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POSSIBILITIES OF RADIOLOGICAL METHODS OF DIAGNOSTICS IN VERIFICATION OF EARLY RHEUMATOID ARTHRITIS

This paper presents diagnostic possibilities of radiological methods in early diagnostics of rheumatoid arthritis. Early diagnostics and treatment is of big importance for improvement of clinical results in the early rheumatoid arthritis patients. Nevertheless, the diagnosis is quite difficult to establish at the early stages of disease because diagnostic criteria of the disease are worked out based on the data obtained from the patients with established diagnosis of rheumatoid arthritis, and hence are not so easily applicable. Magnetic resonance tomography (MRT) is increasingly used in estimation of rheumatoid arthritis at an early stage allowing to reliably detect the key pathological indications of this disease. MRT proved to be more sensitive in detection of synovitis and erosions than clinical examination or conventional X-ray, and may be helpful in establishment of diagnosis of early rheumatoid arthritis. The method also allows to detect bone marrow edema considered to be a precursor of development of erosions at the onset of rheumatoid arthritis and a marker of inflammation activity. Further MRT may help to differentiate rheumatoid arthritis from some other peripheral spondyloarthropathies since it allows to identify inflammations of ligaments and tendons (enthesitis).

Rheumatoid arthritis (RA) is a chronic systemic disease of connective tissue with progressing affection of mainly peripheral (synovial) joints of an erosive and destructive polyarthritis type, possible development of multi-organ affection and heavy complications such as secondary amyloidosis. RA is the most wide-spread autoimmunity disease of man, it is registered in all countries of the world, in all the climatic/geographic zones, among all the age, race, and ethnic groups affecting 0,5–2% adults of the most able-bodied age of 30 to 35 years. RA is of great general medical and social significance as it results in colossal economic losses [14].

During recent years it was persuasively shown that the only realistic way to stop steady progress of the disease is the earliest possible diagnostics and early beginning of active therapy which is to be conducted for a long time and continuously with careful control over efficacy and sensitivity [10, 32]. Therefore importance of RA early diagnostics raises no doubts [15].

Importance of timely and correct RA diagnostics, its dissociation from reactive arthritis and other inflammation diseases of joints is difficult to overestimate because it is only the correct tactics at the onset of the disease that would determine the arthritis course character, rate of joint destruction progress, and functional insufficiency of joints. In clinical practice late RA

diagnostics often takes place which brings about late administration of disease modifying agents and contributes to forming of resistant forms of illness [9, 15].

During recent years, on the basis of a number of clinical observations it was shown that in case of RA during the first 1 to 2 years of disease the irreversible structural damages of joints may occur [15, 17, 38], and depending on the course the following distinctions are made:

- '*Very early RA*'is a disease with symptomatic duration of up to 3 months because during this period a conclusion can be drawn as to arthritis persistence (this very period may be regarded as a potentially reversible period).
- *'Early RA'* (or *'Early established RA'*) means the first 1 to 2 years of the disease when it is possible to identify presence or absence of typical erosive process in joints as well as ascertain the fact of disease progressing.
- *'Non-differentiated arthritis (NDA)'* is an inflammation of joints which does not meet (or does not yet meet?) the RA classification criteria [10].

Early diagnostics, especially that of RA, is much complicated due to lack of specific tests and diagnostic (not classification) criteria [53]. In clinical practice the early arthritis is very often NDA [51]. The early arthritis may be transformed into an authentic RA or another certain rheumatic disease (psoriatic arthritis, reactive arthritis, arthritis in the frame of spondyloarthritis, etc.); it may stop spontaneously (the so-called abortive course) or still remain NDA. According to the data of M. Koller, I. Nobauer-Huhmann (2009), at the primary consulting the share of the patients with differentiated types of arthritis is only 45–65%, and out of 35–55% initially with NDA, later on 35–50% are defined such as have RA; spontaneous remission is observed with 25–55%, persistent NDA - with 25%, other diagnoses — with 15% [37]. Observation over a multitudinous cohort of patients within the RADIKAL investigation in Russia showed that out of 366 patients with inflammatory affections of joints and disease duration of up to 1 year, it was only with 57,9% of patients that the diagnosis of probable RA could be established directly, 36,3% of patients being classified as such as have NDA, and 5,7% at the primary examination were given other diagnoses. After 12 months RA diagnosis was established with 33,1% NDA patients [11].

