

Short-term Repeat Magnetic Resonance Imaging Scans in Suspected Early Axial Spondyloarthritis Are Clinically Relevant Only in HLA-B27–positive Male Subjects

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ABSTRACT. Objective. Our study investigated the natural history of magnetic resonance imaging (MRI)–determined bone marrow edema over a 12-week period in individuals with suspected axial spondyloarthritis.

Methods. There were 109 MRI scans performed on 30 patients who fulfilled the Assessment of Spondyloarthritis international Society inflammatory back pain criteria at baseline and at 4, 8, and 12 weeks.

Results. There were 29 patients who completed the study. Only 4 (14%) patients changed from MRI-negative to MRI-positive (all HLA-B27–positive, OR 2.74). Three of 7 (43%) male HLA-B27–positive patients, 1 of 8 (12.5%) HLA-B27–positive female patients, and no HLA-B27–negative patients changed from MRI-negative to -positive.

Conclusion. Repeat MRI scans within a 12-week period should be considered in HLA-B27–positive males. (J Rheumatol First Release December 1 2017; doi:10.3899/jrheum.170171)

Key Indexing Terms:

MAGNETIC RESONANCE IMAGING DIAGNOSIS AXIAL SPONDYLOARTHRITIS

Sacroiliac joint (SIJ) involvement is a unifying feature in spondyloarthritis (SpA), and radiographic sacroiliitis is a prerequisite for the diagnosis of ankylosing spondylitis (AS). However, radiographic changes may develop slowly, contributing to substantial delays in diagnosis of up to a decade^{1,2}. The Assessment of Spondyloarthritis international Society (ASAS) has reclassified SpA into axial (axSpA) and peripheral (pSpA). The ability of magnetic imaging

resonance (MRI) to demonstrate objective evidence of potentially diagnostic inflammatory lesions early in the course of the disease renders it especially useful for the diagnosis of axSpA, particularly when conventional SIJ radiographs are normal or show equivocal changes^{3,4}. Further, a positive baseline MRI scan is of prognostic value^{4,5} and may predict response to biologic therapy⁶.

However, the sensitivity of MRI is limited because up to 65% of subjects with inflammatory back pain (IBP) suspected of having axSpA have a negative SIJ MRI at baseline⁷, and up to 38% of patients with active AS/axSpA have no inflammatory lesions of the SIJ^{6,8}. AxSpA follows a fluctuating course in early disease and this has been shown both clinically and on MRI^{9,10}. Further, the optimal timing of MRI scanning of IBP cases with normal radiographs is poorly defined. One previous study showed that 27% of HLA-B27–positive patients had a positive repeat MRI scan after 2 years⁷, but clinically, such long waits in symptomatic cases are difficult to justify. Our study evaluates clinically suspected axSpA cases using MRI at 4 timepoints over a 12-week period.

MATERIALS AND METHODS

Participants were recruited from the Defence Medical Rehabilitation Centre, Headley Court, Epsom, and the Royal National Hospital for Rheumatic Diseases, Bath, UK. Local ethical approval was obtained for our study from the Cornwall and Plymouth Research Ethics Committee (reference number 11/SW/0038) and all patients provided informed written consent. Inclusion

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criteria were IBP as defined by the ASAS criteria¹¹ and normal SIJ on anteroposterior pelvis radiographs (scored centrally). Because it is unclear whether nonsteroidal antiinflammatory drugs (NSAID) might affect MRI bone marrow edema (BME), participants were asked to either discontinue all NSAID use or to continue taking a regular dose throughout the study duration to ensure consistency between scans. Additional simple analgesia was permitted if required. Recruited subjects had a total of 4 MRI scans using a predefined protocol at baseline and at 4, 8, and 12 weeks. The protocol included sagittal T1 and short-tau inversion recovery of the cervicothoracic spine, thoracolumbar spine, and coronal oblique of the SIJ. At each visit, patient-reported outcome measures (Bath indices), medication history, and C-reactive protein (CRP) were recorded.

MRI scans. MRI scans were scored according to the Leeds Scoring system^{8,10}. In addition, all images were assessed for ASAS definitions of a positive scan of the SIJ¹² and spine¹³, thereafter referred to as “positive” or “negative” depending on whether definitions were fulfilled, respectively. In the SIJ, although the readers’ focus was on BME lesions, if BME lesions were equivocal and not necessarily highly suggestive of axSpA, the additional presence of structural lesions (erosion, sclerosis, fatty deposition, or fusion) could be used to influence the decision as per the updated ASAS definition¹⁴. Experienced readers (HMO and DMG) scored the scans and radiographs, and were blinded for any clinical data and timepoints. Any disagreement or borderline/equivocal scans were settled by consensus. Radiographs were scored according to the modified New York Criteria (mNYC)¹. Intrareader reliability for ASAS MRI-positive definitions at the SIJ and spine were considered excellent with $\kappa(\text{SE})^{15} = 0.80 (0.19)$, $p = 0.01$, and $1.00 (0.00)$, $p < 0.0001$, respectively. Reliability for mNYC classification of radiographs had 100% agreement ($\text{SE}) = 1.00 (0.00)$, $p < 0.0001$ (absolute agreement).

