Comparing diffusion weighted imaging with clinical and blood parameters, and with short tau inversion recovery sequence in detecting spinal and sacroiliac joint inflammation in axial spondyloarthritis

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Abstract

Objective

To investigate the usefulness of diffusion weighted imaging (DWI) by comparing with clinical features, blood parameters and traditional short tau inversion recovery (STIR) sequence in detecting spinal and sacroiliac (SI) joint inflammation in axial spondyloarthritis (axSpA) patients.

Methods

One hundred and ten axSpA patients were recruited. Clinical, radiological and blood parameters were recorded. DWI and STIR MRI were performed simultaneously and results were scored according to the Spondyloarthritis Research Consortium of Canada (SPARCC) for comparison. Apparent diffusion coefficient (ADC) values were also calculated.

Results

DWI did not correlate with clinical parameters or blood parameters. It also had lowered sensitivity. When compared with STIR sequence, it correlated well with STIR sequence at the SI joint level (CC 0.76, p<0.001), but weakly at the spinal level (CC 0.23, p=0.02). At the SI joint level, the presence of inflammation on both STIR sequence and DWI was associated with an increase in maximum (B=0.24, p=0.02 in STIR; B=0.37, p<0.001 in DWI) and mean ADC values (B=0.17, p=0.003 in STIR; B=0.15, p=0.01 in DWI). Maximum (B=0.19, p=0.04) and mean spinal ADC values (B=0.18, p=0.01) were also positively associated with DWI detected spinal inflammation. Presence of Modic lesions showed positive correlation with STIR sequence (B=7.12, p=0.01) but not spinal ADC values.

Conclusion

Despite DWI correlates with STIR sequence, it has lower sensitivity. However, ADC values appear to be independent of Modic lesions and may supplement STIR sequence to differentiate degeneration.

Key words

spondyloarthritis, diffusion weighted imaging, magnetic resonance imaging, inflammation

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Introduction

Disease activity assessment and monitoring is important in deciding and guiding treatment. In axial spondyloarthritis (axSpA), disease activity indices remain popular and important disease assessment tools. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (1) is an expert-derived assessment method while the Ankylosing Spondylitis Disease Activity Score (ASDAS) (2, 3) is a data driven index. They play important roles in screening candidates with active disease and monitoring disease progress, especially during biologic therapies. Despite their popularity, however, previous studies have shown inconsistent correlation with spinal inflammation (4, 5). Magnetic resonance imaging (MRI) is increasingly used as an objective method of disease assessment in SpA and axial psoriatic arthritis (PsA) (6, 7).

Recommended MRI sequences in detecting spinal inflammation include fat-saturated T2 weighted turbo spin-echo sequence and short tau inversion recovery (STIR) sequence (8). However, both have limited ability in differentiating degeneration (*i.e.* Type I Modic lesions) (9) from axial disease activity. A study had shown that Modic changes were common among 30- to 40-year-old patients and that sacroiliiac (SI) joint bone marrow oedema, sclerosis and erosions were frequently observed in women with pregnancy-related low back pain (10), potentially leading to misdiagnosis and inaccurate disease assessment. Recently, diffusion weighted imaging (DWI) has been proposed as an alternative evaluation method (11). Apparent diffusion coefficient (ADC), a derivation of DWI, quantifies the alterations in water diffusivity resulting from microscopic structural changes. The method can potentially serve as an imaging tool in evaluating and diagnosis of rheumatic diseases as well as differentiating degenerative (Modic) lesions in patients with axial SpA (12). Data on the application of DWI in axSpA is limited. There were only a few studies directly comparing DWI and STIR images at the level of the sacroiliac (SI) joints (12, 13). The utility of DWI in axSpA needs validation. Our goal is, therefore, to evaluate and compare DWI with STIR and other clinical parameters in detecting spinal inflammation in axSpA patients. It is hoped that more information could assist in deciding whether DWI should be used in the management of the disease.

Methods

This is a cross-sectional analysis of 110 axSpA patients recruited consecutively from two rheumatology centres in Hong Kong (Queen Mary Hospital and Pamela Youde Nethersole Eastern Hospital) from March 2014 to October 2015. Our study design is a prospective follow up of at least one year to determine and compare the changes in both STIR sequence and DWI with or without biologics treatment. This analysis only includes data at the initial time point. Written informed consent was obtained from all studied patients. Inclusion criteria included: i) rheumatologist-diagnosed axSpA fulfilling Assessment of SpondyloArthritis International Society (ASAS) classification criteria, ii) age greater than 18 years, iii) current back pain, iv) ability to give written consent, and v) biologics naïve. Exclusion criteria included: i) pregnancy, ii) inability to undergo MRI examination, and inability to give written consent.

