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Clinical importance of inflammatory facet joints of the spine in ankylosing spondylitis: a magnetic resonance imaging study

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Objectives: The aims of this study were to assess the reliability of a novel magnetic resonance imaging (MRI) scoring system for inflammatory lesions of facet joints and to clarify the clinical significance of facet joint inflammation in ankylosing spondylitis (AS).

Method: A total of 53 AS patients (45 males, 84.9%) were assessed for active inflammatory lesions involving the facet joints, as indicated by bone marrow oedema, at 23 discovertebral units (DVUs) between C2 and S1 using a novel scale, the AS Activity of the Facet joint (ASAFacet). The reliability of the ASAFacet was evaluated using intraclass correlation coefficients (ICCs) and Bland–Altman plots.

Results: ICC values for the ASAFacet scores were 0.857 [95% confidence interval (CI) 0.741–0.919] for inter-observer and 0.941 (95% CI 0.873–0.969) for intra-observer reliability. Inflammatory activity scores in facet joints were evenly distributed at all spine levels ($p = 0.294$ for ASAFacet), whereas vertebral body inflammation was more prominent in the thoracic spine than in the cervical and lumbar spine [$p < 0.001$ for the AS spine MRI activity (ASspiMRI-a) score, $p = 0.002$ for the Berlin method, and $p < 0.001$ for the Spondyloarthritis Research Consortium of Canada (SPARCC) MRI index]. ASAFacet scores were closely associated with erythrocyte sediment rate (ESR) and C-reactive protein (CRP) levels ($p < 0.05$, respectively). Patients with peripheral arthritis had fewer lesions involving the vertebral bodies or facet joints than patients without peripheral arthritis ($p < 0.001$ for the four different MRI activity indexes).

Conclusions: This study suggests that recognition of facet joint inflammation has the potential to contribute to our understanding of clinical outcomes in AS.

Ankylosing spondylitis (AS) is a prototypic chronic inflammatory rheumatic disease involving the spine, sacroiliac (SI) joints, and peripheral joints. The disease can lead to joint damage, functional impairment, and decreased quality of life (1, 2). Characteristic radiological changes of AS are first observed at the SI joints and slowly evolve to involve the spine over several years. In clinical practice, assessment of structural damage using diverse radiographic tools is essential for diagnosis and for assessing treatment response and clinical outcomes in AS.

There is accumulating evidence that magnetic resonance imaging (MRI) is being increasingly used for identification of active inflammatory lesions of the spine and the SI joints in AS (3–6). Three reliable and useful MRI scoring systems have been developed to determine acute inflammation or chronic joint changes of the spine in AS: the AS spine MRI activity (ASspiMRI-a) score (6, 7), the Berlin method (8), and the Spondyloarthritis Research Consortium of Canada (SPARCC) MRI index (9). These imaging scoring systems primarily assess bone marrow signal abnormalities and can indicate the presence of active inflammatory lesions in the spinal bodies adjacent to affected discovertebral units (DVUs) without scoring involvement of the facet joint, although the ASspiMRI-a scoring system also assesses bony erosion.

Facet joints (or zygapophysial joints) of the spine are synovial joints that connect the superior and inferior articular processes of the vertebrae. These joints in the spine mainly function to guide and limit spinal motion. In addition to spinal involvement of DVUs in AS, facet joint involvement has been found to be part of disease progression in AS and can present as inflammatory lesions, bony erosion, joint space narrowing, and ankylosis of these joints (10–12). The involvement of facet joints in AS has clinical significance in that it leads to inflammatory pain

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and more severe limitation of spinal mobility due to the formation of bridging syndesmophytes (10).

There is a lack of data about the clinical significance of acute inflammation of the facet joints in AS. Thus, the aims of this study were to (i) test the reliability of a novel MRI scoring index for acute inflammation of the facet joint, which we called the Ankylosing Spondylitis Activity of the Facet joint (ASAFacet); (ii) identify the distribution and presence of active inflammation of bone marrow oedema in the facet joints corresponding to 23 DVUs from C2 to S1 using the ASAFacet index; and (iii) compare MRI scores for the facet joints with other MRI activity scoring indexes, such as the ASspiMRI-a, the Berlin method, and SPARCC, for the 23 DVUs and also to compare MRI findings with clinical disease activity markers, including erythrocyte sediment rate (ESR), C-reactive protein (CRP), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (13), and the Bath Ankylosing Spondylitis Functional Index (BASDFI) (14) in patients with AS.

