Peritenon extensor tendon inflammation at metacarpophalangeal joints level: a valuable ultrasound finding in the differential diagnosis between psoriatic arthritis and rheumatoid arthritis?

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Abstract

Objective

Ultrasound (US) detection of peritenon extensor tendon inflammation (PTI) was found highly specific for spondylo-arthropathies (SpA), including psoriatic arthritis (PsA). However, this finding has not been extensively investigated. This study aimed to investigate the value of PTI at metacarpophalangeal (MCP) joint level in the differential diagnosis between rheumatoid arthritis (RA) and PsA, and analyse the differences between early (less than 1 year of disease duration) and established (more than 1 year of disease duration) disease groups.

Methods

Consecutive RA and PsA patients with clinical involvement of at least one MCP joint were enrolled. The 2nd to the 5th MCP joints of both hands were scanned on the dorsal aspect to detect intra-articular and peri-tendinous inflammatory findings using both B-mode and power Doppler (PD) mode.

Results

The study included a total of 69 patients, 37 patients with RA and 32 patients with PsA. PTI was found in a significantly higher number of patients with PsA rather than in RA patients. Conversely, there was no statistical difference in terms of PTI prevalence between RA and PsA patients in the early disease groups. On the other hand, no statistically significant difference was found in terms of synovitis prevalence between RA and PsA patients.

Conclusion

PTI was found more frequently in PsA rather than in RA patients. Nevertheless, since no statistically significant difference was found between RA and PsA patients with less than 1 year of disease duration, PTI may represent an inflammatory feature of the early phases of both the diseases.

Key words

ultrasound, rheumatoid arthritis, psoriatic arthritis, peritenon extensor tendon inflammation, early arthritis

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Introduction

Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are chronic inflammatory diseases characterised by several similarities and differences. The pathophysiology of RA and PsA is gradually becoming clearer, but many aspects of its cause remain unknown (1, 2). The common feature is represented by a persistent articular inflammation with synovial proliferation, which may generate irreversible joint damage with progressive loss of articular function. Conversely, enthesitis is considered a hallmark feature of seronegative spondyloarthropathies (SpA) and may help to differentiate rheumatoid from psoriatic inflammatory process. However, a number of studies have described an entheseal inflammatory involvement also in patients with RA.

High-resolution ultrasound (US) allows a detailed visualisation of joint and periarticular morpho-structural changes induced by chronic inflammation both in patients with RA and PsA (3-14).

In patients with chronic arthritis, one of the most widely scanned anatomical sites is the hand, and metacarpophalangeal (MCP) joints are frequently involved both in patients with RA and PsA (15, 16).

A pilot study showed that US evidence of peritenon extensor tendon inflammation (PTI) at MCP joint level could be helpful to differentiate PsA from RA patients (17). This inflammation is considered to occur due to enthesitis, because the finger extensor tendons at the MCP joint level are not covered by a synovial tendon sheath (18). However, to date there is still scarce evidence supporting its diagnostic value.

The aim of this study was to investigate the value of PTI at MCP joint level as a potential US finding in the differential diagnosis between RA and PsA. Moreover, we analysed the data with the aim of analysing the differences between early (less than 1 year of disease duration) and established (more than 1 year of disease duration) disease groups.

Methods

Patients

The study included a total of 69 patients, 37 patients with RA classified according to the ACR/EULAR 2010 criteria (19) and 32 patients with PsA classified according to CASPAR criteria (20). Patients had to fulfil the following inclusion criteria: age greater than 18 years, at least one MCP joint clinically involved (defined as the presence of tenderness and/or swelling) and being able to give informed consent. Exclusion criteria were diagnosis of other concomitant rheumatic diseases (*i.e.* osteoarthritis, gout, calcium pyrophosphate deposition disease, connective tissue diseases), history of hand fracture or surgery or presence of severe hand deformities and psoriasis skin involvement at the dorsal surface area of the MCP joints.

