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MR distribution of active inflammatory and chronic structural sacroiliac joint changes in axial spondyloarthropathy: Challenging conventional wisdom

Daria Motamedi[a,*], Rina Patel[a], Kavi K. Devulapalli[a], Lianne S. Gensler[b], Lynne Steinbach[a]

[a] Department of Radiology and Biomedical Imaging, Musculoskeletal Division, University of California San Francisco, United States of America
[b] Department of Medicine, Rheumatology Division, University of California San Francisco, United States of America

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ABSTRACT

Objective: Evaluate the MR distribution of inflammatory sacroiliac joint changes in axial spondyloarthritis phenotypes, including Ankylosing Spondylitis (AS) and non-radiographic Axial Spondyloarthritis (nrAxSpA).
Methods: A retrospective review of 94 patients seen for treatment of axial spondyloarthritis (SpA) who underwent sacroiliac joint MRI between January 2011 and December 2015 was performed. MR images from 68 patients (20 with AS and 48 with nrAxSpA) were reviewed independently by two radiologists. Images were scored on presence of active inflammatory and chronic structural lesions. These lesions were further categorized as unilateral, bilateral and asymmetric, or bilateral and symmetric.
Results: No statistically significant difference was found in the distribution (laterality or symmetry) of bone marrow edema or sclerosis between the AS and nr-axSpA groups. Osseous erosions were more commonly bilateral symmetric in AS than nr-axSpA (11/20 vs. 8/48, $p = 0.01$). No statistically significant difference was noted between bone marrow edema scores in the AS and nr-axSpA subgroups (2.6 vs 3.3, $p = 0.514$). Patients with AS had a significantly higher fat metaplasia score compared to patients with nr-axSpA (7.3 vs 1.1, $p = 0.001$). Patients with nr-axSpA had a higher mean score for erosions (11.6 vs 4.2, $p = 0.001$). Only patients classified as AS were found to have bony ankylosis. Inter-observer reliability was strong to excellent.
Conclusion: Ankylosing spondylitis findings at the sacroiliac joints are classically described as bilateral and symmetric on radiographs. Our study demonstrates that distribution on MRI at an individual time point is variable. The variable distribution should be considered when radiologists evaluate MRI exams of AS patients.

1. Introduction

Spondyloarthritis (SpA) refers to a group of rheumatologic conditions with common clinical, laboratory and genetic features. Specific SpA diseases include ankylosing spondylitis, psoriatic arthritis, reactive arthritis, arthritis related to inflammatory bowel disease, and other undifferentiated forms [1,2]. Patients with axial SpA can be grouped into those with non-radiographic axial spondyloarthritis (nr-axSpA) and radiographic axial spondyloarthritis. Radiographic axial spondyloarthritis is also termed ankylosing spondylitis (AS). Non-radiographic axial spondyloarthritis differs in disease course, gender predilection (nr-axSpA has no gender predilection and AS is more common in males), and levels of inflammatory markers [3]. According to traditional teaching and review of the literature, ankylosing spondylitis is the prototypical SpA characterized by bilateral and symmetric sacroiliitis on radiographs [4].

Imaging findings of SpA at the sacroiliac joints include active inflammatory changes and chronic structural changes. Chronic structural changes include subchondral sclerosis, and erosions with or without back-fill and resultant ankyloses. These chronic findings are generally not visualized on radiographs until greater than five years from disease onset [5,6]. The active inflammatory changes, such as bone marrow edema, capsulitis, and subligamentous enthesitis, often precede chronic structural changes and are best seen on MRI [7,8]. These findings may be less conspicuous on radiographs early in the disease process. Therefore, MRI of the sacroiliac joints is crucial in the early evaluation of patients with radiographically occult disease. When diagnosed early by MRI, these patients can start medications such as immune modulators that reduce disease activity and can improve symptoms [9,10].

Imaging findings of axial SpA are further characterized by pattern of

* Corresponding author at: Department of Radiology and Biomedical Imaging, University of California San Francisco, 505 Parnassus Ave, San Francisco, CA 94110, United States of America.
E-mail address: daria.motamedi@ucsf.edu (D. Motamedi).

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distribution (symmetric vs. asymmetric) at the sacroiliac joints. Ankylosing spondylitis is typically described as bilateral and symmetric sacroiliitis on radiographs [11,12]. Although the MRI findings of SpA have been described, the pattern or distribution are not clearly defined for MRI. Furthermore, the differences in distribution between SpA subgroups (AS and nr-axSpA) have not been clearly defined. Given that MRI can detect active inflammatory findings early in the disease course, the prototypical pattern of findings may not match that described for radiographs. The goal of this investigation, then, is to evaluate the imaging appearance of active inflammatory and chronic structural changes in patients with axial SpA and to describe distribution patterns seen on MRI.

