Sacroiliac Joint Magnetic Resonance Imaging in Asymptomatic Patients with Recurrent Acute Anterior Uveitis: A Proof-of-concept Study

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ABSTRACT. ***Objective.*** Our aim was to quantify bone marrow edema (BME) and/or structural lesions in the sacroiliac joints (SIJ) of patients with recurrent acute anterior uveitis (rAAU) with or without back pain, to evaluate the frequency of axial (axSpA) and peripheral spondyloarthritis (pSpA) and to establish which criterion for magnetic resonance imaging (MRI) positivity best reflected the global assessment of SIJ MRI.

Methods. A total of 50 patients with rAAU without prior rheumatologic diagnosis were included in our cross-sectional study, and these patients were compared to 21 healthy volunteers. SIJ MRI scans were read by 2 rheumatologists according to the Spondyloarthritis Research Consortium of Canada (SPARCC/MORPHO) protocol. Discrepant cases were adjudicated by a radiologist.

Results. Patients with rAAU were diagnosed with axSpA (Group 1, n = 20, 40%) and nonspecific back pain (Group 2, n = 6, 12%), or as being asymptomatic (Group 3, n = 24, 48%). Group 3 results showed 9 patients (37.5%) had SIJ MRI and/or were radiography-positive for axSpA (5 MRI and radiograph, 1 MRI, 3 radiograph). SIJ MRI scans that were compatible with SpA in groups 1 (n = 12) and 3 (n = 6) were similar in acute and structural lesions that were analyzed according to SPARCC/MORPHO. The best sensitivity/specificity criterion for defining a positive global MRI assessment was a BME score ≥ 3 (88%/94%).

Conclusion. This is the first study evaluating SIJ MRI in patients with rAAU without back symptoms, showing positive findings for sacroiliitis. Moreover, a BME score ≥ 3 had better performance to define an SIJ MRI as positive for axSpA. (First Release November 1 2017; J Rheumatol 2017;44:1833–40; doi:10.3899/jrheum.170036)

Key Indexing Terms:
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Anterior uveitis is the most common form of uveitis in several parts of the Western world, accounting for 50% to 92% of cases[1,2]. HLA-B27–associated acute anterior uveitis (AAU) is one of the main causes of anterior uveitis in Western countries, responsible for 18% to 32% of cases[3,4,5]. While AAU occurs less commonly as an isolated condition, it occurs as part of a systemic disease in 50% to 80% of patients, particularly ankylosing spondylitis (AS)[6,7,8,9].

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Few studies have investigated the prevalence of sacroiliitis in patients with AAU but without musculoskeletal symptoms, and none of these studies used magnetic resonance imaging (MRI) as an imaging method[10,11,12,13,14,15].

The aim of our study was to quantify bone marrow edema (BME) and/or structural lesions in the sacroiliac joints (SIJ) of patients with recurrent AAU (rAAU) with or without back pain, and to compare the measurements to those of healthy individuals. In addition, our study investigated the frequency of inflammatory back pain and the occurrence of the HLA-27 allele as well as the diagnostic frequency of axial spondyloarthritis (axSpA) and peripheral SpA (pSpA). We then assessed fulfillment of the Assessment of Spondyloarthritis international Society (ASAS) classification criteria for axSpA[16], pSpA[17], and modified New York (mNY) criteria for AS[18], and sought to establish which criteria for MRI positivity best reflected the global assessment of SIJ MRI.

MATERIALS AND METHODS

A total of 50 patients aged ≥ 18 years having a history of at least 2 episodes of AAU were enrolled in this cross-sectional study. All of them had received care at the Uveitis Outpatient Clinic of the Department of Ophthalmology from the Federal University of São Paulo, Brazil. The participants were

consecutively selected from March 2014 to March 2015. Individuals with nonanterior, granulomatous, or infectious uveitis were excluded, as were those previously diagnosed with any rheumatic disease. The control group comprised 21 blood donors who were considered healthy from the musculoskeletal perspective, as assessed by the Nordic questionnaire[19], and had denied any red-eye episode accompanied by blurred vision. These controls were matched by age, sex, and race to the group of patients with AAU. This study was approved by the Ethics Committee of the Federal University of São Paulo (protocol no. 337.090) and all subjects provided signed informed consent forms.

