Grading of Inflammatory Disease Activity in the Sacroiliac Joints with Magnetic Resonance Imaging: Comparison Between Short-tau Inversion Recovery and Gadolinium Contrast-enhanced Sequences

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ABSTRACT. Objective. We investigated the potential concordance of 2 different magnetic resonance (MR) sequences — short-tau inversion recovery (STIR) and fat-saturated T1-weighted spin-echo after application of gadolinium (Gd) contrast medium to detect active bone marrow abnormalities at the sacroiliac joints (SIJ) in patients with spondyloarthritis (SpA).

Methods. Blinded and using the Danish scoring method, we evaluated transaxial MR images of the 2 sequences in 40 patients with SpA with disease duration of 3–14 years. Both the cartilaginous and ligamentous portions of the SIJ were analyzed.

Results. There was a significant positive correlation between the activity scores obtained by STIR and Gd-enhanced sequences (p < 0.0001). Agreement in the detection of bone marrow abnormalities occurred in 60 of the 80 joints, 35 with and 25 without signs of active disease. Discordance with STIR-positive marrow activity scores occurred in only 11 joints; Gd-enhanced positive scores in 9 joints. The STIR sequence detected remnants of marrow activity in the periphery of chronic fatty replacement not seen or partly obscured on the Gd sequence. Small subchondral enhancing lesions may not be scored on the STIR sequence, mostly because of reduced image resolution.

Conclusion. Active bone marrow abnormalities were detected nearly equally well with STIR and Gd-enhanced fat-suppressed T1 sequences in patients with SpA, with STIR being most sensitive to visualize active abnormalities in the periphery of chronic changes. (First Release Dec 23 2009; J Rheumatol 2010;37:393–400; doi:10.3899/jrheum.090519)

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Magnetic resonance imaging (MRI) has proven to be effective in depicting abnormalities of the sacroiliac joints (SIJ) and the spine in the early stages of ankylosing spondylitis (AS) and other forms of spondyloarthritis (SpA). MRI has also been shown to determine disease activity and to assess change of activity over time in patients treated with anti-tumor necrosis factor-α (anti-TNF-α) agents. Abnormalities of the bone marrow and subchondral bone are hallmarks for the quantitative MR evaluation of disease activity in SpA.

The predominant tissue component of normal bone marrow in adults is fat, determining the bright, intermediate to high signal intensity (SI) by conventional T1-weighted (T1) and T2-weighted (T2) MR sequences and dark, low SI on spectral fat-suppressed T1 and T2 MR sequences. Processes that infiltrate or replace the fat in bone marrow will reduce SI on conventional T1-weighted images and maintain or increase the bright SI on T2-weighted sequences. Fat-suppressed (FS) T2 sequences, in particular the STIR (short-tau inversion recovery) images, are sensitive to increases in water content, and even subtle changes in marrow composition by inflammatory tissue may be detected by increased SI. The same inflammatory processes that infiltrate or replace fat tissue in bone marrow can also effectively be visualized with the use of fat-suppressed T1 MR images after intravenous administration of extracellular MR contrast agents [gadolinium-diethylenetriamine pentaacetic acid, Gd-DTPA (Gd)]. The increase in SI of Gd-enhanced sequences is correlated to a changed vascular composition of the marrow with increased tissue perfusion and permeability. Thus, FS T2 and STIR sequences and Gd-enhanced FS T1 sequences depict different characteristics of the composition and physical properties of tissue. To our knowledge...
it has not been assessed whether and how these differences between the STIR and Gd-enhanced sequences may influence visualization of abnormalities and the scoring of active inflammatory SIJ changes in SpA by MRI. However, in a blinded comparison it has been shown that STIR detected more active spinal lesions in patients with AS than did Gd-enhanced sequences. In assessment of the SIJ in SpA, blinded comparison of STIR and Gd-enhanced T1 FS sequences is still needed.

