

## Correlation between clinical disease activity and sacroiliac magnetic resonance imaging detection in axial spondyloarthritis

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### ABSTRACT

**Objectives:** The study aimed to evaluate the correlation between the clinical disease activity of axial spondyloarthritis (axSpA) and magnetic resonance imaging findings of the sacroiliac joint.

**Patients and methods:** Thirty-two patients (21 males, 11 females; mean age: 39.3±9.2 years; range, 18 to 55 years) who were diagnosed with axSpA according to the Assessment in Spondyloarthritis International Society classification criteria between November 2015 and August 2017 were included in this cross-sectional study. Visual Analog Scale (VAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS)-erythrocyte sedimentation rate (ESR), and ASDAS-C-reactive protein (CRP) were used as the indicators of clinical activity. Magnetic resonance imaging of the sacroiliac joint was performed and the Spondyloarthritis Research Consortium of Canada (SPARCC) score was evaluated by a radiologist who was blinded to the clinical and laboratory parameters of the patients.

**Results:** The mean duration of symptom onset was 9.3±7.7 years, and the mean duration of diagnosis was 3.6±2.8 years. Human leukocyte antigen (HLA)-B27 was positive in 16 (50%) patients. There was no correlation between the SPARCC score and VAS, BASDAI, MASES, BASFI, ASDAS-CRP, ASDAS-ESR, ESR, and CRP values ( $p>0.05$ ). In the HLA-B27 subgroup analyses, a statistically significant correlation was found between HLA-B27-negative patients and SPARCC score ( $r=0.639$ ,  $p=0.008$ ).

**Conclusion:** No relationship was found between other clinical disease parameters and sacroiliac joint imaging findings, except for the relationship between the SPARCC and BASDAI in HLA-B27-negative patients with axSpA.

**Keywords:** Ankylosing spondylitis, axial spondyloarthritis, BASDAI, disease activity, SPARCC score.

Spondyloarthropathies (SpAs) are a heterogeneous group of diseases that include ankylosing spondylitis (AS), psoriatic arthritis, reactive arthritis, enteropathic arthritis, and undifferentiated spondyloarthritis.<sup>1,2</sup> SpAs have varying degrees of relationship with human leukocyte antigen (HLA)-B27.<sup>3</sup> AS is the prototype of SpA and is characterized by erosive radiological findings in the sacroiliac joint (SIJ).<sup>4</sup> In the past 10 years, investigations using magnetic resonance imaging (MRI) of the spine and SIJ in SpA patients have greatly advanced our knowledge

of the disease progression, allowed for an early diagnosis, and served as a reliable indicator for clinical trials.<sup>5</sup> Today, the classification criteria developed in 2009 by the ASAS (Assessment of Spondyloarthritis International Society) are more widely used.

Two aspects of the classification criterion for axial SpA (axSpA) were the clinical arm and the imaging arm. The imaging arm also included SIJ MRI findings that were not included in the previous classification criteria.<sup>5</sup> Along

with these classification criteria, the concept of nonradiographic axSpA (nr-axSpA) was also revealed. Patients who did not match the modified New York criteria for sacroiliitis were also included in nr-axSpA since radiographic sacroiliitis was not identified despite symptoms and indicators. AS and nr-axSpA patients constituted the axSpA group.<sup>6</sup> Studies on the role of SIJ or spinal MRI imaging in demonstrating disease activity are still ongoing.

The Spondyloarthritis Research Consortium of Canada (SPARCC) MRI index was frequently utilized to evaluate the degree of osteitis in AS. Scoring is based on oblique coronal short-tau inversion recovery (STIR) sequences. The SPARCC scoring system was found to be more comprehensive than other suggested methods.<sup>7</sup> In this study, we wanted to see if the SPARCC grading system's evaluation of SIJ MRI data correlates with clinical and laboratory indicators of disease severity.

## PATIENTS AND METHODS

Thirty-two patients (21 males, 11 females; mean age:  $39.3 \pm 9.2$  years; range, 18 to 55 years) who had a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)  $>4$  and who described inflammatory low back pain were included in the cross-sectional study. The patients were diagnosed with axSpA in accordance with the ASAS classification criteria between November 2015 and August 2017 and were routinely followed up in our clinic at the Istanbul Training and Research Hospital.

