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ORIGINAL RESEARCH

Which definitions for MRI sacroiliac joint lesions predict the diagnosis of early axial spondyloarthritis best? A 2-year follow-up in the SPACE cohort

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To cite: de Bruin LJE, Marques ML, van Lunteren M, *et al*. Which definitions for MRI sacroiliac joint lesions predict the diagnosis of early axial spondyloarthritis best? A 2-year follow-up in the SPACE cohort. *RMD Open* 2026;**12**:e006425. doi:10.1136/rmdopen-2025-006425

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/rmdopen-2025-006425).

Received 9 October 2025
Accepted 4 February 2026

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ABSTRACT

Background The Leiden group and the Assessment of Spondyloarthritis International Society (ASAS)-MRI study group have proposed definitions for structural (SL) and active (AL) lesions typical for axial spondyloarthritis (axSpA) on MRI of the sacroiliac joints (MRI-SIJ).

Objectives To analyse the predictive validity of proposed SL and AL MRI-SIJ definitions in early axSpA and compare proposed AL with the current ASAS-MRI-SIJ+ definition.

Methods Patients with chronic back pain (≤2 years) from the Spondyloarthritis Caught Early cohort were diagnosed as axSpA or non-axSpA after 2 years follow-up. Three central readers scored baseline MRI-SIJ for SL (erosions and fat lesions) and AL (bone marrow oedema). Validation required specificity and positive predictive value (PPV) ≥95%.

Results Among 643 patients (52% axSpA), SL were infrequent (2%–14%). All Leiden and most MRI study group SL definitions met the validation threshold, except for 'erosion in ≥2 consecutive slices' and the overall MRI study group definition (PPV <95%). The ASAS-MRI-SIJ+ definition had a higher sensitivity than the MRI study group AL (40% vs 31%) with similar specificity (98% vs 99%). Combining SL and AL, the Leiden SL with ASAS-MRI-SIJ+ definition met the validation threshold with the highest sensitivity (46%). SL increased sensitivity beyond AL alone by 6%–11%.

Conclusions The ASAS-MRI-SIJ+ definition outperforms the MRI study group AL. The Leiden SL combined with the ASAS-MRI-SIJ+ definition is validated, most sensitive and feasible as it simultaneously upholds lesion quantification and detection precision, making it the preferred approach. Nevertheless, SL were uncommon in early axSpA, contributing only marginally beyond AL definitions in early diagnosis.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In 2016, the Leiden group proposed definitions for structural lesions of the MRI of the sacroiliac joints (MRI-SIJ), which have never been validated against the rheumatologist's diagnosis.

⇒ In 2021, the proposed Assessment of Spondyloarthritis International Society (ASAS)-MRI study group definitions for active and structural lesions of the MRI-SIJ in a population with a mean symptom duration of 7 years have not been validated in an early disease cohort, and the active lesion definitions used by the MRI study group have never been compared with the ASAS definition of a positive MRI-SIJ.

WHAT THIS STUDY ADDS

⇒ MRI-SIJ lesions by Leiden and the ASAS-MRI study group were validated in early axial spondyloarthritis (axSpA).

⇒ When evaluating both structural and active lesions, the combination of the Leiden structural lesion definition and the ASAS definition for a positive MRI-SIJ performs best, making it the preferred approach, although structural lesions add little sensitivity beyond that of active lesions alone in early axSpA.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our results are relevant for daily clinical practice, where both active and structural lesions can contribute to identifying the Gestalt of axSpA.

INTRODUCTION

Axial spondyloarthritis (axSpA) is an inflammatory disease, with sacroiliitis being one of its earliest manifestations. Magnetic resonance imaging (MRI) can detect sacroiliitis from the early stages of the disease.[1] The Assessment of SpondyloArthritis international Society (ASAS) definition of a positive sacroiliac joint (SIJ) MRI (ASAS-MRI-SIJ+), introduced in 2009 and updated in 2016, is relatively simple to apply but has limited specificity, as MRI-SIJ of healthy individuals have

been reported to meet this definition.[2–4] This definition focuses solely on active lesions without requiring structural lesions, but includes a qualitative aspect in addition to the quantitative definition.[5] It is debated whether incorporating structural lesions could enhance the ASAS-MRI-SIJ+ definition's performance to identify patients with axSpA.[2 6] The inclusion of structural lesions into the definition could increase its sensitivity, for instance, by capturing patients with axSpA who no longer exhibit active lesions at the time of MRI.

In 2016, definitions for structural lesions of the MRI-SIJ were proposed by the Leiden group, which showed high specificity in early axSpA.[7] A lesion was considered present if visible on ≥2 consecutive slices. Cut-offs for the number of lesions were set at three fatty lesions, three erosions or the combined total of five fatty lesions and/or erosions for high specificity.[7] In 2021, the ASAS-MRI study group (MRI study group) proposed two definitions for active lesions and four definitions for structural lesions on MRI-SIJ typical for axSpA, aiming for high specificity and positive predictive value (PPV; both ≥95%) for the rheumatologist's diagnosis of axSpA.[8] These definitions were based on the number of affected quadrants or consecutive slices within the same quadrants.

Both the Leiden and MRI study group definitions provided valuable insight into the predictive validity of MRI lesions typical of axSpA. However, the Leiden definitions have never been tested against the rheumatologist's diagnosis. Additionally, the MRI study group definitions were developed from a cohort with a mean symptom duration of seven years and have not been validated in early disease cohorts.

