



Ultrasound may improve patient care

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It has been demonstrated sufficiently that ultrasound examination is more sensitive than clinical examination for detecting various arthritic components such as enthesitis, crystal deposits, and especially synovitis—the latter being the key component in many rheumatological diseases and may further be of help in defining the degree of disease activity.

With the better sensitivity for detecting synovitis, ultrasound examinations have been shown to detect subclinical joint involvement resulting in the detection of more joints with synovitis in early and established rheumatoid arthritis (RA) than clinical examination illustrating a low association between the clinical and ultrasound examinations of joint involvement [1]. This has resulted in the incorporation of ultrasound-detected synovitis in the EULAR/ACR classification criteria for RA where the ultrasound findings may assist in establishing a more elaborate joint involvement. Synovitis is classically scored from 0 to 3 according to the degree of severity and grades 0–1 are often considered a normal finding—especially in the feet where synovitis-like changes may be seen in the metatarsophalangeal joints (MTPs) [2]. These findings are likely to be related to pressure on the feet from walking reinforced in overweight patients. This challenge is valid in both very early and in established arthritis patients [3, 4]. However, a recent study has highlighted that even grade 1 in the MTPs may improve in patients with established RA when

initiating treatment [4] pinpointing that cutoffs for what constitute synovitis by ultrasound but also for MRI need to be established for diagnostic purposes. Though it may be natural to challenge the reliability of ultrasound for assessing synovitis, ultrasound has a higher degree of reliability than the clinical joint assessment [5] that repeatedly has been shown to have great variability among clinicians. This divergence in joint evaluation has led to an increasing number of studies exploring the discrepancies between clinical and ultrasound assessments. Before the introduction of ultrasound into clinical practice, assessments of tender and swollen joints were used to define the degree of inflammatory activity in RA patients and are therefore included in all the clinical composite scores frequently used today (DAS, DAS28, SDAI, and CDAI) all of which are developed to be feasible in daily clinical practice and very rarely involve assessment of the joints in the feet. Recent studies, however, challenge the importance of tender joints for assessing disease activity as the risk of having synovitis in a clinically tender joint is low. This has been demonstrated by a very low association between joint tenderness and presence of ultrasound synovitis at joint level whereas clinically swollen joints are highly associated with ultrasound synovitis in established RA [6]. Furthermore, patients with higher number of tender than swollen joints seldom reach composite score remission, even if they had lower degrees of ultrasound synovitis [7] both in RA and psoriatic arthritis [8] illustrating that tender joints, at least in established RA, seem to reflect another component of the arthritic disease than inflammation. The fact that in the DAS28 tender joints have double weight when calculating the composite score index illustrates the complexity of including tender joint when they are not related to inflammation. Conversely, it has been shown that patients who were concordant in terms of DAS and US remission have a slightly lower risk of losing their remission [9]. Several studies have further underlined that the main reason for not obtaining ACR/EULAR Boolean remission is related to the levels of patient's global assessment of disease activity but also to tender joint count [10]. This discrepancy between no inflammatory activity by ultrasound and clinically

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increased composite score levels is highlighting the clinical challenge when not incorporating ultrasound into the evaluation. This may result in increased use of biological treatment in RA patients with concomitant fibromyalgia where the composite scores alone may mistakenly be seen as an indicator of increased inflammatory activity for explaining the persistent joint pain. A study exploring this issue found that RA patients with additional fibromyalgia were more often treated with biological DMARDs than RA patients without fibromyalgia [11]. Though several studies in early RA patients have found no added value of incorporating ultrasound or MRI to a very aggressive treat-to-target approach in all patients [12–14], the studies do not address the role of ultrasound where there is a discrepancy between clinical evaluation and the patient perception of the disease activity which is the dominant application in the clinic. Previous studies have shown that in joints that may clinically be challenging to assess, ultrasound frequently leads the physician to change the diagnosis and consequently the planning of corticosteroid injections [15]. Moreover, ultrasound has shown improved response to local treatment—in the ARCTIC study, it was shown that steroid injections given only to ultrasound-verified inflamed joints caused a reduction of clinically assessed swelling, while injections when given to only clinically assessed swollen joints had less effect on clinical swelling [16]. Even if no added value was found by adding imaging to every clinical control in very early RA, there is nevertheless a need for further randomized studies with a longer follow-up to assess the utility of ultrasound in monitoring of RA patients, but also studies assessing the added value in routine clinical practice where very tight clinical control is not applied are needed.