We aimed to compare STIR MR sequences with Gd-enhanced T1 FS sequences using the Danish scoring method to assess active bone marrow abnormalities adjacent to the cartilaginous and ligamentous portions of the SIJ in patients with SpA. Moreover, we aimed to analyze and discuss differences in scoring and visualization of bone marrow abnormalities between the 2 sequences.

MATERIALS AND METHODS

Patients. From 1998 to 2004, MRI of the SIJ was obtained in 132 patients fulfilling the European Spondylarthropathy Study Group (ESSG) criteria for axial SpA. This SpA cohort was invited to participate in a radiological and clinical followup study including MRI of the SIJ in addition to further imaging. The cohort encompassed 41 patients with early SpA as described in addition to patients with relatively early SpA confirmed by MRI on clinical request from 1999 to 2004. Ninety-five of these patients agreed to participate. To fulfill the aim of the study, at least 32 patients had to be included to obtain a power of 0.80. The first 40 patients included in 2005 were therefore assessed in the present study.

MRI techniques. The followup MR examination of the SIJ was obtained with a 1.5 T unit (Magnetom Symphony, Siemens, Erlangen, Germany) using a body and a multiarray spine coil. The following sequences were obtained: oblique coronal T1 spin-echo, oblique coronal T1 FS, oblique transaxial STIR [recovery time/echo time/inversion time: 4000/30/150 ms; time of acquisition (TA) 7.3 min]. Following intravenous administration of Gd, oblique coronal and transaxial T1 FS images were obtained (recovery time/echo time: 660/12 ms; TA 5.5 min). For all sequences the matrix was 512, the field of view 24 cm and slice thickness 4 mm, with a gap of 0.4 mm. The orientation of sectioning was determined by the slope of the upper endplate of the sacrum (S1) in the sagittal plane. The oblique transaxial sections were parallel to the upper endplate of S1. The Gd used was Magnevist® (Schering AG, Berlin, Germany) or Omniscan® (Nycomed, Oslo, Norway), both with 0.5 mmol Gd-DTPA/ml. We used 0.1 mmol/kg body weight with a maximum of 15 ml.

Only the oblique transaxial STIR and Gd-enhanced oblique transaxial T1 FS sequences were assessed and compared.

MR evaluation. Anatomically, the SIJ consist of a ventral/caudal cartilaginous articulation and a dorsal/cranial syndesmosis or ligamentous articulation (Figure 1). For each joint, 4 osseous locations were evaluated: the iliac and the sacral subchondral bone and adjacent bone marrow in the cartilaginous articulation; and the iliac and the sacral bone marrow adjacent to the ligamentous articulation. Inflammatory bone marrow abnormalities involving both the cartilaginous and ligamentous articulation were registered at both sites independent of their extension along the joint space (Figures 1 and 2). Joint space abnormalities were not assessed, and widening of the cartilaginous joint space due to subchondral bone destruction was considered as part of the joint space.

Inflammatory bone marrow abnormalities (BMA) were defined as localized or diffuse signal hyperintensities on the STIR (BMA-STIR) and the Gd-enhanced T1 FS images (BMA-Gd), relative to the low signal intensity of unaffected bone marrow within the same MR image. The scoring method for inflammatory BMA included a separate assess-
ment of the extent along the cartilaginous and ligamentous joint surfaces, the depth of BMA, and the signal intensity of BMA. The total maximum score for 1 joint was 20 and thus 40 for each patient.

Extent. The 3-dimensional extent of BMA along the cartilaginous and ligamentous joint space had 4 grades: 0 = normal, 1 = slight (< 25% of the total subchondral area), 2 = moderate (25% to 50%), and 3 = severe (≥ 50%). Subtle BMA had to be present at 2 places in 1 MR image or 1 place in 2 consecutive slices to obtain a grade of 1. The extent in percentage of the total subchondral/subcortical areas was calculated as follows: the number of MR sections/images (S) in each sequence with a visible cartilaginous or ligamentous joint space was registered. The number of sections/images with an extent of BMA ≥ 50% along the joint surface (A) and the number of sections with an extent of BMA at < 50% of the joint surface (B) was counted.

