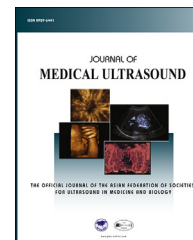


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EDUCATIONAL FORUM

The Third Eye of the Rheumatologist: Applications of Musculoskeletal Ultrasound in Rheumatic Diseases



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Abstract Rheumatologists manage patients with rheumatic diseases, which are of a wide range of musculoskeletal pathologies. Without clarification of the exact location of pathologies and the degree of inflammation, rheumatologists may have an incorrect assessment, leading to inappropriate management. In everyday practice, physical examination is limited by its sensitivity and power of assessment. Musculoskeletal ultrasonography (MSUS) is inexpensive, readily available, and allows side-by-side image comparisons. Thus, during the past 10 years, MSUS has become the “third eye” of the rheumatologist, in that it allows more detailed examination of muscles, bones, and joints, just as the stethoscope provides further details about the respiratory and circulatory systems. We briefly introduce how rheumatologists in Taiwan use MSUS for the diagnosis and treatment for rheumatic diseases.

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Introduction

Rheumatic diseases include a wide range of pathological entities, including connective tissue diseases [e.g., systemic lupus erythematosus, rheumatoid arthritis (RA), scleroderma, dermatomyositis/polymyositis, Sjögren syndrome, mixed connective tissue disease], spondyloarthropathies (e.g., ankylosing spondylitis, reactive arthritis, psoriatic arthritis), degenerative arthritis, metabolic disorders (e.g., gout, pseudogout, other crystal-induced arthritides), septic arthritis, and other diseases that

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affect the joints, bone, cartilage, tendons, and ligaments. The main tissues and organs affected by these diseases are the muscles, bones, joints, and soft tissues. A trained rheumatologist can use differential diagnosis after review of a patient's medical history, the performance of a physical examination and blood tests, and by follow-up after administration of appropriate treatment. However, imaging tests are often required to aid the diagnosis, assess disease severity, and guide treatment follow-ups. With the advancements in imaging technologies over the past decade, musculoskeletal ultrasonography (MSUS) can now provide rheumatologists with very clear gray-scale images of the musculoskeletal system. In addition, color or power Doppler ultrasound can be used to measure blood flow through small vessels to evaluate the extent of inflammation. Moreover, ultrasonography does not expose the patient to radiation, is inexpensive, is readily available, and allows side-by-side image comparisons. Thus, during the past 10 years, MSUS has become the "third eye" of the rheumatologist, in that it allows more detailed examination of muscles, bones, and joints, just as the stethoscope provides further details about the respiratory and circulatory systems. This article will briefly introduce how rheumatologists in Taiwan use MSUS for the diagnosis and treatment of rheumatic diseases.

Advantages and disadvantages of musculoskeletal ultrasound

The main benefits of MSUS are that there is no radiation exposure, it is relatively inexpensive, easy access is available, it is noninvasive and easily accepted by patients, it can be used to assess multiple regions and allows bilateral comparisons, and dynamic scans can be performed. The main disadvantages are that there may be differences in the interpretation of results by different operators, there is a long learning process, there is a need for coordination with physician availability, and it lacks the ability to examine areas behind the bones and air [1].

Why do rheumatologists perform musculoskeletal ultrasound?

Most ultrasound examinations, including abdominal sonography, cardiac sonography, and carotid/intracranial sonography, can be conducted by trained radiology technicians, followed by image interpretation and subsequent issuance of final reports and diagnoses by radiologists or physicians from other departments. Nevertheless, it is very difficult for technicians to perform MSUS, mainly because standardized ultrasound scans of different regions (so-called standard scanning routines) often do not provide physicians with the information they need, and may even mislead them.

