Diagnostic and Interventional Imaging 102 (2021) 171–180

Original article/*Musculoskeletal imaging*

Diagnostic performance of sacroiliac joint MRI and added value of spine MRI to detect active spondyloarthritis

M. Plier[a,b,1], A. Nzeusseu Toukap[a,1], N. Michoux[c], M.S. Stoenoiu[a], T. Kirchgesner[c], P. Durez[a], B. Lauwerys[a], F.E. Lecouvet[c,*]

[a] *Department of Rheumatology, Cliniques Universitaires Saint-Luc, Institut de Recherche Expérimentale et Clinique (IREC), Université Catholique de Louvain (UCLouvain), 1200 Brussels, Belgium*
[b] *Department of Rheumatology, Centre Hospitalier de Luxembourg, 1210 Luxembourg, Luxembourg.*
[c] *Department of Radiology, Cliniques Universitaires Saint-Luc, Institut de Recherche Expérimentale et Clinique (IREC), Université Catholique de Louvain (UCLouvain), 1200 Brussels, Belgium*

ARTICLE INFO

Keywords:
Axial spondyloarthritis
Magnetic resonance imaging (MRI)
Disease activity
Spine
Sacro-iliac joint

ABSTRACT

Purpose: To investigate the diagnostic performance of sacroiliac joint (SIJ) magnetic resonance imaging (MRI) and the incremental value of spine MRI to "predict" clinical disease activity in patients with axial spondyloarthritis (axSpA).
Materials and methods: This cross-sectional study included adult patients with known axSpA according to the SpondyloArthritis International Society (ASAS) classification criteria, radiological arm. MRI disease activity was scored semi-quantitatively for SIJ and total spine MRI in each patient. Two cut-off levels ($\geq$ 1.3 and $\geq$ 2.1) for ankylosing spondylitis disease activity score with C-reactive protein (ASDAS-CRP) were considered for clinical disease activity categorization. MRI scores were first evaluated individually. Then, SIJ score was combined with the score from a spine segment (lumbar, cervical, thoracic or total spine) to build a bi-parametric model using a classification tree. Receiver operating characteristic (ROC) curves were constructed to evaluate the classification performance according to disease activity category of these models.
Results: Forty-four patients (30 men, 14 women; mean age, 37 years $\pm$ 10 [SD] [range: 17–64 years]) with a mean disease duration of 5 years $\pm$ 8 (SD) (range: 0–35 years) were included. Thirty-six patients (36/44; 82%) had ASDAS-CRP $\geq$ 1.3 and 27 patients (27/44; 61%) had ASDAS-CRP $\geq$ 2.1. The most frequently involved spinal segment was mid-thoracic (T7-T8). The SIJ MRI score was an informative model to identify active axSpA (AUC $\geq$ 0.7, regardless of the cut-off level on ASDAS-CRP). Performance of bi-parametric models based on "SIJ + thoracic spine" (for detecting patients with ASDAS-CRP $\geq$ 1.3) or "SIJ + total spine" (for detecting patients with ASDAS-CRP $\geq$ 2.1) outperformed that of the individual SIJ score ($P < 0.05$).
Conclusion: The combination of MRI of the SIJ and spine allows to accurately discriminate between active and inactive axSpA, outperforming SIJ MRI alone.
© 2020 Published by Elsevier Masson SAS on behalf of Société française de radiologie.

1. Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease that mainly affects the axial skeleton. To date, there is no 'gold standard' for measuring disease activity in an individual patient [1]. In daily clinical practice, evaluation of disease activity in patients with axSpA may be challenging when patient reported measures (visual analogic scale of pain, stiffness, and fatigue) of disease activity do not match with evaluation by the rheumatologist [2]. As a result, magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) and spine has gained an increased role as a help in therapeutic decisions in clinical practice and in monitoring treatment efficacy in trials [3,4].

MRI of the SIJ is validated by the SpondyloArthritis International Society (ASAS) as a major classification criteria that helps identify patients with axSPA [5]. MRI of the spine has been recently evaluated as being of limited additional value for testing the presence or absence of axSPA in an individual patient [6]. Yet, the question

Abbreviations: ASAS, Spondyloarthritis International Society; ASDAS-CRP, ankylosing spondylitis disease activity score C-reactive protein; AUC, area under the ROC curve; axSpA, axial spondyloarthritis; BASDAI, ankylosing disease activity index; BME, bone marrow edema; CI, confidence interval; F, frequency of involvement; MRI, magnetic resonance imaging; PGA, patient global assessment; ROC, receiver operating characteristic; SD, standard deviation; SIJ, sacroiliac joint; STIR, short-tau inversion recovery.

* Corresponding author.
E-mail address: frederic.lecouvet@uclouvain.be (F.E. Lecouvet).
[1] M.P. and A.N.T. equally contributed to this article.

https://doi.org/10.1016/j.diii.2020.07.001
2211-5684/© 2020 Published by Elsevier Masson SAS on behalf of Société française de radiologie.

remains whether SIJ MRI provides the necessary and sufficient information on disease activity at the imaging level, or whether combination with MRI of the spine could be of added value. This question has not been analyzed before. The answer to this question is important to confirm the potential of MRI for evaluating disease activity and to determine the choice of regions that should be the main targets of MRI in patients with axSpA in daily practice or in clinical studies.

The purpose of this study was to investigate the performance of MRI scores determined in the SIJ and different anatomical segments of the spine (lumbar spine, cervical spine, thoracic spine, total spine), individually and combined together within bi-parametric models, for "predicting" clinical disease activity in patients with axSpA.

2. Materials and methods

2.1. Patients

We reviewed all medical files of patients in our axSpA Clinic from January 2012 until December 2018 inclusively to identify patients meeting the following criteria. Patients were included in this study:

(i) if they were aged ≥ 18 years;
(ii) if they had a known diagnosis of ankylosing spondylitis according to the ASAS criteria, radiological arm;
(iii) if both SIJ and total spine MRI, as well as the calculated ankylosing spondylitis disease activity score with C-reactive protein (ASDAS-CRP) were available in their medical file and were obtained with an interval < 3 months;

if they were on stable treatment between the clinical and the MRI assessment. Patients were excluded when they had a previous history of disc herniation or of spine or bony pelvis surgery that could interfere with the evaluation of axSpA.

2.2. Clinical and biological data

During the review of the medical files, data about demographical characteristics and laboratory parameters including age, gender, disease duration, medication, HLA B27 status and CRP level were recorded. Bath Ankylosing Disease Activity Index (BASDAI) scores, individual BASDAI questions and Patient Global Assessment (PGA) were collected. Pelvic and SIJ radiographs were reviewed by one expert radiologist blinded for review, and categorized according to the modified New York criteria [7]. ASDAS-CRP was used as reference standard for evaluating clinical disease activity. Two validated cut-off levels were considered: ≥ 1.3 (separating 'inactive disease' from 'active disease' which includes low, high and very high activity) and ≥ 2.1 (separating 'inactive and low disease activity' from 'high and very high disease activity') [8]. Cut-offs were selected according to the European League against rheumatism guidelines for tapering (ASDAS < 1.3) or intensifying treatment (ASDAS ≥ 2.1) in accordance with the rheumatologist's opinion [4].

