Original article

Role of diffusion-weighted imaging in early ankylosing spondylitis

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Keywords: diffusion weighted imaging; ankylosing spondylitis; sacroiliac joint

Background  With the advanced MRI techniques, pathologic features can be detected at an early stage and quantitatively evaluated, resulting in the advantages of early diagnosis and prompt treatment. This study aimed to determine the value of diffusion-weighted MR imaging (DWI) in detection of early ankylosing spondylitis (AS) and investigate the characteristic manifestations of AS on whole body DWI (WB-DWI).

Methods  Twenty patients with the diagnosis of early AS, twenty patients with low back pain (LBP), and twenty-five healthy volunteers were included in this study. The subchondral bone apparent diffusion coefficients (ADC) among these groups in the bilateral ilia and sacrum along the sacroiliac joints were compared. An independent sample t-test was utilized to analyze ADC value differences among groups. P-values less than 0.05 denoted statistical significance. The mean ADC values of focal DWI lesions in AS patients were also measured. Whole body diffusion-weighted imaging was performed in fifteen additional AS patients, and analyzed with MIP and MPR techniques in comparison to conventional MR images in order to evaluate the ability to detect AS lesions with whole body DWI.

Results  Mean ADC values in AS patients were (0.518±0.122)×10⁻³ mm²/s in the ilium and (0.503±0.168)×10⁻³ mm²/s in the sacrum. These were significantly greater than the values measured in the ilium and sacrum of LBP patients, (0.328±0.053)×10⁻³ mm²/s in the ilium and (0.311±0.081)×10⁻³ mm²/s in the sacrum, and control group, (0.325±0.015)×10⁻³ mm²/s in the ilium and (0.318±0.011)×10⁻³ mm²/s in the sacrum respectively. No statistically significant differences were found between LBP group and control group. The mean ADC value of focal DWI lesions in early AS patients was (0. 899±0.265)×10⁻³ mm²/s, which was significantly higher than that of adjacent normal-appearance areas ((0.454±0.079)×10⁻³ mm²/s), WB-DWI detected abnormalities in the 15 additional AS patients both within the sacroiliac joints and at other sites, corresponding to the clinical symptoms of the patients. The mean ADC value of focal DWI lesions of this patient cohort was (1.286±0.311)×10⁻³ mm²/s in the sacrum and (1.220±0.299) ×10⁻³ mm²/s in the ilium.

Conclusions  Subchondral marrow ADC values of subchondral marrows near the sacroiliac joints allow for the differentiation of patients with early AS from normal volunteers and LBP patients. Combined with post-processing techniques such as MIP and MPR, WB-DWI allows for the comprehensive assessment of AS patients, an evaluation potentially helpful in determining prognosis and following the therapeutic response.

Ankylosing spondylitis (AS) is the most common seronegative spondyloarthropathy. This disease is slowly progressive and predominantly affects adolescents. The etiology is unknown. Most frequent symptoms of AS include back and hip pains. The presence of lumbosacral pain in young patients with radiographically-evident sacroiliac joint abnormalities is characteristic of AS; however, conventional radiographic changes of the sacroiliac joints are not detected until 1.5 to 10 years following disease onset. The late onset of radiographic findings may delay diagnosis and treatment; as such recent research has focused on the early detection and diagnosis of AS. As diagnostic imaging techniques continue to develop, advanced magnetic resonance imaging (MRI) techniques, such as diffusion weighted imaging (DWI) and whole-body MRI (WB-MRI), have been utilized in the evaluation of patients with suspected early AS. The aim of this study is to investigate the utility of DWI and WB-MRI in detecting early AS involving in sacroiliac joints.

Methods

Subjects  Written consent form was obtained from all participants in accordance with institutional review board (IRB). Forty patients (age range = 15–40 years, mean age = 30.2 years) with symptoms of low back pain over the last two years were included in this prospective study. Patient symptoms included localized pain in the lumbar or cervical spine, sacroccygeal region, or in the bilateral.