RESULTS

There were 30 participants recruited (Table 1), of whom 29 completed the study, 25 (86%) attended all 4 visits, 2 patients attended 3 visits, and 1 patient attended 2 visits. A total of

Table 1. Baseline characteristics. Values are n (%) unless otherwise specified.

Characteristics, n = 29	Values
HLA-B27–positive	21 (72)
Male	19 (66)
Symptom duration, yrs, mean \pm SD	5 \pm 2.1
Fulfilled ASAS clinical criteria	17 (59)
Fulfilled ASAS imaging criteria	12 (41)
SpA features, ≥ 2	25 (86)
Uveitis	3 (10)
Psoriasis	9 (31)
IBD	0
Regular NSAID	13 (45)
Baseline outcome measures, mean \pm SD	
BASDAI	4.8 \pm 0.7
Back pain score	5.7 \pm 1
BASFI	3.5 \pm 0.7
ASDAS	2.5 \pm 0.3
CRP	2.7 \pm 1.7
Raised CRP	8 (29)

ASAS: Assessment of Spondyloarthritis international Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CRP: C-reactive protein; IBD: inflammatory bowel disease; NSAID: nonsteroidal antiinflammatory drugs; SpA: spondyloarthritis.

109 MRI scans were performed. As well as meeting the inclusion criteria, all patients had ≥ 1 clinical SpA feature (Table 2) and 25 (86%) had ≥ 2 . There were 13 patients (45%) who took regular NSAID throughout the study. All patients were assessed by ANB and RS. Nonradiographic axSpA was diagnosed in 79% and mechanical back pain in 21%. On application of ASAS classification, 26% met the imaging arm, 39% met the clinical arm, and 35% met both arms.

ASAS status. There were 17 participants (59%) who met the ASAS clinical criteria for axSpA prior to any imaging. Eleven (38%) met ASAS imaging arm classification criteria during the study, and a further 3 (10%) had a positive MRI of the spine but normal SIJ (HLA-B27–positive and ≥ 1 clinical feature).

There were 15 (52%) participants who were ASAS MRI-negative (spine and SIJ) at baseline and remained so during the entire study, and 10 (34%) patients were either spine- and/or SIJ-positive for the duration of the study. A total of 4 (14%) patients changed from ASAS axSpA MRI-negative to -positive (spine, $n = 3$ or SIJ, $n = 1$) during the study, which influenced their final diagnosis (Figure 1).

CRP status and change. Of the 28 patients who had blood test results available, CRP levels were normal in 25 subjects (89%) at baseline: 20 remained normal throughout and 5 patients’ CRP became elevated above the upper limit of normal during the study. Three subjects had a raised CRP at baseline: 1 remained raised throughout study and 2 normalized. There was no relationship between CRP change and MRI scans becoming positive at any time during the study.

HLA-B27 status and sex. All 4 patients whose MRI changed from negative to positive were HLA-B27–positive. Comparing patients who were HLA-B27–positive with those who were HLA-B27–negative, the OR for their ASAS MRI status changing from negative to positive was 2.74.

Three of the 4 patients (75%) whose MRI changed from negative to positive were male. Of the 10 patients whose MRI scans were positive throughout, 9 were male (90%). Of the 15 patients who were HLA-B27–positive with negative baseline scans, 4 (27%) developed positive scans during the 12-week study period. Three of 7 (43%) HLA-B27–positive male patients, compared to 1 out of 8 (12.5%) HLA-B27–positive female patients and no HLA-B27–negative patients, changed from ASAS MRI definition–negative to positive during the study.

DISCUSSION

A positive MRI aids diagnosis in clinically suspected axSpA; however, MRI may be negative or inconclusive in a significant proportion of these patients⁷. Our study tested the hypothesis that repeat MRI scanning in suspected but undiagnosed axSpA over 12 weeks may increase the diagnostic yield. In the studied cohort of IBP patients with typical

Table 2. Distribution of SpA features by HLA-B27 status in study population.

ASAS MRI Status	HLA-B27–positive, No. SpA Features					HLA-B27–negative, No. SpA Features					Total
	1	2	3	4	5	1	2	3	4	5	
Negative throughout	2	3	5	0	1	0	3	0	0	1	15
Positive throughout	2	3	1	0	0	0	0	3	1	0	10
Negative to positive	0	2	0	2	0	0	0	0	0	0	4
Total	4	8	6	2	1	0	3	3	1	1	29

ASAS: Assessment of Spondyloarthritis international Society; MRI: magnetic resonance imaging; SpA: spondyloarthritis.