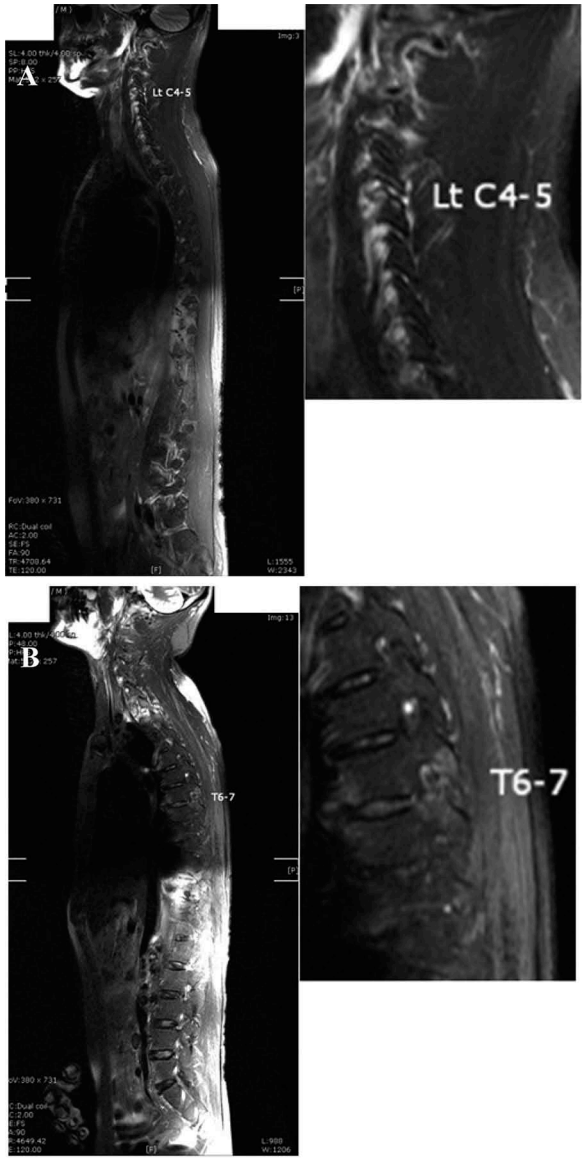

Figure 1. Grading of facet joint inflammation using the ASAFacet. (A) A 39-year-old male patient with less than 50% bone marrow oedema at cervical spine level 4–5, which is grade 1 in the ASAFacet system. (B) A 47-year-old male patient with more than 50% bone marrow oedema at thoracic spine level 6–7, which is grade 2 in the ASAFacet system.

Method

Patients and collection of data for clinical parameters

A total of 53 patients who met the modified New York criteria for AS (15) were recruited for this retrospective study. The patients underwent whole spine MRI to assess the degree of inflammation in the spine as part of routine clinical care between 2011 and 2013. Data regarding the presence of arthritis of peripheral joints, history of uveitis, the presence of human leucocyte antigen (HLA)-B27, and disease duration were obtained through review of medical records or patient interview.

Information about acute phase reactants, including ESR and CRP, and clinical disease activity indexes, such as the BASDAI and BASFI, were obtained if available at the time the spine MRI scan was obtained. Some patients had missing data for ESR, CRP, BASDAI, and BASFI because some of their parameters were not measured at the time of taking the MRI scan. The institutional review board of Hanyang University Medical Centre approved this study.

MRI protocol

The whole spine MRI scans were completed using a 3.0-T MR scanner (Achieva, Philips, The Netherlands) with a spine array coil, and the following sequences were obtained: sagittal T1-weighted (T1), sagittal fat-saturated T2-weighted (T2), and sagittal fat-saturated enhanced T1-weighted sequences.