All patients were recruited consecutively from the outpatient and inpatient clinics of the Rheumatology Unit of the Università Politecnica delle Marche, Carlo Urbani Hospital (Jesi, Italy). This study was conducted as a cross-sectional, single-centre study. Both RA and PsA groups were divided according to disease duration, in order to analyse US PTI prevalence, as follows:

RA group (n=37):
a. less than 1 year of disease duration (early disease) (n=12)
b. more than one year of disease duration (established disease) (n=25)

PsA group (n=32):
a. less than 1 year of disease duration (early disease) (n=10)
b. more than one year of disease duration (established disease) (n=22)

This study was conducted according to the declaration of Helsinki and approved by the Institutional Review Board (Ethics Committee of the Marche Region, no. 262). Informed consent was obtained from all patients.

Clinical and laboratory assessments

An expert rheumatologist (MDC) performed the clinical examinations aiming at detecting tenderness and/or swelling at MCP joint level. Moreover, the collection of the following clinical data was performed: clinical history, disease duration, 28 tender and swollen joints count, disease activity measured by the 28-joint Disease Activity Score (DAS28) (21) for both RA and PsA pa-

tients, Clinical Disease Activity Index (CDAI) (22) for RA patients and Composite Psoriatic Disease Activity Index (CPDAI) (23) for PsA patients, visual analogue scale (VAS) for global pain and Health Assessment Questionnaire (HAQ) (24) for RA patients and a modified Health Assessment Questionnaire for SpA (HAQ-S) (25) for PsA patients. The following laboratory tests were also recorded: rheumatoid factor (RF), anti-citrullinated peptide (anti-CCP) antibodies, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Clinical and laboratory evaluation were performed on the same day as the US assessment.

US assessment

All US examinations were performed by an experienced musculoskeletal sonographer (TO), blinded to the clinical data. Patients were asked not to talk about their clinical condition with the US examiner. The 2nd to the 5th MCP joints of both hands were scanned for the presence/absence of the following pathological US findings using both B-mode and power Doppler (PD) mode:

- joint cavity widening (JCW) (B-mode)
- abnormal increase of intra-articular synovial fluid (B-mode)
- intra-articular synovial hypertrophy (B-mode)
- intra-articular PD signal (inside the fat pad and/or synovial tissue)
- hypoechoic swelling surrounding the extensor digitorum tendon (B-mode)
- peri-tendinous PD signal

The first MCP joint was not included because of its anatomy: different from the other MCP joints and more similar to a proximal interphalangeal joint.

The US examinations were performed using a MyLab Class C system (Esaote S.p.A., Genoa, Italy) equipped with a 6–18 MHz broad band multifrequency linear transducer. All MCP joints were scanned from the dorsal view using a multiplanar technique, adopting the indications provided by the EULAR standardised procedures for US in rheumatology (26). Both longitudinal and transverse scans were performed by slightly moving the transducer from radial to ulnar and from proximal to distal sides on dorsal aspect to enable maximum coverage of the anatomical surface area. To avoid compression of the tissues during the examination an appropriate amount of gel was used and the minimal compression with the probe was made.

US grey-scale imaging parameters were set in order to obtain maximal contrast between all the structures under examination. PD settings were standardised at the following values: pulse repetition frequency; 750 Hz, persistence; 4, wall filter; 3, and Doppler frequency; 9.1 MHz. The gain was set just below the level at which colour noise appears underlying bone (no flow should be visualised at the bony surface) (27). For the identification of synovial fluid and synovial hypertro-

