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Advances in the diagnosis of rheumatoid arthritis

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Abstract: **Rheumatoid arthritis (RA) is a common systemic autoimmune disease characterized by chronic inflammatory diseases of the joints. Nonstandard treatment, the disease will gradually develop, eventually leading to joint deformity, functional loss and high disability rate. Therefore, early diagnosis, intervention and treatment can greatly improve the prognosis of the disease and the quality of life. The purpose of this article is to review and analyze the early diagnosis of joint ultrasound and rheumatoid arthritis.**

Keywords: Rheumatoid arthritis; Early diagnosis; Joint ultrasound

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1. Introduction

Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic progressive erosion of bone and cartilage. Its clinical manifestation is symmetrical and persistent polyarthritis with involvement of facet joints such as hands and wrists. Hand joints are the most common involved joints. The basic pathological changes are synovitis, pannus formation and bone and cartilage destruction. With the progress of the disease, joint deformity and functional loss may eventually occur, seriously affecting the quality of life. Rheumatoid arthritis is a global distribution disease, which is one of the important causes of human labor loss and disability. Its prevalence rate is 0.5%-1.0% worldwide, and the incidence rate is 30/100,000[1]. The prevalence rate in China is about 0.32-0.36%, and the incidence is about 0.28%[2]. The etiology of RA is complex, and its pathogenesis has not yet been clarified. It is generally believed that on the basis of genetic susceptibility, under the interaction of sex hormones, environment, society, physiology, psychology and other factors, the body's immune function disorders lead to chronic inflammatory diseases of joints[3]. With the continuously progress of RA patients, the bone destruction becomes more and more serious, which will affect joint function, bring great inconvenience to life, reduce the quality of life. At the same time, it may cause systemic damage. It is too late to intervene or treat. Therefore, early diagnosis and treatment are very important for the prognosis of patients with rheumatoid arthritis. The purpose of this paper is to summarize the early diagnosis and assessment of rheumatoid arthritis by joint ultrasound.

2. Joint Ultrasound

2.1. Definition of joint ultrasound

Arthrosonography is used to assess joint changes in rheumatoid arthritis by ultrasound in terms of joint effusion, bone erosion, tenosynovitis, peritendinitis and synovitis[4]. Ultrasound technology includes high frequency gray scale imaging and Doppler imaging. Doppler imaging can be divided into color Doppler imaging and energy Doppler imaging. High-frequency ultrasound can not only evaluate synovitis and synovial effusion in RA joints, but also detect multiple joint damage better than other imaging techniques. High-frequency ultrasound has a good value in differential diagnosis of joint effusion, joint capsule thickening and tenosynovitis. Doppler imaging is currently considered to be a sensitive tool for evaluating synovial hyperplasia and neovascularization. Doppler imaging can show synovial congestion and blood supply to the pannus of synovial joint, and can indirectly reflect the degree of inflammation in RA. Therefore, Doppler imaging can be used to treat active RA facet synovitis with high reproducibility and sensitivity[5].

2.2. The role of joint ultrasound in the diagnosis of RA

Joint effusion, synovial thickening and pannus formation are the main manifestations of synovitis defined by ultrasound. It is directly related to the richness of blood flow in synovium and the activity of arthritis. It is also a key factor leading to bone erosion and destruction. High-frequency ultrasound and Doppler imaging describe synovial lesions, record pannus changes of synovial membrane, and measure synovial fluid accumulation and thickness of synovial membrane. Observing the joint blood supply can monitor early joint erosion. Ultrasound has certain value in differentiating synovitis from chronic and fibrosis synovitis[6]. High-frequency ultrasound and energy Doppler ultrasound are effective diagnostic tools for predicting synovial erosion and synovitis of RA hand joint[7]. At the same time, studies have found that there is a significant correlation between joint ultrasound and inflammatory factors and DAS28 score. Joint

ultrasound can be used for early diagnosis and evaluation of rheumatoid arthritis patients with high reference value. Therefore, by observing the lesions of joint effusion, synovium, pannus of synovium, cartilage and bone erosion could provide significant information for the diagnosis, judgment of disease activity and follow-up treatment of RA[8].

2.3. Advantages of joint ultrasound

Muscles are dynamic systems, so they cannot be examined only by static imaging. MRI can't perform real-time dynamic examination, while ultrasound can perform dynamic muscle structure examination. Muscle ultrasound can provide all the information obtained by MRI. Real-time ultrasound examination can obtain more dynamic images of muscle contraction and diastole, so it has its advantages. Ultrasound is simple and cheap. Ultrasound and MRI play the similar roles in the diagnosis of characteristic lesions of RA[9]. It is more practical in the follow-up of damage recovery. Continuous ultrasonography can evaluate the degree and stage of recovery and reduce repetitive injury. Ultrasound examination can detect synovial membrane thickening, bone erosion and osteophyte lesions in the early stage of inflammation. Localization of local lesions and guided puncture are of the great significance for early diagnosis and monitoring of therapeutic response of RA.

