Bone Marrow Edema on Magnetic Resonance Imaging (MRI) of the Sacroiliac Joints Is Associated with Development of Fatty Lesions on MRI over a 1-year Interval in Patients with Early Inflammatory Low Back Pain: A 2-year Followup Study

Marloes van Onna, Astrid van Tubergen, Désirée M. van der Heijde, Anne Grethe Jurik, and Robert Landewé

ABSTRACT. Objective. To assess whether bone marrow edema (BME) detected on magnetic resonance imaging (MRI) of the sacroiliac joints (MRI-SIJ) is associated with development of structural changes on both MRI and pelvic radiographs in patients with early inflammatory back pain (IBP).

Methods. Patients with IBP ≤ 2 years were followed for 2 years with annual MRI-SIJ. MRI were scored for BME and structural changes (erosions and fatty lesions). Pelvic radiographs were graded according to the modified New York (mNY) criteria. With generalized estimated equation analysis, a time trend in the structural change scores was investigated.

Results. Sixty-eight patients [38% male; mean (SD) age 34.9 (10.3) yrs] were included. During the 2-year followup, pelvic radiograph grading remained constant. On MRI, the number of erosions per patient increased significantly (mean score 2.5 at baseline and 3.5 at 2-yr followup; p = 0.05). A trend was found for an increase in the number of fatty lesions per patient (mean score 5.4 at baseline and 8.5 at 2-yr followup; p = 0.06). Overall, BME was associated with the development of fatty lesions (right SIJ: OR 3.13, 95% CI 1.06–9.20; left SIJ: OR 22.13, 95% CI 1.27–384.50), preferentially in quadrants showing resolution of BME. In contrast, BME (or the resolution thereof) was not associated with the development of erosions.

Conclusion. BME at baseline, especially when it disappears over time, results in the development of fatty lesions, but an association with erosions could not be demonstrated. (First Release April 15 2014; J Rheumatol 2014;41:1088–94; doi:10.3899/jrheum.131022)

Key Indexing Terms: MAGNETIC RESONANCE IMAGING AXIAL SPONDYLOARTHRITIS SACROILIITIS

Magnetic resonance imaging of the sacroiliac joints (MRI-SIJ) and pelvic radiographs play an important role in the diagnosis and classification of axial spondyloarthritis (axSpA). Both imaging techniques are included in the

From the School for Public Health and Primary Care (CAPHRI), University of Maastricht, and Department of Medicine, Division of Rheumatology, Maastricht University Medical Center, Maastricht; Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands; Department of Radiology, Aarhus University Hospital, Aarhus, Denmark; Department of Clinical Immunology and Rheumatology, Academic Medical Center Amsterdam, Amsterdam; Department of Rheumatology, Atrium Medical Center Heerlen, Heerlen, The Netherlands.

M. van Onna, MD; A. van Tubergen, MD, PhD, Department of Medicine, Division of Rheumatology, Maastricht University Medical Center; D.M. van der Heijde, MD, PhD, Leiden University Medical Center; A.G. Jurik, MD, PhD, Aarhus University Hospital; R. Landewé, MD, PhD, Academic Medical Center Amsterdam, and Department of Rheumatology, Atrium Medical Center Heerlen.

Address correspondence to Dr. M. van Onna, Department of Medicine, Division of Rheumatology, Maastricht University Medical Center, P. Debyelaan 25, 6202 AZ, Maastricht, The Netherlands. E-mail: m.van.onna@mumc.nl

Accepted for publication February 11, 2014.

"imaging arm" of the Assessment in SpondyloArthritis international Society (ASAS) criteria for axSpA¹. MRI-SIJ has proven especially useful in the early stage of axSpA, because MRI may detect sacroiliitis years before it is seen on a pelvic radiograph. Moreover, MRI can detect both active lesions and structural changes, in contrast to pelvic radiographs, which only detect structural changes². Cases without radiographic sacroiliitis but with active lesions on MRI suggestive for sacroiliitis are labeled nonradiographic axSpA (nr-axSpA)¹.

Active (inflammatory) lesions that can be detected on MRI are bone marrow edema (BME), capsulitis, synovitis, and enthesitis. Structural changes on MRI are erosions, fat deposition (fatty lesions), sclerosis, and ankylosis^{1,3}. To date, only BME is considered mandatory for fulfillment of the ASAS/Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) working group definition of a positive MRI². However, Weber, *et al* suggested that the detection of erosions on MRI-SIJ also may be helpful in making a diagnosis in early axSpA³. There is, however, limited knowledge about the development of structural

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.

