

PSORIATIC ARTHRITIS IMAGING – AN OVERVIEW AND UPDATE

SLIKOVNE METODE U PSORIJATIČNOM ARTRITISU – PREGLED I NOVOSTI

Gordana Ivanac, Eugen Divjak

Clinical Department for Diagnostic and Interventional Radiology, University Hospital Dubrava, Zagreb, Croatia

Corresponding author address:

Assistan Professor Gordana Ivanac, Md, PhD

Clinical Department for Diagnostic and Interventional Radiology

University Hospital Dubrava

Av. Gojka Šuška 6,

10000 Zagreb

Croatia

tel. 01-2903255

e-mail: gordana.augustan@gmail.com

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ABSTRACT

Psoriatic arthritis (PsA) is a chronic inflammatory joint disease that occurs in patients with psoriasis. Typically, involvement of the peripheral joints (with an asymmetric pattern) and the axial skeleton can be recognized. There are no specific laboratory tests for PsA and the diagnosis relies on clinical and imaging findings. Conventional radiology and magnetic resonance are the most valuable imaging modalities, with ultrasound becoming more and more used due to its feasibility and high sensitivity for peripheral disease manifestations. The authors offer a concise overview of PsA, common imaging findings, and literature update.

KEYWORDS: Arthritis, psoriatic – diagnostic imaging, pathology; Diagnostic imaging – methods; Magnetic resonance imaging – methods; Ultrasonography; Tomography, x-ray computed; Joints – diagnostic imaging, pathology; Tenosynovitis – diagnostic imaging; Enthesopathy – diagnostic imaging

SAŽETAK

Psorijatični artritis kronična je upalna bolest zglobova koja se javlja u pacijenata sa psorijazom. Tipično zahvaća periferne zglobove (s asimetričnim uzorkom) te aksijalni skelet. Ne postoje laboratorijski testovi specifični za psorijatični artritis pa dijagnostički postupak počiva na kliničkom nalazu i slikovnim pretragama. Najčešće se rabe klasične radiološke pretrage i magnetska rezonancija, a sve više raste i upotreba ultrazvuka zbog njegove jednostavnosti i visoke osjetljivosti za periferne pokazatelje bolesti. Autori donose sažeti pregled psorijatičnog artritisa, tipičnih nalaza slikovnih metoda i novosti iz literature.

KLJUČNE RIJEČI: Psorijatični artritis – dijagnostički prikaz, patologija; Dijagnostički prikaz – metode; Magnetska rezonancija – metode; Ultrazvuk; Kompjutorizirana tomografija; Zglobovi – dijagnostički prikaz, patologija; Tenosinovitis – dijagnostički prikaz; Entezopatija – dijagnostički prikaz

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy occurring in 6% to 48% of the patients with skin psoriasis (1, 2, 3), typically presenting with arthritis, enthesitis, and/or dactylitis, while the skin symptoms may be subtle (4). Evidence suggests that the underlying pathology includes both genetic and environmental factors that cause profuse proinflammatory processes in the skin and synovium, involving

tumor necrosis factor (TNF)- α , interleukin (IL)-1 β , IL-6, IL-13, and nuclear factor- κ B ligand, which finally leads to osteoclast-driven destruction of the joint (3, 5). Although there are some similarities with rheumatoid arthritis (RA), PsA is often seronegative for rheumatoid factor, and, on closer inspection, different clinical and imaging patterns are evident (4, 6). The disease typically begins as enthesitis of articular capsules, fascia, tendons, and ligaments. Typically, involvement of

the peripheral joints (with an asymmetric pattern) and the axial skeleton can be recognized (7). Based on the clinical presentation, five patterns of PsA have been described by Moll and Wright (1):

(a) asymmetric oligoarticular or monoarticular arthritis primarily affecting the distal interphalangeal (DIP), proximal interphalangeal (PIP), and metatarsophalangeal joints; (b) DIP-predominant arthritis; (c) arthritis mutilans; (d) symmetric, rheumatoid factor (RF)-negative polyarthritis; and (e) psoriatic spondyloarthropathy. As there are no specific laboratory tests for PsA, the diagnosis is mainly based on the clinical presentation and imaging findings (3). Based on a study involving 588 patients with PsA and 536 control subjects, the Classification of Psoriatic Arthritis (CASPAR) study group has formulated criteria for the diagnosis of PsA: the presence of psoriasis or a family history of psoriasis, dactylitis, juxta-articular new bone formation, negative RF, and nail dystrophy (8). If three of the above-mentioned criteria are met, there is a strong indication of PsA.

