EXTENDED REPORT

Low-cost, low-field dedicated extremity magnetic resonance imaging in early rheumatoid arthritis: a 1-year follow-up study

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Objective: To study the ability of low-cost low-field dedicated extremity magnetic resonance imaging (E-MRI) to assess and predict erosive joint damage in the wrist and metacarpophalangeal (MCP) joints of patients with early rheumatoid arthritis.

Methods: 24 previously untreated patients with rheumatoid arthritis with joint symptoms for <1 year were evaluated at the time of diagnosis and after 6 and 12 months of methotrexate treatment with conventional clinical or biochemical examinations, x rays of both hands and wrists, and E-MRI of the dominant wrist and MCP joints.

Results: At baseline, all patients showed magnetic resonance imaging (MRI) synovitis, and MRI erosions were detected in 21 bones (10 patients). 6 (29%) of these, distributed among two patients, were seen on x ray. One x ray erosion was not detected by MRI. At 1 year, MRI and x ray detected 15 and 8 new erosions, respectively, and 19% of MRI erosions at baseline had progressed to x ray erosions. In bones with MRI erosions at baseline, the relative risk of having x ray erosions at the 1-year follow-up was 12.1, compared with bones without baseline MRI erosions (lesion-centred analysis). If bones with baseline x ray erosions were excluded, the relative risk was 5.2. In patients with baseline MRI bone erosion or oedema, the relative risk of having x ray erosions at 1 year was 4.0, compared with patients without these signs at baseline (patient-centred analysis).

Conclusion: In this group of patients with early rheumatoid arthritis who were treated uniformly, baseline E-MRI erosions in MCP or wrist bones markedly increased the risk of x ray erosions at the 1-year follow-up. Low-cost, low-field dedicated extremity MRI is promising for assessment and prognostication of early rheumatoid arthritis.

Efficient methods for diagnosis, monitoring and prognostication are essential in early rheumatoid arthritis.^{1–2} Although conventional x rays only visualise the late signs of preceding disease activity, several studies have verified that magnetic resonance imaging (MRI) is highly sensitive for detecting early inflammatory and destructive changes in joints with rheumatoid arthritis, and a predictive value of early MRI findings for future progressive x ray damage has been reported.^{3–4}

However, except for a few cross-sectional studies, all MRI studies on rheumatoid arthritic joints have been carried out using expensive, high-field, whole-body MRI units. The emergence of low-cost, low-field dedicated extremity MRI units, specifically designed for examination of peripheral joints, have decreased costs and patient discomfort and have increased the feasibility of carrying out MRI in the routine management of rheumatoid arthritis. However, even though a few cross-sectional studies have indicated that low-field dedicated MRI is more sensitive for synovitis and bone erosions than conventional methods,^{5–9} current knowledge on the clinical value of extremity MRI (E-MRI) is limited. In particular, no longitudinal E-MRI studies on patients with early rheumatoid arthritis have been carried out. Consequently, the ability of E-MRI to disclose temporal changes in synovitis and erosions in clinically relevant situations and, importantly, the predictive value of early E-MRI findings, are unknown.

The aim of our 1-year follow-up study of a cohort of patients with early rheumatoid arthritis was to investigate the ability of a low-field dedicated E-MRI system, specifically designed for the examination of peripheral joints, to detect

changes in joint inflammation and destruction in wrist and finger joints and to investigate the predictive value of early E-MRI findings for subsequent development of radiographic and MRI bone erosions.

PATIENTS AND METHODS

Patients and clinical assessments

Twenty five consecutive patients with rheumatoid arthritis of <12 months duration were recruited to this 1-year follow-up study from the Early Synovitis Clinic in South Jutland, Denmark. Further details on recruitment and baseline demographics have previously been reported.⁵ All patients fulfilled the American College of Rheumatology 1987 revised criteria.¹⁰ The median symptom duration at inclusion was 122 days (range 55–360), whereas the median age was 55 years (range 20–69). The female:male ratio was 18:7. Twenty four patients were seropositive for the immunoglobulin M rheumatoid factor. No patients had received corticosteroids or disease-modifying antirheumatic drugs (DMARDs) before inclusion. Twenty four patients completed the follow-up study, whereas one patient withdrew for personal reasons after 18 weeks. At baseline, patients were started on methotrexate 7.5 mg/week. The dose was increased by 2.5 mg/week every 6 weeks to a maximum of

