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Enthesopathy as early manifestation in psoriatic arthritis

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Abstract

Background: Despite the progress made in the study of psoriasis and psoriatic arthritis, their early diagnosis and treatment for practicing physicians continue to be a difficult problem.

Material and methods: 100 people were examined, including 70 patients with psoriatic arthritis aged between 18 and 60 years (23 men and 47 women), admitted to the rheumatology and arthrology departments of the *Timofei Moşneaga* Republican Clinical Hospital 2019-2022 (Favorable opinion of the Committee for Research Ethics, No 21 of 21.12.2019). The control group included 30 people with rheumatoid arthritis.

Results: Ultrasound signs of damage to the joint structures were detected, such as synovitis ($p=0.26$), cartilage changes ($p=0.433$), enthesopathy ($p=0.980$) and tenosynovitis, statistically significant differences ($p=0.800$). Magnetic resonance imaging determined that fluid was the predominant symptom in frequency ($n=13$, 92.86%), including in the small joints of the hands ($n=1$, 100%) and feet ($n=2$, 100%).

Conclusions: In large joints, the proliferation of the synovial membrane was detected in 51.67% of the joints and had predominantly high echogenicity. At small joints, synovial proliferation with predominantly low echogenicity occurred only in 6.1% of the joints.

Key words: psoriatic arthritis, enthesopathy, ultrasound.

Cite this article

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Introduction

Psoriatic arthritis (PsA) is a progressive chronic systemic disease associated with skin psoriasis, the social significance of which is determined by, first of all, an increase in debilitating forms of joint damage and an increase in mortality in patients with PsA compared to population mortality [1-4].

At the current level of development of rheumatology, there is a management in the treatment of PsA associated with the introduction of effective but also expensive antirheumatic drugs, slowing down the progression of joint destruction and the development of functional disorders (anti-TNF-alpha drugs) [5, 6]. Therefore, early diagnosis aimed at identifying morphological changes in bone structures and soft tissues of the joint, determines the effectiveness of conservative therapy and improves long-term prognosis [7-9].

Despite the progress made in the study of psoriasis and PsA, their early diagnosis and treatment for practicing physicians continue to be a difficult problem. The extreme variability of the clinical picture of PsA, various interactions between its various syndromes, the similarity with other

inflammatory diseases of the joints and spine, as well as the absence of mandatory and pathognomonic symptoms create great difficulties in the correct and timely diagnosis of this disease [2, 10-12]. Objective difficulties in diagnosing PsA also include the lack of guidelines, where at the modern level the problems of radiological diagnosis of the given pathology would be presented. All this leads to an extension of the diagnostic process and late administration of appropriate treatment.

Radiological research methods come first in the diagnosis of joint diseases and include all imaging methods such as radiography, ultrasonography, magnetic resonance imaging (MRI) [3, 6, 9]. Despite the fact that radiography continues to be the main method of diagnosis in osteo-articular diseases, it does not allow to assess the condition of those structures of the joint, the impairment of which is of particular clinical importance in early diagnosis [13-15].

Analysis of data from the literature has confirmed the high diagnostic potential of modern diagnostic methods such as radiography, ultrasonography and MRI, in psoriatic arthritis [16, 17]. However, reports on the possibilities of

ultrasound and MRI in the diagnosis of PsA are mainly presented in the literature under a non-systematized character, and there are only isolated reports about the possibilities of MRI in the diagnosis of PsA of a nature S [10, 11, 18]. As for ultrasounds in arthrology, they are mainly represented by the description of rheumatoid arthritis (RA) and osteoarthritis and to a lesser extent PsA [19, 21].

Differential diagnosis of psoriatic and rheumatoid arthritis is quite difficult, belonging to a group of diseases whose morphological basis are proliferative changes in the synovial membrane [22]. In the specialized literature, there are unitary references to the problem of differential diagnosis of these two nosological units using MRI and joint ultrasound [23].

Despite the obvious success of ultrasound diagnosis, a number of diagnostic problems still remain unopened and require further study. Therefore, the ultrasound symptoms of joint damage in patients with PsA have not been definitively systematized. The available sources do not provide data on the relationship between the severity of ultrasound symptoms and clinical and laboratory indications. Accordingly, there is no data on the importance of ultrasound in evaluating the activity of the inflammatory process in PsA, which plays an essential role in monitoring treatment.

