
| Active smoker, n. (%)              | 2 (18.2)                | 10 (34.5)                   | 0.213   | 1 (12.5)                | 11 (34.4)                    | 0.546   |
| Alcohol intake (daily), n. (%)     | 0                       | 0                           | 0.383   | 0                       | 0                            | 0.65    |
| Family history of PsA, n. (%)      | 0                       | 10 (35.7)                   | 0.037   | 1 (12.5)                | 9 (29)                       | 0.653   |
| Obesity, n. (%)                    | 1 (9.1)                 | 3 (10.3)                    | 1.000   | 1 (12.5)                | 3 (9.4)                      | 1.000   |
| Type II diabetes mellitus, n. (%)  | 2 (18.2)                | 1 (3.4)                     | 0.178   | 1 (12.5)                | 2 (6.2)                      | 0.498   |
| Hypertension, n. (%)               | 2 (18.2)                | 4 (13.8)                    | 1.000   | 1 (12.5)                | 5 (15.6)                     | 1.000   |
| Metabolic syndrome, n. (%)         | 1 (9.1)                 | 3 (10.3)                    | 1.000   | 1 (12.5)                | 3 (9.4)                      | 1.000   |
| Fatty liver disease, n. (%)        | 1 (9.1)                 | 3 (10.3)                    | 1.000   | 1 (12.5)                | 3 (9.4)                      | 1.000   |
| Inflammatory bowel disease, n. (%) | 1 (9.1)                 | 0                           | 0.275   | 1 (12.5)                | 0                            | 0.2     |
| Uveitis, n. (%)                    | 1 (9.1)                 | 1 (3.4)                     | 0.479   | 0                       | 2 (6.2)                      | 1.000   |
| Depression, n. (%)                 | 1 (9.1)                 | 1 (3.4)                     | 0.479   | 0                       | 2 (6.2)                      | 1.000   |
| Neoplastic disease, n. (%)         | 1 (9.1)                 | 1 (3.4)                     | 0.479   | 1 (12.5)                | 1 (3.12)                     | 0.364   |
| CV disease, n. (%)                 | 1 (9.1)                 | 2 (6.9)                     | 1.000   | 1 (12.5)                | 2 (6.2)                      | 0.498   |
| PASI, mean $\pm$ SD                | 3.69 (2.49)             | 3.46 (2.71)                 | 0.701   | 4.5 (1.41)              | 3.23 (2.84)                  | 0.034   |
| NAPSI, mean $\pm$ SD               | 10.11 (7.02)            | 7.95 (8.82)                 | 0.188   | 9.86 (7.58)             | 8.04 (8.23)                  | 0.449   |
| NRS pain, mean ( $\pm$ SD)         | 1.73 (2.24)             | 1.8 (2.57)                  | 0.786   | 2.81 (2.7)              | 1.52 (2.36)                  | 0.198   |
| BASDAI, mean ( $\pm$ SD)           | 1.94 (2.33)             | 1.87 (2.27)                 | 0.872   | 2.1 (2.1)               | 1.83 (2.32)                  | 0.629   |
| HAQ, mean ( $\pm$ SD)              | 0.16 (0.28)             | 0.14 (0.32)                 | 0.871   | 0.11 (0.18)             | 0.15 (0.33)                  | 0.618   |

tor factors of developing PsA, will of course be of major additional value to clinical practice in order to identify risk factors to develop PsA in PsO patients. In conclusion, besides corroborating the well-known concept that psoriatic disease may have a subclinical joint involvement, we highlighted that active synovial and enthesal US findings might be useful to identify a subclinical PsA. This could represent a relevant clinical step to better stratify and manage patients with PsO.

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