The traditional imaging method of RA is X-ray, but its specificity is not strong and muscles can not be examined by X-ray. When multiple bone erosion and narrowing of joint space are found on X-ray, RA has entered the middle and late stage. Traditional X-ray is insensitive to early bone erosion[9-11]. CT is easy to detect small bone erosion and overlapping lesions, and can only show the cross-section of lesions, but it can not provide detailed information of lesions, at the same time, the ability to show synovial and cartilage lesions of RA is poor. MRI has many advantages, such as high tissue resolution, multi-plane imaging, etc. But it can not be used as a real-time dynamic examination, long examination time and some taboo restrictions, such as critical, acute, severe patients due to time constraints. It is not easy to perform MRI examination. Patients with ordinary metal objects in vivo are not suitable for MRI examination, so MRI can not be used as a routine examination, and the price is high. The expensive factor also limits the application of MRI in the diagnosis of musculoskeletal soft tissue lesions. Main MRI findings of early RA wrist joint and its diagnostic value. The main MRI signs of early RA include joint synovial thickening, pannus enhancement, joint effusion, bone marrow edema, bone erosion, tenosynovitis and cartilage erosion. Synovial thickening and pannus enhancement: synovial lesion is the earliest pathological change of RA[12].

In the past, ultrasound and magnetic resonance imaging were considered to be more sensitive than radiography in detecting synovitis. Magnetic resonance imaging could also distinguish the differentiation zone of chondrosynovium which was difficult to distinguish by ultrasound. Therefore, magnetic resonance imaging has been regarded as a reference standard for synovial imaging in the past. But the study found that[13] false positive diagnosis of magnetic resonance imaging in healthy people, so the clinical diagnostic criteria of 2010 revised the criteria of 1987, deleting the image part of the criteria. Imaging is an important tool for assisting clinical diagnosis. Ultrasound can not only clearly display synovium and measure its thickness, but also detect blood flow signals in synovium by energy Doppler ultrasound[14]. Ultrasound diagnosis of synovitis has been widely recognized by rheumatologists[15]. Musculoskeletal ultrasonography has its unique advantages over other imaging examinations such as non-radioactive, real-time imaging, simple operation, low cost, repeatable inspection,which is a cost-effective inspection method. Some studies have shown that the specificity of RA diagnosis is up to 91%[16]. This means that joint ultrasound can not only improve the early diagnosis and evaluation of RA patients, but also reduce the cost of patients and non-invasive repetitive operation, so improving patient satisfaction.

2.4. Ultrasonographic manifestations of RA joints

High frequency gray scale display of anatomical structure, Doppler scale of blood flow image. OMERACT team defined common pathological injuries by observing RA patients in 2005[17]. According to OMERACT, synovial thickening is defined as abnormal hypoechoic, immovable and incompressible intra-articular tissue, which may produce Doppler signals. When tenosynovitis has or does not have hydrocele in tenosynovitis, there are low or no echogenic thickening tissues on two vertical planes, which may be accompanied by Doppler signals. Joint effusion is defined as an intra-articular abnormal signal with low or no echo, which is movable, compressible and without Doppler signal. Bone erosion is a discontinuous bone surface visible in two vertical planes. Ultrasonographic Findings of Muscle Bone: Synovitis: Rheumatoid arthritis takes synovitis as its basic pathological change. Synovial congestion, edema and tissue loosening occur in the early stage of rheumatoid arthritis, inflammatory cell infiltration, with different degrees of synovial thickening on ultrasonography. In 2008, E.G. McNally et al. proposed a new semi-quantitative evaluation criterion based on synovial thickness. It was divided into four grades: Grade I, no synovial hyperplasia, 0mm; Grade II, slight synovial hyperplasia, thickness < 2mm; Grade III, moderate

synovial hyperplasia, thickness 2-4mm; Grade IV, synovial hyperplasia, synovial thickness >4mm[18]. Inhomogeneous, visible villous, mass or nodular structure to the articular cavity protruding, showing equal or low echo, pressure is difficult to compress. Pannus: neovascularization and pannus formation in synovium. Energy Doppler flow imaging and color Doppler flow imaging can visually detect the synovial blood flow, showing abnormal increase of blood flow signals around and inside the synovium, which are punctate, star-like or branched. According to the classification standard of Szkudlarek[19] et al, the blood flow signals in synovium were divided into four grades: Grade 0, no blood flow signal; Grade I, single blood flow signal; Grade II, confluent blood flow signals could be seen, but less than 50% of the synovial area; Grade III, more than 50% of synovial area and blood flow signals; Oint cavity effusion: Synovial inflammation leads to the increase of synovial fluid exudation, forming joint cavity effusion. Ultrasound shows the fluid anechoic dark area in the joint cavity, which can be compressed. Its width and depth are used to measure the volume of effusion, and then to assess the severity of the disease. The thickness of anechoic zone in joint space > 1 mm can be judged as joint effusion[6]. Articular cartilage and bone erosion: articular cartilage degeneration, destruction, bone destruction, joint deformity, color Doppler ultrasonography showed rough and blurred articular cartilage surface, increased echo, uneven, irregular shape, local thinning or disappearance in the late stage, increased echo of subchondral bone lines, irregular[20]. The surface echoes of the joints and bones showed unequal depth or insect-like changes, especially when combined with joint effusion[21]. These ultrasonographic images can be used to classify the joint changes of rheumatoid arthritis patients and to identify them early, so as to intervene early and improve the quality of life.