In addition, the problem of differential diagnosis of RA and PsA being diseases with a common morphological substrate in the form of synovial membrane proliferation is practically not revealed in the specialized literature.

The purpose of the study is to substantiate the use of ultrasound examination of patients with psoriatic arthritis to assess the work of the pathological process.

Material and methods

100 people were examined, including 70 patients with PsA aged between 18 and 60 years, of which 23 men and 47 women who were undergoing treatment, admitted to the rheumatology and arthrology departments of the *Timofei Moşneaga* Republican Clinical Hospital or treated in outpatient settings in the period 2018-2022 (Favorable opinion of the Committee for Research Ethics at no.21 of 21.12.2019). The comparison group included 30 people with RA.

The patient was considered included in the study after signing the informed consent form. The diagnosis of PsA was established according to the CASPAR diagnostic criteria (2006) [3-5]. Of the studied patients, patients with polyarticular variant (n=28; 40.0%) and mono-, oligoarthritis (n=29; 41.4%) were detected with the same frequency. In 18.6% (n = 13) of the observations, damage to the distal joints of the hands and plants was detected. The predominance were patients with a minimum degree of activity (n=31; 44.3%) and average (n=24; 34.3%), and patients with a maximum degree of activity (n=12; 17.1%) and patients in remission (n=3; 4.3%) were with lower frequency.

The local activity of inflammation in the joints of interest was evaluated according to the activity index of synovitis, thus taking into account clinical manifestations, such as hyperthermia, inflammation and pain.

The analysis of the clinical material took into account the nature of psoriasis and the stage of its development, the prevalence, type, as well as the age of the disease. Skin manifestations were detected in 69 patients studied with PsA (98.57%).

Peripheral blood parameters were studied in patients with PsA: in 36 people (51.4%) with an average and maximum degree of activity, there was an increase in peripheral blood indicators reflecting inflammatory activity. In the study of biochemical parameters, hypoalbuminemia, an increase of C-reactive protein, seromucoids, was observed.

All patients (n=70; 100.0%) had paired knee joints (n=140; 4.3%), ankle joints (n=46; 1.4%), radiocarpal joints (n=22; 0.7%) and 54 (77.1%) – small hand and plant joints (n=3 024; 93.6%). A total of 3.232 joints were examined.

In order to increase the possibilities of Power Doppler imaging in PsA, the vascularization of the synovial membrane in those joints where its thickening or proliferation was detected was studied. Thus, 296 joints were examined.

Magnetic resonance imaging was used as a reference method and was performed in 15 patients on the “Exselart Vantage” device (Toshiba, Japan) with a magnetic field strength of 1.5 T. In total, 14 knee joints, plant joints (n = 28) and hands (11 = 14) were examined, as a result, 56 joints. Joint examination was performed in previous, sagittal and axial projections in T1, T2 and FSat mode.

The assessment of the degree of synovial vascularization was based on the maximum number of color locus in the area of interest, the size of which depends on the studied area. Thus, in the study of the synovial membrane in the upper inversion of the knee joint, the estimated area area was 5-7 cm², in the study of the wrist and ankle joints – 3-4 cm², small joints of the hands and feet – 1-2 cm².

The comparison group consisted of 30 patients with RA aged 27 to 63 years (average age 45±12.3 years) with a duration of the disease from 6 months to 32 years (average duration 12±5.4 years). Patients in the main group and in the comparison group were comparable in age and duration of the disease. All patients underwent ultrasound of the knee joints and the joints of the hands and feet (n=2320). The analysis of the obtained results was carried out using standard statistical methods (Spearman correlation analysis, Mann-Whitney criterion, X² criterion, Fisher criterion). The differences were considered significant at p<0.05.

Results

The most common changes in the joints in patients with PsA were an increase in the amount of intra-articular fluid and the proliferation of the synovial membrane. The appearance of fluid in the joints occurred in the overwhelming number of patients (n = 63.90%) and only in 10% (n = 7) of the observations there was no liquid. In total,

fluid was detected in 293 out of 3.232 joints (9.1%). Among the knee joints in which there was an increase in the amount of intraarticular fluid ($n = 79$; 100%), in 48.8% ($n = 37$) of the observations were recorded joints with a small amount of fluid (gradation 1). In a smaller number, the amount of liquid corresponding to grade 2 ($n = 24$; 30.4%) and grade 3 ($n = 18$; 20.8%) was observed. In the radiocarpal joints, the maximum thickness of the liquid in the joints was 6 mm, in the ankle joints – 8 mm. The maximum thickness of the fluid in small joints was 2 mm. In this study, homogeneous effusion into the joint cavity prevailed ($n=201$; 68.6%). The heterogeneity of the structure ($n=92$; 31.4%) was due to the appearance of partitions, suspensions or hyperechogenic solid inclusions against the background of anechogenic contents.

