

ORIGINAL ARTICLE

Evaluation of the performances of 'typical' imaging abnormalities of axial spondyloarthritis: results of the cross-sectional ILOS-DESIR study

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ABSTRACT

Objective To evaluate the prevalence and performance as axial Spondyloarthritis (axSpA) diagnostic feature of radiographic and MRI lesions 'typical' of axSpA of the sacroiliac joint (SIJ) and spine in a mechanical chronic back pain (CBP) population and in an axSpA cohort. Methods Cross-sectional multicentre study. Patients: (1) recent onset axSpA (DESIR cohort) and (2) mechanical non-axSpA CBP matched for age and gender (ILOS study). Imaging: radiographs and MR scans were performed identically in both groups. All images were centrally read. blinded for diagnosis and for other imaging findings in the same patient. Statistical analysis: prevalence of lesions 'typical of axSpA' were compared in both groups. Sensitivity, specificity and positive likelihood ratios (LR+) of each lesion (and combination of lesions) were calculated. **Results** A total of 98 patients with CBP were included, and compared with 100 patients with recent onset axSpA. SIJ lesions were consistently more frequent in the axSpA group (35.0% vs 11.8% p<0.001, 35.0% vs 8.4% p<0.001% and 32.0% vs 10.0%. p<0.001 for modified New York criteria, MRI sacroiliitis and ≥3 erosions of the SIJ on MRI, respectively), and performed well (LR+ for ≥3 erosions 3.0 (95% Cl 1.6 to 5.8)). Spine lesions were comparable across groups: radiographic lesions were rare, while all MRI lesions were frequent.

Conclusion Our study confirms that 'typical' lesions can also be observed in patients with non-axSpA CBP but that SIJ lesions by all modalities remain the most valuable for diagnosis, including structural lesions of the SIJ. This suggests the potential interest of adding MRI SIJ structural lesions in the definition of MRI abnormalities for axSpA classification.

INTRODUCTION

Spondyloarthritis (SpA) is a multifaceted systemic disease¹ that encompasses inflammation of the axial skeleton (axial SpA (axSpA)), extra-axial manifestations, that is, enthesitic and peripheral articular involvement, but also extra-articular symptoms, such

Key messages

What is already known about this subject?

- ➤ Some recent data have suggested the so-called 'typical' Spondyloarthritis lesions on X-rays and MRI can be observed in patients without axial Spondyloarthritis (axSpA).
- ▶ Nevertheless, there are virtually no data available regarding the performance of each type of 'typical' Spondyloarthritis lesions to discriminate patients with axSpA from patients with non-axSpA mechanical chronic back pain.

What does this study add?

 Our study confirms that 'typical' lesions of the sacroiliac joints remain the most discriminant ones, including structural lesions.

How might this impact on clinical practice?

► These results suggest the potential interest of also including MRI structural lesions of the sacroiliac joints in the definition of MRI abnormalities for axSpA.

as psoriasis, uveitis or inflammatory bowel disease.

Due to these diverse presentations, diagnosis can be sometimes challenging and, on top of other (mainly clinical) signs, the presence of imaging findings often contributes to the diagnosis. Classically, diagnosis of axSpA is based on the combination of clinical symptoms and unequivocal radiographic damage: either the presence of radiographic sacroiliitis according to the modified New York (mNY) criteria² or the presence of syndesmophytes in the spine.³ However, such structural damage appears after several years since disease onset, leading to significant diagnostic delay.⁴ ⁵ Furthermore, reliability of sacroiliitis on radiographs has been consistently

reported to be poor, regardless the reader (rheumatologists or radiologists) or the type of reading (local reading or central reading campaigns). ⁶⁷ In the late 1990s, MRI allowed to assess the presence of inflammation in the sacroiliac joints (SII) and spine in patients with axSpA. Inflammation could be observed even in patients without structural damage, suggesting that inflammation could be the first step in the sequence that would eventually lead to radiographic progression. Since then, MRI has been used for diagnostic purposes in axSpA, and several definitions have been proposed by the ASAS (Assessment of SpondyloArthritis international Society) group to define a 'positive' MRI of the SIJ.⁸⁹ These lesions (ie, radiographic sacroiliitis and MRI sacroiliitis) have been consistently associated with axSpA and are indeed the entry criteria of the 'imaging arm' of the ASAS classification criteria for axSpA, 10 11 which have been validated in several populations. 12 13 However, other imaging abnormalities have been observed in early axSpA populations, such as structural lesions (ie, erosions, fat deposition and bony bridges/ankylosis of the $\mathrm{SIJ}^{14\,15}$ and also inflammatory and chronic lesions of the spine assessed by MRI¹⁶17).

