Research Article Open Access

Jian Qin, Jianzhong Zhu, Yue Zhang, Changqin Li*

DWI and SPARCC scoring assess curative effect of early ankylosing spondylitis

DOI 10.1515/med-2016-0011
received May 30, 2015; accepted February 11, 2016

Abstract: Background: To investigate the magnetic diffusion weighted imaging (DWI) sequence and Spondyloarthritis Research Consortium of Canada (SPARCC) scoring in assessing curative effect of combined treatment of Chinese and Western medicine for early ankylosing spondylitis (AS).

Methods: 48 cases diagnosed as early AS and treated with Chinese and Western medicine were included in the study. Magnetic routine and DWI sequence scanning image were performed to obtain the mean apparent diffusion coefficient (ADC) value of sub-articular surface bone marrow. Combined with SPARCC scoring, statistical analysis was conducted to compare the difference with the information obtained in the previous study.

Results: The mean ADC value in the sub-articular surface bone marrow of patients after clinical treatment: (4.34±0.55)×10-4mm2/s in ilium and (3.96±0.23)×10-4mm2/s in sacrum, which were both significantly lower than that before treatment ($p< 0.05$). There was highly positive correlation between mean ADC value and SPARCC scoring ($P<0.05$). The regression relationship could be demonstrated as Y=-64.420+21.262X(Y: SPARCC scoring value; X: mean ADC value).

Conclusions: Magnetic DWI and SPARCC scoring could be applied in accessing AS inflammation activity changes and in reflect of curative effect of early AS patients as well as in providing reliable radiologist evidence for clinical therapeutic efficacy.

Keywords: Magnetic resonance, diffusion weighted image, scoring, ankylosing spondylitis, curative effect

1 Introduction

Ankylosing spondylitis (AS) is a kind of seronegative spondyloarthropathy, an autoimmune disease. AS usually starts from sacroiliac joint with an upstream trend to involve axis joints and other auxiliary structures, and in the terminal stage there will be extensive fibrosis, osteo-ankylosis and lesions in multiple systems. Delay of the treatment will result in dysfunction and disability in multiple parts of body, which will severely affect the quality of patients' work and life [1]. Therefore, it is very important to realize the diagnosis and clinical intervention treatment of early AS. Currently, several drugs are used in the treatment of AS, some of which contain "Chinese medicine" (such as tripterygium wilfordii [2], radices paeoniae alba) and "Western medicine" (non-steroid anti-inflammatory drug [3], sulfasalazine [4] , methotrexate [5], thalidomide [6]). TNF-alpha inhibitors have been used in the treatment of AS and satisfactory clinical effects have been achieved. They mainly contain etanercept [7], infliximab [8] and adalimumab [9]. This research was based on the early AS patients with a short course of disease (0.5-12 years) who have been diagnosed and remedied with Chinese and Western medicine. We observed and analyzed the change of water molecular diffusion insub-sacroiliac surface bone marrow before and after treatment through magnetic routine and diffusion weighted imaging (DWI) image examination combined with SPARCC scoring, in order to access the therapeutic efficacy and radiographic changes of early AS, which may provide reliable radiologist evidence and new therapeutic idea for the clinical work.

***Corresponding author: Changqin Li,** Division of Radiology, Taishan Medical School Affiliated Hospital, 706 Taishan Avenue, Taian, Shandong Province 271000, China. E-mail: sdchqli@126.com
Jian Qin, Jianzhong Zhu, Yue Zhang, Division of Radiology, Taishan Medical School Affiliated Hospital, Taian, Shandong Province 271000, China

2 Methods

2.1 Subjects

In this study, 48 patients (male 38, female 10, age range 14-42) of early AS were involved with combined Chinese and Western medicine, all in the early stage research group (course of disease, 0.5-12 years, course of medicine treatment 0.5-0.75 years). 43 patients had low lumbar pain (27 cases with bilateral pain, 16 cases with unilateral pain), 23 cases had morning stiffness, and 7 cases had extra-axis joints symptoms. Upon laboratory examination 48 cases were positive for HLA-B27, and inordinately elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). All patients had no MRI examination contraindication, agreed with MRI examination and signed the written informed consent. Patients were compared before and after treatment of AS. Study did not have a control group.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