2.3. Image analysis

MRI examinations were performed on a 3.0T MRI magnet (Philips Healthcare). The protocol included coronal oblique T1-weighted and short tau inversion recovery (STIR) images of the SIJ and sagittal T1-weighted and STIR images of the whole spine. Detailed sequence parameters can be found in Table 1.

MRI disease activity was evaluated by an expert radiologist, who was blinded to the patients' information. The spine was analyzed using the Berlin method, grading the extent of bone marrow oedema (BME) suggestive of axSPA from 0 (no involvement) to 3 (> 50% of the area) in each of the 23 discovertebral units from C2/C3 to L5/S1, resulting in a score ranging from 0 (minimal value) to 69 (maximal value) [9]. A discovertebral unit was represented by the area defined by 2 imaginary horizontal lines through the middle plane of adjacent vertebras and was assessed on sagittal MRI images. Segmental MRI scores were calculated for the lumbar spine (L1/L2 to L5/S1, range 0–15), the thoracic spine (T1/T2 to T12/L1, range 0–36) and the cervical spine (C2/C3 to C7/T1, range 0–18).

The global score described by Rudwaleit et al. was used to quantify BME in the SIJ [9]. Each sacral and each iliac aspect of both SIJ were scored on a coronal oblique view from 0 to 3 (for none, little, moderate or severe inflammation) with a maximum possible score of 12 (range 0–12). The Berlin MRI spine score and the SIJ scoring system show excellent interobserver reproducibility [10,11].

Table 1
MRI sequence parameters of spine and sacroiliac joint examinations at 3T.

	Spine		Sacroiliac joint	
	T1	STIR	T1	STIR
Plane	Sagittal	Sagittal	Coronal oblique	Coronal oblique
FOV (cm)	340	340	240	240
Slice thickness (mm)	3.5	3.5	3.0	3.0
Gap (%)	0.35	0.35	0.3	0.3
Number of slices	17	17	22	22
TR (ms)	710	3070	570	3700
TE (ms)	10	62	9.4	48
TI (ms)	–	200	–	200
Echo train lenght	2	13	3	16
NEX	1	1	2	2
Duration (min.sec)	2 × 2.05	2 × 2.41	2.12	3.07

SIJ: sacroiliac joint; STIR: short tau inversion recovery; FOV: field of view; TR: repetition time; TE: echo time; TI: inversion time; NEX: number of excitations.

2.4. Statistical analysis

Mean values (or median values when data distribution was not normal according to the Kolmogorov-Smirnov test [12]) with their standard deviation (SD) and range [min–max] were reported for quantitative variables.

Frequency of involvement of each discovertebral segment was investigated. Potential differences in frequency between segments were investigated using mid-P approach or Fisher' exact test [13].

Correlations between MRI scores and markers of disease activity (CRP, BASDAI, PGA, ASDAS-CRP) were searched for using Pearson correlation coefficient or Spearman rank coefficient when data distribution was not normal. Strength of the correlation was interpreted as follows: strong ($r \geq 0.9$), substantial ($0.7 \leq r < 0.9$), moderate ($0.5 \leq r < 0.7$) or weak ($r < 0.5$).

In the assessment of the disease activity by imaging, MRI scores from the SIJ, lumbar spine, cervical spine, thoracic spine and total spine were first evaluated individually as mono-parametric models. In a second step, the SIJ score was combined with the score obtained for each spine segment and for the total spine to constitute a bi-parametric model using a classification tree [14]. The classification performance of the mono- and bi-parametric models was evaluated in reconstructing the receiver operating characteristic (ROC) curve associated to each of these models for 2 different cut-off values of ASDAS-CRP (active disease [i.e., ASDAS-CRP ≥ 1.3] *vs.* inactive disease [i.e., ASDAS-CRP ≥ 1.3] and high or very high disease activity [*i.e.*, ASDAS-CRP ≥ 2.1] *vs.* inactive or low disease activity [*i.e.*, ASDAS-CRP < 2.1]) [15].

True positives (TP), true negatives (TN), false positives (FP), false negatives (FN), sensitivity (Se) and specificity (Sp) along with their 95% confidence intervals (CIs) were calculated. Area under the ROC curves (AUC) and the optimal cut-off value (according to the

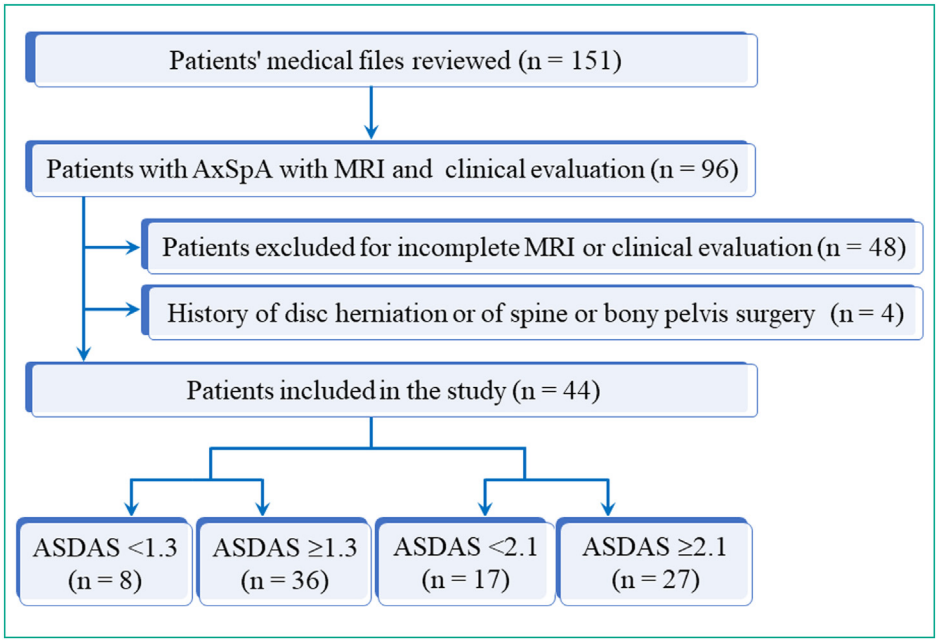

Fig. 1. Study flow chart.

Youden index) were built for the models. The level of performance of the models was interpreted according to AUC value as follows: AUC ≥ 0.9: very informative model, 0.9 > AUC ≥ 0.7: informative model, 0.7 > AUC ≥ 0.5: relatively uninformative model. Finally, a pairwise comparison of AUCs was performed in order to rank the models according to their level of classification performance [16].