Only scarce data are available regarding the sensitivity and specificity of these other imaging abnormalities so-called 'typical of axSpA' (ie, structural lesions of the SIJ, inflammatory and structural lesions of the spine): indeed, their value in the absence of definite lesions of the SIJ (radiographs or MRI) remains unclear, and the prevalence of such abnormalities (eg, chronic changes of the SIJ) in a population of patients suffering from non-axSpA mechanical chronic back pain (CBP) is unknown. Furthermore, recently, the specificity of the findings of MRI sacroiliitis has been challenged by some studies reporting bone marrow oedema (BME) of SIJ in runners and athletes¹⁸ and postpartum females.¹⁹

Only the description of these imaging abnormalities called 'typical of axSpA' in a cohort of patients with non-axSpA mechanical CBP (the main differential diagnosis for axSpA) will allow to assess the performances (ie, sensitivity, specificity, positive likelihood ratio (LR+)) of such abnormalities for the recognition of axSpA in a clinical setting, by comparing the prevalence of such lesions with an early axSpA cohort of patients.

Based on these remarks, the aim of our study was to: (1) to describe the prevalence of SIJ and spine radiographs and MRI abnormalities suggestive of axSpA in a non-axSpA mechanical CBP population (appearing before the age of 45 years) and an early axSpA population and (2) to calculate the sensitivity, specificity and LR+ of each of these abnormalities (and the combination of them).

PATIENTS AND METHODS Study Design

Study Design

ILOS study: observational cross-sectional national multicentric study: four tertiary care hospital centres (rheumatology and radiology departments). *DESIR study*: the multicentre French national early axSpA cohort including 25 centres; inclusion period was 2008–2010.²⁰

Patients

(1) Cases=patients with early axSpA=DESIR patients: in order to compare the prevalence of the other imaging abnormalities and to assess the performances of such abnormalities, a sample of 100 patients sample from DESIR was selected. Inclusion criteria for DESIR have been published elsewhere, 20 but briefly, patients had to present with inflammatory axial back pain for less than 3 years highly suggestive of axSpA. For this present analysis, and in order to ensure the representability of the sample from the whole cohort in terms of imaging, we selected 100 patients based on the results of imaging findings of the SII on the central reading performed at baseline in the cohort: among the whole DESIR cohort (ie, including the 708 patients from baseline) 15% patients presented with radiographic sacroiliitis and MRI sacroiliitis; 6% patients with radiographic sacroiliitis but without MRI sacroiliitis; 20% patients with MRI sacroiliitis but without radiographic sacroiliitis; 59% patients without imaging abnormalities of the SIJ. Therefore, we selected our sample based on the observed abnormalities and their identification (id) number in the cohort (ie, consecutive patients): among all patients without any imaging abnormalities of the SIJ, we selected the first consecutive 59 patients according to their 'id' numerical order; among all patients with MRI sacroiliitis but without radiographic sacroiliitis, we selected the first consecutive 20 patients by 'id' numerical order; among all patients with radiographic sacroiliitis but without MRI sacroiliitis, we selected the first consecutive six patients according to their numerical 'id' order, and among all patients with radiographic and MRI sacroiliitis, we selected the first consecutive 15 patients according to their numerical 'id' order, resulting in a 100-patients sample. (2) Controls=patients with non-axSpA mechanical CBP=ILOS study: One hundred consecutive inpatients and outpatients consulting for definite non-axSpA mechanical CBP were prospectively included in the study, in four tertiary care centres from 2014 to 2015. Patients were interviewed by the investigator before being included: to be included, CBP had to be mechanical and the diagnosis of axSpA had to be excluded; CBP had to initiate before the age of 45 years, and to be lasting for more than 3 months but less than 3 years. All patients gave their informed consent.

Imagings

All patients underwent identical imaging examinations (same modalities and identical imaging protocols): Radiographs: pelvis and lateral cervical and lumbar spine. MRI: SIJ, upper spine (C2 to T10) and lower spine (T8 to S1), using the short-tau inversion recovery and T1 fast spin echo acquisitions.

Imaging data collection

(1) Pelvic radiographs: abnormalities of the SIJ were scored according to the mNY criteria:² the reader reported the grades of each SII (right then left) from 0 to 4 (0=No disease, 1=Suspicious for sacroiliitis, 2=Small localised areas with erosions or sclerosis without alteration in joint width, 3=Moderate/advanced sacroiliitis with one or more of erosions, evidence of sclerosis, widening, narrowing or partial ankylosis; 4=Total ankylosis); after that, for any SII scored 2 or 3, the reader checked for the presence of erosions, sclerosis, joint width widening, joint width narrowing or partial ankylosis; (2) Spine radiographs: abnormalities of the spine were scored according to the mSASSS,²¹ ranging from 0 to 72, by checking at each anterior site of the cervical spine from the lower border of C2 to the upper border of T1 and the lumbar spine from the lower border of T12 to the upper border of the sacrum on a lateral view for the presence of no abnormality, erosion or sclerosis or squaring, syndesmophyte or total bony bridging; (3) MRI of the SIJ: Inflammatory lesions of the SII were scored according to the Spondyloarthritis Research Consortium of Canada MRI index (SPARCC) for the SIJ:22 each SI joint was divided into four quadrants (upper iliac, lower iliac, upper sacral and lower sacral). The reader checked for the presence in any quadrant of: BME in each quadrant and also the presence of intense signal (comparable to signal from adjacent blood vessels) or depth ≥1 cm anywhere within each SI. The score ranges from 0 to 72. The fulfilment of the ASAS definition for MRI sacroiliitis was also assessed.^{8 9} Chronic lesions of the SIJ were scored, in each quadrant, for the presence of erosions, sclerosis, periarticular fat and (partial) ankylosis. Different definitions were tested based on the proposal by de Hooge et al (ie, the presence of at least five erosions or fatty lesions). 23 (4) MRI of the spine: inflammatory lesions of the spine were scored according to the SPARCC for the spine.²⁴ This method was based on the scoring of disco-vertebral units and each of these was divided in four quadrants: anterior/posterior and superior/ inferior. First disco-vertebral unit is C2-C3 and the last L5-S1. The reader checked for the presence in any quadrant of: BME, intensity and depth of BME. The score ranged from 0 to 108. The fulfilment of the ASAS definition of a positive MRI of the spine (ie, at least three inflammatory corners)²⁵ and the fulfilment of the SPACE group definition (ie, at least five inflammatory corners)²³ were also calculated. Chronic spinal MRI lesions were scored according to the Canada-Denmark score: per DUV quadrant dichotomous scores (presence/absence) on corner inflammatory and structural lesions (fatty lesions, erosions, syndesmophytes) were given.²⁶ Different definitions were tested based on the proposal by de Hooge et al (eg, the presence of at least five fatty lesions).²³

