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ORIGINAL ARTICLE

ASDAS is associated with both the extent and intensity of DW-MRI spinal inflammation in active axial spondyloarthritis

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ABSTRACT

Objective To investigate the relationship between Ankylosing Spondylitis Disease Activity Score (ASDAS) and intensity of spinal inflammation measured by apparent diffusion coefficient (ADC) in MRI in participants with active axial spondyloarthritis (SpA).

Methods Participants with axial SpA and back pain were recruited. Clinical, demographic, biochemical and imaging data were collected. ASDAS was calculated based on C reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Inflammatory lesions were identified in short tau inversion recovery images and the corresponding ADC maps to determine the maximum apparent diffusion coefficient (ADCmax), normalised maximum ADC, mean apparent diffusion coefficient (ADCmean) and normalised mean ADC by two independent readers. Spondyloarthritis Research Consortium of Canada (SPARCC) spine and sacroiliac (SI) joint MRI indexes were determined. Univariate and multivariate linear regression models were used to determine the associations between of ASDAS with ADC values, SPARCC spine and SI MRI scores.

Results Eighty-two participants had identifiable ADC lesions. Multivariate analyses using ADCmax and SPARCC spine MRI as independent variables showed associations with ASDAS-CRP (ADCmax: B=0.27, p=0.02; SPARCC: B=0.32, p=0.01) and ASDAS-ESR (ADCmax: B=0.24, p=0.03; SPARCC: B=0.36, p<0.01); using ADCmean and SPARCC spine MRI as independent variables also showed an association with ASDAS-ESR (ADCmean: B=0.22, p=0.05; SPARCC: B=0.36, p<0.01) and a tendency to associate with ASDAS-CRP (ADCmean: B=0.21, p=0.07; SPARCC: B=0.34, p<0.01).

Conclusion ASDAS is associated with both the extent and the intensity of spinal inflammation in patients with detectable inflammatory lesions. Our results showed that ASDAS is an objective disease assessment tool.

Trial registration number HKUCTR-2087.

Key messages

What is already known about this subject?

- Apparent diffusion coefficient (ADC) is a newly validated method of quantifying spinal disease activity in axial spondyloarthritis (SpA).

What does this study add?

- In a group of participants with axial SpA and back pain, we found that the Ankylosing Spondylitis Disease Activity Score (ASDAS) correlated well with the mean and maximum ADC values after adjustment for confounding factors and Spondyloarthritis Research Consortium of Canada spine MRI indices.

How might this impact on clinical practice?

- Our data show evidence that ASDAS is an objective disease assessment tool in patients with axial SpA.
- Our study also provides a new method for validation of future disease assessment tools (eg, biomarkers) in axial SpA.

INTRODUCTION

In the past decade, MRI has gained prominence in both diagnosis and monitoring of disease activity in axial spondyloarthritis (SpA). MRI was included as an imaging criterion in the 2009 Assessment of Spondyloarthritis International Society (ASAS) classification criteria.[1 2] When available, MRI is also recommended prior to consideration for biological disease-modifying antirheumatic drugs.[3]

Disease activity is currently monitored using the Ankylosing Spondylitis Disease Activity Score (ASDAS)[4] according to established ASAS guidelines. ASDAS is a composite index that combines five disease activity variables into a single score. It has been developed as an improvement on previously self-rated tools, such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI),[5] by incorporating objective biochemical measures of C reactive protein (CRP) or erythrocyte sedimentation rate (ESR) into the data-driven index.[6] The score is highly discriminatory[7] and has outperformed other disease

assessment tools[8] in the assessment of disease activity. ASDAS paralleled the levels of inflammatory markers both elevated during active disease and decreased after treatment with biologics.[9]

However, the relationship between clinical disease activity and inflammation on MRI is inconclusive and considerably dependent on the imaging sequence used. In general, ASDAS shows better correlation with MRI inflammation than other clinical disease activity parameters.[10–14] Traditional sequences such short tau inversion recovery (STIR) or T2 fat suppression have reasonable spatial resolution, which is advantageous in showing the extent of inflammation but poorly sensitive in measuring intensity.

Diffusion-weighted imaging (DWI) is a newer MRI sequence that exploits the impedance of water molecules at the tissue level[15] to visualise the bone marrow oedema of spinal inflammation. By removing artefacts, the corresponding computer-generated apparent diffusion coefficient (ADC) maps produce the most objective measures of intensity of inflammation. DWI is shown to outperform STIR imaging in quantifying disease activity,[16 17] and our recent research has proposed ADC as an imaging biomarker of spinal inflammation in SpA.[18]

We hypothesise that ASDAS is associated with intensity of inflammation on diffusion-weighted MRI as represented by ADC values.

