Central Reader Evaluation of MRI Scans of the Sacroiliac Joints from the ASAS Classification Cohort: Discrepancies with Local Readers and Impact on the Performance of the ASAS Criteria

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ABSTRACT

Objectives. The Assessment of SpondyloArthritis international Society (ASAS) MRI working group (WG) conducted a multi-reader exercise on MRI scans from the ASAS classification cohort to assess the spectrum and evolution of lesions in the sacroiliac joint (SIJ) and impact of discrepancies with local readers on numbers of patients classified as axSpA.

Methods. Seven readers assessed baseline scans from 278 cases and 8 readers assessed baseline and follow up scans from 107 cases. Agreement for detection of MRI lesions between central and local readers was assessed descriptively and by the kappa statistic. We calculated the number of patients classified as axSpA by the ASAS criteria after replacing local detection of active lesions by central readers and replacing local reader radiographic sacroiliitis by central reader structural lesions on MRI.

Results. Structural lesions, especially erosions, were as frequent as active lesions (≈40%), the majority of patients having both types of lesions. The ASAS definitions for active MRI lesion typical of axSpA and erosion were comparatively discriminatory between axSpA and non-axSpA. Local reader overcall for active MRI lesions was about 30% but this had a minor impact on the number of patients (6.4%) classified as axSpA. Substitution of radiography with MRI structural lesions also had little impact on classification status (1.4%).

Conclusion. Despite substantial discrepancy between central and local readers in interpretation of both types of MRI lesion, this had a minor impact on the numbers of patients classified as axSpA supporting the robustness of the ASAS criteria for differences in assessment of imaging.

Key Words. Spondyloarthritis, magnetic resonance imaging, sacroiliac joint, lesions, definitions, classification

INTRODUCTION

The ASAS classification cohort study (ASAS-CC) recruited patients referred to a rheumatologist with undiagnosed back pain. It led to the ASAS classification criteria in which patients diagnosed with axial spondyloarthritis (axSpA) could be classified as having axSpA by either an imaging or clinical arm[1]. Imaging criteria for sacroiliitis could be either radiographic or the presence of bone marrow edema (BME) as elaborated in the ASAS consensus definition[2,3]. The sensitivity and specificity of the criteria were 83% and 84%, respectively, and follow up after 4.4 years indicated a high positive predictive value for a rheumatologist's diagnosis of axSpA[4]. The assessment of MRI scans from the ASAS-CC by local readers was limited to determination whether the baseline scan demonstrated active and/or structural lesions typical of axSpA[1]. In the decade since this study our understanding of MRI lesions in the SIJ has increased substantially[5] but longitudinal data has been obtained from cohorts of patients with symptoms restricted to 2-3 years and not the typical patient referred to a rheumatologist where symptom duration averages 8-9 years[6,7]. Moreover, it has been recognized that BME can be observed in the SIJ in other disorders and even in 20-40% of healthy individuals[8-10]. This has led to concerns focused on the accuracy of local reader interpretations of imaging findings on MRI in the ASAS-CC and whether

discrepancies found between local and central readers might alter which patients are classified as having axSpA according to the ASAS criteria. Moreover, diagnosis of axSpA was changed by the local rheumatologist in only 11.2% of patients who were available at follow up after 4.4 years in the ASAS-CC which has also raised concerns regarding diagnostic ascertainment bias[4]. Evaluation of follow up MRI scans from this cohort to determine whether evolution of MRI findings supports these diagnostic conclusions has not been reported.

These considerations led to the decision by ASAS to convene the ASAS-MRI Working Group (WG) to conduct a multi-reader exercise to examine both the baseline and follow up MRI scans from the ASAS-CC. We aimed to address the following questions: A. What was the relative frequency of MRI lesions in the SIJ at baseline and follow up according to the recently updated ASAS definitions[11] and expert rheumatologist diagnosis of axSpA? B. What was the discrepancy between local and central readers in the detection of active and structural MRI lesions in the SIJ and how did this impact which patients were classified as having axSpA? C. Did replacement of local reader assignment of radiographic sacroiliitis by central reader assignment of MRI structural lesions impact which patients were classified as having axSpA? D. What was the evolution of MRI features of axSpA from baseline to follow up and to what degree did this reflect diagnostic assignment by the local rheumatologist?

METHODS

The study cohort, local rheumatologist assessments, imaging assessments, and follow up of the ASAS-CC have been reported previously[1,4,11,12].

ASAS eCRF for evaluation of MRI lesions in the SIJ. The online-available[12] CRF comprised two sections: A. A global scoring page where readers recorded the presence/absence of each type of MRI lesion according to published ASAS definitions[11]. Central readers provided a yes/no response to two primary MRI questions that local readers also addressed in the original baseline ASAS-CC CRF[1]: **MRI Q1**. "*Are there typical acute/active inflammatory lesions compatible with axial SpA present in SI joints or at entheseal sites outside the SI joint?*" **MRI Q2**. "*Are typical chronic inflammatory (structural) lesions present in or around SI joints?*" B. A granular scoring web-based interface where inflammatory and structural lesions were recorded according to established rules[12-14].

