# Comparison of the efficacy of physical examination and radiological imaging in detecting sacroiliitis in patients with juvenile spondyloarthropathies

B. Akdeniz<sup>1</sup>, N. Akyel<sup>2</sup>, M. Yildiz<sup>1</sup>, S. Sahin<sup>1</sup>, A. Adrovic<sup>1</sup>, O. Koker<sup>1</sup>, S. Bektas<sup>1</sup>, E. Dede<sup>1</sup>, K. Barut<sup>1</sup>, S. Kurugoglu<sup>2</sup>, O. Kasapcopur<sup>1</sup>

<sup>1</sup>Department of Paediatric Rheumatology, <sup>2</sup>Department of Radiology, Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Istanbul, Turkey.

# Abstract Objective

To determine and compare the effectiveness of history, physical examination, conventional radiography and magnetic resonance imaging (MRI) in the detection of sacroiliitis in juvenile spondyloarthropathies.

# Methods

One hundred and one patients with JSpA, 33 patients with other diseases and 24 children without rheumatologic complaints were included in the study. Subjects were evaluated using physical examination, laboratory findings, pelvic radiography and MRI. Abdominal or pelvic MRIs of 24 control patients who were obtained in the last 6 months were reevaluated and multivariate logistic regression analyses were used to calculate probability ratios of variables.

# Results

In our study, the rate of active sacroiliitis was 52.4% and in most of them, erosive and sclerotic changes indicating destruction of the sacroiliac joints were recorded. The presence of sacroiliitis on direct x-ray, high JSPADAI score, and hip involvement on MRI were independent risk factors with high predictive potential for active sacroiliitis. Inflammatory lumbar pain, sacroiliac tenderness, modified Schober's limitation, acute phase elevation, HLA-B27 positivity and presence of uveitis failed to predict sacroiliitis. The best specificity was 100% with a high BASFI score (>5), then 94% with a high JSPADAI score (>4). None of the patients in the control group showed active sacroiliitis.

# Conclusion

All patients with possible JSpA should undergo sacroiliac MRI whether HLA-B27 positive or not. In this way, early diagnosis and treatment of axial joint involvement could be possible and it prevents unnecessary examination and loss of time.

# Key words

juvenile spondyloarthropathies, sacroiliitis, magnetic resonance imaging, enthesitis, enthesitis-related arthritis

#### Detecting sacroiliitis in juvenile spondyloarthropathies / B. Akdeniz et al.

Beste Akdeniz, MD Nazli Akvel, MD Mehmet Yildiz, MD Sezgin Sahin, MD, Assoc. Prof. Amra Adrovic, MD, Assoc. Prof. Oya Koker, MD Sule Bektas, MD Elif Dede, MD Kenan Barut, MD, Assoc. Prof. Sebuh Kurugoglu, MD, Prof. Ozgur Kasapcopur, MD, Prof. Please address correspondence to: Ozgur Kasapcopur, Department of Paediatric Rheumatology, Cerrahpasa Medical School, Istanbul University-Cerrahpasa, 34303 Istanbul, Turkey. E-mail: ozgurkasapcopur@hotmail.com ozgurkc@istanbul.edu.tr Received on November 17, 2019; accepted in revised form on February 17, 2020. © Copyright CLINICAL AND

© Copyright Clinical and EXPERIMENTAL RHEUMATOLOGY 2020.

*Competing interests: none declared.* 

### Introduction

Juvenile spondyloarthropathies (JSpA) is a term for chronic inflammatory arthritis with symptoms beginning before the age of 16, affecting the spine and sacroiliac (axial) joints (1-3). Juvenile and adult-onset spondyloarthropathies are separate disease forms with different clinical presentations. Adults mostly present with axial findings, whereas children and adolescents generally present with peripheral oligoarthritis and enthesopathy (4-6). Recently, Martini et al. have grouped these patients under the name of enthesitis/spondylitis-related arthritis (ESRA) as a subtype of juvenile idiopathic arthritis (JIA) (7). Initial axial skeletal involvement is rare in ESRA, but it carries a risk of progression to ankylosing spondylitis (AS) (4, 8). Since the majority of children with ESRA do not initially complain of inflammatory back pain, the physical examination of children cannot be performed clearly or the findings are insufficient, recognition of sacroiliitis is delayed and initiation of treatment before permanent damage sets in could be challenging (9, 10).

Early diagnosis could not be based on physical examination only, because specific clinical features (e.g. axial involvement, sacroiliitis) have late-onset in patients with JSpA. Imaging methods are mandatory for diagnosis and follow-up of JSpA. Magnetic Resonance Imaging (MRI) can visualise the inflammatory changes seen in the axial joints and the lesions in the early stage such as subchondral osteitis (11-15). What we do not know at present is how to define the inflammatory changes such as enthesitis, bone marrow oedema-osteitis in pelvic joints, bones and surrounding tissues other than sacroiliitis on MRI, what it means, what its optimal evaluation is and at what stage it can help the physician.

In this study, we aimed to determine and compare the efficacy of disease history, physical examination and radiological imaging in detecting sacroiliitis in patients with JSpA.