Percentage of BMA extent = (A+(B/2))/S × 100

Depth. The depth of the BMA in the sacral and iliac bone, respectively, had 2 grades: normal (BMA extending < 1 cm beneath the osseous joint surface) and BMA extending ≥ 1 cm beneath the osseous joint surface and covering ≥ 1 cm². If the entire width of the ileum was affected, it was graded 1, irrespective of the thickness of the bone.

Signal intensity. The 2 grades for SI were normal, or slight to moderately increased SI; and pronounced increased SI comparable to the SI of spinal fluid on STIR and great vessels in Gd-enhanced images, respectively, and covering an area of ≥ 1 cm².

Evaluation. The image evaluation was made by a senior radiologist with scientific and clinical experience in the assessment of SpA with MRI using...
a workstation with high-resolution screens. The transaxial STIR and Gd-enhanced T1 FS images were anonymized, with no demographic and patient data on the images, and the images were randomly mixed on 8 CD by an independent person blinded to the study.

Twenty examinations were selected and anonymized in the same way using other codes. They were used for a second evaluation by the same radiologists 14 days after the first assessment. These 20 examinations included the 5 examinations with the most pronounced discrepancies in total scoring between the STIR and Gd-enhanced T1 FS sequences. The radiologist was blinded to the results and the scoring schemes of the first evaluation. Finally, discrepancies between the scorings of the 2 sequences and discrepancies in the intraobserver analysis were assessed in consensus among all authors.

The study complied with the Helsinki Declaration for medical research and was approved by the local ethics committee and the Danish Data Protection Agency. All participants were informed orally and in writing about the study and gave their written consent.

Statistical analysis. A preliminary power calculation verified that 80 SIJ gave a satisfactory power. Using a significance level of 0.05, a minimum expected grading difference of 1, and an expected standard deviation of 2, 63 SIJ were needed to obtain a power of 0.80 and 84 joints a power of 0.90. Further statistical analyses were made using Stata (Stata Corp., College Station, TX, USA) and Analyse-it Software (Leeds, UK). Spearman's correlation was used to analyze the correlation between scoring with the STIR and Gd-enhanced sequences. The intraobserver agreement was assessed using a linear-weighted $\kappa$ test and Bland-Altman plots. Acceptable interobserver agreement for the present scoring method was obtained.

RESULTS

The 40 patients included 21 women and 19 men with a mean age of 36 years at the time of followup (range 16–51 yrs). The mean/median duration of symptoms was 7/6 years (range 3–14 yrs). The mean/median Bath AS Disease Activity Index and Bath AS Functional Index scores obtained in connection with the MRI in 37 patients were 2.9/2.4 (range 0–9) and 1.7/0.7 (range 0–9), respectively; 35 patients also underwent biochemical examination. The mean/median C-reactive protein was 45/15 nmol/l (range 5–761; normal < 75). A total of 26 patients were HLA-B27-positive (not assessed in 1 patient), and 27 patients fulfilled the modified New York criteria for AS. One patient, with AS, received anti-TNF-α therapy. All patients except 4 had chronic SIJ changes determined by MRI.

The intraobserver agreement of the scoring of BMA-STIR and BMA-Gd on 40 joints among the 20 patients showed a linear weighted $\kappa$ value of 0.82 and 0.84, respectively. Bland-Altman plots demonstrated a good agreement between the 2 evaluations.

There was a significant positive correlation between BMA-STIR and BMA-Gd of the 80 joints with a correlation coefficient of 0.78 ($p < 0.0001$). Agreement in the MR visualization of inflammatory bone marrow activity by BMA-STIR and BMA-Gd occurred in 60/80 joints, 35 with and 25 without signs of activity (Figure 3). The ligamentous portion of the 80 SIJ accounted for 34% of BMA-STIR and 36% of BMA-Gd total joint scores.