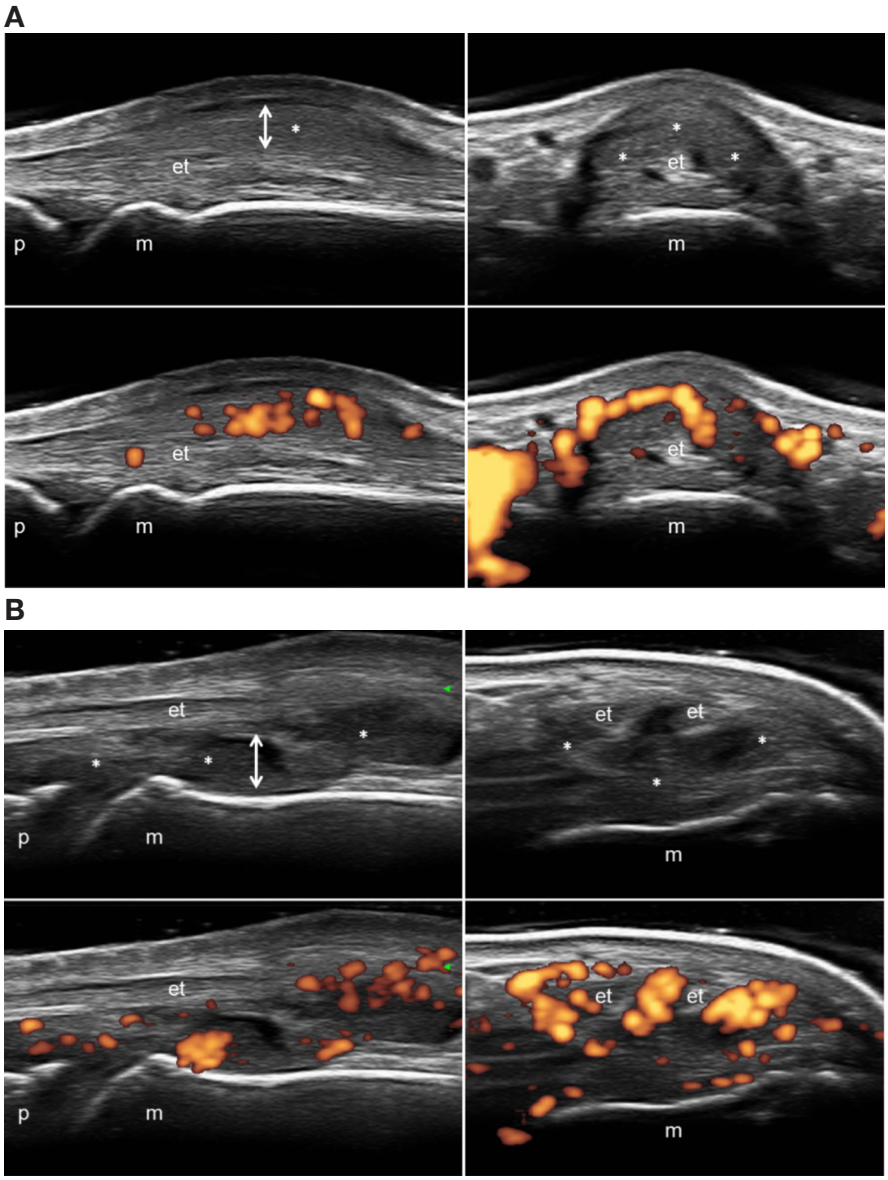

Fig. 1. Representative image of peritenon extensor tendon inflammation (PTI) pattern (**A**) and pseudo-PTI pattern (**B**).

A: Ultrasound image acquired on the dorsal aspect of a 3rd metacarpophalangeal (MCP) joint in patient with psoriatic arthritis showing typical sonographic PTI pattern. Hypoechoic synovial proliferation (*) is found between skin and extensor tendon (**arrow**) and power Doppler signal is at synovial tissue level.

B: Ultrasound image acquired on the dorsal aspect of a 2nd MCP joint in patient with long-standing rheumatoid arthritis showing pseudo-PTI pattern. Note the severe intra-articular synovial proliferation with power Doppler signals (*) which pushes up the joint capsule (**arrow**), reaches the sides of the finger extensor tendons and generates the pseudo-PTI pattern.

et: finger extensor tendon, **p**: proximal phalanx, **m**: metacarpal bone.

phy, the OMERACT preliminary definitions were adopted (28). US PTI was defined as an inflammatory lesion characterised by hypoechoic swelling of the soft tissue surrounding the extensor digitorum tendon, with or without peritendinous PD signal (17). Its presence was confirmed using both longitudinal and transversal views.

Pitfall of PTI pattern

Finger extensor tendons are not surrounded by synovial tissue at MCP joint level and in the case of PTI, PD signal adjacent to the extensor tendon is not a sign of blood flowing into synovial tissue hypertrophy. Figure 1A shows an US image with a representative example of PTI. However, in some cases, especially in patients with long-standing disease, severe intra-articular synovial proliferation, which may exhibit PD signal, can be depicted surrounding the finger extensor tendon. Figure 1B shows a pseudo-PTI pattern due to extensive inflamed intra-articular synovial proliferation which pushes up the joint capsule and reaches the sides of the finger extensor tendon.