Hand is an unique organ of human body taking part in various spheres of man's life activities, and with regard to interconnection of bone structures and surrounding soft tissues, the area of radiocarpal joint and hand belongs to the most sophisticated ones [5, 8]. Bone joints are target organs for a number of inflammatory diseases where the first symptoms of rheumatic diseases may be detected. To detect the first indications of rheumatic affections of bone joints the radiological methods of examination are used. X-ray examination is necessary for estimation of affection of osseous structures and periarticular soft tissues, especially when the disease is manifested in calcification of soft tissues. In cases when soft tissues are not calcified, the standard X-rays of hands show changes in the form of soft tissue thickening or infiltration but do not make it possible to say convincingly which periarticular structures exactly have been changed. Used today in diagnostics of rheumatic diseases, next to the standard radiography of joints, is the method of magnetic resonance tomography (MRT). MRT allows to detect pathological changes in bones and periarticular soft tissues at earlier stages of disease development, when conventional X-ray examination gives normal picture [2]. MRT sensitivity in detection of pathological changes in bones is undoubtedly higher. Use of radiography and

MRT allows to establish correct diagnosis more precisely and at early stages of disease development, and consequently to begin adequate treatment [18].

Examination radiography still remains the chief method of investigation for radiocarpal joint and hand. Since radiography was the only diagnostics method for a long time, the issues of X-ray semiotics of diseases and damages of radiocarpal joint and hand were investigated well enough [13, 19, 24, 33, 50]. Correctness and timeliness of the diagnosis establishment is directly dependent on possibilities of radiography. According to A.Y.Vasylyev (1998) [5], standard radiography at early stages of arthritis formation has a low resolution. Its informativity does not exceed 25%, and therefore it became reasonable to look for a new X-ray method with higher resolution. Microfocal radiography with direct multiple magnification appeared to be one [6, 7]. It was found that X-ray pictures obtained when using very narrow focused bundle of X-rays and holding an object at a remote distance from the film, differed from usual X-ray pictures by higher sharpness and contrast range as well as better visualization of bone details [4]. It was also shown that in case of direct multiple magnification, the additional information obtained was due to significant density contrast between soft tissues and the background (51,6% to 60,2%, compared to 30,8% on conventional X-ray picture) and really unlimited sharpness depth of the area pictured [23]. For this reason the microfocal radiography was put in application to RA diagnostics because it is extremely difficult to interpret the X-ray picture at the early stage [7].

A number of authors attribute big importance to detection of erosions and their localization in early RA diagnostics. Several authors [40] used 4-fold magnification to detect thin erosion in the heads of the main phalanxes of hand denoting that the intermittent toothed picture of 'dot-dash' character is an early and important RA manifestation and is not detected by other investigation methods. According to H. Genant та K. Doi (1975) [33], thin erosions in the heads of the main phalanxes of hand can be detected already 2 weeks after beginning of the pathological process. Other scientists however believe that the marginal attritions are not an early RA indication but testify a widely developed pathological process [10, 12]. Nevertheless it is generally accepted that the presence of erosion is a pathognomic RA indication, so the general attention is focused on detection of the formation of pathological attritions.

During analysis of microfocal radiography data O.Y.Vasylyev (2007) [7, 8] paid attention to the fact that the development of erosions is preceded by the stage of local changes in osseous structure. It allows to admit RA presence at the pre-erosive stage already. It was noted that the course of epiphyses pathology is possible in the form of two versions. In case of the first version a narrow linear strip is seen to appear in the confined area. That strip is located just under the closing plate, most often – in the area of capsule insertion. In case of the second version there is a round shape vaguely outlined area of diluted but completely lost osseous structure which is located near the margin of the joint surface of the phalanx. Such changes were reported in 80% of observations. Complete loss of the cortical layer testifies the rise of the full-scale erosion and beginning of the process stage II [21, 24].

