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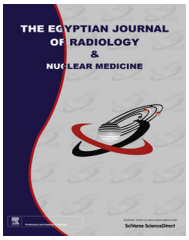

ORIGINAL ARTICLE

Diagnostic value of diffusion weighted magnetic resonance image in early ankylosing spondylitis

Khaled Dewan [a,*], **Hanan El-saadany** [b]

[a] *Diagnostic Radiology Department, Faculty of Medicine, Tanta University, Egypt*
[b] *Physical Medicine, Rheumatology and Rehabilitation Department, Faculty of Medicine, Tanta University, Egypt*

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KEYWORDS

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Abstract *Background:* Diffusion-weighted MRI (DW-MRI) shows the early changes in microscopical movement of water molecules, hence diagnosis of early sacroiliitis which is one of the diagnostic criteria of seronegative spondyloarthropathies.
Objective: To determine the value of DW-MRI in detection of signal characteristics of the sacroiliac joints in patients with early ankylosing spondylitis (AS).
Patients and methods: Fifteen patients with clinically suspected AS, 20 patients with mechanical low back pain and 20 healthy controls underwent conventional MRI and DWI. Apparent diffusion coefficient (ADC) was measured. In addition ten clinically confirmed AS patients underwent whole body-DWI.
Results: Mean ADC values of both sacroiliac joints in AS patients were $(0.523 \pm 0.15) \times 10^{-3}$ mm^2/s in the ilium and $(0.502 \pm 0.15) \times 10^{-3}$ mm^2/s in the sacrum. There was no significant difference between mechanical LBP and healthy controls. But there was a significant difference between AS and LBP patients. Mean ADC value of focal lesions of clinically confirmed AS was $0.965 \pm 0.25 \times 10^{-3}$ mm^2/s in the sacrum and $0.932 \pm 0.31 \times 10^{-3}$ mm^2/s in the ilium.
Conclusion: Subchondral bone marrow ADC values of sacroiliac joints allow differentiation between inflammatory and mechanical LBP. Furthermore, it may be helpful in evaluating the efficacy of the treatment and determine disease prognosis.

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease of unknown cause that affects mainly young adults. Inflammatory back pain and alternating gluteal pain related to sacroiliitis are the leading symptoms in adults with early ankylosing spondylitis and undifferentiated spondyloarthritis (SpA) (1).

* Corresponding author. Tel.: +20 01223598098.
E-mail address: khaledabodewan@yahoo.com (K. Dewan).
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Pain arising from an inflamed sacroiliac joint is typical in ankylosing spondylitis and is always considered a diagnostic criterion (2).

A major challenge in the management of axial spondyloarthritis is the substantial delay in diagnosis, which consistently averages 7–9 years (3). This reflects the lack of specificity of presenting clinical features of the disease, the lack of sensitivity of laboratory markers and the slow rate of radiographic progression in the sacroiliac joints (SIJs) despite ongoing symptoms of inflammatory back pain (IBP) (3).

Imaging studies have always played a prominent role in the diagnosis of ankylosing spondylitis (AS), it yield three major benefits: they ensure the early diagnosis of ankylosing spondylitis in the absence of radiographic sacroiliitis, they provide therapeutic guidance at any time during the course of the disease, and they supply objective information on the degree of inflammation and response to treatment (4).

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 (5–7). This technique has proven to be a valuable method for tracing the microscopic structure of tissue. Molecular diffusion is a physical process that is used to describe the Brownian motion of water molecules (8). The apparent diffusion coefficient (ADC), a quantitative parameter calculated from diffusion-weighted images, combines the effects of capillary perfusion and water diffusion in the extracellular extravascular space. When only high b values are applied, the ADC value approximates the true diffusion. Low b values are influenced by both perfusion and diffusion (8). More recently, DWI has been increasingly used in musculoskeletal structures and diseases. Ward et al. (9), analyzed the diffusion characteristics of normal and posttraumatic bone marrow and concluded that increased ADC values were increased in traumatized bone marrow compared with ADC values of normal bone.