Patients with rAAU and healthy controls were assessed by the same rheumatologist (TLO) for articular and other extraarticular (colitis, psoriasis, and nail dystrophy) manifestations of SpA. Whenever present, back pain was categorized as inflammatory or nonspecific, according to expert opinion and the ASAS definition[20]. The rAAU patients with musculoskeletal symptoms were classified according to ASAS criteria for axSpA and pSpA, and the mNY criteria for AS. The following instruments were used for clinical assessment of patients classified as axSpA: Bath Ankylosing Spondylitis Disease Activity Index[21], Bath Ankylosing Spondylitis Functional Index[22], Bath Ankylosing Spondylitis Metrology Index[23] and Ankylosing Spondylitis Disease Activity Score[24]. Enthesis was assessed by the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)[25].

All patients with rAAU were evaluated by an ophthalmologist; active anterior uveitis was defined as the presence of at least 1 cell per field (grade 0.5+) on biomicroscopy[26]. At the time of imaging method assessment, patients with a cell grade of 0.5 or higher and/or using topical and/or systemic steroids were considered as exhibiting recently active rAAU.

In addition to the HLA-B27 investigation, the erythrocyte sedimentation rate and C-reactive protein were measured for patients with rAAU.

SIJ radiographs were performed in patients with rAAU. These were independently assessed by 2 rheumatologists (TLO and MMP) who were blinded to patient data, using the online Spondyloarthritis Radiography (SPAR) SIJ Scoring Module[27]. When no consensus for meeting mNY criteria was reached, a third reading was conducted by a blinded radiologist specializing in musculoskeletal imaging.

SIJ MRI images were acquired through 1.5T or 3T devices (Siemens Medical Solutions). Semicoronal T1-weighted (T1W) and short-tau inversion recovery (STIR) sequences were obtained from all patients with rAAU and healthy controls as recommended by ASAS[28]. SIJ MRI images were evaluated according to the MORPHO adaptation of the SPARCC SIJ method, which scores both BME and structural lesions through the cartilaginous portion of the SIJ[27]. The evaluated structural lesions were erosion, fat metaplasia, subchondral sclerosis, ankylosis, and backfill. Assessment of MRI scans was conducted on a Web-based interface with online recording of MRI findings. Each scan was first assessed by simultaneous global evaluation of T1W and STIR scans. Readers first had to determine whether they considered the scans as compatible with SpA according to the ASAS criteria for a positive MRI[28] by viewing the STIR sequence, and then through global assessment by viewing T1W and STIR sequences simultaneously. The confidence in these classifications was evaluated on a scale ranging from 0 to 10. Detailed evaluation of specific lesions was then conducted on the subsequent Web page.

MRI readings were performed independently by 2 rheumatologists who were blinded to patient data (TLO and WPM). Adjudication was conducted by a radiologist (RGL) for cases with a difference > 5 for BME, > 3 for any structural lesion, or a disagreement either in the classification as a positive MRI according to the ASAS criteria or in the global assessment between the 2 readers. These cutoffs are based on the estimation of the smallest detectable difference from 2 studies[29,30]. Reader 1's calibration was performed in Edmonton, Alberta, Canada, using online SPARCC SIJ and SPARCC SIJ Structural Score modules[27,31]. STIR images from 40 patients with axSpA were analyzed for calibration of BME readings. The intraclass correlation coefficient (ICC; 3,1) between readers 1 and 2 for BME was 0.88 (95% CI 0.81–0.92). Initially, T1W images from 30 patients with axSpA were analyzed for calibration of structural lesions, followed by discussion of the discrepancies, then assessment of 73 axSpA cases with < 5 years of disease. ICC(3,1) was 0.84 (95% CI 0.79–0.88) for fat metaplasia; 0.66 (95% CI 0.56–0.74) for erosion; 0.77 (95% CI 0.69–0.83) for backfill; and 0.93 (95% CI 0.90–0.95) for ankylosis. Included in the descriptive analysis as group 5 were 30 patients with AS whose T1W and STIR sequences were read during this calibration.