Methods

A computerized literature search, from January 1, 2015 to May 31, 2017, was conducted by the authors to identify articles on imaging in patients with PsA. Articles were retrieved through PubMed search using the US National Library Medical Subject Headings (MeSH) term “Arthritis, Psoriatic/diagnostic imaging”. Publications both in English and in German were considered. Reviews, editorials, case reports, letters, and commentaries were excluded. The search yielded a total of 60 articles and after an abstract review, 32 were found eligible and retrieved as full-text articles. Some articles were excluded due to having been electronically published on an earlier date. A total of 24 articles fulfilling all inclusion criteria were included in the study.

Results

Imaging methods

Various imaging methods are used in patients with suspected or established PsA, mainly conventional radiography (CR), ultrasonography (US), and magnetic resonance imaging (MRI) (4, 9). Computed tomography (CT) is the gold standard for assessment of bone structure, but is only used in exceptional cases of arthritides due to ionizing radiation (4, 7, 10). Other imaging modalities, i.e., scintigraphy, positron emission tomography (PET), single photon emission CT, and dual-emission x-ray absorptiometry, are seldom used in PsA (4, 7).

Conventional radiography

CR remains the most widely used imaging technique, offering high spatial resolution, and fast, reliable,

and relatively inexpensive imaging of the bone structure (4). It is not as sensitive in the detection of erosive lesions as CT, but it has a high specificity (11). The main drawback is the 2-D visualization of a 3-D structure, resulting in suboptimal delineation of bone, especially in complex joints (4). Imaging includes AP and lateral views of painful joints, as well as AP and lateral views of hands and feet for evaluation of the structural changes in DIP joints, which can often show typical radiographic signs, even if the joint is asymptomatic (3, 10). Evaluation of the axial skeleton for atypical syndesmophytes is also recommended, but since higher radiation doses are involved, MRI has recently become the more favoured modality in spine assessment (4, 12). The characteristics of a bone lesion seen in PsA result from a combination of erosive and proliferative bone changes: a large, poorly demarcated erosion of the bony cortex in a para-articular site is often seen, closely associated with new bone formation (3, 6). Typical findings include opera-glass deformity (telescoping erosive joint destruction), fluffy periostitis due to periosteal ossification; pencil-in-cup deformity consisting of destruction of the head of the middle and expansion of the base of the distal phalanx, and acroosteolysis – resorption of the tuft of the distal phalanx (Figures 1 and 2). In patients with axial disease, sacroiliitis, syndesmophytes, paravertebral ossification, and destructive discovertebral lesions can be found (3, 10). Early diagnosis is of utmost importance, and Haroon et al. have shown that even a 6-month delay from symptom onset to the first visit with a rheumatologist contributes to the development of peripheral joint erosions and worse long-term physical function (13). Unfortunately, CR reveals inflammatory changes in peripheral joints months or years after the onset of clinical symptoms (10, 14).

Semi-quantitative scoring methods originally developed for rheumatoid arthritis, designed to measure the degree of radiographically detectable joint damage and changes over time, have been adopted for the use in PsA and described by Wassenberg (15). A novel scoring method called Reductive X-ray Score for Psoriatic Arthritis has been proposed by Tillet et al (16). The method is sensitive to change and includes three hallmark features of PsA: erosion, joint space narrowing (JSN), and osteoproliferation. Fewer joints need to be assessed than in using the most common and most feasible score, PsA-modified Steinbrocker, while the method maintains a similar sensitivity to change as the Sharp/van der Heijde (SvdH) score, which is currently the most sensitive method developed.