ASAS Classification Cohort MRI Resource. Baseline and follow up MRI scans of the SIJ were available from 278 and 170 cases, respectively. Granular assessment for MRI lesions was conducted only in cases where a DICOM series was available in semi-coronal orientation.

Reading exercises. Two multi-reader exercises were conducted. Validated calibration modules aimed at standardization of slice selection and defining SIJ quadrants were provided online for review prior to the readings[15,16]. In the first (exercise A), 7 central readers assessed baseline MRI scans from 275 cases. In the second exercise (exercise B), 8 central readers assessed MRI scans blinded to time point from 108 cases who had MRI performed at baseline and at 4.4 years follow up. The eCRF for this exercise included an additional question that asked the reader to indicate whether the MRI scan was indicative of the presence of axSpA (yes/no).

Statistics. Frequencies of each MRI lesion were assessed descriptively according to individual and majority reader data ($\geq 4/7$ and $\geq 5/8$ readers for exercises A and B, respectively). Comparison of lesion frequencies according to the local rheumatologist final diagnostic ascertainment of axSpA was analyzed using the unpaired t-test and chi-square test for continuous and categorical variables,

respectively. Agreement for detection of MRI lesions between central and local readers was assessed descriptively and using the kappa statistic. We calculated the number of patients that were classified differently after central reader detection of active lesions on MRI replaced local readers and after central reader detection of structural lesions on MRI replaced local reader detection of radiographic sacroiliitis for overall fulfillment of the ASAS criteria and for the imaging arm of the criteria.

RESULTS

Spectrum of MRI lesions at baseline and follow up in the ASAS-CC

In exercise A, 199/275 (72.3%) were diagnosed as having axSpA and 131/170 (77.1%) were diagnosed with axSpA at follow up. For MRI Q1, active lesions typical of axSpA were observed by a majority of readers in 43.2% and 44.3% of cases diagnosed with axSpA at baseline and follow up, respectively, as compared to 3.9% and 5.1% diagnosed without axSpA (Table 1). The most frequent lesion was subchondral inflammation, which was observed in 51.3% and 13.2% of cases diagnosed with and without axSpA, respectively. Inflammation at the site of erosion, enthesitis, and joint space fluid were each observed in 5-10% of cases diagnosed as axSpA. The first two lesions were also 100% specific for axSpA. For MRI Q2, structural lesions typical of axSpA were observed in 39.4% and 44.6% of cases diagnosed with axSpA at baseline and follow up, respectively, as compared to 9.7% and 6.5% without axSpA (Table 1). The most frequent lesion was erosion followed by fat lesion. The frequencies of MRI lesions were similar when individual reader observations were analyzed (supplementary Table 1). Most patients with lesions typical of axSpA had a combination of acute and structural lesions with only 4.6% of cases having only acute lesions and 4.6% having only structural lesions typical of axSpA

(supplementary Table 2). There were 13% of cases who had active or structural lesions typical of axSpA by the majority of readers but were diagnosed as not having axSpA at baseline and follow up.

In exercise B, assessment of MRI scans blinded to baseline and follow up time points demonstrated that central reader detection of active lesions typical of axSpA was 100% and 95.2% specific for rheumatologist diagnosis of axSpA, respectively (Table 2). Sensitivity for diagnosis of axSpA was 41% at baseline and 28% at follow up. There was a decrease of 9.3% in the proportion of cases from the entire cohort with active inflammatory lesions typical of axSpA (MRI Q1) from baseline to follow up (p=0.05). Subchondral inflammation was observed in 49% of cases diagnosed as axSpA at baseline and 36% at follow up but also in 4.2% and 14.3% of baseline and follow up scans from cases without axSpA. There were 19 (17.8%) of cases that were started on tumor necrosis factor inhibitor (TNFi) therapy during the course of follow up. Of these cases, 57.9% had a reduction in inflammatory lesions compared to 5.7% of cases not receiving anti-TNF therapy (p<0.001).

Structural lesions typical of axSpA (MRI Q2) were observed in 38.2% and 51.2% of baseline and follow up scans of cases diagnosed with axSpA, respectively. For the entire cohort there was a significant increase of 9.4% (p=0.02) in cases with structural lesions from baseline to follow up, and this was comprised of an increased proportion with a fat lesion and ankylosis (Table 2). Erosion was the structural lesion observed most frequently in axSpA, was more highly discriminatory than any active lesion per follow up diagnostic assessment, and was highly specific, being present in only a single case diagnosed at baseline as non-axSpA, and in no cases diagnosed as non-axSpA at follow up.