METHODS

This is a cross-sectional study using data from a large DWI observational cohort in participants with axial SpA. It has been registered in the clinical trial registry of The University of Hong Kong. The goals of the cohort are to evaluate the use of DWI in the diagnosis and monitoring of disease activity in patients with axial SpA. We included patients older than 18 years old with back pain and an expert diagnosis of axial SpA from eight rheumatology centres (Queen Mary Hospital, Grantham Hospital, Tung Wah Hospital, Pamela Youde Nethersole Eastern Hospital, Caritas Medical Centre, Tseung Kwan O Hospital, Kwong Wah Hospital and Prince of Wales Hospital) from April 2014 to February 2019. Participants who were pregnant, on biological therapy, on prednisolone (or dose equivalent steroid) dosage of 10 mg or more, or contraindicated for MRI were excluded. All participants were required to sign an informed consent. Details of the cohort have also been reported in our previous publications.[18 19]

Study design

All recruited participants were interviewed for demographic and clinical data. These included age, gender, duration of back pain, family history of SpA, history of inflammatory bowel disease, history of psoriasis and history of enthesitis. Duration of back pain was defined as the time between the first onset of back pain and the date of interview. Physical examination was performed to determine tender joint (44 joints) and swollen joint (44 joints) counts. Participants completed self-assessment questionnaires, including BASDAI and Bath Ankylosing Spondylitis Global Score.[20] The questionnaires were measured as Numerical Rating Score from 1 to 10. Blood tests, including CRP, erythrocyte sedimentation rate (ESR) and human leucocyte antigen (HLA)-B27, were done. ASDAS based on CRP (ASDAS-CRP) and on ESR (ASDAS-ESR) were calculated. Radiographs of the lumbosacral spine were done to determine the presence of radiological AS. Fulfilment of the ASAS classification criteria for axial SpA[1 2] was determined in all participants.

All recruited participants had whole-spine MRI from the cervical (C2) region to the lumbosacral (S1) region and the sacroiliac (SI) joint MRI done on the day of the interview. T1, STIR and diffusion-weighted images were obtained simultaneously. Only STIR and diffusion-weighted images were used in this study. The MRIs were performed using a 3.0 T imaging unit (Achieva; Philips Healthcare, Best, the Netherlands) with participants in supine position. ADC maps were automatically generated by the MRI system. The technical parameters published in our previous publication[18] are summarised as follows: repetition times/echo times 5000/80 (STIR) and 4000/90 (DWI); fields of view 150×240 mm^2 (STIR) and 300×241 mm^2 (DWI); slice thicknesses 3.5 mm (STIR) and 4 mm (DWI); and multiple b values 0, 100, 600 and 1000 sec/mm^2. All magnetic resonance images were performed on a single machine. The acquisition time for STIR sequence and DWI were 2.48 and 2.44 min, respectively.

Reading of images

Anteroposterior view of lumbosacral radiographs were performed and scored for sacroiliitis by a single reader (HHLT). All radiographs were scored according to the modified New York criteria for Ankylosing Spondylitis (AS).[21] The gradings were as follows: 0=normal, 1=suspicious, 2=obvious, 3=partial fusion and 4=complete fusion. Bilateral grade 2 or unilateral grade 3 or above were defined as radiographical axial SpA.

MRI inflammation was defined as hyperintensity in the vertebral bodies in STIR images. The STIR images of the whole spine were scored independently by a rheumatologist and a rheumatology trainee (HYC and SCWC) according to the Spondyloarthritis Research Consortium of Canada (SPARCC) Spine MRI Index[22] and the SPARCC SI MRI Index.[23] HYC had 8 years' experience and SCWC had 4 years' experience in SpA MRI interpretation. The averages of SPARCC scores by the two readers were used in our analyses. A musculoskeletal radiologist (KHL), with 4 years' experience in SpA MRI interpretation, identified all inflammatory lesions in the vertebrae from the scored STIR images. Obvious degenerative lesions were also excluded by KHL. With reference to lesions identified in the STIR sequence, two independent readers (HYC and ETFC) placed regions of interest (ROIs) on the ADC maps of DWI accordingly to determine the maximum apparent diffusion coefficient

(ADCmax) and the mean apparent diffusion coefficient (ADCmean) values. Background apparent diffusion coefficient (ADCbg) values were determined from the average of at least two ADC values measured at the centres of adjacent normal-appearing vertebral bodies. Normalised maximum apparent diffusion coefficient (nADCmax) and normalised mean apparent diffusion coefficient (nADCmean) values were calculated by dividing ADCmax and ADCmean, respectively, by ADCbg. All ADC values used in the analyses were the average of ADC values by the two readers. Magnetic resonance images and ADC values were visualised and determined using OsiriX MD V.9.5.2. All MRI and radiology readers were blinded to the clinical and biochemical data.

Analyses and statistics

Demographic, clinical, biochemical and imaging data were reported as mean±SD. Univariate and multivariate linear regressions were used to determine the associations between ASDAS-CRP or ASDAS-ESR and ADC values or SPARCC spine MRI scores.

