Original paper

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The initial ultrasonographic examination of hands and feet joints in patients with early rheumatoid arthritis

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Abstract

Objectives: The aim was to assess of the morphology, intensity, and activity of changes in the first ultrasonographic (US) examination of hands and feet in patients with early arthritis (lasting up to 12 months) who were ultimately diagnosed with rheumatoid arthritis (RA). An attempt was made to demonstrate a correlation between the intensity of lesions in US and selected laboratory parameters.
Material and methods: Ultrasonographic examination was performed using a LOGIC GE 500 device on a group of 60 patients with arthritis (46 women, 14 men) aged 18–80, previously untreated. In total, 3120 hand and feet joints were examined. The assessment focused on the presence of joint effusion, synovial proliferation and power Doppler signals (assessed on a semi-quantitative scale). Each patient underwent laboratory tests, necessary for making a diagnosis. In order to analyze the correlations between changes in US and laboratory parameters, erythrocyte sedimentation rate (ESR), reactive protein test (CRP), rheumatoid factor (RF), and anti-citrullinated protein antibodies (ACPAs) were used.
Results: In the study group, the average duration of arthritis symptoms until the first US examination was 5.6 months. Among the 3120 examined hand and foot joints, deviations from the norm appeared in 1093 joints, synovial hypertrophy was found in 471 joints (grade 1 synovial hypertrophy was reported most frequently), while presence of signal in Power Doppler was revealed in 261 joints (grade 1 was observed most frequently). A statistically significant correlation was found between the intensity of changes in Power Doppler and CRP concentration.
Conclusions: In patients with increased concentrations of CRP, we may expect arthritis of higher intensity, therefore, in order to prevent the progression of destructive changes, it is necessary to quickly implement effective disease-modifying antirheumatic treatment. The conducted research showed that the activity of joint inflammation is not affected by the values of ESR and the presence of RF or ACPAs.

Key words: early rheumatoid arthritis, synovitis, musculoskeletal ultrasonography.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune-based inflammatory disease with synovium as the main site of inflammation. The ongoing inflammation causes synovial thickening and excessive production of synovial exudate [1, 2]. Progressing inflammation results in the appearance of invasive synovial tissue, called the pannus, and subsequent destructive changes, including marginal and subchondral erosions and joint damage. In recent years, abundant scientific evidence has confirmed the necessity of early diagnostics in RA, which enables to isolate a group of patients requiring intensive disease-modifying anti-rheumatic treatment [3, 4]. It provides the opportunity to improve the patients'

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condition as well as for preventing disability and irreversible joint damage caused by inflammation. Certain benefits of economic nature may also be achieved [5].

Ultrasonography (US) is an invaluable tool facilitating early diagnosis [6]. This diagnostic method enables the acquisition of precise images of the examined organ or pathologically changed sites. It utilizes the spread, dispersion, and reflection of ultrasound waves on the boundaries of various structures. Medical US uses frequencies between approximately 2 and 50 MHz. The use of lower frequencies exposes deeper structures, while higher frequencies are used to visualize elements located superficially. Frequencies between 5 and 18 MHz are usually used for ultrasonographic examination of the osteoarticular system. Synovium is not visible in ultrasonographic image of a healthy joint. In the case of inflammation, this method enables very early imaging of the thickened synovium and other pathological changes, which may not yet be diagnosed in physical examination. The inflamed sections of synovium may also exhibit increased blood flow, which is visible in the power Doppler ultrasound (PDUS) examination. This constitutes another significant element in the diagnostics of joint diseases and the assessment of disease activity. For this reason, US is one of the key methods in the assessment of peripheral joints and plays a very important role in early diagnostics. Moreover, it is an important tool for monitoring treatment effectiveness. An additional advantage provided by US is the ability to simultaneously assess many joints in a relatively short time. Other benefits of this method include its low cost, noninvasiveness, high availability, and repeatability of examination [7–11]. The high sensitivity of US examination is comparable to magnetic resonance imaging (MRI). It is also much more sensitive than classic radiography [4, 12, 13].