T1-weighted spin echo sequences [repetition time (TR)/echo time (TE) 580/10 ms, slice thickness 4 mm, two acquisitions, field of view (FOV) 380 × 731, matrix 512 × 157 pixels] were performed in sagittal views. T1-weighted images were used to detect chronic changes in the bone structure of the spine. The spine was examined in two parts, taking C2 and L5 as orientation points, always starting with cranially. Fat-saturated T2-weighted images (TR/TE 4700/120 ms, slice thickness 4 mm, two acquisitions) and fat-saturated enhanced T1-weighted images (TR/TE 500/10 ms, slice thickness 4 mm, two acquisitions) were also examined to differentiate between chronic and acute spinal lesions.

Evaluated scoring methods

After all patient-identifying information had been removed from the MR images, an independent person randomly selected the image order of the images, which were then independently assessed by two experienced radiologists (SL and JYL) for the presence of changes indicating inflammation or structural alteration of the spine, including

facet oedema. After 8 weeks, one radiologist (SL) evaluated all MR images for intra-observer variability.

Three different methods, including the ASspiMRI-a (6, 7), the Berlin modification of the ASspiMRI-a (8), and the SPARCC (9) scoring methods for spinal inflammation, were applied according to established protocols. The facet joint scoring system was only based on oedema along the facet joint and excluded erosion and ankylosis at 23 DVUs. The presence of bone marrow oedema exhibiting high signal intensity or enhancement below 50% involving a facet joint was given a score of 1 (Figure 1A). The presence of oedema over 50% was given a score of 2 (Figure 1B). Scores ranged between 0 and 4 points for both sides of the facet joints at each DVU, leading to a maximum score of 92 for the evaluated spine between C2 and S1.

Statistical analysis

The inter- and intra-observer reliability of the MRI scoring systems was assessed using the intraclass correlation coefficient (ICC) and Bland and Altman limits of agreement analysis. The ICC was used to examine the extent of agreement between repeated measurements by the same rater (intra-observer reliability) or by different raters (inter-observer reliability) (16, 17). A two-way mixed single measure model (absolute agreement) was used, and in general, an ICC value of more than 0.80 was considered excellent.

The Z-score corresponds to the confidence interval (CI) from a standard normal distribution (i.e. 1.96 for 95% CI in this study) and the standard deviation (sd) represents the sd of all testing scores from the two assessments. In addition, Bland–Altman plots were used to assess the repeatability of a method by comparing repeated measurements (18). These plots show the mean difference between two methods of measurement and the mean with 95% limits of agreement (i.e. mean difference e mean sd of the difference).

For comparison of inflammatory activity scores by spinal level (cervical spine, thoracic spine, and lumbar spine), statistical analysis was performed using the Kruskal–Wallis test and Bonferronitory activityest. To evaluate an association between individual MRI activity scores and clinical findings, including age, disease duration, peripheral arthritis, ESR, CRP, BASDAI, and BASFI, correlation analysis and Wilcoxon rank sum tests were performed. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics 19.0 (IBM Corp, Armonk, NY, USA).

Results

Baseline characteristics of enrolled patients

Demographic, clinical, and radiographic characteristics of the enrolled AS patients are summarized in Table 1. The mean age of the 53 patients was 34.8 years (sd 7.4) and disease duration was 10.1 years (sd 7.0). The proportion of men was 84.9% (n = 45) and 90.6% (n = 48) were HLA-B27 positive. At the time the MRI scans were obtained, the clinical disease activity indicators, ESR, CRP, BASDAI, and BASFI, were 26.5 mm/h (sd 24.4), 1.6 g/dL (sd 2.0), 5.4 (sd 2.2), and 1.6 (sd 1.7), respectively. Based on results for the MRI activity scoring systems from radiologist 1, the mean values of the ASspiMRI-a, Berlin method, and SPARCC for DVU lesions were 10.8 (sd 11.5), 7.7 (sd 8.0), and 25.1 (sd 23.8), respectively. In addition, the inflammatory activity score for facet joints, ASAFacet, was 3.7 (sd 5.3).

