

Erosions Are the Most Relevant Magnetic Resonance Imaging Features in Quantification of Sacroiliac Joints in Ankylosing Spondylitis

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ABSTRACT. *Objective.* To determine the most relevant radiological features in quantitative magnetic resonance imaging (MRI) of sacroiliac (SI) joints in patients with recent-onset ankylosing spondylitis (AS) versus patients with SI involvement due to other rheumatic diseases, or to degenerative SI pain.

Methods. We retrospectively analyzed laboratory values, clinical data, and MRI of the SI joints of 179 patients admitted for evaluation of AS-suspicious SI pain. Standardized MRI sequences were performed at time of first presentation, then archived, and retrospectively quantitatively assessed using a modified SPARCC method for formal statistical comparisons.

Results. Of all patients, 27 (15%) were diagnosed with definite AS. The remainder had SI involvement in other rheumatic diseases, HLA-B27– spondyloarthropathy, or nonspecific degenerative changes. While joint space irregularities, bone marrow edema, subcortical cysts, and contrast medium enhancement were found in MRI of all patients, these features were inconsistent, and only erosions were statistically significantly ($p < 0.02$) in patients diagnosed with AS. Only in AS, the presence of erosions and the quantitative SPARCC erosion subscore correlated to a statistically significant degree ($p < 0.02$) with laboratory levels of inflammation.

Conclusion. Erosions alone, not bone marrow edema or contrast medium enhancement, are the most disease-specific measurable imaging findings in SI MRI of patients with AS. (First Release Jan 15 2010; J Rheumatol 2010;37:622–7; doi:10.3899/jrheum.090602)

Key Indexing Terms:

ANKYLOSING SPONDYLITIS

MAGNETIC RESONANCE IMAGING

OUTCOME ASSESSMENT

Radiological assessments are important prognostic indicators in patients with ankylosing spondylitis (AS), since the entity of structural damage at baseline correlates with both decreased mobility and functional impairment as disease progresses¹⁻⁶. Therefore, imaging assessments of the sacroiliac (SI) joints in patients suspected to have AS, including magnetic resonance imaging (MRI), are important to establish a rapid and reliable diagnosis and to design individual therapies⁷⁻¹¹. Special MRI techniques using, for example, turbo-inversion-recovery-magnitude (TIRM) and contrast medium-enhanced T1 fat-saturated sequences are

the most commonly recommended procedures for detection of bone marrow edema and synovial inflammation, both of which are considered characteristic radiological features in quantitative scoring of AS¹²⁻¹⁸. However, many other conditions of the musculoskeletal system, e.g., “wear and tear” related to aging, osteoarthritis, trauma, malignancies, infection, and other inflammatory rheumatic diseases can present clinical signs and symptoms similar to SI pain in AS. In addition, our own routine clinical experience indicates that the radiological features included in quantitative scoring methods for SI MRI in clinical trials in AS are not totally reliable for translation into “real-life” AS, since they can be found in a variety of conditions causing SI pain.

In our study we determined whether bone marrow edema, subcortical cysts, joint-space irregularities, erosions, and contrast medium enhancement, all of which are radiological features given equal scoring value in the most common present scoring methods of SI joints, are equally helpful for quantitative MRI differentiation between AS and SI involvement in other conditions. We retrospectively analyzed clinical, laboratory, and imaging data of routine rheumatology patients referred to the Radiology Department for causal evaluation of AS-suspicious SI pain. Such information could define the most salient quantification scores in SI MRI of routine AS.

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MATERIALS AND METHODS

Patients. We retrospectively analyzed rheumatology patients referred to the Radiology Department between 2002 and 2006 for radiological evaluation of SI pain. Eligibility for inclusion in our study required that patients (1) presented at the hospital with recent onset of localized SI pain (according to the patient's clinical anamnesis with a disease duration < 1 year); (2) had documented laboratory values and MRI determined within 1 month after their first clinical presentation; (3) had a complete electronically archived set of SI MRI examinations following the standardized protocol detailed below; (4) did not receive systemic antirheumatic or local anesthetic treatment until their MRI examination; (5) were initially clinically suspicious for AS; and (6) had a definite clinical diagnosis at the time of retrospective MRI evaluation.

Our study was approved by the regional ethics committee under a general approval waiver for retrospective studies based on data from local quality registries. According to the hospital's policy, informed consent was obtained from all patients prior to their routine clinical, serological, and radiological examinations.