Estimation of the sample size

The estimated ideal sample size was calculated according to a previous report (17). The results were that a practical design would aim for approximately 15–20 patients per group (*i.e.* 30–40 patients in total), which would typically yield around 60–80 joint evaluations per group if each patient contributes about 4 joints.

Statistical analysis

Two different assessments were taken: the first at MCP joint level, and the second at the patient level. Patients were judged positive for a specific US finding if at least one MCP joint was involved.

Standard descriptive statistics, including proportions for US findings, were expressed as mean and SD for demographic data. Comparison between US findings and clinical diagnosis was performed by χ^2 analysis. Statistical tests were considered significant at $p<0.05$. All p-values were 2-sided. All analyses were performed using GraphPad Prism

Table I. Demographic, clinical and laboratory characteristics of patients with RA and PsA.

Characteristic	RA patients (n=37)	PsA patients (n=32)
Age (years)	55.5 (12.0)	59.4 (10.6)
Women	23 (62.2)	13 (40.6)
Disease duration (months)	98.3 (104.2)	82.3 (89.0)
Rheumatoid factor positive	27 (73.0)	N/A
Anti-CCP antibody positive	26 (70.3)	N/A
ESR (mm/h)	24.0 (21.6)	21.5 (15.2)
CRP (mg/dl)	1.6 (1.8)	1.2 (1.4)
VAS for global pain (mm)	57.6 (27.9)	51.6 (24.0)
HAQ	1.1 (0.8)	1.0 (0.7)
DAS28-ESR	4.1 (1.1)	4.0 (1.2)
CDAI	16.7 (7.2)	NA
CPDAI	NA	3.0 (0.7)
Glucocorticoid use	18 (48.6)	6 (18.8)
Methotrexate use	17 (45.9)	16 (50.0)
Biologics use	9 (24.3)	5 (15.6)

Values are expressed as mean (standard deviation) for continuous variables, n (%) for categorical variables. CCP: cyclic citrullinated peptide; CDAI: Clinical Disease Activity Index; CPDAI: Composite Psoriatic Disease Activity Index; CRP: C-reactive protein; DAS: Disease Activity Score; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; N/A: not applicable; PsA: psoriatic arthritis; RA: rheumatoid arthritis; VAS: visual analogue scale.