Table 1. Baseline characteristics of enrolled patients with ankylosing spondylitis (n = 53).

Demographic features	
Age (years)	34.8 ± 7.4
Gender, male	45 (84.9)
Disease duration (years)	10.1 ± 7.0
HLA-B27 positivity	48 (90.6)
Peripheral arthritis	17 (32.1)
Ocular inflammation	11 (20.8)
Clinical disease activity	
ESR (mm/h), n = 53	26.5 ± 24.4
CRP (g/dL), n = 52	1.6 ± 2.0
BASDAI, n = 33	5.4 ± 2.2
BASFI, n = 28	1.6 ± 1.7
MRI activity scores (radiologist 1, second test 2)	
ASspiMRI-a (0–138)	10.8 ± 11.5
Berlin (0–69)	7.7 ± 8.0
SPARCC (0–108)	25.1 ± 23.8
ASAFacet (0–92)	3.7 ± 5.3

ESR, Erythrocyte sediment rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASspiMRI-a, Ankylosing Spondylitis spine magnetic resonance imaging (MRI) activity; Berlin, the Berlin modification of the ASspiMRI-a; SPARCC, Spondyloarthritis Research Consortium of Canada; ASAFacet, Ankylosing Spondylitis Activity of the Facet joint.
Data are expressed as mean thsd for continuous variables and n (%) for categorical variables.
Statistical analyses for all characteristics were performed for 53 patients with AS, except missing data including ESR (n = 53), CRP (n = 52), BASDAI (n = 33), and BASFI (n = 28).

Reliability of the MRI activity scoring systems

We first assessed inter-observer (radiologist 1 vs. radiologist 2) and intra-observer reliability (between time 1 and time 2 for radiologist 1) for the ASspiMRI-a, Berlin method, and SPARCC for DVU lesions, and observed high ICC values (Table 2). This suggests that the scoring of inflammatory lesions by the two radiologists was reliable. For our new scoring method, ASAFacet, which was used to assess the facet joints of AS patients, the ICC values for inter-observer and intra-observer reliability were 0.857 (95% CI 0.741–0.919) and 0.941 (95%

Table 2. Intraclass correlation coefficients (ICCs) for reliability among the MRI scoring systems.

		First test, mean (sd)	Second test, mean (sd)	ICC (95% CI)
Inter-observer reliability	Radiologist 1 vs. Radiologist 2			
	ASspiMRI-a	10.8 (11.5)	7.5 (8.9)	0.827 (0.588–0.741)
	Berlin	7.7 (8.0)	5.0 (5.9)	0.791 (0.494–0.900)
	SPARCC	25.1 (23.8)	19.9 (20.1)	0.884 (0.746–0.941)
	ASAFacet	3.7 (5.3)	2.8 (3.8)	0.857 (0.741–0.919)
Intra-observer reliability	Between-days (Radiologist 1)			
	ASspiMRI-a	8.8 (10.3)	10.8 (11.5)	0.931 (0.840–0.966)
	Berlin	6.3 (7.6)	7.7 (8.0)	0.942 (0.856–0.972)
	SPARCC	22.5 (24.0)	25.1 (23.8)	0.946 (0.903–0.969)
	ASAFacet	2.9 (5.1)	3.7 (5.3)	0.941 (0.873–0.969)

MRI, Magnetic resonance imaging; sd, standard deviation; CI, confidence interval; ASspiMRI-a, Ankylosing Spondylitis spine MRI activity; Berlin, the Berlin modification of the ASspiMRI-a; SPARCC, Spondyloarthritis Research Consortium of Canada; ASAFacet, Ankylosing Spondylitis Activity of the Facet joint.

CI 0.873–0.969), respectively, suggesting high reliability. The Bland–Altman plots of MRI activity reliability scores for the DVU and facet lesions are shown in Supplementary Figure 1. For all measures using the Bland–Altman plots, 95% of the differences from the mean for each patient were less than 1.96 sd's from the mean difference.