#### Materials and methods

Study design and patients One hundred and one patients with JSpA, aged between 5 and 21 years,

followed up in our paediatric rheumatology clinic and 33 patients with low back and hip pain [27 familial Mediterranean fever (FMF), 4 inflammatory bowel disease (IBD) related arthritis, 1 IBD + psoriasis and 1 Behcet's disease (134 patients in the patient group)] were included in the study. The control group consisted of 24 children who underwent abdominal or pelvic MRI for other reasons without any rheumatologic history or complaints. The diagnosis of ESRA was based on the clinical criteria published by our clinic in 2016, but all of the patients also met the ILAR diagnostic criteria (2, 16, 17). Patients with ESRA and Juvenile Psoriatic Arthritis (JPsA) were included in the JSpA group. FMF, Behçet's disease and IBD patients were evaluated in the 'other diseases' group. Approval was obtained from the Clinical Research Ethics Committee of Istanbul University-Cerrahpasa (04.04.2017/A-23). Each patient and his/her parents were informed about the study and informed consent forms were obtained from the patients and/or their parents.

# Clinical data, measures and examination

All patients with rheumatic disease were evaluated by a blind investigator (BA), unaware of the diagnoses. The BAS-DAI (Bath Ankylosing Spondylitis Disease Activity Index) and BASFI (Bath Ankylosing Spondylitis Functional Index) forms including questions about the disease activity at the time of MRI and the functional status of the patient were filled out for each patient, separately. The BASDAI score of 4 or above and BASFI score of 5 or above are considered as cut off values for serious illness. The JSPADAI (JSpA Disease Activity Index) score of each patient was calculated, and the severity cut-off value was considered to be 4 (disease activity increases as the total score approaches 8). The age, gender, age at onset of disease, duration of diagnosis, age at diagnosis, follow-up period, family history of rheumatologic diseases (AS, FMF), complaints at the onset and follow-up of the disease, presence of uveitis and HLA-B27 positivity of all the patients were recorded. The complaints (inflammatory low back pain, joint complaints), physical examination findings (examination of all joints, limitation of the hip movements, sacroiliac joint tenderness, cervical movements, presence of enthesopathy and modified Schober measurement) and acute phase response were evaluated. Inflammatory back pain was defined as three of the following: low back pain for more than 3 months, insidious onset, recovery with exercise-worsening with rest and morning stiffness. Enthesitis was defined as the presence of spontaneous pain or tenderness by examination of the site of attachment of the Achilles tendon and plantar fascia to the calcaneus, and attachment of the quadriceps femoris tendon to the trochanter major or minor. Hip arthritis was defined as the pain as well as the limitation of hip flexion, extension and rotational movements (FABER or FADIR positivity). Clinical sacroiliitis or sacroiliac joint tenderness was considered in patients with pain or tenderness when compression was applied on the anterior superior level of the iliac spine. Modified Schober limitation was accepted as 4 cm or less in measurements over 15 cm.

# Imaging

During the follow-up, imaging of the patients (pelvic radiography, sacroiliac MRI and hip MRI) obtained in CD format were reevaluated and the clinical status at the time of MRI was noted. Imaging of 10 out of 134 patients could not be reached. Abdominal or pelvic MRIs of the control cases performed due to the non-rheumatologic reasons in the last 6 months from various outpatient clinics (General Paediatrics and Adolescent outpatient clinics, Orthopaedics, Paediatric Surgery, Paediatric Endocrinology outpatient clinics) were obtained by scanning from the system. These imaging studies were evaluated by an experienced radiologist (SK) who was also blind to the diagnoses. Definition of sacroiliitis on Antero-posterior Pelvic x-ray was accepted as bilateral stage 2-4, unilateral stage 3-4 sacroiliitis according to the modified New York criteria (18). MRI sequences used in our study were T2-weighted fatsuppressed fast spin-echo (FSE), short tau inversion recovery (STIR) and

contrast-enhanced T1-weighted FSE. Active sacroiliitis on sacroiliac MRI was defined as diffuse acute inflammatory lesion on the adjacent faces of the sacroiliac joints associated with bone marrow oedema/osteitis (hyperintense lesions on T2 and STIR images, hypointense lesions on non-contrast fatsuppressed T1 images); whereas chronic sacroiliitis on sacroiliac MRI was accepted as unilateral or bilateral erosive and sclerotic area in the sacroiliac joints and presence of enthesitis (hypointense lesions on contrast-enhanced T1 sections) (13, 20). Finally, hip involvement according to hip MRI was considered in those with effusion/erosion/capsulitis in the hip joint space and enthesitis in surrounding tissues.

## Statistical analyses

Comparison of categorical variables was performed by using the Chi-square test or Fisher's exact test. Wilcoxon's rank-sum test was used to compare numerical data, median values were given together with ±SD values. For statistical significance, p<0.05 was accepted. Univariate and multivariate logistic regression analyses were used for odds ratio analysis of variables in patients with active sacroiliitis (MRI positive) and without (MRI negative) on MRI, variables with a probability greater than 1 were considered as risk factors in favor of sacroiliitis. The specificity, sensitivity, negative predictive and positive predictive values were calculated with 2\*2 standard tables; kappa coefficients were calculated for the effectiveness evaluation of the criteria. Kappa value is between 0–1 and the efficiency value of the criterion increases as approaching one. Data were analysed using the SPSS 20.0 programme.