Ultrasound has proven to be important also in other diseases due to its superiority to clinical examinations. Several clinical assessments of enthesitis have been developed and enthesitis is even more difficult to assess clinically than joint synovitis. However, the associations between clinical enthesitis and ultrasound enthesitis are low, and Doppler activity in joints, entheses, and tendons is not associated with clinical composite scores in SpA patients [17]. With the importance of correct diagnosis of active inflammation versus chronic changes for choice of treatment, ultrasound is a useful tool for clinicians. The OMERACT ultrasound group has obtained consensus-based ultrasound definitions of enthesitis and on how to score ultrasound enthesitis to facilitate the reliability [18]. In addition, for patients with gout, the depositions of crystals are easily seen by ultrasound also in asymptomatic joints, tendons, and soft tissues and in patients with no obvious clinical sign of gout. Also for gout, the OMERACT ultrasound group has developed consensus-based ultrasound definitions for the typical lesions (double contour, tophi, and aggregates) [18] and recent data suggest that a treat-to-target approach to lower urate levels causes disappearance of the ultrasound-detected depositions [19]. Thus, ultrasound have

an added value in the clinical setting by detecting depositions that may help in early diagnosis and in the decision of initiating urate lowering treatment as well as showing resolution of the depositions in optimally treated patients which may motivate and help the compliance of taking long-term medical treatment.

The reliability of ultrasound as a clinical tool has often been questioned and has previously hampered the implementation. Ultrasound has, however, been shown to be comparable to MRI—frequently perceived as the gold standard—in detecting synovitis and tenosynovitis, and much work has been done to increase the reliability of ultrasound by eliminating operator dependency which is highlighted as one of the main worries. The operator dependency reported in the literature is mainly related to the skills and experience of the sonographers but may also be related to the quality of the US machines—especially the Doppler mode sensitivity. National and international ultrasound courses are in many countries established to ensure correct training. Consensus-based scoring systems for joint synovitis, tenosynovitis, and enthesitis have been developed to ensure homogeneity among centers [18] and the development of an ultrasound atlas illustrating the different semi-quantitative scores of synovitis in different joints has improved the reliability of scoring joint synovitis [20]. Furthermore, an ultrasound scanning app is available for ensuring optimal image acquisition [21]. However, conditions such as osteoarthritis and erosive osteoarthritis still pose a challenge as a different diagnosis to other arthritic conditions both clinically and for ultrasound and MRI.

Thus, with the low specificity of clinical evaluation, ultrasound stands out as an imaging tool that will improve our clinical examination. The increasing body of evidence of the usefulness of ultrasound as an extension of the clinical examination challenges the rheumatology community in ensuring accessibility in daily clinical practice. The accessibility ought to be facilitated by the rapid development of high-quality equipment with sensitive Doppler modalities to constantly lower prices. As may be seen in the current issue of *Clinical Rheumatology*, ultrasound as a clinical tool is being developed within many different rheumatological disease entities indicating a further widespread use that will improve patient care.

Compliance with ethical standards

Conflict of interest L.T. has received speakers fee from AbbVie, Janssen, Roche, Novartis, Pfizer, MSD, BMS, and GE; H.B.H. has received study grants from AbbVie/Pfizer and Roche. Speaker fees from AbbVie, Bristol-Myers Squibb, Roche, UCB Pharma, and Pfizer.

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