For example, shoulder impingement syndrome may be suspected after an inquiry about the medical history and a physical examination of a patient, in which case additional dynamic ultrasound scanning should be performed to make a definite diagnosis. In addition, abnormalities in the ultrasound images of the rotator cuff ligaments in elderly patients

are often not the genuine reason for pain or movement problems. Thus, it is usually necessary for a physician, who has a greater breadth of knowledge, to interpret such images in concert with the physical examination results and inquiries about medical history before diagnosis. Moreover, if a lesion is discovered, ultrasound-guided aspiration is required so that further testing (such as microscopic examination or culture of synovial fluid) can be performed, or an ultrasound-guided injection may be needed for symptom relief. Only physicians, not technicians, can perform such invasive procedures. In Taiwan, the first MSUS procedures were performed by radiologists who were familiar with imaging of the musculoskeletal system. These doctors can examine the medical history and perform physical examinations to aid in the interpretation of the ultrasonography results, can issue a final report, and can even perform ultrasound-guided aspiration or injection. However, there are too few radiologists specialized in musculoskeletal ultrasound in Taiwan to examine a large number of patients with rheumatic diseases. If rheumatologists can also perform MSUS in person, they can combine the imaging results with their better understanding of patients and rheumatic diseases, and thereby provide better care. Furthermore, during the training of physicians, they can be taught to use ultrasonography as a complement to physical examinations.

Two hypothetical examples illustrate the benefits of rheumatologists performing MSUS. The first example is a patient (female) with early stage RA who has not yet been diagnosed. This patient initially presents with mild joint pain in her right wrist. If the joint pain is only accompanied by mild swelling and joint inflammation, a simple physical examination may falsely interpret the findings as normal. In addition, if serum indicators of inflammation, such as the erythrocyte sedimentation rate or C-reactive protein, are within the normal ranges, and levels of rheumatoid factor and anticitrullinated protein antibody are also normal, then RA may be excluded, and there is no opportunity for pre-emptive treatment. By contrast, if a rheumatologist trained in the use of MSUS examines the wrist inflammation by physical examination and then by MSUS, he/she can determine the presence of RA, administer therapy, and thereby reduce the risks associated with delayed diagnosis. Moreover, if bone erosion is present, active treatment and follow-ups can be managed in a more timely manner.

The second example is a patient who has been diagnosed with RA and is undergoing follow-up treatment. This patient has been treated for RA, and during the follow-up, the inflammatory indices decreased to within their normal ranges, and a simple physical examination indicated no joint inflammation, so the patient may be advised to move toward a more conservative treatment, such as a reduced drug dosage. However, if the rheumatologist performs MSUS to confirm the initial diagnosis and during the follow-up examinations, he/she can better decide on whether dosage reduction is appropriate. Dose reduction may be inappropriate if the Doppler ultrasound signals are still present in the joints and pass through the eroded bone (Figure 1) due to incomplete disease remission. Consequently, rheumatologists must be cautious about drug dose adjustment, and sonographic findings may help them to make better decisions on changes in therapy and dose.

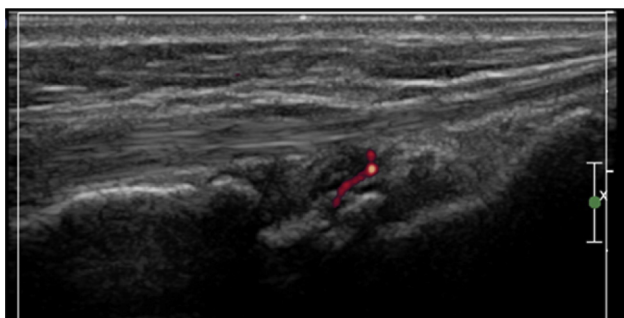


Figure 1 A Doppler ultrasound image of the right wrist of a patient with rheumatoid arthritis shows that the Doppler signal passed through the eroded bone.

To sum up, the benefits of rheumatologists performing ultrasound are that it complements the physical examination and can improve clinical diagnosis; it improves the performance of invasive examinations and treatments; it can detect early stages of arthritis, bone erosion, and cartilage damage; it provides objective evaluation of therapeutic responses; and it aids the evaluation of tendon and ligament disorders in patients with rheumatic diseases.

How do we provide training in musculoskeletal ultrasound?

In the year 2000, with the support of Dr Joung-Liang Lan (former Chief of the Division of Immunology and Rheumatology at Taichung Veterans General Hospital), the author and Dr Der-Yuan Chen (who later succeeded Lan as the Division Chief, and currently serves as the Director of Department of Internal Medicine and Medical Education at Taichung Veterans General Hospital and the Director of the Taiwan Rheumatology Association) attended an international seminar on MSUS in Singapore to learn how to perform this technique. In Taiwan, we also sought advice from radiologists who specialized in MSUS (such as Dr Hong-Jen Chiou at Taipei Veterans General Hospital and Dr Haw-Chang Lan at Taichung Veterans General Hospital) and began to use this technique in clinics and perform some studies. At that time, several rheumatologists in Northern and Southern Taiwan gradually became interested in MSUS and also began using this technique. We also tried to introduce and present the advantages of MSUS at different conferences in Taiwan [2].

