Pro musculoskeletal ultrasonography in rheumatoid arthritis

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ABSTRACT

Musculoskeletal ultrasound has become a widely used imaging diagnostic tool both in the use of daily clinical practice and for clinical studies in monitoring treatment efficiency and predicting disease outcome. By US, detection of inflammatory soft tissue and erosive bone lesions is possible. Grey-scale and power Doppler ultrasound examination is more sensitive and more reliable than clinical examination. Furthermore, patients with unclear arthritic symptoms can be better diagnosed for arthritis by US than by clinical examination. This article gives an overview about the use of US in the diagnosis of early arthritis, especially early rheumatoid arthritis, its role as a prognostic assessor (structural damage), as a monitor for treatment response, as an detector of "real" remission, and a guide to injection procedure.

Introduction

Musculoskeletal ultrasound (US) has meanwhile become an important role as a diagnostic tool in rheumatoid arthritis (RA). US is able to objectify the inflammatory joint process by the detection of both early inflammatory soft tissue lesions (*e.g.* synovitis, tenosynovitis, and bursitis) and early erosive bone lesions in arthritic joint diseases. Studies show good correlation between US and MRI (Magnetic Resonance Imaging) in the detection of inflammatory soft tissue and erosive bone lesions (1-4). US allows a differentiation between exudative and proliferative synovial changes because of good soft tissue contrast. The early detection of synovial proliferation and joint effusion is important in the diagnosis of early arthritis. The application of colour and power Doppler ultrasonography (CDUS/PDUS) is helpful in the differentiation between active and inactive joint process. By accurate assessment of the disease activity and joint damage in RA, both treatment efficiency can be monitored and the outcome of the disease can be predicted by musculoskeletal US. It should be used in a standardise manner for the correct assessment of the disease activity and joint damage in RA (5). Therefore, the OMERACT (Outcome Measurement in Rheumatology Clinical Trials) has defined the typical RA findings that can be detected by musculoskeletal US including effusion, synovial hypertrophy/proliferation, tenosynovitis and erosion as follows (6):

Synovial effusion

Abnormal hypoechoic or anechoic intra-articular material that is displaceable and compressible, but does not exhibit Doppler signal

Synovial hypertrophy/proliferation

abnormal hypoechoic intra-articular tissue that is non-displaceable and poorly compressible and which may exhibit Doppler signal (Fig. 1).

Tenosynovitis

Hypoechoic or anechoic thickened tissue with or without fluid within the tendon sheath with possible signs of Doppler signals, which is seen in 2 perpendicular planes (Fig. 2).

RA bone erosion

an intra-articular discontinuity of the bone surface that is visible in 2 perpendicular planes (Fig. 3).

Musculoskeletal US in daily clinical practice and its role in early undifferentiated/early rheumatoid arthritis

Already at the end of the 90s, it could be presented that 20% of affected finger joints by synovitis which were detected by musculoskeletal US in patients with different arthritic diseases (n=60 patients) had clinically not been presented by swelling or tenderness (1). Later on, Scheel *et al*. analysed the distribution of synovitis in the finger joints MCP and PIP 2-5 of n=46 RA patients and found synovitis mostly (in 86%) in the palmar proximal joint region; the dorsal region alone was only affected in 14% (7). Recently, Vlad *et al*. could