Clinical and demographic data were collected from the recruited patients. This included age, sex, smoking and drinking history, duration of back pain, location and characteristics of back pain, extra-spinal features, and associated medical history. Patients were further classified into 5 subtypes of axSpA: i) ankylosing spondylitis (AS), ii) undifferentiated spondyloarthritis (USpA), iii) psoriatic arthritis (PsA), iv) reactive arthritis (ReA), and v) inflammatory bowel disease related spondyloarthritis (IBD SpA). Blood parameters including human leucocyte antigen (HLA) B27, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were recorded.

The study was approved by both the Institutional Review Boards of The University of Hong Kong and Pamela Youde Nethersole Eastern Hospital. It was conducted in accordance with the

Declaration of Helsinki and the guidance for good clinical practice, 30 November 2006.

Disease activity, functional status and spinal mobility

Patients were asked to complete the Bath Ankylosing Spondylitis Global score (BAS-G) (14). Disease activity was assessed by BASDAI and ASDAS. The latter was calculated based on both CRP (ASDAS-CRP) and ESR (ASDAS-ESR). Funtional status was assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) and spinal mobility by the Bath Ankylosing Spondylitis Metrology Index (BASMI) (15).

Radiographs of cervical and lumbosacral spine

Radiographs of cervical (lateral view) and lumbosacral (anteroposterior and lateral view) spine were performed. They were graded by 2 rheumatologists by concensus to determine the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) (16) and sacroiliitis. SI joint from lumbosacral radiographs (anteroposterior view) were graded into 4 grades according to the Modified New York criteria (17): 0, normal; 1, doubtful; 2, obvious; 3, fusion. Bilateral sacroiliitis grade 2 or above or unilateral sacroiliitis grade 3 or above was defined as radiological AS.

MRI STIR sequence and DWI

All recruited patients underwent whole spine and bilateral SI joint MRI examinations using a 3T Achieva scanner (Philips Healthcare, Best, the Netherlands). A torso coil was used to image both spine and sacroiliac joints. STIR sequence, T1 weighted, T2 weighted TSE and DWI were obtained simultaneously (Table I).

Blinded to clinical data, STIR images of the spine and SI joints were scored by a radiologist (CSW) and a rheumatologist with 6 years of SpA MRI experience (HYC). DWI were scored by 2 radiologists (VWHL, HG). Both sequences were graded according to the spondyloarthritis research consortium of Canada MRI inflammation (SPARCC) scoring method (18, 19) by consensus. Presence of bone marrow oedema (BME) was defined as a positive image in our study. An independent physician (PHL) determined the presence of type I Modic lesions defined by hyperintense STIR and hypointense T1 vertebral endplate changes associated with disc degeneration.

An independent radiologist (XP) blinded to SPARCC manually drew in regions of interests (ROIs). After excluding the false impression of T2 shine-through, regions with elevated diffusion observed on ADC maps were considered lesions, and ROI was drawn along the border of each lesion to include as much abnormality as possible while excluding surrounding normal tissue. The maximum and mean ADC values of the lesion were calculated correspondingly using ImageJ (20). In addition, the mean ADC value of the spine and sacroiliac joint were measured by placing equal sized ROIs on the vertebral body (sagittal plane) and sacroiliac subchondral bone (coronal plane) respectively. Positive STIR/ DWI was defined as presence of inflammatory lesion in respective images. Similarly ADC was defined as the presence of inflammatory lesion via ADC measurement.

Sample size calculation

There is only limited data on the use of DWI in axSpA patients, sample size calculation is not feasible.

Statistical analyses

Continuous and categorical data was compared using a Student's *t*-test and chi-square test respectively. Pearson's correlation was used to test the correlation coefficient (CC) between STIR sequence and DWI scorings. Weighted Cohen's Kappa values were used to assess the agreement in ability to detect inflammation between DWI and STIR images. Agreement was defined as slight, fair, moderate, substantial and almost perfect by values of weighted Cohen's kappa $\kappa<0.2$, $\kappa=0.2-<0.4$, $\kappa=0.4-<0.6$, $=0.6-<0.8$, $\kappa=0.8-1$, respectively. Univariate linear regression and logistic regression were used to determine the associations with a continuous and binary dependent variables respectively. The 95% confidence intervals (CI) were calculated and *p*-values less than 0.05 were considered statistically significant. All statistic analyses were performed using the statistical product and service solutions (SPSS) package 21.0.

Table I. Imaging parameters for STIR, T1 weighted, T2 weighted TSE and DWI sequences.