Intriguingly, the two proposed and then combined active lesion definitions by the MRI study group have never been compared with the ASAS-MRI-SIJ+ definition. Given the widespread use of the ASAS-MRI-SIJ+ definition, any potential replacement should be preceded by a formal comparison. To potentially use MRI lesions typical of axSpA for diagnostic purposes, further validation of MRI lesion definitions is needed in patients with suspected axSpA and no definite diagnosis. Besides the ASAS cohort, in which the proposed MRI study group definitions were developed, an appropriate cohort for this analysis is the Spondyloarthritis Caught Early (SPACE) cohort.[9] By including patients with chronic back pain of ≤2 years, an analysis in SPACE allows testing the predictive validity of the proposed definitions in a cohort of patients with suspicion of early axSpA.[10] Here, we analyse the predictive validity of existing active and structural MRI-SIJ lesion definitions for axSpA using the 2-year diagnosis as outcome. Additionally, we compare the existing definition of ASAS-MRI-SIJ+ with the newly proposed combined active lesion definition from the MRI study group. Finally, we evaluate the additional diagnostic value of structural lesions to that of active lesions.

METHODS

Patients

The present study used baseline and 2-year follow-up data from the SPACE inception cohort. Details of the SPACE cohort were previously described.[9 11] Briefly, the patients included were ≥16 years old with chronic back pain of unknown origin lasting 3 months to 2 years, with an onset before the age of 45 years. Eligibility for follow-up required ≥1 major or ≥2 minor SpA features at baseline.[11] Over a 2-year follow-up, clinical, laboratory and imaging information was collected as part of the visits. After 2 years of follow-up, rheumatologists diagnosed patients as either chronic back pain due to axSpA (axSpA) or not due to axSpA (non-axSpA) based on present SpA features, including imaging findings assessed through local readings.[11]

Diagnoses of axSpA and non-axSpA were categorised as 'definite', 'most likely' or 'possible' based on the level of confidence (LoC), with diagnoses further evaluated on consistency in the last two available visits, if LoC was below 7.[11] Only patients with a 'definite' (LoC of ≥7) or 'most likely' diagnosis (LoC <7 and consistent diagnosis) were included in this study and patients with a 'possible' diagnosis (LoC <7 and inconsistent diagnosis) of axSpA and non-axSpA were excluded (online supplemental figure S1). The 2-year diagnosis by the rheumatologist was then dichotomised into axSpA or non-axSpA and used as the main outcome of this analysis. For the present analysis, the SPACE database was locked on 20 July 2023.

MRI of the sacroiliac joints

The MRI-SIJ were performed using a 1.5T machine, with coronal oblique Short Tau Inversion Recovery (TR2500/TE60, acquisition matrix 304×240) and T1-weighted Turbo Spin-Echo (TR550/TE10, acquisition matrix 320×256) sequences, a field of view of 320×320 mm and a slice thickness of 4 mm. Baseline MRI-SIJ was scored in two reading rounds, each with three trained and well-calibrated central readers independently scoring both sequences simultaneously, while being blinded to clinical and other imaging data. Prior to the reading assessment, readers underwent a calibration procedure to standardise reading methodology and to ensure consistency. In each reading round, bone marrow oedema (BME), erosions and fat lesions were scored. Data were excluded if unavailable for ≥2 readers, or when data were unavailable for BME, erosions and fat lesions. Per the reading round, a consensus was defined when at least two out of three readers agreed on the presence or absence of lesions at the quadrant and slice level. Similarly, consensus was defined for the ASAS-MRI-SIJ+ definition.[5] For both consensus evaluations, the second reading round was supplemented with consensus scores from the first reading round to maximise sample size.

Definitions of lesions on MRI of the sacroiliac joints

MRI-SIJ active (BME) and structural (erosions and fat lesions) lesions were assessed as defined by Leiden

(2016) and the ASAS-MRI study group (2021). A schematic representation of each of the lesions is depicted in figure 1.

Individual Leiden definitions for structural lesions

The Leiden definitions for erosions and fat lesions are based on a modified version of the Spondyloarthritis Research Consortium of Canada Structural Sacroiliac joint Score (SPARCC SSS).[7 12] Lesions are considered present only if visible on two consecutive slices allowing five possible combinations of consecutive slices per quadrant and SIJ, which results in a possible total of 40 lesions (figure 1A,B). Leiden proposed three definitions based on high specificity: ≥3 erosions, ≥3 fat lesions and ≥5 fat lesions and/or erosions.[7]

Individual ASAS-MRI study group definitions for active and structural lesions

The MRI study group defined lesions by the number of affected quadrants (a maximum of eight quadrants) or the number of affected consecutive slices.[8] Their proposed definitions include ≥3 quadrants affected by erosions, ≥2 consecutive slices affected by erosions, ≥5 quadrants affected by fat lesions and ≥3 consecutive slices affected by fat lesions.

Besides structural lesion definitions, the MRI study group proposed two definitions for active lesions: ≥4 quadrants affected by BME and ≥2 consecutive slices affected by BME.

(Overall) definitions for active lesions

The ASAS-MRI-SIJ+ definition requires the following features: BME clearly present and located in a typical anatomical area (subchondral bone) and the MRI appearance must be highly suggestive of SpA.[5] To compare with the ASAS-MRI-SIJ+ definition, the proposed MRI study group active lesions were combined into an overall definition for active lesions: ≥4 quadrants and/or ≥2 consecutive slices affected by BME. Although there are other lesions that can indicate signs of activity (eg, capsulitis, enthesitis, among others), we have only considered BME in the active lesions category, as this is the lesion type that is also considered to define a positive MRI according to the ASAS-MRI-SIJ definition. An overview of the overall lesion definitions is presented in figure 2.

Overall definitions of structural lesions and combined definitions for active and structural lesions

Similarly, the proposed structural lesion definitions were combined (figure 2). The overall Leiden structural lesion definition was positive if any of the earlier described individually proposed Leiden structural lesions were present. The same was applicable to the MRI study group. The overall definitions were used to evaluate the additional diagnostic value of structural lesions to that of active lesions.

