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# Early Rheumatoid Arthritis: Possibilities Of Mri Diagnosis

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**Annotation:** The article presents the results of a clinical and radiological examination of 65 patients with early rheumatoid arthritis with a duration of articular syndrome up to 12 months. The frequency of detection of erosions in standard radiography of the hands and magnetic resonance imaging (MRI) was analyzed depending on clinical and laboratory features. A standard examination protocol and image evaluation sequence have been developed. MRI is a more informative method for the topical diagnosis of early arthritis compared to standard radiography. In early rheumatoid arthritis, MRI made it possible to diagnose erosive changes in the joints in 36 patients out of 65, which is significantly more than with conventional X-ray examination (2 patients out of 65). Using MRI, erosive changes in the joints of the hands were diagnosed 12 months before their detection on radiographs, the most significant differences in the definition of destructive changes are observed in the area of the carpal bones and metacarpal heads. The frequency of detection of erosions in MRI of the hand correlated with seropositivity for antibodies to citrated proteins and did not depend on the activity of the process according to DAS28.

**Key words:** early rheumatoid arthritis, radiography standard, MRI, hand joints, erosions, diagnostics.

## Introduction

Rheumatoid arthritis (RA) occupies a major place among joint diseases leading to severe disability in people of working age. In most cases, RA has a progressive course and during the first two years leads to the formation of bone erosions in 70% of patients [12]. As a result, about 90% of patients lose their ability to work after 20 years from the onset of the disease. It should be noted that the optimization of the use of basic drugs in the treatment of RA requires the improvement of research methods in order to verify the diagnosis at the initial stages of the disease and control the progression of bone-destructive changes [5]. Most patients with early polyarthritis have an initially non-erosive nature of the process. The early appearance of erosions and destructive changes (in the first 3-6 months from the onset of the disease) is a prognostically unfavorable factor and requires an aggressive treatment strategy. The diagnostic gap in the detection of erosions by various methods is well described in the literature, primarily with standard X-ray examination and magnetic resonance imaging (MRI). Irreversible changes in the articular cartilage and subordinate bone occur mainly during the first 12 months of the disease, and radiologically these changes are detected only after 2-3 years [2, 6, 16]. At the present stage, an alternative method for assessing joint lesions at the initial stages of the disease and monitoring the effectiveness of therapy is MRI [1, 3, 8], which makes it possible to assess the structure of cartilage, soft tissues and subchondral bone, as well as to detect erosive changes in the joints much earlier compared to standard radiography.

The aim of our study was to improve the diagnosis of the erosive process in early rheumatoid arthritis (RA) and to establish the frequency of detection of erosions in standard X-ray and MRI; assessment of the dependence of the erosive process on the clinical features of the course of the disease.

## Material and research methods

The study involved 65 patients diagnosed with rheumatoid arthritis according to the classification criteria ARC/EULAR, 2010 [4], in which the duration of the articular syndrome did not exceed 12 months. The duration of the articular syndrome averaged 8.2±2.6 months. The average age of patients was 38.3±6.3 years.

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Among the examined patients there were 48 women, 17 men. All patients underwent a clinical examination with the determination of the DAS28 activity index. In general, all patients had active RA, with an average DAS28 score of 5.2 ± 2.1, which corresponds to high disease activity. Thus, low RA activity (DAS28<3.2) was found only in 7 patients; moderate (3.2 □ DAS28 □ 5.1) — in 30 patients; high (DAS28 > 5.1) - in 28. At the same time, the serological variant of the disease was determined by positivity to rheumatoid factor (RF) and citrated proteins - antibodies to cyclic citrated peptide (anti-CCP) and cyclic modified vimentin (anti-CMV). To assess RF, an immunoturbodimetric method was used, the level of antiCCP and antiCMV was assessed by enzyme immunoassay (ELISA). Among the examined patients, 45 patients were seropositive in the Russian Federation, 20 people were sero-negative, respectively. Seropositive antiCCP were 40 patients, seronegative — 25; seropositive anti-CMV were 27 people, sero-negative - 38. Positive for two types of antibodies to citrated proteins was established in 27 patients, sero-negative - in 25. Clinical and laboratory characteristics of patients are given in Table. one.