Blood tests and sacroiliac MRI were performed within the same week. Patients who could not undergo MRI and patients who did not have blood test results were excluded from the study. Data including demographic characteristics of the patients (age, sex, education level, marital status), duration of symptoms, duration of diagnosis, HLA-B27, disease history (uveitis, inflammatory bowel disease, psoriasis, tuberculosis, other diseases), family history, drug use (nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, tumor necrosis factor-alpha [TNF- $\alpha$ ] blocker usage) were recorded.

To measure disease severity, the Ankylosing Spondylitis Disease Activity Score (ASDAS)-erythrocyte sedimentation rate (ESR), BASDAI, and ASDAS-C-reactive protein (CRP) were computed and reported. Six items make up the BASDAI, a self-reported questionnaire that assesses the severity of each of the five main AS symptoms: fatigue, back pain, joint pain/swelling, enthesitis, duration, and morning stiffness. The final BASDAI score is based on the average of five significant symptoms measured during the previous week, with a higher score indicating more severe disease activity.<sup>5</sup> A 10-cm Visual Analog Scale (VAS) was used by the patients to respond to the questions. BASDAI's Turkish validity and reliability study was conducted in 2005.<sup>8</sup>

The patient's global evaluation of disease activity, the CRP (mg/L) for the ASDAS-CRP, or the ESR (mm/h) for the ASDAS-ESR, were used to construct the ASDAS-ESR and ASDAS-CRP, and the scores were then calculated using the responses from questions 2, 3, and 6 on the BASDAI. The VAS was employed to evaluate inflammatory low back discomfort in the last week, and the patients were asked to score between 0 and 100 points (0=no pain, 100=unbearable pain).<sup>5</sup>

Sacroiliac joint MRI examination was performed in the supine position with the head in front using a spine coil in a HDX model 1.5 Tesla MRI device (GE HealthCare Technologies Inc., Chicago, IL, USA). Plans were made to coincide with the oblique coronal plan according to the sagittal and axial planes on the localizing image. Sequences used in MRI examination were as follows: (i) COR T1 (echo time [TE]: min.full; repetition time [TR]: 620 msec); (ii) COR STIR (TE: 42; TR: 5,225 msec); (iii) T2 fat-saturated axial/coronal (TE: 85; TR: 4,240 msec); (iv) T1 axial/coronal (TE: min.full; TR: 620 msec).

The SPARCC scoring system is based on the evaluation of the enhanced signal in the fat-suppressed T2 sequence or STIR sequences indicating bone marrow edema in the oblique coronal sections of the SIJ. The SIJ is divided into six consecutive sections to examine all signal changes in the sacrum up to the iliac bone and sacral foramina. Sacral interforaminal bone marrow is used as a reference in evaluating the

increased signal in SIJ in the STIR sequence. Each SIJ is divided into four quadrants (upper iliac, upper sacral, lower sacral, and lower iliac). The presence of an increased signal in each quadrant is recorded. The maximum score for two SIJs in each coronal slice is 8. The maximum score for six coronal slices is 48. The fact that the lesion either shows an intense signal (when venous blood in the nearby presacral veins is taken as reference) or the signal depth is  $\geq 1$  cm from the articular surface in any of the six sections of each SIJ provides an additional score. If the signal is intense in any SIJ quadrant in a single section, it gets 1 point, and considering there are two SIJs and six sections, the maximum score is 12. It is calculated in the same way for depth, with a depth maximum score of 12. With this calculation, the maximum total score is 72.<sup>9</sup> A radiologist employed by our institution reviewed SPARCC grading without knowledge of the patients' clinical or laboratory data.

**Statistical analysis**

Data were analyzed using IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA).

The Kolmogorov-Smirnov test was used to confirm the normality of distributions. The data were summarized as median (min-max); categorical data were summarized as frequency and percentage. Correlation analysis was performed using the Spearman correlation technique. A correlation coefficient ( $r$ )  $>0.30$  and a  $p$ -value  $<0.05$  was considered statistically significant.

**RESULTS**

The mean duration of symptom onset was  $9.3 \pm 7.7$  years, and the mean duration of diagnosis was  $3.6 \pm 2.8$  years. Table 1 lists the patients' demographic details. The clinical features and

**Table 1.** Demographic characteristics and comorbid diseases of patients

	Frequency	Percent
Sex		
Female	11	34.4
Male	21	65.6
Marital status		
Divorced	9	28.1
Married	23	71.9
Education		
Illiterate	14	43.8
Primary	3	9.4
Secondary	10	31.3
University	5	15.6
Family history		
(-)	27	84.4
(+)	5	15.6
Father	1	3.1
Brother/sister	4	12.5
Additional disease		
(-)	24	75.0
(+)	8	25.0
Diabetes insipidus	1	3.1
Diabetes mellitus	1	3.1
Hepatitis B carrier	1	3.1
Hypertension	2	6.3
Hypothyroidism	1	3.1
Coronary artery disease	2	6.3
Palmoplantar pustulosis	1	3.1