Material and methods

The patients from the present study were selected from a group of 200 individuals showing symptoms of early arthritis, diagnosed at the Department of Rheumatology and internal diseases in the years 2010–2013. There were 60 patients qualified (46 women, 14 men) in whom diagnostics and clinical monitoring led to the diagnosis of RA. The inclusion criteria were symptoms duration of up to 12 months and the presence of swelling in at least 1 joint. The exclusion criteria were use of disease-modifying antirheumatic drugs (DMARDs) and glucocorticoids (GC), the diagnosis of an active infection, and neoplasms. The average age of the patients during the first ultrasonographic examination was 48 years (18–80 years). The average symptom duration before the first examination was 5 months (1–12 months). All patients met the RA classification criteria according to ACR and EULAR from 2010. Before inclusion in the study written informed consent were required from all patients. The study protocol was accepted by the local Ethic Committee.

On the day of the first US examination, all patients underwent the laboratory tests necessary for clinical diagnosis, especially: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), and anti-citrullinated proteins (ACPA). Moreover, all patients received physical examination and provided their medical history; DAS28 factor was assessed in order to establish disease activity. The US examiner was not familiar with the results of laboratory tests.

Ultrasonographic examination was performed in all patients by the same examiner using the LOGIC GE 500 device; 12 MHz linear head was used in all cases. Power Doppler signal, allowing for the imaging of tissue flow, was acquired after artifact reduction.

The examination was focused on the following joints: bilateral radiocarpal joints (2), metacarpophalangeal joints (10), proximal interphalangeal joints (8), distal interphalangeal joints (10), talocrural joints (2), metatarsophalangeal joints (10), hallux interphalangeal joints (2), proximal interphalangeal joints of the foot (8). In total, 52 joints were examined in every patients; average examination time was 40 minutes.

The elements assessed during US examination included: joint effusion, synovial thickening, intensity of hypervascularity in power Doppler, and also the presence of erosions, and tendon abnormalities (tenosynovitis).

For the purpose of the present study, joint effusion, synovial thickening, and intensity of hipervascularity in power Doppler were assessed in 4-grade scales, published for the first time by Szkudlarek et al. [14].

The following parameters were assessed: joint effusion (JE) defined as abnormal, usually echo lucent, intra-articular material subject to compression: 0 – no effusion, 1 – minimal amount of joint effusion, 2 – moderate amount of joint effusion, 3 – extensive amount of joint effusion [14].

Joint Effusion Index (JEI) – an index calculated for every patient, which is the sum of all grades received due to the presence of effusion in all joints.

Synovial thickening (synovitis) – abnormal, hypoechogenic, intra-articular tissue assessed in grey scale (GS) as follows: 0 – no synovial thickening; 1 – minimal synovial thickening visible only in the physiological space of a joint; 2 – moderate synovial thickening with joint capsule elevation; 3 – significant synovial thickening forming numerous pathological joint capsule recesses [14].

Synovial Thickening Index (GSI) – an index calculated for every patient, which is the sum of all grades received due to the intensity of synovial thickening in all joints.

Power Doppler (PD) signal is defined as the presence of vascular flow signals within thickening synovial membrane: 0 – no flow in the synovium; 1 – single vessel signals; 2 – the present vascular signals take up less than 50% of the synovium; 3 – diffuse vascular signals visible in over 50% of the synovium [14].

Power Doppler Index (PDI) – an index calculated for every patient, which is the sum of all grades received due to the presence of vascular flow signals within thickening synovial membrane in all joints.

Erosions on joint surfaces – in accordance with the definition proposed by OMERACT, discontinuity of the cortical bone surface, that was visualized in at least two perpendicular planes [15, 16]. The presence of erosions was assessed on a 2-grade scale: 0 – lack of erosions, 1 – erosions present.

Tendon abnormalities, such as: tenosynovitis (according to the OMERACT it is hypoechogenic or anechoic thickened tissue within the tendon sheath which is seen in two perpendicular planes and which may exhibit Doppler signal) or enthesitis, were cumulatively assessed on a 2-grade scale: 0 – absent, 1 – present [16–18]. The localization of changes was restricted to establishing the presence of pathologies in hands and feet.

Joint effusion, synovial thickening, and inflammation activity in PDUS were compared with the values of laboratory parameters: ESR, CRP, RF, and ACPA, which were assessed on a 2-grade scale:

- ESR: 0 – normal value (3–15 mm/h for women; 1–10 mm/h for men); 1 – increased value (over 15 mm/h for women; over 10 mm/h for men),
- CRP: 0 – normal concentration (0–5 mg/l); 1 – increased concentration (over 5 mg/l),
- RF: 0 – normal level (0–14 IU/ml); 1 – increased level (over 14 IU/ml),
- ACPA: 0 – antibodies absent (less than 5.0 U/ml); 1 – antibodies present (over U/ml).

