The Value of Ultrasound in Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic systemic disease characterized by symmetrical joint inflammation that can lead to progressive joint destruction and disability. RA is one of the commonest inflammatory arthritides with a prevalence rate in most industrialized countries of between 0.3 and 1% of the population. This article summarizes the role of ultrasonography in the diagnosis and management of patients with RA.

The management of RA has changed dramatically over the last few years. Early diagnosis and effective treatment have been shown to be able to improve symptom control, long-term structural damage and functional status [1]. With increasing use of disease modifying anti-rheumatic drug (DMARDs) and the early introduction of biologics, the number of RA patients who are able to achieve remission has been increasing [2, 3, 4, 5]. The ‘treat-to-target’ approach which has set remission as the primary treatment goal for RA in clinical practice has been shown to improve clinical outcomes [6, 7]. Sensitivity and accurate measurement tools are increasingly important, not only to establish diagnosis but also to monitor disease activity for appropriate guidance on therapy.

CURRENT MEASUREMENT TOOLS FOR DIAGNOSIS AND DISEASE MONITORING

In clinical practice, judgements for diagnosis and disease activity are largely based on clinical evaluation with the interpretation by clinicians of patients’ symptoms being combined with the laboratory assay of inflammatory markers as well as conventional radiography of the joints. Studies have shown that the increased joint damage can develop despite apparent clinical improvement [8]. Remission — as defined by clinical remission criteria — does not always equate to the complete absence of inflammation as measured by modern sensitive imaging techniques such as ultrasound and magnetic resonance imaging (MRI) [9]. This reflects the suboptimal sensitivity of traditional clinical approaches to the detection of synovitis and shows the superiority of advanced imaging techniques over clinical assessment alone in defining disease activity.

There are increasing amounts of data to support the validity of ultrasound as a disease assessment tool which has superior sensitivity for the detection of inflammation than clinical assessment [10, 11, 12, 13, 14, 15, 16, 17]. Ultrasound is gaining popularity among rheumatologists, as increasing evidence supports the added value of ultrasound assessment over traditional clinical measures, thus enabling greater confidence in diagnostic and management decisions.

STRENGTH OF ULTRASOUND

Musculoskeletal ultrasound and MRI are capable of directly visualizing and objectively quantifying synovial inflammation and bone damage. However, MRI is expensive, time consuming and has the disadvantage that only a few joints can be scanned at a time. Ultrasound on the other hand, allows real-time ‘point of care’ assessment of multiple joints in multiple planes and is relatively inexpensive compared to MRI. It is easily repeatable, is easy to carry out and has a shorter scanning time.

Ultrasound can be considered to be the extension of the physical examination.

Our practical experience is that patients prefer ultrasound over MRI examinations because of the increased possibility of direct interaction between the patient and the clinician.

USE OF ULTRASONOUND IN RA

Ultrasound examination has been shown to be more sensitive and accurate than clinical examinations in detecting synovitis [12, 15, 18, 19]. The technique can be used in different ways to assess different aspects of synovitis: gray-scale to demonstrate the morphology and quantity of synovium and power Doppler or color Doppler to measure the synovial vascularity, which is an indicator of active inflammation [22, 23].
Power or color Doppler has in particular attracted recent attention, as this approach has been shown to correlate better with inflammatory activity than gray-scale alone. Ultrasound is also more sensitive than conventional radiography in detecting bone erosions [10, 11, 15, 20, 21] [Figure 2]. Ultrasound should however not be regarded as a substitute for good clinical evaluation, but as a complementary tool which can help in the clinical assessment. The technique has been likened to a ‘joint stethoscope’ [24].

ACCELERATED DIAGNOSIS

Studies show that the identification of subclinical disease using ultrasound can alter disease classification. For example, a diagnosis of monoarthritis can be modified to oligoarthritis and/or polyarthritis when ultrasound is used in the very early window of the disease time-course [25]. In addition, adding ultrasound findings to the 2010 ACR/EULAR (American College of Rheumatology/European League against Rheumatism) classification criteria for RA increased the number of patients who fulfilled the 1987 ACR revised criteria for RA after 18 months of follow-up [25]. Ultrasound examination thus allows reclassification of the disease and provides earlier confirmation that the diagnostic criteria of RA have been fulfilled. This can allow earlier initiation of DMARDs therapy. The detection of increased Doppler signals within the joints has been shown to predict future bone damage. The identification of such joints should help stratify patients and indicate those patients who should receive more aggressive therapy.

FIGURE 1A. Physical examination of the metatarsophalangeal joint.

FIGURE 1B. Longitudinal section through the metatarsophalangeal joint showing gray-scale synovitis.

FIGURE 1C. Image corresponding to 1a showing increased power Doppler signal within the synovitis which is suggestive of active disease.

BETTER DISEASE MONITORING

Ultrasound is a more objective assessment tool than clinical examination alone and correlates well with clinical parameters for disease activity. The sensitivity of ultrasound has been shown, in follow-up studies of RA patients treated with corticosteroids [26] and tumor necrosis factor blocking agents [27], to be good for the detection of changes in joint inflammation. Indeed, one study has demonstrated that, over a 12-month period ultrasound exhibits a greater sensitivity for detecting erosive progression than plain radiography [28].