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groups (n = All subjects in the AS (MRI examination and lab test did not support the diagnosis of chronic low back pain (LBP) because imaging examination and lab test did not support the diagnosis of early AS. Twenty-five healthy volunteers without any history of back pains during the last two years were enrolled in our study as a control group. Fifteen additional patients (10 men, 5 women, age range = 19–38 years, mean age = 27.4 years) with clinically confirmed AS (disease course = 2–5 years) were enrolled for WB-DWI.

MRI examination

All subjects in the AS (n = 20), LBP (n = 20) and control groups (n = 25) underwent conventional MRI and DW-MRI of the sacroiliac joints. A 1.5T MR scanner (GE Healthcare, Signa HDxt, Milwaukee, WI, USA) with a gradient amplitude of 40 mT/m and a slew rate of 150 T/m/s was utilized with an 8-channel CLT array coil employed for dedicated sacroiliac joint imaging and a built-in body coil for the whole body DWI scan.

MR Parameters for the sacroiliac joints included: axial spin echo T1-weighted imaging (T1WI, TR 420 ms, TE 7.2 ms, NEX 2, matrix 320×192, FOV 36×36), fat-saturated fast spin echo T2-weighted imaging (FS T2WI, TR 380 ms, TE 85.5 ms, NEX 2, matrix 256×224, FOV 36×36), oblique coronal short TI inversion recovery (STIR: TR 4100 ms, TE 70.6 ms, TI 150 ms, NEX 4, matrix 288×224, FOV 36×36, 16 slices, slice thickness 7 mm, no slice gap) and axial DWI with a SE-EPI sequence (TR 2000 ms, TE 63.3 ms, NEX 2, matrix 128×128, FOV 36×36). Other parameters, including the number of acquired slices (16), slice thickness (7 mm), and interslice gaps (none), were kept constant for the above scans. Total scan time was less than 10 minutes.

WB-DWI was performed in 15 AS patients. Segmental scanning in the supine position with 30 slices per segment was performed: 7 or 8 segments (i.e., Location 1 through Location 7 or Location 8) were evenly divided between the head and the upper tibia according to subjects’ heights. The center frequency (CF) of segments including the head and upper abdomen (i.e., Location 1 and Location 4) was recorded by auto prescan functionality, and the mean CF value was calculated and maintained consistent among all subjects.

A spin echo, echo planar DWI sequence, was employed with spectral presaturation inversion recovery imaging (SPIR; TR 3380 ms, TE 74.1 ms, TI 180 ms, NEX 4, matrix 96×96, FOV 40×40, slice thickness 6 mm, no slice gaps). The diffusion coefficient of b-value was 600 s/mm². Scan time per segment was 2 minutes 52 seconds with a total scan time from 20 to 30 minutes per subject.

Image analysis

Original DWI images of the sacroiliac joints were transmitted to a professional post-processing workstation (GE Healthcare ADW 4.4). Utilizing the function tool of the apparent diffusion coefficient (ADC) software, multiple regions of interest (ROI) 71 mm² in area were placed in the regions of normal appearing marrow, avoiding regions of artifact, vessels, or cortical bone. If a focal abnormality was detected, the slice containing the majority of the lesion was selected and an ROI centered on the lesion on that slice to measure the ADC value. An additional ROI was placed in the adjacent area relatively normal in DWI appearance. For LBP patients and healthy volunteers, six ROIs were placed in subchondral marrow for both the bilateral sacrum and ilium (three ROIs for each) along sacroiliac joint to measure the mean ADC values. No diffusion abnormalities were seen in these patient subsets.

The original multi-segmented WB-DWI images were transmitted to a post-processing workstation and combined into one single DWI image. Multiplanar reconstructions (MPR), three dimensional maximum intensity projections (MIP) and curved reformatted images were obtained and provided for assessment of the WB-DWI images. A color ADC map was converted to gray scale, providing a PET-like image (gray scale conversion technique). Typical DWI lesions on the whole body scan occurred within the sacroiliac joints, in the spine, and at attachment points of various tendons and ligaments (i.e., enthesisopathy). The ADC values of lesions were measured and the mean ADC values of lesions in different anatomic locations were also calculated.

Statistical analysis

Statistical analysis was performed with standard software (Statistical Package for the Social Sciences; SPSS; USA). Differences in mean ADC values of the sacrum and ilium between the AS, LBP and control groups were assessed using an independent sample t-test. The ADC values of lesions identified in early AS patients were compared to those of adjacent normal appearing marrow utilizing a paired t-test. P values less than 0.05 were considered statistically significant.