The objective of this study was to determine the value of DW-MRI in the detection of active inflammatory changes and signal characteristics of the sacroiliac joints in patients with early ankylosing spondylitis in addition to determining the role of DWI in the differentiation between inflammatory and mechanical low back pain.

2. Patients and methods

Thirty-five patients with simple chronic low back pain with symptoms duration from 6 months to 2 years were recruited from the out- patient clinic of Rheumatology and Rehabilitation Department. Inclusion criteria for the study required the presence of chronic low back pain without a confirmed diagnosis and an age of 16–40 years (mean age: 29 years). Exclusion criteria were current infections (including brucellosis) of the bone and joints, pregnancy, metallic implants, history of traumatic injury, severe disk prolapse, osseous neoplastic or metastatic disease and claustrophobia. We followed the diagnostic algorithm suggested by the Berlin group for the early diagnosis of axial spondyloarthritis (10). The Berlin algorithm is based on the probability of early axial spondyloarthritis in patients with chronic back pain according to the absence or presence of certain clinical features, laboratory tests, and skeletal imaging. The entry criteria were inflammatory back pain and the presence of at least three of seven spondyloarthritis features: family history of spondyloarthritis, heel pain, uveitis, synovitis, dactylitis, good response to non-steroidal anti-inflammatory drugs, and HLA (human leukocyte antigen)-B27 positivity. The result of the algorithm is expressed as a percentage of probability of axial spondyloarthritis (10). The rate above which axial spondyloarthritis is considered a definite diagnosis is 90%. Of thirty-five patients, fifteen patients (13 men and 2 women) had been diagnosed with early AS. The other twenty patients (15 men, 5 women) were diagnosed as simple mechanical low back pain (LBP) because clinical examination, lab test and radiographs did not support the diagnosis of early AS. Twenty age and sex matched healthy volunteers without any history of back pain during the last 6 months were enrolled in our study as a control group. Ten additional patients (7 men, 3 women, age range: 18–39 years, mean age: 27 years) with clinically confirmed AS (disease duration: 3–6 years) were enrolled for WB-DWI.

2.1. MRI examination

All subjects in the AS ($n = 15$), LBP ($n = 20$) and control group ($n = 20$) underwent conventional MRI and DW-MRI of the sacroiliac joints. A 1.5T MR scanner (Siemens, MAGNETOM ASSENZA Muenchen, Germany) with a gradient amplitude of 40 mT/m and a slew rate of 150 T/m/s was utilized with an 16-channel CLT array coil employed for dedicated sacroiliac joint imaging and a built-in body coil for the whole body DWI scan.

MRI Parameters for the sacroiliac joints included: axial spin echo T1-weighted imaging (T1WI, TR 420 ms, TE7.2 ms, NEX 2, matrix 320×192, FOV 36×36), fat-saturated fast spin echo T2-weighted imaging (FST2WI, 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, FOV36×36). Other parameters, including the number of acquired slices (16), slice thickness (7 mm), and interslice gap (none), were kept constant for the above scans. Total scan time was less than 10 min.

WB-DWI was performed in 10 clinically confirmed 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 pre-scan 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 pre-saturation 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/mm^2. Scan time per segment was 2 min 52 s with a total scan time from 20 to 30 min per subject.

2.2. Image processing

An ROI (region of interest) of 73–83 mm was placed on superior, middle and inferior subchondral areas of iliac and sacral sides of both sacroiliac joints (total of 12). ADC measurements are made in AS, LBP and the control group (Fig. 1). The areas which were hypo-intense on T1-weighted and hyper- intense on T2-weighted images were determined to be bone marrow edema, and ADC measurements from these areas are compared to the ADC values of the equivalent areas of the LBP group and control subjects. ADC values from the normal appearing areas of AS patients showing no edema were calculated at 3 points (superior, middle and inferior) on both sacral and iliac surfaces of both sacroiliac joints. MRI examinations were reviewed at a Workstation for qualitative and quantitative evaluation.