# Results

## Demographic findings

134 patients (101 JSpA and 33 FMF+Behçet's Disease+IBD) and 24 control subjects were included in the study. Demographic, clinical and laboratory characteristics of the patient and control groups are given in Table I. Of these parameters, the mean age of the whole patient group (n: 134) was about 3 years more than that of the control

group (n=24). When the age of diagnosis was compared, it was found that the patients in the JSpA group were diagnosed later than the other patients' group. While the proportion of males in the patient group (n=134) was 70%, it was 37.5% in the control group.

## MRI findings

Active sacroiliitis on MRI (diffuse subchondral bone marrow oedema) was detected in 65 of 124 (52%) patients (95 spondylitis, 29 other sacroiliitis), whereas sclerotic and erosive changes of chronic character were detected in 59 (48%) and ankylosis was observed in 2 cases. Only in JSpA patients, active sacroiliitis was detected in 48% and chronic changes (erosive/sclerotic) were observed in 47%.

## Radiographic findings

According to the New York staging system (20), 48 patients (38.7%) had normal pelvic radiographs, 32 (25.8%) had stage 1 (suspicious), 42 (33.8%) had stage 2 (erosion and sclerosis), and 2 (1.6%) had stage 3 (erosion, sclerosis and partial ankylosis) radiographs. Active sacroiliitis was detected on MRI in two patients whose radiographs were interpreted as normal, in 27 patients with suspected findings and in 36 of 44 patients (81%) with stage 2 and 3 sacroiliitis on pelvic radiography. All of the patients with erosion and sclerosis on x-ray also had these chronic changes on MRI. Pathological changes in pelvic radiographs were found to be a strong risk factor for sacroiliitis. (p=0.000, OR: 7.486).

# Efficacy of symptoms, clinical findings, examination and laboratory in detecting sacroiliitis & risk factors

When the clinical and laboratory findings were compared; the ratio of patients with modified Schober limitation, high VAS score, high JSPADAI score, and CRP positivity was higher in patients with FMF and IBD (the other patient group).

The clinical findings of patients in JSpA and other disease groups with sacroiliitis (MRI+) and without sacroiliitis (MRI-) on MRI are compared in Table II. Hip pain, presence of sacroiliitis on pelvic Table I. Demographic and clinical findings of patient and control group.

	Patient group		Control group	<i>p</i> -value
	*JSpA (n=101) (%)	Other (n=33) (%)	(n=24)	
Mean age at the study (years)	15.50 ± 3.43	15.00 ± 3.29	12.12 ± 3.88	<0.05
Mean age at diagnosis (years)	$12.50 \pm 3.25$	$10.83 \pm 3.68$	-	< 0.05
Mean follow-up duration (months)	$35.93 \pm 34.28$	$49.94 \pm 46.80$	-	>0.05
Mean duration of the disease (months)	$43.83 \pm 35.64$	$58.63 \pm 45.82$	-	>0.05
Gender				
Male, n (%)	70 (69.3)	24 (72.7)	9 (37.5)	< 0.05
Female, n (%)	31 (30.7)	9 (27.3)	15 (62.5)	
Inflammatory back pain	22 (21.7)	10 (30.3)	-	>0.05 (0,275)
Hip pain	24 (23.7)	11 (33.3)	-	>0.05 (0.277)
Morning stiffness	29 (28.7)	10 (30.3)	-	>0.05 (0.840)
Mean duration of morning stiffness (min)	10.94 ± 26.70	$10 \pm 22$	-	>0.05 (0.538)
Affected joint				
No arthritis	62 (61.3)	18 (54.5)	-	>0.05 (0.585)
• Hip	20 (19.8)	11 (33.3)		
• Knee	3 (2.9)	0 (0)		
• Ankle	7 (6.9)	3 (9)		
Metatarsal joint	6 (5.9)	1 (3)		
Dactylitis	2 (1.9)	0 (0)		
• Elbow	1 (0.99)	0 (0)		
Enthesitis				
No enthesitis	83 (82.1)	31 (93.9)	-	>0.05 (0.416)
Achilles tendon	7 (6.9)	1 (3)		
Plantar fascia	9 (8.9)	1 (3)		
Tuberositas tibia	2 (1.9)	0 (0)		
Sacroiliac joint tenderness	17 (16.8)	7 (21.2)	-	>0.05 (0.569)
Limitation in modified Schober test	10 (9.9)	8 (24.2)	-	<0,05
Mean value of modified Schober test (cm)	$5.9 \pm 1.3$	$5.2 \pm 1.3$	-	< 0.05
BASDAI score (0-10)**	$1.36 \pm 1.77$	$1.81 \pm 2.18$	-	>0.05 (0,193)
BASFI score (0-10)***	$0.55 \pm 1.23$	$0.58 \pm 1.05$	-	>0.05 (0.535)
VAS – Patient $(0-10)^{\dagger}$	$1.2 \pm 1.6$	$1.8 \pm 1.8$	-	<0.05
VAS – Physician $(0-10)^{\dagger}$	$1 \pm 1.5$	$1.5 \pm 1.5$	-	< 0.05
JSPADAI score (0-10) <sup>±</sup>	$1.44 \pm 1.51$	$2.13 \pm 1.48$	-	< 0.05
CRP positivity (>0.5 mg/dl)	33 (32.6)	19 (57.5)	-	< 0.05
Elevation of erythrocyte sedimentation rate (>15 mm/h)	39 (29,7)	18 (54,5)	-	>0.05 (0.128)
Thrombocytosis (>450000/mm <sup>3</sup> )	7 (6,9)	3 (9)	-	>0.05 (0.704)