Synovial proliferation was detected in 296 (9.16%) joints. In most observations ($n = 286$; 96.6%) diffuse thickening of the synovial membrane was determined. The echogenicity of the synovial membrane was different: in predominant quantity – low ($n = 200$; 67.6%), in the smaller amount – increased ($n= 96$; 32.4%). Cartilage thickening was detected in 4 joints (2.9%). In 58 (97.1%) cases, there was a thinning of the cartilage, which in a number of observations was accompanied by a change in the contours in the form of unevenness and blur, and in a number of cases – a change in the normal ecostructure. In some patients with thinning of cartilage (22%), an increase in its echogenicity was observed.

A number of authors believe that the main target in PsA is not the synovial membrane, but bone tissue and inflamed entheses [7-9]. Therefore, special attention was paid to the search of bone erosions and to assess the condition of the tendon-ligament apparatus. The ultrasound image of ligament and tendon changes included enthesopathy of the patellar ligament and the quadriceps tendon of the femoral and tenosynovitis.

In the enthesopathies of the patellar tendons and tendons of the quadriceps, in all cases thickening of the ligament at the site of attachment, loss of the typical stratified structure and the appearance of small hyperechogenic inclusions were observed. Changes in the bone in enthesopathy were manifested in the form of bumps of the cortical layer.

In some patients ($n = 7$; 10%), there was a significant decrease in the echogenicity of the patellar ligament at the site of bone insertion, also with the loss of the typical structure. These were patients with marked activity of the disease, and the visible clinical picture was considered as an enthesis.

Tenosynovitis of the flexors of the fingers, flexors and extensors of the hands was detected in 30 localizations. In most observations ($n = 28$; 93.3%), the appearance of fluid in the synovial sheath of the tendon was combined with the preservation of the normal echostructure of the tendon itself. And only in 2 cases (6.7%) there was a thickening of the tendon with loss of the typical echostructure of the tendon.

According to ultrasound data, bone erosions were detected only in 2 people (1.4%) in the ends of the metacarpal bones, while on radiography and magnetic resonance imaging, the frequency of severity of this symptom was higher.

However, data from the literature indicate a higher sensitivity of ultrasound in detecting erosions compared to classical radiography [1, 4, 8].

The lesion of the small joints of the hands and feet was characterized primarily by diffuse proliferation of the synovial membrane, mainly with low echogenicity ($p = 0.0001$), which in 92% of cases is accompanied by a homogeneous effusion ($p = 0.005$). Changes in the ligament apparatus in all observations are represented by tenosynovitis. From the data in the literature it is known that the low echogenicity of the synovial membrane is due to its edema against the background of active inflammation, and this pattern was reflected in the clinical picture of the lesion of the small joints of the hands and plants in this study. It remains unclear the frequent detection of the synovial membrane, mainly with high echogenicity, in the knee joints, independent of the activity of the disease. Perhaps this fact is due to the earlier fibrosis of the synovial membrane in this localization.

Magnetic resonance imaging was the second method of investigation in the complex diagnosis of PsA and was used as a reference method. In the study group, fluid was the predominant symptom in frequency ($n = 13$, 92.86%), including in the small joints of the hands ($n = 1$, 100%) and legs ($n = 2$, 100%). Synovial proliferation was the second most common sign of damage to the knee joint ($n = 10$; 71.43%) and was detected in 3.6% of the foot joints and 7.1% of the joints of the hands.

In the present study, erosions were detected in 3 joints and localized in the condyles of the femoral and tibial bones and in the ends of the metatarsal bones II, III on all surfaces. The changes in cartilage consisted of its thinning and structural changes and were observed in 28.57% of cases in the observed contingent ($n = 4$). In one observation, fragmentation of cartilage occurred, in the other, changes in the type of crack were revealed, which fall within the manifestations of chondromalacia.

