Gadolinium contrast-enhanced MRI sequence does not have an incremental value in the assessment of sacroiliitis in patients with early inflammatory back pain by using MRI in combination with pelvic radiographs: a 2-year follow-up study

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Abstract

Objective

To evaluate the potential incremental value in detecting sacroiliitis of the T1 post-gadolinium diethylenetriaminepenta-acetic acid (Gd-DTPA) MRI sequence of the sacroiliac joints (SIJ) compared with the combination of short tau inversion recovery (STIR) MRI sequence and pelvic radiographs in patients with inflammatory back pain (IBP) suspected for axial spondyloarthritis.

Methods

A 2-year follow-up study was conducted in patients with IBP of less than 2 years duration. Annual MRI of the SIJ (MRI-SIJ) was performed and scored for bone marrow oedema (BME). Pelvic radiographs were scored according to the modified New York (mNY) criteria. Agreement on the presence of BME detected by the STIR and post-Gd-DTPA sequence and the incremental value of post-Gd-DTPA sequence over STIR plus radiographs was analysed by descriptive methods and kappa statistics.

Results

At baseline, 20 (29%) out of 68 patients (38% male; mean (SD) age 34.9 (10.3) years) enrolled had BME both on the STIR and post-Gd-DTPA sequences; 4 patients (6%) on the STIR sequence only; none on the post-Gd-DTPA sequence only (kappa value: 0.87). Fifteen (22%) patients fulfilled the mNY criteria at baseline.

Sixty-two (91%) patients had at least 1 follow-up MRI-SIJ. At 2-year follow-up, 2 patients had BME on the post-Gd-DTPA sequence without BME on the STIR sequence. These 2 patients already fulfilled the mNY criteria at baseline.

Conclusion

In this cohort of patients with early IBP, the post-Gd-DTPA sequence of the MRI-SIJ did not have an incremental value in the detection of sacroiliitis compared with the STIR sequence plus pelvic radiographs.

Key words

MRI, sacroiliitis, ankylosing spondylitis, axial spondyloarthritis.

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Introduction

Pelvic radiographs and magnetic resonance imaging (MRI) are important imaging techniques to detect sacroiliitis in patients with a suspicion of axial spondyloarthritis (axSpA). In the Assessment in SpondyloArthritis international Society (ASAS) axSpA classification criteria, sacroiliitis on either MRI or pelvic radiograph is used as the entry criterion for fulfillment of the 'imaging arm' (1). With MRI, both active lesions and structural changes can be detected, in contrast to pelvic radiographs that only visualise structural changes. Typical 'active lesions' in the sacroiliac joints (SIJ) detected by MRI are subchondral bone marrow oedema (BME), as well as synovitis, enthesitis and capsulitis (2). Different MRI techniques can be used to detect active lesions; these are short tau inversion recovery (STIR) that suppresses the signal intensity of fat, and T1 with or without fat suppression after administration of the contrast agent gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA). Only BME on the STIR or post-Gd-DTPA sequence is considered for the definition of active sacroiliitis according to the ASAS/Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) consensus (2). The ASAS/OMERACT MRI working group further states that the STIR sequence alone is usually sufficient to detect sacroiliitis. This statement is supported by several studies that found no additional value of the post-Gd-DTPA sequence compared with the STIR sequence in detecting sacroiliitis in patients with early or established axSpA (3, 4). However, these studies were cross-sectional (3) or had a 3-month follow-up period only (4). Furthermore, these studies did not include pelvic radiographs. Besides that in the ASAS classification criteria both pelvic radiographs and MRI-SIJ are considered for fulfilment of the imaging arm, also in daily practice, usually the first step for making a diagnosis is to perform a pelvic radiograph. When negative of equivocal, the next step is to make an MRI-SIJ. Although on the short term, the post-Gd-DTPA MRI sequence does not seem to be of additional value, it is unknown what its value is over a longer follow-up period, especially in patients with early disease, and taking the pelvic radiograph into account. Fluctuating or subsiding BME on either the STIR or post-Gd-DTPA sequence may affect the sensitivity and specificity of MRI in detecting sacroiliitis and hamper the diagnostic process (5). Combining the information on pelvic radiographs with the information on MRI-SIJ may yield an higher probability of detecting sacroiliitis (6).