RESULTS

Sacroiliac joint DWI

The mean ADC values of the bilateral sacral and iliac subchondral bone marrows were shown in Figure 1. The

hips. Of forty patients, twenty patients (13 men and 7 women) had been diagnosed with early AS by a combination of typical clinical symptoms, laboratory results including positive human leukocyte antigen (HLA) B27, elevating in erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), and either radiographically normal sacroiliac joints or radiographic findings supporting degree I sacroilitis. The other twenty patients (12 men, 8 women) were diagnosed as simple chronic low back pain (LBP) because imaging examination and lab test did not support the diagnosis of early AS. Twenty-five healthy volunteers without any history of back pains during the last two years were enrolled in our study as a control group. Fifteen additional patients (10 men, 5 women, age range = 19–38 years, mean age = 27.4 years) with clinically confirmed AS (disease course = 2–5 years) were enrolled for WB-DWI.

Exclusion criteria include patient medical history of rheumatoid arthritis, surgery, history of traumatic injury, severe disc protrusion, tuberculosis of the bone, and osseous neoplastic or metastatic disease. Patients with MRI contraindications such as claustrophobia were also excluded.

MRI examination

All subjects in the AS (n = 20), LBP (n = 20) and control groups (n = 25) underwent conventional MRI and DW-MRI of the sacroiliac joints. A 1.5T MR scanner (GE Healthcare, Signa HDxt, Milwaukee, WI, USA) with a gradient amplitude of 40 mT/m and a slew rate of 150 T/m/s was utilized with an 8-channel CLT array coil employed for dedicated sacroiliac joint imaging and a built-in body coil for the whole body DWI scan.

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RESULTS

Sacroiliac joint DWI

The mean ADC values of the bilateral sacral and iliac subchondral bone marrows were shown in Figure 1. The
mean ADC values of the control group were 

\((0.325\pm0.015)\times10^{-3}\ \text{mm}^2/\text{s}\) in the ilium and 

\((0.318\pm0.011)\times10^{-3}\ \text{mm}^2/\text{s}\) in the sacrum. The mean ADC values of the LBP group were 

\((0.328\pm0.053)\times10^{-3}\ \text{mm}^2/\text{s}\) in the ilium and 

\((0.311\pm0.081)\times10^{-3}\ \text{mm}^2/\text{s}\) in the sacrum. There was no significant difference between the control group and LBP group \((P=0.658)\). The mean ADC values of the AS group were 

\((0.518\pm0.122)\times10^{-3}\ \text{mm}^2/\text{s}\) in the ilium and 

\((0.503\pm0.168)\times10^{-3}\ \text{mm}^2/\text{s}\) in the sacrum, which were significantly greater than those in the LBP and control groups \((P=0.003)\).

There were no evident abnormalities identified in the subchondral bone marrow of the 20 subjects in LBP group, and no edema in the bilateral subchondral bone marrow of the sacrum or ilium was detected (Figure 2). Normal structure of “low-medium-low” signal intensity (SI) was displayed along the sacroiliac joint, which represents the bilateral bone cortices (low SI) surrounding the sacroiliac joint articular cartilage (medium SI). Similar conventional MRI and DWI findings were demonstrated in 25 subjects in control group.

For 13/20 subjects in the early AS group, no definite focal osseous abnormalities were demonstrated by either conventional MRI or DW-MRI (Figure 3). In these cases, homogeneous signal intensity was present in the subchondral bone marrow and cartilage of the sacroiliac joint. Focal bone marrow edema was detected in 7/20 early AS patients as manifest by high signal intensity lesions (Figure 4). The comparison of ADC values in focal lesions of early AS patients with those in adjacent relatively normal appearing marrows was shown in Table 1. The mean ADC value of all lesions was 

\(0.899\times10^{-3}\ \text{mm}^2/\text{s}\), which was significantly higher than that of adjacent relatively normal regions \((0.454\times10^{-3}\ \text{mm}^2/\text{s}, \ P<0.001)\).

