Imaging

Ultrasound imaging for the rheumatologist XXVI. Sonographic assessment of the knee in patients with psoriatic arthritis

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ABSTRACT

Psoriatic arthritis (PsA) is an arthropathy associated to psoriasis, which is part of the spondyloarthropathy family, and which may present with various forms, from mono-oligoarthritis to symmetric polyarthritis mimicking rheumatoid arthritis. In longstanding disease, the symmetric polyarthritis is the most common pattern of PsA, involving small joint of hands, feet, wrists, ankles and, very frequently, knees. Other common features are represented by the inflammation of enthesis and tendons. Ultrasound (US) examinations were performed using a Logiq 9 (General Electric Medical Systems, Milwaukee, WI) equipped with a multifrequency linear probe, working at 10-14 MHz. One-hundred and sixty-six knee joints were investigated in a total of 83 patients. Prior to US assessment, all patients underwent a clinical examination by an expert rheumatologist who recorded the presence/absence of pain, tenderness (detected by palpation and/or active or passive mobilisation of the knee), and knee swelling. Sixty-two (74.7%) knee joints were found clinically involved, while at least one US finding indicative of joint inflammation was obtained in 70 (84.3%) knee joints. In the 59% of the patients we noticed synovial hypertrophy. Enthesitis was present in 39.7% of the subjects studied.

This study demonstrated that US detected a higher number of inflamed knee joints and enthesis with respect to clinical assessment in PsA patients.

Introduction

Psoriatic arthritis (PsA) is an inflammatory joint disease associated with psoriasis, classified within the family of spondyloarthropathies. The exact prevalence of PsA is unknown but in Italy it should be close to 30% in psoriatic subjects (1-4) or to 0.42% of the general population (5). A great variability in clinical features and severity is observed in patients affected by such an arthropathy. In fact, mono-oligoarthritis or symmetric polyarthritis mimicking rheumatoid arthritis (RA) and benign or seriously destructive disease (the so-called mutilans arthritis) can be identified. In longstanding disease, the symmetric polyarthritis is the most common pattern of PsA, involving the small joints of hands and feet, wrists, ankles and knees. However, knee involvement is seen, with high frequency, also in early PsA (in about 30% of patients). Other common features are represented by the inflammation of enthesis and tendons.

It is well known that musculoskeletal ultrasound (US) is a reliable technique with greater sensitivity than clinical examination in the detection of synovitis, enthesitis and tenosynovitis in most of the rheumatic diseases (7-17). However, to date, few studies have evaluated articular involvement in PsA using sonographic examination (15-19) and, in particular, the number of studies focused on the knee involvement is very low.

The aims of our study were to investigate, by US examination, the prevalence and the features of knee involvement in PsA and to describe their correlations with clinical findings.

Methods

We performed a multicentre study in 4 different Rheumatology Units in Italy: University of Pisa, University of Pavia,

Università Politecnica delle Marche and the Sapienza University of Rome. In each unit, US examinations were performed by a rheumatologist experienced in musculoskeletal US using a Logiq 9 (General Electrics Medical Systems, Milwaukee, WI) with a linear probe operating at 10 MHz for joint assessment and 14 MHz for tendon and enthesis evaluation. The inter-observer agreement of sonographers in detecting and scoring US features of joint inflammation, enthesitis and bone erosions has been calculated and reported in previous studies (14, 20). Good-to-excellent agreement rates were found in the detection and semiquantitative assessment of US signs of joint and entheseal inflammation and bone erosion, The study was conducted according to the Declaration of Helsinki and local regulations, and informed consent was obtained from all patients.

Patients

Eighty-three patients with PsA, either out-patients or in-patients, were consecutively enrolled in the study. The diagnosis of PsA was established according to the CASPAR criteria (21). Exclusion criteria included history of severe trauma or surgery of the knee. Demographic and clinical characteristics of the study population are reported in Table I.

Study design

Prior to US assessment, all patients underwent a clinical examination by an expert rheumatologist who recorded the presence/absence of pain, tenderness (by palpation and/or active or passive mobilisation of the knee), and knee swelling.

All US examinations were performed by experienced sonographers, one for each centre involved in the study, who were blind to both clinical and laboratory data.