Geijer et al. (17) obtained hand and foot radiographs for 72 of 197 PsA patients enrolled in the Swedish psoriatic arthritis registry and followed for 5 years. Radiographic progression in early PsA was generally slow

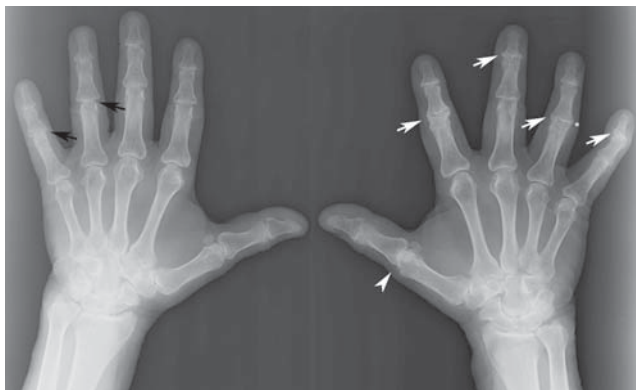


FIGURE 1 Conventional AP radiographs of the hands of an 85-year-old male patient with PsA. Note the narrowing of the interphalangeal joint spaces with osteophytosis and sclerosis – classic signs of osteoarthritic changes (white arrows). Fluffy bone appearance is seen at the site of active disease (asterisk). Erosion of the heads of the proximal phalanges results in the “pencil-in-cup” sign (black arrows). Subluxation of the first MCP joint can also be seen (white arrowhead). Typically of PsA, changes are asymmetric and seen in the distal joints.

SLIKA 1. Standardne rendgenske snimke obiju šaka 85-godišnjega muškog pacijenta sa PsA učinjene u AP projekciji.

Vidljivo je suženje interfalangealnih zglobnih prostora s osteofitozom i sklerozacijom zglobnih tijela – tipični znakovi osteoartritičkih promjena (bijele strjelice). Kost na mjestu aktivne bolesti ima „čupav” izgled (zvjezdica). Erozijska glava proksimalnih falangi dovodi do pojave znaka „olovke u šalici” (crne strjelice). Također je vidljiva subluksacija prvog MCP zgloba (bijeli vrh strjelice). Uobičajeno za PsA, promjene su asimetrične i zahvaćaju distalne zglobove.

but substantial. Male sex appeared to be a risk factor for early radiographic damage while the presence of baseline radiographic damage and dactylitis developing during follow-up could predict further destruction.

Jadon et al. reported on differences between clinical characteristics of patients with PsA with PsA mutilans (PAM) and without PAM (18). In a retrospective cohort study including 610 patients (36 of who had PAM), PAM cases were diagnosed with PsA at an earlier age, had poorer function, more prevalent nail dystrophy, and more severe radiographic axial disease/sacroiliitis. The rate of osteolysis was higher in earlier disease, and more severe in those with nail dystrophy.

Kavanaugh et al. (19) reported results from a randomized, placebo-controlled phase III trial that evaluated clinical efficacy and radiographic benefit through two years of ustekinumab therapy in patients with active PsA. A total of 615 adult patients with PsA were enrolled and radiographic progression was scored using the modified SvdH score with modifications for PsA. The results showed that mean changes were numerically lower in the ustekinumab groups than in the placebo crossover group.

Kavanaugh et al. recently published another paper (20) on evaluation of long-term outcomes in 395 PsA



FIGURE 2 Conventional AP radiographs of the feet of an 85-year-old male patient with PsA. Erosion of the head of the proximal phalanx resulting in the “pencil-in-cup” sign is seen in the right big toe (black arrowhead). Some soft tissue swelling is also present.

SLIKA 2. Standardne rendgenske snimke obaju stopala 85-godišnjeg muškog pacijenta sa PsA učinjene u AP projekciji.