**WB-DWI**

Fifteen patients with the clinically confirmed AS underwent WB-DWI. Hyperintense lesions of subchondral bone marrows were demonstrated on ADC maps, correlating to inflammatory bone marrow edema. MIP, MPR and PET-like evaluation of the left anterior sacrum on the FS T2WI (3B). DWI (3C) and color map (3D) images show homogeneous signal intensity in the bilateral subchondral bone marrow.

**Figure 4.** A 32-year old man with early AS suffering from lumbosacral pain more than 1 years. Focal lesions related to bone marrow edema are identified in the left-anterior sacrum and superior right ilium on FS T2WI (4A, arrows). Hyperintense lesions corresponding to the FS T2WI in the left sacrum are seen on ADC image (4B) and color map (4C).
Table 1. Mean ADC values (10^{-3} mm^2/s) of focal lesions and adjacent normal bone marrows for early AS group

<table>
<thead>
<tr>
<th>Locations</th>
<th>Lesions (SD)</th>
<th>Adjacent bone marrows (SD)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacrum</td>
<td>0.886 ± 0.265</td>
<td>0.453 ± 0.079</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sacrum</td>
<td>0.840 ± 0.322</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Sacrum</td>
<td>1.240 ± 0.468</td>
<td>0.468 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Sacrum</td>
<td>0.906 ± 0.296</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Sacrum</td>
<td>0.874 ± 0.458</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Ilium</td>
<td>0.861 ± 0.576</td>
<td>0.450 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Ilium</td>
<td>0.588 ± 0.450</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Ilium</td>
<td>0.671 ± 0.528</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Ilium</td>
<td>0.830 ± 0.462</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Ilium</td>
<td>0.705 ± 0.510</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
<tr>
<td>Ilium</td>
<td>0.812 ± 0.493</td>
<td>0.430 ± 0.089</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA: not available.

DISCUSSION

Ankylosing spondylitis involves in numerous inflammatory pathologies including sacroiliitis, peripheral arthritis and enthesopathy. These lesions progress superiorly along the axial skeleton and may eventually develop into spondyloarthropathy. With disease progression, ossification of cartilage results in joint ankylosis and eventually joint deformity with associated mobility restriction. Such disability is common in patients with severe AS. Early recognition of AS before the disease reaching this irreversible point is thus crucial. Subchondral bilateral or unilateral sacroiliac marrow edema is characteristic of AS. In currently clinical practice, early diagnosis of AS is primarily dependent on identification of subjective symptoms of sacroiliitis or identification of abnormal laboratory values. Radiographic findings in the sacroiliac joints frequently lag or absent at early disease. This has led to interest in utilizing MRI, which is highly sensitive for the detection of marrow edema, facilitating the early diagnosis of AS. In recent years, DWI has been increasingly utilized in early diagnosis as well as the monitoring and estimation of therapeutic response, in particular for central nervous system diseases, liver diseases and metastatic diseases. With continued improvements of DWI sequences and MR hardware, DWI has become increasingly important for musculoskeletal imaging in the applications varying from the differentiation between benign and malignant fractures to the detection of multiple metastases. Because of dense cellularity within tumors due to the rapid growth of tumor cells, restricting the motion of extracellular free water, hyperintensity on DWI and decreased ADC values can be seen. Meanwhile water molecular diffusion is often increased in inflammatory processes, leading to the increase in ADC values above baseline.

Dietrich et al measured the mean ADC value of vertebral bodies in healthy subjects utilizing b-values ranging from...
Table 2. Mean ADC values of multiple lesions in AS patients (mean ± SD, 10^-3 mm²/s)

<table>
<thead>
<tr>
<th>Locations</th>
<th>Number of lesions</th>
<th>Mean ADC values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacrum</td>
<td>16</td>
<td>1.286 ± 0.311</td>
</tr>
<tr>
<td>Ilium</td>
<td>13</td>
<td>1.220 ± 0.299</td>
</tr>
<tr>
<td>Costovertebral joint</td>
<td>9</td>
<td>1.388 ± 0.125</td>
</tr>
<tr>
<td>Vertebræ</td>
<td>14</td>
<td>1.311 ± 0.268</td>
</tr>
<tr>
<td>Hip joint</td>
<td>8</td>
<td>1.288 ± 0.307</td>
</tr>
<tr>
<td>Ischial tuberosity</td>
<td>6</td>
<td>1.485 ± 0.298</td>
</tr>
</tbody>
</table>