As MRI was chosen as the reference method for correctly evaluating the diagnostic efficacy of ultrasonography in detecting existing changes, MRI results obtained in 15 patients in 56 joints were compared with ultrasound data of the same patients (tab. 1).

Table 1. Comparison of signs, viewed at USG and MRI, in 16 patients

Symptom	Number of joints with detected changes	
	USG PD	MRI
Liquid	16 (28.6%)	16 (28.6%)
Proliferation of synovial membrane	11 (19.6%)	12 (24.1%)
Cartilage modification	4 (7.1%)	4 (7.1%)
Bone erosions	2 (3.5%)	4 (7.1%)
Osteophytes	7 (12.5%)	7 (12.5%)
Degenerative changes in tendons	6 (42.9%)	7 (50%)
Tenosynovitis	3 (5.4%)	3 (5.4%)

In these studies, MRI data have generally been consistent with the results of ultrasound in the diagnosis of the

presence of intraarticular fluid, synovial proliferation, cartilage changes, osteophytes, as well as tenosynovitis and enthesopathy.

The greatest diagnostic efficacy of ultrasound was achieved in detecting fluids, cartilage changes, osteophytes and tenosynovitis, at which sensitivity and specificity were 100%. These high rates were due to the exclusion of the possibility of diagnostic errors, given the sufficiently clear ultrasonic visualization of these joint structures. Slightly lower diagnostic efficiency was achieved in the detection of synovial proliferation and enthesopathy, in which the sensitivity was 91.7% and 85.7%, specificity – 100%, diagnostic accuracy – 95.6%, respectively, 92.9%. The lowest efficiency was achieved in identifying marginal bone erosion; sensitivity was 50%, specificity – 100%, accuracy of diagnosis – 75%.

In order to assess the possibilities of energy Doppler mapping in the reflection of PsA activity, the results of ultrasound studies and clinical and laboratory study data were compared. Indicators were studied that reflect the general activity of the disease (ESR and number of leukocytes) and indicators that directly reflect the presence and activity of the inflammatory process in the studied joint: pain, inflammation and hyperemia, first of all, it was necessary to identify the severity of the main ultrasound symptoms of synovitis in the knee and small joints of the hands and feet, depending on the clinical manifestations of inflammation. At the same time, for the knee joints, the thickness and degree of synovial vascularization and the amount of fluid were taken into account, for small joints — the fact of the presence of thickened synovial, its vascularization and the presence of fluid (tab. 2 and 3).

Table 2. Expression of ultrasound symptoms of synovitis depending on the clinical activity of inflammation in the knee joints

Ultrasonographic sign	Group No 1 (n=46) low activity	Group No 2 (n=12) average activity	Group No 3 (n=10) high activity
The thickness of the synovial membrane			
grade 1	44 (95.7%)	1 (8.3%)	-
grade 2	2 (4.3%)	10 (83.4%)	-
grade 3	-	1 (8.3%)	10 (100%)
Degree of vascularization			
grade 0	26 (56.5%)	0	0
grade 1	20 (43.5%)	0	0
grade 2	0	12 (100%)	0
grade 3	0	0	10 (100%)
Quantity of liquid			
grade 0	24 (52.2%)	0	0
grade 1	22 (47.8%)	0	0
grade 2	0	10 (83.3%)	2 (20%)
grade 3	0	2 (16.7%)	8 (80%)

Cartilage changes			
thickeners	0	0	4 (40%)
thinning	40 (87.0%)	12 (100%)	6 (60%)
change strokes	30 (65.2%)	8 (66.7%)	10 (100%)
modification of the echostructure	30 (65.2%)	8 (66.7%)	10 (100%)
Decrease in the echogenicity of the ligament in the place of fixation (enthesitis)	0	0	7 (70%)

Table 3. Expression of ultrasound symptoms of synovitis depending on the clinical activity of inflammation in small joints

Ultrasonographic sign	Group No 1 (n=84) low activity	Group No 2 (n=10) average activity	Group No 3 (n=90) high activity
Thickening of the synovial membrane:			
up to 3 mm	84 (100%)	2 (20%)	0
more than 3 mm	0	8 (80%)	90 (100%)
Degree of vascularization:			
grade 0	70 (83.3%)	0	0
grade 1	14 (16.7%)	0	0
grade 2	0	8 (80%)	3 (3.3%)
grade 3	0	2 (20%)	87 (96.7%)
Presence of liquid	76 (90.5%)	10 (100%)	90 (100%)
The appearance of fluid in the tendon sheath (tenosynovitis)	0	2 (20%)	36 (40%)
Defect in the cortical layer (bone erosion)	0	0	2 (2.2%)