2. Material and methods

A retrospective review of patients clinically evaluated by the rheumatologist (author LG) at UCSF's Spondyloarthritis Clinic between January 2011 and December 2015 was performed. Patients were included in the review if they had MR imaging of the sacroiliac joints and were diagnosed as having axSpA (either nrAxSpA or AS if patients had radiographic sacroiliitis meeting the Modified New York Criteria) [13]. The MR exams of 94 patients meeting these criteria were included in the study.

2.1. MR evaluation and lesion scoring

All MR images were acquired on a 1.5 Tesla or 3 Tesla MR scanner. 59 patients underwent imaging at our institution on a 1.5 Tesla or 3 Tesla MR Scanner (GE) with an established protocol including coronal oblique short tau inversion recovery (STIR) and unenhanced non fat saturated T1 images. The examination was performed in a supine position using a whole-body surface coil system. An additional 35 patients were imaged at outside facilities on either 1.5 Tesla or 3 Tesla scanners. Outside MR images were assessed by two radiologists, a diagnostic radiology resident with 3 years of experience (Rater 1) and a fellowship-trained musculoskeletal radiologist with 8 years of experience (Rater 2) for the presence of dedicated coronal oblique STIR or T2 fat saturated sequences, in addition to coronal oblique unenhanced non-fat saturated T1 sequences. Patients with insufficient MR images including lack of coronal oblique sequences (N = 15), wide field of view precluding appropriate SI joint resolution (N = 5), and poor quality fluid sensitive sequences (N = 6) were excluded. After excluding for the above limitations, a total of 68 patients were included in the study, 48 had nrAxSpA and 20 had AS, as diagnosed by the rheumatologist.

All MR sacroiliac joint exams from 68 patients were reviewed independently by Raters 1 and 2 using the Assessment of SpondyloArthritis International Society (ASAS) criteria and modified Berlin Classification [14] after a 30-minute training and calibration session. Axial and coronal sequences were used to evaluate for the presence of acute or chronic inflammatory findings according to ASAS criteria. These active or chronic inflammatory findings were scored on the coronal sequences using the Berlin Classification, and distribution of findings was assessed. Independent imaging analysis was reviewed and adjudicated by a fellowship-trained musculoskeletal radiologist with 30 years of experience. Consensus imaging reads were established and used for subsequent data analysis.

2.2. Definition of MR lesions

Images were assessed for the presence of active inflammatory and chronic structural changes as defined by ASAS criteria [15]. The ASAS criteria identify and describe findings on MRI that are used in the classification of sacroilitis. Theses active and chronic findings include bone marrow edema, fat metaplasia, sclerosis, erosions and anklyosis. Examples of active inflammatory and chronic structural changes are shown in Figs. 1–3. All sequences in each exam was evaluated for the presence or absence of the aforementioned inflammatory findings.

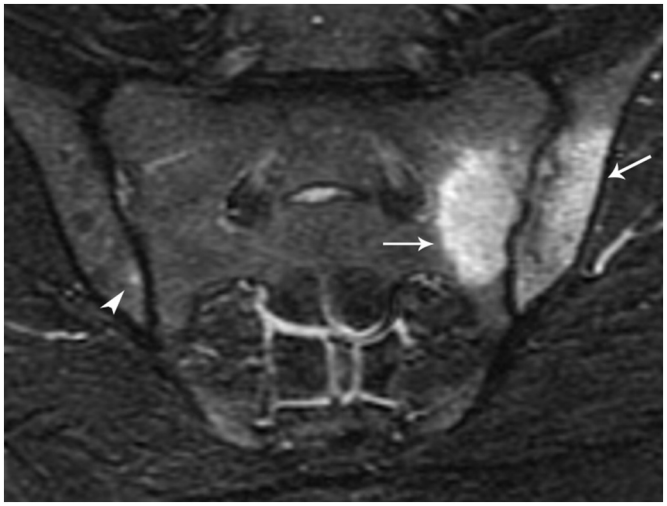

Fig. 1. MRI findings of sacroiliitis. 35 year old male with HLA B27 positive ankylosing spondylitis. Coronal oblique STIR sequence shows predominantly unilateral inflammatory lesions, including osteitis at the left sacroiliac joint, and osseous erosions (white arrows). A very small erosion is noted at the right sacroiliac joint (arrowhead).