We included only patients with measurable ADC lesions in the analyses. ASDAS-CRP or ASDAS-ESR was the dependent variable in univariate regression models. In addition to the independent variables nADCmax, nADCmean, SPARCC spine MRI score and SPARCC SI MRI score, other known or expected associated factors, including age, male gender, HLA-B27 positivity, duration of back pain, family history of SpA, radiological AS, tender joint count, swollen joint count, and current or history of enthesitis were also involved in the analyses. Independent variables with p values less than 0.1 in univariate analyses were retested in multivariate regression models using either ASDAS-CRP or ASDAS-ESR as dependent variables. 'Enter' mode was used in the analyses. Two independent multivariate models using nADCmax and nADCmean were built for each multivariate ASDAS model. Results were reported as regression coefficient (β) and standard coefficient with 95% CI in linear regression models. Intraclass correlation coefficient was used to determine the interobserver agreement between the two SPARCC MRI spine scores, SPARCC MRI SI scores and different ADC parameters. The degree of reliability was interpreted as 0.00–0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; and 0.81–1.00, almost perfect. Unless specified, p values less than 0.05 were considered statistically significant. All statistics were performed with commercial software (IBM SPSS Statistics V.25). Listwise deletions were performed for missing data.

RESULTS

Three hundred one participants with axial SpA and back pain were recruited for the study. Most of them had HLA-B27 positivity and established radiographical SpA. Among our participants, 14.8% had psoriasis and 2.7% had inflammatory bowel disease. Our study population was characterised by a slight male predominance, prolonged disease duration and significant back pain. Participants had high clinical disease activity (ASDAS-CRP 2.0±0.9 and ASDAS-ESR 3.1±1.0).[6] The average SPARCC spine MRI score was 6.3±8.6 and the average SPARCC SI MRI score was 3.2±6.0. The group with identifiable ADC lesions had more men, fewer peripheral arthritis, fewer tender and swollen joint count, and higher ESR (table 1).

Three hundred twenty-five STIR lesions were found in 98 (32.6%) participants. Two hundred seventy-four (84.3%) STIR lesions from 82 (83.7%) participants could be located in ADC maps (figure 1). The technical success rates of the ADC measurement of inflammatory lesions in STIR images at individual spinal levels were 24/38 (63.2%), cervical spine; 188/203 (92.6%), thoracic spine; and 62/84 (73.8%), lumbosacral spine. Intraclass correlation coefficient of ADCmax, ADCmean, nADCmax and nADCmean between the two readers were 0.86, 0.82, 0.75 and 0.63, respectively. When compared with normal vertebrae (ADCbg), the maximum and average ADCs of inflammatory lesions were 6.4 and 3.4 times higher, respectively. Most of the measurable ADC lesions were located in the midthoracic spine. Figure 2 shows the details of their distribution.

Inter-reader reliability of SPARCC spine MRI scores and SPARCC SI MRI score by the two readers was almost perfect (intraclass correlation coefficient was 0.92 for SPARCC spine MRI score and 0.95 for SPARCC SI MRI score).

Univariate and multivariate regression analyses

In univariate analyses, ASDAS-CRP was positively associated with swollen joint count, ADCmax, ADCmean and SPARCC spine MRI score. It was negatively associated with HLA-B27 positivity (table 2). ASDAS-ESR was also positively associated with swollen joint count, ADCmax, ADCmean and SPARCC spine MRI score. It was negatively associated with male gender and HLA-B27 positivity (table 3).

Multivariate regression analyses showed that ADCmax and SPARCC spine MRI score were independently associated with both ASDAS-CRP and ASDAS-ESR. ADCmean was associated with ASDAS-ESR and tended to associate with ASDAS-CRP. HLA-B27 positivity had negative associations with ASDAS-ESR and had a tendency to associate negatively with ASDAS-CRP. Male gender tended to associate negatively with ASDAS-ESR when ADCmax was used as an independent variable. Results are shown in tables 2 and 3.

Figure 3 shows an example of a female participant with moderate clinical disease activity and moderate level of ADC values.

DISCUSSION

As ASDAS is a recommended by ASAS guidelines[24] for assessment of disease activity, much research has attempted to show its relationship with STIR–MRI

Table 1 Comparing demographic, clinical, biochemical and imaging features between participants with and without identifiable ADC lesions

	With identifiable ADC lesions	Without identifiable ADC lesions	P value
Age (N=301) (years)	45.7±13.1	42.7±13.1	0.09
Male gender (N=301)	55 (67.1%)	115 (52.5%)	0.02
Duration of back pain (N=299) (years)	13.4±10.7	11.2±11.2	0.13
HLA-B27 positivity (N=290)	69 (85.2%)	164 (78.5%)	0.20
History of inflammatory bowel disease (N=298)	3 (3.8%)	5 (2.3%)	0.49
History of psoriasis (N=298)	8 (10.0%)	36 (16.5%)	0.16
Family history of SpA (N=286)	15 (19.5%)	48 (23.0%)	0.53
Radiographical axial SpA (N=294)	5 (71.4%)	21 (52.5%)	0.35
Fulfilled ASAS axial SpA criteria (N=300)	79 (97.5%)	200 (91.3%)	0.06
Back pain NRS (N=294)	5.8±2.4	5.6±2.4	0.50
Ever peripheral arthritis (N=298)	36 (45.0%)	132 (60.6%)	0.02
Tender joint count (N=292)	0.8±1.5	1.6±3.1	0.02
Swollen joint count (N=293)	0.3±0.9	0.7±1.6	0.02
Ever enthesitis (N=297)	35 (43.8%)	97 (44.7%)	0.88
CRP (N=300) (mg/dL)	1.2±1.4	1.0±1.9	0.48
ESR (N=299) (mm/hour)	37.1±23.3	30.1±24.9	0.03
ASDAS-CRP (N=292)	2.1±0.8	2.0±0.9	0.44
ASDAS-ESR (N=291)	3.3±1.0	3.1±1.1	0.11
ADC background (N=82) (mm^2/s)		–	–
ADCmax (N=82) (mm^2/s)	$1.45\pm0.31\times10^{-3}$	–	–
ADCmean (N=82) (mm^2/s)	$0.77\pm0.19\times10^{-3}$	–	–
nADCmax (N=82)	6.5±2.1	–	–
nADCmean (N=82)	3.4±1.0	–	–
SPARCC SI MRI score (N=297)	3.4±5.9	3.1±6.1	0.68
SPARCC spine MRI score (N=294)	13.7±10.2	3.5±6.0	<0.001