A *P* value < 0.05 was regarded as statistically significant for all tests cited above. All analyses were performed using StatsDirect statistical software version 2.7.8 (http://www.statsdirect.com/). The function *classregtree* from Matlab software version R2017a (http://www. mathworks.com) was used to optimize the classification tree for assessing disease activity by imaging from combined MRI scores (with equal prior probabilities for both classes of disease activity, 'inactive disease' versus 'active disease' when using an ASDAS-CRP ≥ 1.3, and 'inactive or low disease activity' versus 'high or very high disease activity when using an ASDAS-CRP ≥ 2.1).

3. Results

3.1. Descriptive measurements

Based on our inclusion and exclusion criteria, 44 patients were included in this study (Fig. 1). There were 30 men and 14 women. Thirty-six patients had an ASDAS-CRP ≥ 1.3 and 27 had an ASDAS-CRP ≥ 2.1. Demographical, clinical and radiological data are given in Table 2. Patient disease activity levels did not differ in terms of male/female ratio, age, radiographic sacroiliitis or disease duration (all *P* values > 0.05), regardless of the cut-off level on ASDAS-CRP.

Frequency of involvement (F) of each discovertebral segment is displayed in Fig. 2. The most frequently affected segment was T7-T8 (22/44; F = 50%) patients. Frequency of involvement in the thoracolumbar junction (from T10-T11 to L1-L2) and L3-L4 was between 50% and 40%. Less affected segments were the cervical spine (C2-C3 to C7-T1), the upper (T1-T2 to T6-T7) and lower (T8-T9, T9-T10) thoracic spine, the L2-L3 level, and the lower lumbar spine (L4-L5 and L5-S1) (F < 40%).

Correlations between individual MRI scores (SIJ, lumbar, thoracic, cervical and total spine) and measures of clinical disease

Table 2
Demographic, clinical and MRI characteristics of 44 patients with axial spondyloarthritis.

Demographic parameters	
Gender	
Male	30/44 (68%)
Female	14/44 (32%)
Age (years)	37 ± 10 [17–64]
Disease duration (years)	5 ± 8 [0–35]
Age of onset (years)	27 ± 11 [11–56]
HLA B27 positive	34/44 (77%)
Radiographic sacroiliitis according to New York criteria	36/44 (82%)
Current treatment	
None	7/44 (16%)
NSAID	31/44 (70%)
ATNF of AIL17	6/44 (14%)
Clinical parameters	
Serum CRP level (mg/L)	10 ± 11 [1–50]
CRP ≥ 5 mg/l	21/44 (48%)
BASMI (0–10)	1.0 ± 1.4 [0–5]
BASFI (0–10)	3.2 ± 2.5 [0–10]
BASDAI (0–10)	4.3 ± 2.3 [0–10]
Patient global assessment (0–10)	4.6 ± 3.0 [0–9]
ASDAS-CRP (total)	2.6 ± 1.2 [0.8–5.8]
ASDAS-CRP ≥ 1.3	36/44 (82%)
ASDAS-CRP ≥ 2.1	27/44 (61%)
MRI scores	
Global MRI score for SIJ (0–12)	4.1 ± 3.2 [0–12]
Berlin MRI spine score	-
Total spine (0–69)	7.5 ± 6.5 [0–23]
Lumbar spine (0–15)	2.1 ± 1.9 [0–6]
Thoracic spine (0–36)	4.7 ± 4.4 [0–16]
Cervical spine (0–18)	0.7 ± 1.1 [0–4]
Delay between MRI & clinical scoring (days)	28 ± 21 [0–80]

Quantitative variables are reported as mean ± standard deviation; numbers in brackets are ranges. Qualitative variables are expressed as proportions; numbers in parentheses are percentages. NSAIDs: nonsteroidal anti-inflammatory drugs; ATNF: anti-tumor necrosis factor; AIL-17: anti-interleukin-17 monoclonal antibody; CRP: C-reactive protein; BASMI: bath ankylosing spondylitis metrology index; BASFI: bath ankylosing spondylitis functionnal index; BASDAI: bath ankylosing spondylitis disease activity index; ASDAS-CRP: ankylosing spondylitis disease activity score C-reactive protein; MRI: magnetic resonance imaging; SIJ: sacroiliac joints.