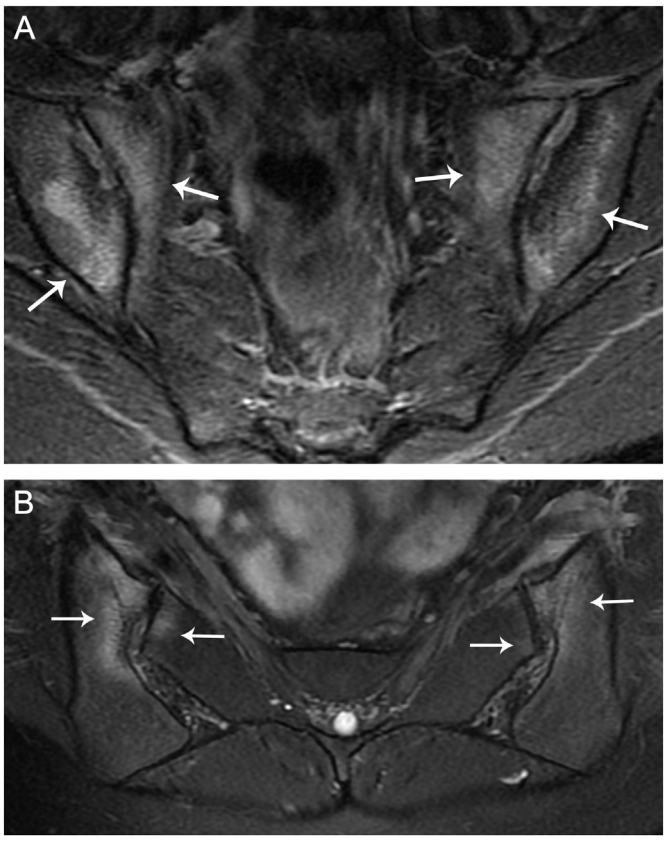

Fig. 2. MRI findings of sacroiliitis. 29 year old female with HLA-B27 positive ankylosing spondylitis. A. Coronal oblique STIR and B. axial T2 fat saturations images show predominantly bilateral symmetric inflammatory lesions, including osteitis and erosions at the bilateral sacroiliac joints (white arrows).

2.3. Scoring of MR lesions

Once active inflammatory and chronic structural changes were identified, these were scored and further classified according to the

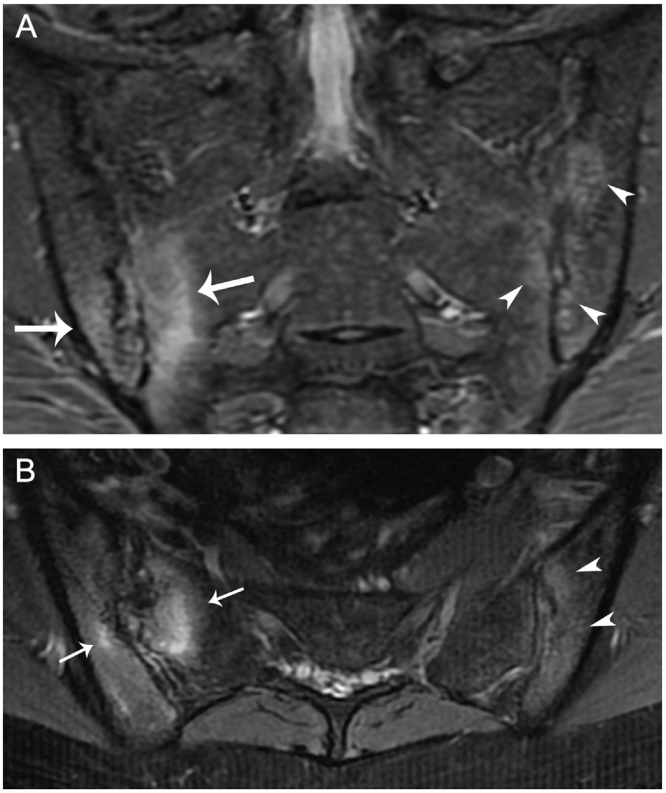

Fig. 3. MRI findings of sacroiliitis. 27 year old male with HLA-B27 positive ankylosing spondylitis. A. Coronal oblique STIR and B. axial T2 fat saturation images show predominantly bilateral asymmetric inflammatory lesions, including osteitis and erosions that are more severe at the right sacroiliac joint (white arrows) than the left (arrowheads).

modified Berlin classification. The modified Berlin Classification utilizes a quadrant based approach separating the ilium from the sacrum and divides the upper (anterosuperior) and lower (posteroinferior) portions of the joint by a fictional line along the bottom of the first sacral neural foramina. This results in a total of 8 quadrants, bilateraly. The coronal oblique images are the standard method for scoring using the Berlin method [16], so all imaging slices in a given coronal oblique sequence were utilized for evaluation.