Image reading

Images from the cases (axSpA DESIR patients) and the controls (non-axSpA mechanical CBP ILOS patients) were fully anonymised and pooled together in a random order. An experienced reader (AM) scored all 198 imaging studies, blinded for the group the patient belonged to (eg, to the axSpA or the CBP group) and also for the findings on the other imaging modalities, since all modalities (X-ray SIJ, X-ray Spine, MRI SIJ and MRI of the spine) were scored separately.

Statistical methods

Sample size: In order to calculate the sample size of this study, due to the scarce data available regarding the diagnostic/classification performances of each type of lesions, we assumed that the specificity of BME of the SIJ detected by MRI (eg, as in the axSpA ASAS criteria) was 95%.²⁷ With this hypothesis, a sample of 100 cases (axSpA) and 100 controls (mechanical non-axSpA patients with CBP) would allow us to estimate specificity with a ±5% accuracy. Analysis: a descriptive analysis of the different imaging abnormalities suggestive of axSpA in the SIJ and spine was performed (number (%) of patients with a lesion, and mean (SD) for the continuous scores). Proportions and continuous variables were compared in both groups by χ^2 test and T-test, respectively. Statistical significance was set for p<0.05. The performances of the presence of each type of lesion as well as the combination of different types of lesions were calculated: sensitivity (SE: imaging positives/patients with axSpA), specificity (Spe: imaging negatives/patients with CBP) and positive LR (LR+=sensitivity/1-specificity or the probability of a person who has the disease testing positive divided by the probability of a person who does not have the disease testing positive) and their 95% CI, using the group as the 'gold-standard'. LR+ captures both sensitivity and specificity of a given test, or in this case 'lesion or combination of lesions' in a single figure and is an indicator of the diagnostic/classification value of the respective findings: the higher the LR+, the better the diagnostic value of the finding.²⁸ All analyses were performed using R-CRAN software.²⁹

RESULTS

Among the 100 included patients with non-axSpA mechanical back pain, imaging was only available in 98 patients. Age and gender were comparable (mean (SD) 36.2 (9.9) vs 32.2 (8.7) years, and 41.8% and 45% males, in the mechanical CBP vs axSpA groups, respectively).

Descriptive analysis

Pelvic radiographs: patients with axSpA had consistently more lesions suggestive of patients with axSpA than CBP: 9/97 (9.3%) vs 35 (35%), 21/97 (21.6%) vs 50 (50.0%) and 13/97 (13.4%) vs 25 (25.0%) for erosions, sclerosis and joint widening, respectively. The number

of patients presenting at least a grade 2 unilaterally and the number of patients fulfilling the mNY criteria were significantly higher in the axSpA group (54 (54%) vs 26/96 (27.1%), p<0.001 and 35 (35%) vs 11/95 (11.6%), p<0.001, respectively) (table 1).

Spine radiographs: Prevalence of spine lesions was very low, and only squaring was significantly more frequent in the axSpA group (mean (SD) number of squaring lesions per patient: 0.2 (0.8) vs 0.01 (0.1), p=0.037). The mSASSS did not differ across groups: 2.0 (14.5) vs 2.2 (15.1), p=NS, for the mechanical CBP and axSpA groups, respectively) (table 1).

MRI inflammatory lesions of the SIJ: the presence of at least one inflammatory lesion was quite frequent in both groups, but significantly more frequently observed in the axSpA group (24 (25.3%) vs 40 (40.0%), p=0.028). The number of patients who fulfilled the ASAS definition for a positive sacroiliitis on MRI was low in the mechanical CBP group: 35 (35.0%) vs 8 (8.4%), p<0.001; furthermore, almost no patient (or no patient) from the mechanical CBP group fulfilled the definition when lesions were scored as deep or intense (24 (24%) vs 3/95 (3.2%), p<0.001) or both (13 (13%) vs 0 (0%), p<0.001, in the axSpA vs CBP groups, respectively) (table 1). The mean SIJ-SPARCC score was significantly higher in the axSpA group: 4.9 (8.8) vs 0.6 (1.3), p<0.001.