2.2 MRI equipment and sequence

Superconducting magnetic resonance scanner was used at 3.0 T MR Scanner (GE Discovery MR 750, USA, GE corporation), and 15ml gadopentetate meglumine was used as contrast agent. MRI examination routine sequence: routine sequence T1 weighted image TR=400ms, TE=10ms;T2 weighted image (T2WI) TR=2400ms, TE=110ms; field of vision 28cm X 28cm; slice thickness 4.0 mm; slice space 1.0 mm; number of scanner piles 16. Oblique coronal short TI inversion recovery (STIR): TR=2700ms, TE=110ms; field of vision 28cm X 28cm; slice thickness 4.0 mm; slice space 1.0 mm; number of scanner piles 18; direction of scanner parallel with the ligature between the 1st and 2nd sacral vertebrae.

DWI scanner parameters: TR=5000ms, TE=50ms, field of vision 38×38cm, slice thickness 4.0 mm, slice space 1.5 mm, number of scanner piles 20, excitations 4 or 6, b=600s/mm^2.

2.3 MRI image process analysis

GE MRAW4.6 workstation was used for the original data processing.

DWI [10]: 1. The choice of region of interest: region with obvious lesion in the image was chosen, of which the location and area were in accordance with previous research; for patients without obvious lesion, 12 ROI was chosen from upper, middle and lower area of bilateral sacrum surface and sacrum surface bone marrow. 2. Apparent diffusion coefficient (ADC) value: the ADC value of ROI was documented with the mean value.

2.3.1 SPARCC scoring system

Bone marrow edema SPARCC scoring [11]: sacroiliac joint was scanned in T2WI STIR, and 6 layers were chosen from 4th to 9th layer to be scored in 3 aspects: 1. Involved area: sacroiliac joint of every layer in both sides was divided into 4 quadrant, 1 point will be added if the area with bone marrow edema (high signal) and 0 point added if not; Total points of 6 layer will be 48 points. 2. Edema intensity: 1 point will be added if the signal of lesion approximates or exceeds that of anterior iliac vein every layer in both sides, and the total points will be 12 in 6 layers. 3. Edema depth: 1 point will be added if the edema depth of lesion exceeds 1cm in every layer, and the total points will be 12 points. Total SPARCC scoring would be known after putting involved area scoring, edema intensity scoring and edema depth scoring together, and full mark is 72 points. It has been found in the study that some early and small bone marrow lesion wasn't showed perfectly in the T2WI STIR image, but with a more sensitive result in the DWI image. Therefore, combined analysis of oblique coronal T2WI STIR and DWI image were applied in the actual research. Continuous 6 layers' DWI images were chosen with relative good cross section results and approximately similar area and position to oblique coronal image result, while scoring was the same as above. Additional scoring was given for lesion shown in the DWI images but not seen in the oblique coronal T2WI STIR images.

2.3.2 Observation

With two experienced diagnostician participating, double-blinding study was used to read the images. Comprehensive observation was performed about MRI multiple sequences (FSE T1WI, FSE T2WI, Oblique coronal T2 pressed fat sequence, DWI sequence) images. Compared

with the data before treatment, analysis of ADC value changes and SPARCC scoring of sacroiliac joints inflammation was made, in order to make sure the inflammation and its severity after clinical intervention treatment for tested AS patients. At last, a comprehensive evaluation of clinical therapeutic efficacy was accomplished.

2.3.3 Statistical analysis

Statistical analysis was performed using SPSS16.0 software. Intraclass correlation coefficient (ICC) was used to evaluate the reliability of observers. Paired T test was performed by two observers. ADC value was shown using mean ±SD, with confident interval 95% (95% CI). ADC and SPARCC scoring were conducted using correlation and regression analysis. A P value < 0.05 was considered statistically significant.