Statistical analysis. Differences in demographic and clinical characteristics between rAAU patients and controls were assessed by chi-square test or Fisher's exact test for nominal, and Kolmogorov-Smirnov, Student t test, ANOVA, or the nonparametric Mann-Whitney and Kruskal-Wallis tests when appropriate for continuous variables. Mean ICC was calculated to assess reproducibility among MRI readers, κ coefficient for radiograph readers, and radiograph and MRI SIJ agreement for detection of sacroiliitis. For that purpose, an ICC(3,1), 2-way mixed model with absolute agreement and individual measures, was used. ICC and κ values > 0.4, > 0.6, > 0.8, and > 0.9 were regarded as representing moderate, good, very good, and excellent reproducibility, respectively. The frequency of MRI lesions at the group level was analyzed descriptively as the mean [median; interquartile range (IQR)] for each lesion for both MRI readers. When adjudication was necessary, the average among the third reading and the closest value from TLO or WPM was considered for analysis. In addition, the mean values of 2 readers for sensitivity, specificity, and positive/negative likelihood ratios were calculated for the following: ASAS definition of a positive MRI, and derived additional candidate lesion-based criteria for global positive MRI based on the combination of a number of SIJ quadrants with BME and/or structural lesions. The gold standard was global assessment of the MRI images that were compatible with SpA, and a level of confidence being ≥ 7 according to both readers. In addition, the area under the receiver-operating characteristic (ROC) curve was calculated for each criterion.

Pearson correlation was calculated between the sum of mNY sacroiliitis grade of both SIJ for each patient (score 0 to 8) and the mean number of quadrants for each MRI lesion.

The statistical analysis was performed with the statistical software SPSS 20.0 and STATA 12.0. P values < 0.05 were considered significant.

RESULTS

Following clinical, laboratory, and imaging evaluation, the 50 patients with rAAU were divided into 3 groups according to expert opinion diagnosis: group 1 (axSpA, n = 20, 40%), group 2 [nonspecific back pain (NSBP), n = 6, 12%], and group 3 (asymptomatic, n = 24, 48%). Healthy controls were in group 4 (n = 21) and AS patients were in group 5 (n = 30).

Among the 20 patients diagnosed with axSpA according to expert opinion, 11 (55%) were classified as AS. The remainder met only the ASAS criteria for axSpA, 5 (25%) based on the presence of sacroiliitis (imaging arm) and 4 on HLA-B27 positivity associated with at least 1 other clinical manifestation besides rAAU (clinical arm). Among the first subgroup (i.e., the one comprising 5 patients), only 1 (20%) was classified as nonradiographic axSpA. The other 4 patients were not classified as AS because they did not have inflammatory back pain, reduced Schober test, or chest expansion, despite having radiographic sacroiliitis. Comparison of demographic, clinical, and laboratory characteristics among these subgroups did not detect any statistically significant differences, and these groups were therefore analyzed together. None of the rAAU patients had taken any synthetic or biological disease-modifying drugs. The demographic data, eye disease, back pain duration, and laboratory characteristics are described in Table 1.

Table 1. Clinical and laboratory characteristics of patients with recurrent AAU and healthy controls. Values are n (%) unless otherwise specified.