	STIR	T1w	T2w	DWI
TR/TE (ms)	5000/80	800/8	3000/110	4000/90
Field-of-view (mm^2)	150 × 240	150 × 240	150 × 240	300 × 241
Matrix size	152 × 157	168 × 217	168 × 215	124 × 100
Slice thickness (mm)	3.5	3.5	3.5	4
SENSE factor	-	-	-	2

Results

All one hundred and ten recruited patients had MRI examinations performed. SI joint DWI data was missing in one patient (0.9%) and 2 ADC measurements (1.8%) were missing from analyses. Of all recruited patients, 48.6% had positive STIR sequence and 41.8% had positive DWI at the spinal level. A significant portion (18%) of studied patients were found to have spine degeneration (Modic lesions) in STIR MRI. At the SI joint level, 45.8% were found to have positive STIR images while 22.2% had positive DWI.

AS (n=72/110; 65.5%) was the major subtype in our axSpA cohort, followed by PsA (n=21/1110; 19.1%), USpA (n=14/110; 12.7%), IBP SpA (n=2/110; 1.8%), and ReA (n=1/110; 0.9%). Table II shows the baseline characteristics of patients. They were characterized by prolonged disease duration, moderate to high disease activity, moderate functional impairment, and significant degree of radiolographic changes. The majority of them were on non-steroidal anti-inflammatory drugs (NSAID) or cyclooxygenase II (COX II) inhibitors and suffered from inflammatory back pain (IBP).

Table II. Baseline characteristics of studied patients.

Age	43.05±15.53 years
Duration of back pain	11.82±11.25 years
Male: Female	5.4:4.6
B27 positivity	80.8%
Smoker	27.3%
Drinker	13.2%
ASDAS-ESR	3.09±1.08
ASDAS-CRP	1.84±0.91
BASDAI	4.63±2.22
BASFI	2.92±2.51
BASMI	3.39±1.47
Radiological AS	81.5%
mSASSS	11.24±17.00
STIR SPARCC (spine)	5.30±9.95
STIR SPARCC (SI joints)	5.30±10.34
DWI SPARCC (spine)	2.66±5.43
DWI SPARCC (SI joints)	1.21±2.85
Maximum spine ADC values	1.94±0.34
Mean spine ADC values	1.40±2.56
Maximum SI joints ADC values	1.19±0.37
Mean SI joints ADC values	0.65±0.21
Patients with inflammatory back pain	66.4%
Ever use NSAIDs/ COX2	76.9%
Present of Modic lesion(s)	18.0%

Regression models: associations between clinical parameters, inflammatory markers and positive STIR/ DWI

Univariate logistic regressions were performed using positive STIR sequence, and positive DWI as dependent variables. Clinical parameters and inflammatory markers including back pain numerical rating scale (NRS), BASDAI, ESR, CRP, ASDAS-ESR, and ASDAS-CRP were used as independent variables. Results are in Table III. None of the independent variables showed significant association with MRI detected inflammation in the regression models.

Comparing STIR sequence and DWI

Correlations between SPARCC STIR and DWI were calculated. At the SI joint level, STIR correlated well with DWI (CC 0.76; $p<0.001$). At the spinal level, STIR and DWI showed weak correlation only (CC 0.22; $p=0.02$).

Table IV shows the agreements in detecting BME between STIR and DWI at different axial joints levels. Despite good correlations between SPARCC STIR and DWI at SI joints level, the agreements between the two images were only fair and DWI showed lower sensitivity in detecting inflammatory lesions.

Table III. Association between clinical parameters, inflammatory markers and positive STIR/ DWI.

	Positive STIR		Positive DWI	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Back pain NRS	0.91 (0.76; 1.08) n=109	0.26	0.93 (0.80; 1.08) n=109	0.35
BASDAI	0.89 (0.74; 1.08) n=109	0.23	0.90 (0.76; 1.07) n=109	0.25
ESR	1.01 (0.99; 1.02) n=108	0.38	1.01 (0.99; 1.02) n=108	0.37
CRP	1.41 (0.94; 2.12) n=109	0.10	1.02 (0.90; 1.16) n=109	0.71
ASDAS-ESR	0.82 (0.55; 1.21) n=107	0.31	0.88 (0.61; 1.26) n=107	0.47
ASDAS-CRP	0.95 (0.59; 1.50) n=108	0.81	0.83 (0.54; 1.28) n=108	0.41

Table IV. Agreements between STIR and DWI at spine, SI joints, and spine and SI joints levels.