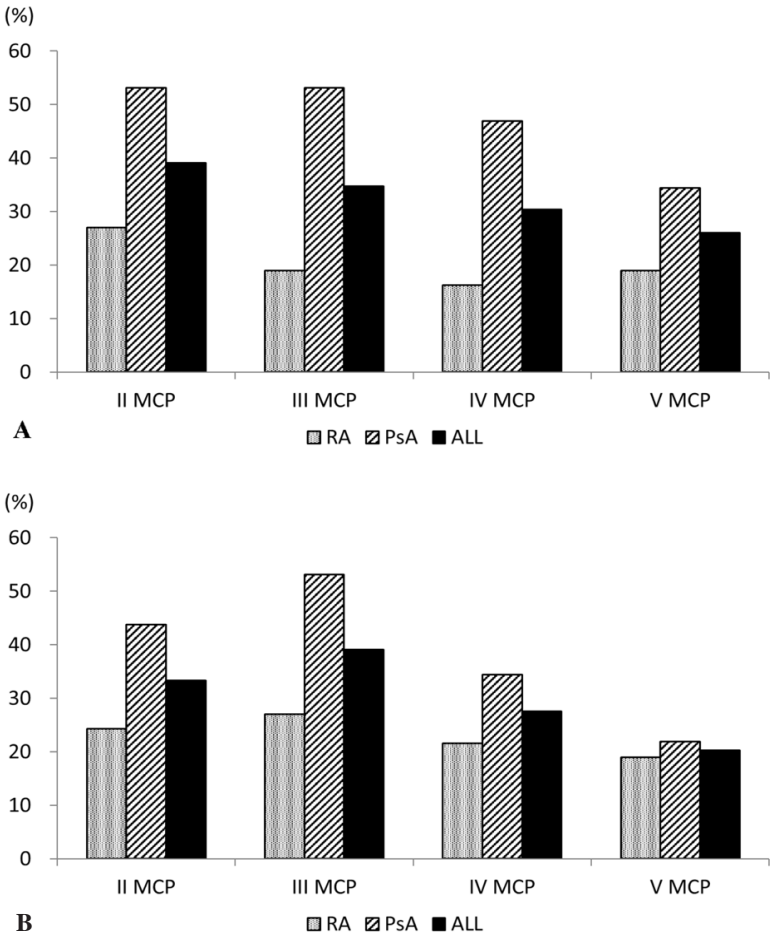

Fig. 2. Distribution of peritenon extensor tendon inflammation (PTI) sonographic patterns from 2nd to 5th metacarpophalangeal (MCP) joints.
A: Distribution of hypoechoic swelling surrounding the extensor digitorum tendon in B-mode assessment.
B: Distribution of peritendinous power Doppler signal.
Both findings were more frequently found in 2nd and 3rd MCP joints rather than in 4th and 5th MCP joints.

Table II. US assessment at MCP joint level.

US findings	All			Less than 1 year of disease duration			More than 1 year of disease duration		
	RA (n=296)	PsA (n=256)	*p*-value	RA (n=96)	PsA (n=80)	*p*-value	RA (n=200)	PsA (n=176)	*p*-value
Hypoechoic swelling surrounding the extensor digitorum tendon	30 (10.1%)	60 (23.4%)	<0.001	17 (17.7%)	14 (17.5%)	0.971	13 (6.5%)	46 (26.1%)	<0.001
Peri-tendinous PD signal	34 (11.5%)	49 (19.1%)	0.012	16 (16.7%)	13 (16.3%)	0.941	18 (9.0%)	36 (20.5%)	0.002
Joint cavity widening	146 (49.3%)	110 (43.0%)	0.135	36 (37.5%)	33 (41.3%)	0.612	110 (55.0%)	77 (43.8%)	0.030
Synovial fluid	19 (6.4%)	15 (5.9%)	0.785	6 (6.3%)	5 (6.3%)	1.000	13 (6.5%)	10 (5.7%)	0.741
Synovial hypertrophy	158 (53.4%)	118 (46.1%)	0.088	44 (45.8%)	34 (42.5%)	0.658	114 (57.0%)	84 (47.7%)	0.072
Intra-articular PD	108 (36.5%)	72 (28.1%)	0.037	24 (25.0%)	25 (31.3%)	0.357	80 (40.0%)	47 (26.7%)	0.007

Values are expressed in terms of number of joints (%).
MCP: metacarpophalangeal; PD: power Doppler; PsA: psoriatic arthritis; RA: rheumatoid arthritis; US: ultrasound.

Table III. US assessment at patient level.

US findings	All			Less than 1 year of disease duration			More than 1 year of disease duration		
	RA (n=37)	PsA (n=32)	*p*-value	RA (n=12)	PsA (n=10)	*p*-value	RA (n=25)	PsA (n=22)	*p*-value
Hypoechoic swelling surrounding the extensor digitorum tendon	13 (35.1%)	23 (71.9%)	0.002	6 (50.0%)	8 (80.0%)	0.145	7 (28.0%)	15 (68.2%)	0.006
Peri-tendinous PD signal	12 (32.4%)	21 (65.6%)	0.006	6 (50.0%)	7 (70.0%)	0.342	6 (24.0%)	14 (63.6%)	0.006
Joint cavity widening	33 (89.2%)	29 (90.6%)	0.844	9 (75.0%)	10 (100%)	0.090	24 (96.0%)	19 (86.4%)	0.238
Synovial fluid	12 (32.4%)	11 (34.4%)	0.865	3 (25.0%)	3 (30.0%)	0.793	9 (36.0%)	8 (36.4%)	0.979
Synovial hypertrophy	33 (89.2%)	30 (93.8%)	0.503	9 (75.0%)	9 (90.0%)	0.364	24 (96.0%)	21 (95.5%)	0.926
Intra-articular PD	32 (86.5%)	28 (87.5%)	0.901	8 (66.7%)	10 (100%)	0.044	24 (96.0%)	18 (%)	0.116

Values are expressed in terms of number of patients.
PD: power Doppler; PsA: psoriatic arthritis; RA: rheumatoid arthritis; US: ultrasound.

5 v. 5.04 (GraphPad Software Inc., La Jolla, CA, USA).

