Usefulness of Joint Ultrasonography in Medical Care for Rheumatoid Arthritis

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Ultrasonography (US) using a high frequency probe has recently gained attention as a useful diagnostic imaging tool in the routine medical care of musculoskeletal diseases including rheumatoid arthritis (RA) because it allows detailed real-time observation of soft tissues in shallow layers including the synovium, tendons, muscles, blood vessels, and nerves. Using a gray scale, US plots synovial thickening and synovial fluid retention in joint capsules and tendon sheaths, and then shows blood flow signals using the Doppler method. This allows diagnosis of active synovitis, arthritis, and tenosynovitis depending on whether the observed Doppler signal appears as an accumulation of spotty signals in line with the site of synovial thickening. US is useful for the early diagnosis, determination of activity and remission, and prediction of prognosis of arthritis because of its higher sensitivity to detect inflammation in an articular site compared with that of conventional and blood examinations. Because performing routine joint US for an articular site in every patient is difficult due to temporal restriction, it is practical to perform joint US only in selected cases and when conventional examinations fail to detect inflammation around the articular sites. Therapeutic agents for RA have significantly advanced in recent years. Improvements in the diagnostic techniques for RA are also needed. Joint US is a useful diagnostic imaging tool that promises better medical care through complementation of judgment based on conventional examination.

**Key words:** ultrasound, rheumatoid arthritis, early diagnosis, differential diagnosis

**Introduction**

In medical care of patients with musculoskeletal diseases presenting with rheumatoid arthritis (RA), the presence or absence of synovitis is a characteristic finding that needs to be confirmed when judging whether or not an illness is arthritis. In physical examination, the judgment is made by indirectly supposing the presence or absence base on redness, heat sensation, joint swelling, tenderness, and values of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP). Understanding of the presence or absence, degree, number, and distribution of synovitis through detailed examination is the basis of differential diagnosis, evaluation of disease activity, and decision of a treatment strategy. Different from that in diseases of the internal organs, palpation is aggressively conducted for many of the joints because they are located in shallow layers where palpation from the body surface is possible. Palpation is a basic examination technique for which skill and knowledge of physicians engaged in medical care for RA are required. However, determination of articular findings based on this examination depends on the experiences and techniques of each physician, resulting in a low concordance rate among examiners. A test using systemic inflammatory markers such as CRP and ESR is useful for the determination of the presence or absence of arthritis. However, interpretation of the results require care because the test values are influenced by pathological changes other than arthritis, and the markers do not increase in local inflammation in some cases.

For this reason, joint ultrasonography (US) has been gaining attention in recent years, and it has
been used in the diagnosis and evaluation of disease activity of not only RA \(^{4-6}\) but also many musculoskeletal diseases, including polymyalgia rheumatica \(^7\) and psoriatic arthritis \(^8\). This is because joint US is superior to conventional examination in terms of image plotting capacity of lesions of soft tissues such as synovium and tendon, as well as bone erosion, leading to superior judgment of the presence or absence of the lesions. Judgment using high-resolution images provided by joint US allows improvement in sensitivity for detection of joint swelling lesions and correction of divergence in examination ability among physicians \(^9\), leading to confirmation of the correctness of judgment in conventional examination. Joint US allows direct judgment of the presence or absence of synovitis through plotting of the thickened synovium and visual capturing of its pathologically characteristic neovessels as minute blood flow, using power Doppler imaging \(^10\). Therefore, joint US is superior in terms of detection sensitivity of synovitis \(^2\), allowing more accurate judgment of the presence or absence of synovitis, compared with clinical evaluations such as blood examination and palpation.

1. Pathological changes that can be observed using US

Use of a high-frequency (10–20 MHz) probe allows detailed observation of various soft tissues close to the body surface, including subcutaneous tissue, muscles, blood vessels, and nerves. Judgment is made by combining blood flow signals detected by power Doppler imaging to plotting in grayscale.

In rheumatic diseases, lesions mainly of the synovium are the main subjects of the observation \(^11\).

1) Synovial fluid retention and synovial thickening

Synovial fluid retention and synovial thickening are observed as no/low echo in the joint, tendon sheath, or bursa of the lesion. Synovial fluid retention shows no/low echo in many cases, is mobile and compressible, and is characterized by the absence of blood flow signal (PD signal) in the observation using power Doppler imaging. Meanwhile, synovial thickening is characterized by the absence of mobility and by poor compressibility by the probe, and the site shows a PD signal in some cases (Figure-1b, c). It is judged that there is active synovitis when the PD signal appears as an accumulation image of spotty signals in line with the site of synovial thickening, characteristic of synovitis findings. Care needs to be taken to avoid mistaking existing vessels in sites other than that of the thickened synovium.

2) Bone erosion

Bone erosion is defined in US as discontinuous dots on the bone surface in the joint observed in longitudinal and transverse planes (Figure-2a, b). US is also superior in terms of detection capacity for bone erosion that is difficult to plot on plain radiography, which is generally used for confirmation of bone erosion. Although there is unevenness on the bone surface in healthy subjects as well, this can be distinguished by observation in at least 2 directions, namely longitudinal and transverse directions, instead of using only 1 direction. Bone erosion is characterized by a disrupted white line on the US monitor that plots the outline of the bone.
surface and is a finding highly specific to RA. A PD signal detected inside the bone erosion indicates that the erosion is active and progressive.

3) Tenosynovitis

Tenosynovitis is observed in longitudinal and transverse planes as a thickened tissue with low or no echo in the tendon sheath. This synovitis shows a Doppler signal in some cases (Figure-3a, b) and is observed in RA very frequently. In particular, the findings of tenosynovitis are frequently seen in the wrist joints, flexor tendon of the palm, and tendon sheath of the long head of biceps brachii muscle.

