Ultrasound imaging for the rheumatologist XXI. Role of ultrasound imaging in early arthritis

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ABSTRACT

Identification of early indicators of diagnosis and prognosis together with tight control of disease activity are the current goals of management of early arthritis.

Several studies in the literature to date suggest that musculoskeletal ultrasonography (US) may have a role in this setting. US is a valid and reliable tool for the assessment of inflammatory arthritis – either as an ultra-sensitive measure of inflammation or joint damage. US is also useful in the differential diagnosis of early arthritis, both identifying disease specific findings and integrating clinical findings into structured diagnostic algorithms. Grey scale and power Doppler US are sensitive disease activity and severity markers, identifying subgroups of patients with poorer clinical and radiological outcomes, even once clinical remission has been achieved.

The present review provides an update of the available data and discusses research issues of ultrasound imaging in early arthritis.

Introduction

Early arthritis is a clinical entity which includes classifiable and undifferentiated arthritides.

It is vital to make early diagnosis and aim towards tight control of disease activity in order to modify the course of rheumatoid arthritis (RA) (1, 2).

Musculoskeletal ultrasound (US) is well established as a useful imaging modality in different types of inflammatory arthritis (IA) (3). Most of the published work centres upon established RA but in recent years there has been increasing focus on the early phases of RA and undifferentiated synovitis.

The present review deals with the potential application of US in the assessment of patients with early IA.

Is US useful in the early detection of synovitis?

US has become an important diagnostic tool in the assessment of rheumatologic diseases, as it can accurately detect a number of elementary lesions including joint effusion, synovial hypertrophy, tenosynovitis, enthesopathy, bursitis, bone erosions and cartilage abnormalities (4-7).

These properties make US an invaluable tool in the diagnosis of early IA. The first way in which US can assist the clinician in making diagnosis of IA is by allowing the patient with non-specific hand and/or wrist pain to be differentiated from the patient with true synovitis.

US has been shown to compare favourably with several other imaging techniques, including contrast-enhanced MRI, arthroscopy, scintigraphy, and histology in the detection of synovitis (8, 9). In a study examining a cohort of patients with early RA, US was found to be even more useful than MRI at identifying joint and tendon sheath effusion (10). When compared with clinical examination US demonstrates higher sensitivity in detecting synovitis in both longstanding and early RA (4). This seems particularly useful in discriminating oligo-arthritis from polyarthritis, with obvious prognostic implications, especially in the setting of an early assessment (11, 12).

The addition of power Doppler (PD) to conventional gray scale (GS) US allows assessment of soft tissue vascularity (13, 14). PD has been validated against MRI and histology, and was proven to identify active synovitis in RA (15-17).

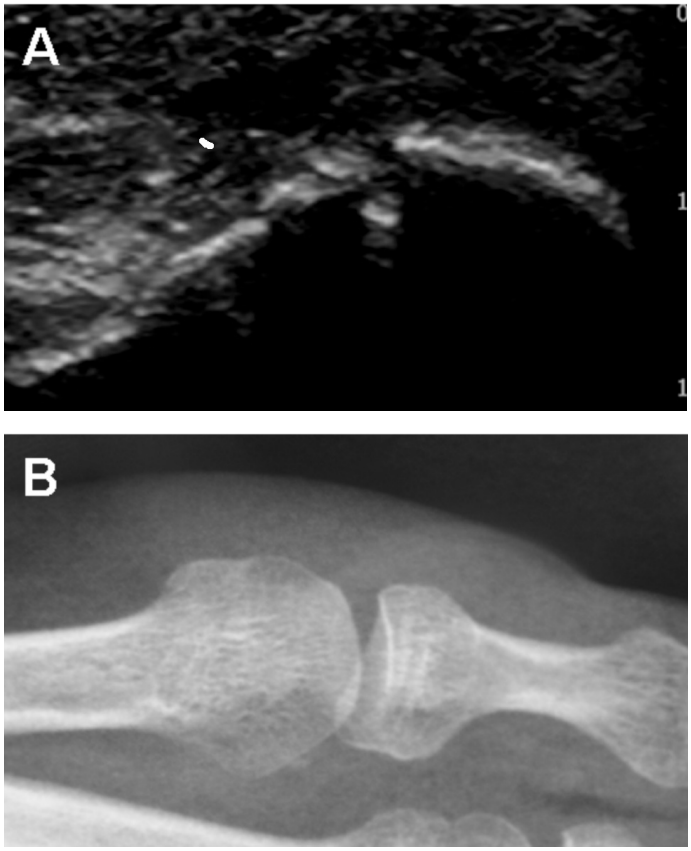

Fig. 1. US shows an erosion of the lateral aspect of the fifth metatarsophalangeal joint (**A**) in a patient with early rheumatoid arthritis, while conventional radiography fails to image the same lesion (**B**).
For further ultrasound images, go to www.clinexprheumatol.org/ultrasound

Is US useful in early detection of joint damage?

There is overwhelming evidence that the high resolution and multi-planar properties of US scanning can sensitively detect erosions, even before plain radiography. We are also aware that US performs well compared with computerised tomography (CT) as a gold standard for bone erosion detection. From the analysis performed on metacarpophalangeal joints (MCP) of erosive RA patients, US was more sensitive than conventional radiography (42% *vs*. 19%) and also highly specific (91%) (18).

Several studies have documented that US depicts erosions up to 6 times as much as x-rays in early RA patients (19-22). However, no increased sensitivity was reported in two cross sectional studies (10,23). These differences may relate to the different resolution of the US equipment employed and to the different joints assessed. In spite of this the reliability of US in the detection of erosions is now well established (24) and the accuracy appears to depend on the acoustic window of individual joints, being maximal for the1st, 2nd, 5th MCP and 1st and 5th metatarsophalangeal joints (MTP).