3 Results

3.1 Analysis of the reliability of the observers

ICC of observer A was 0.988, and observer B was 0.984. That showed there was high reliability of the observation. And there was no significant difference in the observational data between different observers (P =0.846).

3.1.1 Comparison of ADC value before and after treatment along ilium and sacrum surface of sacroiliac joint in case group

The ADC value along ilium and sacrum surface of sacroiliac joint was significantly lower than that of the contrast group (P<0.05) (Table 1).

3.1.2 SPARCC scoring of bone marrow in sacroiliac joint

Score range after treatment was 1-46 points (3-58 points before treatment), and MRI grade difference between before and after treatment was: 8-16 points. Wilcoxon symbol rank test analysis was performed, showing the effective result of the treatment in the case group(P=0.000 <0.05).

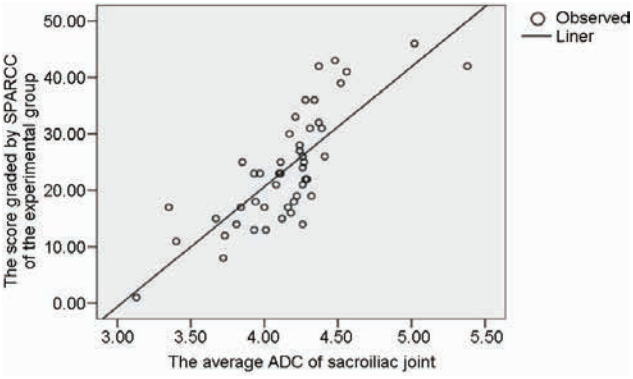

Figure 1: SPARCC scoring in experimental group

Table 1: Index difference between control and experimental group

		Before treatment	After treatment	t value	P value
ADC value (×10^{-4} mm^2/s)	Sacrum	5.05 ±1.10	4.34 ± 0.55	8.359	0.000
	Ilium	4.63 ± 0.79	3.96 ± 0.23	11.699	0.000

Notes: Paired T test was performed.

Table 2: Correlation and linear regression analysis of ADC value and SPARCC scoring

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	0.623	75.943	1	46	0.000	-64.420	21.262

3.1.3 Correlation and linear regression analysis of ADC value and SPARCC scoring

Spearman's rho correlation analysis was performed with a result of highly-positive correlation relationship (P=0.000<0.05), r= 0.784; linear regression (definition Y: SPARCC scoring value; X: ADC mean value) was performed (P=0.000 <0.05), independent variable X (ADC value) was statistically significant. The regression equation was Y=-64.420+21.262X, (R2 value 0.623) showing a good regression effect (Table 2, Figure 1).

4 Discussion

The main manifestation of AS is the progressive inflammation in the sacroiliac joint and spine little joints with an unclear pathogenesis and a possible correlation with heredity and environment [12]. AS is seen mostly in teenagers and males, MRI is more sensitive to early AS active inflammation compared to traditional X ray and CT examination [13]. The reflection of bone marrow edema [14] could provide important information for the pre-and-post diagnose, therapy and evaluation of disease.

DWI changes of early AS after treatment: magnetic DWI is conducted to show the water content and water molecular activity of human tissue through the detection of water molecular irregular free diffusion activity in the living body tissue, which is the only image method based on water molecular detection [15,16]. It has been reported [17] that peri-sacroiliac joint tissue' structure like skeleton and muscle will be better reflected and the clinical observation will be better performed with a best "b value" of 600s/mm2. For early AS patients, in sacroiliac joints, with synovium stave cells layer thicker, inflammatory cells infiltrating and pannus forming and invading into sub-articular sclerotin, bone marrow edema formed and existed, which was reflected in sub-sacroiliac joint surface bone marrow area as spot or even patchy diffusion restricted region (highly signal) on DWI image (Figure 2). After clinical intervention treatment, the inflammation infiltration decreased, and pannus reduced, and bone marrow edema relieved. Water molecular diffusion restricted region became smaller in corresponding position, and DWI diffusion restricted region' signal reduced with ADC value lower compared to contrast group. Statistical analysis was conducted with the ADC value before and after treatment (P <0.05), significantly revealing that AS inflammation activity was reduced after treatment in the case group. The ADC value was still lightly higher than that of contrast group because of slight or chronic inflammation.