**Table 2.** Patients' clinical disease activity evaluations, laboratory parameters, SPARCC scores, HLA-B27 status, and drugs used

	n	%	Mean $\pm$ SD
VAS			79.2 $\pm$ 16.3
BASDAI			5.9 $\pm$ 1.3
ESR (mm/h)			20.3 $\pm$ 17.2
CRP (mg/dL)			1.1 $\pm$ 1.1
SPARCC score			10.4 $\pm$ 11.5
ASDAS-ESR			3.5 $\pm$ 0.7
ASDAS-CRP			3.8 $\pm$ 0.7
Psoriasis (+)	0	0.0	
IBH (+)	0	0.0	
Uveitis (+)	3	9.4	
Tuberculosis (+)	1	3.1	
HLA-B27 (+)	16	50.0	
NSAID (user)	31	96.9	
Sulfasalazine (user)	17	53.1	
TNF- $\alpha$ blocker (user)	4	53.1	
ASDAS-ESR			
$\leq 3.5$	19	59.4	
$> 3.5$	13	40.6	
ASDAS-CRP			
$\leq 3.5$	11	34.4	
$> 3.5$	21	65.6	

SPARCC: Spondyloarthritis Research Consortium of Canada; HLA-B27: Human leukocyte antigen-B27; SD: Standard deviation; VAS: Visual Analog Scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; IBH: Inflammatory bowel disease; NSAID: Non-steroidal anti-inflammatory drug; TNF- $\alpha$ : Tumor necrosis factor-alpha.

**Table 3.** Correlation between clinical disease parameters and SPARCC scores

	VAS	BASDAI	ESR	CRP	ASDAS-ESR	ASDAS-CRP
SPARCC score						
r	0.233	0.214	-0.091	-0.125	-0.073	-0.081
p	0.200	0.239	0.622	0.494	0.691	0.658

SPARCC: Spondyloarthritis Research Consortium of Canada; VAS: Visual Analog Scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; Spearman correlation.

**Table 4.** Correlation between clinical disease parameters and SPARCC score in males and females

	VAS	BASDAI	ESR	CRP	ASDAS-ESR	ASDAS-CRP
Female SPARCC score						
r	0.036	0.396	0.453	0.294	0.230	0.042
p	0.917	0.228	0.162	0.380	0.495	0.903
Male SPARCC score						
r	0.346	0.241	-0.143	-0.340	-0.021	-0.039
p	0.124	0.294	0.536	0.132	0.927	0.868

SPARCC: Spondyloarthritis Research Consortium of Canada; VAS: Visual Analog Scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; Spearman correlation.

**Table 5.** Correlation between clinical disease parameters and SPARCC score according to HLA-B27 status

	VAS	BASDAI	ESR	CRP	ASDAS-ESR	ASDAS-CRP
<b>HLA-B27 (-)</b>						
SPARCC score						
r	0.118	0.639	-0.266	-0.295	0.001	-0.135
p	0.664	<b>0.008</b>	0.320	0.268	0.998	0.618
<b>HLA-B27 (+)</b>						
SPARCC score						
r	0.287	-0.228	0.054	0.023	-0.022	-0.003
p	0.281	0.395	0.844	0.933	0.936	0.991

SPARCC: Spondyloarthritis Research Consortium of Canada, Spondyloarthritis Research Consortium of Canada; HLA-B27: Human leukocyte antigen B27; VAS: Visual Analog Scale; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ESR: Erythrocyte Sedimentation Rate; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; Spearman correlation.

disease activity scores of the patients related to AS are given in Table 2.

No relationship was found between the SPARCC score and the VAS, BASDAI, ASDAS-CRP, ASDAS-ESR, ESR, or CRP levels in all patients or between sexes (Tables 3, 4). HLA-B27 was positive in 16 (50%) patients. When the HLA-B27 positivity subgroup analysis was

performed, a strong positive correlation was found between BASDAI and SPARCC score in only HLA-B27-negative patients ( $r=0.639$ ,  $p=0.008$ , Table 5). There was a strong positive association between the VAS score and BASDAI, ASDAS-ESR, and ASDAS-CRP when the correlation between clinical parameters of the disease and laboratory measures was evaluated ( $p<0.05$ ).