The Journal of Rheumatology 2014; 41:6; doi:10.3899/jrheum.131022

changes as detected on MRI-SIJ in patients with early inflammatory back pain (IBP) who may have or develop axSpA. Further, data on the association between BME and development of structural changes are scarce. Only 1 study suggested that fatty lesions on MRI-SIJ may be the first sign of structural damage after previous active inflammation⁴.

The aims of our study were to assess (1) the presence of structural changes on both MRI-SIJ and pelvic radiographs, and (2) whether BME detected on MRI-SIJ is associated with the development of structural changes on both MRI-SIJ and pelvic radiographs in patients with recent-onset IBP over a 2-year followup period.

MATERIALS AND METHODS

Study population. Patients with IBP of < 2 years duration were enrolled in the Early SpondyloArthritis Clinic (ESpAC) study. In this prospective inception cohort study, 3 identical clinical and radiological examinations were performed at baseline and after 1 and 2 years. A more detailed description of the study population and inclusion can be found in previous reports^{5,6,7}. The Calin criteria were used to define the presence of IBP. Patients had to fulfill at least 4 of the criteria: onset before the age of 40 years, duration of back pain more than 3 months, insidious onset, morning stiffness, and improvement with exercise⁸. Patients who fulfilled only 3 out of 5 of the Calin criteria but reported night pain were also included. Presence of other SpA features was preferred but not obligatory. Patients were not treated with biological therapy during the entire study period, but the use of nonsteroidal antiinflammatory drugs was allowed. The study was approved by the ethics committee from the Maastricht University Medical Center. All patients gave written informed consent.

MRI protocol. MRI-SIJ was performed using a 1.5 Tesla Philips Gyro scan ACS-NT. Patients were placed in supine position in a spine surface coil. The following sequences were used in an oblique coronal plane: T1-weighted spin echo (SE), short-tau inversion recovery (STIR), and T2-weighted fast SE with fat saturation. The MRI set of each individual was scored independently and in a random time order by 1 experienced radiologist (AGJ), without knowledge of clinical or laboratory findings. The SIJ were scored using a combination of the Spondyloarthritis Research Consortium of Canada (SPARCC) method and a modified version of the Aarhus MRI scoring system9,10. In contrast to the original SPARCC system, there was no maximum to the number of evaluated slices, but the number of slices within a patient was kept the same for all timepoints. First, each SIJ was divided into 4 quadrants (upper/lower sacral and upper/lower iliac quadrant) and both BME and structural changes were scored separately per slice in a dichotomous manner (absent vs present). Second, a total count of both BME and structural changes per SIJ was performed. The method for scoring BME has been published¹¹. The structural change scores included scoring of both erosions and fatty deposition of the bone marrow (fatty lesions). Erosions, defined as cortical defects of the SIJ lining, are detected as hypointense signal on the T1 sequence. Subcortical fatty lesions, defined as replacement of normal bone marrow by fatty tissue, are detected as an increased signal on the T1 sequence. According to the ASAS/OMERACT working group definition for active lesions on MRI-SIJ, an MRI-SIJ is considered positive for active sacroiliitis when at least 1 active lesion is present in at least 2 successive slices or when ≥ 2 lesions are detected in 1 slice². Analogous to the ASAS/OMERACT working group definition for active lesions on MRI-SIJ, we defined an MRI-SIJ as positive for structural changes when at least 1 erosion or fatty lesion is present in at least 2 successive slices or when \geq 2 erosions or fatty lesions are detected in 1 slice.

Pelvic radiographs. Anteroposterior pelvic radiographs of the SIJ were obtained and independently scored in a random time order by 2 readers (AT and RL) who were blinded to clinical and laboratory findings and were not

involved in the MRI reading. In case of disagreement, the judgment of a third reader (DH) was decisive. The pelvic radiographs were scored according to the modified New York (mNY) criteria for sacroiliitis, in which sacroiliitis of at least grade 2 bilaterally or grade 3–4 unilaterally must be present for fulfillment¹².