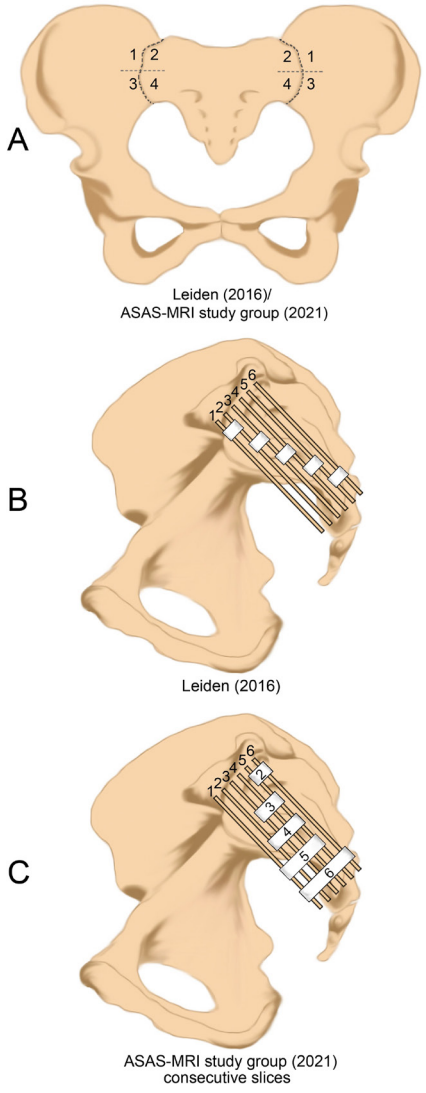

Figure 1 Visual representation of the quantification and extent of lesion definitions proposed by Leiden and ASAS-MRI study group, including quadrants and sagittal slices used for scoring lesions in the SIJ. (A) Frontal perspective presenting the individual quadrants per SIJ used by both the Leiden and the ASAS-MRI study group. (B) Sagittal view illustrating an SIJ with five rectangles, each corresponding to a pair of two consecutive slices. (C) Sagittal perspective of an SIJ with rectangles illustrating five variations in the number of consecutive slices. Leiden defined a structural lesion only when identified in two consecutive slices within the same quadrant (A).[7] Per structural lesion, there are five possible positions within one quadrant, based on the number of consecutive slices (B). The proposed definitions by Leiden are the number of lesions present across both SIJ. Therefore, the total possible number of lesions is 40 (5 possible lesions×4 quadrants×2 SIJ). The ASAS-MRI study group proposed definitions in two categories.[8] One category is the number of quadrants (A) affected (0–8 quadrants: 4 quadrantsx2 SIJ) by either inflammatory or structural lesions regardless of slice location or number of consecutive slices. The second category is the number of consecutive slices (C) affected (2–6 consecutive slices) by either inflammatory or structural lesions within the same quadrant. ASAS, Assessment of Spondyloarthritis international Society; MRI, magnetic resonance imaging; SIJ, sacroiliac joint(s).

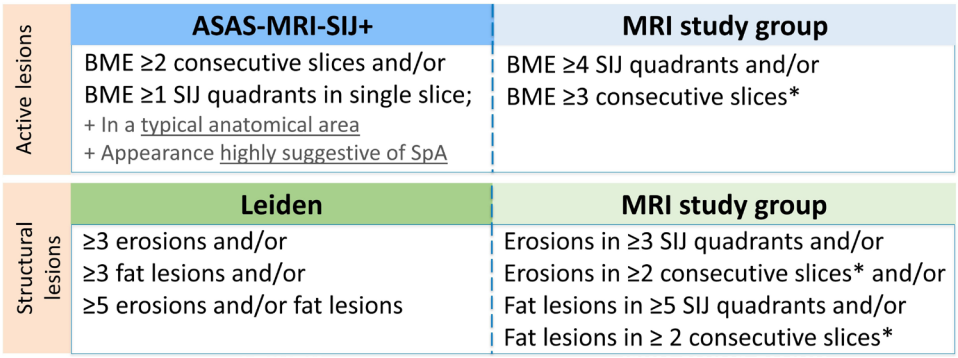

Figure 2 Overview of the MRI-SIJ lesion definitions. All lesions are characteristic of axSpA and in typical anatomic location. The Leiden definitions require lesions to be present in at least two consecutive slices and were based on the modified SPARCC SSS. *Consecutive slices are irrespective of quadrant location. ASAS, Assessment of SpondyloArthritis international Society; axSpA, axial spondyloarthritis; BME, bone marrow oedema; MRI, magnetic resonance imaging; SIJ, sacroiliac joint(s); SPARCC SSS, Spondyloarthritis Research Consortium of Canada Structural Sacroiliac joint Score.

Data analysis

First, for each MRI-SIJ definition (individual lesions and overall lesion definitions), the number of patients fulfilling that definition was calculated. To assess the predictive validity of each of the MRI-SIJ definitions (predictor), sensitivity, specificity, PPV and negative predictive values (NPVs) were calculated using the 2-year axSpA/non-axSpA diagnosis as the outcome. Definitions were considered validated within the SPACE cohort if a combination of specificity ≥95% and PPV ≥95% was achieved, following the methodology outlined by the MRI study group.[8]

Subsequently, subgroup analyses were performed for sex, HLA-B27 status and their combination. Because part of the population has been included in the study describing the development of the Leiden structural lesions, a sensitivity analysis was performed only in the patients who were not part of the first analysis. Next, sensitivity analyses were performed for each reading round, including the complete reading rounds and only the overlapping patients between reading rounds. Furthermore, definitions were assessed for the individual readers of the second reading round.