Vidljiva je erozija glave proksimalne falange palca desnog stopala koja uzrokuje znak „olovke u šalici” (crni vrh strjelice). Prisutan je i edem mekih česti.

patients who achieved or did not achieve minimal disease activity (MDA) through 5 years of golimumab treatment in the GO-REVEAL trial. Golimumab treatment yielded significantly higher MDA response rates versus patients randomized to placebo, and achievement of MDA at ≥ 3 and ≥ 4 consecutive visits was associated with significantly less radiographic progression (measured by SvdH score).

Jadon et al. also reported on prevalence as well as clinical and radiographic characteristics of psoriatic spondyloarthritis (PsSpA) in PsA with ankylosing spondylitis (AS) (21). In a combined cohort of 201 patients with PsA and 201 patients with AS from a single centre, 24% fulfilled the classification criteria for both conditions. The pattern of axial disease was significantly influenced by the presence of skin psoriasis and HLA-B*27.

In a recent study on 45 PsA patients (22) CR was used to establish an association between nail psoriasis and DIP involvement. The results showed that a significant proportion of PsA patients had nail involvement and DIP arthritis.

Haroon et al. conducted a study on axial involvement (23), aiming to identify clinical and genetic as-

sociations of sacroiliitis (SI) in patients with PsA, and to describe the radiographic patterns of SI in PsA. The study showed that early onset of PsA, severe skin disease, peripheral joint erosions, and HLA-B*0801 are significantly associated with SI, whereas HLA-B*2705 only showed marginal significance. In this study, HLA-B*27 positive Axial-PsA patients resembled AS, while HLA-B*0801 positive Axial-PsA patients had asymmetrical and/or unilateral SI, typical of PsA.

Computed tomography

While CT offers excellent imaging of bone structures and is considered to be the “gold standard” in the evaluation of bone, this modality is still not able to detect active inflammation sites. Besides, there is the issue of the ionizing radiation exposure limit applicability of CT in routine diagnosis and management of PsA (4, 7, 10). Findings of micro-CT scans of peripheral joints in PsA patients include Ω -shaped erosions in the metacarpophalangeal joints (24), and new bone formation at entheses can be detected in both psoriasis patients without arthritis and PsA patients (25, 26). Regarding the assessment of the axial skeleton, although CT of the SI joints can give a satisfactory display of bone erosion, sclerosis, and joint space alterations including ankylosis, MRI is the preferred technique. In the assessment of the spine, CT is mainly used when vertebral fracture is suspected in PsA patients (4, 12).

A study by Kocijan et al. (27) evaluated bone microstructure and volumetric bone mineral density (BMD) in patients with PsA and psoriasis using high-resolution peripheral quantitative CT (HR-pQCT) scans at the ultradistal and periarticular radius. The study enrolled 50 PsA patients, 30 psoriasis patients, and 70 healthy, age- and sex-related controls. The results suggest that PsA is associated with significantly decreased trabecular volumetric BMD and deterioration of trabecular bone microstructure. The cortical BMD and microstructure in PsA patients didn't differ from the control group, in contrast with current findings in RA. Also, the duration of skin disease was associated with trabecular bone loss in PsA patients, a finding supporting the concept of subclinical musculoskeletal disease in psoriasis patients.

Magnetic resonance

MRI allows high-resolution imaging of all structures involved in arthritis, and is sensitive for peripheral and axial disease manifestations (4). Today, all joints can be evaluated with similar efficacy, and the technique is sufficiently standardized (7). Dynamic contrast-enhanced MRI in combination with current software offers acquisition of quantitative data about inflammatory processes, such as: ME (maximum enhancement), IRE (initial rate of enhancement), GD (gadolinium)

distribution, and Tonset (time of onset) that can be coded in color maps for further analysis (28).