In exercise B, MRI was considered indicative of axSpA in 44/108 (40.7%) of cases at baseline and in 43/86 (50.0%) diagnosed as axSpA by the rheumatologist. Change in MRI diagnosis from baseline to follow up assessments was recorded in only 10/108 (9.3%) cases (4 from axSpA to not axSpA, and 6 from not axSpA to axSpA) according to agreement by ≥2 readers (Table 3). Change in MRI diagnosis was recorded in only 3 cases according to a majority of readers (≥5/8). Change in rheumatologist diagnosis was recorded in 9/108 (8.3%) cases, 2 of which had a change in MRI diagnosis.

Local Versus Central Reader Detection of MRI Lesions in the Sacroiliac Joint

The frequency of active lesions reported by local readers (61%) in cases diagnosed with axSpA was greater than for central readers (43.2% and 49.7% for majority (≥4/7) and ≥2 reader data, respectively) (Table 4). This difference was similar for scans limited to cases that attended for follow up evaluation and cases where only data from DICOM scans was analyzed (supplementary Table 3). Structural lesions typical of axSpA were reported by local readers in 44.4% of cases who were diagnosed with axSpA. This compares with 39.5% and 54.9% of cases when assessed by a majority and ≥2 central readers, respectively.

Discordance between central and local readers for detection of active lesions (MRI Q1) was recorded in 46 (17.8%) and 47 (18.2%) of cases according to ≥2 and majority (≥4/7) central reader data, respectively (kappa (95%CI) of 0.64 (0.54-0.73) and 0.62 (0.53-0.72)) (Table 5). With central reading as external standard the false-positive rate for active lesions was 27.4% and 33.3% ('local overcall') for ≥2 and majority reader data, respectively. Reliability between the 7 central readers was higher with a median kappa value of 0.74 and range of 0.63-0.83 for all possible reader pairs (supplementary Table 4). Discordance between central and local readers for detection of structural lesions (MRI Q2) was noted in 66 (30.0%) and 67 (30.5%) of cases according to ≥2 and majority (≥4/7) central

reader data, respectively (kappa (95%CI) of 0.44 (0.32 to 0.55) and 0.38 (0.25 to 0.50)). Local versus central reader discrepancies were less evident when only data from DICOM scans was assessed (Table 5).

Impact of Central versus Local Reader Discrepancies in Detection of Active Lesions Typical of axSpA (MRI Q1) on Classification of Axial SpA

There were 159(63.1%) patients who fulfilled the ASAS axSpA criteria based on local-reading, and 148 (58.7%) and 143 (56.7%) patients based on ≥2 and majority central-reading, respectively (Table 6). A total of 19 (7.5%) and 20 (7.9%) patients who were classified as axSpA after local reading were re-classified as not having axSpA after ≥2 and majority reader central evaluation. Conversely, 8 (3.2%) and 4 (1.6%) cases who were classified as having axSpA after ≥2 and majority reader central evaluation, respectively, would have been re-classified as not having axSpA after local assessment. The numbers were similar when fulfillment of the imaging arm was the primary consideration (irrespective of the clinical arm).

Impact of Replacing Local Reader Detection of Radiographic Sacroiliitis by Central Reader Detection of MRI Structural Lesions (MRI Q2) on classification of axSpA

In total, 120 (55.3%) cases fulfilled the axSpA criteria based on local reading of radiographic sacroiliitis and central reading of active inflammation on MRI. This changed to 125 (57.6%) and 117 (53.9%) of cases after replacement of radiographic sacroiliitis by ≥2 and majority central reader MRI structural lesions, respectively (Table 6). A total of 9 (4.1%) and 4 (1.8%) cases who were classified as not having axSpA were re-classified as having axSpA after replacing radiographic sacroiliitis with ≥2 and majority reader MRI structural lesions, respectively. Conversely, 7 (3.2%) and 8 (3.7%) cases were re-classified as not having axSpA after substitution by

≥2 and majority reader MRI structural lesions, respectively. The numbers were similar when fulfillment of the imaging arm was the primary consideration (irrespective of the clinical arm).

DISCUSSION

This first central reader evaluation of MRI scans from the ASAS-CC study applying consensus definitions for MRI lesions recently reported by ASAS[11] demonstrates several observations of major importance to the interpretation of MRI scans relevant to both diagnosis and classification of axSpA. First, structural lesions occur almost as frequently as active lesions in patients presenting with undiagnosed back pain to a rheumatologist. Second, subchondral bone marrow inflammation may occur in 10-15% of cases diagnosed as non-axSpA while other active lesions such as inflammation in an erosion cavity, capsulitis, and enthesitis are highly specific for axSpA but each occur in only 5-10% of cases. Third, central reader detection of active MRI lesions considered typical of axSpA and erosions was comparatively discriminatory between axSpA and non-axSpA. Fourth, there was relatively little change in the frequencies of active and structural lesions over a mean follow up period of 4.4 years in this cohort of patients who received mainly conservative therapy. Fifth, although clear discrepancy between local and central readers in detection of MRI lesions was evident this had a minor impact on the total number of patients classified as axSpA using the ASAS criteria. Even substitution of radiography with structural lesions detected on T1W MRI by central readers did not materially impact the number of patients classified as having axSpA.