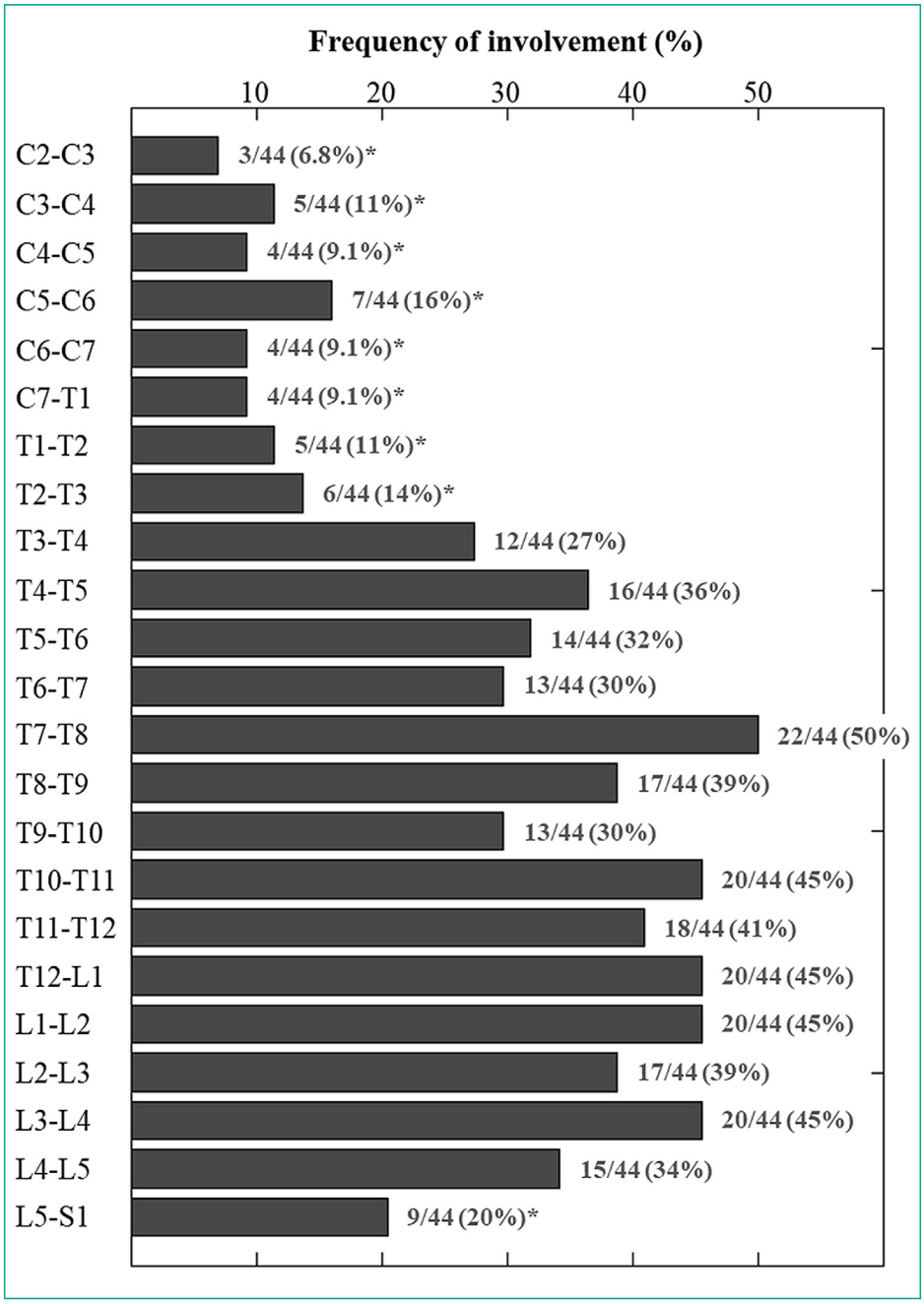

Fig. 2. Graph shows distribution (frequency) of spinal lesions in 44 patients with axial spondyloarthritis according to MRI. Significant differences in frequencies were observed between segment T7-T8 and segments * (Fisher exact test, $P < 0.05$).

activity are reported in Table 3. Although statistically significant correlations were observed (mainly between SIJ score and ASDAS-CRP, CRP, and BASDAI-Question 2 values, *i.e.*, axial pain), the strength of these correlations were moderate at best.

3.2. Performances of individual MRI scores

The level of performance of the mono-parametric models to classify the patients according to their clinical disease activity level is reported in Table 4 and Fig. 3. Considering a cut-off level on ASDAS-CRP ≥ 1.3, the performance of the MRI scores (based on AUC value) ranged from relatively uninformative (cervical spine, lumbar spine, total spine) to informative (thoracic spine, SIJ). In considering a cut-off level on ASDAS-CRP ≥ 2.1, the classification performance of the MRI scores ranged from relatively uninformative (lumbar spine, total spine, cervical spine, thoracic spine) to informative (SIJ). The mono-parametric analyses showed that using a threshold score of either 4 or 6, SIJ MRI had a specificity of 100% (95%CI: 63–100%), hence allowing the correct identification of patients with active disease (ASDAS-CRP ≥ 1.3) and of those with high or very high disease activity (ASDAS-CRP ≥ 2.1).

3.3. Performances of combined MRI scores

Two examples of bi-parametric model using a classification tree are shown on Figs. 4 and 5. The level of performance of these models is reported in Table 5 and Fig. 3. The performance of these models to predict clinical disease activity was at least informative,

Table 3
Correlations observed between clinical measurements of disease activity and mono-parametric models based on individual MRI scores.

MRI scores	ASDAS-CRP	CRP	PGA	BASDAI	BASDAI-Q2
	r (95% CI)	r (95% CI)	r (95% CI)	r (95% CI)	r (95% CI)
	P-value	*P*-value	*P*-value	*P*-value	*P*-value
SIJ	0.50 (0.24; 0.69)[a]	0.52 (0.27; 0.71)[b]	0.46 (0.19; 0.67)[a]	–	0.31 (0.02; 0.56)[a]
	0.001	0.000	0.002	0.055	0.039
Lumbar spine	–	–	–	–	–
	0.845	0.385	0.839	0.675	0.692
Thoracic spine	0.31 (0.01; 0.56)[b]	0.47 (0.20; 0.67)[b]	–	–	–
	0.041	0.001	0.134	0.875	0.210
Cervical spine	–	–	–	–	–
	0.055	0.056	0.083	0.384	0.305
Total spine	–	0.40 (0.12; 0.63)[b]	–	–	–
	0.097	0.007	0.227	0.286	0.190

MRI: magnetic resonance imaging; ASDAS-CRP: ankylosing spondylitis disease activity score C-reactive protein; CRP: C-reactive protein; PGA: patient global assessment; BASDAI: bath ankylosing spondylitis disease activity index; BASDAI-Q2: bath ankylosing spondylitis disease activity index question 2 (axial pain); SIJ: sacroiliac joint. Correlations range from weak to moderate.
[a] Pearson correlation coefficient.
[b] Spearman correlation coefficient

Table 4
Levels of performance of mono-parametric models based on individual MRI scores using 2 different cut-off levels of ASDAS-CRP.

Model	Cut-off	TP	TN	FP	FN	Se (%) (95% CI)	Sp (%) (95% CI)	AUC (95% CI)	*P*-value
ASDAS ≥ 1.3									
SIJ	> 4	16	8	0	20	44 (28; 62)	100 (63; 100)	0.70 (0.55; 0.83)	0.011
Lumbar spine	–	–	–	–	–	–	–	0.62 (0.46; 0.76)	0.190
Cervical spine	–	–	–	–	–	–	–	0.57 (0.42; 0.72)	0.388
Thoracic spine	> 0	32	4	4	4	89 (74; 97)	50 (16; 84)	0.74 (0.59; 0.86)	0.016
Total spine	> 5	21	7	1	15	58 (41; 75)	88 (47; 100)	0.68 (0.53; 0.81)	0.046
ASDAS ≥ 2.1									
SIJ	> 6	10	17	0	17	37 (19; 58)	100 (81; 100)	0.72 (0.56; 0.84)	0.006
Lumbar spine	–	–	–	–	–	–	–	0.55 (0.39; 0.70)	0.578
Cervical spine	> 1	9	16	1	18	33 (17; 54)	94 (71; 100)	0.66 (0.50; 0.79)	0.017
Thoracic spine	> 1	22	9	8	5	81 (62; 94)	53 (28; 77)	0.68 (0.52; 0.81)	0.038
Total spine	–	–	–	–	–	–	–	0.65 (0.49; 0.79)	0.081

Receiver operating characteristic (ROC) curve analysis: sensitivity and specificity are reported only when the test was statistically significant ($P < 0.05$); Se: sensitivity; Sp: specificity; TP: true-positive; TN: true-negative; FP: false-positive; FN: false-negative; AUC: area under the ROC curve; SIJ: sacroiliac joints. The table reads as follows: a SIJ score > 4 yields a model with a sensitivity of 44% and a specificity of 100% for assessing disease activity using an ASDAS-CRP ≥ 1.3. Cut-off values result from ROC curves analysis.