More recently, Bajaj *et al*. prospectively investigated US bone erosions at the 2nd, 5th MCP, 5th MTP and the 2 most involved proximal interphalangeal joints (PIP) in early RA, confirming a higher sensitivity compared with plan radiography and detection of bone damage by US before it became evident on x-rays (25). This property will make US an invaluable tool for the detection of bony erosions in early RA (Fig. 1) (21, 26).

Cartilage damage can also be quantified by US in early RA as well as in established RA and osteoarthritis (27).

Is US useful in the differential diagnosis of early IA?

Freeston *et al*. proposed a diagnostic algorithm which includes US for the prediction of persistent arthritis in patients presenting with IA from less than 12 weeks. This study showed clear benefit of GS and PD US particularly in seronegative patients, in which the prediction of persistence clinically is much more difficult because of the absence of defined prognostic factors. In this subgroup the presence of US features such as a high GS score , PD signal and at least one US erosion increased the probability of persistent IA from 30% to 94%, while if US features were absent, the probability felt to 0-5%.(28)

US is able to clearly depict entheseal pathology and would appear to be a valid tool for the discrimination between spondyloarthropathies and RA (29-31). Whilst this is an area requiring more research, sub-clinical entheseal inflammation detected by US could identify those patients with psoriasis and an increased risk to develop psoriatic arthritis (32).

Several studies have demonstrated the diagnostic utility of US in the diagnosis of crystal-associated arthropathies (7, 33).

It is clear that much additional research needs to be done in the area of disease differentiation in early IA and that US findings are only relevant when coupled with clinical parameters.

Invasive US guided techniques such as joint fluid aspiration and synovial biopsies may be useful in the early diagnosis of IA. Furthermore US-guided injection may assist in the accurate delivery of drug therapy to joints and tendon sheaths (34). US-guided mini-invasive biopsy procedures can now be performed in both large and small joints and may add valuable information to the assessment of early IA (35, 36).

Is US scan a reliable tool for disease activity and severity assessment in early IA?

Semi-quantitative grading systems (grade 0-3) have been generally applied to all joints investigated with US to date (13, 14, 37) Using this technique an overall US score can be obtained using the sum of the grade of each investigated joint. A gathering body of evidence supports the validity and reliability of such measures in early IA.

In early RA Naredo *et al*. showed a significant correlation between DAS28, CRP and PD scores (assessed at 28 joints) throughout the clinical course of patients recently commenced onto disease modifying drugs and a correlation between persistent PD signal and the

progression of radiographic damage (38). A significant correlation with ESR and CRP has been recently reported in a larger cohort of early RA both for GS and PD assessed in 44 joints (39). Correlation between US measures and inflammatory indices was significant even if patients with early undifferentiated IA were included (40).

As for the number and pattern of the joints to be scanned, several simplified joint counts have been proposed to avoid time consuming extensive examinations (41-43). Further applications of a systematic assessment by US pointed toward the prediction and the assessment of the response to treatment in early IA.

The effectiveness of intramuscular steroids was tested in 102 patients with recent-onset inflammatory hand pain. In this study the predictive value of clinical, laboratory and US variables was evaluated. A significant association with clinical response to intramuscular steroids was found only for US-proven synovitis and presence of rheumatoid factor, whilst clinical synovitis or raised CRP were not predictive. Such results indicate that an objective measure of inflammation in early IA can drive the therapeutic decision towards the right way (44).

In patients with erosive early RA randomized to receive methotrexate plus infliximab or methotrexate plus placebo, the quantification of PD in the MCP joints was predictive of progression of radiographic erosion after 12 months in the placebo group (45). This study provided evidence of a modification of both grey scale and PD synovitis according to clinical response to therapy and a more profound suppression of US signs of inflammation in the infliximab group.

A recent study has shown that modification of US characters was lower than that of standard clinical measures, such as manual joint count in early IA (46).

Can US identify sub-clinical joint inflammation and ongoing structural damage in early IA?

A considerable body of evidence exists in support of the application of US in the assessment of residual disease activity. The majority of RA patients in clinical remission show signs of persistent inflammation on US scanning at the wrists and MCPs (41, 47). It is well recognised that some patients with RA in clinical remission still have radiographic progression. Brown *et al*. have investigated the predictive value of sub-clinical inflammation in terms of radiographic progression. This study clearly indicated that the patients with PD signal in clinical remission had the highest risk of progressive joint damage (48).

Analyzing a smaller group of patients with early RA in clinical remission, it has also been shown that the presence of sub-clinical inflammation detected by US may help in discriminating patients with short-lived or unstable clinical remission. In particular these patients with PD positive synovitis showed a significantly increased risk of early relapse compared with PD negative (39).

Research agenda and conclusions

US is a valuable imaging tool in early IA where a very sensitive and highly reproducible analysis of joint inflammation is particularly required. Technical advances will further improve the resolution and the sensitivity of this technique. The introduction of three-dimensional probes could also overcome the operator dependence of US allowing for the standardized acquisition of images for reliable monitoring (21, 26, 49).

Further innovation includes fusion imaging, which conjugates different modalities, US and MRI, improving the diagnostic accuracy by highlighting strengths and weakening limitations of each imaging technique (50).

Further study of sub-clinical disease might permit the differentiation of patients with different clinical entities: those with potentially favourable outcomes from those with a poor outcome. There may also be merit in integrating clinical and US findings in the decision making process of patients with early IA.

Link

For ultrasound images, go to www.clinexprheumatol.org/ultrasound

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