For the 80 joints, the mean score values and ranges of inflammatory joint activity by BMA-STIR and BMA-Gd were 2.90 (range 0–15) and 2.89 (range 0–15), respectively. In the 40 patients the mean scores were 5.93 (range 0–26) and 5.75 (range 0–25), respectively. Thus, by both sequences the joints had a relatively minor degree of activity compared to the maximal score of 20 per joint and 40 per patient. In the 35 joints with signs of activity by both sequences, the mean score values for BMA-STIR were 6.09 (range 1–15) and 6.11 (range 2–15) for BMA-Gd.

Disagreements with inflammatory activity scored by 1 sequence only, STIR or Gd-enhanced, occurred in 20 joints. Seventeen of these disagreements occurred in the cartilaginous and 3 in the ligamentous SIJ portion. Eleven joints demonstrated inflammatory activity visualized only by BMA-STIR; 4 joints had a score value of 1 and 7 had a score of 2. Nine joints had a positive score on BMA-Gd only; 3 joints had a score value of 1, 5 had a score of 2, while 1 had a score of 3. All these disagreements except 1 had an extent of < 25% of the subchondral area in the cartilaginous and ligamentous joint portion, respectively (score value 1). Eleven activity changes had a depth of BMA-STIR or BMA-Gd ≥ 1 cm and thereby obtained a score value of 2.

Consensus evaluation of disagreements in 11 joints with inflammatory activity by STIR only. Six joints with a score value of 2 on the STIR sequence had bone marrow activity in the periphery of chronic BMA (Figures 2 and 4). Retrospectively, there was no Gd enhancement in 4 of the 6
joints. In 2 joints a faint Gd enhancement could be recognized on 1 slice only and was therefore according to the definition not registered (Figure 2). The same applied to 1 joint with slight activity on both sides of the joint space (score 2). The remaining 4 joints had a score of 1. Retrospectively, 3 had no enhancement and 1 had a slight Gd enhancement, which should have been registered.

Consensus evaluation of disagreements in 9 joints with inflammatory activity by Gd-enhanced sequences only. Three joints had small localized subchondral Gd-enhancement score 1, and 2 had scores of 2. Retrospectively, 3 of these lesions could partly be identified by STIR, but were probably interpreted as part of an abnormal joint space because of reduced image resolution and noise on the STIR sequence (Figure 5). This was not the case in 2 patients. In 3 joints, slight diffuse Gd enhancements posterior/distally (2 scores of 2 and 1 score of 3) were interpreted as coil effects on the STIR sequence. In 1 joint (score of 2) a slight diffuse enhancement in the periphery of chronic iliac bone abnormalities was also detectable by STIR retrospectively.

Consensus evaluation of 4 BMA-STIR and BMA-Gd disagreements exceeding 95% limits by the Bland-Altman plot (Figure 3). One joint had a score value of 8 on BMA-STIR in the cartilaginous portion of the right SIJ and a score of 3
The BMA-STIR with an extent of 50% in the iliac bone in the periphery of extensive chronic changes was not detected on BMA-Gd before evaluation of disagreements (Figure 2). The second joint with BMA-STIR (score 4) greater than BMA-Gd (score 0) was primarily interpreted to have signs of activity at the sacral and iliac side with a depth of >1 cm. At the second evaluation and at consensus, the BMA-STIR findings were deemed to be due to noise. One joint had a BMA-Gd score value of 8 and only 2 on BMA-STIR. In this joint there was a mixture of chronic and active inflammatory changes, and diffuse signal hyperintensity subchondrally in the ligamentous portion of the SJJ. In the fourth joint there was a difference in score values of 5 in favor of BMA-Gd; at the second intraobserver evaluation this difference was not observed.