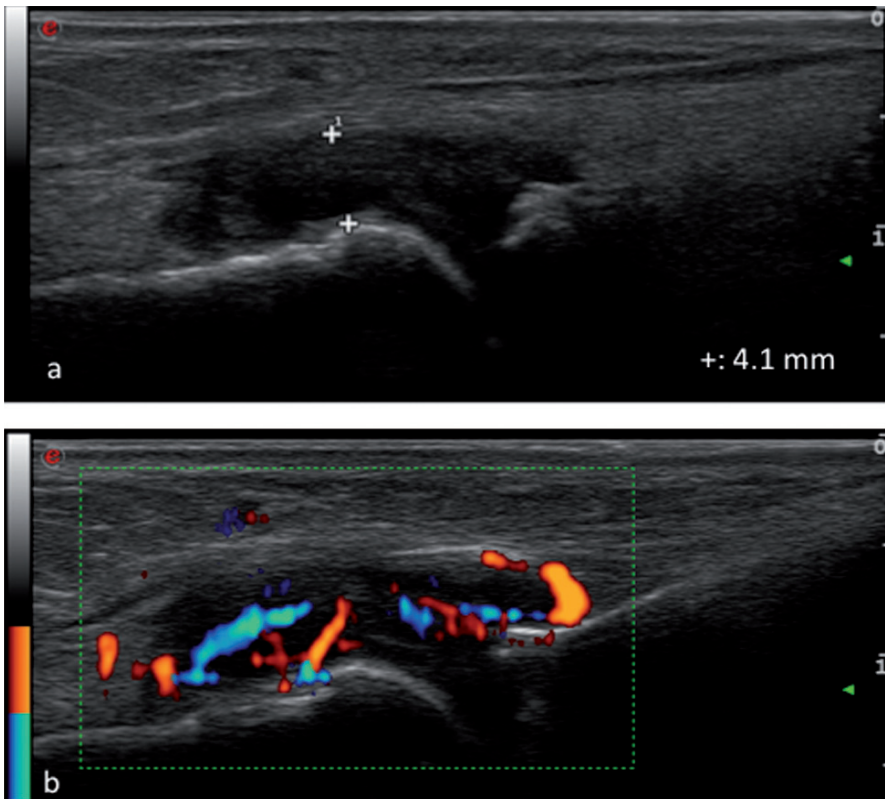

Fig. 1. synovitis of the MTP joint 2 at dorsal aspect in grey scale ultrasound (**a**), grade 3 and in power Doppler ultrasound (**b**), grade 2.

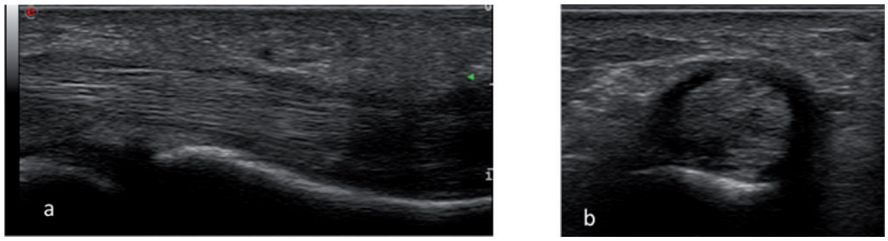

Fig. 2. tenosynovitis of the flexor digitorum tendon at palmar aspect of MCP joint 2 level in long (**a**) and short (**b**) axis.

confirm those results. In the study with 42 RA patients *palmar* synovitis scores correlated better to clinical data (HAQ; CDAI; SDAI, HAQ) than *dorsal* synovitis scores - both for greyscale and power Doppler mode (8).

In a study by Mandl *et al*. sonographical findings were combined to valid clinical scores (DAS28; SDAI; CDAI). In this study, GSUS and PDUS were more reliable than the examined clinical scores; furthermore discriminate capacity of PDUS was at least as high as that of the clinical score in the discrimination of different therapeutic groups. Consequently, US should be integrated into clinical practice additional to clinical evaluation (9).

Musculoskeletal US is also very helpful in patients with unclear clinical arthritic symptoms and minimal disease activity, which was presented in a study by Ciechomska A *et al*. In the study, n=44 patients with unclear arthritis, of which 26 were firstly visited, were sonographically assessed. The results of the study showed that 70% of the included patients had an active synovitis in musculoskeletal US and even 41% had a severe synovitis with an active erosion. The diagnosis of an arthritis was found in 65% of the firstly visited patient group (n=26) of which 31% already had erosions in musculoskeletal US, but not in conventional radiography (10).

Sommier *et al*. analysed the distribution of erosions in both side MCP joints 2, 3, 5 and MTP joints 2, 3, 5 in the dorsal, palmar/plantar and medial/lateral (only MCP 2, 5 and MTP 5) joint regions of n=82 patients with early (<2 years disease duration) and longstanding (≥2 years disease duration) RA. In 50% of all patients, erosions were detected in the medial/lateral region of the MCP 2, 5 and MTP 5 joints. In the early RA group, 90% of the erosions were detected in the medial MCP 2 and/or lateral MTP 5 joint region (11), consequently, especially these joint regions should be assessed by musculoskeletal US in the early diagnosis of RA.