Table 5
Levels of performance of bi-parametric MRI models (using a classification tree approach) with 2 different cut-off levels of ankylosing spondylitis disease activity score C-reactive protein.

bi-parametric model	TP	TN	FP	FN	Se (%) (95% CI)	Sp (%) (95% CI)	AUC (95% CI)	*P*-value
ASDAS ≥ 1.3								
SIJ + lumbar spine	25	7	1	11	69 (52; 84)	88 (47; 100)	0.79 (0.64; 0.89)	< 0.001
SIJ + cervical spine	26	7	1	10	72 (55; 86)	88 (47; 100)	0.80 (0.65; 0.90)	< 0.001
SIJ + thoracic spine	26	8	0	10	72 (55; 86)	100 (63; 100)	0.86 (0.72; 0.95)	< 0.001
SIJ + total spine	28	7	1	8	78 (61; 90)	88 (47; 100)	0.83 (0.68; 0.92)	< 0.001
ASDAS ≥ 2.1								
SIJ + lumbar spine	22	13	4	5	81 (62; 94)	76 (50; 93)	0.79 (0.64; 0.90)	< 0.001
SIJ + cervical spine	18	15	2	9	67 (46; 84)	88 (64; 99)	0.78 (0.62; 0.89)	< 0.001
SIJ + thoracic spine	20	15	2	7	74 (54; 89)	88 (64; 99)	0.81 (0.67; 0.91)	< 0.001
SIJ + total spine	22	16	1	5	81 (62; 94)	94 (71; 100)	0.88 (0.74; 0.96)	< 0.001

The table reads as follows: a model based on 'SIJ + lumbar spine' scores yields a sensitivity of 69% and a specificity of 88% for assessing disease activity using an ankylosing spondylitis disease activity score C-reactive protein (ASDAS-CRP) ≥ 1.3. As classification trees reconstructed here are binary classifiers, not cut-off value is reported. Receiver operating characteristic (ROC) curve analysis: capabilities are reported only when the test was statistically significant ($P < 0.05$); Se: sensitivity; Sp: specificity; TP: true-positive; TN: true-negative; FP: false-positive; FN: false-negative; AUC: area under the ROC curve; SIJ: sacroiliac joints.

regardless of the model or the cut-off level on ASDAS-CRP (all AUC values ≥ 0.7).

3.4. Comparison of performance between models

When considering a cut-off level on ASDAS-CRP ≥ 1.3, the pairwise comparison of AUCs derived from mono-parametric models did not yield any significant difference (all *P* values > 0.251). No individual MRI score significantly outperformed another one. The same observation was made when considering a cut-off level on ASDAS-CRP ≥ 2.1 (all *P* values > 0.100).

The pairwise comparison of AUCs derived from bi-parametric models did not reveal any significant difference, regardless of the cut-off level on ASDAS-CRP (all *P*-values > 0.208). No bi-parametric model significantly outperformed another one.

When considering a cut-off level ASDAS-CRP ≥ 1.3, the model "SIJ + thoracic spine" significantly outperformed the mono-parametric models based on cervical spine ($P = 0.003$), lumbar spine ($P = 0.014$) and SIJ ($P = 0.050$) but not those based on thoracic

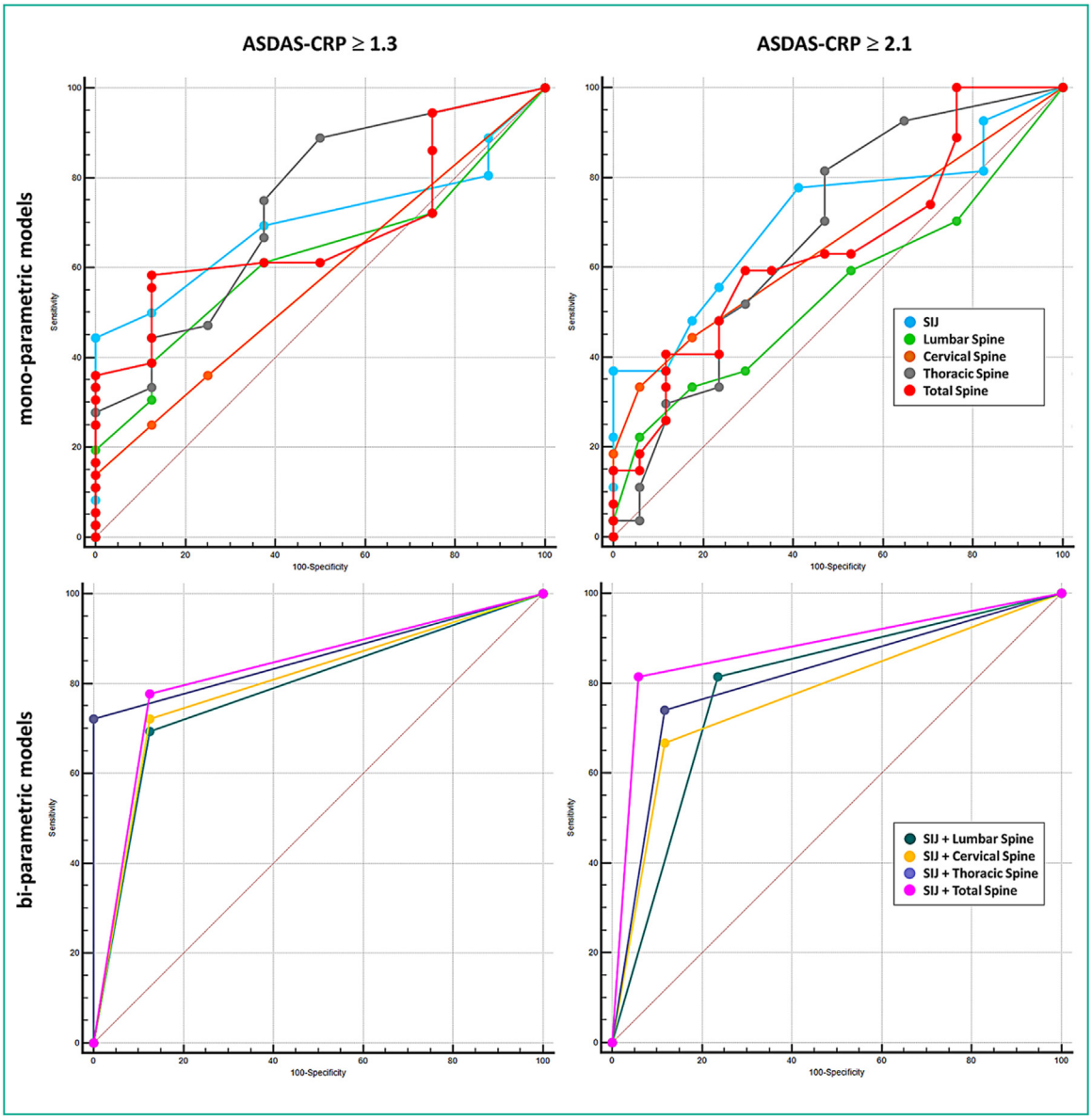

Fig. 3. Receiver operating characteristic (ROC) curve analysis of the mono- and bi-parametric models (reconstructed from MRI scores) using 2 different cut-off levels of ankylosing spondylitis disease activity score C-reactive protein (ASDAS-CRP). SIJ: sacroiliac joints.

spine ($P = 0.239$) and total spine ($P = 0.064$). The model "SIJ + total spine" also significantly outperformed the mono-parametric models based on cervical spine ($P = 0.026$), lumbar spine ($P = 0.039$) and total spine ($P = 0.044$) but not those based on SIJ ($P = 0.214$) and thoracic spine ($P = 0.244$).