Variables	Group 1, AxSpA, n = 20	Group 2, NSBP, n = 6	Group 3, Asymptomatic, n = 24	Group 4, Controls, n = 21	Group 5, AS, n = 30	p
Female	13 (75)	0 (0)	12 (50)	14 (66.7)	6 (20)	0.921*
White	11 (55)	3 (50)	14 (58.3)	12 (57.1)	—	1.000*
Age, yrs, mean ± SD	44.8 ± 14.3	44.5 ± 11.2	42.3 ± 11.8	47.1 ± 12	40.40 ± 11	0.378$^{\Delta}$
Age at onset of uveitis, yrs, mean ± SD	38.9 ± 14	35.5 ± 14.8	36.8 ± 12.8	NA	NA	0.817$^{\Delta}$
Eye disease duration, yr, mean ± SD	6.2 ± 6.1	7.2 ± 6.2	5.5 ± 6.4	NA	NA	0.491¶
Active uveitis	7 (35)	2 (33.3)	14 (58.3)	NA	NA	0.252*
Age at onset of back pain, yrs, mean ± SD	31.2 ± 10	30.5 ± 11.3	NA	NA	NA	0.893$^{€}$
Back pain duration, yrs, mean ± SD	13.8 ± 10.5	14.8 ± 14.3	NA	NA	17 ± 11.52	0.629$^{\Delta}$
Inflammatory back pain (expert opinion/ ASAS definition)	9 (45)	NA	NA	NA	30 (100)	
Assessment instruments, mean ± SD	BASDAI 4.2 ± 2.3 BASFI 2.9 ± 2.7 BASMI 3.0 ± 1.2 ASDAS-ESR 3.1 ± 1.1 ASDAS-CRP 3.1 ± 1.1	NA	NA	NA	BASDAI 4.9 ± 2.6, BASFI 3.7 ± 2.8 — — ASDAS-CRP 3.8 ± 1.3	0.356$^{€}$ 0.296$^{€}$ 0.059$^{€}$
Enthesitis score (MASES) ≥ 2	6 (30)	1 (16.7)	1 (4.17)	0 (0)	—	0.007*
ESR, mm/1st h, mean ± SD	23.7 ± 18	9.5 ± 6.2	26.4 ± 22.4	NA	—	0.176$^{\Delta}$
CRP, mg/l, mean ± SD	7.7 ± 9.2	2.5 ± 2.3	4.3 ± 4.7	NA	10.9 ± 10.6	0.014¶
HLA-B27+	12 (60)	0 (0)	12 (50)	NA	26 (87)	0.025*

*Fisher's exact test; $^{€}$Student t test; $^{\Delta}$ANOVA; ¶Kruskal-Wallis test; NA: not applicable; —: data not available. AAU: acute anterior uveitis; axSpA: axial spondyloarthritis; NSBP: nonspecific back pain; AS: ankylosing spondylitis; ASAS: Assessment of Spondyloarthritis international Society; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; ESR: erythrocyte sedimentation rate; ASDAS-ESR: Ankylosing Spondylitis Disease Activity Score-ESR; CRP: C-reactive protein.

The number of patients with MASES ≥ 2 on clinical examination was larger in group 1 compared to the other groups. Only 1 patient in group 3 (4.17%) had a MASES score ≥ 2 and it was because he had bilateral Haglund's deformity (Table 1).

Regarding non-AAU extraarticular involvement, 1 female patient from group 1 (HLA-B27–negative) reported chronic diarrhea, but no evidence of macroscopic colitis was observed on colonoscopy. A male patient from group 1 (HLA-B27–positive) had nail pitting and only 1 patient (group 3 and HLA-B27–negative) had plaque psoriasis confirmed by skin biopsy. Another patient from group 3 (HLA-B27–positive) reported a previous circinate balanitis.

The individual readings performed by readers 1 and 2 are presented in a descriptive manner (Table 2). Adjudication was necessary in 18 (39%) cases: BME (n = 7), erosion (n = 6), subchondral sclerosis (n = 7), backfill (n = 1), SpA presence according to ASAS (n = 16), and SpA presence according to global assessment (n = 9). The ICC (3,1) between readers 1 and 2 was 0.54 (95% CI 0.31-0.71) for BME; 0.68 (95% CI 0.53-0.79) for erosion; 0.73 (95% CI 0.53-0.84) for subchondral sclerosis; 0.72 (95% CI 0.59-0.82) for fat metaplasia; 0.70 (95% CI 0.56-0.80) for backfill; and 0.62 (95% CI 0.44-0.75) for ankylosis.

The κ coefficient for assessment of radiographic sacroiliitis according to mNY criteria between the 2 rheumatologists was 0.49. A discrepancy occurred in 12 cases (24%), which were submitted to a third reading. The final SIJ scores were right SIJ, grade 0 (n = 17), grade 1 (n = 10), grade 2 (n = 10), grade 3 (n = 13), and grade 4 (n = 0), and left SIJ grade 0 (n = 10), grade 1 (n = 12), grade 2 (n = 7), grade 3 (n = 20), and grade 4 (n = 1).

Regarding the images, 4 patients from group 1 and 3 from group 3 had positive SIJ radiographs according to the mNY criteria, but the MRI scans were considered negative for SpA. Only 1 patient from group 1 and another from group 3 had positive SIJ MRI but normal radiographs. The κ coefficient value between SIJ radiograph reading and global assessment of MRI for diagnosis of SpA was 0.60. Pearson correlation between the sum of mNY sacroiliitis grade for each patient (0 to 8) and the mean number of quadrants for each MRI lesion was r = 0.382 (BME), r = 0.377 (erosion), r = 0.217 (subchondral sclerosis), r = 0.358 (fat metaplasia), r = 0.371 (backfill), and r = 0.463 (ankylosis).