In 2009, under the guidance of Dr Shu-Fen Luo (former Director of the Taiwan Rheumatology Association), the Taiwan Rheumatology Association established the Taiwan Rheumatology UltraSound Team (TRUST) to hold regular ultrasonography seminars at different levels. The basic-level training focuses on basic scanning techniques (patient position, probe selection, instrument settings, the order of standard scans, comparisons between left and right sides of the body, dynamic examinations, etc.), familiarity with normal anatomical ultrasound images of various regions, interpretation of structural lesions, and basic ultrasound-guided injection. The mid-level training provides a more in-depth understanding of commonly seen pitfalls in imaging

and teaches about the use of more advanced operations. The high-level training teaches about techniques that can be used for diseases that are less commonly targeted by ultrasonography, such as vasculitis, scleroderma, Sjögren syndrome, and psoriasis, and also introduces new ultrasound techniques, such as three-dimensional ultrasound, elastography, and combined magnetic resonance imaging/ultrasound.

In April 2010, TRUST developed the first ultrasound atlas of rheumatic diseases in the Chinese language [3]. In 2011, TRUST finished writing a textbook on the use of MSUS in rheumatic diseases and held an ultrasound seminar at the Asia Pacific League of Associations for Rheumatology Symposium [4]. From 2012 to 2013, we completed the standardized format for ultrasound reports and an assessment of consistency in ultrasound image interpretation between physicians. In 2014, a rheumatology group (previously merged into the panel for the musculoskeletal systems) was established within the Taiwan Society of Ultrasound in Medicine. In recent years, MSUS has become a necessary part of the rheumatology specialist examination in Taiwan.

From the author's perspective, it is important to be passionate about ultrasonography, take the time to delve into the details of ultrasound, and promote the adoption of MSUS among rheumatologists. As far as possible, scans should be performed using high-quality ultrasound scanners. Given insufficient funding at the hospital where the author worked, he even took out a loan to purchase a Philips iU22 ultrasound machine (Bothell, WA, USA) with 2D and 3D transducers (without a pay raise) to obtain better quality images and to conduct studies using three-dimensional ultrasound. Lastly, successful establishment of a dedicated ultrasound team is an essential factor for increasing the adoption and use of ultrasound!

Currently, the most common applications of MSUS for rheumatic diseases are as follows [5]:

Regional pain syndrome/tumor, mass

For a patient with a regional pain, gray-scale ultrasonography can help to determine whether the lesion is primarily located in the skin, subcutaneous tissue, tendon, ligament, nerve, blood vessel, joint, or bone. Doppler ultrasound can then be used to determine whether there is increased blood flow at the site of the lesion. A pathological examination of a biopsy sample remains necessary for a definite diagnosis of most masses, but MSUS can help to narrow the range of diagnostic possibilities. For example, a patient (male) received a firm diagnosis of gout based on analysis of the synovial fluid. Administration of uric acid-lowering medication reduced his serum level of uric acid to below 5 mg/dL for more than 1 year. Nonetheless, the lump on his finger, which was long considered to be a gouty tophus, continued to grow larger (Figure 2). Furthermore, dynamic ultrasonography examination indicated no signs of small and shiny hyperechoic particles or chronic tophi, but did indicate a hypoechoic tumor, which possibly originated from the tendon sheath (Figure 3). Accordingly, the patient was transferred to the hand surgery department for removal of the lesion. The



Figure 2 A lump classified as a gouty tophus on the finger of a patient initially diagnosed with gout based on a physical examination.