## DISCUSSION

Studies on the place of SIJ or spinal MRI in showing disease activity are still ongoing. Our study has shown that there is no relationship between clinical disease parameters and SIJ findings except for the SPARCC score relationship with BASDAI in HLA-B27-negative patients with axSpA. Therefore, we have concluded that SIJ MRI does not need to be used for routine follow-up of disease activity.

The phenotypic heterogeneity of axSpA and the accompanying large number of clinical manifestations might result in a misunderstanding of the disease severity. Therefore, the use of a combined index is useful in evaluating disease activity in axSpA.<sup>10</sup> The disease severity composite index primarily employed in axSpA is the BASDAI. However, it has been demonstrated in the past that there is a discrepancy between the clinician's and the patient's assessment of the disease activity in axSpA.<sup>11</sup> The inability of BASDAI to show disease activity has led to different examinations and the development of ASDAS. Studies have shown that ASDAS is superior to BASDAI, patient global assessment, clinician global assessment, and acute phase reactants.<sup>10,11</sup> At the same time, the advantage of ASDAS over BASDAI is that only subjective parameters are used when calculating BASDAI; however, when calculating ASDAS, the objective parameters ESR and CRP are also used. Various trials have been conducted on the place of MRI in monitoring disease severity in SpA. European Alliance of Associations for Rheumatology published a guide on the application of imaging techniques to the diagnosis and treatment of the disease in SpA in 2015. In this guide, 34 studies on MRI in axSpA were evaluated. As a result, it has been stated that SIJ or spine MRI imaging can provide additional information in addition to biochemical and clinical evaluations in showing disease activity in axSpA.<sup>12</sup> Hence, in our study, we wanted to evaluate whether the SIJ MRI reflects the clinical disease activity.

In a study by Zhang et al.,<sup>7</sup> 52 patients who met the ASAS classification criteria and 16 volunteers were recruited. BASDAI, ESR, and high-sensitivity CRP were examined as clinical AS activity index, and SPARCC score and apparent diffusion coefficient values in diffusion-weighted imaging were used as SIJ MRI activity. It was found that the BASDAI score had a significant positive

relationship with the SPARCC score. At the same time, it was determined that ESR had a significant positive correlation with high-sensitivity CRP. In a study conducted by MacKay et al.,<sup>13</sup> spine and SIJ MRI were performed in 40 patients who met the ASAS axSpA criteria. The patients were evaluated with the SPARCC score, and BASDAI and ASDAS were examined as clinical disease activity. There was no significant relationship between the total (spine and SIJ) SPARCC score of the patients and BASDAI, ASDAS-ESR, and ASDAS-CRP. In our study, no positive significant correlation was found between many clinical disease parameters and the SPARCC score. The reason for this may be that only the acute condition is evaluated as the disease activity in SIJ MRI in SPARCC scoring. However, persistent axSpA characteristics including ankylosis and erosion may potentially worsen clinical disease activity. In the SPARCC score, chronic changes of SIJ are not evaluated. Another reason we could not find a positive significant correlation may be that clinical disease activity consists of subjective parameters. Although ASDAS-CRP and ASDAS-ESR include ESR and CRP parameters, subjective questions are also used when calculating ASDAS. This suggests that acute-phase reactants may remain limited in demonstrating disease activity. Although subjective parameters are used in querying ASDAS, four different versions of ASDAS were used in a study by van der Heijde et al.<sup>14</sup> All four versions were consistent with the patient's global assessment and the clinician's global assessment. However, BASDAI correlated with the patient's global assessment but not with the clinician's global assessment. Likewise, there was no relationship between acute phase reactants and patient global evaluation. Accordingly, it can be thought that ASDAS can reflect the disease activity more objectively than BASDAI.

In a cohort study by Navarro-Compan et al.,<sup>15</sup> 167 patients with axSpA according to the ASAS criteria were monitored for two years to assess the correlation between clinical disease activity characteristics and the SIJ MRI SPARCC score. As clinical disease parameters, BASDAI, ASDAS, night pain, global assessment of the patient, ESR, and CRP were examined, and these parameters were compared with the SIJ MRI SPARCC score. A statistically significant relationship was observed between the SPARCC value in males and clinical disease activity parameters other than BASDAI,

but this relationship was not observed in females. Our investigation differs from this study in that we only found a correlation between BASDAI and SPARCC score in HLA-B27-negative patients, and we did not find a statistically significant correlation between SPARCC score and clinical disease activity parameters when female and male subgroups were examined.

