The role of very early diagnosis and treatment of RA in the reversibility of bone edema, synovitis and bone erosions evaluated by Magnetic Resonance Imaging of the dominant hand

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Purpose

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by symmetrical articular involvement. The diagnosis of rheumatoid arthritis is difficult to establish early in the disease process, since no specific tests are available.

Magnetic resonance (MR) imaging has demonstrated greater sensitivity for the detection of synovitis and erosions than either clinical examination or conventional radiography and can help to establish an early diagnosis of rheumatoid arthritis. MRI allows the detection of bone marrow edema, which is thought to be a precursor for the development of erosions in early rheumatoid arthritis as well as a marker of active inflammation. Early aggressive therapy with disease-modifying antirheumatic drugs (DMARDs) can improve outcome and prevent joint damage.

Erosions are known to occur within 2 years of the onset of rheumatoid arthritis in the absence of effective therapy. To prevent irreversible damage to joints, the diagnosis must be confirmed within a few months of the onset of synovitis (preferably within 3-6 months of the onset of joint symptoms) [1]. A hypothesis in RA research is that early in the disease process, a "window of opportunity" exists, where therapeutic intervention has a disproportionate impact on outcome [2-4].

MRI has been largely used for evaluation of therapeutic response with DMARDs and biologic agents in patients with early RA [5-9].

The purpose of this study was to evaluate the MRI findings of hand involvement before and one year after treatment with DMARDs in patients with very early rheumatoid arthritis (VERA) (disease duration < 3 months), early rheumatoid arthritis (ERA) (disease duration < 12 months) and established rheumatoid arthritis (ESTRA) (disease duration >12 months).
Methods and Materials

Patients. Twenty-two patients (9/13 men/women, 30-83 years (57.09±14.4ys) with RA according to the American College of Rheumatology (ACR) criteria and without prior use of DMARDs were enrolled in the study. Patients were divided in three groups according to the disease duration. Group 1: 9 patients, 6/3 men/women, 30-83 years (61.22±18.41ys) with very early RA (disease duration < 3 months) (VERA), group 2: 7 patients, all women, 41-75 years (52.42±11.14ys) with early RA (disease duration < 12 months) (ERA) and group 3: 6 patients, 3/3 men/women, 41-70 years (56.33±10.83ys) with established RA (disease duration > 12 months) (ESTRA).

Clinical and laboratory evaluation. Each patient underwent complete physical examination. Clinical disease variables included: duration of morning stiffness (min), grip strength (mm Hg), total joint count with tenderness or swelling, number of swollen joints, number of tender joints and pain score [on visual analog scale (VAS)] (cm). Laboratory disease variables included: Ht, Hb, CRP, ESR, C3, C4, ANA, RF and anti-CCP. For assessing disease activity, the Disease Activity Score for 28 joints (DAS-28) was calculated.

Imaging evaluation.

MRI of the dominant was performed in the same MR unit (1.5 Tesla Gyroscan ACS NT, Philips Medical Systems, Best, The Netherlands) using a surface coil with 20 cm field of view. The patient laid prone with the arm to be studied extended overhead toward the midline. The imaging protocol consisted of: coronal and axial STIR images with 2500,60,160 (repetition time, ms/echo time, ms/ inversion time, ms) 3 mm slice thickness, 0.3 mm intersection gap, 256 x 256 imaging matrix, coronal spin-echo T1-weighted images with 500,16 (repetition time, ms/echo time, ms) 3 mm slice thickness, 0.3 mm intersection gap, 256 x 256 imaging matrix; and coronal spin-echo fat-suppressed, T1-weighted images with 500,16 (repetition time, ms/echo time, ms) 3 mm slice thickness, 0.3 mm intersection gap, 256 x 256 imaging matrix before and coronal and axial images immediately after intravenous administration of 0.1 mmol/kg Gd-DTPA. Intravenous contrast injection was performed through a vein in the contralateral arm. Diffusion of contrast material into joint effusions was avoided in coronal scans performed immediately after contrast administration since the duration of post-contrast scans was 2.5 min. Hand involvement was evaluated using the OMERACT RA MRI scoring system to assess bone edema, synovitis and erosions [10, 11]. According to this method definitions, (a) bone edema is a lesion within the trabecular bone, with ill defined margins and signal characteristics consistent with increased water content; (b) bone erosion is a sharply margined bone lesion, with correct juxta-articular localisation and typical signal characteristics, which is visible in two planes with a cortical break seen in at least one plane; (c) synovitis is characterised by synovial thickening associated with...
increased contrast enhancement. Evaluation of all MRI examinations were performed independently by two musculoskeletal radiologists (PK, AZ) blinded to the patients' identity, clinical status and disease duration. STIR images were evaluated for bone edema and plain and-contrast enhanced fat suppressed T1-weighted coronal and axial images were evaluated for erosions and synovitis. Wrist and metacarpophalangeal (MCP) joints were scored separately for bone edema and erosions. The scale was 0-3 for edema and 0-10 for erosions, based on the proportion of pathologic bone compared with the "assessed bone volume" judged on all available images. Because the lowest slice thickness that could be obtained was 3 mm, attention was paid to avoid considering as bone erosions areas of irregular bone contours or ligamentous attachments. Synovitis was also assessed in wrist and MCP joint areas. The scale was 0-3 (0=normal [no synovitis], 1 to 3 [mild, moderate, severe]).

The study was approved by the institutional Review Board and informed consent was obtained from all subjects.

Statistical analysis

Statistical analysis was performed with SPSS base 15 for Windows. The normality of distribution of parameters was assessed using the Kolmogorov-Smirnov test. Unpaired 2-tailed Student t test was used to study differences of MRI findings (bone edema, synovitis and erosions) in the three groups one year after treatment with DMARDs.
Results

Clinical assessment was evaluated using the disease activity score for 28 joint indices (DAS-28). After treatment DAS-28 was significantly decreased in VERA (before treatment 6.2±0.9, after 2.4±1.2), in ERA (before treatment 5.3±0.8, after 2.8±1.0) and in ESTRA patients (before treatment 5.7±8.0, after 2.7±0.7).

Unpaired 2-tailed Student t test before and after treatment showed significant differences in patients with VERA in bone edema (before treatment 16.77±13.78, after treatment 5.88±6.31) (figures 1,2) and synovitis (before treatment 12.44±6.44, after treatment 2.88±3.25) and those with ERA in synovitis (before treatment 7.57±6.32, after treatment 1.42±1.81), p<0.05 (figures 3,4). No significant difference was found in erosions in any group.
Fig. 0: Coronal STIR (TR/2500 ms, TE/60 ms, TI/160 ms) scan at baseline MRI shows bone edema in carpal bones

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Fig. 0: Coronal STIR (TR/2500 ms, TE/60 ms, TI/160 ms) scan on follow up MRI one year after treatment, shows a decrease of bone edema in carpal bones (same patient as in fig 1).

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Fig. 0: Axial contrast enhanced T1 weighted (TR/500 ms, TE/16 ms) fat suppressed scan at baseline MRI shows synovitis in the third and fifth MCP joins

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**Fig. 0:** Axial contrast enhanced T1 weighted (TR/500 ms, TE/16 ms) fat suppressed scan, on follow up MRI one year after treatment, shows reversibility of synovitis in the third and fifth MCP joins (same patient as in fig 3).

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Conclusion

MRI showed that the therapeutic response of DMARDs is greater during the first months of the disease, in which bone edema and synovitis can be reversible.
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