Statistical analysis. Descriptive statistics were used to describe the presence or absence of structural changes on MRI-SIJ and pelvic radiographs during the 2-year followup period. The presence of BME at baseline and during followup in relation to the development of fatty lesions and/or erosions at the site of BME was investigated per quadrant of SIJ (8 quadrants per patient) using descriptive analysis. Generalized estimated equation (GEE) analysis was performed to investigate a time trend in the MRI and pelvic radiograph structural change scores. GEE is a model that allows studying time trends while taking the within-subject correlation into account in a dataset with missing values. Further, this technique was used to test whether BME on MRI is associated with erosions and fatty lesions on MRI and structural changes on a pelvic radiograph 1 year later. This was done using a GEE autoregressive time-lag model that correlates the presence of BME on MRI to each structural change score on either MRI or pelvic radiograph 1 year later. On a per-SIJ level, BME was used as an independent variable and the continuous (sum of) MRI or the pelvic radiograph mNY grading in the same location were used as dependent variables. SPSS software version 18.0 was used for all statistical analyses. All p values were 2-tailed, and statistical significance was set at 0.05.

RESULTS

Patient characteristics. Baseline characteristics of the 68 patients included in ESpAC are shown in Table 1. MRI-SIJ and pelvic radiographs were obtained in all patients at baseline. Sixty-two patients (91%) had at least 1 followup MRI and 44 (65%) completed both followup MRI. Sixty-five patients (96%) had at least 1 followup pelvic radiograph and 48 (71%) completed both followup pelvic radiographs. In 10 of 68 patients (15%), adjudication of pelvic radiographs was considered necessary because of disagreement between the first 2 readers.

At baseline, 64 out of 68 patients (94%) fulfilled the European Spondyloarthropathy Study Group and/or Amor and/or ASAS axSpA classification criteria. Sixty-six patients (97%) fulfilled 4 of the 5 Calin criteria. The remaining 2 patients (3%) fulfilled 3 of the 5 Calin criteria and reported "night pain" as well. Forty patients (59%) fulfilled the ASAS axSpA criteria at baseline, of whom 22 fulfilled the imaging and clinical arm of the ASAS axSpA criteria; 9 patients fulfilled only the imaging arm and 9 other patients fulfilled only the clinical arm. Fifteen patients (22%) fulfilled the mNY criteria at baseline.

Structural changes on MRI-SIJ. Scores for BME on MRI-SIJ have been presented in a previous report¹¹. Tables 2 and 3 show the baseline and followup MRI findings for erosions and fatty lesions, respectively, and the relation with fulfillment of the mNY criteria and ASAS axSpA criteria at baseline, and HLA-B27 status.

At baseline, erosions and/or fatty lesions on MRI were detected in 17 patients (25%), of whom 71% were HLA-B27 positive and 9 (53%) fulfilled the mNY criteria. Erosions were detected in 12 (18%) out of 68 patients, of whom 8 (66%) also fulfilled the mNY criteria (Table 2).

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.

Table 1. Baseline characteristics of 68 patients included in the ESpAC. The values are expressed as number (percentage) of patients unless stated otherwise.

| Characteristic | All Patients, n = 68 | Patients with Complete MRI Followup Data, n = 44 | | |
|------------------------------------|-------------------------|--|--|--|
| Male sex | 26 (38) | 15 (34) | | |
| Age, yrs, mean (SD) | 34.9 (10.3) | 36.0 (11.7) | | |
| Median symptom duration, | | | | |
| mos (IQR) | 18 (12-24) | 18 (12-24) | | |
| HLA-B27-positive | 31 (46) | 17 (39) | | |
| History of IBD | 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, mg/l (SD) | 9 (11) | 9 (20) | | |
| Elevated CRP* | 16 (24) | 10 (22) | | |
| Mean ESR, mm/h (SD) | 13 (15) | 13 (30) | | |
| Elevated ESR* | 24 (35) | 13 (30) | | |
| Presence of BME on MRI-SIJ | 24 (35) | 14 (32) | | |
| Fulfillment of ESSG criteria | 58 (85) | 39 (89) | | |
| Fulfillment of Amor criteria | 48 (71) | 31 (70) | | |
| Fulfillment of ASAS axSpA criteria | a 40 (59) | 22 (50) | | |
| Fulfillment of mNY criteria | 15 (22) | 9 (20) | | |