All patients underwent a standard x-ray examination of the hands in a direct (anteroposterior) projection using standard modes. Radiography was performed using BALL films. To take a picture of the hand in a direct palmar projection, such styling was used. The patient sat sideways to the edge of the table. The upper limb was abducted and bent at the elbow joint; the brush was in the position of pronation, the fingers were straightened. Cassette measuring 18 □ 24 cm, half covered with a sheet of provincial plate, located in the plane of the table. The palm fit snugly against the cassette. The median transverse line of the cassette corresponded to the projection of the heads of the metacarpal bones. The X-ray beam was directed vertically to the head of the III metacarpal bone. The radiological stage of RA was established according to the generally accepted classification by O. Steinbrocker (1949) [15].

Quantitative changes in the joints were described according to the J.T. Sharp (1989) [12] modified by van der Heijde et al. (1999)[16]. To visualize erosions, 16 joints and bones of each hand were used: II–V proximal interphalangeal joints, I–V metacarpophalangeal joints, I carpometacarpal joint, I interphalangeal joint, trapezius, boat, semiulna. To assess the narrowing of the joint spaces, 15 joints of each hand were used: II–V proximal interphalangeal joints,

I–V metacarpophalangeal joints, III–V carpometacarpal joints, navicular-trapezoid joint, capitate-boat-semilunar joint, radiocarpal joint [13]. MRI of the dominant hand was performed on a high-field GE SIGNA EXPLORER MRI scanner with a magnetic field induction of 1.5 T. The wrist was in a neutral position, parallel to the plane of the table, the hand with straightened fingers was in the pronation position. In this position, the hands were fixed with their backs. pillows and side rollers in order to exclude motor artifacts and image distortion. When fixing the hand, they tried to achieve a comfortable position for the patient. Centering was performed on the site of the proximal row of carpal bones. Images with the aim of studying the state of all structures of the wrist joint, wrist and fingers were obtained in the frontal, sagittal and axial planes, the thickness of the sections was 3 mm, the field of view (FOV) was 9–12 cm [3]. The studies were carried out with prevenous administration of a contrast agent containing dimeglumine gadopentetate. (Gd-DTPA) at the rate of 0.1 mmol per 1 kg of patient weight. The drug was injected into the contralateral limb. The study was carried out before and after the administration of a contrast agent.

Table 1. Clinical and laboratory characteristics of patients with early rheumatoid arthritis included in the study

| Clinical and laboratory parameters | Low activity (DAS28 < 3,2), n = 7 | Moderate activity (3,2 ≤ DAS28 ≤5,1), n = 30 | High activity (DAS28 > 5,1), n = 28 |
|---|---|---|---|
| | Number of patients | | |
| Men (n=17) | 3 | 9 | 5 |
| Women (n=48) | 4 | 21 | 23 |
| RF positive (n=45)/RF negative (n=20) | 2/5 | 19/11 | 24/4 |
| Anti-CCP positive (n=40)/anti-CCP negative (n=25) | 1/6 | 16/14 | 25/3 |

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Date of Publication: 24-02-2022

| | | | |
|---|---|---|---|
| Anti-CMV positive (n = 27)/anti-CMV negative (n = 38) | 0/7 | 9/21 | 18/10 |