The frequency of a positive MRI compatible with axSpA was highest in group 1; this result was expected because MRI was used to diagnose and then classify these patients. Of more interest is that 9 patients (37.5%) from group 3 had

Table 2. SIJ quadrants of each type of lesion on SIJ MRI of patients with recurrent AAU and healthy controls. Values are mean ± SD (median; interquartile range).

Variables	Group 1, AxSpA, n = 20	Group 2, NSBP, n = 6	Group 3, Asymptomatic, n = 24	Group 4, Controls, n = 21	Group 5, AS
BME					
Reader 1	6.8 ± 6.6 (5; 10)	1.3 ± 1.2 (1.5; 2)	2.5 ± 5.5 (0; 3)	1.5 ± 3 (0; 1)	4.8 ± 6.64 (2; 8)
Reader 2	2.9 ± 4.0 (1; 6)	1.1 ± 1 (1.5; 2)	0.9 ± 1.8 (0; 1)	0.9 ± 2.0 (0; 1)	5.10 ± 9.35 (2; 6.5)
Mean	5.8 ± 6.4 (3.3; 8.5)	1.1 ± 1 (1.3; 1.8)	2.1 ± 4.8 (0; 1.9)	1.2 ± 2.5 (0; 1)	4.9 ± 7.5 (2.5; 6.5)
Erosion					
Reader 1	2 ± 2.6 (1; 3)	0	1 ± 2.6 (0; 1)	0.5 ± 1.4 (0; 0)	8.9 ± 6.6 (10; 12.5)
Reader 2	2.5 ± 4.5 (0; 2)	0	0.6 ± 1.4 (0; 0)	0.1 ± 0.4 (0; 0)	3.3 ± 4.4 (2; 5)
Mean	2.5 ± 3.8 (0.8; 3)	0	0.6 ± 1.3 (0; 0.9)	0.2 ± 0.4 (0; 0)	6.1 ± 4.7 (5; 7)
Subchondral sclerosis					
Reader 1	1.8 ± 3.9 (0; 2)	1 ± 1.1 (1; 2)	2.2 ± 3.9 (0.5; 4)	0.9 ± 2.3 (0; 1)	—
Reader 2	1.1 ± 3.6 (0; 0)	0	0.7 ± 2.1 (0; 0)	0.3 ± 1.1 (0; 0)	—
Mean	1.5 ± 3.6 (0.5; 1.4)	0.5 ± 0.5 (0.5; 1)	1.3 ± 3 (0; 0.5)	0.7 ± 2 (0; 0.5)	—
Fat metaplasia					
Reader 1	1.7 ± 3.5 (0; 2)	0	0.5 ± 1.4 (0; 0)	0.1 ± 0.3 (0; 0)	9.6 ± 8.6 (6; 15)
Reader 2	2.5 ± 6.7 (0; 1)	0	0.7 ± 2 (0; 0)	0	3.3 ± 4.6 (2; 5)
Mean	1.7 ± 3.7 (0; 0.9)	0	0.6 ± 1.8 (0; 0)	0 ± 0.2 (0; 0)	6.4 ± 6.1(4.5; 10.5)
Ankylosis					
Reader 1	1.7 ± 3.3 (0; 3)	0	1 ± 2.5 (0; 0)	0	1.3 ± 3.7 (0; 0.5)
Reader 2	0.2 ± 0.9 (0; 0)	0	0.5 ± 1.9 (0; 0)	0	1.7 ± 3.8 (0; 1.5)
Mean	0.9 ± 2.7 (0; 0.5)	0	0.6 ± 2.1 (0; 0)	0	1.5 ± 3.7 (0; 0.75)
Backfill					
Reader 1	0.9 ± 1.3 (0; 1)	0	0.7 ± 2.6 (0; 0)	0.1 ± 0.4 (0; 0)	4.9 ± 7 (1; 9)
Reader 2	1.2 ± 3.8 (0; 0)	0	0.7 ± 2.5 (0; 0)	0 (0; 0)	4.6 ± 4.9 (3; 6.5)
Mean	0.7 ± 1.2 (0; 0.9)	0	0.7 ± 2.6 (0; 0)	0 ± 0.2 (0; 0)	4.7 ± 5.47 (2.5; 6.5)

