Combining information obtained from MRI and conventional radiographs in order to detect sacroiliitis in patients with recent-onset inflammatory back pain

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Abstract
Aim: To compare the contribution of changes on MRI and changes on conventional radiography (CR) in SI joints of patients with recent onset inflammatory back pain (IBP) in making an early diagnosis of SpA.

Materials and Methods: 68 patients with IBP (38% male; mean age 34.9 year (SD 10.3)) were included if symptom duration was <2 years. Coronal MRI scans of the SI joints were scored for inflammation and structural changes and pelvic radiographs were scored according to the modified New York grading (mNY). Agreement between MRI and CR was analysed by cross-tabulation per SI joint and per patient.

Results: A structural change was detected in 20 SI-joints by MRI and in 37 SI joints by CR. Inflammation was detected in 36 SI-joints by MRI, and 22 of these joints showed radiographic sacroiliitis. Fourteen patients fulfilled the mNY criteria based on CR. Based on structural changes on MRI 8 patients would fulfil the mNY criteria, 14 (partly different patients as with CR) based on MRI for inflammation only, 16 based on MRI for inflammation and structural changes combined, 19 based on CR combined with MRI for inflammation, and 19 (same patients) based on CR combined with MRI for inflammation and structural changes.

Conclusions: CR can detect structural changes in SI joints with higher sensitivity than MRI. But inflammation on MRI can be found in a substantial proportion of patients with IBP with (yet) normal radiographs. Assessment of structural changes by CR followed by assessment of inflammation on MRI in patients with negative findings gives the highest returns in terms of detecting involvement of the SI joints by imaging in patients with recent onset IBP.
Introduction

Ankylosing spondylitis (AS) is the prototype disease in the group of spondyloarthritides (SpA). For the classification of patients as having AS according to the most widely used criteria, the modified New York criteria (mNY), radiographic sacroiliitis is obligatory. (1) A classification as SpA can also be made without sacroiliitis on radiographs, according to the Amor or European Spondylarthropathy Study Group (ESSG) criteria. (2, 3) It has been hypothesised that SpA with axial involvement not (yet) fulfilling the modified New York criteria may involve an earlier and less severe part of the spectrum of AS. (4)

Making an early diagnosis of SpA with axial involvement is challenging. One of the reasons is that sacroiliitis on radiographs is a rather late phenomenon and difficult to interpret reliably. (5) Magnetic resonance imaging (MRI) has been proposed as an imaging method to detect sacroiliitis earlier. (6) MRI can provide insight in both inflammation as well as in structural changes caused by inflammation, while radiographs show only structural changes. MRI may be particularly useful in making a diagnosis of SpA in patients presenting with inflammatory back pain (IBP). In the present study we compared the performance of MRI and conventional radiographs (CR) of SI joints in patients with recent onset IBP with a relatively high level of suspicion of SpA. We compared both imaging modalities with respect to structural changes, and we compared inflammation on MRI and structural changes on CR. Comparisons were made on the level of single joints and on the level of patients, by applying the mNY criteria by substituting CR information by MRI information in the radiographic criterion.

Methods

Patients

Patients with inflammatory low back pain present for 2 years at most, were eligible to this study. IBP was defined according to the Calin criteria which are positive if 4 out of the 5 following characteristics are present: insidious onset; onset before the age of 40 years; persistence for at least 3 months; association with morning stiffness; and improvement with exercise. (7) Patients could also be included if 3 out of 5 criteria were present plus night pain. Preferably, but not obligatory, patients should have at least one feature of SpA according to the ESSG criteria: presence of a family member with AS; presence or history of psoriasis, inflammatory bowel disease (IBD) or uveitis. The study was approved by the institutional review board and all patients gave written informed consent.

MRI

A MRI examination of the sacroiliac joints was performed using a 1.5 Tesla Philips Gyro scan ACS-NT (Philips, Best, the Netherlands). Patients were scanned in supine position using a Synergy-spine coil as surface coil. We chose a coronal oblique scan plane parallel to the length of the sacrum and two slabs: one transversal slab positioned cranially to the region of interest to diminish flow-artefacts, and one frontally through the bowel and anterior abdominal wall, to diminish motion artefacts of breathing and bowel movements. The following sequences were used: T1- weighted Spin Echo (SE), Short Tau Inversion Recovery (STIR), T2-weighted fast SE with fat sat and T1 -weighted SE with fat suppression after the intravenous administration of contrast medium (Gadolinium diethylenetriaminepentate (Gd), 0.1 mmol/kg body weight).