MRI inflammatory lesions of the spine: prevalence of at least one lesion was high in both groups (44 (44.9%) vs 52 (52.5%), p=NS, for the mechanical CBP and axSpA groups, respectively). The number of patients fulfilling the different definitions for a positive MRI was greater, but not significantly, in the axSpA group: 44 (44.4%) vs 33 (33.7%), NS, and 30 (30.3%) vs 25 (25.5%), NS, in the axSpA group versus mechanical CBP groups, for the ASAS and for the SPACE group definitions, respectively. The SPARCC score was lower in the mechanical CBP group, but this difference did not reach statistical significance (3.3 (5.8) vs 5.6 (13.5), NS, in the mechanical CBP vs axSpA groups, respectively).

MRI structural lesions of the SIJ: Up to 17% patients with mechanical CBP (vs 24% of patients with axSpA) presented at least one chronic lesion of the SIJ, but the number of patients presenting the different combinations of structural lesions of the SIJ proposed was consistently and significantly greater in the axSpA group (table 1).

MRI structural lesions of the spine: prevalence was comparable in both groups, with 21 (21.4%) vs 15 (15.2%) patients in the mechanical CBP and axSpA groups, respectively, presenting with at least three fatty lesions (NS).

Performances as diagnostic features for axSpA

Performances (SE, Spe and LR+) for all imaging abnormalities are reported in table 2. Among radiographic lesions, the presence of SIJ erosions and the fulfilment of mNY criteria were the only lesions/combination of lesions with LR+ above 3 (3.8 (95% CI 1.9 to 7.4) and 3.0

(1.6 to 5.6), respectively; all radiographic spine lesions presented poor performances.

The ASAS definition of MRI sacroiliitis presented a high specificity (0.9 (0.8 to 0.9)) and a good positive LR (4.2 (2.0 to 8.5)) and even better performances when the definition included deep or intense lesions (Spe: 1.0 (0.9 to 1.0) and LR+: 7.6 (2.4 to 24.2)). The presence of different combinations of structural lesions of the SIJ performed well, in particular the presence of at least three erosions (Spe: 0.9 (0.8 to 1.0), LR+: 3.0 (1.6 to 5.8)), However in the spine, regardless of the MRI lesions or combination or lesions (ie, inflammatory or structural), performances were poor, with all positive LRs below 2.

DISCUSSION

Our study confirms that 'typical lesions of axSpA' can also be observed in patients with non-axSpA mechanical CBP. Indeed, 21%, 25.3% and 50.0% of patients from the non-axSpA mechanical CBP group presented with sclerosis on the pelvis radiograph, at least one inflammatory lesion of the SII and at least one structural lesion of the spine, respectively. However, among the non-axSpA mechanical CBP group, only 11.6% and 8% fulfilled the mNY criteria and ASAS MRI sacroiliitis definition, respectively. Interestingly, the number of patients with structural lesions of the SIJ on MRI was consistently higher in the axSpA group, in particular for the presence of at least three erosions, for which the difference was more important across groups (10% vs 32%, respectively). Finally, our finding confirms previous data regarding spine imaging findings in patients with early disease: indeed, the number of lesions detected on spine radiographs was so low in both groups that no differences could be observed; regarding MRI of the spine, inflammatory lesions were consistently more frequent in the axSpA group, but the differences did not reach a statistical significance, neither for the ASAS definition (ie, at least three lesions) nor for the SPACE group definition (ie, at least five inflammatory lesions). Spinal structural lesions on MRI were even more frequent in the mechanical non-axSpA, for example, 21% vs 15% patients presenting with at least three fatty lesions in the non-axSpA mechanical CBP versus axSpA groups; this finding regarding structural lesions of the spine has already been reported by the SPACE group²³ and they suggested a cut-off of at least five fatty lesions. Nevertheless, in our analysis, even this high cut-off performed poorly (LR=0.6 (95% CI 0.3 to 1.4)). This is probably reflecting the fact that fatty lesions can also be observed as a consequence of mechanical spinal disorders.

Although most of the lesions were observed in both groups, some lesions (or combination of lesions) performed very well for axSpA recognition, particularly at the SIJ level. Indeed, despite all the well-known limitations regarding the poor inter-reader and intrareader reliability for the radiographic sacroiliitis