Showed mean results after adjudication for groups 1 to 4. Mean results for group 5 are not adjudicated (cases read during calibration). Because subchondral sclerosis is not a lesion read in SPARCC SIJ Structural Score (SSS), data are not available. SIJ: sacroiliac joint; MRI: magnetic resonance imaging; AAU: acute anterior uveitis; BME: bone marrow edema; axSpA: axial spondyloarthritis; NSBP: nonspecific back pain; AS: ankylosing spondylitis.

images compatible with SpA, with 6 (25%) being detected on SIJ MRI and 8 (33.3%) on SIJ radiographs. Also, 2 controls (9.5%) had MRI images compatible with SpA, confirming that MRI findings can occur independently of back pain. However, the difference between groups 2 and 3, or group 3 and healthy controls, was not statistically significant, likely because of the small sample size of each group. Also, a higher number of patients in group 1 had a positive MRI according to global assessment as compared to the ASAS definition. In contrast, the number of controls with a positive MRI was lower when considering global assessment (Table 3).

The mean (median; IQR) number of quadrants for all lesions did not differ between groups 1 and 3 when considering those patients who had positive global assessment MRI by both readers (Table 4). The 2 patients from the control group with an MRI compatible with SpA exhibited BME, subchondral sclerosis, and fat metaplasia, but no erosion.

To establish which criterion for positive SIJ MRI might best reflect the global assessment for SpA, several cutoffs for numbers of quadrants with lesions were tested. The global assessment of SIJ MRI with a level of confidence being ≥ 7 according to readers 1 and 2 (or 1 of these readers and reader 3 in cases of discrepancy) was used as the gold standard for

Table 3. Diagnosis of SIJ radiographs and MRI scans of patients with AAU and healthy controls. Values are n (%).

Variables	Group 1, AxSpA, n = 20	Group 2, NSBP, n = 6	Group 3, Asymptomatic, n = 24	Group 4, Controls, n = 21	p
MRI+ (ASAS definition)	8 (40)	1 (16.7)	3 (12.5)	3 (14.3)	0.13
MRI+ (global assessment)	12 (60)[β]	0	6 (25)	2 (9.5)	0.001
Radiograph (mNY)	15 (75)[β]	0	8 (33.3)	NA	0.001
Imaging+ (global positive MRI and/or radiograph)	16 (80)[β]	0	9 (37.5)	NA	< 0.001

[β] Different from the other groups (Fisher's exact test). SIJ: sacroiliac joint; AAU: acute anterior uveitis; axSpA: axial spondyloarthritis; NSBP: nonspecific back pain; MRI: magnetic resonance imaging; ASAS: Assessment of Spondyloarthritis international Society; mNY: modified New York; NA: not applicable.

Table 4. Comparison of lesions between patients with MRI that were compatible with SpA from groups 1 and 3. Values are mean ± SD (median; interquartile range).

	Group 1, AxSpA with Positive Global MRI Assessment, n = 12	Group 3, Asymptomatic with Positive Global MRI Assessment, n = 6	p[&]
BME	8.91 ± 6.59 (8; 9.75)	6.83 ± 8.22 (3; 13.75)	0.384
Erosion	4.04 ± 4.26 (2.25; 7.88)	2.33 ± 1.63 (2.5; 3)	0.750
Subchondral sclerosis	2.20 ± 4.62 (1; 1.88)	4.08 ± 5.23 (2; 7.88)	0.437
Fat metaplasia	2.7 ± 4.58 (0.25; 4.75)	2.5 ± 3.09 (1.25; 5.63)	0.750
Ankylosis	1.54 ± 3.41 (0.25; 1.38)	2.58 ± 3.95 (0.75; 5.5)	0.682
Backfill	1.12 ± 1.5 (0.5; 1.88)	2.83 ± 4.78 (0; 7)	0.892

[&]Mann-Whitney U test. SpA: spondyloarthritis; BME: bone marrow edema; axSpA: axial spondyloarthritis; MRI: magnetic resonance imaging.

the estimation of sensitivity, specificity, and positive/negative likelihood ratios. The images that were considered compatible with SpA on global assessment (20 cases) were compared to those considered noncompatible with SpA (51 cases, Table 5). BME ≥ 3 was the criterion with the best sensitivity and specificity for the definition of positive MRI, followed by the ASAS definition.