The aim of this study was to evaluate the potential incremental value of the post-Gd-DTPA sequence for detecting sacroiliitis compared with the combination of STIR MRI sequence and pelvic radiographs in patients presenting with IBP of short duration suspected for axSpA. These patients were followed for 2 years with repeated radiological examinations.

Materials and methods

Study population

Patients with IBP of less than 2 years duration were enrolled in the Early SpondyloArthritis Clinic (ESpAC) study. In this prospective cohort study, systematic clinical and radiological examinations were performed at baseline and after 1 and 2 years. A more detailed description of the study population has been reported previously (7). For IBP to be present, patients had to fulfil 4 of the following 5 Calin criteria: onset of symptoms before the age of 40 years, duration of back pain more than 3 months, insidious onset, morning stiffness and improvement with exercise (8). Patients who fulfilled only 3 out of 5 of the Calin criteria but reported night pain, were also eligible. Presence of extra-axial manifestations of SpA was preferred but not obligatory. Patients were not treated with biological therapy during the entire study period. The use of non-steroidal anti-inflammatory drugs (NSAIDs) was allowed. The study has been approved by the ethics committee of the Maastricht University Medical Center. All patients have given written informed consent.

MRI protocol

MRI of the SI joints was obtained with a 1.5 Tesla Philips Gyro Scan ACS-NT

(Philips, The Netherlands). Patients were examined while lying in a supine position. By using an oblique coronal slice orientation, the following sequences were obtained:

- T1-weighted spin echo (SE), 256 x 256 matrix
- STIR, 256 x 256 matrix
- T1-weighted SE with fat suppression after administration of the intravenous contrast agent Gd-DTPA (0.1 mmol/kg body weight), 512 x 256 matrix

The slice thickness was 4 mm with 0.4 mm intervals. Each MRI set was scored with unknown time sequence by one experienced radiologist (AGJ), without knowledge of clinical or laboratory findings.

MRI and pelvic radiograph scoring

The MR images were scored using a combination of the Spondyloarthritis Research Consortium of Canada (SPARCC) method and a modified version of the Aarhus MRI scoring method (9, 10). In contrast to the original SPARCC system, there was no maximum to the number of evaluated slices, in order to maximise the detection of abnormal MRI findings. The number of evaluated slices within a individual patient was kept the same for all time points. Each SIJ was divided into 4 quadrants: upper iliac, lower iliac, upper sacral and lower sacral. All images (STIR and post-Gd-DTPA) were scored for the presence of subchondral BME with the corresponding T1 sequence without contrast simultaneously. BME present in the cartilaginous part of the joint was scored per slice in a dichotomous manner (present *vs*. absent). BME was defined as areas of increased signal intensity on both the STIR and post-Gd-DTPA images compared with normal bone marrow, and its presence was estimated in each of the 4 quadrants. Since synovitis, capsulitis and enthesitis are not considered sufficient for the definition of a positive MRI according to the ASAS/OMERACT definition, only the MRI scores of BME were taken into account (2).

An MRI was considered positive when at least one BME lesion was present in at least two consecutive slices, or when two or more BME lesions were detected in 1 slice, following the ASAS/OMERACT working group definition for BME lesions on MRI-SIJ (2).

Anteroposterior pelvic radiographs of the SIJ were obtained from all patients at baseline and during one- and 2-year follow up. Two readers (AT and RL), who were blinded to the clinical and laboratory findings and were not involved in the MRI reading, independently scored all radiographs with unknown time sequence according to the modified New York (mNY) criteria (11). In case of disagreement, a judgment of a third reader (DH) was conclusive.