| Table | - | ormalities 'typica | Imaging abnormalities 'typical of axSpA' observed in the axSpA and mechanical chronic back pain groups | back pain groups | | | |
|-------|-------------------------|--------------------|--|---|---------------|---------------|---------|
| | | | | | CBP n=98‡ | axSpA n=100 | d |
| Xrays | | Pelvic Xrays | Lesions | Erosion (y/n)* | 9/97 (9.3%) | 35 (35.0 %) | <0.001§ |
| | | | | Sclerosis (y/n) | 21/97 (21.6%) | 50 (50.0%) | <0.001 |
| | | | | Joint widening (y/n) | 13/97 (13.4%) | 25 (25.0%) | NS |
| | | | | Joint narrowing (y/n) | 11/97 (11.3%) | 21 (21.0%) | NS |
| | | | | Partial ankylosis (y/n) 7/97 (7.2%) | 7/97 (7.2%) | 11 (11.0%) | NS |
| | | | | Total ankylosis (y/n) | 0 | 3 (3.0%) | NS |
| | | | At least a grade two unilateral | | 26/96 (27.1%) | 54 (54%) | <0.001 |
| | | | Modified NY criteria | | 11/95 (11.6%) | 35 (35.0%) | <0.001 |
| | | Spine Xrays | Lesions | Number of erosions | 0.4 (0.8) | 0.3 (0.5) | NS |
| | | | | Number of sclerosis lesions | 0.4 (1.6) | 0.5 (1.4) | NS |
| | | | | Number of squaring lesions | 0.01 (0.1) | 0.2 (0.8) | 0.037 |
| | | | | Number of patients with at least one full bone bridge | 2 (2.1%) | 5 (5.0%) | SN |
| M | Inflammatory lesions | Sacroiliac joints | Inflammatory Sacroiliac joints At least one inflammatory lesion lesions | | 24/95 (25.3%) | 40 (40.0%) | 0.028 |
| | | | ASAS definition of MRI sacroiliitis | | 8/95 (8.4%) | 35 (35.0%) | <0.001 |
| | | | ASAS definition of MRI sacroiliitis AND deep lesion† | | 1/95 (1.1%) | 17 (17%) | <0.001 |
| | | | ASAS definition of MRI sacroiliitis AND intense lesion† | | 2/95 (2.1%) | 20 (20%) | <0.001 |
| | | | ASAS definition of MRI sacroiliitis AND (deep OR intense lesion)† | | 3/95 (3.2%) | 24 (24%) | <0.001 |
| | | | ASAS definition of MRI sacroiliitis AND (deep AND intense lesion)† | | 0 | 13 (13%) | <0.001 |
| | | Spine | At least one inflammatory lesion | | 44 (44.9%) | 52/99 (52.5%) | NS |
| | | | At least three inflammatory lesions (ASAS definition of positive spine MRI) | | 33 (33.7%) | 44/99 (44.4%) | SN |
| | | | At least five inflammatory lesions | | 25 (25.5%) | 30/99 (30.3%) | NS |
| | Structural lesions | Sacroiliac joints | At least one structural lesion | | 16/95 (16.8%) | 24 (24%) | NS |
| | | | At least three erosions | | 10/95 (10.5%) | 32 (32%) | <0.001 |
| | | | At least three fatty lesions | | 11/95 (11.6%) | (%62) 62 | 0.004 |
| | | | At least five erosions or fatty lesions | | 13/95 (13.7%) | 33 (33%) | 0.002 |
| | | Spine | At least one structural lesion | | 49 (50.0%) | 42/99 (42.4%) | NS |
| | | | | | | | : |

| able 1 Continued | | | |
|--|------------|---------------|----|
| | CBP n=98‡ | axSpA n=100 | р |
| At least three erosions | 6 (6.1%) | 7/99 (7.1%) | NS |
| At least three fatty lesions | 21 (21.4%) | 15/99 (15.2%) | NS |
| At least five fatty lesions | 12 (12.2%) | 9/99 (9.1%) | NS |
| At least five structural lesions (erosions OR fatty lesions) | 19 (19.4%) | 11/99 (11.1%) | NS |

Results are presented as n(%) for dichotomous variables and as mean (SD) for continuous variables. According to the SPARCC scoring of the SIJ

Spondyloarthritis.

ASSAS, Assessment of SpondyloArthritis international Society; CBP, chronic back pain; NY, New York; SPARCC, Spondyloarthritis Research Consortium of Canada index; axSpA, axial In case no denominator is indicated, the available images are n=98 for CBP and n=100 for axSpA. Significant results are highlighted in bold.

assessment, ⁶⁷ the presence of erosions and sclerosis (and thus, the fulfilment of the mNY criteria) were found to be highly specific. These findings are interesting, particularly in settings where access to MRI can be a challenge due to cost-limitations. Similarly, the presence of an MRI sacroiliitis according to the ASAS definition was found to be as specific as radiographic sacroiliitis, but with higher LR+; furthermore, when the notion of 'depth' or 'intensity' of BME was added to the definition of MRI sacroiliitis, discrimination capacity increased, with increased LR+, and also with larger CIs, due to the small number of patients presenting such lesions (less than four patients) and low sensitivity. Thus, this finding suggests that deep and/or intense BME of the SII is extremely unlikely to be seen in patients with non-axSpA. Another interesting finding of our study was the excellent performances observed for the MRI structural lesions of the SIJ: indeed, the presence of at least three erosions performed as well as the mNY criteria, with an LR+ above three and almost a perfect specificity. However, spine lesions, also including the MRI inflammatory lesions, performed poorly in this early onset population.