* In 66 of 68 patients, baseline CRP and ESR measurements were available. ESR normal range: \leq 7 mm for males; \leq 12 mm for females. CRP cutoff value, normal range: < 10 mg/l. ESpAC: Early Spondyloarthritis Clinic; SpA: spondyloarthritis; IQR: interquartile range; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; BME: bone marrow edema; MRI-SIJ: magnetic resonance imaging of the sacroiliac joints; ESSG: European Spondyloarthropathy Study Group; ASAS: Assessment in SpondyloArthritis international Society; axSpA: axial spondyloarthritis; mNY criteria: modified New York criteria; IBD: inflammatory bowel disease. Fatty lesions were detected in 13 (19%) out of 68 patients, of whom 7 (54%) also fulfilled the mNY criteria (Table 3). Coexistence of both erosions and fatty lesions on MRI occurred in 8 out of 68 patients (9%), of whom 6 (75%) also fulfilled the mNY criteria.

During followup, 4 out of 51 patients (8%) with no signs of erosions at baseline and at least 1 followup MRI present had developed erosions. Of them, 2 patients were HLA-B27-positive and 3 had already fulfilled the mNY criteria at baseline (Table 2). In 2 of these 4 patients, the erosions were accompanied by simultaneous appearance of fatty lesions on MRI. Five out of 50 patients (10%) without fatty lesions at baseline and at least 1 followup MRI developed fatty lesions during followup. Four of them were HLA-B27-positive and 3 fulfilled the mNY criteria at baseline (Table 3).

In 1 out of 12 patients (8%) with erosions on MRI at baseline, the erosions were not detected at the 2-year timepoint (Table 2). In 3 out of 13 patients (23%) with fatty lesions on MRI at baseline, the fatty lesions were not detected during followup (Table 3).

Structural changes on pelvic radiographs. At baseline, 15 patients (22%) fulfilled the mNY criteria for radiographic sacroiliitis, of whom 80% were HLA-B27-positive. Eight of these 15 patients (53%) also had BME at baseline and in 9 patients (60%), erosions and/or fatty lesions were detected on MRI. During followup no changes in mNY grading were found in these 15 patients. Four patients who fulfilled the mNY criteria at baseline developed new erosions and/or fatty lesions on MRI (Tables 2 and 3). No patients were newly classified with radiographic sacroiliitis according to the mNY criteria at followup.

| Table 2. Erosions on MRI-SIJ at baseline and during for | ollowup. |
|---|----------|
|---|----------|

| No. Patients | Baseline | MRI-SIJ 1 Year | 2 Years | mNY Criteria + ^a | ASAS axSpA Criteria+ ^b | HLA-B27+ ^c |
|--------------|----------|-------------------|---------|-----------------------------|---|-----------------------|
| 5 | + | + | + | 3 | 4 | 4 |
| 2 | + | + | NA | 1 | 2 | 2 |
| 3 | + | NA | + | 2 | 3 | 1 |
| 1 | + | + | - | 1 | 1 | 1 |
| 1 | + | NA | NA | 1 | 1 | 1 |
| 35 | _ | _ | - | 3 | 14 | 11 |
| 11 | _ | _ | NA | 1 | 7 | 6 |
| 1 | _ | _ | + | 1 | 1 | 1 |
| 2 | _ | + | + | 1 | 2 | 0 |
| 1 | _ | + | NA | 1 | 1 | 1 |
| 1 | _ | NA | _ | 0 | 1 | 0 |
| 5 | _ | NA | NA | 0 | 3 | 3 |

No. patients with present or absent signs of erosions on MRI-SIJ at baseline and during followup is shown. ^a No. patients who fulfill the mNY criteria at baseline. ^b No. patients who fulfill the ASAS axSpA criteria at baseline. ^c No. patients HLA-B27 positive. + = structural changes present; - = structural changes absent. NA: MRI not available; MRI-SIJ: magnetic resonance imaging of the sacroiliac joints; mNY criteria: modified New York criteria; ASAS axSpA criteria: Assessment in SpondyloArthritis international Society axial spondyloarthritis criteria.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.