ADC, apparent diffusion coefficient; ADCmax, maximum apparent diffusion coefficient; ADCmean, mean apparent diffusion coefficient; ASAS, Assessment of Spondyloarthritis International Society; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; HLA, human leucocyte antigen; N, number; nADCmax, normalised maximum apparent diffusion coefficient; nADCmean, normalised mean apparent diffusion coefficient; NRS, Numerical Rating Score; SPARCC, Spondyloarthritis Research Consortium of Canada; SpA, spondyloarthritis.

inflammation. In this study using DWI–ADC, we have demonstrated its association with the intensity of spinal inflammation in a large cohort of participants with axial SpA.

A positive association between ASDAS and spinal inflammation has been demonstrated in some studies using STIR–MRI[10–12] but has failed in others.[13 14] While STIR sequence is the preferred and recommended MRI sequence for the assessment of disease activity in axial SpA, it is limited by its inability to quantify inflammation. STIR sequence is highly effective in demonstrating the extent of inflammation, but DWI-ADC allows measurement of intensity. The ability of DWI-ADC in quantifying inflammation intensity has been demonstrated in various diseases.[25–27] In previous studies, ADC values were found to correlate with CRP in patients with SpA[28] and to be increased in active sacroiliitis.[29] Our earlier study has also demonstrated that ADC is a potential imaging biomarker of disease activity in axial SpA.[18]

Our results showed that both ADCmax and ADCmean were positively associated with ASDAS, even after adjustments for potential confounding factors and the SPARCC MRI spine score. Although the SPARCC MRI spine score semiquantitatively grades intensity of inflammation by comparison to that of cerebrospinal fluid, this was allocated a less important weighting in the overall score. Therefore, the SPARCC MRI spine score functions more as a description of the extent rather than the intensity of spinal inflammation. Incorporating both STIR and ADC, axial disease activity in SpA may be more comprehensively described.

Participants with and without MRI inflammation had similar back pain and clinical disease activity scores. These findings were consistent with other reports[13 14 30]