Over the course of the study, ultrasonography and clinical and laboratory activity data were compared for all joints as a whole. The results of correlation analysis indicate a positive correlation between the severity of ultrasound symptoms of synovitis and the level of clinical and laboratory indicators of inflammation. At the same time, the ultrasound symptom, which correlates the most with the level of local activity, is the degree of vascularization of the synovial membrane, which appeared both in the large joints ($r = 0.508$) and in the small ones ($r = 0.500$). The strongest correlation is observed between the amount of fluid ($r = 0.401$) and the degree of vascularization of the synovial membrane in the knee ($r = 0.508$), small joints ($r = 0.500$) and the level of ESR and leukocytosis. A weaker correlation is observed between the level of laboratory parameters and the thickness of the synovial membrane ($r = 0.383$).

When analysing the frequency of occurrence of ultrasound signs, depending on the duration of the disease, statistically significant differences were found only in the

frequency of occurrence of marginal bone growths, which were significantly more often determined in the group of patients with a duration of the disease of more than 10 years ($p = 0.04$). For other ultrasound signs of damage to the joint structures, such as synovitis ($p = 0.26$), changes in cartilage ($p = 0.433$), enthesopathy ($p = 0.980$) and tenosynovitis, statistically significant differences ($p = 0.800$) depending on the occurrence were not detected. The possibility of using modern radiographic diagnostic methods in monitoring the treatment of arthritis is widely discussed in modern literature [5, 9, 17]. The possibilities of Dopplerography have been studied in terms of evaluating the dynamics of the treatment of patients with PsA. The study was conducted in 10 patients with early diagnosed PsA. Ultrasound was performed at the time of launch of treatment and 1 month after taking nonsteroidal anti-inflammatory drugs and DMARD therapy with methotrexate. 13 knee joints and 9 metatarsophalangeal joints (22 joints in total) were examined. Before the start of treatment, vascularization was detected in all joints, and joints with the degree of vascularization 2 and 3 prevailed. Against the background of treatment was determined the number of joints in which blood flow was not recorded or a low degree of vascularization (grade 1).

When comparing the vascularization indices in the groups before and during the treatment, a significant decrease in the degree of vascularization of the synovial membrane in the joints of the knee ($p = 0.018$) and of the small ones ($p = 0.002$) was observed against the background of therapy with non-steroidal anti-inflammatories and methotrexate. Simultaneously with this, there was a decrease in indicators of laboratory activity of arthritis. To evaluate the changes in these indicators, the non-parametric criterion of Wilcoxon's paired comparison with materiality level ($p < 0.05$) was used. As a result of the comparison, statistically significant differences were obtained for ESR ($p = 0.012$) and leukocytes ($p = 0.005$) before and during treatment.

Comparison of ultrasound data and magnetic resonance imaging demonstrated the comparability of methods for detecting intra-articular inflammatory fluid, synovial proliferation, cartilage changes, detection of tenosynovitis and enthesopathies.

Ultrasound examination of the joints in patients with PsA, including the determination of the amount of intra-articular inflammatory fluid, the thickness of the synovial membrane and the degree of its vascularization, the assessment of the state of the tendon-ligament apparatus, allows to assess the activity of the inflammatory process. An essential role in determining the activity is played by the evaluation of the degree of vascularization, as indicated by a positive correlation between local inflammatory activity and synovial vascularization ($r = 0.591$).

The use of ultrasound to assess the dynamics of treatment was justified and was characterized by a decrease in the degree of vascularization of the synovial membrane in combination with a decrease in the amount of intra-articular inflammatory fluid and the thickness of the synovial membrane.

Based on the systematization of the ultrasound image, certain diagnostic differential visual signs of joint changes in psoriatic and rheumatoid arthritis were obtained, namely the predominance of ligament and tendon enthesopathies of the knee joint in PsA.

Discussion

Ultrasound examination was the main method in the complex diagnosis of PsA. The results of the study demonstrated that in patients with PsA damage to all anatomical structures of the joint with polymorphism of the ultrasound model is detected.