Finzel *et al*. compared the erosions assessed by musculoskeletal US to those detected by micro Computertomography imaging (uCT) in n=26 patients with RA (n=14) and psoriatic arthritis (n=6) as well as 6 healthy controls. In the study, good correlation between both imaging modalities could be presented (12).

Rahmani *et al*. compared the erosions detected by musculoskeletal US to those that were found by MRI and conventional radiography in patients with early RA. In the study, there was an acceptable agreement between US and MRI findings, but not to radiography for early rheumatoid arthritis (13).

Prognosis and outcome of RA - is musculoskeletal US a helpful tool?

Synovitis plays an important role in the joint destroying process. It could be shown that no bone destruction occurs without the presence of synovitis. The persistence of synovitis in the finger joints beyond insufficient therapy is responsible for later joint destruction. High synovitis sum scores and high erosion sum scores in grey scale (GS) US as well as high DAS28 scores at baseline have a predictive value for bone destructions 12 months later (14).

Macchioni *et al*. presented that persistent power Doppler positive joints and joints with persistent synovitis in GSUS develop erosions in radiography significantly more often (p=0.001 and p=0.02). Power Doppler positive joints with PDUS scores ≥2 had an odds ratio (OR) = 8.51 for the devel-

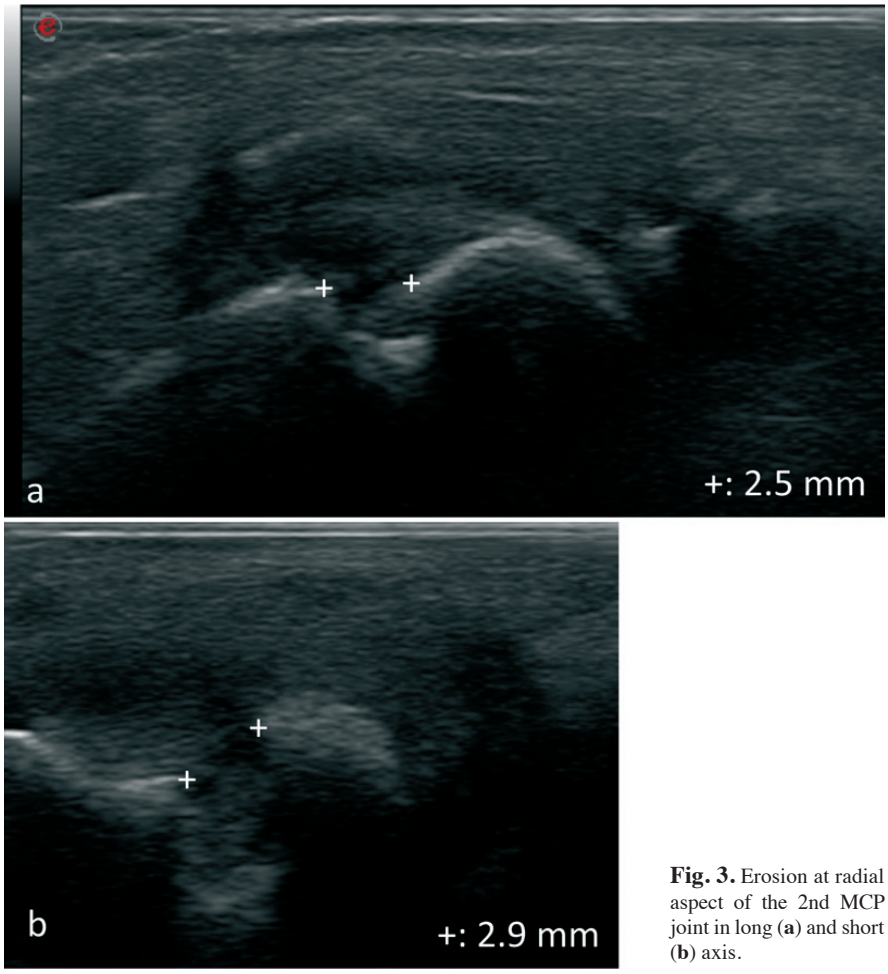

Fig. 3. Erosion at radial aspect of the 2nd MCP joint in long (**a**) and short (**b**) axis.