DISCUSSION

In our study, all 40 patients fulfilled the ESSG criteria for SpA10. A total of 36 patients had chronic abnormalities of the SJJ in the form of erosions and MR signs of fatty marrow replacement at followup8. These chronic changes were not assessed in our study. Using the Danish scoring system8, our study was confined to a blinded comparison of 2 commonly used MR sequences in the assessment of inflammatory activity in the bone marrow in the form of localized or diffuse MR signal hyperintensities, commonly known as “bone marrow edema.” The results showed that 35 joints with chronic changes demonstrated persistent inflammatory activity by both sequences. Another 11 and 9 joints demonstrated slight activity by either STIR or the Gd-enhanced sequence.

MRI is exquisitely sensitive to visualize changes in the cellular composition of bone marrow. Therefore it constitutes the most important and sensitive imaging technique for evaluation of bone marrow lesions such as detection and longitudinal control of primary and secondary bone marrow malignancies, occult fractures, and reparative changes secondary to arthritis as well as degenerative joint disorders. The combination of T1 fast spin-echo and the FS STIR sequence represents the most commonly used MR technique for assessment of bone marrow lesions. However, specific sequences and MR techniques such as diffusion-weighted sequences may be required in the differentiation between conditions16.

The STIR sequence may overestimate the extent of bone marrow involvement7 because of its high sensitivity to small changes in cellular and extracellular water content. The STIR sequence may therefore not be able to separate signal intensities from the lesion itself and signal from surrounding tissue edema. This separation may be better obtained by use of Gd-enhanced MRI in combination with FS T1 sequences9. This technique, however, requires a defined timing between the intravenous Gd-enhanced injection and MR image acquisition. In our study there was a general agreement between the 2 sequences, indicating that the fatty and hematopoietic marrow has been replaced by tissue with an increased vascular component in active marrow abnormalities. This is in accord with the findings of Francois, et al17, who studied the histological pattern of AS from early to late stages using 5 biopsies and 12 autopsies of the SJJ. In the active early stage of AS there was osteoblastic activity in the subchondral bone and adjacent bone marrow, with replacement of hematopoietic cells by plasma cells and lymphocytes around vessels as well as myxofibroblast replacement17. In later chronic stages the marrow was described as osteoporotic.

Knowledge is sparse about the correlation between histopathology and MRI of the SJJ in SpA. The normal MR anatomy with correlation to histology has been described in detail11. Bollow, et al18 correlated MR images with computed tomography-guided core biopsies of the cartilaginous joint space in 32 patients, including 18 with AS. To our knowledge, there are no studies available on correlation between MRI and histology of subchondral and bone marrow changes adjacent to abnormalities of the SJJ spaces in SpA. However, the 2 main types of bone marrow alteration
observed by MRI adjacent to disk degeneration have MR appearances similar to those of sacroiliitis. In type 1, the active stage, the low signal intensity on T1 and increased signal intensity on T2 correspond histopathologically to fibrovascular replacement in the marrow. In type 2, the chronic stage, with high fat signal intensity on T1, histology demonstrated fat deposition in the marrow. Bone marrow edema was not described by these authors. Zanetti, et al described similar MRI and histological appearances of subchondral marrow changes in osteoarthritis of the knee. These authors were searching for histological evidence of bone marrow edema but found a mixture of reparative tissue that included fibrovascular changes, osteonecrosis, and trabecular abnormalities rather than marrow edema. In our study, 11 joints showed slight diffuse hyperintensities on the STIR sequence with or without less increased signal intensity on the following Gd-enhanced MR images. All these discordances occurred in the periphery of chronic marrow abnormalities in the form of fatty replacement (Figures 2 and 4). These marrow changes may represent marrow edema and/or remnants of active changes in a phase of transition from active marrow abnormalities to fatty replacement.