\*Juvenile Spondyloarthritis \*\*Bath Ankylosing Spondylitis Disease Activity Index \*\*\*Bath Ankylosing Spondylitis Functional Index <sup>†</sup>Visual Analogue Scale <sup>‡</sup>Juvenile Spondyloarthritis Disease Activity Index.

radiography and hip joint involvement on MRI were detected more in the JSpA group than the control group. There was no significant difference between the two groups in the other parameters. In the univariate and multivariate model of 124 patients in the JSpA and other patient groups, the probability analysis (efficacy in predicting sacroiliitis, risk factors for sacroiliitis) for the use of clinical findings in the differentiation of patients with and without sacroiliitis on MRI is indicated in Table III. Hip pain, high JSPADAI score (>4), detection of sacroiliitis on pelvic direct radiography and presence of hip arthritis (capsulitis/synovitis) on MRI were found as risk factors (OR >1, positive) in univariate model and according to this, their effectiveness of predicting

the presence of sacroiliitis was statistically significant. In the multivariate reduced model, the presence of sacroiliitis on pelvic direct radiography, high JSPADAI score, and presence of hip arthritis (capsulitis/synovitis) on hip MRI were independent risk factors (OR > 1, positively) and their efficacy in predicting the presence of sacroiliitis was significant (p < 0.05). None of the other parameters, including hip pain, were considered as a risk factor in favour of sacroiliitis (p>0.05). Besides, the probability rates of univariate and multivariate models of HLA-B27 positivity on the presence of oligoarthritis, enthesopathy, uveitis and hip arthritis on hip MRI in patients with spondylitis, which were not specified in the table, were also examined. Accordingly, HLA-B27 is a positive independent risk factor only for uveitis (multivariate model p=0.046, OR: 5.12). Nine of eleven spondylitis patients with uveitis were found to be HLA-B27 positive; the sensitivity and specificity of the test for predicting uveitis were 81% and 50%, respectively (p=0.04, kappa: 0.094). Interestingly, HLA-B27 does not constitute a risk factor for enthesopathy, oligoarthritis and, hip arthritis.

#### Sensitivity and specificity results

The sensitivity, specificity, and kappa values of the clinical findings evaluated in the study to determine sacroiliitis are given in Table IV. The best sensitivity was acute phase elevation with 58.4%, followed by pelvic direct radiography with 55.3% and HLA-B27 positiv-

**Table II.** Clinical features of the patients with normal and abnormal magnetic resonance imaging findings.

	Patier	<i>p</i> -value	
	*MRI (+) n=65 (%)	*MRI (-) n=59 (%)	
Mean age at diagnosis (years)	11.92 ± 3.36	12.41 ± 3.44	0.629
Time until the MRI has been performed (months)*	$36.20 \pm 36.38$	$31.79 \pm 39.28$	0.755
Gender (male)	45 (69)	41 (69)	0.975
Back pain	17 (26)	13 (22)	0.593
Hip pain	23 (35)	10 (17)	0.020
HLA-B27 positivity	34 (52)	30 (50.8)	0.871
Uveitis	4 (6)	7 (11.8)	0.264
Sacroiliac joint tenderness	15 (23)	8 (13.5)	0.173
Limitation in modified Schober test	10 (15)	5 (8.4)	0.239
Oligoarthritis	27 (41.5)	24 (40.6)	0.923
Enthesitis	11 (17)	8 (13.5)	0.604
Mean of BASDAI score**	$1.61 \pm 1.76$	$1.20 \pm 2.10$	0.263
Mean of BASFI score***	$0.75 \pm 1.41$	$0.42 \pm 0.96$	0.138
Mean of JSPADAI score <sup>†</sup>	$1.83 \pm 1.67$	$1.47 \pm 1.36$	0.356
Elevation of the acute phase reactants	38 (58)	27 (45.7)	0.157
Stage 2 and 3 sacroiliitis on pelvic radiography	36 (55)	8 (13.5)	0.000
Simultaneous hip involvement on MRI* (n=98)	21 (32)	10 (17)	0.000

\*Magnetic resonance imaging \*\*Bath Ankylosing Spondylitis Disease Activity \*\*\*Bath Ankylosing Spondylitis Functional Index <sup>†</sup>Juvenile Spondyloarthritis Disease Activity Index.

ity with 52.3%. The best specificity was 100% with a high BASFI score (>5), while 94% with a high JSPADAI score (>4) and 91.5% with a modified Schober limitation. Enthesopathy, sacroiliac tenderness and high BASDAI

score (>4) also have a high specificity of 86.4%. While the highest positive predictive value (PPV) was achieved 100% by the BASFI score, the PPV and NPV ratios of pelvic radiographs were 81.8% and 95.8%, respectively.

#### *Comparison of MRI findings in the patient and control groups*

Diffuse bone marrow oedema indicating active sacroiliitis were present only in the patient group (52%), but not in the control group. Focal oedema areas were observed in the pelvic bone in 2 cases in both patient and control groups, whereas, spondylitis was accompanied by diffuse bone marrow oedema in all the patients. These focal lesions in the control group were not evaluated as active sacroiliitis and the cause of these lesions was unknown.