This is the first report that describes the frequencies of the broad spectrum of active and structural MRI lesions according to recently published ASAS definitions in patients presenting to the rheumatologist with undiagnosed back pain. Active or structural lesions typical of axSpA were observed by a majority of central readers in 55% of patients diagnosed by local rheumatologists with axSpA but also in 12.9% of non-axSpA cases suggesting that axSpA may have been under-recognized by local rheumatologists. Subchondral bone marrow edema was observed in about 50% of cases diagnosed with axSpA although the definition of an ASAS positive MRI was met in only 40%. The corresponding frequencies in non-axSpA cases were 13.2% for subchondral BME and 2.6% for an ASAS positive MRI. This is much lower than the 20-40% frequency often cited for an ASAS positive MRI in controls, both healthy and those diagnosed with non-specific back pain, in other cohorts[8-10]. This could be explained by central reader expertise in distinguishing BME lesions suggestive of axSpA versus non-specific findings and also the concomitant presence of structural lesions. It reinforces the importance of contextual interpretation of T1W and fat-suppressed scans for diagnostic interpretation of MRI scans previously emphasized in an ASAS consensus exercise[3].

The revised ASAS definition of erosion was highly discriminatory and was detected in fewer than 10% of non-axSpA cases in both reading exercises although sensitivity of 30-40% was lower than the 50-60% reported in some previous studies of MRI in axSpA[17,18]. This may reflect differences in the definition of erosion. The first ASAS publication on MRI definitions in the SIJ cited only the requirement for a bony defect at the joint margin without specifying alteration in the signal from adjacent bone marrow[2]. The revised ASAS definition stipulates both a bony defect as well as loss of the adjacent bright marrow signal observed on a T1W sequence[11]. Fat lesion with the distinct features of axSpA, namely a sharp border and homogeneous increased T1W signal, was also

discriminatory but sensitivity was less than for erosion at 25-30% while specificity was 90-95%, which was comparable to findings in other cohorts of early SpA that applied a similar definition[18-20].

We observed local reader overcall in the range of 25-35% when using the central reader assessment as external standard raising the possibility of diagnostic overcall. However, this had little impact on the number of patients classified with axSpA since patients could still be classified as axSpA by the clinical arm. Conversely, local readers detected fewer structural lesions than central readers. This could reflect the requirement for good quality T1W images so that the more complex structural lesions can be adequately visualized as the discrepancy was less evident when DICOM images were assessed. Nevertheless, substitution of radiographic sacroiliitis by structural lesions on MRI detected by central readers had a minor impact on the number of patients classified as axSpA. This may not be surprising as most patients with structural lesions also had active lesions typical of axSpA. Similar observations have been reported in two early axSpA cohorts[21,22].

There are some limitations of our data. It has been over a decade since the local MRI reads were conducted and it is possible that discrepancy might be less evident if the study was a contemporary comparison. However, recent clinical trials of non-radiographic axSpA[23,24] have reported similar symptom duration prior to diagnosis as noted for the ASAS-CC suggesting that diagnostic delay has not changed a great deal over the past decade and that imaging findings may therefore not be different. Interpretation of local reader data is compromised by lack of data recorded in the ASAS-CC CRF as to which types of MRI lesion were observed. The assessment of structural lesions, especially erosion, is increasingly being performed using MRI sequences that can enhance the contrast between the joint space and bone[25].

In conclusion, our analysis of MRI scans from patients referred to rheumatologists with undiagnosed back pain demonstrates the importance of both active and structural lesions in diagnostic decision making and the importance of educational initiatives aimed at enhancing interpretation of these lesions. These data also provide reassurance that the ASAS classification criteria have performance characteristics that may circumvent the limitations posed by the widespread lack of reader expertise in the interpretation of MRI scans. However, our study design was retrospective in nature and could not assess the impact of reader discrepancy on diagnostic ascertainment. Consequently, the performance of the ASAS criteria will require further testing in a study design where the impact of differences in interpretation of imaging on diagnostic ascertainment can be addressed.

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Patient and Public Involvement

This consensus-based initiative was done without patient involvement. Patients were not invited to comment on the study design of the MRI reading exercise and were not consulted to interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

Competing Interests

The authors declare no competing interests

Contributorship

All authors contributed to the design of the study, review of study data, drafting of the final manuscript, and agreed to the final version of the manuscript.

Ethical approval

The study did not require ethical approval.

Data sharing statement

The MRI scans and data from the readings reported in this study can be made available after submission of a study proposal to the ASAS MRI-WG.