The original multi-segmented WB-DWI transmitted to a post-processing workstation and combined into one single DWI image. Multi-planar reconstructions (MPR), three dimensional maximum intensity projections (MIP) and curved reformatted images were obtained and provided for assessment of the WB-DW images. A black and white ADC map was converted to gray scale. 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., enthesopathy). The ADC values of lesions were measured and the mean ADC values of lesions in different anatomic locations were also calculated. The ADC values of the three groups were compared by using independent samples *t* test. *P* values less than 0.05 were considered statistically significant.

3. Results

Out of thirty-five patients with chronic low back pain, fifteen patients were diagnosed as inflammatory LBP suggesting ankylosing spondylitis, and 20 patients were diagnosed as mechanical LBP. There was no statistically significant difference between all groups regarding age and sex. In the AS group the mean ADC values were $0.523 \pm 0.15 \times 10^{-3}$ mm^2/s in the ilium and $0.502 \pm 0.15 \times 10^{-3}$ mm^2/s in the sacrum which were statistically significant than LBP group ($p < 0.05$) (Table 1).

The mean ADC values of the LBP group were $0.323 \pm 0.16 \times 10^{-3}$ mm^2/s in the ilium and $0.301 \pm 0.05 \times 10^{-3}$ mm^2/s in the sacrum while in the control group ADC was $0.300 \pm 0.04 \times 10^{-3}$ mm^2/s in the ilium and $(0.302 \pm 0.2)\ 10^{-3}$ mm^2/s in the sacrum. There was no statistically significant difference between LBP and control group ($p > 0.05$) (Table 2).

Our mean ADC values obtained from sub-articular surfaces of both sacroiliac joints bone marrow in all groups are shown in Fig. 1. Regarding bone erosions, there were 5 patients out of 15 AS patients who had bone erosions demonstrated by either conventional MRI or DWI. Subchondral bone marrow edema was detected in 14 out of 15 AS patients as manifested by high signal intensity and higher ADC values (Fig. 2). In LBP and control groups, there were no definite abnormalities detected (Fig. 3) except one LBP patient who has small erosion on the iliac part of right SI joint.

Ten patients with clinically confirmed AS underwent WB-DWI. Hyper-intense lesions of subchondral bone marrows were demonstrated on ADC maps, correlating to inflammatory bone marrow edema. MIP and MPR commonly seen with AS, including sacroiliitis and costovertebral joint arthritis, are demonstrated in Fig. 4. Sacroiliitis, costovertebral joint, ischial tuberosity edema and enthesopathy involving the hip, are illustrated.

4. Discussion

Diagnosing early ankylosing spondylitis (AS) in young patients presenting with inflammatory back pain (IBP) with normal findings on plain radiograph of the sacroiliac joints (SIJs) remains a challenge in routine practice. Radiography detects post inflammatory changes in the subchondral bone of the SIJs, but these changes become evident only after symptoms duration of several years (11). Moreover, the oblique course of the sacroiliac joint, the superposition of the sacral and iliac bones and wavy nature of the joint make the interpretation harder (12).

MRI is the only imaging tool capable of visualizing bone marrow inflammation, a hallmark of SpAs (14). Although routine MRI has high sensitivity in showing the abnormalities related to the sacroiliac joints and the bone marrow, these findings are mostly non-specific. DWI-MRI has the potential of

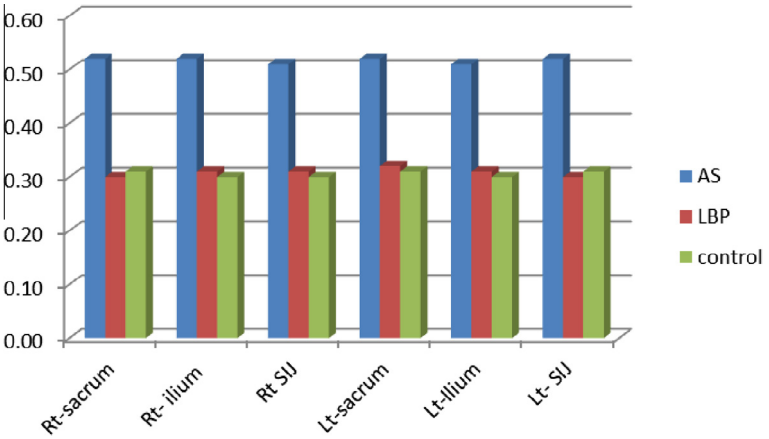

Fig. 1 Mean ADC values of AS patients, LBP patients and healthy controls.