Apart from these lesions in the control group (MRIs taken for orthopaedic reasons); Perthes disease in one case, trochanteric bursitis in femoral neck and osteoid osteoma / post-traumatic stress fracture (no hip effusion or capsulitis) in one case, a simple millimeter cyst on the iliac surface adjacent to the joint in the left sacroiliac joint and one-millimeter synovial cyst in the posterior neighbourhood of the left facet joint in the S1 vertebra in one case, hypointense, stable benign lesion in T1 and T2 sections in one case and lesion filling the spinal canal level in L5-S1 level

**Table III.** The likelihood ratio of clinical findings, laboratory and radiographic imaging in predicting acute sacroiliitis detected by magnetic resonance imaging (odds ratio, OR) (%95 confidence interval, CI).

n=124	Univariate model			Multivariate model		
	OR	%95 CI upper limit-lower limit	р	OR	%95 CI upper limit-lower limit	р
HLA-B27 positivity	1.09	0.53 - 2.22	0.807			
Uveitis	0.17	0.02 - 1.12	0.066			
Inflammatory back pain	1.46	0.40 - 5.30	0.560			
Morning stiffness	0.22	0.04 - 1.16	0.076			
Hip pain	2.69	1.14 - 6.27	0.023	4.65	0.91 - 23.82	0.065
Hip arthritis	1.22	0.09 - 15.35	0.873			
Oligoarthritis	1.03	0.50 - 2.12	0.923			
Enthesitis	0.85	0.36 - 2.03	0.723			
Sacroiliac joint tenderness	1.35	0.27 - 6.80	0.709			
Limitation of FABER maneuvers	1.65	0.18 - 14.53	0.648			
Limitation in modified Schober test	0.41	0.04 - 3.62	0.428			
BASDAI score (<4: mild)*	0.83	0.56 - 1.21	0.345			
BASFI score (<5: mild)**	1.08	0.66 - 1.76	0.735			
VAS – patient (0-10)***	0.61	0.26 - 1.46	0.275			
VAS – physician (0-10)***	1.55	0.56 - 4.28	0.393			
JSPADAI score (<4: mild) <sup>†</sup>	4.22	1.12 - 15.81	0.032	5.96	1.42 - 24.99	0.015
Positivity of C-reactive protein (>0.5 mg/dl)	1.08	0.32 - 3.66	0.893			
Elevation of erythrocyte sedimentation rate (>15 mm/h)	1.90	0.55 - 6.56	0.308			
Presence of thrombocytosis (>450000/mm <sup>3</sup> )	1.35	0.21 - 8.44	0.742			
Time until the MRI has been performed <sup>‡</sup>	0.99	0.94 - 1.03	0.698			
Sacroiliitis detected by pelvic radiography	7.486	3.80 - 14.74	0.000	6.97	3.43 - 14.16	0.000
Hip involvement on MRI (n=98) <sup>‡</sup>	2.262	1.19 - 4.28	0.012	2.78	1.29 - 5.98	0.009

\*Bath Ankylosing Spondylitis Disease Activity Index \*\*Bath Ankylosing Spondylitis Functional Index \*\*\*Visual Analogue Scale †Juvenile Spondyloarthritis Disease Activity Index \*Magnetic resonance imaging.

**Table IV.** Accuracy of symptoms, laboratory data and physical examination for detection of sacroiliitis on magnetic resonance imaging.

(n=124)	Sensitivity	y Specificity	PPV	NPV	Kappa	
	%	%	%	%		
Inflammatory back pain	26.1	77.9	56.6	48.9	0.40	
Hip pain	30.7	79.6	62.5	51	0.102	
Oligoarthritis	41.5	59.3	52.9	47.9	0.009	
Enthesopathy	16.9	86.4	57.8	48.5	0.032	
Sacroiliac joint tenderness	23	86.4	65.2	50.4	0.092	
Limitation in modified Schober test	15.3	91.5	66.6	49.5	0.066	
BASDAI score*	12.3	86.4	50	47.2	-0.012	
BASFI score**	4	100	100	48.7	0.044	
JSPADAI score***	18.4	94	80	51.3	0.129	
Elevation of the acute phase reactants	58.4	54.2	58.4	54.2	0.127	
HLA-B27 positivity	52.3	49.1	53.1	48.3	0.15	
Pelvic radiography	55.3	77.9	81.8	95.8	0.396	
Hip involvement on MRI <sup>†</sup> (n=98)	47.7	81.4	67.7	65.6	0.222	

\*Bath Ankylosing Spondylitis Disease Activity Index \*\*Bath Ankylosing Spondylitis Functional Index \*\*\*Juvenile Spondyloarthritis Disease Activity Index <sup>†</sup>Magnetic resonance imaging.

continued with filum lipoma in one case were detected. But none of these lesions showed inflammatory properties.

### Discussion

Our study is the first to investigate the effectiveness of physical examination, laboratory data and radiographic images in predicting active sacroiliitis lesions detected by MRI in such a large patient population with juvenile spondylarthritis. It provided the opportunity to make a comparison by examining the presence of sacroiliitis not only in JSpA but also in the other diseases such as FMF, IBD related arthritis and Behcet's Disease. The disease activity scoring systems such as BASDAI, BASFI and JSPADAI also have been applied for the first time in such a large series. In this way, the applicability of these scores in the clinic and functional capacity of the patient group was evaluated by examining the relationship between clinical findings and the level of the disease.