For peripheral disease, T1-weighted sequences in 2 planes supplemented by a T2-weighted, fat-suppressed, or short tau inversion recovery sequences are generally performed to visualize synovitis, enthesitis, tenosynovitis, periarticular inflammation, bone marrow edema, bone erosion, and bone proliferation. Additional T1-weighted sequences after intravenous injection of a gadolinium contrast agent can aid identification of inflamed tissue (4, 29, 30). MRI can aid in differential diagnosis between PsA, RA, and OA. Bone marrow edema in PsA is frequently found close to the entheses, while in RA it is located near the capsular attachments, and in OA closer to subchondral areas (4, 31). Bone erosions are commonly located adjacent to collateral ligament insertions in PsA, and in OA they tend to have a central location (4, 32). Periostitis has been shown to be more frequent in PsA, while bone erosions are more common in RA (4, 33). Bone marrow edema and/or enthesitis in diaphyses are much more common in PsA than in RA (4, 34).

There are no specific definitions for MRI assessment of axial PsA, but definitions regarding SpA are available (35, 36). The main lesions assessed are bone marrow edema/osteitis, enthesitis, fat infiltration, bone erosion, bone proliferation, and ankylosis. Regarding the spine, bone marrow edema or soft tissue edema/enthesitis, are commonly seen at the anterior and posterior corners of the vertebral bodies, and at the costovertebral, facet, and costotransverse joints, while erosive discovertebral lesions (Andersson lesions) are less frequent but can be the first sign of the disease (4, 37).

Yanaba et al. (38) used the PsA MRI scoring system (PsAMRIS) (30) to evaluate the effects of adalimumab treatment in five adult Japanese male patients with active PsA. The study indicated that adalimumab treatment is associated with a dramatic improvement of enthesitis, whereas bone erosions may be resistant to such treatment.

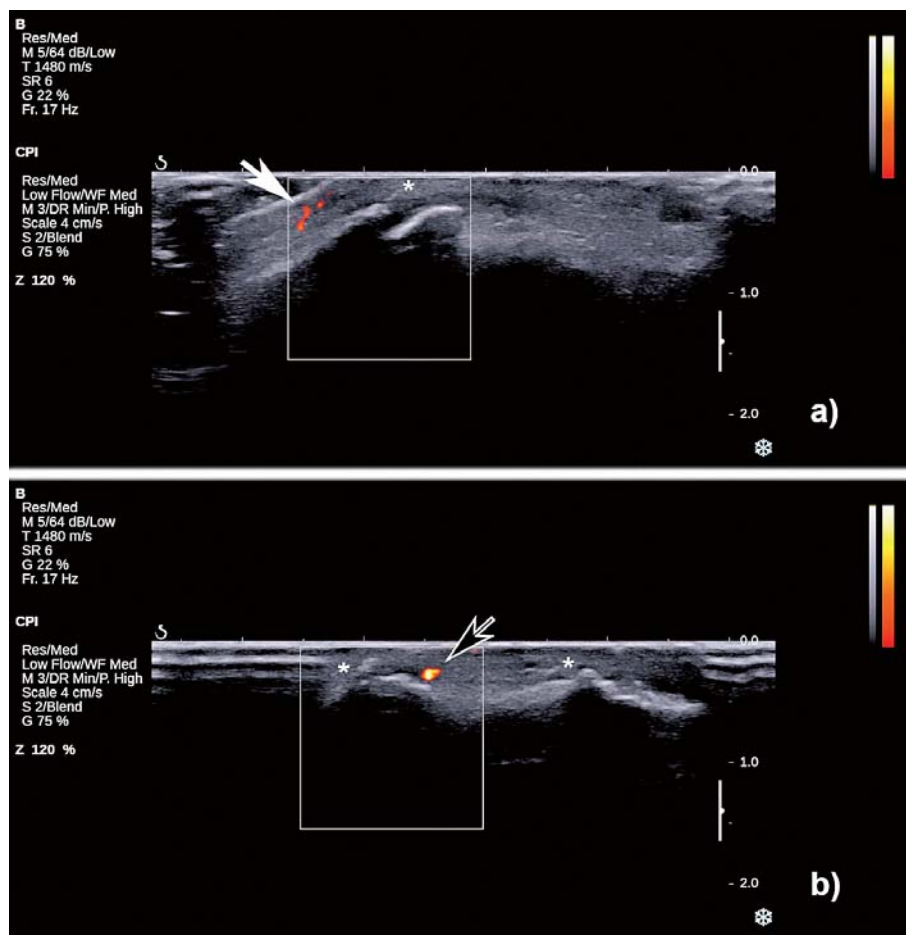
Zubler et al. (39) compared MRI findings of the forefeet in 31 healthy volunteers, 30 patients with symptomatic RA, and 30 patients with symptomatic PsA, to identify MRI patterns of RA or PsA. Mild bone marrow edema was a common finding, and tenosynovitis and joint effusion were occasional findings in healthy volunteers. Tenosynovitis and soft-tissue edema were more frequently observed in patients with PsA, while other arthritis-like findings on MRI were similar in patients with RA and PsA.