Table 1. Frequencies of active and structural lesions in the SIJ of baseline MRI scans at the level of the majority of readers (≥4/7 reader agreement for the same case) according to local rheumatologist diagnosis of AxSpA (present yes/no) at baseline and follow up.

Baseline variables	Local Rheumatologist Diagnosis					
	Baseline			Follow Up		
	Axial SpA=Yes (n=199)	Axial SpA=No (n=76)	P value	Axial SpA=Yes (n=131)	Axial SpA=No (n=39)	P value
Mean age	30.3 (9.4)	33.6 (10.2)	0.016	30.1 (9.8)	35.6 (8.4)	0.001
Mean symptom duration	5.0 (5.8)	6.1 (7.4)	0.25	5.3 (6.1)	6.6 (7.0)	0.34
Males, %	109 (54.8%)	30 (39.5%)	0.024	77 (58.8%)	13 (33.3%)	0.005
Mean No. of SpA features	2.8 (1.3)	1.3 (1.1)	<0.0001	2.9 (1.4)	1.2 (0.9)	<0.0001
B27 positive, %	126 (63.3%)	18 (23.7%)	<0.0001	93 (71.0%)	6 (15.4%)	<0.0001
Elevated CRP, %	80 (40.2%)	10 (13.2%)	<0.0001	51 (38.9%)	4 (10.3%)	0.0008
Definite radiographic sacroiliitis, %	36 (18.4%)	1 (1.4%)	0.0003	22 (17.3%)	1 (2.6%)	0.02
Active MRI Lesion Variable, Number (%) of cases						
Active lesions typical of axSpA (MRI Q1)	86 (43.2%)	3 (3.9%)	<0.001	58 (44.3%)	2 (5.1%)	<0.001

Active lesions typical of axSpA and meets ASAS definition for positive MRI	79 (39.7%)	2 (2.6%)	<0.001	52 (39.7%)	2 (5.1%)	<0.001
Subchondral inflammation (any)	102 (51.3%)	10 (13.2%)	<0.001	65 (49.6%)	7 (17.9%)	<0.001
Inflammation at the site of erosion	20 (7.2%)	0 (0%)	<0.001	12 (9.2%)	0 (0%)	0.07
Capsulitis	8 (2.9%)	0 (0%)	0.11	5 (3.8%)	0 (0%)	0.59
Joint space fluid	16 (8.0%)	2 (2.6%)	0.17	10 (7.6%)	0 (0%)	0.12
Enthesitis	14 (5.0%)	0 (0%)	0.013	9 (6.9%)	0 (0%)	0.12
BME score, Mean (SD)†	6.3 (12.0)	0.4 (0.6)	<0.001	6.0 (12.5)	0.5(0.8)	<0.001
MRI Structural Lesion Variable, Number (%) of cases						
	Axial SpA=Yes (n=175)	**Axial SpA=No (n=62)**	**p-value**	**Axial SpA=Yes (n=112)**	**Axial SpA=No (n=31)**	**p-value**
Structural lesions typical of axSpA (MRI Q2)	69 (39.4%)	6 (9.7%)	<0.001	50 (44.6%)	2 (6.5%)	<0.001
Subchondral sclerosis	32 (18.3%)	8 (12.9%)	0.43	20 (17.9%)	5 (16.1%)	1.000
Erosion	64 (36.6%)	3 (4.8%)	<0.001	45 (40.2%)	2 (6.5%)	<0.001
Fat lesion	44 (25.1%)	3 (4.8%)	<0.001	28 (25%)	3 (9.9%)	0.085

Bone bud	1 (0.6%)	0 (0%)	1.00	1 (0.9%)	0 (0%)	1.00
Fat metaplasia in an erosion cavity	16 (9.1%)	2 (3.2%)	0.17	14 (12.5%)	1 (3.3%)	0.19
Ankylosis	6 (3.4%)	0 (0%)	0.34	5 (4.5%)	0 (0%)	0.59
Erosion score, mean (SD)*	3.1 (5.0)	0.8 (2.5)	<0.001	3.6 (5.6)	0.6 (1.7)	<0.001
Fat lesion score, mean (SD)*	3.4 (6.4)	0.7 (4.0)	0.003	4.2 (7.6)	0.2(0.6)	<0.001
Sclerosis score, mean (SD)*	2.0 (4.3)	1.9 (6.2)	0.95	1.9 (4.2)	3.3 (9.9)	0.61
Fat metaplasia in an erosion cavity*	0.7 (4.1)	0.0 (0.1)	0.11	1.0 (5.2)	0.0 (0.0)	0.12
Ankylosis score*	0.1 (0.2)	0.05 (0.2)	0.55	0.1 (0.2)	0.0 (0.0)	0.002

† Cases with detailed scoring per SIJ quadrant/halve (mean (SD) available: axSpA at baseline Yes, n=109 No, n=49; axSpA at follow up Yes, n=69 No, n=17

*Cases with detailed scoring per SIJ quadrant/halve (mean (SD) available: axSpA at baseline Yes, n=102 No, n=44; axSpA at follow up Yes, n=63 No, n=16

Table 2. Frequencies of active and structural lesions in the SIJ of baseline and follow up MRI scans at the level of the majority of readers (≥5/8 reader agreement for the same case) according to local rheumatologist diagnosis of AxSpA (present yes/no) at baseline and follow up.