Previous studies have confirmed that bone marrow oedema detected by MRI shows pathological osteitis areas in the bone (19-22). These lesions are found to be the predominant lesions in AS patients indicating severe bone destruction. Although these lesions are not seen on direct radiography, they can be seen as hypointense areas on T1weighted sections and hyperintense areas on T2-weighted and STIR sections (11, 22, 23). This early detection of the precursor bone marrow oedema (osteitis) by MRI enables diagnosis without irreversible destruction of bone structure and ankylosis.

The rate of active sacroiliitis was found in 52.4% of patients in this study. In most of the patients, erosive and sclerotic changes thought to be precursor of the ongoing disease process were noted (3, 23, 24). However, isolated bone marrow oedema seen in asymptomatic patients without any joint damage is still a subject of debate (25, 26).

In our study, in 2 cases of the control group, cystic bone marrow oedema areas of focal character far from the sacroiliac joints were noted and not thought to be compatible with inflammation. None of these control cases had any complaints or symptoms suggestive of spondylitis and MRI showed no sign of active sacroiliitis in this group. As previously noted, the increased signal in bone marrow seen in JSpA is expected to be parallel, diffuse and usually bilateral to the joint faces (27). Focal signal increase in control cases may be due to intensive physical activity causing trauma, infection and malignancy, and also encountered in normal children (11, 28). These lesions in control patients raise doubts if they have inflammatory nature in asymptomatic patients without causing joint damage (26, 29). The presence of other accompanying clinical findings is important in predicting inflammation in these patients.

Active sacroiliitis was detected on MRI in 81% of patients who had stage 2 and

3 sacroiliitis on pelvic radiography. Statistical studies have shown that pathological changes in pelvic radiography are strong risk factors for sacroiliitis. In our study, the high specificity and NPV of radiography for detecting sacroiliitis (80% and 96%, respectively) show that conventional radiology can be used to diagnose this disease in areas that are difficult-to-reach MRI easily. Considering radiation exposure, the low sensitivity and the high number of suspected patients (26%) limit the use of pelvic radiography. If possible, MRI should be performed in the presence of risk factors or serious suspicion of sacroiliitis (29, 30).

One of the most important conclusions of our study is the inadequacy of the disease history, physical examination and laboratory data obtained from the patients in the detection of active sacroiliitis. Inflammatory low back pain, which is an important guide in the history of AS patients and also an established criterion of the ASAS diagnostic criteria is not a risk factor for sacroiliitis in children and adolescents. Its low sensitivity and PPV (26% and 49% respectively) and the presence of sacroiliitis on MRI in 51% of patients without low back pain limit its use in diagnosis similar to recent studies (4, 23).

The presence of enthesitis, sacroiliac tenderness, modified Schober limitation (<4 cm) and FABER limitation did not predict sacroiliitis, but their specificity was relatively high. Also the number of the patients having active sacroiliitis without sacroiliac tenderness and FABER and Schober test limitations was very high. This suggests that patients with active sacroiliitis can easily be overlooked by basic physical examination methods that evaluate mobility of the back and hip joints, which we hope to guide us in the clinic. Low sensitivity of these methods may lead to unnecessary treatment in patients whose MRI cannot be performed. Since the sacroiliac tenderness and inflammatory low back pain are included in the ILAR diagnostic criteria of enthesitisrelated arthritis, it raises questions regarding the adequacy of basic diagnostic criteria (16, 31, 32). As a result of our study, oligoarthritis and enthesopa-

#### Detecting sacroiliitis in juvenile spondyloarthropathies / B. Akdeniz et al.

thy are more reliable findings rather than low back pain for the diagnosis of JSpA in children.

During clinical evaluation, only a high JSPADAI score was found to be an independent risk factor for sacroiliitis compared to other scoring systems. Although they reflect the current disease activity and functional status of the patient with high specificity, they have low sensitivity and cannot predict sacroiliitis. The recent use of JSPADAI scoring among rheumatologists seems promising in early detection of sacroiliitis and in measuring disease activity (33, 34).

Although it was thought that there was a close relationship between acute phase response and sacroiliitis in the previous studies, this relationship could not be proved in our study (4, 35). Increased acute phase markers such as CRP, erythrocyte sedimentation rate and thrombocytosis failed to predict sacroiliitis. This could be explained by the fact that most of the patients were diagnosed previous to the study and were receiving effective treatment at the time of MRI. Generally, the acute phase response is not expected to be too high in JSpA. Acute phase markers can be detected even disproportionately low in patients with active disease. Active sacroiliitis lesions can be seen in patients with an acute phase response that is negative or slightly elevated (36, 37).

HLA-B27 positivity is not sufficient to predict sacroiliitis and has low sensitivity and specificity (Table IV). However, Weiss et al(4) showed that for newly diagnosed 40 JSpA patients, the specificity and sensitivity of HLA-B27 were 69% and 88%, respectively. While HLA-B27 predicted uveitis with 81% sensitivity, its efficacy in predicting oligoarthritis and enthesopathy was also insufficient in our study

MRI-proven hip arthritis is a risk factor in favour of sacroiliitis and is successful in predicting sacroiliitis; in 45% of the patients with hip MRI, hip arthritis was also accompanied by active sacroiliitis in our study. This may be due to the different numbers of samples undergoing sacroiliac MRI (n=124) and hip MRI (n=98), however, there are some studies supporting this situation (35, 38).