Inflammation was scored for each SI joint in joint space, subchondral bone, bone marrow, ligaments and joint capsule. Inflammation was defined as a low signal intensity on T1, with enhancement after Gd-administration, and/or high signal intensity on STIR and/or T2 fast SE. Inflammation in ligaments was defined as areas of low signal intensity running trough high signal intensity tissue on T1, which reflects interosseous ligaments crossing juxta-articular
fatty tissue. Structural changes (erosions, sclerosis, ankylosis) were scored in joint space, subchondral bone, and bone marrow. Each SI joint was labelled as showing inflammation or structural changes if these respective features were present in at least one of the investigated areas. Each set of MRIs was scored independently by two observers, who were blind for the patient identity and for clinical, laboratory and radiological data. All joints that showed a discrepancy between the readers for inflammation and/or structural damage were offered to a third reader. In total 21 discrepant joints were scored for the assessment of structural changes. The final score attributed to the joint was based on a 2 out of 3 majority score. A similar process was followed for discrepancies in inflammation. For this purpose 25 discrepant joints were offered to a third reader.

Conventional radiography
Antero-posterior conventional pelvic radiographs were scored independently by two observers, who were not involved in the MRI reading, without knowledge of clinical information, according to the mNY criteria (from zero (normal) to 4 (complete ankylosis))(1). In case of a discrepancy between the readers a third reader (who was not involved in the MRI scoring) scored the SI joint. In total 42 discrepant SI joints were offered to the third reader. A final score for each SI joint was assigned on the basis of the majority score of the three observers.

Analysis
For CR, the scores were dichotomized. A SI joint with a majority score of 0 or 1 was considered as normal; a SI joint with a majority score of 2 or higher was considered as having radiographic sacroiliitis. For fulfilment of the mNY criteria we also substituted CR information by MRI information in five different ways so that patients could fulfil the mNY criteria as follows; 1) according to the original method based on radiographs; 2) based on structural changes present on MRI in both SI joints; 3) based on inflammation present on MRI in both SI joints; 4) based on inflammation and/or structural changes present on MRI in both SI joints; 5) based on structural changes on CR combined with inflammation with or without structural changes on MRI in both SI joints. If based on radiographs patients with bilateral grade 2 sacroiliitis, or at least unilateral grade 3 sacroiliitis were classified as fulfilling the mNY criteria. If based on MRI, the mere presence of structural damage for definition 2, the mere presence of inflammation for definition 3, or one of both for definition 4 were considered sufficient, and severity or extent of the lesions was ignored. For definition 5 the grading for CR and presence of inflammation on MRI were combined. Agreement between structural changes on MRI and sacroiliitis on CR as well as agreement between inflammation on MRI and sacroiliitis on CR was analysed by cross tabulation. This was done both per SI joint and per classification according to the mNY criteria. Specificity, sensitivity and positive and negative predictive values were calculated with CR as gold standard.

Results
Patients
The characteristics of the 68 patients included in the study are presented in Table 1. Fifteen patients (22%) did not have any of the additional SpA features. Of these 15 patients, seven were HLA B27 positive. Fifty-seven patients fulfilled the ESSG criteria, 48 fulfilled the Amor criteria, and 43 fulfilled both sets of criteria.
Table 1. Baseline characteristics of 68 patients with chronic inflammatory low back pain

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (N=68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (% male)</td>
<td>38</td>
</tr>
<tr>
<td>Mean age (SD) [years]</td>
<td>34.9 (10.3)</td>
</tr>
<tr>
<td>Symptom duration [months] (Median) [IQR]</td>
<td>18.0 [12.0-24.0]</td>
</tr>
</tbody>
</table>

Criteria for inflammatory low back pain:

- 3 criteria present [%] 56
- 4 criteria present [%] 41
- 5 criteria present [%] 3
- Night pain present [%] 96
- HLA-B27 present [%] 46
- History of inflammatory bowel disease present [%] 15
- History of uveitis present [%] 15
- History of psoriasis present [%] 24
- Family history of ankylosing spondylitis present [%] 37
- Fulfilling ESSG criteria 84%
- Fulfilling Amor criteria 71%
- Fulfilling both ESSG and Amor criteria 63%

† 45 of the 47 patients in whom night pain was explored reported confirmatory.