Distribution of inflammatory spinal lesions in DVUs and facet joints

The presence of lesions at 23 DVUs was evaluated according to each MRI scoring system. There were 40 patients with at least one spinal DVU lesion whereas 35 patients had at least one facet joint lesion among the 23 DVUs that were evaluated. All patients with a facet lesion were found to have more than one spinal DVU lesion. The distribution of inflammatory lesions according to the different MRI scoring systems is illustrated in Supplementary Figure 2. Using the ASspiMRI-a, Berlin method, and SPARCC to assess DVU lesions most often identified inflammatory lesions in the upper to middle thoracic spine levels, with a gradual decrease in the number of lesions in the lower lumbar spine. However, inflammatory lesions of the facet joints were largely evenly distributed at all spine levels, with a slightly increased frequency at the T1–2, T5–6, and T10–11 levels.

In addition, we assessed inflammatory activity scores at each cervical, thoracic, and lumbar spine level (Table 3). Inflammatory scores were then compared for those spine levels. We observed significantly more inflammation in the thoracic spine than in the cervical and lumbar spine among the three MRI scoring systems for DVU lesions ($p < 0.001$ for ASspiMRI-a, $p = 0.002$ for the Berlin method, and $p < 0.001$ for SPARCC). By contrast, there were no significant differences in inflammatory scores for the facet joints among those spine levels ($p = 0.294$ for ASAFacet).

Correlation of MRI activity scores for DVUs and facet joints with clinical features

Correlation analysis was performed to compare the facet activity score, ASAFacet, with the other three MRI activity scoring systems, including the ASspiMRI-a, Berlin method, and SPARCC (Supplementary Table 1). The

Table 3. Comparison of inflammatory activity scores in affected lesions at each spinal level (radiologist 2).

	Cervical spine (C2–3 to C7–T1)		Thoracic spine (T1–2 to T12–L1)		Lumbar spine (L1–2 to L5–S1)		
	Mean (sd)	Median (IQR)	Mean (sd)	Median (IQR)	Mean (sd)	Median (IQR)	p
ASspiMRI-a	1.0 (1.7)	0.0 (0.0–1.0)	5.0 (6.6)	2.0 (0.0–9.0)	1.5 (2.2)	1.0 (0.0–2.0)	< 0.001*
Berlin	0.8 (1.5)	0.0 (0.0–1.0)	3.2 (4.0)	2.0 (0.0–5.0)	1.0 (1.4)	0.0 (0.0–2.0)	0.002*
SPARCC	2.7 (4.4)	0.0 (0.0–4.0)	12.6 (14.8)	9.0 (0.08–17.0)	4.6 (7.8)	0.0 (0.0–6.0)	< 0.001*
ASAFacet	0.7 (1.4)	0.0 (0.0–1.0)	1.2 (2.6)	0.0 (0.0–1.0)	0.9 (1.4)	0.0 (0.0–2.0)	0.294†

sd, Standard deviation; IQR, interquartile range; ASspiMRI-a, Ankylosing Spondylitis spine magnetic resonance imaging (MRI) activity; Berlin, the Berlin modification of the ASspiMRI-a; SPARCC, Spondyloarthritis Research Consortium of Canada; ASAFacet, Ankylosing Spondylitis Activity of the Facet joint.
The statistical analyses were performed by the Kruskal–Wallis test. Post-hoc comparisons were made using the Bonferroni method.
* Activity scores at the thoracic spine are higher than those at the cervical spine and lumbar spine.
†ervical spine and lumbar spine.hose at byof the AS

Table 4. Correlation analysis between acute inflammatory makers and individual MRI activity scorings.

		ASspiMRI-a		Berlin		SPARCC		ASAFacet	
		r	p	r	p	r	p	r	p
Radiologist 1	ESR	0.357	0.009	0.413	0.002	0.371	0.006	0.449	0.001
	CRP	0.201	0.154	0.277	0.047	0.216	0.123	0.361	0.009
	BASDAI	−0.168	0.351	−0.220	0.218	−0.233	0.192	−0.301	0.088
	BASFI	0.041	0.837	0.063	0.751	0.022	0.913	−0.043	0.830
Radiologist 2	ESR	0.379	0.005	0.385	0.005	0.366	0.007	0.404	0.003
	CRP	0.241	0.085	0.243	0.083	0.179	0.204	0.295	0.034
	BASDAI	−0.293	0.098	−0.175	0.331	−0.316	0.073	−0.337	0.055
	BASFI	0.029	0.883	0.174	0.376	0.077	0.696	0.030	0.881

