Sensitivity and specificity of ultrasonography and low-field magnetic resonance imaging for diagnosing arthritis

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Abstract

Objectives

To evaluate the value of grey-scale ultrasonography (US) including power Doppler ultrasonography (PDUS) and low-field magnetic resonance imaging (MRI) for the diagnosis of arthritis in a diagnostic phase III study.

Methods

Fifty consecutive patients with suspected arthritis were included in the study. Following a standardised protocol, US of the carpus and the metacarpophalangeal (MCP) joints of the dominant hand was performed. Subsequently, low-field MRI was done using standard sequences, with contrast agent (Gadolinium DTPA) administered to 29 patients.

Results

In 32 out of 50 patients a clinical diagnosis of arthritis was established. In grey-scale ultrasonography including PDUS, sensitivity and specificity were determined as 0.94 and 0.5, respectively, for synovitis (effusion and hypertrophy), 0.72 and 0.94, respectively, for Doppler signals, and 0.38 and 1.0, respectively, for bone erosions. In low-field MRI, sensitivity and specificity values were 0.77 and 0.75, respectively, for synovitis (when using contrast agent), 0.48 and 0.78, respectively, for bone marrow oedema, and 0.58 and 0.83, respectively, for bone erosion.

Conclusions

Both grey-scale ultrasonography including PDUS and low-field MRI are suitable imaging methods for diagnosing arthritis at an early stage. However, PDUS displays a higher specificity and almost the same sensitivity as compared to contrast-enhanced MRI, while being a much simpler and less costly procedure.

Key words
rheumatoid arthritis, ultrasonography, magnetic resonance imaging

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Introduction

The diagnosis of arthritis in rheumatology primarily is based on clinical findings such as the number and distribution of tender and swollen joints or morning stiffness and is supported by laboratory criteria such as positive rheumatoid factor or anti-citrullinated peptide antibodies (ACPA), prior to the new classification criteria (1) also with radiographics.

In addition to the progress in medical treatment of rheumatic diseases, innovative imaging techniques have been developed which facilitate direct visualisation of inflammatory changes in the human body. In particular, ultrasonography and magnetic resonance imaging (MRI) play a significant role in the diagnosis of rheumatic diseases and in monitoring treatment response. Recently, ultrasonography in rheumatology has been refined by the use of power Doppler imaging of increased perfusion in the inflamed synovium of rheumatoid arthritis. (2-4). In addition, low-field MRI has been introduced to clinical practice to facilitate dedicated imaging of peripheral joints suitable even for patients suffering from claustrophobia.

Although ultrasonography and low-field MRI are already in routine use for imaging inflammatory joint diseases, there are only few studies that provide an evaluation of the validity of these imaging methods using the clinical diagnosis as a reference method. Therefore, the aim of this study was to validate grey-scale ultrasonography including PDUS and low-field MRI as diagnostic tests for arthritis with reference to the clinical diagnosis in a phase III study as proposed by Sackett *et al*. (5). It is noteworthy that both imaging methods were performed at a time period in the course of the disease, at which the final rheumatological diagnosis was not yet established.

Materials and methods

Patients

Fifty consecutive patients with suspected arthritis of the wrist or finger joints were included in the study. Inclusion criteria were arthralgia, tenderness, soft-tissue swelling and/or morning stiffness >1 hour in at least one wrist or finger joint, no prior diagnosis of arthritis and no prior treatment with steroids or disease-modifying antirheumatic drugs (DMARDs). Concomitant non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics were allowed. The study was approved by the Ethics Committee of the Justus-Liebig University Giessen, and all patients gave their written informed consent prior to inclusion into the study.

Clinical diagnosis of arthritis was established by the attending physician based on patient history, physical examination, laboratory tests and radiology radiography according to the 1987 American College of Rheumatology (ACR) classification criteria for rheumatoid arthritis.

Imaging Procedures

US examination of the carpus and metacarpophalangeal (MCP) joints of the dominant hand was performed by an experienced investigator (KA), blinded to all clinical findings. The examination followed a standardised protocol according to the "Guidelines for musculoskeletal ultrasound in rheumatology" (6). The linear array ultrasound probe used in this study is a multi-purpose probe with a frequency range of 6–18 MHz for GSUS. For imaging of the finger joints a high frequency of 18 MHz was used. using a linear transducer (6-18 MHz, MyLab 70, Esaote Biomedica, Cologne, Germany). Considering device-specific characteristics for the detection of slow blood flow in small vessels such as the synovial vasculature, the Doppler frequency of 7.7 MHz was chosen due to better tissue penetration. The gain was set to a colour per unit of 65% which was selected by manual elevation of the PDUS gain level until the colour box was almost uniformly filled with the first indication of colour and with only the minimum amount of the next visible signal just beginning to appear (7). Representative PDUS images with the highest amount of Doppler signals were obtained. If any signals were present, an additional movie was obtained by scanning the joint from the lateral to the medial margin to provide real-time data.