For the statistical evaluation was used STATISTICA v.10 software by StatSoft and EXCEL spreadsheet were used for all calculations.

Results

In the studied group of 60 patients, the average duration of symptoms before US joint examination was 5.6 ±3.6 months, while the time from the first examination to RA diagnosis was 0.7 ±2.4 months.

Patient characteristics are shown in Table I.

In total, 3120 joints were assessed; abnormalities were found in 1097. Changes observed in US are presented in Table II.

Table I. Demographic, clinical, and laboratory characteristics of the patients

Total number of patients	60
Age [years]*	48.8 ±17 (18–80)
Female (%)**	46 (76.6)
Durations of symptoms [months]*	5.6 ±3.6 (1–12)
CRP positive (%)**	42 (70)
CRP [mg//l]*	27 ±37.4 (0.3–157.3)
ESR positive (%)**	43 (71.6)
ESR [mm/h]*	36.7 ±31.4 (5–125.7)
RF positive (%)**	41 (68.3)
ACPA positive (%)**	39 (65)
DAS28*	5.5 ±1.1 (3.0–8.3)
Presence of tenosynovitis – hands (%)**	30 (50)
Presence of tenosynovitis – feet (%)**	16 (26.6)
Presence of bone erosions (%)**	10 (16.7)

**Results are presented as: mean ± standard deviation (range)*
***Results are presented as: number of patients (%)*

Table II. Distribution of joints changes in the ultrasonographic examinations

Joint effusion		Grey scale		Power Doppler	
score	*n*	score	*n*	score	*n*
0	2027	0	2649	0	2859
1	459	1	277	1	148
2	492	2	167	2	74
3	142	3	27	3	39

n – number of joints (total number of joints – 3120)

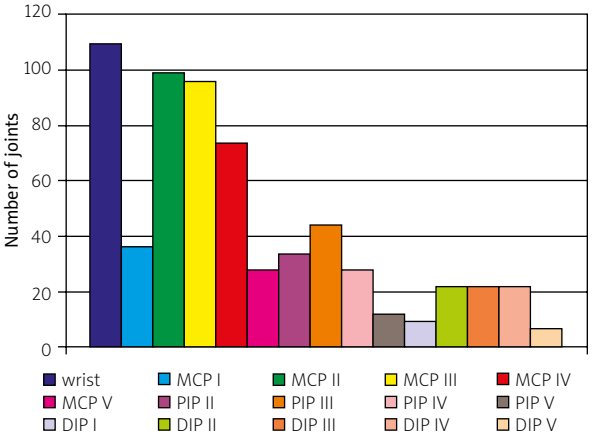

Fig. 1. Location of joint changes in the initial ultrasonographic examination of hands.

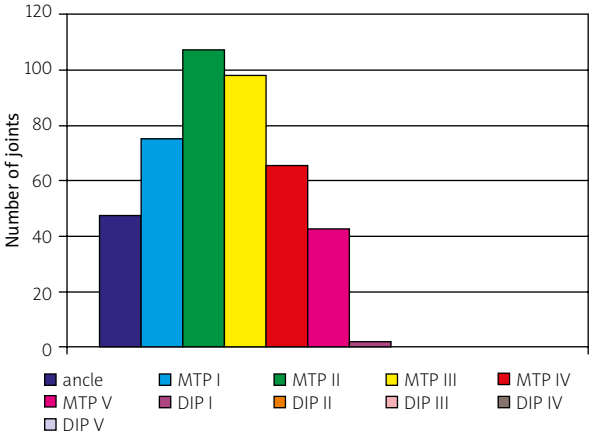

Fig. 2. Location of joint changes in the initial ultrasonographic examination of feet.

In terms of the extent of effusion in the involved joints, the results were as follows: grade 1 – 42%, grade 2 – 45%, grade 3 – 13%. Hypertrophic synovial membrane appeared in 43.1% of joints with present changes, while the percentage distribution of synovial hypertrophy was the following: GS1 – 58.8%, GS2 – 35.5%, GS3 – 5.7%. Taking into consideration only the joints with synovial thickening, changes in power Doppler appeared in 55.4% of cases: PD1 – 31.4%, PD2 – 15.7%, PD3 – 8.3%.