Statistical analysis

Descriptive statistics were used to analyse the presence of BME on MRI-SIJ and structural changes on pelvic radiographs at baseline and during the 2-year follow-up period. Agreement on the presence of BME suggestive for sacroiliitis detected by STIR and post-Gd-DTPA sequences was analysed on a per patient basis by kappa statistics. A kappa value of 0–0.20 indicated poor agreement, 0.21–0.40 indicated fair agreement, 0.40–0.60 indicated moderate agreement, 0.60–0.80 indicated substantial agreement and 0.80–1.0 indicated (almost) perfect agreement (12). Descriptive statistics were used to compare the presence of sacroiliitis detected on either pelvic radiographs or STIR MRI with findings on the post-Gd-DTPA MRI sequences. SPSS software version 18.0 was used for all statistical analyses.

Table I. Baseline characteristics of 68 patients included in the ESpAC.

Characteristic	All patients (n=68)	Patients with complete MRI follow-up data (n=44)
Male sex	26 (38)	15 (34)
Mean age (SD) [years]	34.9 (10.3)	36.0 (11.7)
Median symptom duration (IQR) [months]	18 (12-24)	18 (12-24)
HLA-B27 positive	31 (46)	17 (39)
History of inflammatory bowel disease	10 (15)	7 (16)
History of anterior uveitis	10 (15)	8 (18)
History of psoriasis	16 (24)	12 (27)
History of peripheral arthritis	19 (28)	12 (27)
Family history of SpA	37 (54)	26 (59)
Mean CRP (SD) [mg/l]	9 (11)	9 (12)
Elevated CRP[a]	16 (24)	10 (22)
Mean ESR (SD) [mm]	13 (15)	13 (16)
Elevated ESR[a]	24 (36)	13 (30)
Presence of BME on MRI	24 (35)	14 (32)
Fulfillment ESSG criteria	58 (85)	39 (89)
Fulfillment Amor criteria	48 (71)	31 (70)
Fulfillment ASAS axSpA criteria	40 (59)	22 (50)
Fulfillment mNY criteria	15 (22)	9 (20)

The values are expressed as number (percentage) of patients unless stated otherwise.
ESpAC: Early Spondyloarthritis Clinic; SpA: spondyloarthritis; IQR: interquartile range; SD: standard deviation; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BME: bone marrow oedema; MRI: magnetic resonance imaging; ESSG: European Spondyloarthropathy Study Group; ASAS: Assessment in SpondyloArthritis international Society; axSpA: axial spondyloarthritis; mNY criteria: modified New York criteria
[a] In 66 of 68 patients baseline CRP and ESR measurements were available. ESR normal range: ≤7 mm for males; ≤12 mm for females. CRP cut-off value, normal range: <10 mg/l

Results

Patient characteristics

Baseline MRI-SIJ and pelvic radiographs were available in all 68 patients included in the ESpAC. Baseline characteristics are shown in Table I.

Sixty-two (91%) patients had at least 1 follow-up MRI and 44 (65%) patients completed both follow-up MRIs. Sixty-five (96%) patients had at least 1 follow-up pelvic radiograph and 48 (71%) patients completed both follow-up pelvic radiographs.

At baseline, 64 (94%) out of 68 pa-

Table II. Detection of BME on the STIR and post-Gd-DTPA sequences per patient at baseline and follow-up.

		Follow-up*			
		BME on both STIR and post-Gd-DTPA	BME on STIR only	BME on post-Gd-GTPA only	No BME
Baseline	BME on both STIR and post- Gd-DTPA (n=19)	13	1	2	3
	BME on STIR only (n=4)	1	1	0	2
	No BME (n=39)	3	2	0	34

Bone marrow oedema (BME) on the Short τ Inversion Recovery (STIR) and post-gadolinium diethylenetriaminepentaacetic acid (post-Gd-DTPA) sequence in 62 patients with at least 1 follow-up MRI
*Follow-up MRI at 1 or 2 years, depending on last available MRI.

tients fulfilled the European Spondyloarthropathy Study Group (ESSG) and/or Amor and/or ASAS axSpA classification criteria. Fifteen (22%) patients fulfilled the mNY criteria at baseline and in 24 (35%) patients BME was detected on MRI-SIJ. Eight (53%) of 15 patients who fulfilled the mNY criteria at baseline had signs of BME on both the STIR and post-Gd-DTPA sequence at baseline.