Adjudication for structural and inflammatory changes on MRI

After the read of the two observers, there was agreement on the presence of structural changes in 17 joints, and on the absence of structural changes in 98 joints. Adjudication of 21 joints with a discrepancy for structural changes led to a positive assignment of erosions in 3 joints. One joint was scored positive in a patient in which already the other joint was scored positive, and the other two joints were in one patient that was scored as having structural changes by one of the two readers in the original read in both joints.

There was agreement on the presence of inflammation in 32 joints, and on the absence of inflammation in 79 joints after the read of the two observers. Adjudication of 25 joints with a discrepancy for inflammatory changes led to an assignment of inflammation in 4 joints. These 4 joints all occurred in patients in which both readers already considered unilateral inflammatory changes present. Adjudication did not yield additional patients with inflammation.

Adjudication for changes on CR

There was agreement on the presence of sacroiliitis in 29 SI-joints, and on the absence of sacroiliitis in 65 SI-joints. The adjudication of the 42 discrepant joints led to the assignment of 8 joints as positive for sacroiliitis. In 4 patients adjudication resulted in fulfilment of the mNY criteria, as these patients showed already grade 2 abnormalities in the contra-lateral SI joint.
Abnormalities on MRI
In total, twenty SI joints in 12 patients showed structural changes on MRI (Tables 2a and 2b). Thirty-six joints in 22 patients showed signs of inflammation on MRI (Tables 3a and 3b). Twelve of these 22 patients also had structural changes on MRI. None of the patients had structural changes on MRI without inflammation.

Table 2a. Single SI-joint analysis comparing structural changes observed on MRI with structural changes on conventional radiographs based on the modified New York criteria

<table>
<thead>
<tr>
<th>Structural changes on MRI</th>
<th>Radiographs of SI-joint*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>abnormal</td>
<td>normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>18</td>
<td>2</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>19</td>
<td>97</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>99</td>
<td>136</td>
<td></td>
</tr>
</tbody>
</table>

* Patients fulfilled the modified New York criteria on MRI if structural changes were present and on CR if bilateral at least grade 2 or unilateral at least grade 3

Table 2b. Per patient analysis comparing structural changes observed on MRI with structural changes on conventional radiographs based on the modified New York criteria

<table>
<thead>
<tr>
<th>Structural changes on MRI</th>
<th>Radiographs of SI-joint*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sacroiliitis</td>
<td>normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>present in both SI-joints</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>present in one SI-joint</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>4</td>
<td>52</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>14</td>
<td>54</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

Table 3a. Per joint analysis comparing inflammation observed on MRI with structural changes on conventional radiographs based on the modified New York criteria

<table>
<thead>
<tr>
<th>Inflammation on MRI</th>
<th>Radiographs of SI-joint*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sacroiliitis</td>
<td>normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>present</td>
<td>22</td>
<td>14</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>15</td>
<td>85</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>37</td>
<td>99</td>
<td>136</td>
<td></td>
</tr>
</tbody>
</table>

Table 3b. Per patient analysis comparing inflammation observed on MRI with structural changes on conventional radiographs based on the modified New York criteria

<table>
<thead>
<tr>
<th>Inflammation on MRI</th>
<th>Radiographs of SI-joint*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sacroiliitis</td>
<td>normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>present in both SI-joints</td>
<td>9</td>
<td>5</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>present in one SI-joint</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>2</td>
<td>44</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>14</td>
<td>54</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

* Radiographs of the SI-joints were scored according to the modified New York criteria, which were met if bilateral grade 2 or unilateral grade 3 or 4 Sacroiliitis was scored.
Abnormalities on CR
On CR 37 SI-joints of 23 patients showed radiographic sacroiliitis; 28 SI joints grade 2, and 9 SI joints grade 3. Fourteen patients fulfilled the radiographic criterion of the mNY criteria for AS: nine patients due to bilateral grade 2 sacroiliitis; 4 patients because of bilateral grade 3 sacroiliitis, and the remaining patient because of grade 2 and grade 3 sacroiliitis combined. The remaining 9 patients showed unilateral grade 2 sacroiliitis.

MRI findings compared with radiographic findings
A comparison between structural changes on MRI and CR is presented in Tables 2a and 2b. In total 12 patients showed structural changes on MRI: 8 in both joints and 4 in one joint. In 20 SI-joints structural changes on MRI were detected, as compared to 37 SI-joints with radiographic sacroiliitis (54%). In two SI-joints that were normal on CR, structural changes were scored on MRI. If radiographic sacroiliitis graded according to the mNY criteria is considered the gold standard, the sensitivity of detecting chronic changes by MRI per SI joint is 49% (18/37) and the specificity is 98% (97/99). Corresponding positive predictive value and negative predictive value were 90% and 84% respectively.