Ultrasonographic signs of arthritis comprised distension of the joint capsule by

a weakly or non-echogenic joint effusion, thickening of the synovial layer, bone erosions presenting as discontinuity of the cortical bone and the presence of power Doppler signals. In order to exclude physiological and arteficial signals, only Doppler signals that were confined to the thickened synovial layer were regarded as significant.

Subsequently, low-field MRI performed by another investigator (MB) who was blinded to all clinical and also the ultrasonographic findings. A solenoid volume coil (cylindrical coil geometry) and a multi-channel (dual-phased-array) volume coil were used for MR imaging of the same hand in coronar and axial planes based on standard sequences (C-scan, Esaote Biomedica). Contrast agent (Gadolinium DTPA) was administered to 29 patients. Indicators of arthritis were synovial thickening with enhanced uptake of contrast agent, cortical bone erosions and bone marrow oedema (Fig. 1).

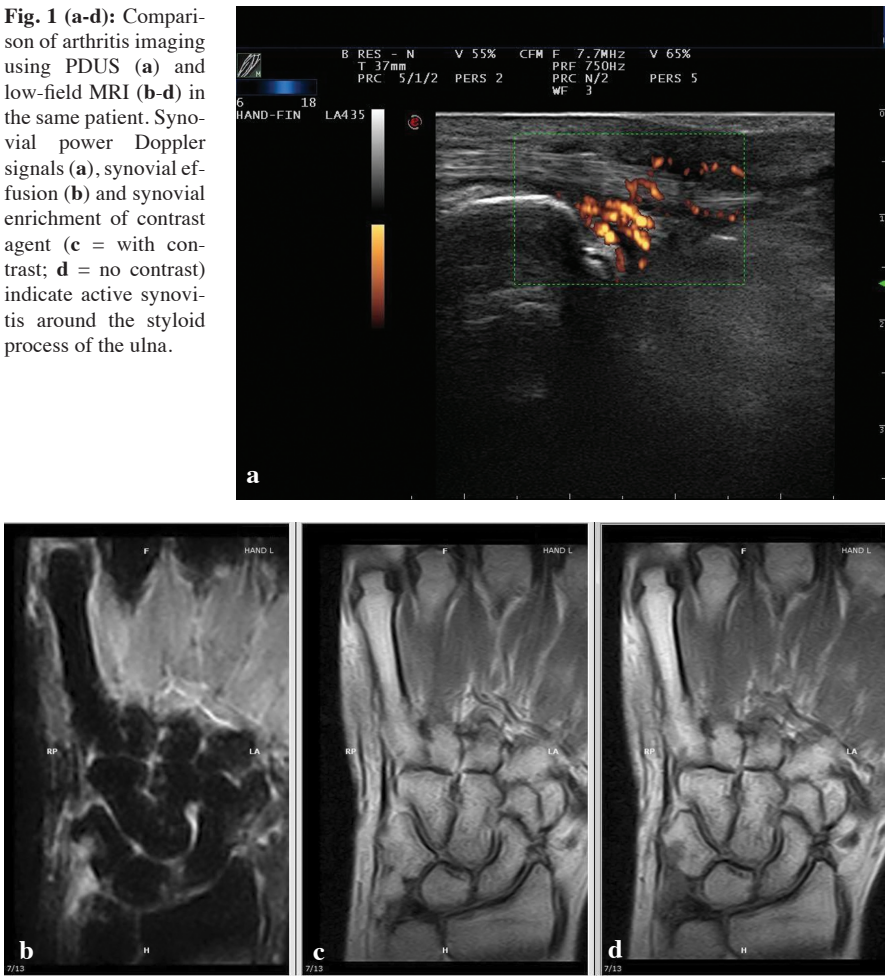

Fig. 1 (a-d): Comparison of arthritis imaging using PDUS (**a**) and low-field MRI (**b**-**d**) in the same patient. Synovial power Doppler signals (**a**), synovial effusion (**b**) and synovial enrichment of contrast agent (**c** = with contrast; **d** = no contrast) indicate active synovitis around the styloid process of the ulna.