Taking into consideration all assessed joints, changes were most frequently found in radiocarpal joints, bilateral MCP II-IV, bilateral PIP II–III, and bilateral MTP II–IV (Figs. 1 and 2). Synovial thickening and signal in power Doppler usually occurred in wrists, MCP II–III joints, and MTP II–III joints.

Intensified changes (JE ≥ 2) in foot joints appeared first in 6.7% of patients, with minor deviations (JE ≤ 1) in hand joints; only 5% of patients showed no abnormalities in foot joints. Intensified changes (JE ≥ 2) in both hand and foot joints were observed in 65% of patients.

Abnormalities in tendons (tenosynovitis, enthesitis) were found in 38.3% of cases. When separately analyzing the changes occurring in hand and foot tendons, 50% of patients exhibited changes in hand tendons, but only 26.7% in foot tendons (Fig. 3).

Erosions were observed in 10 patients; they appeared significantly more frequently in foot joints (65.5%) than in hand joints (34.5%). The erosions were found in radiocarpal joints, metacarpophalangeal joints from I to III, proximal interphalangeal joints II and IV, and metatarsophalangeal joints I to V (Fig. 4). Erosions were most frequent in MTP II joints. In joints with synovial hypertrophy, erosions were present in 6.1% of cases.

The analysis was based on the values of laboratory parameters and serological markers. In the examined group, increased concentration of CRP was found in 70% of patients, increased ESR – in 86%, RF presence – in 68%, and ACPA presence – in 65%.

An attempt was made to assess the correlation between the changes present in US and selected values

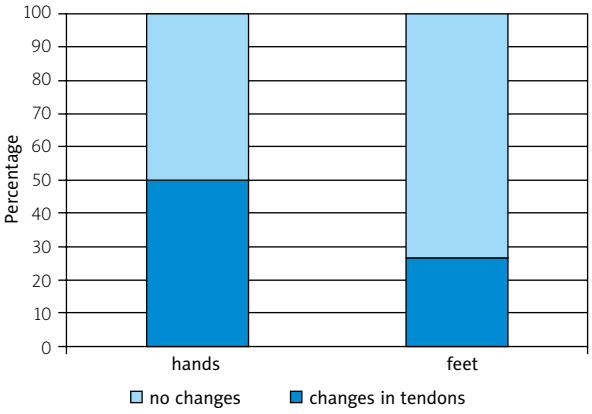

Fig. 3. Distribution of changes in hand and foot tendons.

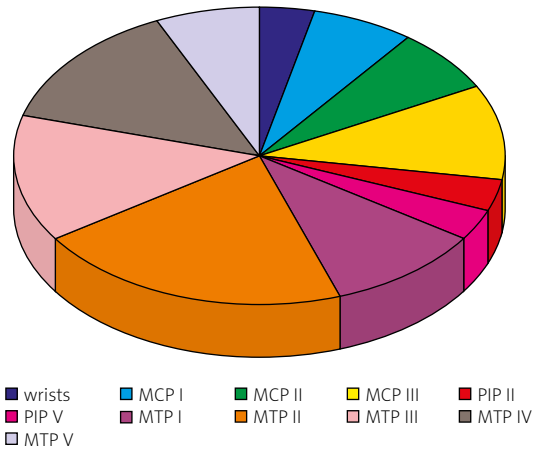

Fig. 4. Location of erosions in foot and hand joints.

of laboratory parameters and serological markers (ESR, CRP, RF, ACPA). The presence of joint effusion, synovial thickening, and changes in power Doppler were taken into consideration. A statistically significant correlation was found between CRP concentration and the intensity of vascularization in power Doppler (PDI); (R = 0.2902; p = 0.025). No correlations were found between the remaining assessed parameters (ESR, RF, ACPA) and the above-mentioned US changes (presence of effusion and synovial thickening).