US scanning technique

A multiplanar US examination was performed according to the indications provided by the EULAR guidelines for musculoskeletal ultrasound in rheumatology (22). Additional scans, performed to evaluate wider cartilage surface, included medial para-patellar views which were carried out with knee in maximal flexion. Dynamic examination during both compression with the probe and flexion-extension of the knee was carried out to identify the superficial margin of the hyaline cartilage. Lateral and medial longitudinal views, during flexion-extension of the knee, were adopted to investigate the presence of meniscal calcification. Quadriceps and patellar tendons and entheses were scanned firstly with the patient supine and the lower limbs in extended neutral position (in order to avoid vascular compression) and then with a 30° knee flexion angle. Sonographic measurements of entheses thickness were performed where it appeared maximum. A detailed description of the scans adopted is reported in Table II.

The setting parameters were standardised as follows:

- grey scale gain was initially set in order to obtain the maximal contrast between the different tissues under examination, and successively reduced to the lowest level allowing the visualisation of only hyperechoic structures using the bony cortex as reference;
- pulse repetition frequency of 500 Hz, Doppler frequency of 7.5 MHz and Doppler gain to avoid random noise visualisation.

US image interpretation

Joint effusion, synovial hypertrophy, and bone erosion were registered by US according to the preliminary definitions provided by the Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Special Interest Group for Musculoskeletal Ultrasound in Rheumatology (23). Enthesitis was defined as hypoechogenicity and/or thickening of the entheses, as well as the presence of power Doppler signal at entheseal level (24).

In the evaluation of cartilage, the morphostructural changes used to detect the presence of monosodium urate (MSU) or of calcium pyrophosphate dihydrate (CPPD) crystal deposits, were the hy-

Table I. Demographic and clinical data.

Number of patients	83
Gender (female/male)	26/57
Age in years (average ± SD; range)	53.4 ± 12.4; 34–78
Disease duration in months (average ± SD; range)	109.7 ± 25.3; 8–590

SD: standard deviation.

Table II. Scanning technique adopted for the study.

Scanning planes	Position of the patient	Anatomic structures under examination
Anterior tranverse and longitudinal scans (medial, midline and lateral)	Patient in supine position with the knee in neutral extended position and with the knee semiflexed at 30°	Supra-patellar pouch and medial and lateral recesses Quadriceps and patellar tendons and entheses
Anterior supra-patellar tranverse and longitudinal scans	Patient in supine position with the knee in maximal flexion (>90°)	Hyaline cartilage of the femoral trochlea and the anterior portion of the femoral condyles
Anterior para-patellar transverse and longitudinal scans	Patient in supine position with the knee in maximal flexion (>90°)	The lateral portion of the hyaline cartilage of the femoral condyles
Lateral and medial transverseand longitudinal scans	Patients in supine position with the knee in neutral extended and in maximal flexion positions.	The external portion of the menisci
Posterior tranverse and longitudinal scans	Patient in prone position with the knee in neutral extended position.	Hyaline cartilage of the posterior portion of the femoral condyles Gastrocnemius-semimembranosus bursa

Table III. Comparison between sonographic and clinical findings indicative of knee joint inflammation (**a**) and enthesitis (**b**) obtained from a total of 83 patients with PsA.

a.		Clinical findings		Total
US findings		Presence	Absence	
Joint effusion	Presence	54	16	70
	Absence	8	5	13
Synovial hypertrophy	Presence	49	0	49
	Absence	13	21	34
Intra-articular power Doppler signal	Presence	13	0	13
	Absence	49	21	70
Total		62	21	83
b.				
B-mode signs of enthesitis	Presence	21	18	39
	Absence	14	30	44
Power Doppler signal at entheseal level	Presence	13	0	13
	Absence	49	21	70
Total		62	21	83

perechoic enhancement of the superficial margin or the hyperechoic spots within the cartilage layer respectively (25). How to identify meniscal calcification was described in a previous study (26).