Data analysis

All US and MR imaging parameters (synovitis, synovial power Doppler signals, erosions and bone marrow oedema) were recorded in 2x2 contingency tables and compared with the clinical diagnosis. Specificity, sensitivity and positive and negative predictive values were calculated for each parameter in order to determine the value of either imaging modality as a diagnostic test in arthritis. Statistical analysis was performed in collaboration with MoReData GmbH in Giessen. Mann-Whitney U-test and McNemar's test were used to compare patient characteristics. Fisher's exact test was used to test for independence of the variables in the contingency table analysis.

Results

Demographic and clinical data of the patient cohort is presented in Table I. In 32 (64%) of the 50 patients enrolled in the study, the clinical diagnosis of arthritis was established. Of these, 26 patients were found to have rheumatoid arthritis, 4 had a spondylo arthropathy with involvement of the wrist and finger joints, 1 had psoriatic arthritis and 1 had oligoarthritis which could not be classified any further. Among the remaining 18 patients (36%) who did not reveal clinical signs of arthritis, 12 were found to have osteoarthritis of the finger joints, 3 were diagnosed as having fibromyalgia syndrome, and 3 presented other non-inflammatory symptoms.

In 29 of 50 study patients the application of an MRI contrast agent was performed. In a patient with existing contraindication for an MRI scan only the ultrasound examination was performed. The results of the contingency table analysis is shown in Table II. In US including PDUS, sensitivity and specificity were determined as 0.94 and 0.5, respectively, for synovitis (effusion and hypertrophy), 0.72 and 0.94, respectively, for Doppler signals, and 0.38 and 1.0, respectively, for bone erosions. In low-field MRI, sensitivity and specificity values were 0.77 and 0.75, respectively, for synovitis (when using contrast agent), 0.48 and 0.78, respectively, for bone marrow oedema, and 0.58 and 0.83, respectively, for bone erosion.

In the present study, the initial MRI examinations were performed without using a contrast agent (Gd-enhanced MRI). The sub-analysis carried out (n=20, synovitis without contrast agent to n=29, with contrast agent) of the study revealed, however, a non-significant association in the prospective study design.

Discussion

The primary aim of this study was to determine the prospective value of articular ultrasound and low-field MRI for the diagnosis of arthritis according to the OMERACT criteria applied (8-10).

The results of the study confirm that the presence of synovial power Doppler signals inherits a higher specificity for the clinical diagnosis of arthritis than B-mode detection of synovial effusion or

Table I. Patient characteristics.

	Total	Arthritis	No Arthritis
Number of patients	50	32 (64%)	18 (36%)
RA	26 (52%)	26 (100%)	0
PsA/SpA/Oligoarthritis	6 (12%)	6 (100%)	0
Osteoarthritis	12 (24%)	0	12 (100%)
Fibromyalgia syndrome	3 (6%)	0	3 (100%)
Other diagnosis	3 (6%)	0	3 (100%)
Age (years, mean ± SD)	57 ± 11.4	59± 11.2	54.5 ± 9.3
Sex (male/female)	17/33	15/17	2/16
Duration of symptoms (months)	23.0 ± 40.8	19.6± 24,9	28.5 ± 33.8
Duration of morning stiffness (minutes)	22.3 ± 34.8	22.4± 34.6	22.2 ± 36.0
Number of swollen joints	2.2 ± 2.7	2.8± 2.9	1.1 ± 1.9
Number of tender joints	6 ± 4.4	5.3± 4.1	7.2 ± 4.9
Disease severity VAS (0-100)	59.7 ± 16.5	58.9± 17.8	61.3 ± 14.4
Radiographic erosions	5 (10.2 %)	5 (16.1%)	0 (0%)
ESR (mm/h)	24.2 ± 20.0	28.4± 20.9	17.3 ± 16.5
CRP (mg/dl)	1.2 ± 1.7	1.7± 1.9	0.4 ± 0.7
RF positive (>14 U/l)	12 (24%)	10 (31.3%)	2 (11.1%)
ACPA positive (>5 RE/ml)	7 (14%)	7 (21.9%)	0 (0%)

RA: Rheumatoid arthritis; PsA: Psoriatic arthritis; SpA: Spondylo-arthropathy; SD: Standard deviation; VAS: visual analogue scale; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; RF: Rheumatoid factor; ACPA: anti-cyclic citrullinated peptide antibodies.