Results

Clinical characteristics of patients with RA and PsA

A total of 69 patients, 37 patients with RA (mean age: 55.5±12.0 years, 62.2% women) and 32 patients with PsA (mean age: 59.4±10.6 years, 40.6% women) were assessed. Demographic, clinical and laboratory characteristics are summarised in Table I. Mean disease duration was 98.3 months±104.2 standard deviation (SD) and 82.3 months 89.0 SD for RA and PsA patients, respectively. In RA patients, RF and anti-CCP antibodies were found positive in 73.0% and 70.3% of the cases, respectively; the mean DAS28-ESR was 4.1±1.1 SD and CDAI was 16.7±7.2 SD. Among PsA patients, the mean DAS28-ESR was 4.0±1.2 SD and CPDAI was 3.0±0.7 SD.

US findings at joint level

US assessments were performed in a total of 552 MCP joints (69 patients), 296 joints in 37 patients with RA and 256 joints in 32 patients with PsA. The results are reported in Table II.

Hypoechoic swelling surrounding the extensor digitorum tendon was found in 30 (10.1%) and 60 (23.4%) MCP joints in all patients with RA and PsA ($p<0.001$), respectively, and peri-tendinous PD signal was detected in 34 (11.5%) and 49 (19.1%) MCP joints in all patients with RA and PsA ($p=0.012$), respectively. In patients with early disease, the PTI prevalence was not significantly different between RA and PsA joints. Conversely, such a prevalence was significantly higher in the MCP joints of patients with established PsA with respect to the joints of patients with established RA (26.1% *vs*. 6.5% for B-mode findings and 20.5% *vs*. 9% for peritendinous PD signal).

On the other hand, as regards synovial hypertrophy, no statistically significant difference was found in terms of prevalence of involved joints between RA and PsA, neither in the early disease groups ($p=0.658$), nor in the established disease groups ($p=0.741$), nor considering all the patients independently of the disease duration.

Figure 2 shows the distribution of PTI pattern. Both hypoechoic swelling surrounding the extensor digitorum tendon (Fig. 2A) and peri-tendinous PD signal (Fig. 2B) were found more frequently at MCP joint level of the second and third fingers rather than of the fourth and fifth fingers.

US findings at patient level

Peri-articular and intra-articular US findings of 37 patients with RA and 32 with PsA were compared (Table III).

Hypoechoic swelling surrounding the extensor digitorum tendon and peri-tendinous PD signal were detected in about two-third of the PsA patients (71.9% and 65.6%, respectively) and in about one-third of the RA patients (35.1% and 32.4%, respectively). A statistically significant difference in

the prevalence of US findings indicative of PTI was found between RA and PsA patients when disease duration was more than one year (p=0.006), and no significant difference was observed comparing early disease groups.

US findings indicative of synovitis were frequently found in both patients with RA and PsA, and no significant difference was found.

Discussion

Modern imaging techniques, such as high-resolution US and magnetic resonance imaging (MRI), provide useful information for the rheumatologist in terms of detailed morpho-structural characterisation of both joint and peri-articular inflammation in patients with chronic arthritis. Moreover, the PD technique with high frequency probes allows for a sensitive assessment of the topographical distribution of blood flow perfusion at small joints and superficial peri-articular soft tissues (29-34).

Very few studies have been carried out to assess the ability of US to distinguish different patterns of soft tissue inflammatory involvement in patients with RA and PsA. These studies have focused at the level of the entheses (35-38), knee (39), shoulder (40), temporomandibular joint (41, 42) and nails (43). Enthesitis is a key feature in the diagnosis of SpA, including PsA. Therefore, the US detection of enthesitis (*i.e*. Achilles enthesitis, plantar fasciitis, and/or other peripheral entheseal involvement) is certainly important in the differential diagnosis of RA and PsA. The MCP joints are frequently affected both in RA and PsA patients, they can be easily assessed with US, and they have not yet been extensively investigated by US for estimating its value in differential diagnosis. Iurassich *et al*. compared the US patterns of RA and PsA at finger joints level in 1999, however this study was conducted using only B-mode without PD assessment and the obtained results should be interpreted considering the technology available at that time (44).