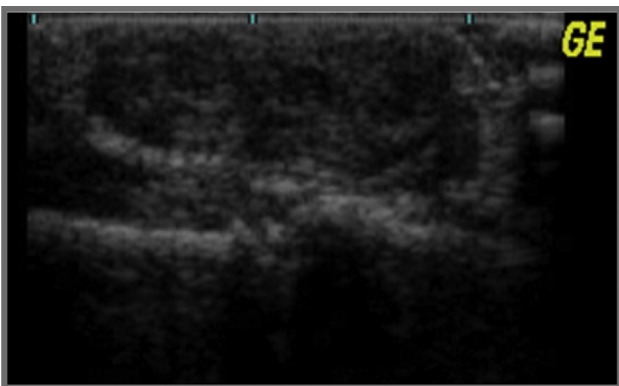


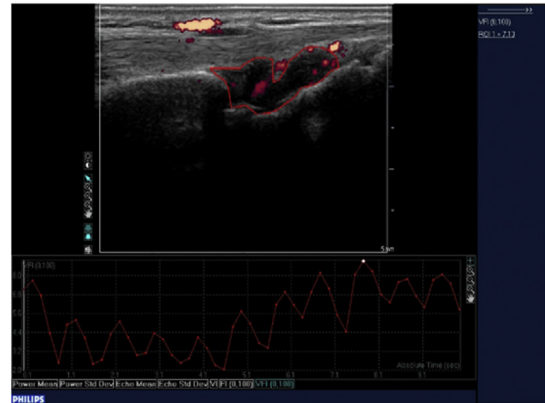
Figure 3 A hypoechoic tumor, possibly from the tendon sheath, was detected by ultrasound of the same patient as in Figure 2.

resulting pathology report described a giant cell tumor of the tendon sheath.

Diagnosis of arthritis and assessment of prognosis

MSUS can increase the reliability of the diagnosis of arthritis. A study by Matsos et al showed that among a population of patients, 9.7% were originally diagnosed with arthritis based on clinical criteria, but 38.7% had arthritis based on ultrasonography [6]. Furthermore, MSUS may also influence doctors' treatment decisions. For instance, a study at the Taichung Veterans General Hospital reported that if synovial membrane proliferation or bone erosion appears in a patient with palindromic rheumatism, then the patient will very likely develop RA [7]. This means that the treatment strategy can be adjusted upon the appearance of palindromic rheumatism with synovial membrane proliferation or bone erosion.

(A)



(B)

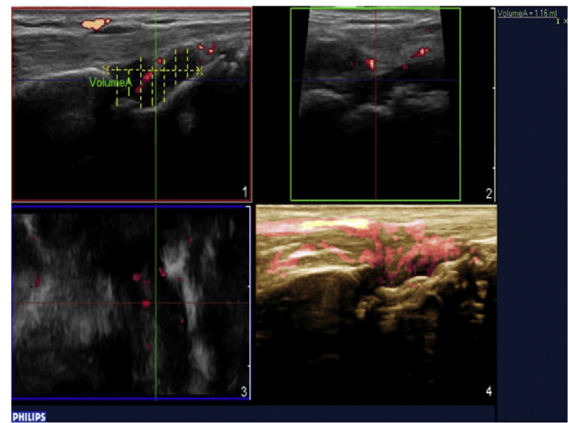


Figure 4 Quantification of the Doppler signals of an inflamed joint by (A) two-dimensional and (B) three-dimensional ultrasound using the computer-aided software QLAB provided by Philips (Bothell, WA, USA).

Assessment of inflammatory responses

Rheumatologists usually determine whether there is increased blood flow at an articular lesion using Doppler ultrasound. For example, a previous study indicated that greater blood flow correlates with more subsynovial infiltration of polymorphonuclear leucocytes and surface fibrin in the joints of patients with synovitis [8]. Hence, rheumatologists currently use semiquantitative methods to evaluate the extent of inflammation in the joints of patients with RA. Rheumatologists at the Taichung Veterans General Hospital quantify Doppler signals obtained with two-dimensional and three-dimensional ultrasound by computer-aided software, leading to an even more accurate assessment of the extent of joint inflammation (Figure 4).

Evaluation of therapy at follow-up

Some clinical trials for new RA drugs showed that as the medication works, Doppler ultrasound shows reduced blood flow in the joint [9,10]. In addition, the presence of Doppler signals in the joint after a period of treatment is the most

significant predictor of disease relapse [11]. Therefore, MSUS in conjunction with Doppler ultrasound can provide physicians with valuable information regarding treatment decisions for patients with RA, such as the effectiveness of biologics, the decision for drug withdrawal, and the risk of relapse after drug withdrawal.

Ultrasound-guided aspiration and injection and synovial biopsy

The use of MSUS to guide invasive examinations provides better accuracy and can help prevent damage to the skin and blood vessels [12]. The ultrasound-guided synovial biopsy requires only local anesthesia, making this a more convenient and faster procedure, and also allowing biopsy of small joints.

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