The Journal of Rheumatology 2014; 41:6; doi:10.3899/jrheum.131022

Table 3. Fatty lesions on MRI-SIJ at baseline and during followup.

| No. Patients | | MRI-SIJ | | mNY Criteria + ^a | ASAS axSpA | HLA-B27+ ^c | |
|--------------|----------|---------|---------|-----------------------------|------------------------|-----------------------|--|
| Η | Baseline | 1 Year | 2 Years | | Criteria+ ^b | | |
| 6 | + | + | + | 3 | 5 | 5 | |
| 2 | + | + | NA | 1 | 2 | 2 | |
| 1 | + | NA | + | 1 | 1 | 0 | |
| 1 | + | NA | _ | 0 | 1 | 0 | |
| 2 | + | _ | + | 1 | 2 | 1 | |
| 1 | + | NA | NA | 1 | 1 | 1 | |
| 35 | _ | _ | _ | 4 | 14 | 11 | |
| 9 | _ | _ | NA | 1 | 5 | 4 | |
| 1 | _ | NA | _ | 0 | 1 | 0 | |
| 1 | _ | + | + | 1 | 1 | 0 | |
| 3 | _ | + | NA | 1 | 3 | 3 | |
| 1 | _ | NA | + | 1 | 1 | 1 | |
| 5 | _ | NA | NA | 0 | 3 | 3 | |

^a No. patients who fulfill the mNY criteria at baseline. ^b No. patients who fulfill the ASAS axSpA criteria at baseline. ^c No. patients who are HLA-B27 positive. + = structural changes present; - = structural changes absent. NA: MRI not available; MRI-SIJ: magnetic resonance imaging of the sacroiliac joints; mNY criteria: modified New York criteria; ASAS axSpA criteria: Assessment in SpondyloArthritis international Society axial spondyloarthritis criteria.

Association between BME and structural changes on MRI-SIJ. The first analysis was a GEE analysis (scores of 58 patients with at least 2 successive timepoints available included) showing that the number of erosions per patient increased significantly during followup [estimated marginal (EM) mean score of 2.5 at baseline, 3.3 at 1-year followup and 3.5 at 2-year followup; p = 0.05]. There was also a trend for an increase in the number of fatty lesions (EM mean score of 5.4 at baseline, 7.7 at 1-year followup, and 8.5 at 2-year followup; p = 0.06).

The second analysis was a GEE analysis per SIJ (2 per patient) showing an association between BME and the development of fatty lesions on MRI (Table 4). An association between BME and subsequent development of erosions on MRI could not be proven (Table 4).

The third analysis was a detailed descriptive analysis at the level of quadrants of SIJ, to investigate the association between the presence of BME and the development of erosions and/or fatty lesions at the same site. This analysis was done to investigate how an inflammatory lesion at a particular site associates with the development of a structural lesion at the same site. Every patient had 8 quadrants (4 left and 4 right) available for comparison.

The starting point of this analysis was the presence of BME. Continuous presence of BME over time versus resolution of BME was taken into consideration. The results of this analysis, which are presented in Table 5, show that an increase of fatty lesions preferentially occurs in quadrants in which BME has resolved over time (55%) in comparison with quadrants in which BME has persisted over time (26%). With regard to the development of erosions, such a disparity could not be confirmed (26% vs 30%).

DISCUSSION

Our study demonstrated that BME on MRI-SIJ is associated with the development of fatty lesions in a cohort of patients with early IBP. Such an association could not be demonstrated for erosions, despite a significant overall numerical increase of erosions over time. Further, about 10% of the patients without erosions and fatty lesions at baseline developed new structural changes on MRI during the 2-year followup period.

Table 4. GEE analysis (continuous MRI-SIJ score) showing association between bone marrow edema on MRI-SIJ and the development of structural changes on MRI-SIJ during followup.

| Per Joint An | OR (95% CI) | р | | |
|---|---|--|--|------------------------------|
| MRI Development of Structural Changes (per-unit change) | Fatty Degeneration, per unit Erosions, per unit | Right SIJ Left SIJ Right SIJ Left SIJ | 3.13 (1.06–9.20) 22.13 (1.27–384.50) 0.24 (0.07–8.24) 1.24 (0.09–18.03) | 0.04 0.03 0.43 0.88 |

N = 58. GEE: generalized estimated equation; MRI-SIJ: magnetic resonance imaging of the sacroiliac joints.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.