Table II. Sensitivity and specificity of US and low-field MRI parameters.

Indicator of the imaging	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Synovial power Doppler signals (ultrasonography)	71.9%	94.4%	95.8%	65.4%
Erosions (ultrasonography)	37.5%	100%	100%	47.4%
Synovitis (ultrasonography)	93.8%	50%	76.9%	81.8%
Synovial thickening with enhanced uptake of contrast agent (low-field MRI)	76.2%	75%	88.9%	54.5%
Synovial thickening without use of contrast agent (low-field MRI)	80%	20%	50%	50%
Erosions (low-field MRI)	58.1%	83.3%	85.7%	53.5%
Bone marrow oedema (low-field MRI)	45.8%	77.8%	78.9%	46.7%

thickening alone. The latter also occurs in osteoarthritis, joint trauma and other non-inflammatory conditions. Overall, the sensitivity of PDUS is good, with a high positive and a moderate negative predictive value resulting in good test efficiency. Using high-end ultrasound devices, the acquisition of US images is simple and its evaluation is easy to learn even for inexperienced investigators as indicated by good inter-investigator agreement (11). On the other hand, it has to be taken into account that with growing sensitivity of US Doppler devices, Doppler signals become more susceptible to artefacts. Furthermore, signals deriving from physiological blood vessels may sometimes also occur in non-inflamed joints (12).

The detection of erosions by ultrasonography is also highly specific, but lacks sufficient sensitivity. In contrast to increased synovial perfusions as detected by US, erosions tend to occur later in disease and thus are of limited use for the early diagnosis of arthritis. Thus, the relatively low sensitivity of erosions in our study may be due to the low incidence of erosions in our study population of early arthritis patients.

For the use of low-field MRI as a diagnostic method in rheumatology, it is recommended to perform all examinations with at least 4 sequences: T1-weighted sequences in coronal and axial planes, a fat-suppressed T2-weighted sequence (short tau inversion recovery, STIR) and a T1-weighted three-dimensional gradient echo (3D GE) sequence. Especially the used 3D GE T1-weighted sequence facilitated a better assessment of pathologic contrast enhancement during the course of this study. In addition, the lower thickness and higher number of sections compared with the other sequences provided a more detailed image of the articulating bones. When examining the wrist and finger joints by low-field MRI in this study, the detection of bone marrow oedema proved to more specific for arthritis than the signs of synovitis, particularly when the examination was done without contrast agent.

Analysis of conventional high-field-strength MRI and low-field-MRI showed a high agreement related to inflammatory manifestation at the joints when using standardised scoring systems (13-14).

Of note, the use of contrast agent improved the specificity of synovitis nearly fourfold and the positive predictive value approximately 1.8-fold. In contrast, the sensitivity of bone marrow oedema is low, whereas the sensitivity of synovitis is high, independent of the use of a contrast agent. Thus, the number of false negative results would be rather high when applying bone marrow oedema as the sole parameter for diagnosing arthritis. Synovitis, therefore, is a good screening parameter whereas the detection of bone marrow oedema or contrast enhancement confirms the presence of arthritis. As for erosions, the results are similar to those in US but sensitivity is higher. We consider this finding to be due to the technical advantage of low-field MRI of providing multiplanar views of all bones of the hand not all of which are also accessible to ultrasonography.

Comparing the two imaging modalities, there is a high concordance between US including PDUS and low-field MRI in the detection of inflammatory soft tissue lesions. Not surprisingly, the diagnosis of arthritis is more certain the more criteria are compiled and the more inflammatory changes are detectable. Our study shows that both ultrasound and low-field MRI are suitable imaging methods for diagnosing arthritis at an early stage

thus facilitating the identification of patients who benefit from early use of anti-rheumatic therapy. Especially the positive detection of Doppler signals in PDUS displayed a very high specificity in terms of arthritis.

However, grey-scale ultrasound including PDUS displays a higher specificity and almost the same sensitivity as compared to contrast-enhanced MRI, while being a much simpler, less time-consuming and less costly procedure. In addition, signs of synovitis and positive power Doppler signals in PDUS have a higher negative predictive value than signs of synovitis and bone marrow oedema in low-field MRI indicating that ultrasound is more suitable for the exclusion of arthritis.

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