Results

Joint inflammation

One hundred and sixty-six knee joints were investigated in a total of 83 patients. Signs suggestive of articular inflammation were detected in 62 (74.7%) knee joints at clinical examination while, by US, were visualised in 70 (84.3%) knee joints. Clinical examination results were in agreement with US assessment in 54 patients, while in 16 subjects joint effusion was identified only by US. In 8 patients with clinical signs of knee joint inflammation, US could not reveal any effusion. In the 70 knee joints defined inflamed by US, effusion was always found, while synovial hypertrophy with or without intra-articular power Doppler signal was detected in 49 (59%) knees of 58 (70%) patients. Table IIIa reports the findings obtained by clinical examination and US assessment of the knee joint.

Enthesitis

Tenderness at entheses was elicited in 35 patients when performing clinical examination, while US findings of enthesitis were detected in 39 patients, with a total of 64 entheses involved (16 quadriceps, 26 proximal patellar and 22 distal patellar enthesis). Clinical examination results agree with US findings in 21 patients, while in 18 subjects enthesitis was identified only by US. In 14 PsA patients, tenderness at enthesis was present at clinical evaluation but no signs of enthesitis were visualised by US. Power Doppler signal at the enthesis was imaged in only 10 out of 39 patients (for a total number of 11 enthesis). Table IIIb shows the relationship between US and clinical findings indicative of enthesitis.

Other findings

We detected 29 Baker's cysts (or gastrocnemius-semimembranosus bursae) in 26 patients (21.3%), and all of the cysts but one were associated with ipsilateral knee joint effusion. Besides findings related to joint synovitis or enthesitis, we recorded the typical "double line" pattern (hyperechoic line at the upper part of the cartilage layer) in the knee of two patients, suggestive of the presence of a MSU crystals deposition. No US findings indicative of CPPD disease were found at knee cartilage level.

Discussion

To date, few studies have been reported in the literature on the applications of US in the assessment of joint, tendon and entheseal involvement in the course of PsA. In particular, only few investigators have pointed their attention to the features of knee inflammation in such a disorder (27-30) so no data are available on knee involvement in a large PsA population.

By sonographic examination, only two papers evaluated signs of synovitis regarding therapy monitoring (27, 28) in a limited number of PsA patients.

In the first study (27), in order to investigate the efficacy of intra-articular methotrexate (MTX) in 10 RA and 19 PsA patients with knee arthritis, synovial thickness of the suprapatellar bursa was measured and the presence of effusion and Baker's cyst reported. At follow-up US examinations, significant differences were demonstrated in both the mean thickness of the synovial membrane and the presence of joint effusion.

The aim of the study by Fiocco *et al*. (28) was to visualise the effect of the therapy with etanercept, in refractory knee joint synovitis of 12 RA and 8 PsA patients. After 3-month, a reduction in power Doppler signal was observed, which lasted up to 12 months. After one year, a reduction of the synovial thickening was also assessed.

The other structures involved in PsA disease, the "enthesis organ", were studied by Frediani *et al*. (29, 30), and by Balint *et al*. (17). Various papers are pointed on enthesopathy in SpA (24, 31-37) but most of time the results are reported without distinguish between the different forms of SpA or are regarding a few patients.

Frediani *et al*. (29, 30) studied quadricipital enthesis in 40 patients with RA and 40 with PsA both with the knee in an extended position and with a 30° flexion. Thickening or hypoechogenicity of enthesis, loss of normal fibrillar structure, gross irregularity of the patella and enthesophytes longer than 5 mm were considered indicative of enthesitis. They reported the presence of effusion in the suprapatellar joint recess also. Enthesitis was demonstrated in 45% of PsA patients (higher than in the RA group), while effusion was significantly more frequent in RA patients (95% *vs*. 60% in PsA group). No isolated enthesitis was found in RA patients, while it was reported in PsA group. Interestingly, quadricipital enthesitis was