4.1 SPARCC scoring

The latest scoring method of AS sacroiliac joint inflammation is Spondyloarthritis Research Consortium of Canada (SPARCC [18,19]) which is recommended by most scholars. Besides that there are other scoring systems like Leeds, Berlin and so on.

In practice, the horizontal axis pressure grease T2WI images are better than oblique coronary pressure grease T2WI images on image resolution with a relative easier operation. In the previous and middle phase of this study, some early and regional bone marrow edema wasn't

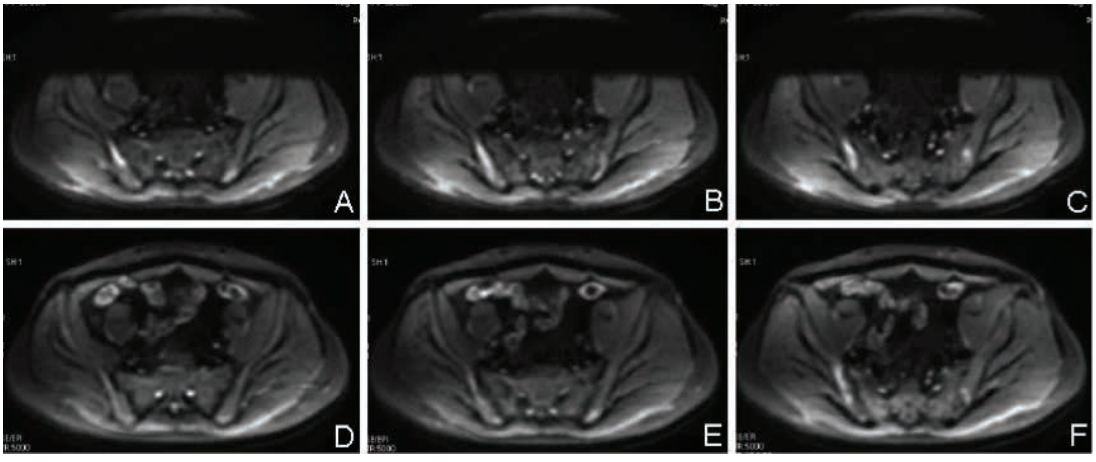

Figure 2: Comparison of DWI image in one patient before and after treatment (A, B, C: before treatment; D, E, F: after treatment). DWI image before treatment showed bilateral post-ilium striped diffusion restricted region; after 4 months' treatment, reexamination showed decreased signal in diffusion restricted region, shrink area and dwindled ADC value, reflecting a good therapy.