T.B.Prokayeva et al. (1994) [16] are of the opinion that, next to erosion, RA stage I features joint capsule infiltration and loss of structural character of elements in soft tissues. According to their data edema of soft tissues is visualized in 81,1% of cases.

It is proved that using micrifocal radiography in case of RA stage II it is possible not only to clearly visualize the marginal osseous defects in the area of the joint but also identify the type of erosions. It is suggested that three types of erosions be specified:

1) flat defect with exposed spongy substance;

2) sphere shape or wedge shape defect of cortical plate without sclerotic rim on the bottom;

3) erosion with sclerotic bottom in the form of sclerotic border on the bottom of the erosive crater — in case of the most long-term course of the process [5, 23].

So the traditional method verified by dozens of years of practical experience and a number of clinical investigations — radiography — has sufficient specificity and accuracy — 93,7 and 85,5% respectively and slightly lower sensitivity — 77,2% [17, 18]. However due to physical parameters the standard radiography cannot detect changes of soft tissues, and the result obtained — a two-dimensional picture representing the summation picture of various areas of the bone has a certain sensitivity limit and cannot be repeated frequently because of peculiarities of summing-up of radiological dose load the patient is exposed to. Several investigations proved that, firstly, the radiography made during up to 1 year investigation does not allow to predict RA development in RA patients though being of high specificity (96%) and low sensitivity (17%) [27]. Secondly, the radiography data are correlated with RA diagnosis within longer terms from the moment of the diagnosis establishment [44], which is confirmed by the data of other investigations [29, 31].

Today MRT is gaining priority importance in visualization of extra- and intraarticular structures of radiocarpal joint, wrist and hand. High contrast range of soft tissues and possibility to obtain multi-plane pictures provide optimal visualization of extra- and intraarticular structures of joints: muscles, tendons, hyaline and fibrous cartilages, joint capsule, adipose tissue, articular bursae, and bone marrow [1, 2, 18, 20, 35]. MRT is of a special value for examination of RA patients, mainly at early, not yet differentiated stages. In case of RA early stages the main MRT advantage over other methods of radiological diagnostics was proved to lie in possibility to detect intra-articular and extra-articular aggregations of liquid, changes of synovial membrane, cartilaginous, fibrous and soft tissue structures. In estimation of condition of osseous structures MRT allows to visualize edema and fibrosis of bone marrow not visible with X-ray, and more distinctly estimate presence, size and localization of bone erosions, subchondral and intra-epiphysis cysts.

MRT is an unique possibility to obtain picture of bone marrow and a very sensitive, though not quite specific technique to detect osteonecrosis, osteomyelitis, primary infiltrations and traumas, especially osseous contusion and fractures without displacement. Indications of these diseases are not detected by X-ray before cortical and/or trabecular sections of the bone are affected [1].

In addition, this method is a matter of great expectations because using MRT examination results makes it possible to conduct earlier and more complete RA diagnostics, to stratify patients depending on risk rates of development of erosive changes, and formulate correct treatment tactics of early RA patients. Due to absence of radiological load on the patient MRT allows to repeat such examination quite often — to monitor changes in condition of joints and periarticular soft tissues on the background of the treatment conducted including use of the newest biological agents.

High cost of conventional MRT sets with magnetic field strength of 1,5 T used to restrict wide implementation of this method. Therefore a relatively cheap model was made having lower magnetic field strength (0,2T — the so called low field MRT) for examination of peripheral sections of osseous and articular system — upper and lower limbs [17]. This resulted in issue of a series of studies on comparative analysis of diagnostic efficiency of the models with magnetic field strength of 0,2 T and 1,5 T [26, 30, 39, 54]. Finally it was shown that both set modalities possess similar possibilities as to estimation of changes of synovial membrane, width of articular cavity and other indications. At the analysis of separate picture elements the low field MRT (0,2 T) has even better accuracy. At the same time it was noted that this apparatus was less sensitive in detection of bone marrow edema [30]. According to H. Yoshioka [54], its flaw consists in non-selectivity of STIR-sequence and non-homogeneity of magnetic field.