The standard protocol included pulse sequences that allowed obtaining weighted T1, T2, T2 images with tissue inhibition from tissue signal (STIR). The following programs were performed on patients:
1. Survey program (Scout-tra-sag-cor) in three study projections (axial, sagittal and frontal): fast spin echo pulse sequence; FOV - 299 mm; TO - 6 ms; TR - 15 ms; number of slices - 3, slice thickness - 10 mm; matrix size - 256 □ 256.
2. T1-FSE in frontal, sagittal and axial projections: FOV - 200 mm; TO - 20 ms; TR - 570 ms; number of slices - 21, slice thickness - 3 mm; matrix size - 1024 □ 314.
3. T2-fl2d in frontal and axial projections: FOV - 200 mm; TO - 15 ms; TR - 867 ms; number of slices - 24, slice thickness - 3 mm; matrix size 1024 □ 224.
4. T2-tirm in frontal projection: FOV - 249 mm; TO - 30 ms; TR - 3975 ms; number of slices - 14, slice thickness - 2-3 mm; matrix size – 512 □ 512.
5. Tl-fs-fl3d in axial and frontal projections: FOV - 100 mm; TO - 11 ms; TR - 24 ms; number of slices - 30, slice thickness - 3 mm; matrix size 512 □ 512.
The joints of the hand and wrist were assessed qualitatively, as well as using the OMERACT RAMRIS scoring system [6]. When analyzing bone erosions, each bone in the area of interest was evaluated. carpal bones, distal section of the radius and distal section of the ulna, bases of the metacarpal bones; metacarpophalangeal joints - the heads of the metacarpal bones and the base of the phalanges). Erosion was quantified according to the recommendations of OMERACT RAMRIS on a scale from 0 to 10: 0 - no erosion, 1 - erosion occupies 1-10% of the volume / articular surface of the bone, 2 - 11-20%, 3 - 21-30%, 4 - 31-40%, 5 - 41-50%, 6 - 51-60%, 7 - 61-70%, 8 - 71-80%, 9 - 81-90%, 10 - 91-100% [11]. The analysis of the received data was carried out on the main console of the tomograph or on the Magic View workstation using the Canvas software. Statistical processing of the obtained results was carried out using the Statistica 6.1 program using the methods of parametric and nonparametric statistics. The test values are given as: sample mean ± standard error of the mean. The degree of relationship between pairs of independent features was assessed using the rank correlation coefficient.
Comparison of groups according to a qualitative binary trait was carried out using criterion 2 with the analysis of contingency tables. Statistically significant differences in the results of the study were determined at $p<0.05$. All patients involved in the study signed an informed consent to participate in the clinical study. The moral commission agreed to conduct this study.

## Research results and discussion

Standard X-ray of the hands in direct projection was performed in all examined patients. Given the early onset of the articular syndrome (up to 12 months), the main attention was paid to such radiological symptoms as periarticular osteoporosis, narrowing of the joint space, and the presence of erosions. In the vast majority of patients, radiographic changes were not detected during standard X-ray examination of the hands. Periarticular osteoporosis was found in 15 (23.07%) patients, stage II - in 8 (13.3%).
In addition, stage II was divided into pre-erosive, when only narrowing of the joint space was observed without erosive changes, and erosive, when single (1-2) erosions were found in the bones forming the cyst. Thus, pre-erosive stage II was established in 6 patients (10.0%), and single erosions were verified in 2 (3.33%) patients. At the same time, stage III and IV were not found in any patient with RRA.
It is well known that antibodies to citrated peptides are specific markers of RA detected in the blood at early stages of the disease. In table. Table 2 shows the frequency of detection of erosions and narrowing of the joint spaces in the joints of the hands in the examined patients, depending on the presence or absence of anti-CCP and anti-CMV. It should be noted that radiographic erosions were detected only in 2 patients who were simultaneously seropositive for two citrated proteins - anti-CCP and anti-CMV. Given the small number of patients, it is impossible to establish significant relationships between the detection of erosions and the serological status of patients

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Date of Publication: 24-02-2022

Table 2 - Correlation between the data of clinical laboratory and radiological methods of examination in patients with early rheumatoid arthritis

| Citrated peptides in the blood | Erosion | | Narrowing of the joint space | |
|---|---|---|---|---|
| | Yes (n=2) | No (n=48) | Yes (n=7) | No (n=43) |
| Anti-CCP positive (n=34) | 2 (5,9 %) | 32 (94,1 %) | 6 (17,6 %) | 32 28 (82,4 %) |
| Anti-CCP negative (n=16) | 0 (0 %) | 16 (100 %) | 1 (6,25 %) | 15 (93,75 %) |
| R | 0,046 | | 0,017 | |
| Anti-CMV positive (n=31) | 2 (6,5 %) | 29 (93,5 %) | 5 (16,1 %) | 26 (83,9 %) |
| Anti-CMV negative (n=19) | 0 (0 %) | 19 (100 %) | 2 (10,5 %) | 17 (89,5 %) |
| R | 0,012 | | 0,048 | |
| Positive anti-CCP and anti-CMV (n=25) | 2 (8,0 %) | 23 (92,0 %) | 3 (12 %) | 22 (88 %) |
| Negative anti-CCP and anti-CMV (n=14) | 0 (0 %) | 14 (100 %) | 1 (7,1 %) | 13 (92,9 %) |
| R | 0,027 | | 0,013 | |

At the same time, narrowing of the joint space was radiologically established in 7 patients (in 2 of them, single erosions were additionally detected). Among these patients, 6 were seropositive for anti-CCP, 5 were seropositive for antiCMV, three patients were positive for two markers simultaneously. This made it possible to draw a conclusion about more pronounced radiographic changes in patients with a positive titer of citrated proteins.