Lesions were assigned a score of 0–3 (based on increasing severity from "none to severe", 0: no lesions, 1: ≤ 33%, 2: 33% to 66%, 3: > 66% of the subchondral bone area in the respective quadrant) per quadrant for a maximum score of 12 per side and 24 overall. Ankylosis was defined as osseous bridging across the sacroiliac joint. A point was assigned for every two adjacent quadrants noted to be bridged for a maximum of 2 points per side and 4 overall.

For each patient, lesions were categorized as unilateral, bilateral and asymmetric, or bilateral and symmetric. Bilateral and symmetric designation was assigned if lesions mirrored each other in location and intensity across the anatomic midline. Bilateral findings varying in either location or intensity were designated bilateral and asymmetric. Lesions involving only one joint were categorized as unilateral.

2.4. Statistical analysis

Baseline characteristics of AS and nr-axSpA groups were compared using chi-square test and Mann-Whitney *U* test for categorical and continuous variables, respectively. The agreement between raters for MR scores was determined by calculating interclass correlation coefficients (ICC). Correlation values were defined as follows: 0–0.2, poor; 0.3–0.4, fair; 0.5–0.6, moderate; 0.7–0.8, strong; > 0.8, excellent agreement. All statistical analyses were performed using SPSS 24.0 (Cary, NC).

Table 1
Demographic features.

Characteristics	AS (n = 20)	nr-axSpA (n = 48)	All patients	*p*-value
Age in years, mean (SD)	39.7 (15.8)	35.9 (10)	37.0 (12)	0.46
Symptom duration in years mean (SD)	12.1 (11.6)	7.1 (6)	8.6 (8)	0.09
Male patients, n (%)	16 (80)	23 (48)	29 (43)	**0.02**
Anti-TNF treatment, n (%)	4 (20)	9 (19)	11 (16)	0.58

Statistically significant results (p-value < 0.05) are given in bold.

3. Results

3.1. Demographics

68 patients with a clinical diagnosis of axSpA met inclusion criteria for imaging analysis. Of those 68 patients, 47 (69%) were HLA-B27 positive, 17 (25%) were HLA-B27 negative, and 4 (6%) did not have reliable data on HLA-B27 status. 48 (75.8%) met clinical criteria for nr-axSpA, while 20 (24.2%) were classified as AS. A statistically significant predominance of males was seen in the AS group compared to the nr-axSpA group ($p = 0.015$). Otherwise, no significant differences were noted between the groups (Table 1).

3.2. Reader correlation statistics

MR evaluation using the modified Berlin Classification revealed strong to excellent agreement between the two readers. Excellent correlation was achieved for rating of bone marrow edema and fat metaplasia (ICC scores of 0.94–0.98 and 0.96–1.00, respectively). Strong to excellent correlation was achieved for identification of subchondral sclerosis and osseous erosions with several quadrants demonstrating strong correlation (ICC scores of 0.73–0.98 and 0.79–0.98, respectively). Perfect correlation was achieved for MR evaluation of bony ankylosis.

3.3. Aggregate modified Berlin score findings

Average bone marrow edema (BME) score of 3.1 was seen in the overall cohort (Table 2). No statistically significant differences were noted between BME scores in the AS and nr-axSpA subgroups (2.6 vs 3.3, $p = 0.514$). Patients with AS had a significantly higher fat metaplasia score compared to patients with nr-axSpA (7.3 vs 1.1, $p = 0.001$). Patients with nr-axSpA had a higher mean score for erosions (11.6 vs 4.2, $p = 0.001$). Only patients with a diagnosis of AS were found to have bony ankylosis.

3.4. Distribution of inflammatory and structural changes on MR

Of the 68 patients evaluated, 2 had no active inflammatory or chronic structural changes seen on MRI. Only one category of lesion (bone marrow edema, fat metaplasia, erosions, sclerosis, or ankylosis)

Table 2
Modified Berlin criteria scores, mean (SD).

Characteristics	AS	nr-axSpA	All patients	*p*-value
BME	2.6 (3.6)	3.3 (4.0)	3.1 (3.9)	0.51
Fat metaplasia	7.3 (8.3)	1.1 (2.9)	2.9 (5.8)	**0.001**
Erosions	4.2 (4.7)	11.6 (8.2)	6.4 (6.8)	**0.001**
Sclerosis	2.1 (2.4)	1.4 (2.2)	1.6 (2.2)	0.29
Ankylosis	0.9 (1.5)	0	0.3 (0.9)	**0.001**

Statistically significant results (p-value < 0.05) are given in bold.