Measurements. Routine clinical and laboratory evaluations were performed in all patients within < 1 month after their first clinical presentation. In each patient, the referring physicians made the final clinical diagnosis according to the respective established disease classification criteria¹⁹⁻²⁵. In this retrospective study, we retrieved the clinical diagnoses from the electronic patient file archive. Patients classified with definite AS were HLA-B27+. MRI scans following a standardized sequence protocol were performed and nonquantitatively assessed at time of first presentation, archived, and retrospectively quantitatively assessed utilizing a modification of the Spondyloarthritis Research Consortium of Canada (SPARCC) method for formal statistical comparisons¹⁵. Of note, the quantitative SPARCC evaluation of MRI was performed retrospectively and was not decisive for establishing clinical diagnosis since none of the clinical disease classification criteria include MRI findings. For the calculations in this study, C-reactive protein (CRP; mg/l) was used as a marker for inflammation. Radiological and clinical values were used for formal statistical comparisons.

Statistical analysis. All data are given as mean \pm standard deviation (SD). Statistical comparisons were performed using analyses of variance (ANOVA) followed by *posthoc* Bonferroni test. The intraobserver reproducibility of modified SPARCC sum scores and of subscores was calculated using ANOVA to provide the intraclass correlation coefficient (ICC) and kappa statistics. All statistical analyses were performed using SPSS 11.5 for Windows (SPSS Inc., Chicago, IL, USA).

MRI. In each patient, MRI were performed with a 1.5-Tesla (T) system (Siemens, Magnetom Vision, Erlangen, Germany) using appropriate surface coils. In accord with the SPARCC MRI index for assessment of SI joint inflammation in AS spondylitis score, sequences were acquired in semicoronal planes tilted parallel to the axis of the SI joints and semiaxial planes of all patients, all with 4 mm slice thickness¹⁵. Sequences of this protocol (inhouse designation: "Bechterew-protocol") were as follows: (1) T1-weighted semicoronal spin-echo [SE, time to recovery (TR) 517–618 ms, time to echo (TE) 13 ms, echo train length (ETL) 3, matrix frequency 512, phase 256]; (2) semicoronal TIRM (TR 2.720–3.170 ms, time to inversion 140 ms, TE 38–61 ms, ETL 7, matrix frequency 384, phase 256); (3) semicoronal T2-weighted MEDIC with fat saturation (FS) (TR 715 ms, TE 27 ms); (4) semicoronal T1-weighted SE with FS (TR 517–618 ms, TE 13 ms); (5) semiaxial T1-weighted SE with FS (TR 517–618 ms, TE 13 ms); and (6) semiaxial T1-weighted SE without and (7) with FS after intravenous (IV) administration of gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA; Magnevist, Schering, Germany) at 0.1 mmol/kg body weight.

Scoring of MRI lesions. An experienced investigator (MCW) retrospectively quantitatively scored all archived MRI blinded to patient demographics, laboratory values, and definite clinical diagnosis. MRI were scored after extensive investigator training and after achieving high performance reproducibility (ICC = 0.91; kappa = 0.81–0.90) on complete sets of 10 SI joint