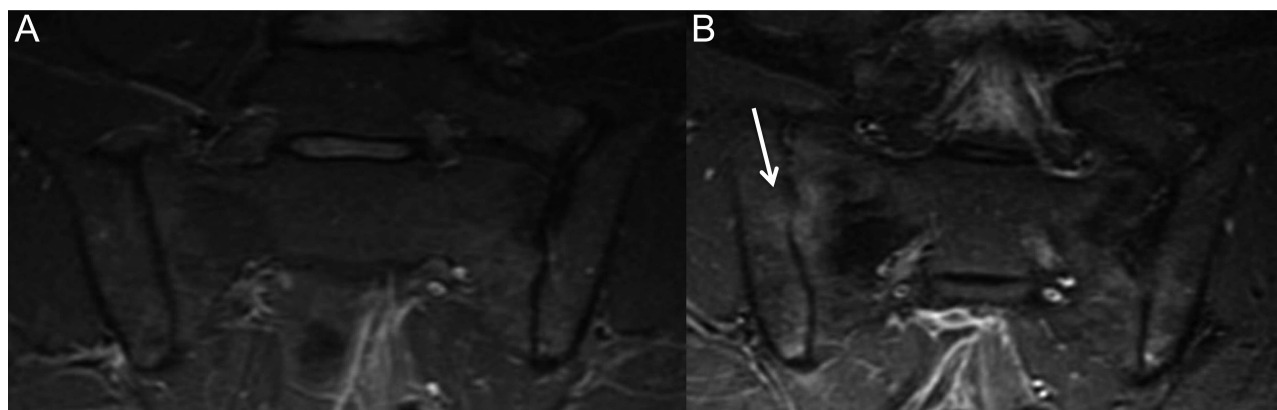


Figure 1. MRI changes in 1 patient between (A) the negative scan at baseline; and (B) the development of active inflammatory sacroiliitis (arrow) in the right SIJ (present on > 1 slice) at Week 4, which resulted in a change from ASAS SIJ definition “negative” to “positive”. ASAS: Assessment of Spondyloarthritis international Society; MRI: magnetic resonance imaging; SIJ: sacroiliac joint.

axSpA features (HLA-B27–positive = 72%, ≥ 2 SpA features = 86%), only 14% of patients changed their ASAS MRI definition from negative to positive over the 12-week period. While the yield of repeating an MRI scan in patients with IBP and a normal baseline scan is low, there may be benefit in repeating the scan within 12 weeks, especially in HLA-B27–positive males, because 43% of these patients changed from negative MRI to positive during the study period. Neither baseline CRP nor presence of other SpA features (dactylitis, arthritis, enthesitis) predicted change in MRI status.

The majority of our cohort (59%) met ASAS clinical criteria at baseline. There were 52% who were ASAS imaging–negative at baseline and remained so throughout the study. Overall, in our 12-week study, there was little change in MRI inflammatory lesions.

The natural variation of inflammatory MRI lesions of BME in axSpA remains poorly defined. From an SIJ perspective, 1 study showed that 73.5% of patients who had SIJ BME at baseline had persistent lesions 1 year later¹⁰, even in the absence of clinical symptoms. In the spine, 31% of vertebral corners showed persistence of inflammatory lesions at a 2-year timepoint¹⁶. These observations, together with the findings from our study, suggest that once an inflammatory lesion develops, there is likely to be little change in the spine and in SIJ lesions within the first year unless biologic

therapies are introduced. However, our study supports the findings of van Onna, *et al*⁷ that if the baseline scan is negative, then the proportion changing to a positive scan at followup is higher in HLA-B27–positive patients (27%) compared to patients who are HLA-B27–negative (0%).

The strengths of our study include the realistic clinical time frames for potential followup scans and the fact that the study was specifically designed to investigate the usefulness of repeat scans within a 12-week window, which has not previously been performed, to our knowledge. Other strong aspects include the minimal absence of followup MRI scans in the cohort as well as data on NSAID use collected on all patients throughout the study. The main limitations of our study were the lack of asymptomatic and/or mechanical back pain control arms.

Our study evaluated the natural history of axSpA-related inflammatory lesions on MRI and the role of repeat MRI scanning within a 12-week period in clinically suspected early axSpA. In a symptomatic patient with suspected axSpA, where baseline MRI scanning is normal, a repeat MRI scan may be of diagnostic utility in HLA-B27–positive males but not in females or HLA-B27–negative subjects. These results are highly relevant to aid in clinical decision making and to add to the body of evidence on MRI use in axSpA diagnosis.

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