2.5. Joint ultrasound score

Articular ultrasound score refers to Hartung[22] et al. According to the joint ultrasound on synovial thickness, joint effusion, bone erosion and synovial blood flow signals, the corresponding scores are given to their performance (Table 1). Including Ultrasound Score and Simplified Ultrasound Score, Ultrasound scoring was used to examine 19 joints including bilateral elbow joint, wrist joint, 1-5 metacarpophalangeal joint, 1-5 proximal interphalangeal joint, knee joint, ankle joint and 1-5 metatarsophalangeal joint. Simplified Ultrasound Score was used to examine 8 pairs of joints including bilateral elbow joint, wrist joint, knee joint, metacarpophalangeal joint 3, metacarpophalangeal joint 4, proximal interphalangeal joint 3, metatarsophalangeal joint 4 and proximal interphalangeal joint 1. Hammer and others compared 7-78 joints of RA patients. It was found that the ultrasound scores of different number of joint combinations could well reflect the disease activity of RA patients, and the best simplified joint combinations need to be further explored[23]. The study found that the joint ultrasound score was closely related to the degree of activity of rheumatoid arthritis[24].

Table 1. Ultrasound Scoring of RA Indicators

Score	Synovial thickness	Joint effusion	Bone erosion	CDFI or PDUS
0	No abnormalities	No effusion	Bone surface is smooth	No color flow signal in synovium
1	The synovium was slightly thickened. The synovial membrane of the facet joint was not higher than the level of the connection between the highest points of the two bones. The synovial membrane thickness of the major joints was > 2 mm and < 5 mm.	Joint effusion did not reach the edge of articular junction.	Bone surface is not smooth, but there is no bone defect.	Intrasynovial measurements and a few punctate blood flow signals that is < 3 punctate blood flow signals.
2	The synovium was moderately thickened. The synovial membrane of the facet joint protruded, the highest point of the two bones connected, not reaching the skeleton, and the synovial membrane thickness of the major joints was > 5 mm and< 9 mm.	Joint effusion reaching the edge of articular junction.	Slight bone defect on bone surface.	More than 3 punctate blood flow or blood flow fused into slices, but less than 50% synovial area.
3	The synovial membrane of the facet joints extends to the skeleton and the synovial membrane thickness of the major joints is more than 9 mm.	Joint effusion beyond the edge of the articular junction.	Extensive bone destruction due to bone defect on bone surface.	There were abundant dendritic or reticular blood flow signals in the synovium, and the blood flow signals were more than 50% in the synovium.

3. Concluding remarks

Rheumatoid arthritis is an immune disorder involving multiple systems. As the disease progresses, it can cause irreversible joint damage and other serious complications of the system, which can endanger life. Therefore, the early diagnosis, assessment of the disease and the timing of drug use are particularly important for the prognosis of rheumatoid arthritis. Early intervention can significantly improve the quality of life of patients. At present, the diagnosis of RA and judgment of disease activity at home and abroad mainly depend on clinical manifestation and laboratory examination, For example, DAS-28, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, anti-CCP antibody, joint X-ray, magnetic resonance and so on. ESR and C-reactive protein are relatively simple in clinic. However, due to its lack of specificity, it is susceptible to interference from other factors (such as infection, tumors, serum diseases, etc.), which reduces its accuracy and credibility[25]. Rheumatoid factor can be elevated in a variety of connective tissue diseases, and its sensitivity is not high. Anti-CCP antibody is a diagnostic index of RA. The increase of anti-CCP antibody has no significant correlation with the disease activity of rheumatoid arthritis, and it can not represent the disease activity. At present, DAS-28 is the most commonly used comprehensive index to evaluate the disease activity of RA in the world. Because of its wide range, it has been proved that DAS-28 is significantly related to the disease activity of RA. Although DAS-28 score can evaluate the condition of RA patients better, it needs to sum up the number of joint tenderness, and individual pain threshold is different, so it has certain subjectivity. The joint ultrasound is not limited by subjective pain and physical examination, and can objectively evaluate the condition and disease activity. Studies have confirmed that joint ultrasound is positively correlated with DAS-28, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor and disease activity of RA. It should be an effective method for early diagnosis and disease activity evaluation.

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