Rheumatoid factor is one of the classification criteria for RA, but its absence does not exclude the establishment of such a diagnosis. It seems interesting to us to establish the presence or absence of a relationship between changes on radiographs and seropositivity in the Russian Federation. The results are given in table. 3.

Erosions were found in one RF-positive patient and one sero-negative patient, so it was not possible to establish probable differences between the groups (P = 0.951). With regard to joint space narrowing, this radiographic finding was more common in RF-positive patients (P<0.05). In a patient with NDA, narrowing of the joint space was found in the sero-negative variant of the disease.

Destructive processes in bone tissue are the result of a generalized inflammatory reaction, the integral indicator of which is the DAS28 inflammatory activity index. We analyzed the relationship between this parameter and changes detected on radiographs in patients with RRA. Erosions were found in patients with high and moderate activity, however, due to the small size of the groups, it was not possible to establish a probable correlation between these indicators. Joint space narrowing was probably more common with high disease activity (DAS28 > 5.1).

Therefore, the erosive stage of RRA was established in 2 patients. When analyzing the identified erosive lesions, it should be noted that they were verified in patients with high and moderate activity of the process and the presence of seropositivity in anti-CCP and anti-CMV. In one patient, one erosion of the trapezoid bone of the right hand was found, in another patient, two erosions were found - the distal radius of the left hand and the head of the third metacarpal bone of the right hand. The narrowing of the joint spaces was detected in 7 patients, which made it possible to establish stage II of the rheumatoid process in them, despite the short duration of the disease (up to 12 months). MRI makes it possible to more accurately detect bone erosions in RRA and predict the further course of RA.

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Date of Publication: 24-02-2022

Erosions were visualized on MRI as well-defined disturbances in the signaling characteristics of the bone marrow as a low-intensity signal on T1-33 and a high signal on T2-33 structures. Erosions were mostly flat, their width was greater than the depth, from 1 mm in size, with clear uneven contours. More often they were registered in the area of attachment of the joint capsule and ligaments. According to the recommendations of OMERACT RAMRIS [7], bone erosion on MRI was considered as a bone lesion with sharp edges, with a clear juxta-articular localization and typical characteristics of the visualized signal in two planes with a break in the cortical layer, which is visible in at least one plane. Rapid post-gadolin enhancement was interpreted as the presence of an active hypervascularized panus in the erosion. In total, erosions were detected in 36 patients with RRA, which significantly exceeded the number of erosions found during standard X-ray examination. More often they were localized in the zone of the semilunar bone of the wrist (24 patients), the capitate bone (23 patients), the heads of the metacarpal bones (24 patients), and the trapezius bone (17 patients).
We also performed a scoring of the intensity of the erosive process according to OMERACT RAMRIS in patients with RRA. The results are given in table. 4

Table 3 - Correlations between indicators of radiological examination of patients with early rheumatoid arthritis

| Rheumatoid factor in the blood | Erosion | | Joint space narrowing | |
|---|---|---|---|---|
| | Yes (n=2) | No (n=48) | Yes (n=7) | No (n=43) |
| RF positive (n=39) | 1 (2,5 %) | 38 (97,5 %) | 5 (12,8 %) | 35 (87,2 %) |
| RF negative (n=11) | 1 (9,1 %) | 10 (90,9 %) | 2 (18,2 %) | 9 (81,8 %) |
| R | 0,951 | | 0,046 | |

Table 4 - The frequency of verification of erosions in the joints of the hands in patients with early rheumatoid arthritis (according to MRI), depending on the radiological stage

| | Metacarpal bones | | | | | wrist bones | | | | | | | Radial bone | ulna |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | I | II | III | IV | V | Trapezoidal | Trapeze bone | Lunar | Boat-shaped | trihedral | Hook-shaped | pea-shapedя | | |
| The number of patients found erosion | 24 | | | | | 17 | 110 | 23 | 24 | 0 | 4 | 0 | 4 | 6 |
| Sum of points | 0 | 39 | 44 | 18 | 0 | 63 | 31 | 48 | 53 | 0 | 12 | 0 | 17 | 21 |