MRI. Changes of the lumbar-sacral junction, e.g., lumbar disc herniations or lumbar osteoarthritis, were not scored. Subchondral sclerosis and SI ankylosis were not scored. Scoring of the SI joints was confined to the synovial portion of the joint¹⁵. SI joints were semiquantitatively assessed for the following: joint-space width, erosions, bone marrow edema, subcortical cysts, and contrast medium enhancement. The aggregate SPARCC method, which originally scored only 6 consecutive slices from posterior to anterior, was modified slightly to assess all slices on which the SI joints within the iliac bone and within the sacrum up to the sacral foramina were assessable, to simplify and to score the presence or absence of the radiological features on any slices¹⁵. Increased signals in the SI joint space or in the SI ligaments were not scored. For all radiological features assessed (except joint-space width), each SI joint was divided into 4 quadrants: upper iliac, lower iliac, upper sacral, and lower sacral. The presence of an increased signal on TIRM in each of these 4 quadrants was scored, where score 1 indicated an increased signal of depth < 1 cm from the articular surface, and score 0 indicated a normal signal. Each joint that included a lesion demonstrating continuous increased signal of depth > 1 cm from the articular surface was given an additional score of 1. Similarly, detectable erosions on any of the obtained sequences in each of the 4 quadrants were scored as 1 or 0, where 1 indicated the presence and 0 the absence of erosions. Each joint that included an erosive lesion > 1 cm was given an additional score of 1. According to the Outcome Measures in Rheumatology Clinical Trials (OMERACT) scoring system, erosion is defined as a sharply marginated bone lesion with correct juxtaarticular localization and typical signal characteristics. To be labeled erosion, the cortical break should be seen in at least 2 planes²⁶. Detectable subcortical cysts on any of the obtained sequences in each of the 4 quadrants were scored as 1 or 0, where 1 indicated the presence and 0 the absence of subcortical cysts. The maximum possible score for subcortical cysts was 8. The presence of both joint-space widening and joint-space narrowing was scored as 1, resulting in a maximum possible score for joint-space irregularities of 2. Joint-space irregularities were scored as an independent feature despite a possible presence/absence of erosions. A uniform joint space of less than 2 mm infrequently occurs either unilaterally or bilaterally in the asymptomatic population and therefore, when present, has been considered a significant sign²⁷. The presence of an increased signal on either T1-weighted SE or T1-weighted SE with FS or both after IV administration of Gd-DTPA in each of these 4 quadrants was scored, with a score of 1 for an increased signal of depth < 1 cm from the articular surface and 0 for normal signal. Each joint that included a contrast medium enhancing lesion demonstrating a signal of depth > 1 cm from the articular surface was given an additional score of 1. Therefore, the maximum possible modified SPARCC radiological sum score on sacroiliac MRI was 58.

RESULTS

Table 1 summarizes the demographic values of the 179 patients (46 men and 133 women) included in this analysis. Of note, this was not a randomized trial, because the choice of MRI for each patient was determined by the referring physicians based on individual patient clinical considerations. However, MRI were performed in patients whose radiographs were inconclusive as well as consecutively in most patients suspected of having AS during the observation period. Thus, these patients represented a "real-life" sample of patients who presented with AS-suspicious SI pain at the Rheumatology Department and were referred to the Radiology Department. The mean age of all 179 patients at MRI was 48.6 (12.3) years. The mean time from onset of SI pain (as recorded by the patient) until the MRI examination was 6.7 (3.1) months. No patient received any systemic antirheumatic or local anesthetic treatment prior to MRI.

Table 1. Demographic and radiological characteristics of 179 patients admitted for magnetic resonance imaging (MRI) evaluation of sacroiliac pain. Values are means (\pm SD).

	HLA-B27– SpA, n = 101	SI Changes, n = 28	AS, n = 27	Diagnosis				
				PsA, n = 9	RA, n = 8	Oligoarthritis, n = 3	SS, n = 2	SLE, n = 1
Demographic characteristics								
Age, yrs	49.4 (12.0)	48.3 (12.3)	42.9 (16.7)	48.6 (16.2)	56.7 (8.0)	54.6 (18.7)	46.2 (5.6)	47.3
CRP, mg/l	6.1 (5.4)	8.1 (6.6)	15.6 (7.1)	12.3 (7.4)	13.1 (6.4)	11.7 (7.4)	15.1 (10.4)	16.8
MRI Characteristics								
Total MRI score	1.2 (1.5)	0.9 (1.3)	2.2 (1.2)	1.8 (2.0)	1.6 (1.9)	1.7 (2.9)	0	2
JSI								
n	4	0	5	0	1	0	0	0
Score	0.06 (0.2)	—	0.2 (0.3)	—	0.1 (0.3)	—	—	—
BME								
n	29	6	16	4	2	1	0	0
Score	0.4 (0.7)	0.4 (0.9)	0.8 (0.7)	0.8 (1.0)	0.6 (1.3)	0.7 (1.0)	—	—
Erosion								
n	2	0	12	1	2	1	0	0
Score	0.04 (0.2)	—	0.6 (0.6)	0.1 (0.3)	0.2 (0.4)	0.3 (0.5)	—	—
SCC								
n	9	0	0	1	0	0	0	1
Score	0.1 (0.4)	—	—	0.1 (0.3)	—	—	—	2.0
CME								
n	28	4	14	4	2	1	0	0
Score	0.5 (0.8)	0.4 (1.0)	0.6 (0.7)	0.8 (1.0)	0.6 (1.1)	0.7 (1.0)	—	—

AS: ankylosing spondylitis; BME: bone marrow edema; CME: contrast medium enhancement; CRP: C-reactive protein; HLA-B27– SpA: HLA-B27– spondyloarthropathy; JSI: joint space irregularities; PsA: psoriatic arthritis; RA: rheumatoid arthritis; SCC: subcortical cysts; SS: Sjögren's syndrome; SLE: systemic lupus erythematosus; SI: Changes: nonspecific degenerative sacroiliac changes.