Synovitis of peripheral joints makes a physical basis for RA diagnostic data, and this indication may be trustworthily detected by MRT using various modes — T1, T2, or STIR-mode with suppression of signal from adipose tissue. The method allows to perform correct as well as the earliest possible diagnostics. The generally accepted method for estimation of synovitis is examination before and after intravenous injection of the contrast substance containing gadolinium chelates — Gd-DTPA [48]. It allows to strictly quantify the volume of hypertrophic synovia [25, 45]. These MRT data are extremely important as it is shown that the increased synovial volume (or the rate of synovitis aggravation by the contrasting agent) is correlated with other disease activity criteria – edema of joint soft tissues, its painfulness at palpation, laboratory indications.

On MRT synovitis is identified as an area of signal gain in the modes T1, T2 or STIR, on the areas related to anatomic location of synovia. In this case as a rule the pictures obtained before and after contrasting are compared in T1-modes [43].

With the help of 3D-reconstructions MRT allows to calculate the quantity of free synovial liquid in joints. This method may be very helpful for monitoring of RA patients response to treatment or for study of normal physiological functioning of synovial liquid in joint *in vivo.* MR-signal of non-hemorrhagic synovial liquid has low intensity at T1–33 and high at T2–33 due to presence of free water. Hemorrhagic synovial liquid may contain methemoglobin which has short T1 and gives high intensity signal at T1–33, and/or desoxyhemoglobin which has a form of low intensity signal at T2–33 [2].

Specific find for MRT of bones is bone marrow edema (Bone Marrow Oedema, BMO) or osteitis which is detected in the spongy osseous tissue of bone epiphyses [52]. Most of MRT examinations held today have the purpose to estimate correlation between the data concerning bone narrow edema and prediction of osseous tissue destruction development. This phenomenon is described as disturbance of trabecular structure of bone, with vague boundaries, and with MR-signal parameters which correspond to increased content of liquid; it may be detected in the area around the erosion or separately [43]. In case of bone marrow edema medium intensity reduction of MR-signal is observed in T1-mode and significant increase of signal intensity – in T2-mode. These signal parameters correspond to increased content of free liquid inside the bone – symptom of osteitis. Several investigations carried out confirmed that bone marrow edema corresponds to inflammatory infiltration of bone substance, according to the results of histological examination of joint tissues obtained during operations of fixation of prosthetic joints in RA patients [17, 18].

Many scientific studies of today are done to estimate possibilities to make use of changes in bone marrow edema for monitoring of treatment with various new agents belonging to the group of biological agents. This application of MRT is very important because the new agents feature the need for frequent instrumental dynamic control of changes in condition of osseous-muscular system, which is impossible with traditional radiography due to high radiological load.

Further study of MRT possibilities for inflammatory processes showed its efficiency in detection of cartilage erosions [3]. Depending on destruction depth and type five forms of changes in hyaline cartilaginous tissue may be distinguished: 1) nidal heterogeneity in the form of dotty surface or penetrating the entire depth of affection area in the area of synovial membrane insertion without disturbance to the integrity of the rest of the cartilage surface; 2) surface multitudinous defects (flat erosions); 3) erosions with different penetration depths (from 1,5 mm along the thickness of the cartilage to the subhondral layer; 4) focal thinning of the cartilage due to proliferative changes; 5) complete diffusive thinning of the cartilaginous tissue (development of ankyloses) [34].