MRI, Magnetic resonance imaging; ESR, erythrocyte sediment rate; CRP, C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASspiMRI-a, Ankylosing Spondylitis spine MRI activity; Berlin, the Berlin modification of the ASspiMRI-a; SPARCC, Spondyloarthritis Research Consortium of Canada; ASAFacet, Ankylosing Spondylitis Activity of the Facet joint.
The statistical analyses were performed by SpearmanspiMRI-a; SPARCC, Spondyloarthritis g data including CRP (n = 52), BASDAI (n = 33), and BASFI (n = 28).

ASAFacet was significantly associated with the ASspiMRI-a, the Berlin method, and SPARCC, with correlation coefficients ranging from 0.507 to 0.642 ($p < 0.001$ for all indexes).

We then compared the MRI activity scoring systems with clinical activity indicators, including ESR, CRP, BASDAI, and BASFI (Table 4). Berlin and SPARCC scores from the two radiologists were closely associated with ESR values. CRP was marginally related to the Berlin score (r = 0.277, p = 0.047) but not to the SPARCC. By contrast, the ASAFacet score was significantly associated with the ESR level (r = 0.449, p = 0.001 for radiologist 1 and r = 0.404, p = 0.003 for radiologist 2) and CRP level (r = 0.361, p = 0.009 for radiologist 1 and r = 0.295, p = 0.034 for radiologist 2). However, the BASDAI and BASFI were not associated with any of the other MRI disease activity scoring systems.

Among the 53 patients, 17 patients had a history of peripheral joint involvement. We assessed differences in MRI activity scores according to the presence and absence of peripheral arthritis. Table 5 shows that there were fewer lesions in the DVUs or facet joints in patients with peripheral arthritis than in patients without peripheral arthritis ($p < 0.001$ for all MRI activity scoring indexes). However, there were no significant differences in inflammatory activity scores among the different MRI activity scoring systems between patients with and without peripheral arthritis.

Discussion

The measurement of inflammatory changes and structural damage using imaging modalities is considered essential for evaluation of disease activity and progression of AS. There are several MRI scoring systems for the assessment of acute spinal lesions, including the ASspiMRI-a (6, 7), the Berlin modification of the ASspiMRI-a (8), and SPARCC (9), which mainly focus on evaluation of DVU. However, there is a lack of methods for evaluating

Table 5. Comparison of inflammation at facet joint lesions according to the presence of peripheral arthritis.

	Number of affected lesions					Activity score at affected lesion				
	Peripheral arthritis (n = 17)		No peripheral arthritis (n = 36)			Peripheral arthritis (n = 17)		No peripheral arthritis (n = 36)		
	Mean (sd)	Median (IQR)	Mean (sd)	Median (IQR)	p	Mean (sd)	Median (IQR)	Mean (sd)	Median (IQR)	p
ASspiMRI-a	2.3 (5.0)	0.0 (0.0–0.5)	8.0 (5.7)	8.0 (2.3–13.5)	< 0.001	8.8 (11.2)	5.0 (0.0–11.0)	11.8 (11.6)	11.0 (1.0–17.0)	0.191
Berlin	2.1 (4.3)	0.0 (0.0–1.5)	8.0 (5.1)	7.0 (3.5–12.0)	< 0.001	6.5 (8.4)	2.0 (0.0–11.0)	8.2 (7.9)	7.0 (1.0–14.0)	0.237
SPARCC	1.0 (2.1)	0.0 (0.0–0.5)	4.5 (2.1)	6.0 (2.3–6.0)	< 0.001	19.2 (24.2)	9.0 (0.0–26.0)	27.9 (23.5)	26.0 (4.0–49.5)	0.139
ASAFacet	1.6 (4.1)	0.0 (0.0–0.0)	2.8 (2.1)	2.0 (1.0–4.0)	< 0.001	4.8 (8.0)	2.0 (0.0–6.0)	3.2 (3.3)	3.0 (0.0–5.5)	0.884

sd, Standard deviation; IQR, interquartile range; ASspiMRI-a, the Ankylosing Spondylitis spine magnetic resonance imaging (MRI) activity; Berlin, the Berlin modification of the ASspiMRI-a; SPARCC, Spondyloarthritis Research Consortium of Canada; ASAFacet, Ankylosing Spondylitis Activity of the Facet joint.
The statistical analyses were performed by the Wilcoxon rank sum test.