Agreement between the STIR- and post-Gd-DTPA MRI sequences

At baseline, a good agreement between the STIR and post-Gd-DTPA sequence on a per patient basis was found (kappa=0.87). Twenty (29%) patients showed BME on MRI-SIJ suggestive for sacroiliitis on both STIR and post-Gd-DTPA sequences. In 4 (6%) patients, BME was detected on the STIR sequence only, but this was minimal in 3 of these 4 patients. None of the patients had signs of BME on the post-Gd-DTPA sequence only.

Twenty-three (96%) of 24 patients with BME on MRI at baseline had at least one follow-up MRI. A moderate to good agreement between the STIR and post-Gd-DTPA sequence on a per patient basis was also found at 1-year (kappa=0.83) and 2-year (kappa=0.75) follow-up.

Detection of BME on the STIR and post-Gd-DTPA sequence at follow-up

Table II shows that in 5 (26%) of 19 patients with BME on both STIR and post-Gd-DTPA sequences at baseline, BME could no longer be detected on STIR sequence at 2-years follow-up. In 2 of these 5 patients, however, BME was still visible on the post-Gd-DTPA sequence. In the remaining 3 patients BME has disappeared on both the STIR and post-Gd-DTPA sequence at 2-years follow-up. These 3 patients were all HLA-B27-negative. In 2 of 4 patients with BME on the STIR sequence only at baseline, BME was no longer present at 2-years follow-up. Both patients were HLA-B27-negative.

Five (13%) of 39 patients without signs of BME on both the STIR and post-Gd-DTPA sequences at baseline, developed BME at follow-up. None of these 5 patients developed BME on the post-Gd-DTPA sequence only.

Incremental value of the post-Gd-DTPA sequence compared with the combination of STIR sequence and pelvic radiograph

At baseline, 31 (46%) patients had BME on MRI-SIJ and/or fulfilled the mNY criteria for radiographic sacroiliitis. None of these 31 patients had signs of BME on the post-Gd-DTPA sequence only at baseline. Thirty (97%) of 31 patients had both at least one follow-up MRI-SIJ and at least one follow up pelvic radiograph. At follow-up, no new patients fulfilled the mNY criteria for radiographic sacroiliitis. BME on the post-Gd-DTPA sequence only was found in 2 (7%) of these 30 patients at follow up. However, both patients already fulfilled the mNY criteria.

Discussion

The present study showed that the post-Gd-DTPA MRI sequence does not have an incremental value in the detection of sacroiliitis in a cohort of patients with early IBP who were followed for 2 years compared to the combination of STIR MRI sequence and pelvic radiographs.

Both MRI sequences can be used to detect sacroiliitis with similar efficiency, as is reflected in the high kappa values found in our study. Earlier studies also compared the concordance between STIR and post-Gd-DTPA sequences in detecting BME on MRI-SIJ (3, 4). De Hooge et al. found a 100% agreement between the STIR and post-Gd-DTPA MRI sequence in detecting BME on MRI-SIJ in a prospective cohort study of 127 patients with chronic back pain of less than 2 years duration with onset below 45 years (4). In 8 (6%) of the 127 patients, synovitis and/or capsulitis and/or enthesitis was detected on the post-Gd-DTPA sequence, but without corresponding BME. However, these findings are not solely considered in the ASAS/OMERACT definition of active sacroiliitis. Also in this study, it was concluded that the post-Gd-DTPA sequence does not have an additional value in the assessment of active sacroiliitis over the STIR sequence (4). Madsen et al. found in 40 patients with established axSpA, who were assessed by an oblique transaxial MRI of the SIJ, that the STIR sequence can replace the post-Gd-DTPA sequence (3). There was agreement between both imaging sequences in 60 (75%) of the 80 SIJs. With the STIR sequence more BME, mainly in the periphery of structural changes, was detected. However, the authors suggested that the post-Gd-DTPA sequence might be superior to the STIR sequence with respect to detecting small subcortical lesions (3). In contrast to these two studies, our longitudinal study also compared the MRI findings to the findings of pelvic radiographs over a 2-year follow-up period. In a small subset of patients, BME could be detected on the post-Gd-DTPA sequence only during follow-up. However, these patients already fulfilled the mNY criteria. This suggests that post-Gd-DTPA sequence does not provide additional diagnostic information in the detection of sacroiliitis in this cohort of patients with early

IBP when information from the STIR sequence and pelvic radiographs are combined.