Finally, the predictive validity was assessed for different combinations of structural and active lesions. An overview of all performed data analyses is shown in online supplemental figure S1.

RESULTS

A total of 643 patients were included in the main analysis, with a mean age of 30 (SD 8) years, 39% males and a mean symptom duration of 13 (SD 7) months (table 1, online supplemental figure S1). There were 335 (52%) patients with axSpA and 308 (48%) patients with non-axSpA. Online supplemental table S1 presents the descriptive statistics of the individual readers per type of lesion.

Individual lesions

Table 2 shows the performance of the proposed definitions for individual structural and active lesions. All individual Leiden and MRI study group structural lesion definitions showed a low frequency of fulfilment, ranging from 2% to 9% of all patients. In general, definitions had low sensitivity and NPV, but high specificity and PPV. All structural lesion definitions proposed by Leiden met the threshold of specificity and PPV ≥95% and were therefore considered validated. Most of the structural lesion definitions proposed by the MRI study group were considered validated. Only the definition of ≥2 consecutive slices affected by erosions did not meet the threshold (specificity 98.4% and PPV 91.2%). The active lesion definitions proposed by the MRI study group were also validated, and active lesions were more common (in 7%–16% of all patients) than structural lesions.

Overall definitions of structural and active lesions

The overall MRI study group active lesion definition met the threshold and was validated (table 3A). The ASAS-MRI-SIJ+ definition was validated and additionally showed a higher sensitivity compared with the MRI study group active lesion definition (39.7% vs 30.7%). This gain in sensitivity (9%) was obtained with a comparable specificity (98.1% vs 99.4%) (figure 3).

The overall Leiden structural lesion definition (ie, meeting at least one of the three proposed definitions) met the predefined thresholds and was validated (table 3B). Contrarily, the overall MRI study group structural lesion definition did not meet the threshold (specificity 98.1% but PPV 93%) and therefore was not validated, despite higher sensitivity compared with the Leiden structural lesion definition (23.9% vs 16.1%) (table 3C).

Combined structural and active lesions

All combinations of the Leiden structural lesion definition with any active lesion definition (ASAS-MRI-SIJ+ or MRI study group) met the threshold (table 3). The MRI study group structural lesion met the threshold only when combined with the presence of any of the active lesion definitions. Since the MRI study group structural lesion definition did not independently meet the threshold with a PPV of

Table 1 Baseline characteristics of patients with chronic back pain of unknown origin, stratified by the 2-year diagnosis (axSpA or non-axSpA)

Baseline variables	All (N=643)	axSpA (N=335)	Non-axSpA (N=308)
Age (years)	30.2 (8.1)	29.6 (7.7)	31.0 (8.4)
Symptom duration (months)	13 (7)	13 (7)	13 (7)
Male	252 (39%)	173 (52%)	79 (26%)
HLA-B27-positive	283 (44%)	233 (70%)	50 (16%)
Positive family history (ASAS definition)	280 (44%)	157 (47%)	123 (40%)
IBP	458 (71%)	281 (84%)	177 (58%)
Psoriasis	79 (12%)	55 (16%)	24 (8%)
Peripheral arthritis	95 (15%)	73 (22%)	22 (7%)
Dactylitis	40 (6%)	36 (11%)	4 (1%)
Heel enthesitis	135 (21%)	109 (33%)	26 (8%)
Uveitis	49 (8%)	41 (12%)	8 (3%)
IBD	45 (7%)	25 (8%)	20 (7%)
Good response to NSAIDs	224 (35%)	154 (46%)	70 (23%)
Elevated CRP (>5 mg/L)	176 (27%)	113 (34%)	63 (20%)
CRP (mg/L)	5.8 (9.1)	6.8 (10.4)	5.1 (7.4)
Radiographic sacroiliitis (mNY; local)	78 (12%)	78 (23%)	0 (0%)
Sacroiliitis on MRI (ASAS criteria; local)	219 (34%)	200 (60%)	19 (6%)
Radiographic sacroiliitis (mNY; central)	21 (3%)	18 (5%)	3 (1%)
Sacroiliitis on MRI (ASAS criteria; central)	139 (22%)	133 (40%)	6 (2%)
Number of SpA features	3 (2)	4 (2)	2 (1)

Data are presented as mean (SD) or n (%), as appropriate. The number of SpA features is the sum of all SpA features present in the population excluding HLA-B27 status and imaging.
ASAS, Assessment of Spondyloarthritis international Society; axSpA, axial spondyloarthritis; CRP, C-reactive protein; HLA, human leucocyte antigen; IBD, inflammatory bowel disease; IBP, inflammatory back pain; mNY, modified New York criteria for sacroiliitis; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs.

93%, its combinations with any active lesion definition met the threshold solely due to the performance of the active lesion definitions. Upon comparison of all combinations of the overall definitions for structural and active lesions, the Leiden structural lesion definition with the ASAS-MRI-SIJ+ definition met the threshold, while having the highest sensitivity (46%). The ASAS-MRI-SIJ+ definition combined with the Leiden structural lesion definition met the threshold in any scenario, that is, with structural lesions in the presence or absence of active lesions, which did not apply for the combination with the MRI study group structural lesion definition. In general, the two overall structural lesion definitions independently contributed slightly (6%–11%) to the sensitivity of active lesion definitions (31%–40%) (figure 3). Notably, combining active and structural lesions showed little specificity loss compared with the individual lesions while increasing sensitivity.