During the ultrasound, some differences were found in the visual image depending on the location of the changes. Thus, the lesions of the knee joint are characterized by a high frequency of heterogeneous occurrence of overflow into the joint cavity, proliferation of the synovial membrane of a diffuse or focal nature, high echogenicity of the synovial membrane and its poorly expressed vascularization, changes in the tendon-ligament apparatus in the form of enthesopathies.

The introduction into practice of Doppler energy mapping, according to a significant number of authors [3-8], provides fundamental diagnostic capabilities. The possibilities of Dopplerography of the synovial membrane in rheumatoid arthritis are described in detail [19, 21-23]. Reports on the study of synovial vascularization in PsA are still isolated. In the studies, a high sensitivity of ultrasound was reported in detecting signs of synovitis and tenosynovitis in lesions of the joints of the hands and feet in PsA, however, the data of energetic Doppler drifting did not have correlations with clinical and laboratory signs of inflammatory activity.

The activity of synovitis plays a central role in the formation of the clinical picture of joint diseases [2, 7, 15]. How actively it evolves also depends on the choice of treatment and the prognosis of the disease. In practice, it is very important not only to establish that the patient has synovitis, but also to have an objective tool to assess his activity and dynamics of the process under the influence of the treatment that is prescribed to the patient. The use of quantitative research methods in medicine can significantly increase the reliability of assessing the patient's condition. Sources in the literature indicate the ability of ultrasonography to assess the activity of inflammation in the knee joint in RA based on the positive correlations between clinical and laboratory activity, arthritis and the symptoms detected during ultrasound, namely between the thickness and degree of vascularization of the synovial membrane, the amount of intra-articular fluid [12, 13, 16-19].

At the same time, was analyzed the severity of the changes of other joint structures whose involvement is of clinical importance, namely the presence/absence of bone erosions, the condition of cartilage and tendon-ligament apparatus.

PsA and RA are similar in morphology and clinical course

of disease. In order to study the ultrasound possibilities in identifying the differences of these two diseases, in 30 patients with RA (comparison group) ultrasound of the knee joints and small joints of the hands and feet (2.320 joints) was performed. The results of the ultrasound were compared with the data of clinical and laboratory activity. When comparing the frequency of occurrence of distinctive signs at ultrasonography of damage to the knee and small joints, depending on the nosological affiliation, the following results were obtained. In the group of patients with PsA, enthesopathy and enthesitis of their own patellar ligaments and tendons of the femoral quadriceps were detected significantly more often ($p = 0.007$). In the study of small joints in patients of the PsA group, inflammatory fluid was detected more often than in patients in the comparison group ($p = 0.009$). For patients with RA, a feature of the visual picture was the more frequent detection of proliferative changes in the synovial membrane in both the knee joints ($p = 0.03$) and in the small ones ($p = 0.001$), compared to PsA. Statistically there were no significant differences in the frequency of detection of inflammatory fluid in the knee joints, tenosynovitis, the nature of joint effusion and changes in cartilage structure in patients with PsA and RA.

Analysis depending on the lasting changes in the disease detected at USG has shown that marginal bone growths are equally often detected in a group of patients with the duration of the disease more than 10 years, regardless of nosology.

Thus, the study carried out showed the effectiveness of the ultrasonographic method in detecting morphological changes in joints in patients with PsA, determining the activity and evaluating the results of treatment.

Conclusions

1. Ultrasound is a highly informative method in detecting a wide range of morphological changes in the joints of patients with PsA. The highest index of sensitivity appeared when inflammatory fluid, cartilage changes, osteophytes and tenosynovitis were detected. Less sensitivity was achieved in the detection of synovial membrane proliferation, enthesopathy, the slightest sensitivity was observed in the visualization of marginal bone erosions. At the same time, the indicators of specificity were equally high.

2. In large joints, the proliferation of the synovial membrane was detected in 51.67% of the joints and had predominantly high echogenicity, as well as accompanied by intra-articular overflow in all observations. In small joints, synovial proliferation with predominantly low echogenicity occurred only in 6.1% of the joints, due to their rarer lesion, and was combined with an increase in intra-articular fluid in 92% of cases. Tendon-ligament injury in PsA included enthesopathy in the knee joints, tenosynovitis in the ankle, radiocarpal joints, and in small joints of hands and plants.