Table 5. Presence of bone marrow edema on MRI at baseline and followup in relation to the subsequent development of fatty lesions and erosions at the same sacroiliac joint quadrant.

| Baseline | | | Last Followup MRI* | | | | |
|---------------|---------------|----------------|---|---------------|--|--|--|
| | BME (present) | BME (present)* | BME Present AND Increase of FL at the Same Quadrant (%) | BME (absent)* | BME Absent AND Increase of FL at the Same Quadrant (%) | | |
| All Quadrants | 89 | 47 | 12 of 47 SI quadrants (26) | 42 | 23 of 42 SI quadrants (55) | | |
| | BME (present) | BME (present) | BME Present AND Increase of Erosions at the Same Ouadrant | BME (absent) | BME Absent AND Increase of Erosions at the Same Quadrant | | |
| All Quadrants | 89 | 47 | 14 of 47 SI quadrants (30) | 42 | 11 of 42 SI quadrants (26) | | |

N = 62 patients. * Followup at 1 or 2 years, depending on last MRI. SIJ: sacroiliac joint; BME: bone marrow edema; FL: fatty lesion; MRI: magnetic resonance imaging.

An increase in the number of structural changes on MRI over time was demonstrated in a previous study evaluating MRI-SIJ abnormalities in patients with early axSpA¹³. In that study by Madsen, et al, 80 out of 94 patients (85%) with axSpA had erosions and fatty lesions present on MRI at baseline. After a mean followup period of 51 months, both the number of erosions and fatty lesions significantly increased¹³. We also found a significant increase in the number of erosions, as well as a strong trend for an increase in the number of fatty lesions. In the study by Madsen, et al, the proportion of patients with structural changes was higher at baseline compared with our cohort (85% vs 25%), and their followup duration was longer, which might explain the difference in time trends found for fatty lesions. The presence of fatty lesions might also be underestimated in our study because the presence of intense BME may prevent the detection of fatty lesions owing to counteracting MR signals on the T1 MRI sequence (BME low-signal intensity; fatty lesions high-signal intensity)⁴.

In our present study, we demonstrated statistically an association between the presence of BME and the subsequent development of fatty lesions on MRI. Even more important is the indication that these fatty lesions seem to have preferentially occurred at the sites (quadrants) in which existing BME has resolved over time. This is entirely in line with existing theories about the role of fatty lesions as a repair reaction in response to inflammatory triggers. A study by Song, et al⁴ described an association between disappearance of BME on MRI in both the SIJ and spine and the subsequent appearance of fatty lesions on MRI in patients with early axial SpA treated with either etanercept or sulfasalazine over a 1-year followup period. In patients in whom BME resolved, fatty lesions occurred in 10.5% of the SIJ quadrants 1 year later, but in those in whom BME persisted, fatty lesions occurred in only 2.4% of the SIJ quadrants 1 year later⁴. In a study by Maksymowych, et al, 76 patients with axSpA were followed for 1 year with repeated MRI of the spine¹⁴. The chance of developing new fatty lesions was significantly higher at vertebral corners with BME at baseline compared to vertebral corners without BME at baseline (18% vs 3%)¹⁴. A correlation between BME and the subsequent development of fatty lesions on MRI-SIJ could not be demonstrated in the SPondylo-Arthritis Caught Early (SPACE)-cohort over a 3-month followup period¹⁵. This last finding suggests that a longer followup period is necessary before fatty lesions can be detected in response to subsiding BME.

While we found an increase in the number of erosions in our study, we failed to demonstrate a significant association between the presence of BME and the development of erosions. A possible explanation is that the erosions occur independently of inflammation. Larger cohorts are necessary to provide sufficient statistical power to clarify the relation between BME and development of both fatty lesions and erosions.

The rate of development from nonradiographic to radiographic axSpA in patients with a clinical diagnosis of axSpA without signs of radiographic sacroiliitis is estimated to be about 10% per 2 years¹⁶. In patients with BME on MRI-SIJ, this percentage increases to around 20% per 2 years¹⁷. Our study failed to demonstrate an association between BME and development of structural changes detected on pelvic radiographs, nor could we demonstrate a change in the level of sacroiliitis according to the mNY criteria during the 2-year followup. The short followup period and the relatively small sample size may have hindered detection of these changes.

There are several concerns when assessing structural changes of the SIJ on either an MRI or pelvic radiograph, and it is debatable which imaging modality is approaching the truth or whether they are complementary. Both imaging modalities are subject to observer errors, and especially the evaluation of pelvic radiographs may be hampered by projection artifacts and poor visibility^{18,19}. Erosions on MRI may not be reliably detected if the slice thickness is too big, or movement artifacts may limit an accurate image interpretation. The natural irregular shape of the cortical lining of the SIJ may also limit detection of erosions. In our study, of

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.