50 to 500 s/mm². The mean ADC value of spinal vertebræ was 0.30 × 10^-3 mm²/s with a b-value of 500 s/mm². Chan et al evaluated 46 patients with acute vertebral fractures utilizing DW-MRI with a b-value of 1000 s/mm². The mean ADC values were 0.23 × 10^-3 mm²/s for normal vertebra, 1.94 × 10^-3 mm²/s for benign fracture sites and 0.82 × 10^-3 mm²/s for malignant fracture sites. Utilizing a b-value of 600 s/mm² in our study, the mean sacral and ilial ADC values of healthy volunteers were higher than those found in the aforementioned studies. The reason potentially relating to this difference may be the age range of the patients (64.2 years in Chan’s study, 26.5 years in our study). The bone mineral density (BMD) in younger people is generally higher than that of older individuals. Yeung et al reported that the ADC value of bone marrow was decreased with the declining BMD. In our study, the mean ADC value of lesions in early AS patients was lower than the ADC value reported by Chan for traumatic and infectious lesions, likely reflecting less edema with AS.

Bozgeyik et al measured sacral and ilial ADC values in patients with sacroiliitis and low back pain. The results showed that mean ADC value of sacroiliitis patients was higher than simple low back pain patients, but this difference was not statistically significant (b-value = 600 s/mm²). In our study, however, mean sacral and ilial ADC values in AS patients were significantly greater than corresponding values in LBP patients. These results are partially consistent with Bozgeyik’s study. This may indicate that it is possible to differentiate early AS patients from LBP patients by measuring subchondral ADC value along the bilateral sacroiliac joints. This may relate to the distribution/extent of ongoing inflammatory changes associated with AS, which may eventually result in the appearance of bone marrow edema. Such quantitative assessments may be useful for predicting the diagnosis of early AS in patients without typical symptoms, signs and evident abnormalities on conventional MRI and DWI.

Although sacroiliitis is the most common manifestation in AS patients and routinely examined in clinical practice, inflammatory abnormalities of AS can occur in multiple regions involving in the whole body. WB-DWI is capable of detecting the multiple abnormalities in sacroiliac joints, small joints in spine, peripheral joints and ligamentous and tendinous attachments by a single MR scan within 20 minutes. This technique allows for a comprehensive AS evaluation.

WB-DWI is a non-invasive method of detecting the multiple abnormalities present in AS patients, providing early detection and the potential for earlier treatment. Compared with conventional MRI, WB-DWI combined with fat suppression technique was more sensitive in the detection of bone marrow edema and more intuitive in determining the systemic distribution of lesions. Meanwhile, MIP, MPR, curved reformatted and PET-like image (gray scale conversion) can be utilized with WB-DWI technique, allowing for the observation of

Figure 6. A 32-year old man with AS suffering from low back pain for 5 years. Lesion in the 10th costovertebral joint and bilateral sacroiliac joints are illustrated by MIP image, PET-like image, coronal MPR image and DWI images (arrows). Costovertebral arthritis, sacroiliitis and Romanus lesions are also well-demonstrated by axial, sagittal and coronal MPR images. The presence of sacroiliitis is confirmed on conventional MRI images (coronal FS T2WI, axial T1WI and axial FS T2WI).
lesion distribution without interference from the normal signal of the intra-abdominal organs. PET-type image analysis in our study demonstrated a high contrast of lesions against the suppressed background signal, providing a comparable detectability of AS lesions compared with PET.23 WB-DWI and Color maps were also helpful with the direct evaluation of lesions by different ADC values. Although the details of anatomic structure were not well demonstrated in WB-DWI images, sufficient contrast between the abnormalities and normal tissues on DWI can be obtained.

In conclusion, DWI and WB-DWI have been proved to be valuable for the diagnosis and differentiation of early AS from the patients with simple low back pains and healthy populations, showing a huge promise in determining prognosis and following the therapeutic response. With the further development of MRI techniques, such as faster scan acquisitions with higher spatial resolutions, this application of DW and WB-DWI will be further extended.

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