Our study has some limitations that are worth noting. The study population might be considered as not optimal since the selection of the patients with axSpA was not based on any classification criteria but on the judgement of the rheumatologist. This was also the case for the group of patients suffering from mechanical disorder. However, this situation is perfectly reflecting daily practice (eg, in case of patients presenting with recent onset back pain before the age of 45 years, what is the probability to observe MRI findings at the SIJ level suggestive of spondyloarthritis in patients with a diagnosis (based on rheumatologist's opinion) of spondyloarthritis versus a diagnosis of mechanical disorders. This design (eg, focusing on patients with recent onset disease) probably explains the low prevalence of structural lesions observed in this study. Another limitation was that only one reader performed the reading. Indeed, central reading exercises usually include at least two readers since average scores are closer to the truth. However, the purpose of this exercise was not really to have a 'true' score, but rather to try to reproduce a situation that often occurs in clinical practice: that is, in front of a patient with recent onset CBP, to what extent the presence of these so-called 'typical axSpA' lesions contributes to the likelihood of an axSpA diagnosis. Furthermore, the reader was trained for several central-reading campaigns, and this one-reader exercise yielded very similar results to those obtained by the central reading of DESIR: the percentage of patients with axSpA fulfilling the mNY criteria and the ASAS definition of an MRI sacroiliitis were 35% vs 21% and 35% vs 35%³⁰ in this study versus the central reading, respectively. The prevalence of mNY criteria fulfilment in the axSpA population in this present study was indeed higher than the central reading exercise. This observed difference can be explained by the poor inter-reader reliability of the assessment of the pelvis radiograph,

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| Table 2 | | es of the differe | Performances of the different imaging abnormalities 'typical of axSpA' with regard to axSpA recognition | axSpA recognition | | | |
|---------|--|------------------------|---|-------------------------------|----------------|----------------|-------------------|
| | | | | | Se (95% CI) | Spe (95% CI) | LR+ (95% CI) |
| Xrays | | Pelvic Xrays | Lesions | Erosion (y/n)* | 0.4 (0.3, 0.5) | 0.9 (0.8, 0.9) | 3.8 (1.9, 7.4) |
| | | | | Sclerosis (y/n) | 0.5 (0.4, 0.6) | 0.8 (0.7, 0.9) | 2.3 (1.5, 3.5) |
| | | | | Joint widening (y/n) | 0.3 (0.2, 0.4) | 0.9 (0.8, 0.9) | 1.9 (1.0, 3.4) |
| | | | | Joint narrowing (y/n) | 0.2 (0.1, 0.3) | 0.9 (0.8, 0.9) | 1.9 (0.9, 3.6) |
| | | | | Partial ankylosis (y/n) | 0.1 (0.1, 0.2) | 0.9 (0.9, 0.9) | 1.5 (0.6, 3.8) |
| | | | | Total ankylosis (y/n) | 0.0 (0.0, 0.1) | 1.0 (0.9, 1.0) | NA* |
| | | | At least a grade two unilaterally | | 0.54 (0.4,0.6) | 0.7 (0.6,0.8) | 2.0 (1.4, 2.9) |
| | | | Modified NY criteria | | 0.4 (0.3, 0.5) | 0.9 (0.8, 0.9) | 3.0 (1.6, 5.6) |
| | | Spine Xrays | Lesions | At least one erosion | 0.1 (0.1,0.2) | 0.8 (0.7,0.9) | 0.7 (0.4, 1.2) |
| | | | | At least one sclerosis lesion | 0.2 (0.2,0.3) | 0.8 (0.7,0.9) | 1.3 (0.7, 2.3) |
| | | | | At least one squaring lesions | 0.1 (0.0, 0.1) | 1.0 (0.9, 1.0) | 5.7 (0.7, 46.5) |
| | | | | At least one full bone bridge | 0.1 (0.0,0.1) | 1.0 (0.9,1.0) | 2.5 (0.5, 12.7) |
| M | Inflammatory Sacroiliac lesions joints | y Sacroiliac joints | At least one inflammatory lesion | | 0.4 (0.3, 0.5) | 0.8 (0.7, 0.8) | 1.6 (1.0, 2.4) |
| | | | ASAS definition of positive MRI sacroiliitis | | 0.4 (0.3, 0.5) | 0.9 (0.8, 0.9) | 4.2 (2.0, 8.5) |
| | | | ASAS definition of MRI sacroiliitis AND deep lesion† | | 0.2 (0.1, 0.3) | 1.0 (0.9, 1.0) | 16.2 (2.2, 119.0) |
| | | | ASAS definition of MRI sacroiliitis AND intense lesion† | | 0.2 (0.1, 0.3) | 1.0 (0.9, 1.0) | 9.5 (2.3, 39.6) |
| | | | ASAS definition of MRI sacroillitis AND (deep OR intense lesion)† | | 0.2 (0.2, 0.3) | 1.0 (0.9, 1.0) | 7.6 (2.4, 24.2) |
| | | | ASAS definition of MRI sacrolliitis AND (deep AND intense lesion)† | | 0.1 (0.1, 0.2) | 1.0 (0.9, 1.0) | NA* |
| | | Spine | At least one inflammatory lesion | | 0.5 (0.4, 0.6) | 0.6 (0.5, 0.7) | 1.2 (0.9, 1.6) |
| | | | At least three inflammatory lesions (ASAS definition of positive spine MRI) | | 0.4 (0.3, 0.6) | 0.7 (0.6, 0.8) | 1.4 (0.9, 1.9) |
| | | | At least five inflammatory lesions | | 0.3 (0.2, 0.4) | 0.7 (0.7, 0.8) | 1.2 (0.8, 1.9) |
| | Structural lesions | Sacroiliac joints | At least one structural lesion | | 0.2 (0.2, 0.3) | 0.8 (0.7, 0.0) | 1.4 (0.8, 2.5) |
| | | | At least three erosions | | 0.3 (0.2, 0.4) | 0.9 (0.8, 1.0) | 3.0 (1.6, 5.8) |
| | | | At least three fatty lesions | | 0.3 (0.2, 0.4) | 0.9 (0.8, 0.9) | 2.5 (1.3, 4.7) |
| | | | | | | | Conditation |