BETTER DEFINITION OF THE STATUS OF REMISSION

Early intervention with DMARDs and biologics has made clinical remission a realistic target. However, even when patients are in remission, according to the standard definitions of clinical remission, patients can continue to progress structurally. The first study illustrating such a discrepancy between ultrasound findings and the clinical composite indices of remission was that of Brown AK et al [9]. The dominant wrist and 2-5 metacarpophalangeal joints of 106 asymptomatic RA patients in complete clinical remission for at least 6 months were scanned using both ultrasound and MRI. In at least one scanned joint, 73% and 43% of patients had evidence of gray-scale or power Doppler joint synovitis respectively. MRI confirmed the ultrasound findings. More recent studies have demonstrated similar findings [29, 30, 31, 32, 33]. All this suggests that ultrasound is more sensitive than clinical assessment on its own in the detection of subclinical synovitis. When used in addition to clinical assessment, ultrasound allows more accurate and objective evaluation of disease status, especially for the establishment of true remission. This is of significant help in guiding treatment decisions and optimizing maintenance therapy in order to avoid under- or over-treatment.

PREDICTIVE VALUE IN REMISSION STATES

In RA patients with low disease activity or remission it has been shown that power Doppler activity is better than clinical examination alone in the prediction of radiographic progression, disease flare and persistence of disease [32, 33, 34]. Saleem et al [34] studied 93 RA patients in clinical remission over a 12-month period of whom 26 patients had a flare over the period. The presence of power Doppler activity was found to be the strongest independent predictor of flare (OR 4.08 (1.26–13.19); p=0.014) as none of the routine clinical indices of remission were predictive. Peluso et al [33] noted that only 20% of patients without power Doppler activity had a flare over 12 months compared to 47.1% who did. Similarly, Scirè et al noted that power Doppler activity was a better predictor of short-term relapse than clinical approaches [32]. Ultrasound-detected synovitis has also been shown to correlate with subsequent radiological and functional outcomes [28 35 36].

ULTRASOUND GUIDED INJECTION

Ultrasound provides more precise guidance in diagnostic procedures such as joint aspiration, synovial biopsy and joint injection therapies at target sites. There is some evidence suggesting that this approach may improve clinical outcomes with fewer complications than standard ‘blind’ approaches [37, 38, 39, 40].
FIGURE 2. Longitudinal section through the lateral aspect of the 5th metatarsophalangeal joint. This shows an erosion (bone defect) on the metatarsal head which is a classical site for early damage in patients with RA. This damage is often not seen on conventional XR in early RA and therefore ultrasound is particularly advantageous.

LIMITATIONS OF ULTRASOUND

However, there are several factors which can limit the use of ultrasound in rheumatology. The ultrasound beam is not able to penetrate bone, thus making it impossible to visualize intraosseous changes such as bone marrow edema. Due to the restricted access of ultrasound in certain joints e.g. wrists and metacarpophalangeal joints, the sensitivity of the technique in the detection of synovitis and erosions at such sites is lower than those of MRI and computed tomography (CT). Nevertheless, the sensitivity of ultrasound remains superior to the current standard of clinical examination and radiography.

The major concern about the accuracy of ultrasound is its operator dependence. To ensure that ultrasonography findings are comparable, it is important to use standardized examination procedures and methods of image interpretation. In 2005, the EULAR and OMERACT (Outcome Measures in Rheumatology) Ultrasound Task Force published an expert consensus on ultrasonography-specific definitions and image acquisition for various inflammatory pathologies (synovial fluid, synovial hyper trophy, tenosynovitis, bone erosion, entheseopathy) [41]. After the establishment of the consensus, intraobserver reliability was shown to be moderate-to-excellent and the interobserver reliability was moderate-to-good for the detection of synovitis (i.e. effusion, synovial hypertrophy, and power Doppler signal) and grading [42]. Work is ongoing on the further development of reliable standardized ultrasonography scoring systems in RA for both synovitis and bone damage.

FUTURE PERSPECTIVES

Three-dimensional (3D) ultrasound allows volumetric assessment of tissue blocks and quantification of regions of interest. The technique is considered to be operator-independent at least as far as the acquisition of the images is concerned, although the interpretation of 3D images is technically more challenging than 2D images. However, there is good-to-excellent agreement between 3D and 2D ultrasound for the sensitivity for the detection of synovitis and bone erosion [43]. The long image acquisition times of 3D ultrasound however hampers its use in dynamic scans. Fusion of ultrasound image with MRI or CT images could combine the advantages of real-time image acquisition in ultrasound with the better depiction of bone and soft-tissue lesions in MRI or CT. The fusion of ultrasound and CT images has been shown to improve the accuracy of injections in the sacroiliac joints [44]. SonoeLASTography evaluates tissue elasticity. Its role in RA is unknown except for the differentiation of rheumatoid nodules and gouty tophi [45]. The technique has however shown promising results in the evaluation of other conditions such as Achilles tendinopathy, lateral epicondylitis and scleroderma. [46, 47, 48, 49].

CONCLUSIONS

The role of ultrasound in the diagnosis and management of RA has evolved significantly in recent years. When combined with clinical assessment, gray-scale and power Doppler ultrasound allows a more accurate and objective evaluation of disease status and can result in the optimization of disease suppression and of disease outcomes. As the cost of the technique falls and the resolution of the acquired image increases, ultrasound is fast becoming the essential assessment tool for the rheumatologist.

We predict that in the future, no rheumatology department will be deemed to be competent without ultrasound facilities.

REFERENCES