Abbreviations: CRP, C reactive protein; DMARD, disease-modifying antirheumatic drug; E-MRI, extremity magnetic resonance imaging; ESR, erythrocyte sedimentation rate; FOV, field of view; IQR, interquartile range; MCP, metacarpophalangeal; MRI, magnetic resonance imaging; OMERACT, Outcome Measures in Rheumatology; STIR, short T1-inversion recovery

20 mg weekly or a dose-limiting adverse event. Patients with a high disease activity, who were considered unable to await the onset of methotrexate, were offered prednisolone 7.5 mg orally per day, which was tapered down as quickly as allowed by the disease activity. Parenteral and local corticosteroids and DMARDs other than methotrexate were not allowed. All patients were assessed clinically every 6 weeks—that is, nine times within 1 year—while conventional radiography of both hands and wrists and MRI of the dominant wrist and metacarpophalangeal (MCP) joints were carried out at baseline, 6 and 12 months. The clinical examination included assessments of joint swelling and joint tenderness as suggested by the European League Against Rheumatism.¹¹ All clinical examinations were carried out by the same rheumatologist (HML). Serum levels of C reactive protein (CRP), erythrocyte sedimentation rate (ESR) and immunoglobulin M rheumatoid factor were measured according to standard methods. The study was conducted in accordance with the Declaration of Helsinki, and signed informed consent was obtained from each patient.

Extremity MRI

Image acquisition

MRI of the dominant wrist and 2nd–5th MCP joints was carried out at baseline, 6 and 12 months, using a 0.2-T Artoscan system (ESAOTE Biomedica, Genova, Italy), a dedicated extremity MRI unit. Patients were comfortably seated in an adjustable scanning chair, with the dominant hand positioned in a wrist coil in the magnet and kept in neutral position with the thumb up and the fingers extended. The imaging protocol comprised a coronal short T1 inversion–recovery (STIR) sequence, followed by coronal and axial T1-weighted spin-echo images obtained before and after intravenous injection of gadodiamide (Omniscan, Chester, UK), 0.1 mmol/kg body weight, via a peripheral vein. The post-contrast coronal and axial images were started 3 min after the injection of gadodiamide. The imaging parameters for the STIR sequence were as follows: repetition time 500 ms, echo time 18 ms, matrix size 256×160, field of view (FOV) 200 mm, slice thickness 3 mm. For the T1-weighted spin-echo sequences, the imaging parameters were as follows: repetition time 500 ms, echo time 18 ms, matrix size 256×192, FOV 200 mm, slice thickness 3 mm. Owing to the small magnet size, the true FOV of the coronal images was 120 mm. Owing to the restricted FOV, the radius, the ulna and the distal radioulnar joint were not consistently visualised and were, consequently, not evaluated. The approximate imaging time in each patient was 45 min.

Image evaluation

All the MRIs were scored for synovitis, bone oedema and bone erosions, as defined in the Outcome Measures in Rheumatology (OMERACT) MRI rheumatoid arthritis recommendations (see Conaghan *et al*¹² for details), by one rheumatologist (MØ), with documented experience and high inter-reader agreement with readers from other countries.¹³ The assessor was blinded to clinical and radiographic findings.

The numbers of erosions were also counted (MRI erosion count). The maximum was one erosion per MCP joint quadrant or per wrist joint bone.

Tenosynovitis was defined as the presence of post-contrast enhancement in at least one tendon sheath on at least two consecutive axial T1-weighted images. Tenosynovitis was scored per patient, as absent or present.

x Rays

Conventional x rays of both wrists and hands in anteroposterior and Nørgaard projections were obtained at inclusion and after 6 and 12 months. A single-coated mammography film (MRF 31 Du-Med, Herning, Denmark) was used. The x rays were assessed by an experienced musculoskeletal radiologist (JV) who was blinded to the MRI and clinical findings. Fourteen joints were scored: 2 wrists, 10 MCP and 2 thumb interphalangeal joints. The radiographs were scored according to the Larsen method, in which each joint was assigned a score between 0 (normal) and 5 (mutilating changes) based on comparison with standard reference films.^{14, 15} A Larsen score was calculated by summation of scores in the individual joints (the wrist joint scores were multiplied by 5).