Ultrasound

Ultrasound (US) provides feasible, high-resolution visualization of all structures involved in peripheral arthritis, and is sensitive for peripheral disease manifes-

FIGURE 3 US imaging of the interphalangeal joints in the hand of an 85-year-old male patient with PsA. Longitudinal scan (a) and transversal scan (b) show periarticular calcifications, some osteophytes (asterisks), and soft tissue swelling. Power-Doppler scan verifies increased vascularization in the extensor tendon (white arrow) and synovial membrane (black arrow).

SLIKA 3. UZ pregled interfalangealnih zglobova šake stopala 85-godišnjega muškog pacijenta sa PsA. Uzdužni (a) i poprečni (b) prikaz pokazuju periartikularne kalcifikacije i nekoliko osteofita (zvjezdice) te edem mekih česti. Prikaz Power Dopplerom potvrđuje pojačanu vaskularizaciju u području tetive ekstenzora (bijela strjelica) i u sinovijalnoj membrani (crna strjelica).



tations, but is not recommended for the assessment of axial involvement (4). The current European League Against Rheumatism (EULAR) recommendations on the use of imaging techniques encourage the use of US in chronic arthritides (12, 40), and over recent years research has proved US to be valid, sensitive, and reliable in the assessment of synovitis, tenosynovitis, and enthesitis, including anatomical damage (bone and/or tendon erosions) in patients with RA or PsA (Figure 3). Moreover, there are also promising results regarding its prognostic value (41, 42). Because an US wave cannot penetrate bones, the technique is less sensitive than MRI and CT for diagnosing bone erosions and unable to diagnose osteitis (4). US findings in clinical or subclinical synovitis are nonspecific and the diagnostic value lies in recognizing the joint inflammation (4, 12). US diagnosis of enthesitis has received a lot of scientific attention lately. The hallmark lesions of enthesitis are (a) chronic changes: presence of enthesophytes, calcifications, and erosions at the insertion site and (b) inflammatory changes: increased thickness, hypoechogenicity, and Doppler activity in the enthesitis (4, 43). An example of US imaging in PsA is shown in Figure 3.

Acquacalda et al. conducted a study on the prevalence of ultrasonographic enthesitis in psoriasis pa-

tients with or without musculoskeletal symptoms (44). Data were obtained from 340 entheses in 34 patients. At baseline, US abnormalities were found in 97.1% of the total population and in 86.4% of the asymptomatic patients. At 6 months under systemic treatment, US morphological abnormalities were likely to improve.

Lin et al. (45) aimed to compare high-frequency ultrasound (HFU) findings in the fingers with PsA and RA and to explore the potential use of HFU in the early diagnosis of PsA. The study enrolled 44 PsA and 39 RA patients, and 20 healthy individuals. The results suggested that HFU is valuable in the detection of soft tissue inflammation and enthesitis in the fingers of PsA patients, and that it may be an easy, safe, and effective examination method in the early diagnosis of PsA as well as in the observation of related pathological changes.