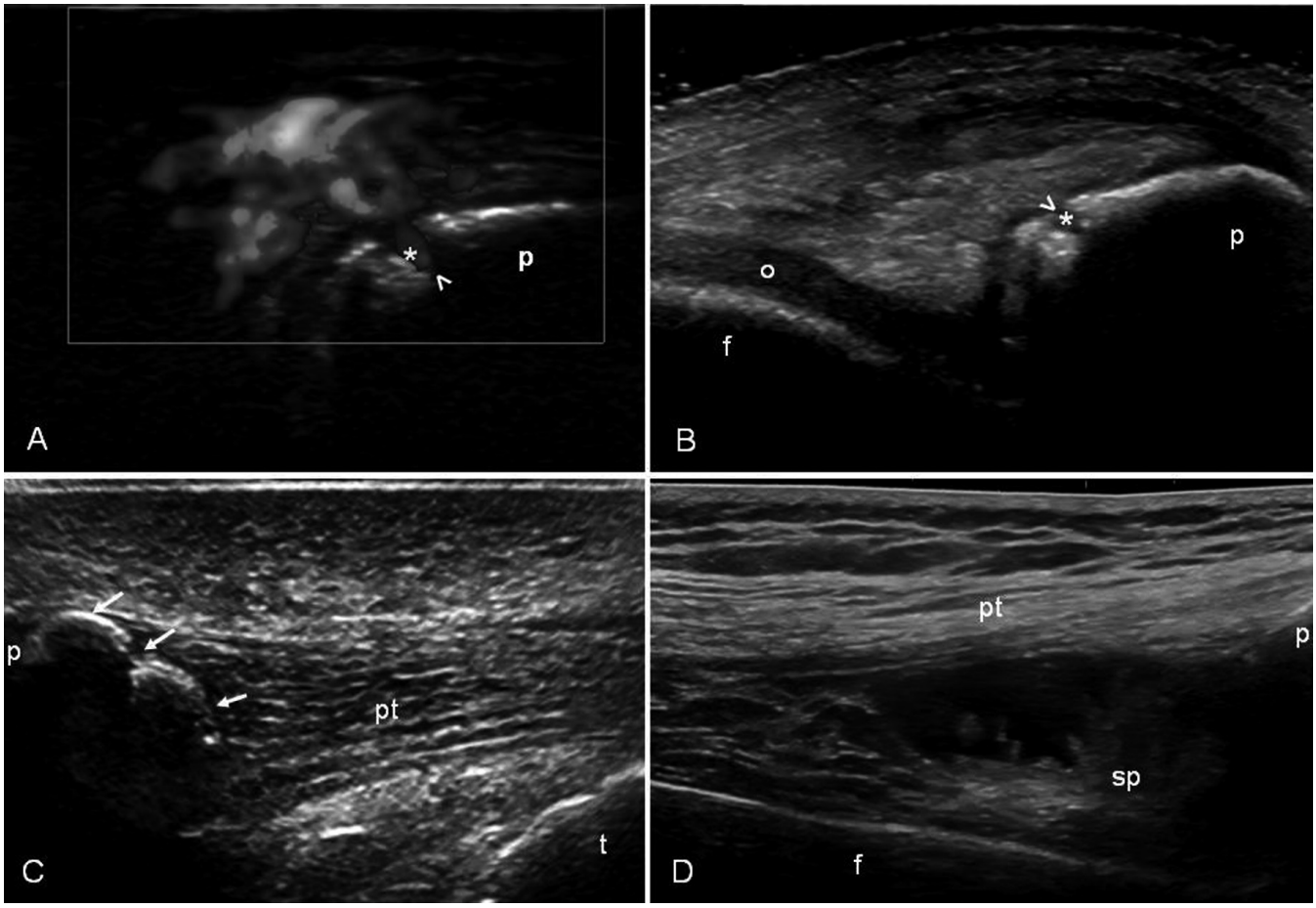

Fig. 1. A. Dorsal transverse scan of the upper pole of the patella. Power Doppler technique showing the presence of signal in the quadricipital enthesis and into an erosion. **p**: patella; arrowhead: patellar cortical bone erosion.
B. Anterior para-patellar longitudinal scan showing the presence of an erosion in the cortical bone of the patella. Grey scale US. **p**: patella; **f**: femur; arrowhead: patellar cortical bone erosion; °: lateral portion of the hyaline cartilage of the femoral condyles.
C. Dorsal longitudinal scan of the patellar tendon showing a big enthesophyte starting from the lower pole of the patella and producing acoustic shadowing. Grey scale US. **p**: lower pole of the patella; **t**: tibia; **pt**: patellar tendon; the arrows indicate the enthesophyte.
D. Anterior suprapatellar longitudinal scan showing a marked suprapatellar pouch enlargement with evident signs of synovial proliferation (**sp**). Grey scale US. **p**: upper pole of the patella; **pt**: patellar tendon; **f**: femur.

more frequent in the male sex both in PsA and RA population. Sonographic examinations of the 18 PsA patients with enthesitis revealed irregular bone profiles (in 17 cases), while enthesophytosis, tendinous fiber thickening and hypoechogenicity were present in 9 patients. The presence of psoriatic skin lesions (at any site) does not seem to be associated with the presence of enthesitis. US assessment was demonstrated to be superior to the clinical examination in identifying both enthesitis and joint effusion.