Presence of erosions of articular surfaces is the most characteristic for chronic polyarthritis X-ray symptom. Erosions show up in connection with destruction of subhondral closing plate and area of spongy bone of joint epiphysis. Three types of osseous erosions are distinguished [28, 36]. Most often in small joints of hands marginal surface erosions are formed in the spots of the bone intraarticular area where the bone is not protected by the cartilage covering the joint. It is those 'exposed' areas of bone epiphysis at the margins of articular surfaces that are primary targets for the 'attack' of the actively proliferating joint synovial membrane [28, 41]. Compressive erosions take place in the cases of falling-in (collapse) of the spongy bone subhondral part on the background of juxta-articular osteoporosis and bone-like reformation of osseous structure resulting in invagination of the articular surface into epiphysis. Important spots where this type erosions appear are metacarpophalangeal joints in which collapse and invagination of articular surfaces of proximal epiphysis of main finger phalanxes and displacement of carpal heads into these areas form joint deformations typical for RA. Erosions of the third type come out in the form of surface resorption of the bone closing plate at the spot of tendon insertion and are usually connected with inflammatory changes in a contiguous tendon. Emergence of such erosion along the external margin of styloid process of ulna is an important find making up one of the early X-ray symptoms of RA.

MRT higher diagnostic capacity in detecting the destruction of osseous tissue are determined by the physical parameters of this type of examination. Unlike radiography whose method is based on absorption of X-rays by osseous tissue, magnetic resonance method is based on detection of quantitative differences in the content of hydrogen ions (protons, H^+), which make part, first of all, of water composition, the main component of man's tissues [8]. This feature of the method and also the fact that MR-tomographic method (layer-after-layer picture section unlike with standard radiography giving summation picture) allows to detect much more changes in bones, joints and juxtaposed soft tissues, erosions which are located on the fore or rear surface of bones. In addition the intraosseous cysts which in case of standard radiography are 'closed' by the juxtaposed osseous tissue and thus might not be detected by radiography, are well visualized in case of MRT [17].

Anatomy of bones features the availability of a significant number of differently formed structures which are tightly interconnected and perform various functions. Surrounded with fascial vaginas tendons occupy a certain place among them but from the viewpoint of RA diagnostics their affection *per se* is not significant and does not belong to diagnostics criteria. However, since the changes in tendons of muscles may be important for differential RA diagnostics and contribute to development of joint rigidity as well as accompany synovites, it is necessary to consider this factor in a diagnostic search.

Tendinitis and tenosynovitis are most frequently detected in the wrist area when the pathological process involves wrist ligaments or changes are detected in the area of styloid process of ulna [49]. X-ray-wise they are manifested by thickening and infiltration of ligaments and tendons at the spots of their location and insertion of bones (enthesopathy). Any soft tissue structures may be calcified which is very clearly seen on X-ray pictures. MRT is a sensitive method to estimate the entire spectrum of tendon pathology detecting tendinitis and tendon ruptures in most cases with better accuracy than clinical examination. Normal tendons have the even margins and homogenous signal of low intensity at T2–33. Tendon rupture may be partial or complete, it is depicted by different rates of tendon breakage (high intensity signal inside the tendon at T2–33). In case of tenosynovitis the liquid may be seen under the tendon membrane with the tendon itself having normal appearance. Tendinitis usually results from thickening and unevenness of the tendon but the most reliable symptom is signal intensity increase inside the tendon at T2–33 [2].

MR-signal is assessed in the areas which surround tendons of flexor muscles and protractor muscles, taking into consideration synovitis by the scale from 0 to 3. Development of tendinitis is an unfavourable factor in prediction of the functional condition of the joints of bones and is also defined as a risk factor in destructive affection of joints [42].

A number of investigations note that classical manifestation of RA onset in hands and feet is preceded by tenosynovitis of protractor muscles (in 65,0% of observations), more seldom — tendons of flexor muscles (30,0%). The important advantage of MRT lies in possibility to visualize tendons during the entire period in interconnection with the surrounding soft tissues, vessels and joints [20, 47]. On MR pictures the tendons which are within norm are uniformly hypointensive in T1- and T2-modes [20, 22]. However if tendons or ligament are oriented at 45–65° to the direction of magnetic field vector, then increase of MR-signal intensity is generated from them. This phenomenon was called the phenomenon of 'magic angle' and it appears in case spin-echo and gradient-echo sequences with short T1 are used [22, 46]. So T.H. Berquist (2003) [20] described the phenomenon of 'magic angle' with regard to tendon pollicis longus, located at the angle of 45° to the magnetic field at T1–33 in frontal plane. Further the hypertrophy of synovial membrane develops with formation of synovitis, accumulation of free liquid on hand being most frequently observed in the area intermetacarpal articulations [8].