The Journal of Rheumatology 2014; 41:6; doi:10.3899/jrheum.131022

the 15 patients with sacroiliitis on pelvic radiographs according to independent readers, erosions and/or fatty lesions on MRI were detected in only 9 (60%) at baseline. The majority of the patients who developed new erosions and/or fatty lesions on MRI during followup already fulfilled the mNY criteria at baseline.

Some limitations of our study need to be addressed. First, the MRI were scored by 1 reader only, which may in theory influence the reliability of the data. However, the reader was very experienced and the MRI scores showed a high consistency over time despite scoring each MRI set independently and blinding of the reader for time order. Further, and in contrast to scoring pelvic radiographs, a number of studies have shown a rather high interobserver agreement when scoring MRI-SIJ^{9,20}. Second, in our present study, the T1 and STIR sequences were simultaneously scored for active lesions and structural changes. This scoring method could have resulted in reader bias, because the presence of BME on the STIR sequence may possibly have triggered the reader to screen more carefully for structural changes on the T1 sequence or vice versa. This may influence the sensitivity for scoring structural changes on MRI-SIJ. In 16 of the 17 patients with erosions and/or fatty lesions at baseline, concomitant BME was also found. However, one could also postulate that concomitant BME decreases the specificity of scoring structural changes on MRI, because a reader is more likely to score an indeterminate lesion as a structural change. Scoring the T1 and STIR sequence independently could possibly lower the risk of reader bias when evaluating the presence of active lesions and structural changes on MRI-SIJ. Third, in the MRI scoring system we used, we applied an unlimited number of evaluated slices. Serial image acquisition of the same anatomical region offers advantages to monitor changes over time. However, this scoring method may be limited by the possibility of misalignment between 2 successive MRI examinations, which may cause measurement error. Last, ESpAC is a relatively small cohort with selected patients. Patients were referred by (related) medical specialties (i.e., dermatology, gastroenterology) and through family members of the local ankylosing spondylitis society. This referral strategy may explain the relative high proportion of patients with extraaxial manifestations and/or positive family history for SpA. As a consequence, a high proportion of patients fulfilled at least one of the classification criteria for SpA. Further, the proportion of female patients in ESpAC was relatively high (62%) and the proportion of patients with a positive HLA-B27 status was relatively low (46%). However, these percentages are in accordance with other cohorts that included patients with early IBP^{21,22}. Nevertheless, extrapolation of the study findings should be done with caution.

In this cohort of patients presenting with IBP of recent onset and suspected for axSpA, the number of patients with erosions and fatty lesions detected on MRI-SIJ remained relatively stable during the 2 years of followup, but the overall number of MRI erosions in patients who already had erosions at baseline increased. Signs of BME on MRI, and especially the resolution of it, were significantly correlated with the development of fatty lesions on MRI, but not with the development of structural changes visible on pelvic radiographs.

REFERENCES

- Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al. The development of Assessment of Spondyloarthritis international society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 2009;68:777-83.
- Rudwaleit M, Jurik AG, Hermann KG, Landewé R, van der Heijde D, Baraliakos X, et al. Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by the ASAS/OMERACT MRI group. Ann Rheum Dis 2009:68:1520-7.
- Weber U, Zubler V, Pedersen SJ, Rufibach K, Lambert RG, Chan SM, et al. Development and validation of an MRI reference criterion for defining a positive SIJ MRI in spondyloarthritis. Arthritis Care Res 2013;65:977-85.
- 4. Song IH, Hermann KG, Haibel H, Althoff CE, Poddubnyy D, Listing J, et al. Relationship between active inflammatory lesions in the spine and sacroiliac joints and new development of chronic lesions on whole-body MRI in early axial spondyloarthritis: results of the ESTHER trial at week 48. Ann Rheum Dis 2011;70:1257-63.
- Heuft-Dorenbosch L, Landewé R, Weijers R, Houben H, van der Linden S, Jacobs P, et al. Performance of various criteria sets in patients with inflammatory back pain of short duration; the Maastricht early spondyloarthritis clinic. Ann Rheum Dis 2007;66:92-8.
- Heuft-Dorenbosch L, Landewé R, Weijers R, Wanders A, Houben H, van der Linden S, et al. Combining information obtained from magnetic resonance imaging and conventional radiographs to detect sacroiliitis in patients with recent onset inflammatory back pain. Ann Rheum Dis 2006;65:804-8.
- Heuft-Dorenbosch L, Weijers R, Landewé R, van der Linden S, van der Heijde D. Magnetic resonance imaging changes of sacroiliac joints in patients with recent-onset inflammatory back pain. Arthritis Res Ther 2006;8:R11.
- Calin A, Porta J, Fries JF, Schurman DJ. Clinical history as a screening test for ankylosing spondylitis. JAMA 1977;237:2613-4.
- Maksymowych WP, Inman RD, Salonen D, Dhillon SS, Williams M, Stone M, et al. Spondyloarthritis research consortium of Canada magnetic resonance imaging index for assessment of sacroiliac joint inflammation in ankylosing spondylitis. Arthritis Rheum 2005;53:703-9.
- Puhakka KB, Jurik AG, Egund N, Schiottz-Christensen B, Stengaard-Pedersen K, van Overeem Hansen G, et al. Imaging of sacroiliitis in early seronegative spondyloarthropathy. Assessment of abnormalities by MR in comparison with radiography and CT. Acta Radiol 2003;44:218-29.
- 11. Van Onna M, Jurik AG, van der Heijde D, van Tubergen A, Heuft-Dorenbosch L, Landewé R. HLA-B27 and gender independently determine the likelihood of a positive MRI of the sacroiliac joints in patients with early inflammatory back pain: A two-year MRI follow-up study. Ann Rheum Dis 2011;70:1981-5.
- Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York Criteria. Arthritis Rheum 1984;27:361-8.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.