| e 2 Continued | | | | |
|---------------|--|----------------|-------------------------------|----------------|
| | | Se (95% CI) | Spe (95% CI) LR+ (95% CI) | LR+ (95% CI) |
| | At least five structural lesions (erosions or fatty lesions) | 0.3 (0.2, 0.4) | 0.9 (0.8, 0.9) 2.4 (1.4, 4.3) | 2.4 (1.4, 4.3) |
| Spine | At least one structural lesion | 0.4 (0.3, 0.5) | 0.5 (0.4, 0.6) | 0.8 (0.6, 1.2) |
| | At least three erosions | 0.1 (0.0, 0.1) | 0.9 (0.9, 1.0) | 1.2 (0.4, 3.3) |
| | At least three fatty lesions | 0.2 (0.1, 0.2) | 0.8 (0.7, 0.9) | 0.7 (0.4, 1.2) |
| | At least five fatty lesions | 0.1 (0.0, 0.2) | 0.9 (0.8, 0.9) | 0.7 (0.3, 1.7) |
| | At least five structural lesions (erosions OR fatty lesions) | 0.1 (0.1, 0.2) | 0.8 (0.7, 0.9) | 0.6 (0.3, 1.1) |

*NA=not applicable, since one of the categories is 0, thus not calculable. †According to the SPARCC scoring method.

SAS, Assessment of SpondyloArthritis international Society; CBP, chronic back pain; NY, New York; axSpA, axial Spondyloarthritis. => 2 (considered relevant) are highlighted in bold

widely reported in the literature, which is not improved by training of readers. ^{6 7} Furthermore, the scores from this present exercise were somehow more 'conservative' than the local reading by the investigators of DESIR, ²⁰ who reported 39% and 50% patients fulfilling the mNY criteria and MRI sacroiliitis definitions, respectively.

Our study confirms that some of these 'typical axSpA' lesions can also be observed in patients without axSpA particularly at the spine level on MRI, but that lesions of the SIJ by all modalities remain the most valuables for diagnosis, including structural lesions of the SIJ. These very good performances of structural lesions of the SIJ for diagnostic purposes suggest a potential interest of adding MRI SIJ structural lesions to the ASAS classification criteria, and further studies assessing whether their inclusion in classification criteria might increase the criteria's performance are needed.

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REFERENCES

- Smolen JS, Schöls M, Braun J, et al. Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international Task Force. Ann Rheum Dis 2018;77:3–17.
- van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.
- Sieper J, Rudwaleit M, Baraliakos X, et al. The assessment of spondyloarthritis International Society (ASAS) Handbook: a guide to assess spondyloarthritis. Ann Rheum Dis 2009;68 Suppl 2:ii1–44.
- Feldtkeller E, Bruckel J, Khan MA. Scientific contributions of ankylosing spondylitis patient advocacy groups. Curr Opin Rheumatol 2000;12:239–47.
- Masson Behar V, Dougados M, Etcheto A, et al. Diagnostic delay in axial spondyloarthritis: A cross-sectional study of 432 patients. Joint Bone Spine 2017;84:467–71.
- van den Berg R, Lenczner G, Feydy A, et al. Agreement between clinical practice and trained central reading in reading of sacroiliac joints on plain pelvic radiographs. Results from the DESIR cohort. Arthritis Rheumatol 2014;66:2403–11.
- van Tubergen A, Heuft-Dorenbosch L, Schulpen G, et al. Radiographic assessment of sacroiliitis by radiologists and rheumatologists: does training improve quality? Ann Rheum Dis 2003;62:519–25.
- Lambert RGW, Bakker PAC, van der Heijde D, et al. Defining active sacroillitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI Working Group. Ann Rheum Dis 2016;75:1958–63.
- Rudwaleit M, Jurik AG, Hermann K-GA, et al. Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by the ASAS/ OMERACT MRI group. Ann Rheum Dis 2009;68:1520–7.
- Rudwaleit M, Landewé R, van der Heijde D, et al. The development of assessment of spondyloarthritis International Society classification criteria for axial spondyloarthritis (Part I): classification of paper patients by expert opinion including uncertainty appraisal. Ann Rheum Dis 2009;68:770–6.
- Rudwaleit M, van der Heijde D, Landewé R, et al. The development of assessment of spondyloarthritis International Society classification criteria for axial spondyloarthritis (Part II): validation and final selection. Ann Rheum Dis 2009;68:777–83.
- Moltó A, Paternotte S, van der Heijde D, et al. Evaluation of the validity of the different arms of the ASAS set of criteria for axial spondyloarthritis and description of the different imaging abnormalities suggestive of spondyloarthritis: data from the DESIR cohort. Ann Rheum Dis 2015;74:746–51.
- Sepriano A, Rubio R, Ramiro S, et al. Performance of the ASAS classification criteria for axial and peripheral spondyloarthritis: a systematic literature review and meta-analysis. Ann Rheum Dis 2017;76:886–90.
- Jacquemin C, Rubio Vargas R, van den Berg R, et al. What is the reliability of non-trained Investigators in recognising structural MRI lesions of sacroiliac joints in patients with recent inflammatory back pain? Results of the DESIR cohort. RMD Open 2016;2:e000303.
- de Hooge M, Pialat J-B, Reijnierse M, et al. Assessment of typical spa lesions on MRI of the spine: do local readers and central readers agree in the DESIR-cohort at baseline? Clin Rheumatol 2017;36:1551–9.