	Local Rheumatologist Diagnosis							
	Baseline				Follow Up			
	All Cases (n=108)	Axial SpA=Yes (n=86)	Axial SpA=No (n=22)	P-value	All Cases (n=108)	Axial SpA=Yes (n=87)	Axial SpA=No (n=21)	P-value
MRI indicative of axSpA according to central readers	44 (40.7%)	43 (50.0%)	1(4.5%)	<0.001	47 (43.9%)	46 (52.9%)	1(4.8%)	<0.001
Active MRI Lesion Variable, Number (%) of cases								
Cases with global assessment of active lesions	All Cases (n=107)	Axial SpA=Yes (n=85)	Axial SpA=No (n=22)	P-value	All Cases (n=107)	Axial SpA=Yes (n=86)	Axial SpA=No (n=21)	P-value
Active lesions typical of axSpA	35 (32.7%)	35 (41.2%)	0 (0%)	<0.001	25 (23.4%)	24 (27.9%)	1 (4.8%)	0.023

	All Cases (n=80)	Axial SpA=Yes (n=64)	Axial SpA=No (n=16)	P-value	All Cases (n=66)	Axial SpA=Yes (n=66)	Axial SpA=No (n=14)	P value
Active lesions typical of axSpA and meets ASAS definition for positive MRI	35 (32.7%)	35 (41.2%)	0 (0%)	<0.001	24 (22.4%)	23 (26.7%)	1 (4.8%)	0.039
Subchondral inflammation	43 (40.2%)	42 (49.4%)	1 (4.5%)	<0.001	34 (31.8%)	31 (36.0%)	3 (14.3%)	0.056
Inflammation at the site of erosion	3 (2.8%)	3 (3.5%)	0 (0%)	1.00	2 (1.9%)	2 (2.3%)	0 (0%)	1.00
Capsulitis	3 (2.8%)	3 (3.5%)	0 (0%)	1.00	0 (0%)	0 (0%)	0 (0%)	1.00
Joint space fluid	12 (11.2%)	12 (14.1%)	0 (0%)	0.121	4 (3.7%)	4 (4.7%)	0 (0%)	0.58
Enthesitis	2 (1.9%)	2 (2.4%)	0 (0%)	1.00	2 (1.9%)	2 (2.3%)	0 (0%)	1.00
Cases with Detailed Scoring of Active Lesions	**All Cases (n=80)**	**Axial SpA=Yes (n=64)**	**Axial SpA=No (n=16)**	**P-value**	**All Cases (n=66)**	**Axial SpA=Yes (n=66)**	**Axial SpA=No (n=14)**	**P value**
BME score, Mean (SD)	4.6 (8.8)	5.8 (9.5)	0.4 (0.5)	<0.001	3.4 (7.5)	4.0 (8.1)	0.8 (2.1)	0.007
Structural MRI Lesion Variable, Number (%) of cases**								

Cases with global assessment of structural lesions	All n=85	Axial SpA=Yes (n=68)	Axial SpA=No (n=17)	P-value	All n=85	Axial SpA=Yes (n=70)	Axial SpA=No (n=15)	P-value
Structural lesions typical of axSpA	28 (32.9%)	26 (38.2%)	2 (11.8%)	0.039	36 (42.3%)	36 (51.4%)	0 (0%)	<0.001
Subchondral sclerosis	8 (9.4%)	6 (8.8%)	2 (11.8%)	0.66	5 (5.9%)	5 (7.1%)	0 (0%)	0.58
Erosion	24 (28.2%)	23 (33.8%)	1 (5.9%)	0.032	24 (28.2%)	24 (34.3%)	0 (0%)	0.005
Fat lesion	21 (24.7%)	18 (26.5%)	3 (17.6%)	0.55	23 (27.1%)	22 (31.4%)	1 (6.7%)	0.059
Bone bud	1 (1.2%)	1 (1.5%)	0 (0%)	1.00	0 (0%)	0 (0%)	0 (0%)	1.00
Fat metaplasia in an erosion cavity (FM-EC)	5 (5.9%)	4 (5.9%)	1 (5.9%)	1.00	5 (5.9%)	5 (7.1%)	0 (0%)	0.58
Ankylosis	3 (3.5%)	3 (4.4%)	0 (0%)	1.00	5 (5.9%)	5 (7.1%)	0 (0%)	0.58
Cases with Detailed Scoring of Structural Lesions	**All Cases (n=49)**	Axial SpA=Yes (n=39)	Axial SpA=No (n=10)	**P-value**	**All Cases (n=49)**	Axial SpA=Yes (n=41)	Axial SpA=No (n=8)	**P-value**
Erosion score, mean (SD)	2.3 (4.2)	2.6 (4.3)	1.2 (3.8)	0.37	2.3 (5.3)	2.8 (5.8)	0.1 (0.2)	0.004