When considering a cut-off level ASDAS-CRP ≥ 2.1, the model "SIJ + thoracic spine" significantly outperformed the model based on lumbar spine ($P = 0.010$) but not the other mono-parametric models ($P^{versus\ \text{cervical spine}} = 0.069$, $P^{versus\ \text{thoracic spine}} = 0.166$, $P^{versus\ \text{total spine}} = 0.088$, $P^{versus\ \text{SIJ}} = 0.106$). In contrast, the model "SIJ + total spine" significantly outperformed almost all mono-parametric models ($P^{versus\ \text{lumbar spine}} = 0.002$, $P^{versus\ \text{cervical spine}} = 0.006$, $P^{versus\ \text{total spine}} = 0.028$, $P^{versus\ \text{SIJ}} = 0.041$) expect that based on thoracic spine ($P = 0.061$).

4. Discussion

This study addressed the performance of MRI of the SIJ and the incremental value of spine MRI in assessing disease activity in axSpA. First, we found that the individual SIJ MRI score represents an informative model for identifying patients with more severe *versus* less severe clinical disease activity, regardless of the clinical cut-off level considered on the basis of ASDAS-CRP (≥ 1.3 or ≥ 2.1). Second, this study demonstrated for the first time that the combination of SIJ and spine MRI scores within a classification tree yielded bi-parametric models performing significantly better than certain individual MRI scores for identifying patients with higher versus lower disease activity. This study highlights that the bi-parametric "SIJ + thoracic spine" model outperforms the mono-parametric model based on SIJ scoring for identifying patients with an ASDAS-CRP ≥ 1.3, and that the biparametric "SIJ + total spine" model outperformed the mono-parametric model based on SIJ scoring for identifying patients with an ASDAS-CRP ≥ 2.1.

MRI of the SIJ is an important contributor to the diagnosis of axSpA, with well-defined acquisition and reading protocols [17]. MRI coverage of the SIJ is sufficient in the vast majority of patients to identify axSPA in an accurate clinical setting. The diagnostic role of spine MRI is still unclear and under investigation but it seems that

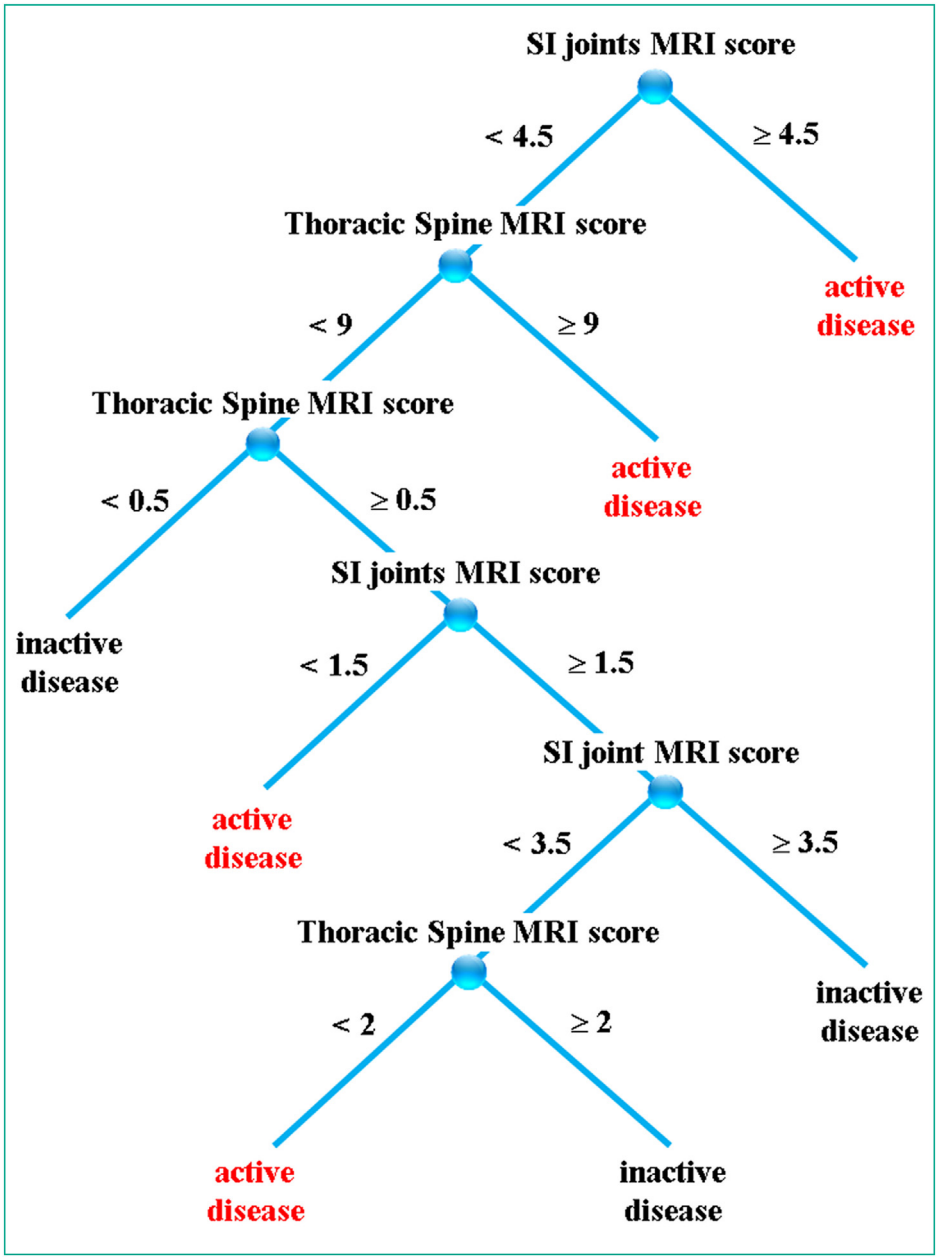

Fig. 4. Graph shows bi-parametric model based on "SIJ + thoracic spine" scores (using a classification tree) for assessing clinical disease activity in patients with axial spondyloarthritis, with a cut-off level on ankylosing spondylitis disease activity score C-reactive protein (ASDAS-CRP) ≥ 1.3. The tree reads as follows: if the SIJ score ≥ 4.5 (first top node), then the patient is identified as presenting active disease and the test stops. However, if the SIJ score < 4.5, then the test continues to the second top node. If the thoracic score ≥ 9, then the patient is identified as presenting active disease, and so forth. The tree has thus 6 nodes (corresponding to 6 thresholding tests either applied on the SIJ or thoracic spine score) that may be tested consecutively (from top to bottom), if necessary, to classify patients according to disease activity. Of note, the number of nodes and the thresholding test associated to each node of the tree are both optimized by the *classregtree* function (Matlab) that performs an "exact search" to find the best split. MRI: magnetic resonance imaging; SI: sacroiliac.

spinal lesions alone are unlikely to have sufficient diagnostic performance [18]. Ez-Zaitouni et al. demonstrated that in patients with chronic back pain without sacroiliitis, 382 MRIs of the spine must be performed in patients with negative SIJ MRI to identify only one patient with non-radiological-axSpA, questioning the indication of spinal MRI to help diagnose axSPA [6]. On the other hand, Weber et al. found that MRI assessment of the spine in addition to SIJ MRI can lead to misclassification in up to 17.5% of healthy volunteers without axSpA [19]. In this study, we assessed the value of spine MRI for the evaluation of disease activity in addition to SIJ MRI.