The majority of our discordances with Gd-positive and STIR-negative (score 0) scorings could be explained by technical, sequence-related errors or artifacts. Most abnormalities that obtained a score value on the Gd sequence were also recognized on the STIR sequence, but were interpreted as, for example, erosions adjacent to destructive widening of the cartilaginous joint space (Figure 5). Although we used a matrix of 512 and an acquisition time of 7 minutes for the STIR sequence with a short inversion time at 1.5 Tesla, it was not possible to obtain an image resolution with precise anatomical landmarks comparable to that of the Gd-enhanced FS T1 sequence. Another reason for discordances with Gd-positive scoring was diffuse hyperintensities of the bone marrow close to the coil at both sequences.

In an unblinded MR study of sacroiliitis, the STIR sequences were found to be less sensitive than the Gd-enhanced sequences, but mainly regarding abnormalities of the joint space. Examining 17 patients with different stages of AS, Bredella, et al found that all enhancements of bone marrow lesions were also seen by STIR and fat-saturated T2 images; they were seen slightly better on the STIR images. However, in 4 of 10 patients with active disease by MRI, more extensive activity was seen on Gd-enhanced images compared with the STIR sequence. These discordances between the sequences may not concern the bone marrow, but rather abnormalities as well as normal vascular anatomy in the ligamentous joint space. However, the interreader reliability for Gd-enhanced images has been shown to be superior to STIR images. Baraliakos, et al performed a blinded comparison of FS Gd-enhanced sequences and STIR sequences for spinal evaluation in patients with AS. Those results are in agreement with ours: more lesions are detected by the STIR sequence, while the Gd-enhanced sequences may be more selective and specific. In our study, STIR was superior with regard to “rim lesions” around chronic changes, while Gd-enhanced sequences were superior for detecting tiny subcortical “threshold” lesions. Such threshold lesions may be difficult to detect by STIR and also to differentiate from normal variants in healthy persons. Equivocal small signal alterations seen only on Gd-enhanced sequences therefore ought to be reassessed after a few years of followup.

More than one-third of the score values in this study were obtained from the ligamentous portion of the SIJ. These figures cannot be recognized from previous reports. Francois, et al concluded from histopathological studies that “myxoid” marrow was not seen close to ligamentous insertions. Using coronal MRI only, Muche, et al did not address the 3-dimensional anatomy of the SIJ and were apparently unable to assess inflammatory lesions and bone marrow abnormalities in the ligamentous portions of the joints. It is a prerequisite for precise visualization and assessment of the structures such as synovia, ligaments, and menisci, etc. in the periphery of a joint that images are obtained perpendicular to the surface of the joint space (Figure 1). Therefore the common MRI of the SIJ confined to oblique coronal sequences with a slice direction tangential to the edges of the joint space and partial volume averaging has considerable limitations in the assessment of anatomical structures in the ventrocaudal and dorsocranial portions of the joint; as well, separation between the cartilaginous and ligamentous joint portions may be difficult.

Limitations of the study. First, our study did not include patients with early acute inflammatory bone marrow lesions, but later stages with chronic fatty marrow replacement and different stages of remaining active marrow inflammation, because they are a diagnostic challenge. The primary MR examination of the SIJ in these patients did not include both STIR and Gd-enhanced sequences with the same oblique transaxial slice direction. Second, there is no histopathologic correlation to disease activity and chronic changes. Further, the availability of a concomitant high-resolution T1 sequence may have facilitated the assessment of both sequences, in particular the STIR sequence.

In summary, active bone marrow abnormalities were depicted nearly equally well by STIR and Gd-enhanced FS sequences in patients with SpA. The STIR sequence depicted marrow activity in the periphery of chronic fatty replacement not seen or less well seen on the Gd-enhanced sequence. The Gd-enhanced sequence detected small subchondral lesions not seen or less well seen on the STIR sequence, mainly because of its reduced image resolution. The significance of these differences has to be analyzed in followup studies. Taking this into account, high-resolution STIR sequences can substitute for Gd-enhanced sequence studies when performed in the oblique transaxial plane.
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REFERENCES