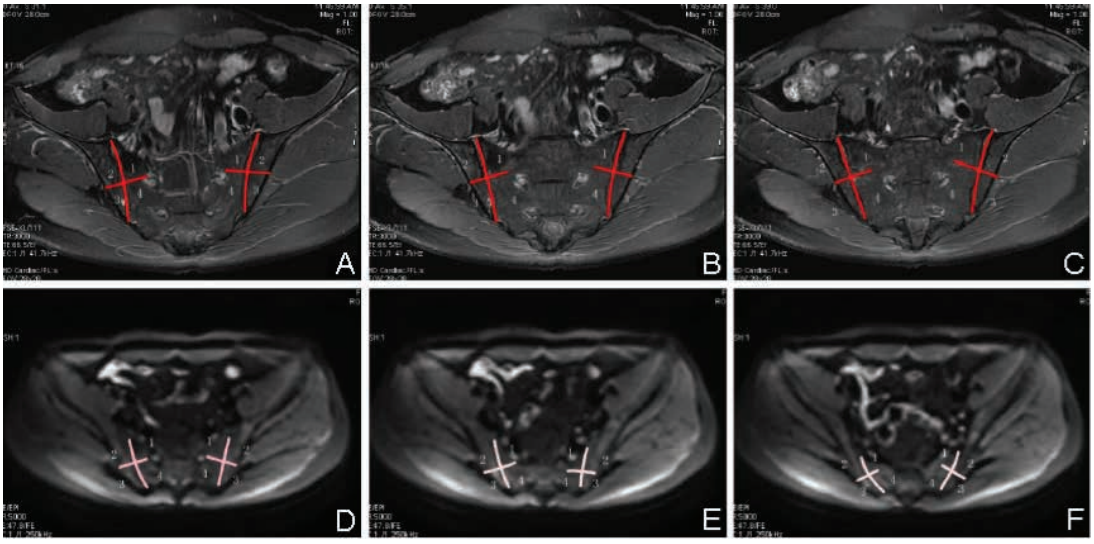

Figure 3: Bone marrow edema scoring on T2WI STIR sequence and DWI sequence in one patient. Bilateral sacroiliac joint was divided into four quadrants (1 supra-sacral, 2 supra-iliac, 3 infra-iliac, 4 infra-sacral), and scoring was performed following the principles above. A, B and C were STIR images, cumulative scoring was 2 points; D, E and F were DWI images, and the cumulative scoring was 15 points. This method could reflect some bone marrow edema which did exist but not shown in STIR sequence.

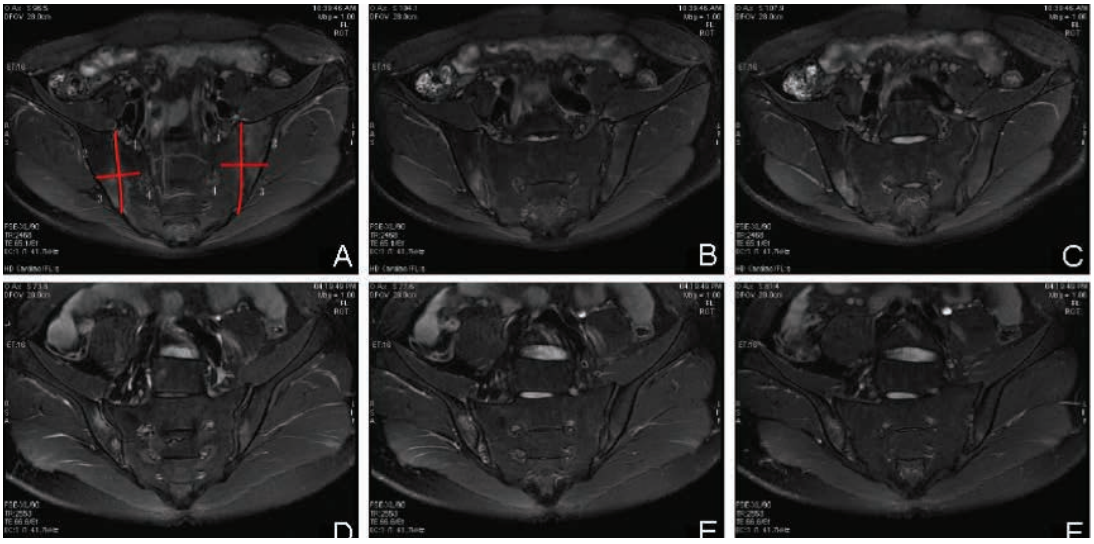

Figure 4: SPARCC scoring comparison of bone marrow edema before and after treatment in AS patients. Scoring of A, B and C (before treatment): 10, 8, 9; scoring of D, E and F (after treatment): 7, 5, 5. The scoring of bone marrow edema decreased significantly after treatment, showing reduced bone marrow edema and an effective therapy.

reflected well in the T2WI STIR images while more sensitive in the DWI images. Therefore, combined analysis of oblique coronal T2WI STIR and DWI image was applied in the comprehensive scoring. Continuous 6 layers' DWI images were chosen with relative good cross section results and approximately similar area and position to oblique coronal image result, and scoring is the same as SPARCC scoring. With this method there would be greater possibility to find out the bone marrow edema region which did exist without reflected in the oblique coronal T2WI STIR images. We think SPARCC scoring will be further completed and supplemented combined with DWI sequence (Figure 3).