Another important contribution to the literature, for the study of enthesis, is by Balint *et al*. (17), who compared US with clinical examination in the detection of entheseal abnormalities of the lower limbs in patients with SpA. They studied 35 patients affected by SpA (only 7 with PsA), examining five entheseal sites at lower limbs (including superior and inferior poles of the patella and anterior tibial tuberosity) to detect bursitis, structure thickness, bony erosion, and enthesophyte, with the knee flexed at 30°. An enthesitis score (GUESS) was formulated based on the US imaging. Findings were reported for the whole SpA group and not for each disease, in any case, US demonstrated enthesis abnormalities in 195/348 (56%) sites, showing higher sensitivity than clinical examination. The most frequent finding was tendon thickening (at any site, but mostly at the infrapatellar enthesis), bursitis (or subquadricipital recess), bone erosions and enthesophytes were relatively more frequent at the suprapatellar region (while considering only the knee). Enthesophytes were frequently reported (3-30% of the sites) but they may represent the end stage of inflammation or may relate to other pathologic conditions such as trauma or degenerative changes (which are common in the general population); on the other hand, bony erosions are generally less frequent (1-13% of the sites). About 54% of the enthesis were symmetrically involved. No significant correlation were noted between the GUESS and acute phase parameters (*i.e*. ESR or CRP).

Our results support the higher sensitivity of US than clinical examination in the detection of joint and entheseal inflammation at knee level in patients with PsA. Since we did not use a gold stand-

ard imaging technique for the detection of synovitis, possible explanations of the lack of agreement between clinical and US data (in 8 patients with knee swelling on clinical examination, US could not find any signs of joint inflammation) include an incorrect interpretation of either clinical or US findings.

The percentage of knee effusion in our cohort of patients is extremely high (84.3%), higher than the one reported by Frediani *et al*. (29, 30). The quantity of intra-articular fluid considered "normal" in healthy knee is not standardised, thus a different interpretation of this pathologic finding may explain this discrepancy. Furthermore, the number of patients recruited by Frediani *et al*. was less than half the one of the present study. Finally, we used a more sensitive US machine.

We noticed a low number of patients with intra-articular power Doppler signal. This is due to the enrollment in the study of also asymptomatic patients (25 of whom did not complain of knee pain) and to the relatively lower sensitivity of the Doppler technique in detecting low flow in large joints where synovial tissue is located far from the skin surface.

Regarding enthesitis, we demonstrated a slightly lower percentage of entheseal inflammation (39.7%) with regard to Frediani *et al*. (45%) (29, 30). The difference can be explained by the different number of patients enrolled and by the US findings used to state the presence of enthesitis. In our study, enthesophytes were not included because of their high prevalence which may also be related to trauma, mechanical overload or tendinosis. Another difference between the study of Frediani *et al*. and our study is that we evaluated all the enthesis in the knee and not only the quadricipital one, where we noticed a lower frequency of enthesitis (results not shown).

Clinical examination detected entheseal tenderness in a group of patients with no US findings indicative for enthesitis. Moreover, our study was not designed to understand if the tenderness was also related to structural alterations (*i.e*. calcification, mechanical or metabolic tendinopathy etc.) or only to the entheseal inflammation.

In conclusion, the present study provides evidence in favour of the higher sensitivity of US in the detection of knee joint and entheseal inflammation with respect to clinical assessment. Our results must be interpreted in the light of the adopted US equipment (Doppler sensitivity may change significantly from one US equipment to others) and study design (patients were consecutively enrolled independently of the disease duration and extent of clinical signs of knee involvement).

Link

For further ultrasound images, please go to www.clinexprheumatol.org

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