Fat lesion score, mean (SD)	4.0 (7.7)	4.3 (7.5)	2.7 (8.6)	0.57	4.5 (7.8)	5.4 (8.3)	0.2 (0.3)	<0.001
Sclerosis score, mean (SD)	1.0 (2.9)	1.1 (3.2)	0.6 (1.3)	0.43	0.9 (2.8)	1.1 (3.0)	0.0 (0.0)	0.032
Fat metaplasia in an erosion cavity (FM-EC)	0.3 (0.8)	0.3 (0.9)	0.3 (0.8)	0.78	0.6 (1.5)	0.7 (1.6)	0.0 (0.0)	0.008
Ankylosis score	0.7 (4.5)	0.9 (5.1)	0.0 (0.1)	0.30	0.9 (4.5)	1.05 (4.89)	0.0 (0.0)	0.18

Table 3. MRI considered indicative of axSpA at baseline and follow up at the level of any 2 central readers or the majority of central readers (≥5/8 reader agreement for the same case) according to local rheumatologist diagnosis of axSpA (present yes/no) at baseline and follow up.

Rheumatologist's diagnosis	MRI indicative of axSpA (any 2 readers)			
	Yes at baseline and yes at follow up (N =48)	Yes at baseline and no at follow up (N = 4)	No at baseline and yes at follow up (N =6)	No at baseline and No at follow up (N = 50)
SpA yes at baseline and follow up (N= 82)	46 (56.1%)	2 (2.4%)	4 (4.9%)	30 (36.6%)
SpA no at baseline and yes at follow up (N =5)	1 (20%)	0 (0%)	1 (20%)	3 (60%)
SpA yes at baseline and no at follow up (N = 4)	1 (25%)	1 (25%)	0 (0%)	2 (50%)
SpA no at baseline and no at follow up (N =17)	0 (0%)	1 (5.9%)	1 (5.9%)	15 (88.2%)
	MRI indicative of axSpA (majority (≥5) of readers)			

Rheumatologist's diagnosis	Yes at baseline and yes at follow up (N =43)	Yes at baseline and no at follow up (N =1)	No at baseline and yes at follow up (N = 4)	No at baseline and No at follow up (N = 60)
SpA yes at baseline and follow up (N =82)	42 (51.2%)	1 (1.2%)	2 (2.4%)	37 (61.7%)
SpA no at baseline and yes at follow up (N = 5)	1 (20%)	0 (0%)	1 (20%)	3 (60%)
SpA yes at baseline and no at follow up (N =4)	0 (0%)	0 (0%)	0 (0%)	4 (100%)
SpA no at baseline and no at follow up (N =17)	0 (0%)	0 (0%)	1 (5.9%)	16 (94.1%)

Table 4. Central and local MRI reader assessment of active and structural MRI lesions in the SIJ according to diagnostic ascertainment by the local physician at baseline and follow up in the ASAS classification study.

Reader	MRI Lesion Type	Local Rheumatologist Diagnosis at baseline		P value	Local Rheumatologist Diagnosis at follow up		P value
		AxSpA (n=187)	Not AxSpA (n=70)		AxSpA (n=122)	Not AxSpA (n=35)	
ACTIVE LESIONS							
Local	Active lesions typical of axSpA	114 (61.0%)	3 (4.3%)	<0.001	75 (61.5%)	5 (14.3%)	<0.001
Central (≥4/7 reader agreement)	Active lesions typical of axSpA	83 (43.2%)	3 (4.3%)	<0.001	56 (45.9%)	2 (5.7%)	<0.001
Central (≥4/7 reader agreement)	ASAS MRI positive	76 (40.6%)	2 (2.9%)	<0.001	50 (41%)	2 (5.7%)	<0.001

		AxSpA	Not AxSpA		AxSpA	Not AxSpA	
Central (any 2 readers)	Active lesions typical of axSpA	93 (49.7%)	6 (8.6%)	<0.001	60 (49.2%)	5 (14.3%)	<0.001
Central (any 2 readers)	ASAS MRI positive	89 (47.6%)	5 (7.1%)	<0.001	57 (46.7%)	4 (11.4%)	<0.001
STRUCTURAL LESIONS							
		AxSpA (n=162)	Not AxSpA (n=58)		AxSpA (n=103)	Not AxSpA (n=28)	
Local	Structural lesions typical of axSpA	72 (44.4%)	3 (5.2%)	<0.001	44 (42.7%)	4 (14.3%)	0.007
Central (any 2 readers)	Structural lesions typical of axSpA	89 (54.9%)	10 (17.2%)	<0.001	56 (54.4%)	6 (21.4%)	0.003
Central (≥4/7 reader agreement)	Structural lesions typical of axSpA	64 (39.5%)	6 (10.3%)	<0.001	46 (44.7%)	2 (7.1%)	<0.001

Table 5. Agreement between central and local readers for active (MRI Q1) and structural (MRI Q2) lesions typical for axSpA observed on all available MRI scans from patients in the ASAS classification cohort.