	Negative DWI	Positive DWI	Cohen's Kappa Value
Spine and SI joints			
Negative STIR	19/108 (17.6%)	11/108 (10.2%)	0.23
Positive STIR	28/108 (25.9%)	50/108 (46.3%)	
Spine			
Negative STIR	38/109 (34.9%)	18/109 (16.5%)	0.21
Positive STIR	25/109 (22.9%)	28/109 (25.7%)	
SI joints			
Negative STIR	53/106 (50.0%)	4/106 (3.77%)	0.35
Positive STIR	29/106 (27.4%)	20/106 (18.9%)	

Table V. Associations betweeen positive STIR/ DWI with ADC values.

	SI max lesional ADC		SI mean lesional ADC	
	B (95% CI)	*p*-value	B (95% CI)	*p*-value
Positive STIR	0.24 (0.04; 0.44) n=58	0.02	0.17 (0.06; 0.28) n=58	0.003
Positive DWI	0.37 (0.20; 0.55) n=58	<0.001	0.15 (0.04; 0.25) n=58	0.01
	Spine max lesional ADC		Spine mean lesional ADC	
	B (95% CI)	*p*-value	B (95% CI)	*p*-value
Positive STIR	-0.03 (-0.26; 0.19) n=54	0.77	-0.04 (-0.21; 0.13) n=55	0.62
Positive DWI	0.19 (0.01; 0.37) n=54	0.04	0.18 (0.05; 0.32) n=55	0.01
Presence of Modic lesion	0.18 (-0.04; 0.40) n=49	0.11	0.04 (-0.12; 0.20) n=50	0.63

Regression models: associations betweeen positive STIR/ DWI with ADC values

Univariate linear regressions were peformed using maximum and mean ADC values as dependent variables at both the spinal and SI joint level. Independent variables used at the SI joint level included positive STIR and positive DWI. At the spine level, positive

STIR, positive DWI and presence of Modic lesions were used as independent variables. Both positive STIR and DWI associated positively with maximum and mean ADC values at the SI joint level while at the spinal level, positive STIR and presence of Modic lesion failed to show any association with ADC. The results are shown in Table V.

Regression models: associations between clinical parameters, inflammatory markers and ADC values

Table VI shows the results. Only ASDAS-CRP was associated with SI joints mean lesional ADC.

Regression model: association between SPARCC (spine) STIR and degeneration

Univariate linear regression using SPARCC (spine) STIR sequence as dependent variable and presence of Modic lesions as independent variable showed the two were positively associated (B=7.17, CI 2.11; 12.24, p=0.01).

Table VI. Associations between clinical parameters, inflammatory markers and ADC values.

	Spinal max lesional ADC		Spinal mean lesional ADC		Spinal mean non-lesional ADC	
	B (95% CI)	p-value	B (95% CI)	p-value	B (95% CI)	p-value
Back pain NRS	0.00 (-0.04; 0.04) n=54	0.89	-0.01 (-0.04; 0.02) n=55	0.48	0.00 (-0.04; 0.04) n=54	0.89
BASDAI	0.01 (-0.03; 0.06) n=54	0.57	-0.01 (-0.04; 0.02) n=55	0.47	0.01 (-0.03; 0.06) n=54	0.57
ESR	0.00 (-0.00; 0.00) n=54	0.99	-0.00 (-0.00; 0.00) n=55	0.65	0.00 (-0.00; 0.00) n=54	0.99
CRP	0.00 (-0.05; 0.04) n=54	0.92	-0.01 (-0.05; 0.02) n=55	0.45	0.00 (-0.05; 0.04) n=54	0.92
ASDAS-ESR	0.01 (-0.07; 0.10) n=54	0.75	-0.02 (-0.09; 0.04) n=55	0.50	0.01 (-0.07; 0.10) n=54	0.75
ASDAS-CRP	0.02 (-0.10; 0.13) n=54	0.74	-0.04 (-0.12; 0.05) n=55	0.37	0.02 (-0.10; 0.13) n=54	0.74
	SI joints max lesional ADC		SI joints mean lesional ADC		SI joints mean non-lesional ADC	
Back pain NRS	0.02 (-0.02; 0.06) n=58	0.29	0.02 (-0.01; 0.04) n=58	0.15	0.02 (-0.02; 0.06) n=58	0.29
BASDAI	0.01 (-0.04; 0.05) n=58	0.68	0.01 (-0.01; 0.04) n=58	0.26	0.01 (-0.04; 0.05) n=58	0.68
ESR	-0.00 (-0.00; 0.00) n=58	0.73	0.00 (-0.00; 0.00) n=58	0.39	-0.00 (-0.00; 0.00) n=58	0.73
CRP	0.01 (-0.04; 0.05) n=58	0.81 n=58	0.02 (-0.01; 0.04)	0.19	0.01 (-0.04; 0.05) n=58	0.81
ASDAS-ESR	0.02 (-0.07; 0.11) n=58	0.69	0.04 (-0.01; 0.01) n=58	0.10	0.02 (-0.07; 0.11) n=58	0.69
ASDAS-CRP	0.06 (-0.05; 0.16) n=58	0.30	0.07 (0.01; 0.12) n=58	0.03	0.06 (-0.05; 0.16) n=58	0.30