The limitations of our study were the heterogeneity of our patient population, the high incidence of patients with FMF and being a single-centre study. It is known that the rate of sacroiliac involvement in FMF is quite high making the differentiation between isolated JSpA and FMF-associated spondylitis challenging. A recent study from our clinic showed that the rate of patients diagnosed with both FMF and JSpA in the FMF population was 10.2% (39). There is no doubt about the diagnosis of FMF patients in our study because of their mutation analyses and the clinical criteria for diagnosis.

Another limitation was that the imaging of the control group was not aimed at rheumatic sacroiliac involvement, so the imaging techniques could not be standardised in those cases. The sacroiliac joint spaces could be evaluated clearly by our specialist radiologist for any inflammatory process.

The differences in interpretation in regions with a low socioeconomic level, which do not have the same imaging service and physician quality are other problems to keep in mind. The risk of inadequacy, delay or inaccuracy in diagnosis is more common for patients who cannot be evaluated by an expert radiologist and rheumatologist. This limits the use of MRI, an advanced and relatively expensive imaging method (26).

In our study, clinical findings were shown to be unreliable in detecting active sacroiliitis in both spondylitis and FMF patients. All the patients with suspicion of JSpA should undergo sacroiliac MRI regardless of the presence of symptoms, HLA-B27 positivity and elevated acute phase response. In this way, early diagnosis and treatment of axial joint involvement are possible by preventing unnecessary examination and loss of time.

#### References

- BARUT K, ADROVIC A, SAHIN S, KASAP-COPUR O: Juvenile idiopathic arthritis. *Balkan Med J* 2017; 34: 90-101.
- ADROVIC A, BARUT K, SAHIN S, KASAP-COPUR O: Juvenile spondyloarthropathies. *Curr Rheumatol Rep* 2016; 18: 55.
- SUDOL-SZOPINSKA I, ESHED I, JANS L, HER-REGODS N, TEH J, VOJINOVIC J: Classifications and imaging of juvenile spondyloarthropathy. J Ultrason 2018; 18: 224-33.

- 4. WEISS PF, XIAO R, BIKO DM, CHAUVIN NA: Assessment of sacroiliitis at diagnosis of juvenile spondyloarthropathy by radiography, magnetic resonance imaging, and clinical examination. *Arthritis Care Res* (Hoboken) 2016; 68: 187-94.
- KASAPCOPUR O, DEMIRLI N, OZDOGAN H et al.: Evaluation of classification criteria for juvenile-onset spondyloarthropathies. *Rheu*matol Int 2005; 25: 414-8.
- GOIRAND M, BRETON S, CHEVALLIER F et al.: Clinical features of children with enthesitis-related juvenile idiopathic arthritis / juvenile spondyloarthropathy followed in a french tertiary care pediatric rheumatology centre. *Pediatr Rheumatol Online J* 2018; 16: 21.
- MARTINI A, RAVELLI A, AVCIN T *et al.*: Toward new classification criteria for juvenile idiopathic arthritis: First steps, pediatric rheumatology international trials organization international consensus. *J Rheumatol* 2019; 46: 190-7.
- TSE SML, LAXER RM: New advances in juvenile spondyloarthropathy. *Nat Rev Rheu*matol 2012; 8: 269-79.
- SIEPER J, RUDWALEIT M: How early should ankylosing spondylitis be treated with tumour necrosis factor blockers? *Ann Rheum Dis* 2005; 64: iv61.
- MAKAY B, GUCENMEZ OA, UNSAL E: Inactive disease in enthesitis-related arthritis: Association of increased body mass index. *J Rheumatol* 2016; 43: 937.
- 11. LAMBERT RGW, BAKKER PAC, VAN DER HEI-JDE D et al.: Defining active sacroiliitis on MRI for classification of axial spondyloarthropathy: Update by the asas mri working group. Ann Rheum Dis 2016; 75: 1958.
- WEISS PF, COLBERT RA: Radiography versus magnetic resonance imaging (MRI) in juvenile spondyloarthropathy: Is the MR image everything? J Rheumatol 2014; 41: 832.
- HERREGODS N, JAREMKO JL, BARALIAKOS X et al.: Limited role of gadolinium to detect active sacroiliitis on MRI in juvenile spondyloarthropathy. Skeletal Radiol 2015; 44: 1637-46.
- YILMAZ MH, OZBAYRAK M, KASAPCOPUR O, KURUGOGLU S, KANBEROGLU K: Pelvic MRI findings of juvenile-onset ankylosing spondylitis. *Clin Rheumatol* 2010; 29: 1007-13.
- WEISS PF, CHAUVIN NA, ROTH J: Imaging in juvenile spondyloarthropathy. *Curr Rheumatol Rep* 2016; 18: 75.
- ADROVIC A, SEZEN M, BARUT K *et al.*: The performance of classification criteria for juvenile spondyloarthropathies. *Rheumatol Int* 2017; 37: 2013-8.
- PETTY RE, SOUTHWOOD TR, MANNERS P et al.: International league of associations for rheumatology classification of juvenile idiopathic arthritis: Second revision, Edmonton, 2001. J Rheumatol 2004; 31: 390-2.
- 18. SIEPER J, RUDWALEIT M, BARALIAKOS X et al.: The Assessment of Spondyloarthropathy International Society (ASAS) handbook: A guide to assess spondyloarthropathy. Ann Rheum Dis 2009; 68: ii1.
- 19. SUDOŁ-SZOPIŃSKA I, GIETKA P, ZNAJDEK M

#### Detecting sacroiliitis in juvenile spondyloarthropathies / B. Akdeniz et al.

*et al.*: Imaging of juvenile spondyloarthropathy. Part I: Classifications and radiographs. *J Ultrason* 2017; 17: 167-75.