Only 8 of the 14 patients (57%) fulfilling the mNY criteria for AS would fulfil the radiographic criterion if this was based on the presence of structural changes on MRI (Table 2b), but 9 of these 14 patients had signs of inflammation on MRI in both joints and 3 in one joint (Table 3). The 2 remaining patients showed only structural changes on MRI in one joint. In 22 of the 37 SI-joints with radiographic sacroiliitis (59%) inflammation was observed on MRI (Table 3a). Of the 9 patients with unilateral radiographic sacroiliitis, only one patient had signs of inflammation on MRI (in both SI joints). Of the 36 SI-joints with inflammation on MRI (17 left, 19 right) radiographic sacroiliitis was detected in 22 SI-joints (61%; 11 left and 11 right).

If we consider either inflammation or structural changes on MRI as positive findings and compare this to radiographic abnormalities, there is only a small gain as compared to the information provided by inflammation alone (Tables 4a and 4b). Two more joints with MRI abnormalities could be identified, that appeared to be concordant with the findings on the radiographs. This resulted in two more patients fulfilling the mNY criteria. Based on the combined information of either inflammation or structural changes on MRI 11 of the 14 patients (79%) can be picked up that fulfil the mNY criteria according to CR and another 5 patients showing abnormalities on MRI while there were no abnormalities on CR. Based on MRI findings 16 patients would fulfil the mNY criteria. If we combine the information obtained by CR with that obtained by MRI, 19 patients would fulfil the mNY criteria. In addition there are 5 patients showing abnormalities on MRI in a single joint in patients not fulfilling the mNY criteria on CR. CR in combination with inflammation on MRI, or CR in combination with inflammation and structural changes on MRI is equally informative.

Summarising the above mentioned information, classification according to the mNY criteria would be justified for 8 patients, if classification is based on MRI for structural changes only, 14 patients if classification is based on structural changes on CR, 14 (partly) different patients if classification is based on MRI for inflammation only, 16 patients if classification is based on MRI for inflammation and structural changes, 19 patients if classification is based on CR combined with MRI for inflammation, and 19 patients (the same patients as for CR combined with MRI inflammation only) if classification is based on CR combined with MRI for inflammation and structural damage. All patients defined as fulfilment of the radiographic mNY criteria according to the various definitions fulfil both the ESSG and the Amor criteria, except one patient with bilateral inflammation on MRI, but without structural changes on MRI or CR, who did not fulfil any of the SpA criteria. This patient, which presented with
arthritis and was HLA-B27 positive, would fulfil the ESSG criteria and the Amor criteria if MRI inflammation would substitute structural changes on CR with a similar weight. In the 6 patients with structural changes on CR but not on MRI, other than radiographic features made these patients fulfil the ESSG and Amor criteria.

Table 4a. Per joint analysis comparing inflammation or structural changes observed on MRI with structural changes on the conventional radiograph based on the modified New York criteria

<table>
<thead>
<tr>
<th>Inflammation and/or structural changes on MRI</th>
<th>Radiographs of SI-joint*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sacroiliitis</td>
<td>normal</td>
</tr>
<tr>
<td>present</td>
<td>24</td>
<td>14</td>
</tr>
<tr>
<td>absent</td>
<td>13</td>
<td>85</td>
</tr>
<tr>
<td>total</td>
<td>37</td>
<td>99</td>
</tr>
</tbody>
</table>

Table 4b. Per patient analysis comparing inflammation or structural changes observed on MRI with structural changes on the conventional radiograph based on the modified New York criteria

<table>
<thead>
<tr>
<th>Inflammation and/or structural changes on MRI</th>
<th>Radiographs of SI-joint*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sacroiliitis</td>
<td>normal</td>
</tr>
<tr>
<td>present in both SI-joints</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>present in one SI-joint</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>absent</td>
<td>2</td>
<td>44</td>
</tr>
<tr>
<td>total</td>
<td>14</td>
<td>54</td>
</tr>
</tbody>
</table>

* Radiographs of the SI-joints were scored according to the modified New York criteria, which were met if bilateral grade 2 or unilateral grade 3 or 4 Sacroiliitis was scored.