In addition, an x ray bone erosion count was calculated, as described for MRI.

Statistical analysis

Non-parametric statistical methods were applied and descriptive statistics (numbers, medians, ranges and interquartile ranges (IQRs)) were calculated. In analyses including more than two groups, the Kruskal–Wallis equality of populations rank test was used. In case of significance of the Kruskal–Wallis test, the Mann–Whitney U test was used for pairwise group comparisons. The Wilcoxon matched pairs rank signed test was used to compare baseline values with data at 1 year. Correlations were calculated by means of the Spearman's rank correlation test. p values <0.05 were considered significant. The statistical analyses were carried out with STATA.

Results

Clinical measures of disease activity at baseline and at follow-up

Table 1 presents baseline and follow-up characteristics of the 24 patients. The study population exhibited significant decreases in all measures of disease activity after 1 year ($p<0.001$ – 0.02), whereas the physical capability, expressed by the Health Assessment Questionnaire score, increased through the observation period ($p<0.001$). All patients remained on methotrexate, although the proportion of patients on oral prednisolone was low during the entire period (8% (two patients) starting at baseline, 12.5% at 1 year).

Bone erosions on x ray and MRI at baseline and at follow-up

At baseline, the total number of bone erosions detected by x ray of both hands and wrists was 15, distributed among 6 patients. Most erosions were detected in the right hand (67%). Two patients had erosions in wrist joints only, two in finger joints only, and two in both wrist and finger joints. The median Larsen score was 0 (range 0–26), as 75% had the score 0 (mean 12). At the 1-year follow-up, 17 erosions, distributed among 7 patients, were detected. Six erosions were no longer visible and eight new erosions had emerged. Four patients had new radiographic joint involvement and one had progressive erosive changes. Thus, x ray progression occurred in a total of five patients (table 1).

At baseline, 21 erosions were detected by MRI of the dominant wrist and 2nd–5th MCP joints, distributed among 10 patients. Six (29%) of the MRI erosions, distributed among two patients, were seen on x ray. One x ray erosion was not shown by MRI. Thus, the ratio of MRI erosions:radiographic erosions was 21:7, that is 3:1.

At 1 year, 15 new MRI erosions (8 patients) were seen, while 1 of the 21 baseline MRI erosions (5%) was no longer

Table 1 Clinical, biochemical and imaging data at baseline, 6 and 12 months

	Baseline (n = 25)	6 months (n = 24)	12 months (n = 24)	p Value (baseline v 1 year)
Clinical and biochemical parameters				
Swollen joint count (0–28)	8 (4–11)	1 (0–4)	1 (0–5)	<0.001
Tender joint count (0–28)	7 (4–10)	1 (0–5)	1 (0–5)	0.013
Pain score (0–100 mm)	60 (21–79)	21 (4–30)	25 (4–43)	0.001
Patient's global assessment (0–100 mm)	67 (38–82)	19 (3–39)	21 (3–50)	<0.001
Doctor's global assessment (0–100 mm)	37 (22–55)	17 (10–22)	11 (6–19)	<0.001
HAQ (0–3)	0.55 (0.35–1.35)	0.23 (0.08–0.61)	0.25 (0–0.67)	<0.001
ESR (mm/h)	30 (18–55)	17 (10–30)	16 (11–25)	0.002
CRP (mg/l)	21 (8–65)	10 (5–18)	6 (4–10)	0.002
Drug				
No of patients receiving methotrexate	25 (100%)	24 (100%)	24 (100%)	
No of patients receiving oral glucocorticosteroids	2 (8%)	3 (12.5%)	3 (12.5%)	
x Ray findings (both hands and wrists)				
No of patients with bone erosions	6	6	7	NS
Larsen score (per patient)	0(0–4.25)	0(0–3)	0(0–2.25)	NS
Number of bones with erosions, all patients	15	13	17	NS
MRI findings (dominant wrist and 2nd–5th MCP joints)				
No of patients with synovitis	24	20	16	
No of patients with bone oedema	7	6	4	
No of patients with bone erosions	11	11	12	
No of patients with tenosynovitis	15	7	6	
Synovitis score, per patient	8 (4–11)	6 (2.5–10)	4 (0–7)	<0.001
Bone oedema score, per patient	0 (0–1.5)	0 (0–0.25)	0 (0–0)	NS
Erosion score, per patient	0 (0–2)	0 (0–2)	0.5 (0–2.25)	NS
Number of erosions, all patients	21	25	35	NS

CRP serum, C reactive protein; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; NS, not significant.