Discussion

To the best of our knowledge, this is the first study directly comparing DWI with the traditional STIR sequence at both the spinal and SI joint levels in axSpA patients. Ours is also the largest axial DWI cohort of SpA patients reported so far. Although not as sensitive as STIR, we show DWI has the ability in demonstrating active BME in SI joints. At the spinal level, despite a positive but weak correlation, there is discrepancy in the imaging findings between the two MRI techniques.

Compared to international cohorts, our population has more active sacroiliitis (45.8%) and spondylitis (41.8%) in STIR MRI (2, 21). This is due to inclusion of patients with current back pain in our study, aiming to recruit more active MRIs for comparison. In this way, our cohort is more representative of real day to day clinical practice. In daily practice, rheumatologists tend to order MRI for SpA patients with back pain in order to determine whether biologic therapy is indicated, although the role of MRI for disease monitoring is still under development (22).

We correlate clinical and blood parameters with positive spine and SI joints MRI, instead of with SPARCC MRI scores. SPARCC is designed to assess spinal and SI joint inflammation independently (18, 19) without a score to assess total axial joint inflammation. It was not the original purpose of this study to correlate with an individual part of the axial joints. In addition, in daily practice, rheumatologists are more interested in the presence of active axial inflammation rather than the extent of inflammation by SPARCC. Once again, our data resembles more actual day to day practice.

There are no associations between MRI (STIR and DWI) inflammation and clinical or blood parameters (back pain NRS, BASDAI, ESR, CRP, ASDAS-ESR, ASDAS-CRP). Despite the popularity of disease activity scores and inflammatory markers, our study shows that these perform poorly in screening for axial disease activity. The associations between clinical parameters, inflammatory markers, and MRI inflammation are inconsistent, and a lack of association has been demonstrated in previous studies (4, 23-24). Our cohort, however, selects only patients with back pain which may potentially lead to bias in the analyses. It is worth noting that in an international cohort, clinical parameters and inflammatory markers were found to correlate with MRI sacroiliitis cross-sectionally and longitudinally in male patients only (25).

SPARCC scores describe the extend of MRI inflammation. At SI joints level, good correlation between that of STIR and DWI suggests the two imaging techniques are able to detect similar pattern of inflammation. Despite the observation, the sensitivity of DWI is lower than STIR in detecting inflamma-