Regarding the distribution of MRI lesions across the spine, we observed that the most frequently involved segment was the mid-thoracic spine (T7-T8). It was followed by the thoraco-lumbar junction (T10-T11 to L1-L2) and the mid-lumbar spine (L3-L4). The cervical spine and upper thoracic segment were the less affected regions. These results are in line with the data from other studies that found that the mid-thoracic is the most frequently and severely affected spinal segment [20–23].

Active inflammation on MRI is mainly represented by BME. At the imaging level, the best indicators of active disease are subchondral BME in the SIJ [24] and BME of the vertebral corners [25]. Our results confirm that MRI evaluation of BME in the SIJ is a valuable tool for the evaluation of disease activity. The high specificity of SIJ MRI highlights its accuracy in identifying truly active patients.

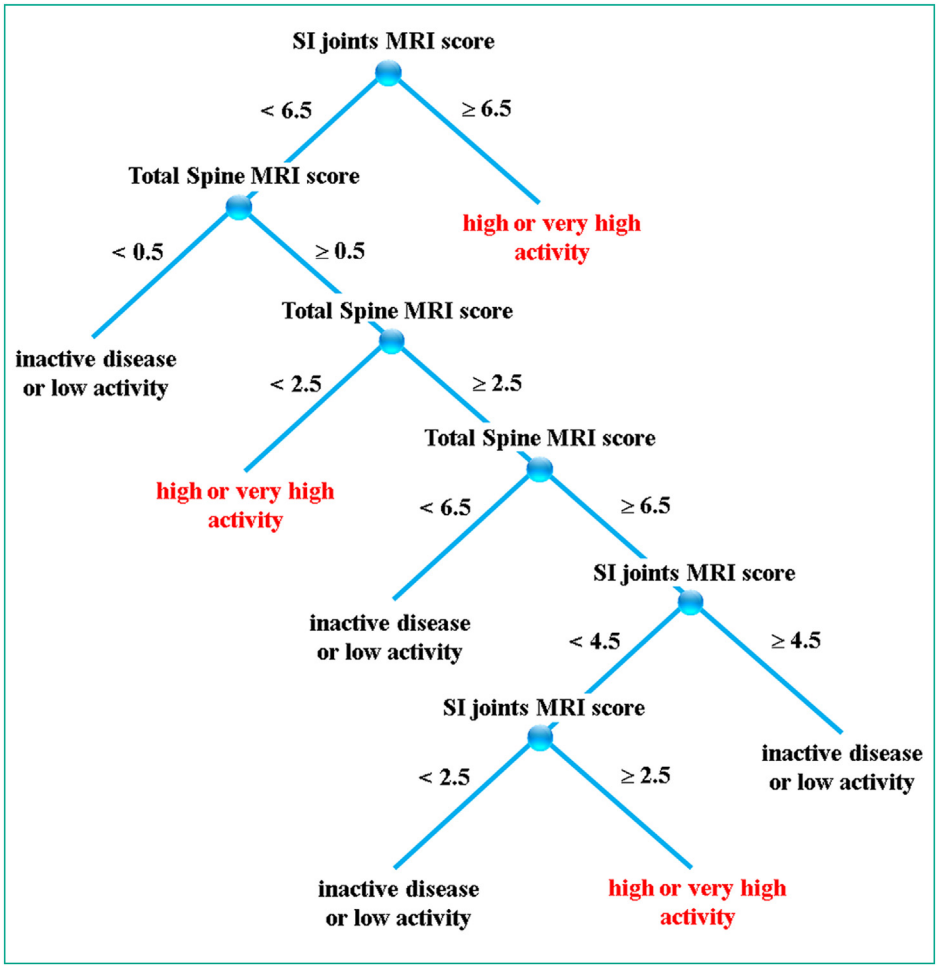

Fig. 5. Bi-parametric model based on "SIJ + total spine" scores (using a classification tree) in assessing clinical disease activity in patients with axial spondyloarthritis, with a cut-off level on ankylosing spondylitis disease activity score C-reactive protein (ASDAS-CRP) ≥ 2.1. The tree reads as follows. If the SIJ score ≥ 6.5 (first top node), then the patient is identified as presenting a high or very high disease activity and the test stops. However, if the SIJ score < 6.5, then if the total Spine score ≥ 0.5 (second top node) but is also < 2.5 (third node), then the patient is identified as presenting a high or very high disease activity. This tree has also 6 nodes (*i.e.*, 6 thresholding tests either applied on the SIJ or total spine score) that may be tested consecutively (from top to bottom), if necessary, to classify the patients according to disease activity. Of note, the number of nodes and the thresholding test associated to each node of the tree are both optimized by the *classregtree* function (Matlab) that performs an "exact search" to find the best split. MRI: magnetic resonance imaging; SI: sacroiliac.

In addition, significant correlations between MRI inflammation scores and measures of clinical disease activity were observed. Indeed, SIJ MRI scores correlated significantly with ASDAS-CRP, CRP levels, PGA and BASDAI question 2 (axial pain), in agreement with previous reports made by Navarro-Compán et al. [26]. In line with Konca et al., we also found that thoracic MRI scores had a significant positive correlation with ASDAS-CRP and CRP levels [23]. Beside this, no relation was observed between clinical parameters and lumbar or cervical MRI scores.

Importantly, our results demonstrate that the categorization of patients according to their clinical disease activity may be improved when spine MRI is performed in addition to SIJ MRI. Bi-parametric models showed that SIJ MRI complemented with thoracic spine MRI (for an ASDAS-CRP ≥ 1.3) or with total Spine MRI (for an ASDAS-CRP ≥ 2.1) outperformed SIJ MRI alone.