Table 3
MR distribution of inflammatory and structural findings.

Characteristics		AS	nr-axSpA	*p*-value
BME	Unilateral	3	15	0.16
	Bilateral asymmetric	5	13	0.89
	Bilateral symmetric	5	4	0.06
Fat metaplasia	Unilateral	0	3	**0.04**
	Bilateral asymmetric	3	3	0.77
	Bilateral symmetric	8	3	0.08
Erosions	Unilateral	1	11	**0.04**
	Bilateral asymmetric	8	21	0.36
	Bilateral symmetric	11	8	**0.01**
Sclerosis	Unilateral	0	4	0.11
	Bilateral asymmetric	0	3	0.18
	Bilateral symmetric	9	10	0.09
Ankylosis	Unilateral	0	0	–
	Bilateral asymmetric	0	0	–
	Bilateral symmetric	6	0	**0.01**

Statistically significant results (p-value < 0.05) are given in bold.

was found in 4 of the 68 patients. The remaining 62 of 68 patients had findings in at least two of the categories. Summarized findings characterizing the distribution of SI joint changes on MR are provided in Table 3. Overall, 45 (66.2%) patients had bone marrow edema. No statistically significant differences in distribution of bone marrow edema was seen among AS and nr-axSpA groups, but there was a trend towards bilateral symmetric distribution in AS ($p = 0.055$).

Twenty patients (20.4%) had findings of fat metaplasia and twenty-six patients (38.2%) had subchondral sclerosis on MR. No statistically significant difference in pattern of distribution was found for subchondral sclerosis. Unilateral distribution of fat metaplasia was associated with nr-axSpA ($p = 0.040$). Presence of bilateral and asymmetric fat metaplasia was not statistically significant between the AS and nr-axSpA groups. Bilateral and symmetric distribution of fat metaplasia was also not statistically significant between the two groups, though there was a trend towards more common distribution of bilateral symmetric fat metaplasia in patients with AS ($p = 0.078$).

Sixty patients (88.2%) had erosive changes on MR. The differences in distribution of osseous erosions between AS and nr-axSpA groups were statistically significant. Unilateral erosions were significantly associated with nr-axSpA ($p = 0.040$) compared to the AS group. Bilateral and symmetric erosions were significantly associated with AS ($p = 0.006$).

4. Discussion

The distribution of ankylosing spondylitis on pelvic radiographs is described as bilateral and symmetric according to traditional teaching and review of the literature [11,12]. However, distribution of findings on MRI of the sacroiliac joints and differences in distribution between axial SpA subgroups has not been characterized. Our study shows that the distribution pattern of findings on MRI does not necessarily match that of radiographic findings. The distribution of inflammatory sacroiliac findings on MRI is variable for those with AS. The only finding that was significantly associated with the AS subgroup over nr-asSpA was bilateral and symmetric osseous erosions. The only findings associated with nr-asSpA over AS were unilateral fat metaplasia and unilateral erosions. Even though bilateral symmetric osseous erosions were more commonly seen with AS, 9 of 20 patients with AS demonstrated erosions which were unilateral or bilateral and asymmetric.

Our study has several limitations. First, this is a retrospective analysis which is subject to inherent observation bias. Second, despite an overall sample size of 68 patients, the relatively few number of patients with a clinical diagnosis of AS yields low power and may preclude findings from reaching statistical significance. Third, treatment-related factors such as timing of anti-TNF medication regimens were not included in our review but may have influenced active inflammatory or chronic structural findings on MR. Finally, MR exams are obtained at an individual time point within the patient's clinical course and may only show active inflammatory lesions occurring at that single time point, which may have implications for pattern of distribution.

Despite these limitations, this to the knowledge of the authors is the only imaging study to date to formally evaluate and characterize the distribution of MR findings of the sacroiliac joints in patients with axial SpA. Strengths of our study include the use of a validated and reproducible instrument for assessing findings of sacroiliitis on MRI, strong to excellent correlation among readers, and rheumatologic correlation in all cases.

5. Conclusions

Our evaluation of MRI findings of the sacroiliac joints in axial SpA shows that radiologists should not expect patients with AS to have reliably bilateral and symmetric findings on MRI and that distribution of findings may be variable. Future directions of study include larger, prospective studies to further characterize the distribution of MR findings in patients with axial spondyloarthritis.

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