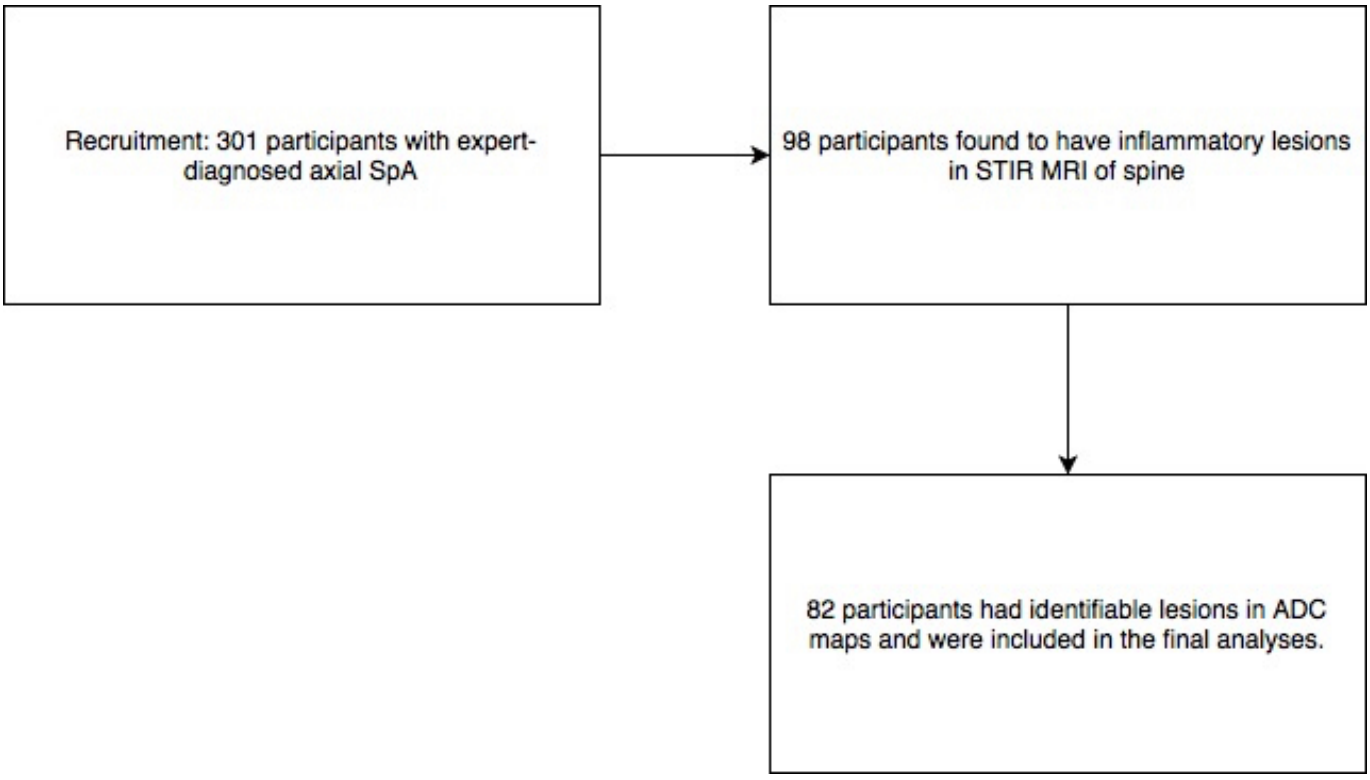

Figure 1 Flowchart diagram. ADC, apparent diffusion coefficient; STIR, short tau inversion recovery.

highlighting the importance of MRI imaging in addition to clinical disease activity. As a data-driven disease activity index, ASDAS has been repeatedly shown to outperform another widely used clinical disease assessment tool, the BASDAI.[7 8] Very high disease activity measured by ASDAS predicted radiological progression better than by BASDAI.[31] In addition, superior correlations between ASDAS and STIR–MRI inflammation have also been demonstrated in various studies.[10–12] Despite an association between ADC and back pain score in our previous study[18] and with ASDAS in this study, it had no association with BASDAI.[18] Based on the two studies, ASDAS surpasses BASDAI in describing the intensity of spinal inflammation and should be the preferred choice in the assessment of axial SpA.

HLA-B27 has been reported to associate with earlier disease onset, severity of spinal and SI joint inflammation, and radiological sacroiliitis.[32–34] The negative associations between HLA-B27 positivity and clinical disease activities (ASDAS-CRP and ASDAS-ESR) in our analyses were not expected. Interestingly, such an association has also been reported previously by another international study.[34] Further studies may help to reveal their true relationship.

A major challenge of using spinal ADC is the high degree of variability between MRI machines. A proposed solution is to use normalised apparent diffusion coefficient (nADC), which compares ADC values of inflammatory sites to normal tissues (ADCbg). In this study, the mean of two apparently normal regions near the site of inflammation was used to calculate ADCbg. However, this method has not been validated. Factors such as age, osteoporosis[35] and skeletal maturity[36] may affect the ADC values, and axial SpA patients are more prone to osteoporosis.[37] On normalisation, nADC values showed decreased interobserver reliability, and the associations with ASDAS were lost. A possible reason was the lack of standardisation in drawing the ROIs of the normal non-inflamed regions. AS was also known to be associated with other spinal pathologies, such as osteoporosis and vertebral fractures, which could affect the measured ADC values. This further increased the variability of ADCbg measurements. Having said that, the loss of associations between nADC values and ASDAS should not affect our conclusion. Normalisation of ADC values would not be essential since only a single MRI machine and ADC software to acquire the ADC data were used. Future studies should attempt to find out the best way of ADC normalisation to allow accurate comparison of ADC values between different MRI machines.

Potential measurement errors of mean ADC values may be another challenge. Inflammation is rarely homogenous, and inadvertent inclusion of normal tissues within the boundaries of ROIs may result in falsely diluted mean ADC values. Poor visuospatial resolution of ADC maps and small inflammatory lesions, such as corner inflammatory lesions,[38] also contributed to errors in measurements. As such, ADCmax may be a more objective way to represent spinal inflammation in axial SpA. Despite this, the two readers had good interobserver reliabilities in both ADCmean and ADCmax measurements. ADC technical failure was another limitation.[39] Nevertheless, we