Subgroup and sensitivity analyses

HLA-B27 status and sex stratification

After stratification for sex and HLA-B27 status (online supplemental table S2), structural lesions were rare among HLA-B27-negative patients, both in males (0%–8%) and especially in females (0%–4%). Structural and active lesion definitions performed similarly in HLA-B27-positive males and females. In HLA-B27-negative males, Leiden structural lesions outperformed the MRI study group structural lesions, while in HLA-B27-negative females, definitions rarely met the threshold (specificity ≥95% and PPV ≥94%). Performance by sex and HLA-B27 status of individual definitions can be found in online supplemental tables S3, S4

Patients not included in the study by the Leiden group

In the sensitivity analysis, only including those patients not previously considered in the analysis of the development of the Leiden structural lesions, the performance across definitions was in line with the main analysis, with two exceptions among the individual structural lesions by the MRI study group (online supplemental table S5). The ≥2 consecutive slices affected with erosions met the threshold of specificity and PPV ≥95%, while the ≥3 quadrants affected by erosions did not.

Reading rounds considering overlapping patients

In the second reading round, more structural lesions were scored compared with the first reading round (2%–16% vs 1%–8%)(online supplemental table S6).

Table 2 Validation of individual and overall lesion definitions proposed by Leiden and the MRI study group for structural and active lesions in MRI-SIJ typical for axSpA, assessed against the rheumatologist's diagnosis at 2-year follow-up, based on consensus between readers

		axSpA at follow-up (yes/no) **N=643 (52% axSpA)**			
Baseline MRI data	**n (%)**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Leiden structural lesions					
Erosions ≥3	18 (3)	5.4	**100.0**	**100.0**	49.3
Fat lesions ≥3	42 (7)	12.2	**99.7**	**97.6**	51.1
Fat lesions and/or erosions ≥5	40 (6)	11.6	**99.7**	**97.5**	50.9
Overall Leiden structural lesion definition	55 (9)	16.1	**99.7**	**98.2**	52.2
MRI study group structural lesions					
Erosion score in ≥3 SIJ quadrants	21 (3)	6.0	**99.7**	**95.2**	49.4
Erosion in ≥2 consecutive slices	57 (9)	15.5	98.4	91.2	51.7
Fat lesion in ≥5 SIJ quadrants	12 (2)	3.6	**100.0**	**100.0**	48.8
Fat lesion in ≥3 consecutive slices	49 (8)	14.3	**99.7**	**98.0**	51.7
Overall MRI study group structural lesion definition	86 (13)	23.9	98.1	93.0	54.2
MRI study group active lesions					
BME score in ≥4 SIJ quadrants	47 (7)	14.0	**100.0**	**100.0**	51.7
BME in ≥3 consecutive slices	104 (16)	30.4	**99.4**	**98.1**	56.8
Overall MRI study group active lesion definition	105 (16)	30.7	**99.4**	**98.1**	56.9

This analysis corresponds to analysis number 1 of the flow diagram displayed in online supplemental figure S1. Bold values indicate all definitions that meet the threshold consensus for specificity and PPV. Overall MRI study group active lesion definition is defined by having BME score in ≥4 SIJ quadrants or BME in ≥3 consecutive slices. Overall Leiden structural lesion definition is defined by having ≥3 erosions, ≥3 fat lesions or ≥5 fat lesions and/or erosions. Overall MRI study group structural lesion definition is defined by having an erosion score in ≥3 SIJ quadrants, erosion in ≥2 consecutive slices, fat lesion in ≥5 SIJ quadrants or fat lesion in ≥3 consecutive slices.
AxSpA, axial spondyloarthritis; BME, bone marrow oedema; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value; SIJ, sacroiliac joint.

Table 3 Validation of combinations of active and/or structural lesions based on definitions proposed by Leiden and the MRI study group for active and/or structural lesions in MRI-SIJ typical for axSpA, assessed against the rheumatologist's diagnosis at 2-year follow-up, based on consensus between readers

		axSpA at follow-up (yes/no) **N=643 (52% axSpA)**			
Baseline MRI data	**n (%)**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
(A) Active lesions					
ASAS-MRI-SIJ+	139 (22)	39.7	**98.1**	**95.7**	59.9
MRI study group+	105 (16)	30.7	**99.4**	**98.1**	56.9
(B) Leiden structural lesions					
Structural lesions+	55 (9)	16.1	**99.7**	**98.2**	52.2
- Combined with ASAS-MRI-SIJ+					
Structural lesions+ and ASAS-MRI-SIJ+	35 (5)	10.1	**99.7**	**97.1**	50.5
Structural lesions+ and ASAS-MRI-SIJ-	20 (3)	6.0	**100.0**	**100.0**	49.4
Structural lesions+ and/or ASAS-MRI-SIJ+	159 (25)	45.7	**98.1**	**96.2**	62.4
- Combined with MRI study group active lesions					
Structural lesions+ and active MRI study group+	28 (4)	8.1	**99.7**	**96.4**	49.9
Structural lesions+ and active MRI study group-	27 (4)	8.1	**100.0**	**100.0**	50.0
Structural lesions+ and/or active MRI study group+	132 (21)	38.8	**99.4**	**98.5**	59.9
(C) MRI study group structural lesions					
Structural lesions+	86 (13)	23.9	98.1	93.0	54.2
- Combined with ASAS-MRI-SIJ+					
Structural lesions+ and ASAS-MRI-SIJ+	55 (9)	15.8	**99.4**	**96.4**	52.0
Structural lesions+ and ASAS-MRI-SIJ-	31 (5)	8.1	98.7	87.1	49.7
Structural lesions+ and/or ASAS-MRI-SIJ+	170 (26)	47.8	96.8	94.1	63.0
- Combined with MRI study group active lesions					
Structural lesions+ and active MRI study group+	44 (7)	12.5	**99.4**	**95.5**	51.1
Structural lesions+ and active MRI study group–	42 (7)	11.3	98.7	90.5	50.6
Structural lesions+ and/or active MRI study group+	147 (23)	42.1	**98.1**	**95.9**	60.9