Table 5. The frequency of detection of erosions depending on seropositivity in anti-CCP and anti-CMV in patients with early rheumatoid arthritis

| Serovariant | Erosion (number patients%) |
|---|---|
| Anti-CCP positive (n=34) | 29/85,3 |
| Anti-CCP negative (n=16) | 7/43,75 |
| R | < 0,05 |
| Anti-CMV positive (n=31) | 29/93,5 |
| Anti-CMV negative (n=19) | 7/36,8 |
| R | < 0,01 |
| Anti-CCP and anti-CMV positive (n=25) | 25/100 |

ISSN NO: 2770-0003
Date of Publication: 24-02-2022

| | |
|---|---|
| Anti-CCP and anti-CMV negative (n=14) | 6/42,8 |
| R | < 0,01 |

Thus, the total number of erosions found in 36 patients is 143, and the total score of bone erosions is 364. The data obtained allow us to state that the vast majority of patients had a multiple erosive process with damage to several areas of the hand. However, the severity of erosion was minimal, ranging from 1 to 3 points according to the OMERACT RAMRIS criteria. The average score of erosive lesions was 2.54 on a 10-point scoring system.

We also analyzed the dependence of the detection of bone erosions in accordance with the serobelonging of patients. Interestingly, no possible differences were found between the groups of seropositive or seronegative patients in the Russian Federation. Erosions were verified in 30 patients with positive RF (76.9%) and in 6 (54.5%) patients with negative RF ($P > 0.05$). At the same time, in patients with positive antibodies to citrated proteins, bone erosions, shown in Table 5, were probably more likely to be verified.

The result obtained is especially important in relation to the early diagnosis of RA. Due to the fact that the ability to visualize erosion radiographically appears approximately 1–2 years later than with MRI [6, 9], and RF in some studies is considered an insufficiently sensitive criterion in the early stages of the disease [10, 14], it is MRI and analysis of the results obtained may be of greater significance at the stage of early differential diagnosis. Thus, the establishment of the fact of seropositivity for these markers can be not only a diagnostic sign of RA, but also a predictor of a prognostically unfavorable erosive process, which is clearly manifested in MRI. At the same time, the degree of RA activity, determined using DAS28, did not affect the frequency of detection of erosions: in all groups of patients, the frequency of detection of erosions of the bones of the hand was approximately the same, statistically possible differences were not established between the groups. Therefore, single-time RA activity generally does not correlate with qualitative changes on MRI, except for the synovitis of the hand joints, when the number of patients with established synovitis increased with an increase in DAS28 activity [1]. The frequency of erosion detection was also the highest in patients with positive anti-CCP and anti-CMV markers - 2.74±0.12 points, but did not depend on RA activity according to DAS28. Between the degrees of activity and the frequency of erosions on MRI, statistically possible differences were not established. Thus, an MRI study in patients with RRA made it possible to objectify and visualize changes in the joints of the hands, confirm the diagnosis of rheumatoid arthritis and evaluate the prognosis. Identification of an erosive process indicates an aggressive course of the disease and a poor prognosis.

## Conclusions

1. An integrated approach to the diagnosis of hand lesions in early rheumatoid arthritis is a necessary condition for obtaining the most probable diagnostic conclusion, taking into account pathological processes developing in the synovial membrane, subchondral bone and periarticular tissues.
2. Magnetic resonance imaging of the wrist joint and hand should be performed in the frontal, axial and sagittal projections; The standard protocol should include pulse sequences to obtain T1-33, T2-33 and T2-33 with fat suppression.
3. MRI is a more informative method for the topical diagnosis of early arthritis compared to standard radiography. In early rheumatoid arthritis, MRI made it possible to diagnose erosive changes in the joints in 36 patients out of 65, which is significantly more than with conventional X-ray examination (2 patients out of 65). Using MRI, erosive changes in the joints of the hands were diagnosed 12 months before their detection on radiographs, and the most significant differences in the definition of destructive changes are observed in the areas of the carpal bones and metacarpal heads.
4. The frequency of detection of erosions in MRI of the hand correlated with seropositivity for antibodies to citrated proteins and did not depend on the activity of the process according to DAS28.

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