In patients with chronic arthritis, synovitis and PTI are pathologic conditions which can be easily visualised by high-resolution US on the dorsal aspect of MCP joint level. Synovitis can be frequently found in both RA and PsA. It is commonly assumed that the primary abnormality in RA is joint synovitis and SpA is associated not only with synovitis, but also with enthesitis which represents the inflammation of tendon, ligament, or capsule insertion into the bone. McGonagle *et al*. proposed the hypothesis that enthesitis could explain all the rheumatic signs of SpA being synovitis in SpA secondary to liberation of pro-inflammatory mediators from the enthesis (45). Moroever, according to the concept of the 'enthesis organ', the enthesis itself has an elaborate functional integration with the adjacent soft tissues including the synovial tissue (46). Anatomical unit termed the synovio-entheseal complex (SEC), whereby the normal enthesis-related fibrocartilages were critically dependent on immediately adjacent synovium (47). The SEC exists in both intra- and extra-articular tissues and the inflammation at the SEC level offers an explanation for both intra- and extra-articular soft tissue inflammation in patients with SpA.

Some studies have pointed out that the involvement of extra-articular tissues may be more characteristic in patients with PsA than RA (48, 49). Although extensor tendon inflammation was observed less frequently than flexor tenosynovitis, inflammation surrounding extensor tendon at finger level was recognised by MRI as peritendinous fluid and enhancement in patients with PsA (50).

At the MCP joint level, the finger extensor tendon is not covered by a synovial tendon sheath. Therefore, the PTI should not be interpreted as a sign of tenosynovitis, but a an enthesitis related lesion (18).

In the present study, no statistically significant difference was found in terms of synovitis prevalence between RA and PsA patients. Conversely, PTI was found by US in a significantly higher number of patients with PsA rather than in those with RA. However, such a difference was not detected in the early phase of the diseases. These findings agree with the theory that primary inflammatory lesion is enthesitis in both PsA and RA patients.

Gutierrez *et al*. reported that no US PTI was found in 18 patients with RA (17). Our results confirmed the high specificity of US PTI for PsA: it was detected in 23 (71.9%) of the 32 PsA patients, and in only 13 (35.1%) of the 37 RA patients. However, its discriminant value was lower than that initially found, confined to the patients with established disease, and irrelevant in the early phase of both RA and PsA. In fact, in our cohort, the RA patients with PTI were found more frequently in the early RA group rather than in the established RA group (50% *vs*. 28%), and the frequency of PTI between patients with RA and PsA of less than 1 year duration was not statistically different. Wakefield *et al*. also detected periextensor tendon disease using B-mode US in 14 (7%) of 200 MCP joints in 9 (18%) of 50 patients with early, untreated RA (51). Thus, US PTI may be an inflammatory pattern of the early phase in both RA and PsA.

The possible reason we found PTI pattern in patients with RA may be the similarity of joint findings in two diseases. The diagnosis of both RA and PsA is usually made using the classification criteria that enable the stratification of groups of individuals into those with and those without RA and PsA (19). In fact, the clinical features at joint level of both diseases are similar and sometimes difficult to distinguish. Therefore, some patients with RA who have characteristics of PsA might be included in this study. Moreover, sonographic PTI pattern is sometimes difficult to distinguish with intra-articular severe arthritis, as mentioned in the result, pitfall of PTI pattern. This fact may be another possible explanation. At least, two perpendicular views obtained on longitudinal and transverse scans on the dorsal aspect of a MCP joint are required to distinguish PTI pattern and intra-articular inflammation. This aspect should be considered in further studies.

There are some limitations in this study. First, this is a monocentric study carried out in a relatively small number of patients; however, to the best of our knowledge this is to date the largest cohort investigated on this topic, and the new insights provided especially in the

early phases of the RA and PsA, justify the implementation of a multicentre study. Second, there was a relatively low prevalence of US findings indicative of joint inflammation; this could be due to the study design, which included consecutive patients with RA and PsA, regardless of the disease activity. Finally, this study did not consider the treatment applied at the time of US examination, which could lead to relevant changes in the PD signal (52).

In conclusion, high-resolution US with PD technique confirmed the detection of PTI at MCP joint level in a higher number of patients with PsA rather than in RA. Nevertheless, since no statistically significant difference was found between RA and PsA patients with less than 1 year of disease duration, the PTI pattern may represent an inflammatory feature of the early phases of both the diseases.

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