This analysis corresponds to analysis number 1 of the flow diagram displayed in online supplemental figure S1. Bold values indicate all definitions that meet the threshold consensus for specificity and PPV (both >95%). ASAS-MRI-SIJ± indicates a positive or negative MRI of the SIJ according to the ASAS definition. MRI study group+ indicates a positive or negative MRI of the SIJ defined by having a bone marrow oedema score in ≥4 SIJ quadrants or bone marrow oedema in ≥3 consecutive slices. Structural lesions+ by Leiden are defined by having ≥3 erosions, ≥3 fat lesions or ≥5 fat lesions and/or erosions. Structural lesions+ by the MRI study group are defined by having an erosion score in ≥3 SIJ quadrants, erosion in ≥2 consecutive slices, fat lesion in ≥5 SIJ quadrants or fat lesion in ≥3 consecutive slices.
ASAS, Assessment of SpondyloArthritis International Society; AxSpA, axial spondyloarthritis; MRI, magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value; SIJ, sacroiliac joint(s).

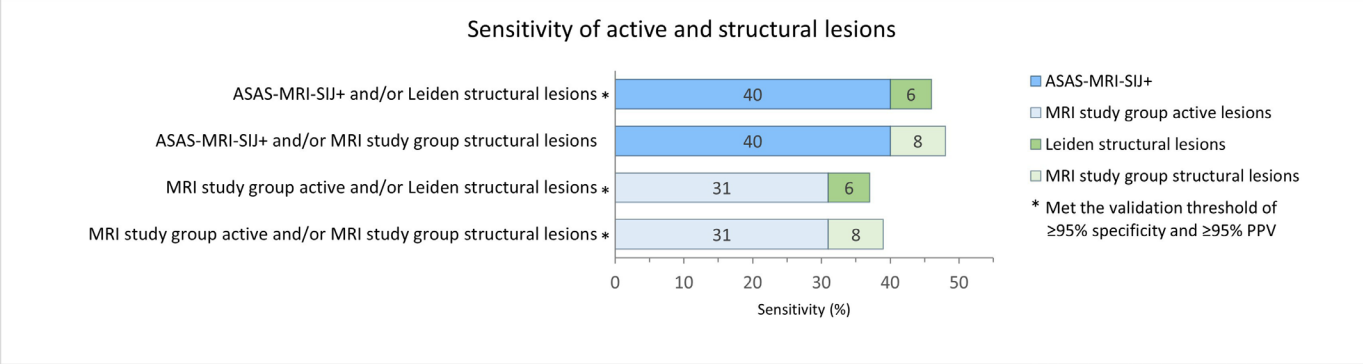

Figure 3 Added value of the identification of structural lesions alone, compared with the identification of active lesions, as measured with sensitivity to identify patients with axSpA (n=643). ASAS, Assessment of SpondyloArthritis international Society; axSpA, axial spondyloarthritis; MRI, magnetic resonance imaging; PPV, positive predictive value; SIJ, sacroiliac joints.

Notwithstanding, specificity and PPV remained consistently high in the second reading round (specificity ≥97.1% and PPV ≥87.0%). Considering both reading rounds for overlapping patients, the performance of all definitions was similar and in line with the main analysis. All individual MRI study group structural lesions and the overall MRI study group structural lesion definition met the threshold of specificity and PPV ≥95% in the first reading round.

Reading rounds considering all patients

When comparing definition performance across the two reading rounds, including all patients, specificity and PPV remained high (specificity ≥94.7% and PPV ≥86.7%; online supplemental table S7). Results were generally consistent with the main analysis. Deviating from it, the ≥2 consecutive slices affected with erosions met the threshold of specificity and PPV ≥95% only in the first reading round, along with the overall MRI study group structural lesion definition.

Individual readers

Analysis of individual reader scores of the second reading round showed that the individual Leiden structural lesions, MRI study group active lesions, overall Leiden structural lesion definition, overall MRI study group active lesion definition, and the ASAS-MRI-SIJ+ definition all met the threshold of specificity ≥95% and PPV ≥94% in ≥2 readers (table 4). Most individual MRI study group structural lesions met the threshold in ≥2 readers, except for ≥2 consecutive slices with erosions. The overall MRI study group structural lesion definition did not meet the threshold in any reader.

DISCUSSION

This study validated definitions for MRI-SIJ active and structural lesions proposed by Leiden and the MRI study group against the 2-year diagnosis in patients with (suspected) early axSpA from the SPACE cohort, confirming their high specificity and PPV. Particularly, the assessed definitions for structural lesions were infrequently observed in patients with early axSpA (average symptom duration: 13 months). All individual definitions by Leiden and the MRI study group met the validation threshold of specificity ≥95% and PPV ≥95%, except for the MRI study group definition requiring ≥2 consecutive slices affected by erosions. The overall Leiden structural lesion definition was validated, whereas the MRI study group structural lesion definition was not. Both the ASAS-MRI-SIJ+ and the overall MRI study group active lesion definitions met the validation threshold, with the ASAS-MRI-SIJ+ definition offering higher sensitivity. When combining active and structural lesions, the Leiden structural lesion definition with the ASAS-MRI-SIJ+ definition meets the validation threshold while maintaining high sensitivity. Structural lesions contributed only marginally to the identification of patients with axSpA, increasing sensitivity by 6%–11% beyond the 31%–40% sensitivity of active lesion definitions alone.