In this study, score range in case group was 1-46 points (3-58 points in contrast group), and MRI grade difference between before and after treatment was 8-16 points. Wilcoxon symbol rank test analysis was conducted, showing the effective result of the treatment (P=0.000), which decreased bone marrow edema and reduced AS inflammation progress.

4.2 Correlation and linear regression analysis of ADC value and SPARCC scoring

There was a highly positive correlation relationship between ADC value and SPARCC scoring (P=0.000<0.05) (Figure 4). Linear regression analysis was conducted with a result of good regression effect. The regression equation: Y=-64.420+21.262X (definition Y: SPARCC scoring value; X: ADC mean value), showing that a higher ADC value (AS inflammation activity higher) accompanied with a higher SPARCC value. There was a linear relationship between them through which possible ADC value or SPARCC scoring value could be known.

In this study, MRI routine sequence examination showed a greater sensibility for AS inflammation activity while a limited evaluation value for early AS patients without obvious bone marrow edema or with only small regional bone marrow edema. For those patients above, it couldn't be done to find out whether the post-treatment inflammation activity changed or not through MRI signal changes, so the curative effect couldn't be evaluated. However, DWI sequence and SPARCC scoring could be combined to effectively assess early AS curative situation, to provide radiologist standards for clinical therapy evaluation and to make up the insufficiency of routine MRI examination.

It is objective that we have data with great discrete value in this study, but the general rule between them could still be used to study and predict the inflammation changes and development of AS, and to provide quantized standards for clinic research. Because most of the patients involved in this study were of I level, whether AS inflammation of II level accords with this linear regression relationship is still uncertain, which is worthy of further investigation.

Abbreviations

ADC: apparent diffusion coefficient
AS: ankylosing spondylitis
DWI: diffusion weighted imaging
SPARCC: Spondyloarthritis Research Consortium of Canada
STIR: short TI inversion recovery
T2WI: T2 weighted image