Michelsen et al. conducted a cross-sectional study involving 141 PsA outpatients to investigate the association between clinical and ultrasonographic (US) evidence of inflammation in psoriatic arthritis (PsA), as well as to compare clinical and US remission criteria (46). The Disease Activity Index for Psoriatic Arthritis (DAPSA) and 28-joint Disease Activity Score (DAS28) reflected US findings better than the Composite Psori-

atic Disease Activity Index (CPDAI) and Psoriatic Arthritis Disease Activity Score (PASDAS). MDA was fulfilled in 22.7% and the clinical remission criteria in 5.7%–9.9% of the patients. US remission (no Power Doppler activity in all examined joints, entheses, and tendons) was found in 49.6% of the patients. Minimal disease activity (MDA), DAPSA, and Boolean's remission criteria predicted US remission.

Fiocco et al. have recently investigated contrast-enhanced US (CEUS) imaging with histopathological and immunohistochemical quantitative estimation of microvascular proliferation on synovial samples of patients affected by PsA (47) and investigated a possible association with the frequencies of pathogenic T helper (Th)-17 cells in PsA joints in eight patients (48). The results indicate that CEUS can truly measure synovial inflammation, and could be a useful tool to develop a quantitative imaging biomarker for monitoring target therapeutics in PsA.

Cozzi et al. (49) used CEUS to assess synovial inflammation in hand joints and evaluate the effects of mud-bath therapy on the clinical picture of PsA patients treated with TNF inhibitors. Their results suggest a decrease of residual synovial inflammation and a beneficial clinical effect of spa therapy in PsA patients treated with TNF inhibitors.

A study by Bandinelli et al. (50) has shown that US abnormalities of the hand and wrist were independent of early clinical PsA indices (except erosions), while they correlated to dermatological (except PASI), serological, and genetic parameters of disease.

Janta et al. (51) compared clinical and musculoskeletal (MS) US features between PsA patients treated with full and tapered dosages of biologic (b) disease-modifying antirheumatic drugs (DMARDs). The secondary objective was to compare clinical and MSUS features between PsA patients treated with bDMARDs with and without concomitant synthetic (s) DMARDs. The presence of B-mode and Doppler synovitis, tenosynovitis, enthesopathy, and paratenonitis was investigated. No significant differences were found between clinical, laboratory, and US variables, both for BM and CD, between patients with full and tapered dosages and between patients with and without concomitant sDMARD. Clinical assessment, MSUS variables, and MDA status are similar in patients receiving full and tapered dosages of bDMARDs.

Batmaz et al. (52) compared the femoral cartilage thickness of 33 PsA patients with that of 31 healthy controls. The results were similar between the two groups. In PsA patients the cartilage thickness was associated with disease activity, functional inadequacy, and enthesopathy scores.

Højgaard et al. (53) published a study protocol, aiming to investigate the association and prognostic value of pain mechanisms, ultrasonic activity, and clinical

outcomes in PsA patients on intensified antirheumatic treatment.

Other modalities

Other modalities, such as PET-CT and scintigraphy, are rarely used in clinical practice, but are an important focus of clinical research. The authors have found articles on use of PET-CT in the detection of asymptomatic enthesitis in psoriasis patients, which could be a prognostic factor of the onset of psoriatic arthritis (54). Another group investigated the role of PET-CT in the assessment of disease activity in PsA and RA (55). A group of authors from Italy offered a novel approach to the assessment of peripheral PsA, using functional infrared imaging (fIRI) with promising results (56).

Conclusion

PsA is an inflammatory joint disease that is similar to RA but can be easily distinguished from it upon a closer inspection. It usually shows a specific pattern of joint involvement: peripheral joints with an asymmetric pattern and the axial skeleton are most commonly affected. The clinical diagnosis relies heavily on imaging findings. Typical findings result from a combination of erosive and proliferative bone changes and inflammatory changes in the synovia, tendons, and entheses. Various imaging methods have a role in PsA diagnosis, but CR and US are mostly used due to their feasibility and relatively low cost. There is an increasing interest among researchers in the investigation of new possibilities in PsA diagnosis and follow-up of patients using both conventional US and CEUS.

CONFLICT OF INTEREST STATEMENT: The authors have no conflict of interest.

IZJAVA O SUKOBU INTERESA: Autori izjavljuju da nisu u sukobu interesa.

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