The initial studies by Leiden and the MRI study group and the current study scored structural MRI-SIJ lesions based on lesion definitions adapted from the SPARCC SSS from 2010, which aligned with the ASAS-MRI-SIJ definitions of the individual structural lesions as updated in 2019.[7 13 14] We consider the individual structural lesions as defined by Leiden and the MRI study group as similar, apart from Leiden requiring every lesion to be present in ≥2 consecutive slices.[7] This criterion increases detection certainty of lesions by reducing the likelihood of false-positive findings while meeting the prespecified validation threshold. Unlike the Leiden structural lesion definition, the MRI study group definition variously quantifies structural lesions using either quadrants or consecutive slices but does not consider lesion quantification and proportion simultaneously. While this approach increases sensitivity, it reduces certainty in lesion identification and may introduce complexity in the assessment compared with the Leiden definition.

The Leiden definition requires ≥3 lesions in ≥2 consecutive slices for high specificity, whereas the MRI study group definition allows only ≥1 lesion in ≥2 consecutive slices or ≥3 affected quadrants in only ≥1 slice. These differences make the MRI study group definition easier to attain. Given the rarity of structural lesions in early

Table 4 Performance of definitions for active and structural lesions in MRI-SIJ typical for axSpA, assessed against the rheumatologist's diagnosis at 2-year follow-up, using MRI reading round 2 of the individual readers

	axSpA at follow-up (yes/no) **N=447 (66% axSpA)**					
	Specificity			**PPV**		
Baseline MRI data	**Reader 1**	**Reader 2**	**Reader 3**	**Reader 1**	**Reader 2**	**Reader 3**
1. Individual lesion definitions						
(A) Leiden (2016) structural lesions						
Erosions ≥3	**100.0**	**97.4**	**98.7**	**100.0**	**94.4**	**94.1**
Fat lesions ≥3	**99.3**	**98.0**	**99.3**	**97.6**	**95.7**	**97.9**
Fat lesions and/or erosions ≥5	**99.3**	96.0	**98.7**	**96.9**	92.8	**95.7**
(B) MRI study group (2021) structural lesions						
Erosion score in ≥3 SIJ quadrants	**99.3**	97.4	**98.7**	**94.1**	92.7	**94.7**
Erosion in ≥2 consecutive slices	95.4	87.4	94.7	85.4	86.4	90.8
Fat lesion in ≥5 SIJ quadrants	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**
Fat lesion in ≥3 consecutive slices	**98.0**	96.0	**98.7**	**94.4**	92.1	**96.1**
(C) MRI study group (2021) active lesions						
BME score in ≥4 SIJ quadrants	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**
BME in ≥3 consecutive slices	**98.7**	**97.4**	**98.7**	**97.8**	**96.7**	**98.1**
2. 'Overall' definitions						
(A) Active lesions						
ASAS-MRI-SIJ+	**96.0**	**95.4**	93.4	**94.8**	**95.2**	93.2
Active MRI study group	**98.7**	**97.4**	**98.7**	**97.8**	**96.7**	**98.1**
(B) Structural lesions						
Leiden definition	**99.3**	**96.0**	**98.0**	**98.0**	**94.2**	**95.4**
MRI study group definition	94.0	86.8	93.4	89.7	87.3	90.9

This analysis corresponds to analysis number 4 of the flow diagram displayed in online supplemental figure S1. When a value is bold a reader has met the specificity of ≥95% and PPV of ≥94%. ASAS-MRI-SIJ+ indicates a positive MRI of the SIJ according to the ASAS definition. MRI study group indicates a positive MRI of the SIJ defined by having BME score in ≥4 SIJ quadrants or BME in ≥3 consecutive slices; The Leiden definition is defined by having ≥3 erosions, ≥3 fat lesions or ≥5 fat lesions and/or erosions. The MRI study group definition is defined by having an erosion score in ≥3 SIJ quadrants, erosion in ≥2 consecutive slices, fat lesion in ≥5 SIJ quadrants or fat lesion in ≥3 consecutive slices.
ASAS, Assessment of SpondyloArthritis International Society; AxSpA, axial Spondyloarthritis; BME, bone marrow oedema; MRI, magnetic resonance imaging; PPV, positive predictive value; SIJ, sacroiliac joint(s).

axSpA, confirming multiple lesions in consecutive slices enhances a reliable lesion detection and helps maintain high disease specificity. Also, the Leiden definitions align more closely with a reader's overall assessment, as they identify individual lesions in specific quadrants, with the requirement of ≥2 consecutive slices adding accuracy to the assessment. Hence, the Leiden definition is most feasible for research due to its ability to provide greater certainty and consistency in identifying structural lesions, even when both definitions show comparable performance.

The finding that structural lesions are infrequently present in patients with early axSpA has been seen before in studies from the DESIR cohort.[15 16] Our findings show that, when structural lesions are present in patients with early axSpA, active lesions are usually simultaneously present. Our data show that structural lesion definitions alone offer, at the group level, little additional sensitivity compared with active lesion definitions for identifying axSpA. These findings are relevant for daily clinical practice, where both active and structural lesions can contribute to identifying the *Gestalt* of axSpA. At the individual patient level, structural lesions can be seen without active lesions; however, this is rare in early axSpA, and active lesions alone are more common. Thereby, definitions for the presence of either structural lesions, active lesions or both should be considered. Among such combinations within our analysis, the Leiden structural lesion definition with the ASAS-MRI-SIJ+ definition showed the highest sensitivity while meeting the validation threshold. Additionally, the Leiden structural lesion and ASAS-MRI-SIJ+ definitions individually have an advantageous performance compared with the MRI study group definitions, making their combination most preferable for clinical practice and research.

Our subgroup analyses showed that lesions were seldom present in HLA-B27-negative patients, especially females. Our sensitivity analysis showed consistent performance across reading rounds, confirming the definitions' robustness and indicating that the readers were well-calibrated and experienced. In our study, the assessment of the individual readers of the second reading round reflects clinical practice, where a single reader assesses the MRI and reports lesions. This assessment demonstrated consistently high specificity and PPV across readers, aligning with the results of the consensus of readers and reinforcing the robustness of the readings and our findings.