Table 1 Mean ADC values of AS patients and LBP patients on the sacral and iliac bones of both sacroiliac joints.

ADC	AS (n = 15) Mean ± SD	LBP (n = 20) Mean ± SD	p
Superior R. sacral	$0.40 \times 10^{-3} \pm 0.14$	$0.32 \times 10^{-3} \pm 0.07$	< 0.05
Middle R. sacral	$0.50 \times 10^{-3} \pm 0.19$	$0.21 \times 10^{-3} \pm 0.07$	< 0.05
Inferior R sacral	$0.57 \times 10^{-3} \pm 0.13$	$0.33 \times 10^{-3} \pm 0.08$	< 0.05
Superior R iliac	$0.55 \times 10^{-3} \pm 0.13$	$0.21 \times 10^{-3} \pm 0.06$	< 0.05
Middle R iliac	$0.60 \times 10^{-3} \pm 0.14$	$0.32 \times 10^{-3} \pm 0.06$	< 0.05
Inferior R iliac	$0.57 \times 10^{-3} \pm 0.15$	$0.33 \times 10^{-3} \pm 0.06$	< 0.05
Superior L sacral	$0.56 \times 10^{-3} \pm 0.12$	$0.31 \times 10^{-3} \pm 0.06$	< 0.05
Middle L sacral	$0.57 \times 10^{-3} \pm 0.13$	$0.33 \times 10^{-3} \pm 0.03$	< 0.05
Inferior L sacral	$0.58 \times 10^{-3} \pm 0.14$	$0.32 \times 10^{-3} \pm 0.02$	< 0.05
Superior L iliac	$0.55 \times 10^{-3} \pm 0.12$	$0.31 \times 10^{-3} \pm 0.07$	< 0.05
Middle L iliac	$0.46 \times 10^{-3} \pm 0.12$	$0.32 \times 10^{-3} \pm 0.05$	< 0.05
Inferior L iliac	$0.58 \times 10^{-3} \pm 0.11$	$0.31 \times 10^{-3} \pm 0.08$	< 0.05

AS: anklosing spondylitis, LBP: low back pain.
Significant $p < 0.05$.

Table 2 Mean ADC values of LBP group and healthy control group on the sacral and iliac bones of both sacroiliac joints.

ADC	LBP (n = 20) Mean ± SD	Control (n = 20) Mean ± SD	p
Superior R. sacral	$0.32 \times 10^{-3} \pm 0.07$	$0.31 \times 10^{-3} \pm 0.03$	> 0.05
Middle R. sacral	$0.21 \times 10^{-3} \pm 0.07$	$0.32 \times 10^{-3} \pm 0.02$	> 0.05
Inferior R sacral	$0.33 \times 10^{-3} \pm 0.08$	$0.33 \times 10^{-3} \pm 0.01$	> 0.05
Superior R iliac	$0.21 \times 10^{-3} \pm 0.06$	$0.32 \times 10^{-3} \pm 0.03$	> 0.05
Middle R iliac	$0.32 \times 10^{-3} \pm 0.06$	$0.31 \times 10^{-3} \pm 0.04$	> 0.05
Inferior R iliac	$0.33 \times 10^{-3} \pm 0.06$	$0.33 \times 10^{-3} \pm 0.03$	> 0.05
Superior L sacral	$0.31 \times 10^{-3} \pm 0.06$	$0.32 \times 10^{-3} \pm 0.02$	> 0.05
Middle L sacral	$0.33 \times 10^{-3} \pm 0.03$	$0.31 \times 10^{-3} \pm 0.01$	> 0.05
Inferior L sacral	$0.32 \times 10^{-3} \pm 0.02$	$0.31 \times 10^{-3} \pm 0.03$	> 0.05
Superior L iliac	$0.31 \times 10^{-3} \pm 0.07$	$0.31 \times 10^{-3} \pm 0.02$	> 0.05
Middle L iliac	$0.32 \times 10^{-3} \pm 0.05$	$0.30 \times 10^{-3} \pm 0.01$	> 0.05
Inferior L iliac	$0.31 \times 10^{-3} \pm 0.08$	$0.31 \times 10^{-3} \pm 0.01$	> 0.05

LBP: low back pain.
Significant $p < 0.05$.