According to the electronic patient file archive, 27 (15%) of these patients were ultimately diagnosed with definite AS, including those with preradiographic HLA-B27+ axial spondyloarthropathy (Table 1). The remainder showed SI involvement of other conditions: 9 fulfilled criteria for diagnosis of psoriatic arthritis (PsA); 8 were diagnosed with rheumatoid arthritis (RA), 2 with Sjögren's syndrome (SS), 1 with systemic lupus erythematosus (SLE), 3 with oligoarthritis, 28 with unspecific degenerative SI changes, and the remainder with HLA-B27– axial spondyloarthropathies.

In all patients, the mean CRP at the time of MRI was 8.1 (8.2) mg/l. When patients were grouped according to their later diagnosis, those with AS had a mean CRP value of 15.6 (7.1) mg/l, which was statistically significantly higher than patients with HLA-B27– spondyloarthropathy [6.1 (5.4) mg/l; $p < 0.02$] or patients with unspecific degenerative sacroiliac changes [8.1 (6.6) mg/l; $p < 0.03$]. However, patients diagnosed with RA [13.1 (6.4) mg/l] or SLE (16.8 mg/l) had equally high CRP values ($p =$ nonsignificant, respectively). Patients with oligoarthritis [11.7 (7.4) mg/l; $p =$ NS], PsA [12.3 (7.4) mg/l; $p =$ NS], or SS [15.1 (10.4) mg/l; $p =$ NS] had CRP values statistically similar to those of patients with AS, RA, or SLE.

On MRI, only 5.6% ($n = 10$) of patients showed joint-space irregularities (Table 1), an occurrence highest

among patients diagnosed with AS (50%), followed by patients with HLA-B27– spondyloarthropathy (40%), and RA (10%; $p =$ NS, respectively). In 11/179 patients (6%), subcortical cysts were found on MRI, with the highest proportion among those later diagnosed with HLA-B27– spondyloarthropathy (82%, $n = 9$; $p < 0.03$), followed by patients with SLE and AS (9%, $n = 1$, respectively; Table 1). Ten percent ($n = 18$) of all patients showed bone erosions on MRI. Of those, 67% were found in patients diagnosed with AS ($n = 12$; $p < 0.02$), followed by patients with HLA-B27– spondyloarthropathy or RA (11%, $n = 2$, respectively), and PsA or oligoarthritis (6%, $n = 1$, respectively; Table 1).

On TIRM sequences, 32% of patients ($n = 58$) showed SI bone marrow edema. This group comprised 50% with HLA-B27– spondyloarthropathy ($n = 58$), 28% with AS ($n = 16$), 10% with unspecific degenerative SI changes ($n = 6$), 7% with PsA, 3% with RA, and 2% (1 patient) with oligoarthritis ($p =$ NS, respectively; Table 1). After IV administration of contrast medium, 30% ($n = 53$) of all patients showed enhancement on T1-weighted SE with FS. The majority of individuals in this group were later diagnosed with HLA-B27– spondyloarthropathy (53%; $p =$ NS). Twenty-six percent of patients with contrast medium enhancement were later diagnosed with AS, 8% with PsA or unspecific degenerative SI changes, 4% with RA, and 2% with oligoarthritis ($p =$ NS, respectively; Table 1).

When grouping patients according to their definite clinical diagnosis, the mean total SPARCC MRI score was not statistically significantly different between AS patients and those with HLA-B27– spondyloarthritis, PsA, RA, SLE, or oligoarthritis ($p = \text{NS}$, respectively), but differed markedly from those of patients with unspecific degenerative SI changes or SS ($p < 0.05$).

However, among patients with erosions, patients with AS and MRI erosions (67% of all patients with erosions) had a significantly increased mean CRP [19.3 (10.3) mg/l; $p < 0.02$] compared to patients with HLA-B27– spondyloarthritis, PsA, or oligoarthritis, but not RA ($p = \text{NS}$, respectively).