Values are medians (interquartile ranges), when not otherwise stated.

p values indicate significant differences between baseline and 1 year (Wilcoxon signed ranks test).

visible. Four MRI erosions had enlarged. By contrast, x rays of both hands and wrists detected eight new erosions only.

Four (19%) of the MRI erosions progressed to an x ray erosion during the 1-year follow-up period.

MRI synovitis, bone oedema and tenosynovitis at baseline and follow-up

At baseline, the median synovitis score was 8 (IQR 4–11). At 1 year, the median synovitis score was reduced to 4 (IQR 0–7, $p < 0.001$). This coincided with a reduction in tender and swollen joint counts and considerable decreases in laboratory markers of inflammation (CRP and ESR; table 1). At baseline, the median bone oedema score was 0 (IQR 0–1.5). At 1 year, the median oedema score remained 0 (IQR 0–0, NS). Tenosynovitis was less frequent at 6 months (7 patients) and 12 months (6 patients) compared with baseline (15 patients).

Relationship between MRI synovitis scores and clinical or biochemical assessments

Significant positive correlations were found between total MRI synovitis scores and pain score, patients' global assessment and the Health Assessment Questionnaire score at baseline ($\rho = 0.44$ – 0.47 , $p < 0.05$), but with no other clinical or biochemical disease activity measures. At baseline, CRP in patients with a total MRI synovitis score ≥ 8 (the median) was significantly higher than that in patients with a score < 8 (57 mg/l (IQR 21–89) v 13 mg/l (IQR 6–38); $p < 0.05$).

Relationship between baseline MRI synovitis and follow-up MRI bone erosions

In joints with MRI synovitis at baseline (grades 1–3), the relative risk of having MRI erosions at the 1-year follow-up was 7.3, compared with joints without MRI synovitis (grade 0). When patients with baseline moderate or severe synovitis (grades 2–3) were compared with no or mild MRI baseline synovitis (grades 0–1), the corresponding relative risk for bone erosions by year 1 was 10.7. The number of new MRI

bone erosions during the 1-year study was significantly correlated with the baseline synovitis score ($r = 0.61$, $p < 0.001$).

Baseline MRI bone changes as predictors of x ray erosions

In bones with MRI erosions at baseline, the relative risk of having radiographic bone erosions by the 1-year follow-up was 12.1, compared with bones without baseline MRI erosions. If bones with baseline radiographic erosions were excluded from the analysis, the relative risk was 5.2.

In a patient-centred analysis, 12 patients showed MRI erosions or bone oedema at baseline. Of these, 4 (33%) had x ray erosions at 1 year. Of the 12 patients with no bone erosion or oedema at baseline MRI, 1 (8%) had x ray erosions at 1 year, resulting in a relative risk of 4.0 for having x ray erosions after 1 year, if baseline bone erosion or oedema are present. Separate patient-centred analyses of MRI bone oedema and bone erosion gave lower relative risk values. Thus, baseline MRI bone changes both in lesion-centred and patient-centred analyses markedly increased the risk of radiographic erosive damage 1 year later. Correspondingly, only 1 of 14 (7%) patients without baseline MRI erosions had x ray erosions after 1 year.

The baseline OMERACT MRI erosion score was strongly correlated with the 1-year follow-up x ray erosion count in the same joints ($\rho = 0.69$, $p < 0.001$) and the x ray Larsen score of both wrists and hands ($\rho = 0.64$, $p < 0.001$).

DISCUSSION

In the present 1-year follow-up study of a cohort of patients with early rheumatoid arthritis, bone changes visualised by a low-cost, low-field, dedicated E-MRI unit markedly increased the risk of x ray joint damage 1 year later. The relative risk of radiographic erosion at follow-up was > 5 in bones with baseline E-MRI bone erosion (lesion-centred analysis) and 4 in patients with baseline E-MRI bone erosion or oedema (patient-centred analysis).