1093

van Onna, et al: Structural changes on MRI-SIJ

- Madsen KB, Schiøttz-Christensen B, Jurik AG. Prognostic significance of magnetic resonance imaging changes of the sacroiliac joints in spondyloarthritis—a follow-up study. J Rheumatol 2010;37:1718-27.
- Maksymowych WP, Morency N, Conner-Spady B, Lambert RG. Suppression of inflammation and effects on new bone formation in ankylosing spondylitis: evidence for a window of opportunity in disease modification. Ann Rheum Dis 2013;72:23-8.
- 15. De Hooge M, Van den Berg R, Navarro Compán MV, Reijnierse M, Van Gaalen F, Fagerli KM, et al. Do bone marrow edema (BME) lesions in the sacroiliac joint (SIJ) change into fatty lesions over a 3-month period in patients with axial spondyloathritis (axSpA) [abstract]? Ann Rheum Dis 2013;72 Suppl:656.
- Poddubnyy D, Rudwaleit M, Haibel H, Listing J, Märker-Hermann E, Zeidler H, et al. Rates and predictors of radiographic sacroiliitis progression over 2 years in patients with axial spondyloarthritis. Ann Rheum Dis 2011;70:1369-74.
- Sieper J, van der Heijde D. Review: Nonradiographic axial spondyloarthritis: new definition of an old disease? Arthritis Rheum 2013;65:543-51.
- 18. Braun J, Sieper J, Bollow M. Imaging of sacroiliitis. Clin Rheumatol 2000;19:51-7.

- Van Tubergen A, Heuft-Dorenbosch L, Schulpen G, Landewé R, Wijers R, van der Heijde D, et al. Radiographic assessment of sacroiliitis by radiologists and rheumatologists: does training improve quality? Ann Rheum Dis 2003;62:519-25.
- 20. Weber U, Maksymowych WP, Jurik AG, Pfirrmann CW, Rufibach K, Kissling RO, et al. Validation of whole-body against conventional magnetic resonance imaging for scoring acute inflammatory lesions in the sacroiliac joints of patients with spondylarthritis. Arthritis Rheum 2009;61:893-9.
- 21. van den Berg R, de Hooge M, Rudwaleit M, Sieper J, van Gaalen F, Reijnierse M, et al. ASAS modification of the Berlin algorithm for diagnosing axial spondyloarthritis: results from the SPondyloArthritis Caught Early (SPACE)-cohort and from the Assessment of SpondyloArthritis international Society (ASAS)-cohort. Ann Rheum Dis 2013;72:1646-53.
- 22. Dougados M, d'Agostino MA, Benessiano J, Berenbaum F, Breban M, Claudepierre P, et al. The DESIR cohort: a 10-year follow-up of early inflammatory back pain in France: study design and baseline characteristics of the 708 recruited patients. Joint Bone Spine 2011;78:598-603.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2014. All rights reserved.