- 20. BURGOS-VARGAS R: The assessment of the spondyloarthropathy international society concept and criteria for the classification of axial spondyloarthropathy and peripheral spondyloarthropathy: A critical appraisal for the pediatric rheumatologist. *Pediatr Rheumatol Online J* 2012; 10: 14.
- MARZO-ORTEGA H, MCGONAGLE D, BEN-NETT NA: Magnetic resonance imaging in spondyloarthritis. *Curr Opin Rheumatol* 2010; 22: 381-87.
- 22. MADSEN KB, EGUND N, JURIK AG: Grading of inflammatory disease activity in the sacroiliac joints with magnetic resonance imaging: Comparison between short-tau inversion recovery and gadolinium contrast-enhanced sequences. J Rheumatol 2010;37:393.
- 23. ORR KE, ANDRONIKOU S, BRAMHAM MJ, HOLJAR-ERLIC I, MENEGOTTO F, RAMANAN AV: Magnetic resonance imaging of sacroiliitis in children: Frequency of findings and interobserver reliability. *Pediatr Radiol* 2018; 48: 1621-8.
- 24. ROBINSON PC, SENGUPTA R, SIEBERT S: Non-radiographic axial spondyloarthropathy (nr-axSpa): Advances in classification, imaging and therapy. *Rheumatol Ther* 2019; 6: 165-77.
- 25. MARZO-ORTEGA H, MCGONAGLE D, O'CONNOR P et al.: Baseline and 1-year magnetic resonance imaging of the sacroiliac joint

and lumbar spine in very early inflammatory back pain. Relationship between symptoms, HLA-B27 and disease extent and persistence. *Ann Rheum Dis* 2009; 68: 1721.

- 26. ORR KE, ANDRONIKOU S, BRAMHAM MJ, HOLJAR-ERLIC I, MENEGOTTO F, RAMANAN AV: Overcoming two technical pitfalls in MRI of paediatric and adolescent sacroiliitis. *Clin Radiol* 2019; 74: 235-41.
- 27. RUDWALEIT M, JURIK AG, HERMANN KGA et al.: Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthropathy: A consensual approach by the asas/omeract mri group. Ann Rheum Dis 2009; 68: 1520.
- CHAUVIN NA, XIAO R, BRANDON TG et al.: MRI of the sacroiliac joint in healthy children. AJR Am J Roentgenol 2019; 212: 1303-9.
- 29. BOU ANTOUN M, ADAMSBAUM C, SEME-RANO L, KONÉ-PAUT I, ROSSI-SEMERANO L: Clinical predictors of magnetic resonance imaging-detected sacroiliitis in children with enthesitis related arthritis. *Joint Bone Spine* 2017; 84: 699-702.
- 30. WEISS PF, XIAO R, BRANDON TG et al.: Radiographs in screening for sacroiliitis in children: What is the value? Arthritis Care Res (Hoboken) 2018; 20: 141.
- 31. HERREGODS N, DEHOORNE J, VAN DEN BOSCH F et al.: ASAS definition for sacroiliitis on MRI in SpA: Applicable to children? Pediatr Rheumatol Online J 2017; 15: 24.
- 32. HERREGODS N, DEHOORNE J, JAREMKO J et al.: Diagnostic value of MRI of the sacro-

iliac joints in juvenile spondyloarthropathy. *J Belg Soc Radiol* 2016; 100: 95.

- 33. WEISS PF, COLBERT RA, XIAO R et al.: Development and retrospective validation of the juvenile spondyloarthropathy disease activity index. Arthritis Care Res (Hoboken) 2014; 66: 1775-82.
- 34. ZANWAR A, PHATAK S, AGGARWAL A: Prospective validation of the juvenile spondyloarthropathy disease activity index in children with enthesitis-related arthritis. *Rheumatology* (Oxford) 2018; 57: 2167-71.
- 35. STOLL ML, BHORE R, DEMPSEY-ROBERT-SON M, PUNARO M: Spondyloarthropathy in a pediatric population: Risk factors for sacroiliitis. *J Rheumatol* 2010; 37: 2402-8.
- AGGARWAL A, MISRA DP: Enthesitis-related arthritis. *Clin Rheumatol* 2015; 34: 1839-46.
- 37. TSE SM, PETTY RE: Enthesitis related arthritis. *In*: CASSIDY JT, PETTY RE, LAXER RM, LINDSLEY CB (Eds.). Textbook of Pediatric Rheumatology e-book: Expert consult: Online and print: Elsevier Health Sciences; 2010.
- LIN C, MACKENZIE JD, COURTIER JL, GU JT, MILOJEVIC D: Magnetic resonance imaging findings in juvenile spondyloarthropathy and effects of treatment observed on subsequent imaging. *Pediatr Rheumatol Online J* 2014; 12: 25.
- 39. OZER E, SEKER D, TANER E *et al.*: The frequency of juvenile spondyloarthropathies in childhood familial Mediterranean fever. *Clin Exp Rheumatol* 2018; 36: 141-5.