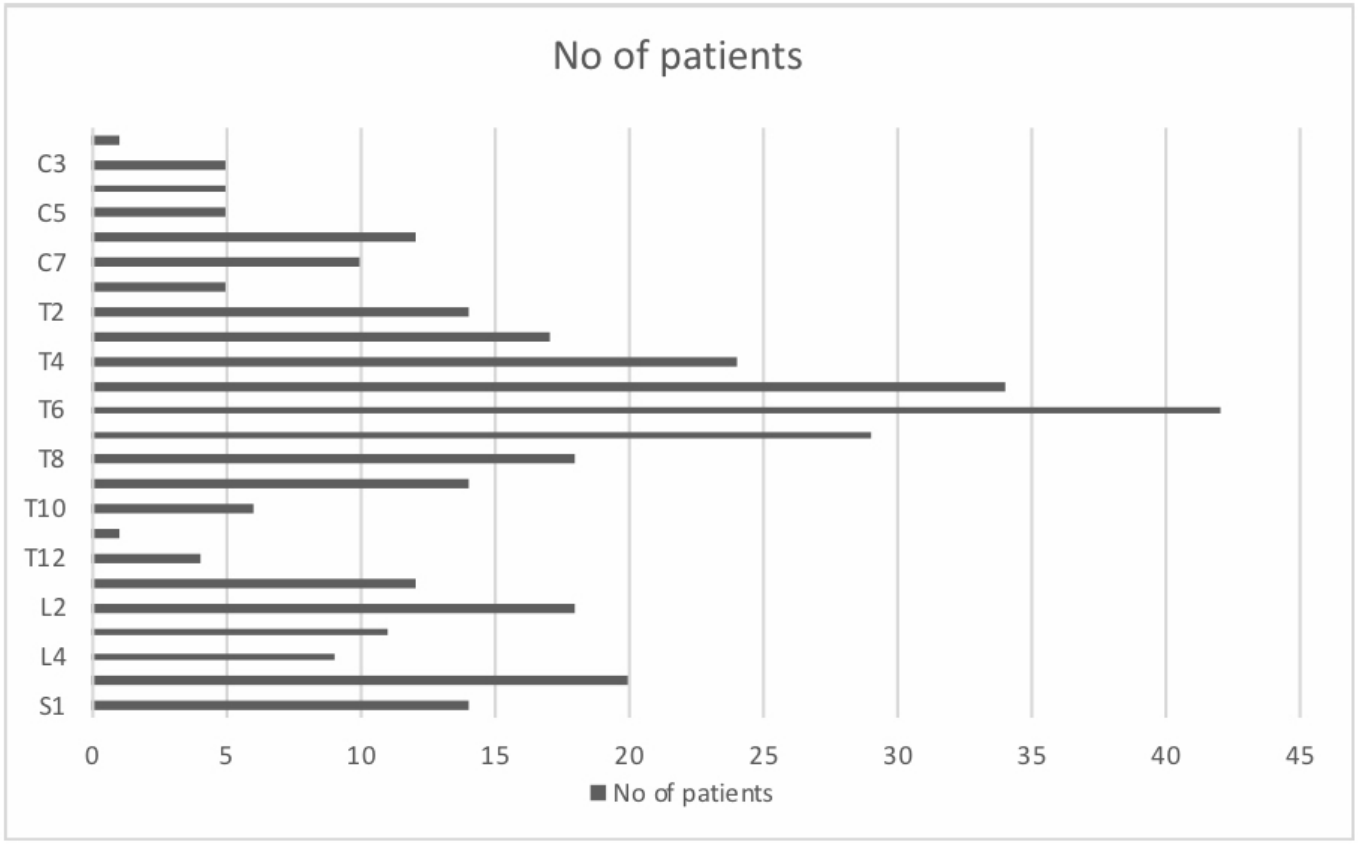

Figure 2 Distribution of inflammatory lesions on short tau inversion recovery MRI.

encountered extensive inflammatory lesions visualised on STIR images with minimal intensity that render them undetectable on ADC. Because each imaging technique characterises unique aspects of spinal inflammation, the addition of ADC to the more traditional STIR imaging has an added value of quantifying inflammation.

Our study has other limitations. Application of ADC is limited to patients with identifiable MRI inflammation only. The technique focuses on quantifying intensity of inflammation, and no meaningful values could be drawn from patients without MRI inflammation. This restricted the number of participants included in our analyses. In contrast to other international studies, we included mainly participants with advanced axial SpA with high clinical activity. It is not clear whether the same results could be replicated in the early disease group. Our inclusion of participants with prerequisite back pain may have excluded those with asymptomatic yet active inflammation, hence contributing to selection bias. Despite this, the percentage of participants with active spinal inflammation was compatible with another international study.[40] The exclusion of obvious degenerative lesions might also falsely exclude coexisting inflammatory lesions. Finally, we did not include SI joint ADC values into the analyses because ADC acquisition in SI joints has not been validated. Yet, SPARCC SI MRI was not associated with ASDAS in our study.

CONCLUSION AND FUTURE DIRECTION

Using DWI-ADC, we demonstrated that ASDAS is associated with both the extent and intensity of spinal inflammation in patients with detectable inflammatory lesions. Data from other ethnic groups and prospective analyses would provide a more complete picture of this relationship.

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Contributors Study conception and design: HYC, KHL and CSL. Acquisition of data: HYC, HHLT and SCWC. Interpretation of imaging: HYC, ETFC, KHL, HHLT and SCWC. Analysis and interpretation of data: HYC, ETFC and CSL. Drafting of the article: HYC and ETFC. Revision of the article: HYC and ETFC.

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Competing interests None.

Patient consent for publication Not required.

Ethics approval The study was approved by the institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (reference number UW 14-085) and local ethics committees. It was conducted in accordance with the Declaration of Helsinki and the guidance of Good Clinical Practice on 30 November 2006. All participants gave written informed consent before recruitment.

Provenance and peer review Not commissioned; externally peer reviewed.