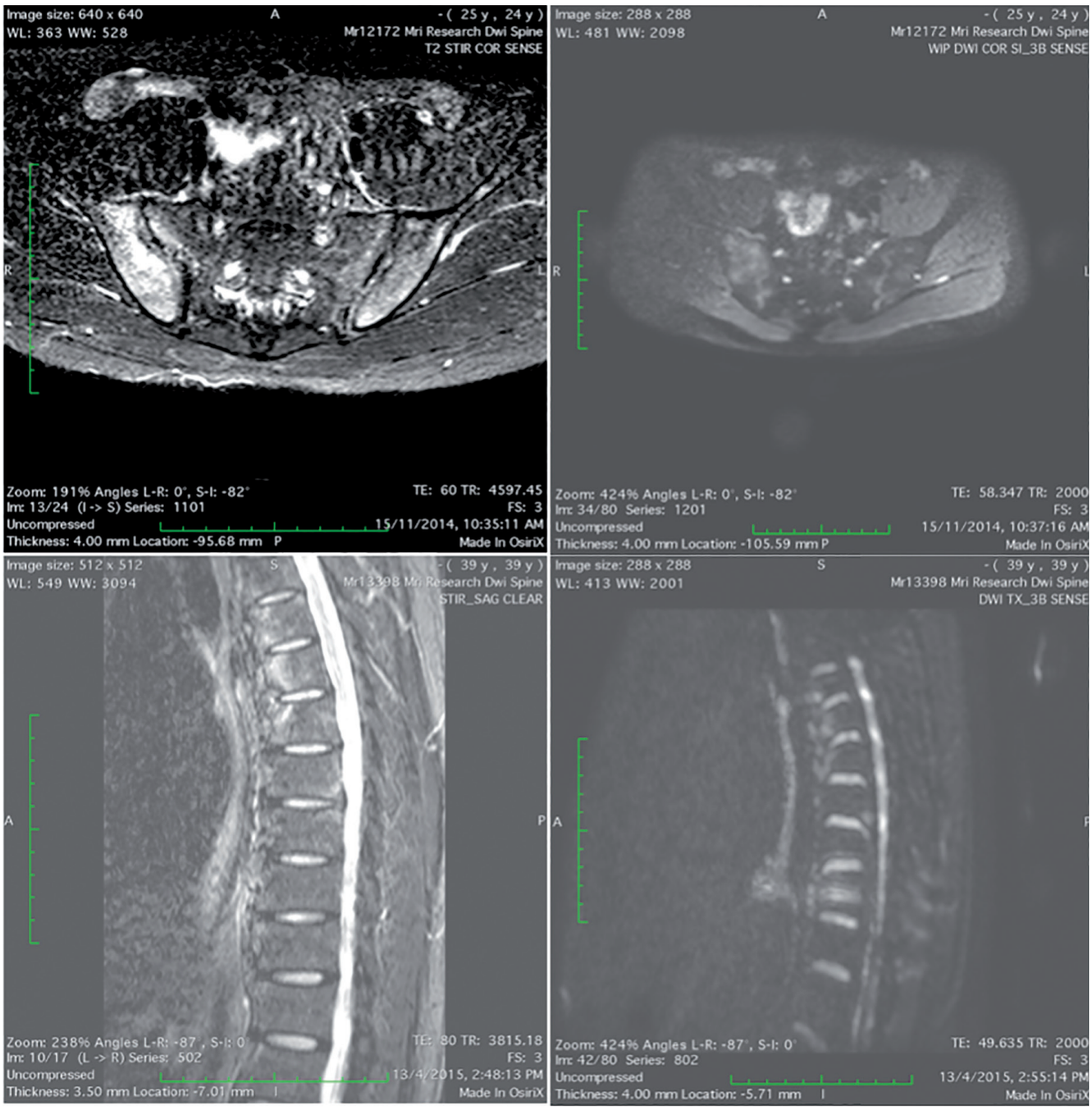

Fig. 1. DWI images have poorer resolution. Left upper: STIR SI joints image; right upper: DWI SI joints image. Left lower: STIR spine image; right lower: DWI spine image.

tion and the agreement between the two images is only fair. At the spinal level, the agreement is even weaker. DWI has lowered spatial resolution (Fig. 1), leading to a lowered sensitivity. Despite the lowered resolution, a previous study of 42 patients showed DWI to be sensitive when compared to T1-weighted gadolinium images in detecting active sacroiliitis (12). It is worth to note that the study measured lesional ADC based on T1-weighted gadolinium images which were also used as the images for comparison, created potential bias. Instead of using STIR/DWI deduced lesional ADC, we avoid the same bias by also comparing independent SPARCC scores of STIR and DWI images.

SI joint BME in STIR sequence has been proven to correlate with inflammation by histology (26, 27). As DWI and STIR correlate well at SI joints level, we can deduce that SI joint BME in DWI would also correlate with histological inflammation. In contrast, the correlation of SPARCC scores between STIR and DWI of the spine is weak. The reasons for the discrepancy would need further study. We propose the images of STIR could detect small inflammatory lesions like the conrner inflammatory lesions (CIL) (28) which would be difficult to be detected in

DWI images. Although a small study had validated DWI spine as a method of disease monitoring (29), data on its usefulness in axSpA is still lacking. Further studies will be needed to identify differences between STIR and DWI images at the spinal level.

Few studies investigated lesional ADC values (30-32). Our mean lesional value appears to be compatible with other reports, but the true cut off value has not been validated. As expected, positive STIR and DWI predicts higher maximum and mean ADC values at SI joints. Nevertheless, it is interesting to observe that positive STIR at the spinal level had no association with maximum and mean ADC values. As pointed out, STIR images have better sensitivity than DWI. STIR sequence has greater ability to pick up lesions with low ADC values, leading to the loss of association between ADC and positive STIR. Our results also show that the presence of Modic lesions is associated with higher SPARCC spine score in the STIR sequence but has no association with both maximum and mean spine ADC values. This suggests that degenerations in the spine may have effects on disease activity interpretation in STIR images. ADC values, in contrast, do not appear to be affected. Studies on the use of ADC to differentiate inflammation from degeneration is limited but prelimiary result seems to be promising (11).

Lastly, we analysed the maximum and mean ADC values for their associations with clinical activity and inflammatory markers aiming to determine the clinical significance of the use of ADC values in axSpA. Unfortunately, none showed positive associations in the regression models. A previous study showed BASDAI to be associated with ADC values (33) while another showed only slight correlation between CRP and ADC values (34). We propose that the ADC values can offer additional information on top of clinical parameters, although its true clinical implication on axSpA patients will need further study.