MRI for acute inflammation of facet joints in patients with AS. Thus, a primary aim of this study was to introduce an MRI activity scoring index for facet joint involvement with good to excellent inter-observer and intra-observer reliability. In contrast to the lesions consistent with vertebral inflammation that were observed mostly in the lower thoracic spine, acute inflammatory lesions involving the facet joints were evenly distributed throughout all assessed spinal levels. In addition, MRI activity scores for the facet joints in AS patients were closely associated with acute phase reactants, such as ESR and CRP, but not with the BASDAI and BASFI.

This study introduces a novel scoring index for the facet joint that identifies acute inflammatory activity. Prior to assessing facet joint inflammation, two independent radiologists assessed the MRI scans using well-established MRI activity scoring systems, such as the ASspiMRI-a, Berlin method, and SPARCC. The intra- and inter-observer reliability of their readings was evaluated using ICCs and Bland-Altman plots, and we observed good to excellent agreement (ICC 0.791 to 0.946). In addition, inter- and intra-observer reliability for facet joint activity was also shown to be excellent (ICC 0.857 and ICC 0.941, respectively). In the analysis of intra-observer reliability between DVU and facet joint scoring indexes (ASspiMRI-a vs. ASAFacet, Berlin vs. ASAFacet, and SPARCC vs. ASAFacet), only the Berlin method was identified to have moderate agreement with the ASAFacet (ICC 0.681 for radiologist 1 and 0.581 for radiologist 2). Agreement scores between the ASAFacet and ASspiMRI-a and SPARCC were poor (data not shown). This might be a result of the inclusion of a measurement of bone erosion in addition to bone marrow oedema in the ASspiMRI-a score and assessment of only the six most severely affected DVUs in the SPARCC rather than all 23 DVUs as in the other scoring systems.

One set of observational data showed that bony ankylosis with or without bridging syndesmophyte formation in the facet joint was present in 10–22% of cases in the cervical or lumbar spine on plain radiographs (10). However, one study reported that approximately 47.5% of AS patients showed facet joint involvement in the cervical spine on plain radiograph (12). Inflammation is a precursor to bony structural damage, including ankylosis and syndesmophyte formation; therefore, inflammatory changes in the facet joints of AS patients could be viewed as an incipient feature in the clinical progression of AS. Weber et al reported detection of inflammatory changes in a proportion of established (n = 2/10, four lesions) and early (n = 1/10, two lesions) AS patients using whole body MRI (11). We evaluated acute inflammatory lesions of facet joints in 23 corresponding DVUs for each patient and found that 35 patients had at least one inflammatory facet joint lesion, and 18 patients had no facet joint lesions. There was involvement of the facet joints in approximately two-thirds of the patients enrolled in this study, which is a greater proportion than noted in previous studies using plain radiographs (10, 12). Previous studies also proposed that inflammation of the facet joint in AS is non-specific and occurs secondary to ankylosis of the corresponding intervertebral disc (19, 20). However, the synchronous occurrence of vertebral body and facet joint involvement has not always been identified in plain radiographs in AS patients (10, 12). This suggests that inflammation of the facet joint is potentially an essential prerequisite to joint damage, but does not always progress to structural changes, such as bony ankylosis.