Thus in connection with implementation of new methods of RA treatment and need for early disease diagnostics, MRT of joints became widely practised in rheumatology. At the same time the traditional method of radiological diagnostics i.e. standard radiography of joints, did not lose its importance either [17]. Nevertheless, despite wide development of CT and MRT the radiological diagnostics of changes in radiocarpal joint and hand, especially at early stages, is not yet well enough investigated [8]. Small number of studies are devoted to description of CT-,MRT-semiotics of changes in bones and tendon-ligament apparatus of

radiocarpal joint and hand. In both domestic and foreign literature the data are missing concerning comparative analysis of radiography, CT, MRT efficiency. So far the standard algorithm has not been worked out for application of radiological methods of examination of this category patients. Directions as to application of different methods of radiological diagnostics are not formulated either. At the same time solution of the problem of radiological diagnostics of changes in radiocarpal joint and hand in case of RA would allow to substantially raise quality of treatment of patients and postpone disability.

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POSSIBILITIES OF RADIOLOGICAL METHODS OF DIAGNOSTICS IN VERIFICATION OF EARLY RHEUMATOID ARTHRITIS

V.N. Ryzhyk, D.V. Vershynina, E.M. Mykhalchenko, P.F. Dudiy, I.Y. Golovach

This paper presents diagnostic possibilities of radiological methods in early diagnostics of rheumatoid arthritis. Early diagnostics and treatment is of big importance for improvement of clinical results in the early rheumatoid arthritis patients. Nevertheless, the diagnosis is quite difficult to establish at the early stages of disease because diagnostic criteria of the disease are worked out based on the data obtained from the patients with established diagnosis of rheumatoid arthritis, and hence are not so easily applicable. Magnetic resonance tomography (MRT) is increasingly used in estimation of rheumatoid arthritis at an early stage allowing to reliably detect the key pathological indications of this disease. MRT proved to be more sensitive in detection of synovitis and erosions than clinical examination or conventional X-ray, and may be helpful in establishment of diagnosis of early rheumatoid arthritis. The method also allows to detect bone marrow edema considered to be a precursor of development of erosions at the onset of rheumatoid arthritis and a marker of inflammation activity. Further MRT may help to differentiate rheumatoid arthritis from some other peripheral spondyloarthropathies since it allows to identify inflammations of ligaments and tendons (enthesitis).

Keywords: early rheumatoid arthritis, radiological methods, radiography, magnetic resonance tomography.

POSSIBILITIESOFRADIOLOGY METHODS IN DIAGNOSTICS VERIFICATION OF EARLY RHEUMATOID ARTHRITIS

V.M. Ryzhyk, D.V. Vershynina, O.M. Mykhalchenko, P.F. Dudij, I.Yu. Golovach

Summary. The paper presents the possibility of diagnostic radiation in the early diagnosis of rheumatoid arthritis.Early diagnosis and treatment have been recognized as essential forimproving clinical outcomes in patients with early rheumatoid arthritis.However, diagnosis is somewhat difficult in the early stages ofthe disease because the diagnostic criteria were developed from dataobtained in patients with established rheumatoid arthritis and thereforeare not readily applicable. Magnetic resonance (MR) imagingis increasingly being used in the assessment of rheumatoid arthritisdue to its capacity to help identify the key pathologic features of thisdisease entity at presentation. MR imaging has demonstrated greatersensitivity for the detection of synovitis and erosions than either clinicalexamination or conventional radiography and can help establish an early diagnosis of rheumatoid arthritis.It also allows the detection ofbone marrow edema, which is thought to be a precursor for the developmentof erosions in early rheumatoid arthritis as well as a marker ofactive inflammation. In addition, MR imaging can help differentiaterheumatoid arthritis from some clinical subsets of peripheral spondyloarthropathiesby allowing identification of inflammation at the insertionsof ligaments and tendons (enthesitis).

Key words: early rheumatoid arthritis, radiation techniques, radiography, magnetic resonance imaging.

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