Conflict of interest statement: Authors state no conflict of interest

Reference

[1] Gašperšič N., Serša I., Jevtič V., Tomšič M., Praprotnik S., Monitoring ankylosing spondylitis therapy by dynamic contrast-enhanced and diffusion-weighted magnetic resonance imaging, Skeletal Radiol, 2008, 37, 123-131
[2] Ji W, Li J, Lin Y, Song YN, Zhang M, Ke Y, Ren Y, Deng X, Zhang J, Huang F, Yu D. Report of 12 cases of ankylosing spondylitis patients treated with Tripterygium wilfordii. Clin Rheumatol. 2010 Sep;29(9):1067-1072.
[3] Jansen JP, Gaugris S, Choy EH, Ostor A, Nash JT, Stam W.cost effectiveness of etoricoxib versus celecoxib and non-selective nsaids in the treatment of ankylosing spondylitis. Pharmacoeconomics. 2010;28(4):323-344
[4] Braun J, Zochling J, Baraliakos X, Alten R, Burmester G, Grasedyck K, Brandt J, Haibel H, Hammer M, Krause A, Mielke F, Tony HP, Ebner W, Gömör B, Hermann J, Zeidler H, Beck E, Baumgaertner M, Sieper J.efficacy of sulfasalazine in patients with inflammatory back pain due to undifferentiated spondyloarthritis and early ankylosing spondylitis: a multicentre randomised controlled trial. Ann Rheum Dis. 2006 Sep;65(9):1147-1153
[5] Ternant D, Mulleman D, Lauféron F, Vignault C, Ducourau E, Wendling D, Goupille P, Paintaud G.influence of methotrexate on infliximab pharmacokinetics and pharmacodynamics in ankylosing spondylitis. Br J Clin Pharmacol. 2012 Jan;73(1):55-65
[6] Deng X, Zhang J, Zhang J, Huang F. Thalidomide reduces recurrence of ankylosing spondylitis in patients following discontinuation of etanercept. Rheumatol Int. 2013 Jun;33(6):1409-1413
[7] Dougados M, Braun J, Szanto S, Combe B, Elbaz M, Geher P, Thabut G, Leblanc V, Logeart I.Efficacy of etanercept on rheumatic signs and pulmonary function tests in advanced ankylosingspondylitis: results of a randomised double-blind placebo-controlled study (SPINE). Ann Rheum Dis. 2011 May;70(5):799-804
[8] Park W, Hrycaj P, Jeka S, Kovalenko V, Lysenko G, Miranda P, Mikazane H, Gutierrez-Ureña S, Lim M, Lee YA, Lee SJ, Kim H, Yoo DH, Braun J.A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. Ann Rheum Dis. 2013 Oct;72(10):1605-1612
[9] van der Heijde D, Schiff MH, Sieper J, Kivitz AJ, Wong RL, Kupper H, Dijkmans BA, Mease PJ, Davis JC Jr; ATLASStudy Group. Adalimumab effectiveness for the treatment of ankylosing spondylitis is maintained for up to 2 years: long-term results from the ATLAS trial. Ann Rheum Dis. 2009 Jun;68(6):922-929
[10] Weckbach S., Schewe S., Michaely H.J., Steffinger D., Reiser M.F., Glaser C., Whole-body MR imaging in psoriatic arthritis: additional value for therapeutic decision making, Eur J Radiol, 2011, 77, 149-155
[11] Maksymowych W.P., Inman R.D., Salonen D., Dhillon S.S., 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 Rtheum, 2005, 53, 703-709

[12] Végvári A., Szabó Z., Szántó S., Glant T.T., Mikecz K., Szekanecz Z., The genetic background of ankylosing spondylitis, Joint Bone Spine, 2009, 76, 623-628
[13] Chary-Valckenaere I, d'Agostino MA, Loeuille D. Role for imaging studies in ankylosing spondylitis. Joint Bone Spine. 2011 Mar;78(2):138-143
[14] Appel H, Loddenkemper C, Grozdanovic Z, Ebhardt H, Dreimann M, Hempfing A, Stein H, Metz-Stavenhagen P, Rudwaleit M, Sieper J. Correlation of histopathological findings and magnetic resonance imaging in the spine of patients with ankylosing spondylitis. Arthritis Res Ther. 2006;8(5):R143
[15] Zhang C.-y., Rong R., Wang X.-y., Age-related changes of bone marrow of normal adult man on diffusion weighted imaging, Chin Med Sci J, 2008, 23, 162-165
[16] Kwee T.C., Takahara T., Ochiai R., Katahira K., Van Cauteren M., Imai Y., et al., Whole-body diffusion-weighted magnetic resonance imaging, Eur J Radiol, 2009, 70, 409-417
[17] Bozgeyik Z., Ozgocmen S., Kocakoc E., Role of diffusion-weighted MRI in the detection of early active sacroiliitis, Am J Roentgenol, 2008, 191, 980-986
[18] Machado P., Landewé R., Lie E., Kvien T.K., Braun J., Baker D., et al., Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores, Ann Rheum Dis, 2011, 70, 47-53
[19] Maksymowych W.P., Lambert R.G., Brown L.S., Pangan A.L., Defining the Minimally Important Change for the SpondyloArthritis Research Consortium of Canada Spine and Sacroiliac Joint Magnetic Resonance Imaging Indices for Ankylosing Spondylitis, J Rheumatol, 2012, 39, 1666-1674