Table 2 Univariate and multivariate linear regression analyses using ASDAS-CRP as dependent variables

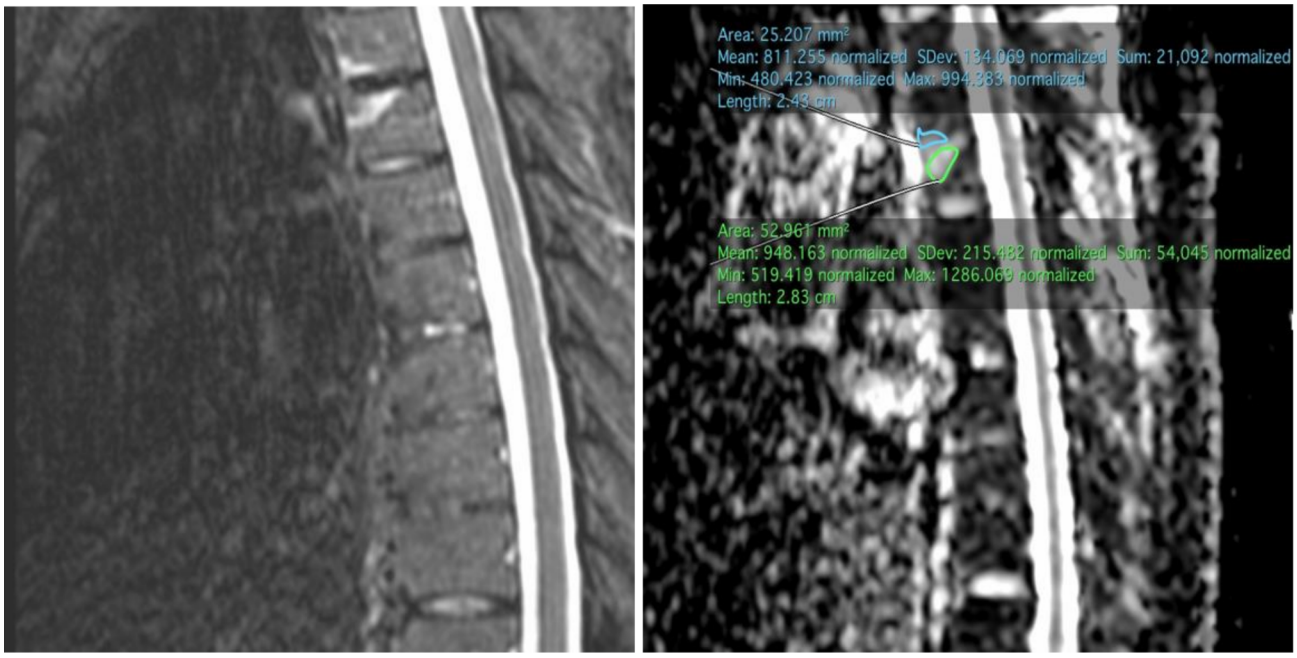
	Univariate analyses using ASDAS-CRP as dependent variable			Multivariate analyses using ASDAS-CRP as dependent variable and ADCmax as independent variable (N=70)			Multivariate analyses using ASDAS-CRP as dependent variable and ADCmean as independent variable (N=70)		
	Standard coefficient	Regression coefficient (95% CI)	P value	Standard coefficient	Regression coefficient (95% CI)	P value	Standard coefficient	Regression coefficient (95% CI)	P value
HLA-B27 positivity (N=77)	–0.19	–0.44 (–0.95 to –0.07)	0.09	–0.21	–0.51 (–1.03 to 0.02)	0.06	–0.21	–0.49 (–1.02 to 0.05)	0.08
Swollen joint count (N=75)	0.19	0.18 (–0.03 to 0.39)	0.10	0.14	0.14 (–0.07 to 0.34)	0.19	0.15	0.14 (–0.06 to 0.35)	0.17
ADCmax (N=78)	0.29	0.001 (0.00 to 0.001)	0.01	0.27	0.001 (0.00 to 0.001)	0.02	–	–	–
ADCmean (N=78)	0.28	0.001 (0.00 to 0.002)	0.01	–	–	–	0.21	0.001 (0.00 to 0.002)	0.07
SPARCC spine MRI score (N=74)	0.31	0.03 (0.01 to 0.04)	0.01	0.32	0.03 (0.01 to 0.05)	0.01	0.34	0.03 (0.01 to 0.05)	<0.01
Age (N=78)	0.05	0.003 (–0.01 to 0.02)	0.67	–	–	–	–	–	–
Male gender (N=78)	–0.09	–0.15 (–0.55 to 0.25)	0.45	–	–	–	–	–	–
Smoker (N=78)	0.17	0.30 (–0.01 to 0.68)	0.13	–	–	–	–	–	–
Drinker (N=78)	0.12	0.31 (–0.27 to 0.89)	0.30	–	–	–	–	–	–
Duration of back pain (N=77)	–0.01	–0.001 (–0.02 to 0.02)	0.94	–	–	–	–	–	–
Family history of SpA (N=75)	0.15	0.30 (–0.16 to 0.77)	0.20	–	–	–	–	–	–
Tender joint count (N=75)	0.16	0.09 (–0.04 to 0.21)	0.18	–	–	–	–	–	–
Ever enthesitis (N=78)	0.10	0.17 (–0.20 to 0.55)	0.37	–	–	–	–	–	–
nADCmax (N=78)	0.01	0.10 (–0.09 to 0.10)	0.91	–	–	–	–	–	–
nADCmean (N=78)	0.04	0.04 (–0.16 to 0.23)	0.73	–	–	–	–	–	–
SPARCC SI MRI score (N=67)	0.13	0.02 (–0.02 to 0.06)	0.30	–	–	–	–	–	–