Limitations of this study include his cross-sectional design, the small sample size who doesn't reflect the whole spectrum of this disease, the lack of a gold standard to measure disease activity, the assessment of BME only in the anterior segment of the spine (inherent to the Berlin method scoring system), and the mean delay of 28 days ± 21 (SD) (range: 0–80 days) between MRI and ASDAS-CRP evaluations. MRI readings were performed by one single reader as the reproducibility of the method has been assessed previously for both the spine and SIJ MRI readings [10,11]. Therefore, our findings must be interpreted with caution and must be confirmed. They should stimulate future research to confirm the value of MRI as a complementary tool to assess disease activity.

In conclusion, despite the limitations of this cross-sectional study, our model combining MRI scoring of both SIJ and spine allows to accurately discriminate between clinically active and inactive axSpA, with a higher effectiveness compared to SIJ scoring alone.

Human rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Author contribution

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Funding

This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Marc Plier:

- conceptualization (equal);
- investigation (lead);
- writing (original draft) (equal);
- writing (review et editing) (equal).

Adrien Nzeusseu Toukap:

- conceptualization (equal);
- investigation (lead);
- writing (original draft) (equal);
- writing (review et editing) (equal).

Nicolas Michoux:

- data curation (equal);
- formal analysis (equal);
- methodology (equal);
- writing (review et editing) (equal).

Maria S. Stoenoiu:

- project administration (equal);
- supervision (equal);
- writing (review et editing) (equal).

Thomas Kirchgesner:

- validation (equal);
- writing (review et editing) (equal).

Patrick Durez

- validation (equal);
- writing (review et editing) (equal).

Bernard Lauwerys:

- supervision (equal);
- writing (review et editing) (equal).

Frédéric E. Lecouvet:

- conceptualization (lead);
- data curation (equal);
- formal analysis (equal);
- investigation (equal);
- methodology (lead);
- project administration (lead);
- supervision (lead);
- validation (lead);
- writing (original draft) (lead);
- writing (review et editing) (lead).

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Braun J, Kiltz U, Sarholz M, Heldmann F, Regel A, Baraliakos X. Monitoring ankylosing spondylitis: clinically useful markers and prediction of clinical outcomes. Expert Rev Clin Immunol 2015;11:935–46.
[2] Landewé R, van Tubergen A. Clinical tools to assess and monitor spondyloarthritis. Curr Rheumatol Rep 2015;17:47.
[3] Mandl P, Navarro-Compán V, Terslev L, Aegerter P, van der Heijde D, D'Agostino MA, et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. Ann Rheum Dis 2015;74:1327–39.
[4] Van der Heijde DM, Ramiro S, Landewé R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017;76:978–91.
[5] Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, 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.
[6] Ez-Zaitouni Z, Bakker PA, van Lunteren M, Hooge M, Van den Bergl R, Reijnierse M, et al. The yield of a positive MRI of the spine as imaging criterion in the ASAS classification criteria for axial spondyloarthritis: results from the SPACE and DESIR cohorts. Ann Rheum Dis 2017;76:1731–6.
[7] Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.
[8] Machado PM, Landewé R, Heijde DV. Ankylosing spondylitis disease activity score (ASDAS): 2018 update of the nomenclature for disease activity states. Ann Rheum Dis 2018;77:1539–40.
[9] Rudwaleit M, Schwarzlose S, Hilgert ES, Listing J, Braun J, Sieper J. MRI in predicting a major clinical response to anti-tumour necrosis factor treatment in ankylosing spondylitis. Ann Rheum Dis 2008;67:1276–81.
[10] Lukas C, Braun J, Van der Heijde D, Hermann KG, Rudwaleit M, Østergaard M, et al. Scoring inflammatory activity of the spine by magnetic resonance imaging in ankylosing spondylitis: a multireader experiment. J Rheumatol 2007;34:862–70.
[11] Landewé RB, Hermann KG, Van der Heijde D, Baraliakos X, Jurik AG, Lambert RG, et al. Scoring sacroiliac joints by magnetic resonance imaging: a multiple-reader reliability experiment. J Rheumatol 2005;32:2050–5.
[12] Altman DG. Practical Statistics for Medical Research. London: Chapman and Hall/CRC; 1991.
[13] Armitage P, Berry G. Statistical methods in medical research (3rd Edition). Oxford: Blackwell Scientific Publications; 1994.
[14] Breiman L, Friedman J, Olshen R, Stone C. Classification and regression trees. Boca Raton Florida: CRC Press; 1984.
[15] Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. Clin Chem 1993;39:561–77.
[16] DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837–45.
[17] Bray TJP, Jones A, Bennett AN, Conaghan PG, Grainger A, Hodgson R, et al. Recommendations for acquisition and interpretation of MRI of the spine and sacroiliac joints in the diagnosis of axial spondyloarthritis in the UK. Rheumatology 2019;58:1831–8.
[18] Jones A, Bray TJP, Mandl P, Hall-Craggs MA, Marzo-Ortega H, Machado PM. Performance of magnetic resonance imaging in the diagnosis of axial spondyloarthritis: a systematic literature review. Rheumatology 2019;58:1955–65.
[19] Weber U, Zubler V, Zhao Z, Lambert RG, Chan SM, Pedersen SJ, et al. Does spinal MRI add incremental diagnostic value to MRI of the sacroiliac joints alone in patients with non-radiographic axial spondyloarthritis? Ann Rheum Dis 2015;74:985–92.
[20] Baraliakos X, Landewé R, Hermann KG, Listing J, Golder W, Brandt J, et al. Inflammation in ankylosing spondylitis: a systematic description of the extent and frequency of acute spinal changes using magnetic resonance imaging. Ann Rheum Dis 2005;64:730–4.
[21] Maksymowych WP, Dhillon SS, Park R, Salonen D, Inman RD, Lambert RG. Validation of the spondyloarthritis research consortium of Canada magnetic resonance imaging spinal inflammation index: is it necessary to score the entire spine? Arthritis Rheum 2007;57:501–7.
[22] Rennie WJ, Dhillon SS, Conner-Spady B, Maksymowych WP, Lambert RG. Magnetic resonance imaging assessment of spinal inflammation in ankylosing spondylitis: standard clinical protocols may omit inflammatory lesions in thoracic vertebrae. Arthritis Rheum 2009;61:1187–93.
[23] Konca S, Keskin D, Cılız D, Bodur H, Sakman B. Spinal inflammation by magnetic resonance imaging in patients with ankylosing spondylitis: association with disease activity and outcome parameters. Rheumatol Int 2012;32:3765–70.

[24] Rudwaleit M, Jurik A, Hermann KG, Landewé R, van der Heijde D, Baraliakos X, 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.
[25] Hermann KG, Baraliakos X, van der Heijde DM, Jurik AG, Landewé R, Marzo-Ortega H, 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.
[26] Navarro-Compán V, Ramiro S, Landewé R, Dougados M, Miceli-Richard C, Richette P, et al. Disease activity is longitudinally related to sacroiliac inflammation on MRI in male patients with axial spondyloarthritis: 2-years of the DESIR cohort. Ann Rheum Dis 2016;75:874–8.