Local Reader		Central Readers (All MRI scans) †				Central Readers (DICOM MRI scans)[#]			
		Active lesion (≥2 readers)		Active Lesion (≥4 readers)		Active lesion (≥2 readers)		Active Lesion (≥4 readers)	
		Yes	No	Yes	No	Yes	No	Yes	No
Active lesion	Yes	85	32	78	39	42	17	37	22
	No	14	127	8	133	11	90	7	94
Kappa (95% CI)		0.64 (0.54-0.73)		0.62 (0.53-0.72)		0.62 (0.49-0.74)		0.59 (0.46-0.72)	
		Structural lesion (≥2 readers)		Structural Lesion (≥4 readers)		Structural lesion (≥2 readers)		Structural Lesion (≥4 readers)	
Structural lesion	Yes	58	25	43	40	29	9	21	17
	No	41	130	27	144	25	75	14	86
Kappa (95% CI)		0.44 (0.32 to 0.55)		0.38 (0.25 to 0.50)		0.62 (0.49-0.74)		0.59 (0.46-0.72)	

† Total with MRI data for assessment of active lesions = 258, total with MRI data for assessment of structural lesions = 220

Total with MRI data for assessment of active lesions = 160, total with MRI data for assessment of structural lesions = 138

Table 6. Impact of reader discrepancy (central versus local) for detection of active SIJ lesions on MRI and replacement of radiographs by MRI structural lesions on classification of axial SpA in the ASAS classification cohort.

Impact of Central Vs. Local Reader SIJ MRI Inflammation Assessment on SpA Classification in cases with all clinical, radiographic, and central and local MRI inflammation data available (n=252)				
MRI assessment used	**Overall SpA Classification=Yes after MRI assessment N(%)**	**Overall SpA Classification=No after MRI assessment N(%)**	**Imaging Arm SpA Classification=Yes after MRI assessment N(%)**	**Imaging Arm SpA Classification=No after MRI assessment N(%)**
Local Reader SIJ MRI Inflammation positive	159 (63.1%)	93 (36.9%)	126 (50%)	126 (50%)
≥2 Central Reader SIJ MRI Inflammation Assessment positive	148 (58.7%)	104 (41.3%)	111 (44.0%)	141 (56.0%)
Majority Central Reader (≥4/7) SIJ MRI inflammation Assessment positive	143 (56.7%)	109 (43.2%)	102 (40.5%)	150 (59.5%)

Impact of Replacement of Radiographic Sacroilitis by MRI Structural Lesions on SpA Classification in cases with all clinical, radiographic, and central and local MRI inflammation data available (n=217)				
Central reader MRI Inflammation Positive*	120 (55.3%)	97 (44.7%)	83(38.2%)	134 (61.8%)
Replace Radiographic Sacroiliitis with Central reader (≥2) MRI Structural Positive**	125 (57.6%)	92 (42.4%)	100 (46.1%)	117 (53.9%)
Replace Radiographic Sacroiliitis with Central Reader (≥4/7) MRI Structural Positive**	117 (53.9%)	100 (46.1%)	85 (39.2%)	132 (60.8%)

*Positive imaging for classification is defined by either local reader positive for radiographic sacroiliitis or majority of central readers positive for MRI inflammation

**Positive imaging for classification is defined by either central readers positive for MRI structural lesions or majority of central readers positive for MRI inflammation

KEY MESSAGES

What is already known?

- MRI of the sacroiliac joints is a crucially important evaluation tool for patients presenting with undiagnosed back pain and suspicion of axial spondyloarthritis although there is limited expertise in image interpretation which may compromise accurate diagnosis and classification of this disease.

What does this study add?

- The Assessments in SpondyloArthritis international Society MRI Working Group reports an expert reader assessment of MRI scans from patients presenting to rheumatologists with undiagnosed back pain and characterizes MRI lesions that are highly specific for a diagnosis of axSpA

- This central reader assessment demonstrates substantial differences in imaging interpretation with local readers. However, this does not affect the number of patients classified as having this disease because the clinical arm of the criteria compensates for differences in disease assignment by the imaging arm.

How might this impact on clinical practice or future developments?

- This report demonstrates the importance of both active and structural MRI lesions in diagnostic decision making and the importance of educational initiatives aimed at enhancing interpretation of these lesions. These data also provide reassurance

that the ASAS classification criteria have performance characteristics that may circumvent the limitations posed by the widespread lack of reader expertise in the interpretation of MRI scans.