Of note, this study found that inflammatory lesions involving the facet joint detected using MRI were evenly distributed in 23 DVUs from C2 to S1, although a small peak was noted at the lower lumbar level (Supplementary Figure 2). de Vlam et al demonstrated equal involvement of facet joints throughout the lumbar spine (χ^2 = 3.97, df = 5, p = 0.15) (10), which might be compatible with our data, although facets at the C2–3 level were more frequently affected than those at C3–4 (χ^2 = 8.2, df = 1, p = 0.0046) and C4–5 (χ^2 = 4.2, df = 1, p = 0.042). Inflammatory lesions of the vertebral bodies have often been noted in the lower thoracic or lumbar spine in established AS and non-radiographic axial spondyloarthritis (6, 21). By contrast, our study evaluated inflammatory changes of the vertebral body and consistently demonstrated these lesions to be more frequent in the upper thoracic spine using the ASspiMRI-a, the Berlin method, and the SPARCC MRI activity scoring systems. Although the observed distribution of spinal inflammation affecting the thoracic spine could be attributed to differences in lifestyle or ethnic diversity, it deserves further investigation in a larger study population.

Several investigations have demonstrated that the involvement of peripheral joints in AS is associated with clinically delayed radiographic progression and less severe spinal disease (22, 23). Based on these clinical observations, our hypothesis was that patients with peripheral joint disease would show few inflammatory findings in the facet joints. We found that AS patients with peripheral arthritis had fewer affected facet joints (p < 0.001 for ASAFacet) and had lower scores on assessment with the ASspiMRI-a, Berlin, and SPARCC indexes. This finding suggests a possible association between less severe involvement of the facet joints and comorbid peripheral joint disease or inflammation of the vertebral body.

Increased acute phase reactants, such as ESR and CRP, have been noted in 50–70% of patients with active disease (1). However, these inflammatory markers have low predictive value for the assessment of disease activity in AS (24). Of note, we found that patients with increased activity scores at the facet joint showed higher ESR and CRP levels, but this was not seen with any of the clinical disease activity indexes, such as the BASDAI and BASFI. By contrast, only the Berlin and SPARCC MRI activity scores were closely related to ESR levels (Table 4), whereas there was no correlation between the ASspiMRI-a score and any acute phase reactants in the present study. Spoorenberg et al

compared ESR and CRP levels of 149 patients with spinal involvement and 42 patients with peripheral arthritis and/or inflammatory bowel disease (IBD) and found higher ESR levels in patients with peripheral arthritis and/or IBD than among patients in the spinal group ($p < 0.02$) (24). Another study also observed a higher ESR level in patients with peripheral joint disease than in those without ($p = 0.0047$) (22). This suggests that the correlation between the ESR level and the facet joint activity score might, in part, originate from the similarity of synovial inflammation of peripheral joints and facet joints of the spine.

Our study has several limitations. First, although this study confirmed the reliability of a newly developed MRI activity scoring method to assess the inflammatory activity of facet joints in AS, further validation studies of the novel MRI scoring system are needed. However, our study did show high intra- and interobserver reliability of the scoring method using ICC and Bland–Altman plots. Second, there was the potential for referral bias in the study population because of retrospective enrolment of patients from a single hospital that specialized in rheumatic diseases. However, general characteristics, such as HLA-B27 positivity and the presence of peripheral arthritis in enrolled patients, were grossly matched to data from other studies (23, 25). Finally, ESR and CRP levels were closely associated with ASAFacet scores in the study. However, the study sample size was small. Therefore, the relationship between ASAFacet scores and inflammatory indexes should be confirmed in a larger study population.

In conclusion, we found that our novel MRI activity scoring system for facet joints was highly reliable for the assessment of inflammatory changes in facet joints. This study has revealed a significant positive correlation of MRI inflammatory scores for facet joints and acute phase reactants, such as ESR and CRP, suggesting that the facet joint may be a potent target for inflammation in AS. These results may enhance our understanding of the clinical significance of facet joint involvement in AS.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Supplementary Figure S1. Bland–Altman plots of differences in reliability. (A) Intra-observer reliability (time 1 vs. time 2), (B) interobserver reliability (radiologist 1 vs. radiologist 2), and (C) intra-observer reliability (ASspiMRI-a, Berlin, and SPARCC vs. ASAFacet).
Supplementary Figure S2. Distribution of inflammatory lesions at 23 discovertebral units (DVUs) according to each MRI scoring system.

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