DISCUSSION

This is the first study that evaluated sacroiliitis on SIJ MRI in patients with rAAU but no axial and peripheral symptoms for SpA. Our results showed that 9 asymptomatic patients (37.5%) had radiograph and/or MRI images that were compatible with axSpA, confirming a close relationship between uveal and axial involvement, independent of the presence of back pain. In addition, when these patients were compared to those from group 1, no statistically significant difference was observed regarding the average number of quadrants exhibiting any of the investigated acute or structural lesions on SIJ MRI. These findings demonstrated that the intensity of the abnormalities, when present, was indistinguishable from those exhibited by the patients classified as axSpA.

Regarding demographic data, we noted a higher prevalence of females among patients with rAAU, particularly among those who were HLA-B27–negative. Few studies have evaluated the relationship between sex and recurrence of AAU, as well as modulation of HLA-B27 and age, but some of them found that women needed longer treatment for the acute episode[32] and that the recurrence of uveitis episodes was higher[33]. Although the HLA-B27 prevalence in group 1 was lower than expected (60%), it was similar to findings in the Brazilian AS population (66%).[34]

Our results showed that in 4 patients (20%) from group 1 and 3 (12.5%) from group 3, the SIJ MRI was negative for SpA, while all of them met the mNY criteria. One patient from group 1 and another from group 3 exhibited the opposite situation (positive SIJ MRI according to the ASAS criteria but normal radiograph). Poddubnyy, *et al* compared conventional radiography and MRI for the detection of chronic sacroiliitis and found that the latter had 84% and 64% sensitivity and specificity, respectively, and a moderate κ coeffi-

Table 5. Sensitivity, specificity, positive/negative likelihood ratios of various criteria for definition of positive MRI.

Variables	Sens.	Sp.	LR+	LR–	ROC Area
ASAS definition	0.71	0.94	12.71	0.31	0.83
BME ≥ 2	0.94	0.83	5.65	0.07	0.89
BME ≥ 3	0.88	0.94	15.88	0.12	0.91
Erosion ≥ 2	0.47	0.96	12.71	0.55	0.72
Erosion ≥ 3	0.41	0.98	22.24	0.60	0.70
Fat metaplasia ≥ 2	0.35	0.98	19.06	0.66	0.67
Fat metaplasia ≥ 3	0.23	0.98	12.71	0.78	0.61
Backfill ≥ 2	0.29	1	NC	0.71	0.65
Backfill ≥ 3	0.24	1	NC	0.76	0.62
BME ≥ 2 and/or erosion ≥ 2	1	0.80	4.91	< 0.01	0.90
BME ≥ 2 and/or fat metaplasia ≥ 2	1	0.82	5.40	< 0.01	0.91
BME ≥ 2 and/or backfill ≥ 2	1	0.83	6	< 0.01	0.92

NC: not calculable (specificity = 1); BME: bone marrow edema; MRI: magnetic resonance imaging; ASAS: Assessment of Spondyloarthritis international Society; Sens.: sensitivity; Sp.: specificity; LR: likelihood ratio; ROC: receiver-operating characteristic.

cient (κ = 0.447). Notably, this was also the case in our study (κ = 0.595)[35]. Also in keeping with the literature, the agreement between radiograph readers was moderate (κ = 0.490) in our study, similar to the agreement reported by van den Berg, *et al* (κ = 0.540)[36]. As is known, interrater reliability between MRI readers for the evaluation of all types of structural lesions is better compared to conventional radiographs[37,38], although the interrater reliability between experienced readers for structural lesions is lower compared to BME[39]. Also, the correlation between mNY sacroiliitis grade and the number of quadrants for each MRI lesion was poor.