Discussion

The changes found at initial US examination of hands and feet joints in patients with early arthritis are not uniform. Synovial thickening is a very important element assessed in US. According to the available literature, synovial thickening assessed on a semi-quantitative scale as GS2 or GS3 usually constitutes a predisposing factor for RA diagnosis. However, as the present study shows, even small changes in synovium require vigilance and patient monitoring for the development of RA [19]. Changes in synovium described as GS1 may constitute a marker of weak response to the implemented therapy; they may also be associated with a lower intensity of clinical symptoms [20]. The analysis of the percentage distribution of synovial thickening in the studied group of patients shows similarities to the percentage distribution reported by Witt et al. [20] among patients diagnosed both with early RA lasting less than 2 years (without the use of DMARDs) and RA lasting more than 2 years. US examination of the patients described in this study revealed a higher frequency of grade GS2 synovial thickening (35.5% vs. 31.7%); GS3 (5.7% vs. 11.9%) was slightly less frequent. Moreover, a small difference in favor of synovial thickening was found in grade GS1 (58.8% vs. 56.4%), which may be explained by the uniform profile of the group and very early stages of arthritis in the examined patients.

Another parameter analyzed in hand and foot US was the presence of increased vascularization in PD. The data from literature indicate that PD signal ≥ 2 is specific to patients with early RA [7, 21]. According to Kawashiri et al. [7], it is even more specific than the RA classification criteria of 2010. In the joints assessed by us, the presence of PD ≥ 2 signal was revealed in only 24% of joints with synovitis, despite the uniformity of the patient group. Power Doppler signal assessment is a very important element of ultrasonographic examination, because it shows the intensity of ongoing inflammation. This should be taken into consideration when making decisions concerning the use of DMARDs. According to the data from literature, PD signal was present even in patients in clinical remission, which is a predictor of fast radiological damage progression in the involved joints [22–24].

In the present study, effusion without synovial thickening was found in 56.9% examined joints. Homogeneous synovial fluid usually is not specific to RA, but the presence of synovial thickening suggests such a diagnosis [25]. We associate the presence of homogeneous synovial fluid in a number of changed joints in the described group of patients with the very early stage of the disease. Moreover, the results are affected by the large number of assessed hand and foot joints in each patient, without singling out the joints characteristic for RA.

The study conducted by us revealed a statistically significant correlation between CRP concentration and the intensity of changes in power Doppler (PDI). Similar results were reported by Scirè et al. [21] in a group of patients with early RA who achieved clinical remission due to previous DMARD therapy. This confirms the general view that active synovitis revealed in PD is correlated with systemic inflammation [21, 26]. Both Scirè et al. [21] and Kawashiri et al. [24] did not find any correlation between ESR values and the intensity of changes in power Doppler, which is also confirmed by us. A study by Xiao et al. [19] revealed the presence of a correlation between CRP, ESR, and ACPA with the intensity of synovial thickening (GS). This study was only concerned with radiocarpal joints, MCP II, III, IV, and PIP II, II, IV; such a correlation was not confirmed by the present study.

Ultrasonographic changes in feet joints were an important element in the studied population. Due to the frequent presence of clinically silent changes, and the fact that the most common location of erosions are MTP joints, US examination should be conducted in this area even in patients who do not report any foot joint ailments.

In the material collected from our patients with early RA, changes in hands tendons (50% of the studied patients) and feet tendons (26.6% of the studied patients) are relatively frequent. This was confirmed in a study by Navalho et al. [27] and a publication by Buryn et al. [28]. Both cited studies confirm the frequent involvement of tendons in patients with early RA and suggest the inclusion of this element into the classification criteria for early RA.

Another element considered in this study are presence of erosions. Conventional radiography shows late erosive changes however due to overlapping of tissue on AP scane, some erosions are missing. US examination can show erosions earlier, it is an important element in both diagnosis confirmation and change progression assessment [12, 29]. Magnetic resonance imaging and computed tomography are most accurate [30]. Erosions

were found in only 10 of the observed patients, while in joints exhibiting synovial thicken (which is an necessary factor initiating the formation of erosions), such changes occurred in only 6.13% of cases. This fact may suggest that the studied patients were observed at an early stage of the disease, before the above-mentioned changes could appear [12, 25]. In our research, erosions most frequently appeared in MTP II, but the majority of reports demonstrate the involvement of MTP V and IP in early RA [12, 15, 31].

Conclusions

In conclusion, it is worth of emphasizing that even US changes of low initial intensity with persistent joint ailments require further monitoring and repeat analysis because failing to reveal subclinically developing RA will have negative and irreversible consequences for the patient. In the analyzed group of patients with early RA, significant changes occurred more frequently in feet therefore it is important to pay special attention to US examination both hands and feet joints during diagnosis of early arthritis.

The authors declare no conflict of interest.

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