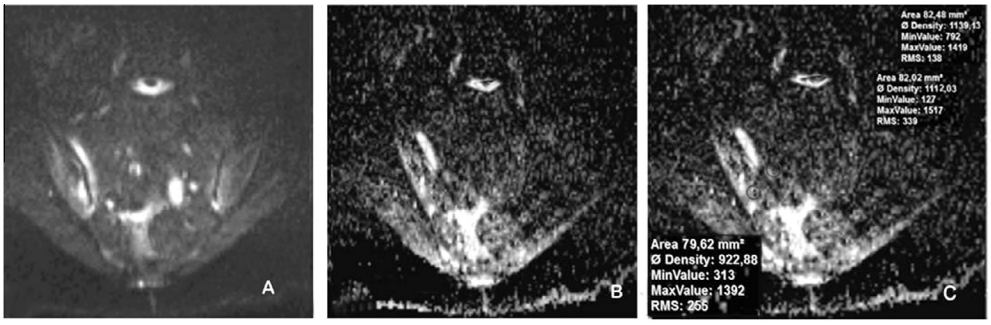

Fig. 2 26 year-old man with early active sacroiliitis. T_2WI shows hyper-intense lesions in sacral and iliac bone marrow of right SIJ_s (A). ADC map shows placement of ROI over affected areas (B, C).

increasing the specificity of MRI (13). The ADC value, a diffusivity index, is a quantitative marker for tissue characterization. The contribution of T2-weighting to DWI may cause false positive results as diffusion restriction, therefore qualitative assessment may not be efficient, and quantitative measurements should be made (12).

In a recently published study Benjamin Dallaudiere et al. (14), studied 46 patients with recent onset lumbar pain (suspected spondyloarthropathy) and 49 patients with purely recent degenerative history. ADC values of active inflammatory lesions from IBP group were 0.788×10^{-3} mm^2/sn, which was significantly higher than degenerative group which was

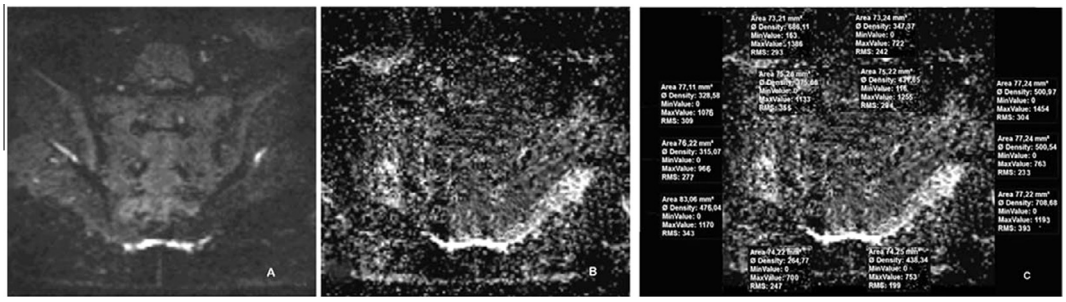

Fig. 3 28 year-old man with chronic LBP of mechanical origin. T_2WI, DWI shows normal both surfaces of both SIJ_s (A, B). ADC map shows 12 ROI placed in sub articular surface of SIJ_s (C).