Limitations and future prospects

Our analysis is limited by its cross-sectional design and the lack of control of normal individuals. Further, we have not examined the use of DWI in early SpA. Our cohort mainly involved patients with long disease duration. As stated in the methods section, we plan to follow up our axSpA patients (with or without biologics treatment) with reassessment STIR and DWI for more complete evaluation. We also plan to include patients with pure spinal degeneration to assess the ability of DWI in differenting degeneration from inflammation.

Conclusion

Clinical disease activities and inflammatory markers correlate poorly with MRI findings. Compare to DWI, STIR sequence has better sensitivity. However, when combine with STIR sequence, DWI-ADC values might be able to differentiate disease activity from degeneration.

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References

1. GARRETT S, JENKINSON T, KENNEDY LG, WHITELOCK H, GAISFORD P, CALIN A: A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994; 21: 2286-91.
2. RUDWALEIT M, LANDEWÉ R, VAN DER HEIJDE D *et al*.: The develoopment of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. *Ann Rheum Dis* 2009; 68: 770-6.
3. RUDWALEIT M, VAN DER HEIJDE D, LANDEWÉ R *et al*.: The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009; 68: 777-83.
4. KILTZ U, BARALIAKOS X, KARAKOSTAS P *et al*.: The degree of spinal inflammation is similar in patients with axial spondyloarthritis who report high or low levels of disease activity: a cohort study. *Ann Rheum Dis* 2012; 71: 1207-11.
5. MACKAY JW, ABOELMAGD S, GAFFNEY JK: Correlation between clinical and MRI disease activity scores in axial spondyloarthritis. *Clin Rheumatol* 2015; 34: 1633-8.
6. OSTERGAARD M, POGGENBORG RP, AXELSEN MB *et al*.: Magnetic resonance imaging in spondyloarthritis – how to quantify findings and measure response. *Best Pract Res Clin Rheumatol* 2010 24: 637-57.
7. POGGENBORG RP, SORENSEN IJ, PEDERSEN SJ, OSTERGAARD M: Magnetic resonance imaging for diagnosing, monitoring and prognostication in psoriatic arthritis. *Clin Exp Rheumatol* 2015; 33 (Suppl. 93): S66-9.
8. SIEPER J, RUDWELEIT M, BARALIAKOS X *et al*.: The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis* 2009; 68 (Suppl. II): ii1-ii4.
9. MODIC MT, STEINBERG PM, ROSS JS, MASARYK TJ, CARTER JR: Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. *Radiology* 1988 Jan; 166: 193-9.
10. ARNBAK B, JENSEN TS, EGUND N *et al*.: Prevalence of degenerative and spondyloarthritis related magnetic resonance imaging findings in the spine and sacroiliac joints in patients with persistant low back pain. *Eur Radiol* 2016; 26: 1191-2013.
11. DALLAUDIERE B, DAUTRY R, PREUX PM *et al*.: Comparison of apparent diffusion coefficient in spondylarthritis axial active inflammatory lesions and type 1 Modic changes. *Eur J Radiol* 2014; 83: 366-70.
12. BOZGEYIK Z, OZGOCMEN S, KOCAKOC E: Role of diffusion-weighted MRI in the detection of early active sacroiliitis. *AJR Am J Roentgenol* 2008; 191: 980-6.
13. SANAL HT, YILMAZ S, KALYONCU U *et al*.: Value of DWI in visual assessment of activity of sacoiliitis in longstanding ankylosing spondylitis patients. *Skeletal Radiol* 2013; 42: 289-93.
14. JONES SD, STEINER A, GARRETT SL, CALIN A: The Bath Ankylosing Spondylitis Patient Global Score (BAS-G). *Br J Rheumatol* 1996; 35: 66-71.
15. JONES SD, PORTER J, GARRETT SL, KENNEDY LG, WHITELOCK H, CALIN A: A new scoring system for the Bath Ankylosing Spondylitis Metrology Index (BASMI). *J Rheumatol* 1995; 22: 1609.
16. CREEMERS MC, FRANSSEN MJ, VAN'T HOF MA, GRIBNAU FW, VAN DE PUTTE LB, VAN RIEL PL: Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. *Ann Rheum Dis* 2005; 64: 127-9.
17. VAN DER LINDEN S, VALKENBURG HA, CATS A: Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984; 27: 361-8.
18. MAKSYMOWYCH WP, INMAN RD, SALONEN D *et al*.: Spondyloarthritis Research Consortium of Canada magnetic resonance imaging index for assessment of spinal inflammation in ankylosing spondylitis. *Arthritis Rheum* 2005; 53: 502-9.
19. MAKSYMOWYCH WP, INMAN RD, SALONEN D *et al*.: Spondyloarthritis Research Consortium of Canada magnetic resonance imaging index for assessment of sacroiliac joint inflammation in ankylosing spondylitis. *Arthrhtis Rheum* 2005; 53: 703-9.
20. SCHNEIDER CA, RASBAND WS, ELICEIRI