4) Enthesopathy

Enthesopathy is observed in the longitudinal and transverse planes as an abnormally low echo or thickening at the site of the bone where the tendon or ligament attaches, and is accompanied by calcification in some cases. Enthesitis shows a Doppler signal in some cases. In addition, bone changes, including osteophytes, bone erosion, and irregular bone surface, are seen at the site where the tendon attaches in some cases. Enthesitis is particularly characteristic of ankylosing spondylitis, reactive arthritis, and psoriatic arthritis that require care for the differentiation from RA, although RA also shows enthesitis. Therefore, those findings indicating enthesitis are helpful information for making a decision in the differential diagnosis of these symptoms.

2. Articular sites where complementation by US is effective

It is occasionally difficult to conduct joint US for many articular sites in ordinary medical care because of temporal restriction and labor intensiveness. Thus, which articular sites should be prioritized in joint US in terms of usefulness?

Salaffi et al. reported lower concordance rate (κ coefficient) between the number of swollen joints and joints with pain among examiners who conducted conventional examinations (0.2, the lowest in the shoulder and 0.4-0.6 in the wrist/knee/ankle) and a higher rate (0.6-0.7) by joint US in GS. The concordance rate of the findings between joint US and conventional examination was high in proximal interphalangeal joint and knee and lowest in the shoulder (κ coefficient: 0.2) followed by metatarsophalangeal joint (MTP).
They mentioned that shoulder and MTP are the sites particularly requiring complementation by US because these are difficult to judge using conventional examination.

Boedec et al. conducted a conventional examination of 66 joints and joint US of 38 joints (DAS28 joints + MTP joints) for 76 RA patients to calculate the concordance rate in the result of determination of the findings between the 2 evaluation methods. The concordance rate of the findings between conventional examination and US varied depending on the articular sites (κ coefficient: −0.08 to 0.51), with the lowest values in the glenohumeral joint (κ coefficient: −0.08 to 0.05) and MTP joint (κ coefficient: −0.08 to 0.28) in particular. Based on the above-mentioned findings, the glenohumeral and MTP joint are the joints to be complemented by US, similar to that suggested by Salaffi et al.

The fingers and wrist joints are the sites most frequently subjected to joint US in many facilities. If possible, it is desirable to choose articular sites for joint US, taking into consideration the above-mentioned parts that particularly require complementation by US.

3. Usefulness of US in early and differential diagnoses

When caring for patients with arthralgia, it is important to examine in detail which site, including the joint, tendon, bursa, and surrounding soft tissue, the lesion originates from, whether the lesion is inflammatory or non-inflammatory, and the expansion and distribution statuses of the lesion. All of these points are difficult to determine in some cases if we use only conventional examination or rely on information from blood examination results. In such cases, US plays an active role. There is divergence between conventional examination-based judgment and US findings-based judgment. For example, in a case diagnosed as swollen hand, multiple arthrosynovitis or tenosynovitis was observed; in a case diagnosed without arthritis due to normal inflammatory reactions, including CRP and ESR, intensive arthrosynovitis was detected; and in a case initially diagnosed as joint swelling, osteoarthritis was the final diagnosis. Confirmation of the presence or absence of the divergence and correction of the judgment are the significance of complementation by US. There are quite a lot of cases in which the diagnosis and treatment strategy are changed according to findings from complementary US. The usefulness in early diagnosis was reported in RA cases in which rheumatoid factor, anti-CCP antibody, were negative. Cases in which US detected a PD signal progresses at high probability to persistent arthritis requiring anti-rheumatic agents such as methotrexate. It led to the improvement of palpation techniques with which physicians can independently confirm the correctness of their examination findings through anatomical understanding of the lesion using US. Moreover, in our experience, the patient developed an understanding of the pathological conditions through US images, facilitating understanding of the necessary changes in the treatment strategy.

4. Usefulness of US in the judgment of disease activity

The PD signal intensity observed in each articular site can be converted into a score by a semiquantitative method. The total sum of the scores representing the findings of multiple joints is well correlated with the comprehensive disease activity index (score calculated by combining examination findings, blood examination results, and patient VAS) such as DAS used in routine care for RA and also well reflects the reduction of disease activity by therapy.

5. Necessity of joint US in cases with clinical remission

It is known that synovitis remains (subclinical synovitis) in a proportion of patients negative for inflammatory reaction and patients judged to have reached clinical remission based on comprehensive disease activity indices. Brown et al. demonstrated that subclinical synovitis judged by joint echo and/or magnetic resonance imaging exists at high probability in patients with remission in RA who received administration of non-biological pharmaceuticals. Moreover, they reported that in these patients, bone destruction based on their chronological observation is proceeding and that the PD signal is the highest contributory factor to joint destruction. Saleem et al. demonstrated that subclinical synovitis still remained in the case in which new and stricter remission criteria were
applied. Joint echo complementation should be attempted in cases with remission as well because it can be important information for determining a true remission and when discussing enhancement or change of pharmacotherapy.

**Conclusion**

The emergence of high-frequency probes and advancements in equipment created a situation in which US plays an active role in the contemporary field of musculoskeletal diseases, including RA. The degree of contribution of imaging information obtained in real time in joint US is inestimable. Now it is nothing more than speculation to diagnose and estimate activity without using joint US. For medical care that requires higher accuracy in diagnosis of musculoskeletal diseases, performing more accurate evaluations through correction of judgment based on conventional examination complemented with joint US is required. It is expected that joint US will infiltrate the medical care system more widely in the future with its necessity based on its proven usefulness.

**References**