The present study shows that in case of discordance between the STIR and post-Gd-DTPA sequences, BME was mainly detected on the STIR sequence. In a previous study in the same cohort we have demonstrated that the combination of a positive MRI scan for BME and a positive HLA-B27 status is associated with a high likelihood of persistent signs of BME on MRI during follow-up (13). Five patients in our cohort showed subsiding BME on the STIR sequence without BME on the post-Gd-DTPA sequence during follow-up, and all of them were HLA-B27 negative. Three of these 5 patients did not fulfil the mNY criteria. Whether the MRI in these 5 patients gave false-positive results or whether these patients showed fluctuating disease activity remains unclear because in ESpAC patients were not given a clinical diagnosis of axSpA that could serve as an external standard.

The MRI scoring method used in the present study is a combination of the SPARCC and Aarhus grading method (9,10). Both scoring systems have proved to be reliable with respect to inter-reader agreement (14). In contrast to the SPARCC method, we applied an unlimited number of slices to be evaluated, and the same (number of) slices were scored per MRI examination per patient over time. The advantage of this method is that all qualitatively optimal slices are scored, thereby maximising the chance of detecting active lesions. A general concern when scoring MRIs of the SIJs is the possibility of misalignment between two successive MRI examinations, which may cause measurement error. We ensured that scoring started and ended at the same anatomical level to minimise the chance of misalignment between two successive MRI examinations. Some limitations of the present study need to be addressed. First, the MRI sets were scored by one reader. However, the reader was experienced and the MRI scores showed high consistency over time despite independent scoring of each MRI set and blinding of the reader for time order. Second, the STIR sequence was not scored independently of the post-Gd-DTPA sequence. This might have contributed to the high per patient kappa values at baseline and follow-up. Third, a number of MRIs and pelvic radiographs was missing at follow-up. Baseline MRIs and pelvic radiographs were nevertheless complete and the baseline results already led to the conclusion that the post-Gd-DTPA sequence can be omitted, a conclusion that did not change when assessing the follow-up MRIs combined with the information from pelvic radiographs. Fourth, discordances between the STIR sequence and the post-Gd-DTPA sequence can be due to MRI coil artefacts, which may have contributed to an overestimation of the presence of BME on the STIR sequence (15). Fifth, in ESpAC, the use of NSAIDs was allowed. The actual use of NSAIDs per patient was not recorded. It is possible that continuous or on-demand treatment with NSAIDs may have led to subsiding BME (16). However, a number of BME lesions may also have subsided due to the natural fluctuating course of the disease (17). Last, patients included in ESpAC were recruited via local rheumatologists, (related) medical specialties (*i.e.* dermatology, gastroenterology) and through family members of the local ankylosing spondylitis society. This selective recruitment may explain the relative high proportion of patients that fulfilled a least one of the classification criteria for axSpA. Furthermore, the proportion of female patients in ESpAC is relatively high (62%) whereas the proportion of patients with a positive HLA-B27 status is relatively low (46%). However, these percentages are in accordance with other cohorts that included patients with early IBP (18, 19). Nevertheless, extrapolation of the study findings should be done cautiously.

In conclusion, combined use of pelvic radiographs and the STIR MRI sequence is sufficient for detecting sacroiliitis in this early IBP cohort suspected for axSpA. The post-Gd-DTPA MRI sequence does not have an incremental value in detecting sacroiliitis, neither at baseline nor during 2 years of follow-up.

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