Discussion
The comparison of abnormalities of SI joints found on MRI and on CR in patients with recent onset IBP yielded important information. First, radiographs are more sensitive than MRI in the detection of structural changes. Second, the majority of the joints showing structural changes on MRI and/or CR also show inflammation on MRI, as did almost all patients with sacroiliitis on CR. Third, quite a number of patients show inflammation on MRI, but without signs of structural changes on either MRI or CR. Combining this information may lead to several conclusions.

To start with, the data add to the hypothesis that inflammation comes first, and structural changes are a subsequent feature. Depending on the lag time between inflammation and structural changes, a diagnosis of sacroiliitis could be made importantly earlier by using MRI inflammation as an early sign of disease. The real causality between MRI inflammation and radiographic sacroiliitis has to be proven in a longitudinal analysis, which will be possible with this cohort once follow up images have been made.

Another, rather unexpected conclusion is that CR is the preferred method for the assessment of structural changes in SI joints. We postulated CR as the gold standard for assessing structural changes. This is arguable for two reasons: CR may either overestimate or underestimate structural changes. In case of underestimation of structural changes by CR, MRI is performing worse as compared to what we already demonstrated. Overestimation of structural changes cannot be ruled out, but is considered unlikely as 12 of the 14 patients fulfilling the mNY criteria show either inflammation or structural changes in one or both SI
joints on MRI (MRI confirms CR), and all these patients fulfil the ESSG and the Amor criteria for SpA. We selected CR as comparator as this is the most widely used method in clinical practice to make a diagnosis of sacroiliitis. It is know that Computer Tomography is a more sensitive method to detect structural changes but if true in this cohort, the difference with MRI would even be larger. Combining information on inflammation and structural changes from MRI seems the most logical way to use the information in clinical practice. By doing so, still only 11 of the 14 patients classified as fulfilling the mNY criteria according to CR can be classified according to MRI. If we would use information from MRI only (both inflammation and structural changes), another 5 patients would be classified according to the mNY criteria which do not fulfil the criteria on CR. Combining information on structural changes on CR with the information of inflammation on MRI classifies the highest number of patients: 14 based on structural changes on CR and 5 additional patients based on inflammation on MRI. Note that we used abnormalities in both SI joints on MRI as a requirement for substituting the mNY criteria. Another 5 patients would have classified if unilateral MRI abnormalities had been sufficient. But in view of the literature, in which the positive predictive value of inflammation in a SI joint with respect to structural changes on the radiograph 3 years later was disappointingly low (60%) (8), we considered unilateral MRI inflammation insufficient. In our view this is the most appropriate way of using imaging modalities in patients with early IBP: first CR of the pelvis, followed by a MRI for the assessment of inflammation only, if patients are not fulfilling the mNY criteria. MRI for chronic changes does not seem to add much information to what is already provided by CR. By following the above-proposed flow diagram we combine the strengths of the two imaging methods.

It is well-known that assessment of sacroiliitis on CR has high inter-observer variation.(5) Therefore we decided to use a 2 out of 3 majority judgement. Assessment was first done by two experienced readers. In case of discrepancy, the joints were offered to a third independent reader. Two trained observers did assessment of the SI joints on MRI. Overall, there was good agreement on the presence on inflammation and structural changes.(9) A similar process was followed in case of discrepancy between the two readers as described for CR. So differences in scoring methodology or handling of data could not influence the likelihood of positive findings. Readers could also not be influenced by prior knowledge: the entire team reading CR was different from the team reading MRI.

Further validation of our results can be derived from follow-up of the patients, which are underway. Follow-up of the patients will be especially interesting for the ten patients that show inflammation on MRI (5 in both joints, 5 in one joint) but not (yet?) structural changes on CR. The data we presented are valid for patients with recent onset IBP with a high suspicion of SpA seen by a rheumatologist. Whether the results are also generalisable to patients with a lower likelihood of SpA is not known.

In conclusion, CR can detect structural changes in SI joints with higher sensitivity than MRI. But inflammation on MRI can be found in a substantial proportion of patients with IBP with (yet) normal radiographs. Applying only MRI for the assessment of both structural changes and inflammation would underestimate sacroiliitis. Assessment of structural changes by CR followed by assessment of inflammation on MRI in patients with negative findings yields the highest probability of detecting involvement of the SI joints in patients with recent onset IBP.
References


Conflict of interest:
The authors declare that they don’t have a conflict of interest with respect to the present study.