A few previous cohorts of patients with early rheumatoid arthritis have been followed up using repeated MRI and *x* ray to assess the predictive value of MRI with respect to subsequent radiographic joint destruction. All these studies were carried out using expensive high-field, whole-body MRI units. MRI bone erosion and bone oedema in patients with early rheumatoid arthritis have previously been shown to predict future radiographic lesions in cohorts followed for up to 6 years.^{3 4 16} A cohort of 40 patients with early rheumatoid arthritis, followed up by Conaghan *et al*,¹⁷ showed a marked relationship between baseline MRI synovitis and subsequent development of bone erosions as assessed by MRI, but the relationship with *x* ray findings was not explored.

Low-field dedicated E-MRI units have previously, in cross-sectional studies, been shown to allow detection of inflammatory and destructive joint damage in rheumatoid arthritis.^{5-7 9 18} However, the ability of E-MRI units to monitor inflammatory and destructive changes, and the importance of the E-MRI findings for the subsequent development of structural joint damage, have not been reported.

E-MRI is favoured by low costs and also because patient positioning is more comfortable and claustrophobia is avoided. The disadvantages of E-MRI include a smaller field of view—meaning that fewer joints can be examined at the same time—and a longer imaging time. The E-MRI technique is limited by a lower spatial resolution and a reduced number of possible imaging techniques. In particular, spectral fat saturation sequences—for example, the T2-weighted fat-saturated sequence, which is used to visualise bone oedema—cannot be acquired. However, the STIR technique, which is possible with E-MRI, can also be used to visualise bone oedema. Recent data show that using the present magnet type, the STIR sequence has a sensitivity of about 40% and a specificity of 99%, if bone oedema on a high-field, T2-weighted, fat-saturation sequence is considered the gold standard reference.¹⁸ The lower sensitivity of the E-MRI STIR sequence compared with the T2-weighted, fat-saturated sequences available on high-field units may explain why bone oedema in our study was less frequently observed and was not as closely related to subsequent development of bone erosions as seen in previous high-field studies.^{3 4 19} In this study, as in most previous studies, including the OMERACT validation studies, a slice thickness of 3 mm was used in the evaluation of bone erosions. Thinner slices—for example, of 1 mm—may improve sensitivity in the detection and progression of erosions. However, this has not been studied formally. MRI signs of inflammation, both in the joint (synovitis) and tendon sheaths (tenosynovitis), were markedly reduced during our study, and coincided with reduction in clinical and biochemical markers of disease activity. This is in accordance with a previous study on DMARD treatment in established rheumatoid arthritis,²⁰ and shows the construct validity of the MRI measures used. MRI scores of synovitis were strongly correlated with the subsequent development of MRI erosions, supporting the close relationship between the extent of MRI synovitis and the risk of developing structural joint damage observed in studies using high-field MRI.^{17 20}

Implementing the modern treatment strategy in early rheumatoid arthritis—that is, early initiation and optimal adjustment of effective treatments—requires early diagnosis and sensitive monitoring of the disease process. Furthermore, concerns about economy, adverse effects and potential interindividual treatment-response differences prompt for focus on reliable prognostic markers to allow stratification of patients to individually tailored treatments, with particular reference to biological agents. In rheumatoid arthritis, early bone erosions seen on conventional *x* ray are correlated with poor long-term radiographic and functional outcome,²¹ and in early undifferentiated arthritis, the presence of *x* ray

erosions increases the risk of developing persistent arthritis.²² However, radiographic erosions are present only in a minority of patients with early rheumatoid arthritis, with prevalences of 8–40% at 6 months,²³⁻²⁷ and *x* ray is not effective in identifying future “non-progressors”—that is, patients without increasing joint damage, who may therefore not require maximally aggressive treatment.²⁸ In our study, a bone erosion visualised by dedicated E-MRI in a radiographically non-eroded bone increased the risk of developing a radiographic erosion at this location within the next year more than fivefold. Furthermore, only 15% of patients without baseline MRI erosions had *x* ray erosions after 1 year. This supports a potential of E-MRI in the differentiation between future progressors and non-progressors in early rheumatoid arthritis.

In conclusion, our study shows that E-MRI at the time of diagnosis of rheumatoid arthritis provides information about the risk of developing irreversible joint damage within the subsequent year. Thus, E-MRI holds promise as a feasible new tool in the initial diagnostic investigation in patients with early and suspected rheumatoid arthritis.

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Ethical approval: This study was conducted in accordance with the Declaration of Helsinki, and approval was obtained from the local ethics committee before starting the study (J No 19980024).

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