Studies have also been conducted evaluating spinal inflammation and clinical disease activity in AS patients. In a study by Konca et al.,<sup>16</sup> laboratory markers ESR and CRP, as well as the BASDAI, ASDAS, Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Radiology Index (BASRI), and Ankylosing Spondylitis Quality of Life scores of 50 patients with diagnoses based on the modified New York criteria, were assessed. Spinal inflammation was assessed by the Ankylosing Spondylitis spine Magnetic Resonance Imaging (ASspiMRI) score. A statistically significant correlation was found between the thoracic MRI score and BASFI, BASMI, BASRI, ASDAS, and patient and clinician global assessment.

Patients with disease activity for more than 10 years were enrolled in a cross-sectional study by Goh et al.,<sup>17</sup> and BASDAI, BASFI, BASMI, Bath Ankylosing Spondylitis Global score (BASG), thoracic and lumbar AS spinal MRI score, ESR, and CRP were evaluated. No significant association was found between MRI results and study parameters.

Magnetic resonance imaging scoring systems have also been used to evaluate TNF- $\alpha$  blocker treatment response in axSpA in various studies. Thirty-seven individuals with nr-axSpA were enrolled by Cantarini et al.<sup>18</sup> to evaluate the impact of adalimumab. Patients received 40 mg of adalimumab every two weeks. ASDAS, BASDAI, BASFI, and SIJ MRI SPARCC scores were used. When evaluated before and after treatment, improvement was observed in the SPARCC score, but this improvement was not found to be statistically significant. Since the disease activity will decrease after the treatment, the improvement in the SPARCC score is an expected result.

In a randomized placebo-controlled study conducted by Rudwaleit et al.,<sup>19</sup> the role of MRI in 50% improvement of the initial BASDAI (BASDAI50) response after TNF- $\alpha$  blocker

treatment in patients with active AS was investigated. Spinal and SIJ MRI of the patients were calculated using the Berlin scoring system. As a result, the odds ratio of reaching BASDAI50 response increased in those with a Berlin MRI score of 11 and CRP of 40 mg/L. In addition, it was stated that the SIJ MRI score could be predictive in reaching BASDAI50 response. This study is valuable since it is a randomized placebo-controlled study that evaluates both SIJ and spinal MRI. It is also a study supporting the good response of CRP elevation to TNF- $\alpha$  inhibitor therapy. In their placebo-controlled randomized study, Machado et al.<sup>20</sup> analyzed the ASSERT (AS study evaluating recombinant infliximab treatment), and the infliximab treatment response was evaluated. The study started with 221 patients and ended with 179 patients in the 102<sup>nd</sup> week. Spinal Berlin scoring system, ASDAS, BASDAI, and ASAS20 ( $\geq 20\%$  improvement of the initial ASAS) responses were examined in the evaluation. As a result, it was found that baseline ASDAS and CRP show a weak correlation with MRI scores. It was determined that the improvement in ASDAS and CRP correlated with the improvement in MRI. BASDAI and patient global assessment were not correlated with MRI. These results suggest that MRI scoring systems have a weak relationship with clinical disease activity but may be a better indicator of how well people are responding to therapy. In a meta-analysis conducted in 2021, Khoury et al.<sup>21</sup> reported that there was insufficient evidence between treatment with anti-TNF agents and SIJ MRI imaging findings.

The limitations of this study are the small number of participants, the absence of a control group, the use of a single clinician to determine the SIJ MRI SPARCC score, the absence of a spinal MRI scan, and the absence of exclusion of accompanying fibromyalgia in our participants.

In conclusion, SIJ MRI, which is an expensive tool, does not need to be used for routine follow-up of disease activity. Nevertheless, there are studies showing a relationship between SIJ MRI and disease activity, as well as that imaging can be useful in the follow-up of TNF- $\alpha$  inhibitor therapy. We believe that this relationship can be revealed better with future studies.

**Ethics Committee Approval:** The study protocol was approved by the Istanbul Training and Research Hospital Clinical Research Ethics Committee (date: 06.11.2015, no: 2015/726). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Material preparation, data collection, and analysis were performed by O.I., E.A., Y.P.D., K.A., N.O.; The first draft of the manuscript was written by E.A., O.I., N.S.C., I.N.M. All authors commented on previous versions of the manuscript. All co-authors read and approved the final manuscript. All authors contributed to the study conception and design.

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