There were differences among groups 2, 3, and 4 regarding the frequency of individuals whose SIJ MRI were positive for SpA as per ASAS criteria or global assessment. However, the difference between the asymptomatic patients with rAAU (group 3) and healthy controls (group 4) was not statistically significant, possibly because of the small sample size in each group. Also, it reinforces the concept that MRI findings are not always connected with back pain. Studies with larger sample sizes are warranted to address this issue. In addition, SIJ MRI scans and radiographs were used to classify the patients in groups 1 and 2. Nevertheless, it should be noted that no MRI image of patients with NSBP and healthy controls exhibited significant amounts (i.e., more than 2 affected quadrants) of erosion, fat metaplasia, backfill, or ankylosis.

In addition, the frequency of individuals with NSBP and healthy controls who met the ASAS criteria and had positive MRI for SpA as per the global assessment (16.7%/14.3% and 0%/9.5%, respectively) was similar to previous studies[40]. This topic is of considerable interest and has been the subject of several studies seeking to improve the definition of SIJ MRI positivity. Such an advance would allow for early diagnosis of the disease but with greater specificity. A previous study assessed several criteria based on the combination of various quadrants exhibiting BME and erosion. The results showed that the criteria that considered both types of lesions had the best performance compared to global assessment of MRI[41]. Moreover, a recent study found that the combination of ≥ 5 fat metaplasia lesions and/or erosions on SIJ MRI had high specificity for axSpA, even in patients with back pain for less than 2 years, but low sensitivity[42]. Regarding the criteria based on the combination of lesions that best reflect the global assessment of SIJ MRI positivity, BME ≥ 3 exhibited the highest sensitivity and specificity (88%/94%) with an excellent area under the ROC curve. Similarly, the criteria combining BME ≥ 2 and/or erosions, fat metaplasia, or backfill ≥ 2 exhibited area under the ROC curve values of at least 0.9. Our results showed that among the proposed criteria for positive SIJ MRI, BME ≥ 3 and those criteria that included structural lesions might be adequate, exhibiting greater specificity than the ASAS criteria. Although our study is too small to draw any definitive conclusions, our data are consistent with the performance of these cutoffs in a larger cohort study[41].

Another topic that should be considered is the classification of patients with rAAU and sacroiliitis but without back pain. Because these patients did not exhibit back pain, arthritis, or enthesitis, they cannot be classified based on any of the existing criteria[43]. However, in addition to having AAU, which is the most frequent extraarticular manifestation of SpA, these patients did exhibit sacroiliitis on imaging tests, with activity and structural changes similar to those of symptomatic patients (group 1). The prospective assessment of this subgroup of patients is crucial to identify the rate of progression of inflammation and bone neoformation, as well as the prognosis and treatment needs of these patients.

Also of note is that despite the high prevalence (40%) of patients with rAAU and musculoskeletal symptoms, these patients had not been previously assessed by a rheumatologist. The relevance of investigation of musculoskeletal symptoms by ophthalmologists was recently supported by a study conducted on 798 patients with AAU. This previous study found that 50.2% of these patients had axSpA, 15.5% had pSpA, and most were HLA-B27– positive[44]. The same phenomenon was shown by Haroon, *et al* who, in addition to finding SpA in exactly 40% of the patients with AAU, also developed an algorithm for referral to rheumatology called the Dublin Uveitis Evaluation Tool (DUET). In this study, the onset of back pain before the age of 45 years and lasting over 3 months, being HLA-27–positive, and having psoriasis were the variables that best improved the performance of the DUET[45]. However, it is worth noting that only half of our rAAU patients were HLA-B27–positive and that the prevalence of psoriasis was low in our study. Therefore, if DUET were used only for referring patients to rheumatology, many cases would be missed.

Our study has some limitations that primarily derive from its small sample size, as well as from the long duration of eye disease and back pain among the symptomatic patients. Another limitation is that SIJ MRI images were acquired through 1.5T and 3T devices, and the latter could have better sensitivity to detect lesions.

Our study in patients with rAAU showed that even patients without any musculoskeletal symptoms might have radiographic and/or MRI sacroiliitis. Moreover, it showed that the lesion-based cutoff criterion that optimally reflected the global assessment for a positive SIJ MRI was BME in ≥ 3 SIJ quadrants. Further studies are necessary to establish the best strategy for early diagnosis of patients with AAU and to determine whether a positive SIJ MRI in the absence of axial symptoms might be used as a marker of high risk for development of spondyloarthritis.

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