Due to the rare presence in controls and early occurrence in the disease course, different definitions of erosions on MRI-SIJ have shown to be most disease-specific for axSpA in four previous studies, having a specificity ranging from 94% to 98%.[13 17–19] Weber *et al.* proposed ≥3 quadrants affected by BME combined with ≥1 or ≥2 quadrants affected by erosion for classification of axSpA.[17] This approach decreased specificity (from 97% to 85%) but increased sensitivity.[17] A Danish study (2019) considered fat lesions disease-specific (≥95%) as well.[19] Altogether, these findings are corroborated by our results, reinforcing that structural lesions, particularly erosions, are highly specific but uncommon in early axSpA, and that combining active and structural lesions may improve sensitivity with limited impact on specificity. Our analysis showed high specificity (≥95%) for ≥3 quadrants affected by erosion but not for ≥1 erosion in ≥2 consecutive slices, so the latter should not be used in early axSpA.

This study did not investigate the anatomic distribution of the MRI-SIJ lesions, though a previous study suggests that these lesions can be location specific, mainly in the middle segments.[20] Future studies could assess the frequency, size and anatomic distribution of MRI-SIJ lesions to fully evaluate their diagnostic value in (early) axSpA. Furthermore, this study did not investigate MRI-SIJ lesions in combination with other SpA features. MRI-SIJ findings alone do not suffice for a diagnosis of axSpA, but should always be combined with clinical features. A limitation of our study could be the substantial overlap of patients (43%) with the cohort from the Leiden study. Similar presence and performance of structural lesions could therefore be expected.[7] Nevertheless, our study analysed over three hundred additional patients and two new centres were included, using scores from a different reading round and readers, while having similar results, strengthening the evidence for the performance of these structural lesions in early disease as well as the generalisability of the findings. This was further confirmed after analysis of only the newly included patients, which also showed similar results. Of note is the use of the follow-up diagnosis as this study's primary outcome, allowing for more certainty and robustness about the diagnosis. One more strength of this analysis is the short symptom duration at baseline (≤2 years). Therefore, our study might be more informative for predicting diagnoses confirmed during follow-up and better reflects clinical practice, aiming at early disease detection.

In conclusion, all MRI-SIJ lesion definitions proposed by Leiden and most proposed definitions by the MRI study group were validated in early axSpA, demonstrating high specificity and PPV. Structural lesions were infrequent, highlighting the limited role of structural changes in early diagnosis. While the Leiden and MRI study group structural lesion definitions performed similarly, the Leiden definition offers a more structured approach by simultaneously incorporating lesion quantification and diagnostic certainty, making it more feasible for clinical and research application. The ASAS-MRI-SIJ+ definition outperformed the MRI study group active lesion definition, and combining structural and active lesions provided only a small increase in sensitivity of early disease.

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Correction notice In the Results section under the 'Combined structural and active lesions' heading, figure 2 was incorrectly cited, when it should have been figure 3. This has now been corrected.

Contributors LJEdB, SR, FAvG and DvdH conceptualised the manuscript's content. DvdH, MvL, LJEdB, MdH, SE, RR, IJB, MR, FAvG, RL and SR collected patient data. MLM, MvL and LJEdB performed data management tasks. LJEdB performed the analysis. LJEdB wrote the first draft of the manuscript. All authors made extensive comments and appropriate changes to the manuscript. SR is the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests LJEdB has received a travelling grant from EULAR. MLM has received consultancy/speaker fees from Novartis; travelling grant from Nordic. Pharma, Novartis. MvL: none to declare. MdH has received consultancy fees from UCB Pharma; speaker fees from UCB Pharma, FWRO-KBS; travelling grants from EULAR, UCB Pharma; voluntary EULAR Congress Committee member and ELAR Imaging taskforce member. MR has received the ISS grant and consultancy fees by ASAS. SE has received speakers bureau fees from Novartis, UCB Pharma, Consultant (Advisory Board member) for AbbVie, Amgen, Eli Lilly, Janssen, Novartis, UCB Pharma. IJB: none to declare. RR has received travelling grants, consulting and/or speaking fees, Advisory Boards fees by Abbvie, Novartis, Janssen, Lilly, MSD, Pfizer and UCB, Amgen, Celltrion and Astra Zeneca. RL has received speaker/consultancy fees from Abbie, UCB, Novartis, Galapagos and Janssen. FAvG has received consultancy fees from Novartis, MSD, AbbVie Bristol Myers Squibb, EL; grants from Stichting Vrienden van Sole Mio, Stichting ASAS, Novartis, UCB. DvdH has received consultancy fees from AbbVie, Alfasigma, ArgenX, BMS, Elly-Lilly, Grey-Wolf Therapeutics, Janssen, Novartis, Pfizer, Takeda, UCB Pharma; director of Imaging Rheumatology bv. SR has received speaker/consultancy fees from Eli Lilly, Novartis, UCB, AbbVie, Galapagos/Alfasigma, Janssen, MSD, Pfizer, Sanofi; grants from AbbVie, Galapagos/Alfasigma, MSD, Novartis, Pfizer, UCB.

Patient consent for publication Not applicable.

Ethics approval The SPACE study protocol was approved by the medical ethical committee of the Leiden University Medical Center (reference number P08.105), the regional committee for medical and health research ethics in South-East Norway (reference number 2014/426), the ethical committee 'Azienda Ospedaliera di Padova' (reference number 2438P) and the regional research ethics committee in Lund, Sweden (reference number 2010/653). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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