ADC, apparent diffusion coefficient; ADCmax, maximum apparent diffusion coefficient; ASAS, Assessment of Spondyloarthritis International Society; CRP, C reactive protein; HLA, human leucocyte antigen; N, number; NaDCmax, normalised maximum apparent diffusion coefficient; SI, sacroiliac; SPARCC, Spondyloarthritis Research Consortium of Canada; SpA, spondyloarthritis.

Table 3 Univariate and multivariate linear regression analyses using ASDAS-ESR as dependent variables

	Univariate analyses using ASDAS-ESR as dependent variable			Multivariate analyses using ASDAS-ESR as dependent variable and ADCmax as independent variable (N=70)			Multivariate analyses using ASDAS-ESR as dependent variable and ADCmean as independent variable (N=70)		
	Standard coefficient	Regression coefficient (95% CI)	P value	Standard coefficient	Regression coefficient (95% CI)	P value	Standard coefficient	Regression coefficient (95% CI)	P value
Male gender (N=78)	−0.30	−0.60 (−1.05 to −0.16)	0.01	−0.21	−0.43 (−0.88 to −0.03)	0.07	−0.18	−0.36 (−0.83 to 0.11)	0.13
HLA-B27 positivity (N=77)	−0.31	−0.82 (−1.40 to −0.24)	0.01	−0.23	−0.63 (−1.23 to −0.02)	0.04	−0.23	−0.62 (−1.22 to −0.01)	0.05
Swollen joint count (N=75)	0.27	0.28 (0.04 to 0.52)	0.02	0.17	0.18 (−0.04 to 0.41)	0.11	0.18	0.20 (−0.03 to 0.42)	0.09
ADCmax (N=78)	0.29	0.001 (0.00 to 0.002)	0.01	0.24	0.001 (0.00 to 0.001)	0.03	–	–	–
ADCmean (N=78)	0.36	0.002 (0.00 to 0.003)	<0.01	–	–	–	0.22	0.001 (0.00 to 0.002)	0.05
SPARCC spine MRI score (N=74)	0.26	0.03 (0.003 to 0.05)	0.02	0.36	0.03 (0.01 to 0.06)	<0.01	0.36	0.03 (0.01 to 0.06)	<0.01
Age (N=78)	0.12	0.01 (−0.01 to 0.03)	0.29	–	–	–	–	–	–
Smoker (N=78)	0.11	0.23 (−0.23 to 0.68)	0.33	–	–	–	–	–	–
Drinker (N=78)	0.13	0.39 (−0.29 to 1.07)	0.25	–	–	–	–	–	–
Duration of back pain (N=77)	−0.08	−0.01 (−0.03 to 0.01)	0.51	–	–	–	–	–	–
Family history of SpA (N=75)	0.13	0.31 (−0.24 to 0.86)	0.26	–	–	–	–	–	–
Tender joint count (N=75)	0.17	0.11 (−0.04 to 0.25)	0.14	–	–	–	–	–	–
Ever enthesitis (N=78)	0.10	0.19 (−0.25 to 0.62)	0.40	–	–	–	–	–	–
nADCmax (N=78)	−0.02	−0.01 (−0.12 to 0.10)	0.85	–	–	–	–	–	–
nADCmean (N=78)	0.08	0.08 (−0.15 to 0.31)	0.49	–	–	–	–	–	–
SPARCC SI MRI score (N=67)	0.11	0.02 (−0.03 to 0.07)	0.38	–	–	–	–	–	–

ADC, mean apparent diffusion coefficient; ADC, apparent diffusion coefficient; ASAS, Assessment of Spondyloarthritis International Society; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; HLA, human leucocyte antigen; N, number; SI, sacroiliac; SPARCC, Spondyloarthritis Research Consortium of Canada; SpA, spondyloarthritis; nADCmax, normalised maximum apparent diffusion coefficient; nADCmean, normalised mean apparent diffusion coefficient.



A 34 years old lady participant with 6 years history of back pain had moderate clinical activity (ASDAS-CRP 2.08, ASDAS-ESR 3.71). The measured ADC max was $1.29x10^{-3}$ mm^2/sec (average$1.45x10^{-3}$ mm^2/sec) and ADC mean was $0.94x10^{-3}$ mm^2/sec (average $0.77x10^{-3}$ mm^2/sec). SPARCC spine MRI score was 8 (average 6.3).

Figure 3 An example showing correlations between ASDAS and different ADC parameters. Short tau inversion recovery image on the left side, ADC map on the right side. ADC, apparent diffusion coefficient; ADCmax, maximum apparent diffusion coefficient; ASDAS, Ankylosing Spondylitis Disease Activity Score; CRP, C reactive protein; SPARCC, Spondyloarthritis Research Consortium of Canada.

Data availability statement Data are available upon reasonable request.

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