- Bakker PAC, van den Berg R, Lenczner G, et al. Can we use structural lesions seen on MRI of the sacroiliac joints reliably for the classification of patients according to the ASAS axial spondyloarthritis criteria? data from the DESIR cohort. Ann Rheum Dis 2017;76:392–8.
- Weber U, Lambert RGW, Pedersen SJ, et al. Assessment of structural lesions in sacroiliac joints enhances diagnostic utility of magnetic resonance imaging in early spondylarthritis. Arthritis Care Res 2010;62:1763–71.
- Weber U, Jurik AG, Zejden A, et al. Frequency and Anatomic Distribution of Magnetic Resonance Imaging Features in the Sacroiliac Joints of Young Athletes: Exploring "Background Noise" Toward a Data-Driven Definition of Sacroilliitis in Early Spondyloarthritis. Arthritis Rheumatol 2018;70.
- A positive MRI of the Sacroiliac joints is not specific for axial spondyloarthritis but frequently occurs in healthy individuals. ACR meeting Abstracts. Available: http://acrabstracts.org/abstract/ a-positive-mri-of-the-sacroiliac-joints-is-not-specific-for-axialspondyloarthritis-but-frequently-occurs-in-healthy-individuals/ [Accessed 6 Mar 2018].
- Dougados M, Etcheto A, Molto A, et al. Clinical presentation of patients suffering from recent onset chronic inflammatory back pain suggestive of spondyloarthritis: the DESIR cohort. Joint Bone Spine 2015;82;345–51.
- Creemers MCW, Franssen MJAM, van't Hof MA, et al. Assessment of outcome in ankylosing spondylitis: an extended radiographic scoring system. Ann Rheum Dis 2005;64:127–9.
- Maksymowych WP, Inman RD, Salonen D, et al. Spondyloarthritis research consortium of Canada magnetic resonance imaging index for assessment of sacroiliac joint inflammation in ankylosing spondylitis. Arthritis Rheum 2005;53:703–9.
- 23. de Hooge M, van den Berg R, Navarro-Compán V, et al. Patients with chronic back pain of short duration from the space cohort: which MRI structural lesions in the sacroiliac joints and inflammatory and structural lesions in the spine are most specific for axial spondyloarthritis? Ann Rheum Dis 2016;75:1308–14.
- Maksymowych WP, Inman RD, Salonen D, et al. Spondyloarthritis research consortium of Canada magnetic resonance imaging index for assessment of spinal inflammation in ankylosing spondylitis. Arthritis Rheum 2005;53:502–9.
- Hermann K-GA, Baraliakos X, van der Heijde DMFM, et al.
 Descriptions of spinal MRI lesions and definition of a positive MRI
 of the spine in axial spondyloarthritis: a consensual approach
 by the ASAS/OMERACT MRI Study Group. Ann Rheum Dis
 2012;71:1278–88.
- Østergaard M, Maksymowych WP, Pedersen SJ, et al. Structural Lesions Detected by Magnetic Resonance Imaging in the Spine of Patients with Spondyloarthritis - Definitions, Assessment System, and Reference Image Set. J Rheumatol Suppl 2009;84:18–34.
- Pedersen SJ, Weber U, Østergaard M. The diagnostic utility of MRI in spondyloarthritis. Best Pract Res Clin Rheumatol 2012;26:751–66.
- 28. McGee S. Simplifying likelihood ratios. *J Gen Intern Med* 2002;17:647–50.
- R: the R project for statistical computing. Available: https://www.r-project.org/ [Accessed 8 Mar 2019].
- van den Berg R, Lenczner G, Thévenin F, et al. Classification of axial spa based on positive imaging (radiographs and/or MRI of the sacroiliac joints) by local rheumatologists or radiologists versus central trained readers in the DESIR cohort. Ann Rheum Dis 2015;74:2016–21.