DISCUSSION

The rapid identification of patients with AS at early clinical disease stages, showing only discrete SI changes, provides an important window of treatment opportunity before irreversible damage occurs²⁸. According to the modified New York criteria, the diagnosis of AS requires radiographic changes in the SI joints²⁴. Although inflammation of the SI joints is considered a hallmark of AS, this inflammatory activity is poorly visualized on standard radiographs, which show only structural changes presumed to result from inflammation^{9,29}. MRI can identify both active inflammatory and chronic structural changes in the SI joints without unnecessary x-ray load, and thus it is increasingly used as an early imaging assessment of the SI joints in patients with AS.

Although the capability of MRI in detecting subtle bony erosions is below that of computerized tomography, one of the most important advantages of MRI is avoidance of x-ray radiation, making it an ideal potential technique for followup of treatment response. Acute changes such as bone marrow edema or inflammation can be uniquely visualized with MRI using TIRM or sequences after IV administration of contrast medium³⁰, revealing acute lesions brightly in contrast to dark normal bone marrow³¹. Moreover, the possibility of diagnosing a patient with SI pain as having early AS rises by a factor of 10 in the presence of typical MRI changes^{23,32}.

OMERACT, in collaboration with the Assessments in Ankylosing Spondylitis (ASAS) international MRI in AS working groups, have published a study on the measurement properties of the SPARCC index for assessment of SI joints in AS¹⁸ and found that it is a good method of measuring acute SI inflammation¹⁵. The precise role of early MRI examinations and the disease-specific significance of typical MRI features in daily practice and quantitative scoring methods of MRI of definite AS, i.e., HLA-B27+, remain to be precisely defined because more simple clinical variables, such as HLA-B27, have a relatively high sensitivity, and MRI assessment of patients with SI pain and possible AS has not yet been well studied.

Utilizing a slight modification of the SPARCC method in the favored MRI sequences in clinical trials in AS, we retrospectively systematically assessed SI joints of patients referred for MRI, including those diagnosed with AS³³. Although only one investigator performed MRI scoring, which must be considered a certain limitation of this study, scoring procedures were done after extensive investigator training and after achieving high performance intraobserver reliability for both modified SPARCC sum scores and sub-scores. Again, although this was not a randomized clinical trial where 2 independent readers are preferred, scoring of images from routine cases by one experienced musculoskeletal reader seemed sufficient for the purpose of our study on a large routine patient cohort sample.

The results of our analyses showed that patients with AS represented the predominant population of patients with erosions on MRI, and that AS patients with erosions had highest mean CRP values. Our results partially agree with another cross-sectional study of patients with moderate to severe AS, wherein only CRP was found to be related to disease activity on MRI, with mean CRP significantly lower in patients without abnormal enhancement or subchondral bone marrow edema on MRI versus those showing MRI changes of active inflammation³⁴. It should be noted, however, that increased CRP values were also found in our study in a few patients with SI involvement in other diseases, limiting the value of CRP in the context of concomitant MRI changes. As mentioned above, identification of AS patients at early clinical disease stages provides an important window of treatment opportunity against irreversible damage. In this context it should be noted that the demographic age of our AS patients was above the reported average age for early disease, indicating that some patients in our cohort might need to be categorized as “late-onset” clinical, recently overt, disease. In addition, this may have partially influenced the results towards a high percentage of unclassifiable disorders, which might clinically have been diagnosed and grouped as HLA-B27– axial spondyloarthropathies.

Our study showed that only erosions on MRI, but not bone marrow edema or contrast medium enhancement (which is inconsistently found in other conditions), are a statistically significant radiological feature unique to AS in patients with initially unspecific SI pain (Figure 1A and 1B). However, one limitation of our study is that the numbers of patients in the different groups were relatively small, limiting the generalizability of our results. The OMERACT and ASAS MRI in AS working groups also noted that developing quantitative scoring methods for the assessment of active inflammation should be given priority over methods assessing structural damage¹⁸. While the SPARCC and other MRI quantification methods give equal scoring value to different MRI features in their “simple” sum scores, erosions being less significant in the presence and intensity of bone marrow edema or contrast medium enhancement, our results