3. Ultrasound criteria for the validity of PsA are: the degree of severity of synovitis, as well as the presence of

tenosynovitis and enthesitis. The strongest correlation was obtained between the activity of inflammation and vascularization of the synovial membrane ($r=0.591$) and tenosynovitis ($r=0.547$), as well as between the levels of ESR and leukocytes, the amount of inflammatory fluid ($r=0.401$) and the degree of vascularization of the synovial membrane ($r=0.508$).

4. An indicator of the positive dynamics of PsA treatment with DMARD drugs is the reduction of synovial membrane vascularization in combination with a decrease in the amount of inflammatory intra-articular fluid and the thickness of the synovial membrane, visualized at Power Doppler mapping.

5. The significant differences between PsA and RA are the presence of enthesopathies of the ligaments proper of the patellar tendon and the quadriceps tendon of the femoral and the predominance of intra-articular overflow in small joints compared to the predominance of the frequency of proliferation in small and knee joints in patients with RA.

References

- Zuliani F, Zabotti A, Errichetti E, Tinazzi I, Zanetti A, Carrara G, et al. Ultrasonographic detection of subclinical enthesitis and synovitis: a possible stratification of psoriatic patients without clinical musculoskeletal involvement. *Clin Exp Rheumatol*. 2019;37(4):593-9.
- Elnady B, El Shaarawy NK, Dawoud NM, Elkhoully T, Desouky DES, El-Shafey EN, et al. Subclinical synovitis and enthesitis in psoriasis patients and controls by ultrasonography in Saudi Arabia; incidence of psoriatic arthritis during two years. *Clin Rheumatol*. 2019;38(6):1627-35. doi: 10.1007/s10067-019-04445-0.
- Tang Y, Cheng S, Yang Y, Xiang X, Wang L, Zhang L, et al. Ultrasound assessment in psoriatic arthritis (PsA) and psoriasis vulgaris (non-PsA): which sites are most commonly involved and what features are more important in PsA? *Quant Imaging Med Surg*. 2020;10(1):86-95. doi: 10.21037/qims.2019.08.09.
- Macchioni P, Salvarani C, Possemato N, Gutierrez M, Grassi W, Gasparini S, et al. Ultrasonographic and clinical assessment of peripheral enthesitis in patients with psoriatic arthritis, psoriasis, and fibromyalgia syndrome: the ULISSE study. *J Rheumatol*. 2019;46(8):904-11. doi: 10.3899/jrheum.171411.
- Florescu A, Vere CC, Florescu LM, Muşetescu AE, Bondari A, Ciurea PL. Clinical and ultrasound assessment of enthesitis in psoriatic arthritis in a Romanian cohort. *Curr Heal Sci J*. 2018;44(4):347-51. doi: 10.12865/CHSJ.44.04.04.
- Yamada Y, Inui K, Okano T, Mandai K, Mamoto K, Koike T, et al. Ultrasound assessment, unlike clinical assessment, reflects enthesitis in patients with psoriatic arthritis. *Clin Exp Rheumatol*. 2021;39(1):139-145.
- Wervers K, Luime JJ, Tchetverikov I, Gerards AH, Kok MR, Appels CWY, et al. Comparison of disease activity measures in early psoriatic arthritis in usual care. *Rheumatology*. 2019;58(12):2251-9. doi: 10.1093/rheumatology/kez215.
- Arslan Alhussain F, Kasapoglu Gunal E, Kurum E, Bakirci S, Ozturk AB, McGonagle D, et al. Greater magnitude of enthesial microdamage and repair in psoriatic arthritis compared with ankylosing spondylitis on ultrasound. *Rheumatology*. 2019;58(2):299-303. doi: 10.1093/rheumatology/key238.
- Zabotti A, McGonagle DG, Giovannini I, Errichetti E, Zuliani F, Zanetti A, et al. Transition phase towards psoriatic arthritis: clinical and ultrasonographic characterisation of psoriatic arthralgia. *RMD Open*. 2019;5(2):e001067. doi: 10.1136/rmdopen-2019-001067.
- Wervers K, Herrings I, Luime JJ, Tchetverikov I, Gerards AH, Hazes JMW, et al. Association of physical activity and medication with enthesitis on