KW: NIH Image to Image J: 25 years of image analysis. *Nat Meth* 2012; 9: 671-5.
21. MOLTO A, PATERNOTTE S, VAN DER HEIJDE D, CLAUDEPIERRE P, RUDWALEIT M, DOUGADOS M: Evaluation of the validity of the different arms of the ASAS set of criteria for axial spondyloarthritis and description of the different imaging abnormalities suggestive of spondyloarthritis: data from the DESIR cohort. *Ann Rheum Dis* 2015; 74: 746-51.
22. OSTERGAARD M, SORENSEN IJ: Magnetic resonance imaging—key to understanding and monitoring disease progression in spondyloarthritis? *J Rheumatol* 2015; 42: 1-4.
23. PUHAKKA KB, JURIK AG, SCHIOTTZ-CHRISTENSEN B *et al*.: Magnetic resonance imaging of sacroiliitis in early seronegative spondylarthropathy. Abnormalities correlated to clinical and laboratory findings. *Rheumatology* (Oxford) 2004; 43: 234-7.
24. DESIREE VAN DER HEIJDE, JOACHIM SIEPER, WALTER P *et al*.: Spinal inflammation in the absence of sacroiliac joint inflammation on magnetic resonance imaging in patients with active nonradiographic axial spondyloarthritis. *Arthritis Rheuamtol* 2014; 66: 667-73.
25. NAVARRO-COMPAN V, RAMIRO S, LANDEWÉ R *et al*.: Disease activity is longitudinally related to sacroiliac inflammation on MRI in male patients with axial spondyloarthritis: 2-years of the DESIR cohort. *Ann Rheum Dis* 2016; 75: 874-8.
26. BOLLOW M, FISCHER T, REIBHAUER H *et al*.: Quantitative analyses of sacroiliac biopies in spondyloarthropathies: T cells and macrophages predominate in early and active sacroiliitis --- cellularity correlates with the degree of enhancement detected by magnetic resonance imaging. *Ann Rheum Dis* 2000; 59: 134-40.
27. CUI Y, ZHANG X, ZHAO Z, LIU Y, ZHENG J: The relationship between histopathological and imaging features of sacroiliitis. *Int J Clin Exp Med* 2015; 8: 5904-10.
28. MAKSYMOWYCH WP, CHIOWCHANWISAWAKIT P, CLARE T, PEDERSEN SJ, ØSTERGAARD M, LAMBERT RG: Inflammatory lesions of the spine on magnetic resonance imaging predict the development of new syndesmophytes in ankylosing spondylitis: evidence of a relationship between inflammation and new bone formation. *Arthritis Rheum* 2009; 60: 93-102.
29. GASPERSIC N, SERSA I, JEVTIC V, TOMSIC M, PRAPROTNIK S: Monitoring ankylosing spondylitis therapy by dynamic contrast-enhanced and diffusion-weighted magnetic resonance imaging. *Skeletal Radiol* 2008; 37: 123-31.
30. SANAL HT, YILMAZ S, SIMESEK L *et al*.: Apparent diffusion coefficients of sacroiliitis in patients with establised ankylosing spondylitis. *Clin Imaging* 2013; 37: 734-9.
31. SAHIN N, HACIBEYOGLU H, INCE O *et al*.: Is there a role for DWI in the diagnosis of sacroiliitis based on ASAS criteria? *Int J Clin Exp Med* 2015; 8: 7544-52.
32. PAN C, HU DY, ZHANG W, LI XM: Role of diffusion-weighted imaging in early ankylosing spondylitis. *Chin Med J* (Engl) 2013; 126: 668-73.
33. ZHAO Y, HAN X, HU S *et al*.: The relevance of ADC value, T_1 intensive rate and the clinical activities in ankylosing spondylitis sacroiliitis. *Zhinghua Yi Xue Za Zhi* 2014; 94: 2750-3.
34. GEZMIS E, DONMEZ FY, AGLIDERE M: Diagnosis of early sacroiliitis in seronegative spondyloarthropathies by DWI and correlation of clinical and laboratory findings with ADC values. *Eur J Radiol* 2013; 82: 2316-21.