opment of new radiographic erosions and an OR=8.30 for the development of a high local Sharp-van der Heijde-Score. Similar results were found for the GSUS synovitis score (15).
A US group from Japan also presented that persistent synovial hypervascularisation detected by PDUS has a predictive value for later erosions (16).
In another study published by Dougados *et al*. it was presented that synovitis detected by US and clinical examination (CE) predicted subsequent structural radiographic destruction irrespective of the modality of examination (GSUS/PDUS/CE) of joints (17).

Patients in DAS28 remission - true remission?

An Italian US group presented by their data that short disease duration is predictive for imaging (US) remission. Only patients with clinical remission (DAS28 <2.6) were included. The patients who have shown synovitis activity in GSUS and/or PDUS were of higher risk for getting a relapse of the inflammatory disease in the next 12 months (18).
The tenosynovitis of the extensor carpi ulnaris (ECU) tendon has a high predictive value in n=61 early arthritis RA patients for the development of erosive bone lesions 12 months later detected by MRI that could be presented by an imaging study from a Norwegian imaging group. In the study, the OR for the development of erosions was 4.21 for the ECU tenosynovitis and 1.38 for the bone edema detected by MRI (19).
By a French US group it could be presented that only PDUS was able to differentiate between patients in remission and in low disease activity (LDA) if compared to GSUS, MRI and x-ray (20).
Yoshimi *et al*. could show that PDUS is able to predict the erosive process on joint level even if the patient is in clinical remission. PDUS scores ≥2 are relevant for the joint destroying process (21) concluding PDUS is essential for the "true" remission.

Disease activity and treatment monitoring by musculoskeletal US

Clinical studies have shown that musculoskeletal US is more sensitive in the detection of inflammatory signs than the clinical examination. A semi quantitative grading system is used for the description of the synovial process in GSUS and PDUS.
Several musculoskeletal ultrasound (US) scores exist to monitor RA disease activity and the therapeutic response to disease modifying anti rheumatic drugs. Different qualitative (0/1) and semi quantitative (0-3) systems as well as quantitative measurements are used. The novel 7-joint ultrasound (US7) score is the first US composite scoring system, which combines soft tissue lesions (synovitis and tenosynovitis) and destructive processes (erosions) in a single scoring system. By that, the implementation of the US7 score can fast and easily give an overview of current disease activity in daily rheumatologic practice. Furthermore, its use in therapy monitoring is very helpful (22).

Guidance of injection procedure by musculoskeletal US

Musculoskeletal is a very important tool in the guidance of diagnostic and therapeutic needle injections of affected joints. Recently, a large study was published by Sibbitt *et al*. in which n= 244 joints with inflammatory arthritis were randomised to injection by conventional palpation-guided anatomic injection (120 joints) compared to sonographic image-guided injection (124 joints). Baseline pain, procedural pain, pain at outcome (2 weeks and 6 months), responders, therapeutic duration, reinjection rates, total cost, and cost per responder were determined in this study. In relation to conventional palpation-guided anatomic injection, sonographic guidance for injection of inflammatory arthritis resulted in a significant reduction in injection pain (p<0.001), significant reduction in pain scores at outcome (p<0.02), significant increase in the responder rate (p<0.003), sig-

nificant reduction in the non-responder rate (p<0.003), significant increase in therapeutic duration (p=0.01), and significant reduction in cost/patient/year. Summarising the results of this study, US guided injections have a positive impact on the clinical outcome and the cost effectiveness (23).

Current success in the use of US

It has recently been published in the new EULAR recommendations that US as an imaging modality has its impact in the clinical management of rheumatoid arthritis (24).

In summary, musculoskeletal US is useful for diagnosing arthritis, especially early RA, offering a prognostic assessment (*i.e.* structural damage), monitoring response to therapies, to identify "real" remission, and guidance of injection procedure.

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