- ultrasound in psoriatic arthritis. *J Rheumatol.* 2019;46(10):1290-4. doi: 10.3899/jrheum.180782.
11. Macía-Villa C, De Miguel E. Updating the use of the Madrid sonographic entheses index (MASEI): a systematic review of the literature. *Rheumatology.* 2020;59(5):1031-40. doi: 10.1093/rheumatology/kez356.
 12. Fiorenza A, Bonitta G, Gerratana E, Marino F, Sarzi-Puttini P, Salaffi F, et al. Assessment of entheses in patients with psoriatic arthritis and fibromyalgia using clinical examination and ultrasound. *Clin Exp Rheumatol.* 2020;38 Suppl 123(1):31-9.
 13. Girolimetto N, Macchioni P, Tinazzi I, Costa L, Peluso R, Tasso M, et al. Predominant ultrasonographic extracapsular changes in symptomatic psoriatic dactylitis: results from a multicenter cross-sectional study comparing symptomatic and asymptomatic hand dactylitis. *Clin Rheumatol.* 2019;39(4):1157-65. doi: 10.1007/s10067-019-04683-2.
 14. Tinazzi I, McGonagle D, Macchioni P, Aydin SZ. Power Doppler enhancement of accessory pulleys confirming disease localization in psoriatic dactylitis. *Rheumatology.* 2019;59(8):2030-2034. doi: 10.1093/rheumatology/kez549.
 15. McGonagle D, Tan AL, Watad A, Helliwell P. Pathophysiology, assessment and treatment of psoriatic dactylitis. *Nat Rev Rheumatol.* 2019;15(2):113-22. doi: 10.1038/s41584-018-0147-9.
 16. Zabotti A, Sakellariou G, Tinazzi I, Batticciotto A, Canzoni M, Carrara G, et al. Clinical science novel and reliable dactylitis global sonographic (DACTOS) score in psoriatic arthritis. *Ann Rheum Dis.* 2020;79(8):1037-1043. doi: 10.1136/annrheumdis-2020-217191.
 17. Sapundzhieva T, Karalilova R, Batalov A. Hand ultrasound patterns in rheumatoid and psoriatic arthritis: the role of ultrasound in the differential diagnosis. *Rheumatol Int.* 2020;40(6):837-48. doi: 10.1007/s00296-020-04559-8.
 18. Sakellariou G, Scirè CA, Adinolfi A, Batticciotto A, Bortoluzzi A, Seidie AD, et al. Differential diagnosis of inflammatory arthropathies by musculoskeletal ultrasonography: a systematic literature review. *Front Med.* 2020;7:141. doi: 10.3389/fmed.2020.00141.
 19. Aydin SZ, Bakirci S, Kasapoglu E, Castillo-Gallego C, Arslan Alhussain F, Ash ZR, et al. The relationship between physical examination and ultrasonography of large entheses of the achilles tendon and patellar tendon origin. *J Rheumatol.* 2019;47(7):1026-30. doi: 10.3899/jrheum.190169.
 20. Bosch P, Husic R, Ficjan A, Gretler J, Lackner A, Graninger WB, et al. Evaluating current definitions of low disease activity in psoriatic arthritis using ultrasound. *Rheumatology.* 2019;58(12):2212-20. doi: 10.1093/rheumatology/kez237.
 21. Wervers K, Vis M, Rasappu N, van der Ven M, Tchetverikov I, Kok MR, et al. Modification of a sonographic enthesitis score to differentiate between psoriatic arthritis and young healthy volunteers. *Scand J Rheumatol.* 2018;47(4):291-4. doi: 10.1080/03009742.2017.1393695.
 22. Hammer HB, Michelsen B, Sexton J, Haugen IK, Provan SA, Haavardsholm EA, et al. Swollen, but not tender joints, are independently associated with ultrasound synovitis: results from a longitudinal observational study of patients with established rheumatoid arthritis. *Ann Rheum Dis.* 2019;78(9):1179-85. doi: 10.1136/annrheumdis-2019-215321.
 23. Helliwell PS, Coates LC, Chew NS, Lettieri G, Moverley AR, Freeston JE, et al. Comparing psoriatic arthritis low-field magnetic resonance imaging, ultrasound and clinical outcomes: data from the TICOPA trial. *J Rheumatol.* 2020;47(9):1338-1343. doi: 10.3899/jrheum.181385.

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