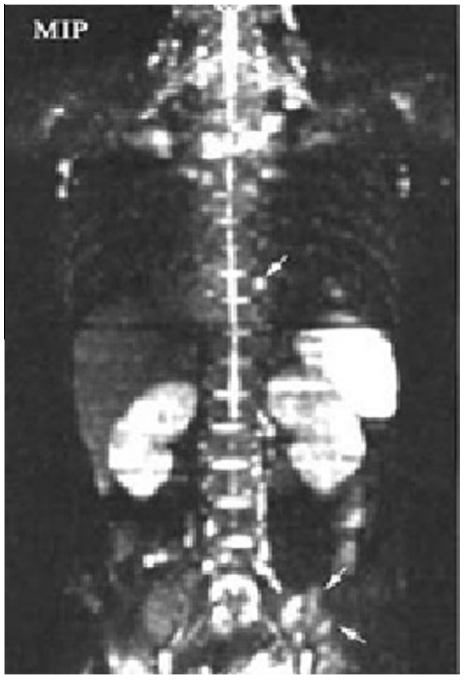

Fig. 4 34 year-old man with clinically confirmed AS. Lesion on both sides of left sacroiliac joint and 9th left cost vertebral joint on MIP image.

0.585×10^{-3} mm^2/s. Moreover, Esin Gesmisetal (12) stated that ADC values on both surfaces of the both sacroiliac joints were found to be 0.23×10^{-3} mm^2/sn in the control group. In the patient group, mean ADC value was 0.48×10^{-3} mm^2/s ($p < 0.001$), which was statistically significant, compatible with the increased diffusion due to medullary edema in early sacroiliitis. These results are consistent with our result, where we found higher ADC values in both sacral and iliac surfaces of both sacroiliac joints which were statistically significant than ADC values found in LBP patients and control group ($p < 0.05$).The difference of ADC values in different studies may be attributed to the different imaging techniques and *b*-value .

Chan et al. (15), evaluated 46 patients with acute vertebral fractures utilizing DW-MRI with a *b*-value of 1000 s/mm^2. The mean ADC values were 0.23 × 10–3 mm^2/s for normal vertebra, 1.94×10^{-3} mm^2/s for benign fracture sites and 0.82×10^{-3} mm^2/s for malignant fracture sites. In our study, utilizing a *b*-value of 600 s/mm^2, the mean sacral and iliac ADC values of healthy volunteers were higher than those in Chan's study. The reason of this difference may be the age range of the patients (64.2 years in Chan's study, 29 years in our study). The bone mineral density (BMD) in younger people is generally higher than that of older individuals. Yeung et al. (16), 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.

Gaspersic et al. (17), evaluated the effects of different therapies on enthesitis and osteitis in active ankylosing spondylitis using DWI and DCE-MRI. They concluded that quantitative MRI parameters diminished significantly with regression of the inflammatory activity. DWI and DCE-MRI were shown to be effective in quantifying changes in inflammation during the treatment of ankylosing spondylitis and may be convenient for assessing treatment efficacy (17). Moreover, Bozgeyik et al. (8), concluded that DWI is a sensitive, fast sequence and does not require a contrast agent, which makes it a good and cost-effective alternative for imaging sacroiliac joints. DWI also offers the possibility of quantifying diffusion coefficients of the lesions, which can discriminate between normal and involved subchondral bone, and it offers a new alternative for follow-up. DWI may be useful in the early diagnosis and follow-up of the acute inflammatory lesions that occur in early axial spondyloarthritis.

In our study, we found higher ADC values in both sacral and iliac surfaces of both sacroiliac joints which were statistically significant than ADC values found in LBP patients and control group ($p < 0.05$). Bone marrow edema causes a local increase in water movement, resulting in increased local diffusion that is expressed by high ADC values. These results are more or less consistent with Bozgeyik's (8) study who stated that mean ADC value in AS patients was higher in AS patients than LBP patients but this difference was not statistically significant. 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 in predicting early AS patients without typical symptoms, signs and evident abnormalities on conventional MRI.

Ankylosing spondylitis involves numerous inflammatory pathologies including sacroiliitis, peripheral arthritis and enthesopathy. 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 determining the systemic distribution of the lesions. Meanwhile, MIP and MPR can be utilized with WB-DWI technique, allowing for the observation of signal of the intra-abdominal organs (18). WB-DWI and maps were also helpful in 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 (19).

5. Conclusion

DWI and WB-DWI by measuring ADC values shown to be sensitive and fast sequence that allow differentiation between inflammatory and mechanical low back pain. Furthermore, both techniques are likely to play an important role in the early diagnosis of AS and assessment of treatment response.

Conflict of interest

None.

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