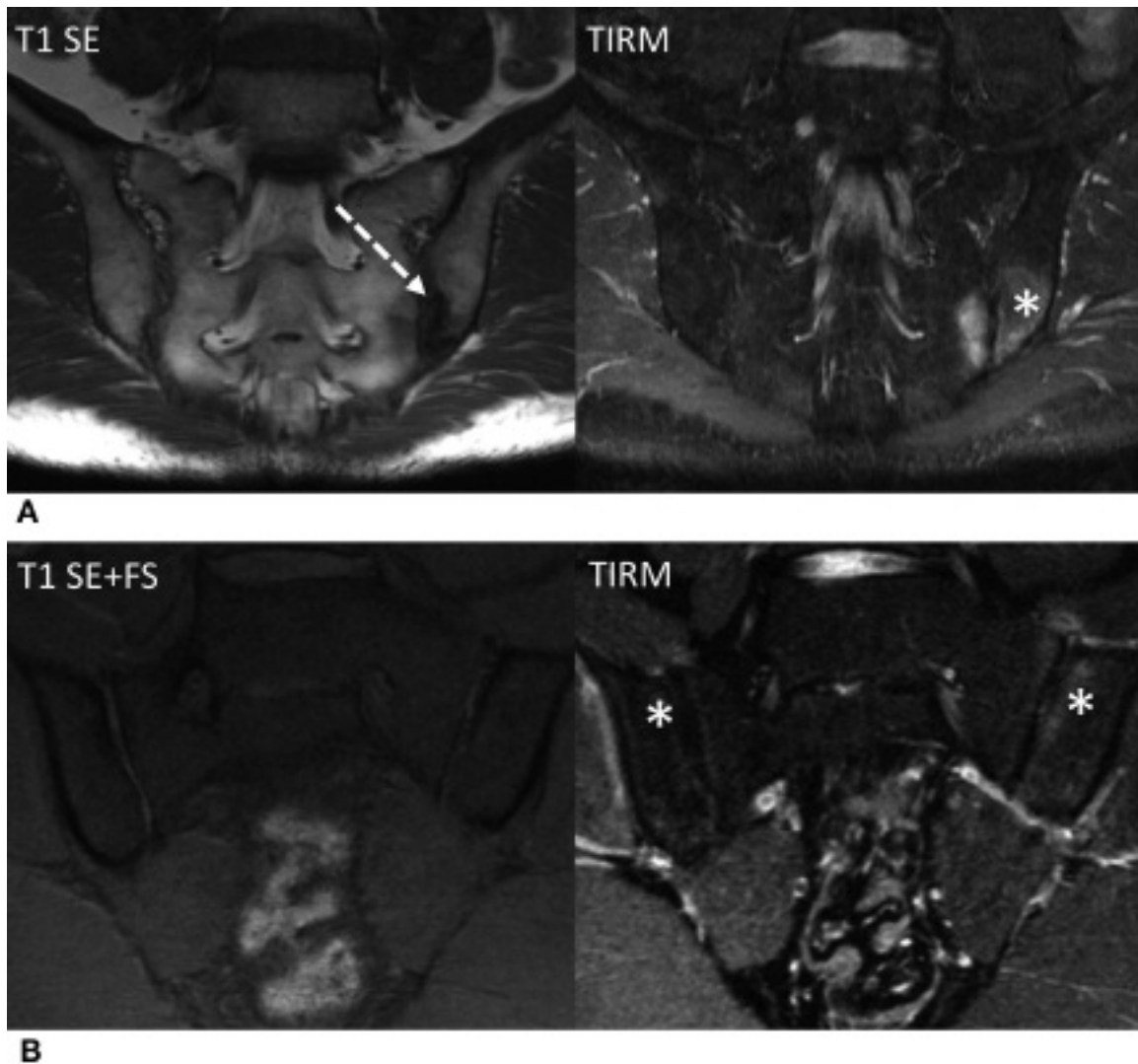


Figure 1. A. Representative T1 SE (left) and TIRM (right) images show erosive changes (broken arrow) and bone marrow edema (*) on MRI of sacroiliac joints in a patient later diagnosed with AS. B. In comparison to panel A, representative T1 SE + FS (left) and TIRM (right) images on MRI of sacroiliac joints of a patient later diagnosed with psoriatic arthritis show only bone marrow edema (*), but no erosive changes.

suggest that these erosions, because of their radiological specificity for AS, should be a major consideration in quantitative MRI assessment scores of SI joints.

Erosions alone, not bone marrow edema or contrast medium enhancement, are the most disease-specific measurable imaging findings in SI MRI of AS patients in clinical practice and merit special consideration for both diagnostic radiological MRI classification and assessments of the effect of therapeutic agents. Therefore, a more prominent role for the presence or absence of erosive changes in quantitative MRI scoring rather than for equal scoring value of unspecific features such as bone marrow edema or contrast medium enhancement, as is the case within the sum score of the SPARCC method, warrants further research.

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