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Sacroiliac joint involvement in psoriatic arthritis – MRI, radiographic and clinical findings in 581 European routine care patients

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Abstract

Background Axial involvement in psoriatic arthritis (axPsA) is associated with more severe disease and increased pain, yet no consensus definition of axPsA exists. This study aims to describe the occurrence and characteristics of MRI and radiographic sacroiliac joint (SIJ) involvement in a European PsA cohort.

Methods Patients with a clinical diagnosis of PsA or of axial spondyloarthritis with psoriasis and available routine care SIJ MRIs were included from five European registries in the EuroSpA collaboration. SIJ MRIs and radiographs were centrally assessed for inflammatory and structural lesions, differential diagnoses, and globally evaluated for SpA-indicative findings.

Results Among 581 PsA patients (mean age 45 years, 47% male), 31% exhibited SpA-indicative SIJ-MRI findings (MRI-axPsA). In MRI-axPsA patients, the most common lesions were bone marrow edema (BME) (69%), erosions (68%), and fat lesions (58%), generally present bilaterally. BME ≥ 1 cm, inflammation in an erosion cavity, capsulitis, fat lesions ≥ 1 cm, backfill, and ankylosis were observed almost exclusively in MRI-AxPsA patients. Differential diagnoses included osteitis condensans ilii (8%), probable strain-related BME (11%) and degenerative disease (16%). Among 259 patients with radiographs, 29% met the radiographic mNY criteria for ankylosing spondylitis and 38% had SpA-indicative MRI findings. Male sex, HLA-B27 positivity, elevated CRP and history of inflammatory back pain (but not current back pain) were independently associated with MRI-detected axial involvement.

Conclusion In this large European cohort, one-third of routine care PsA patients had axial involvement, based on global SIJ MRI assessment. The study supports incorporating MRI into the future definition of axPsA to enable early identification.

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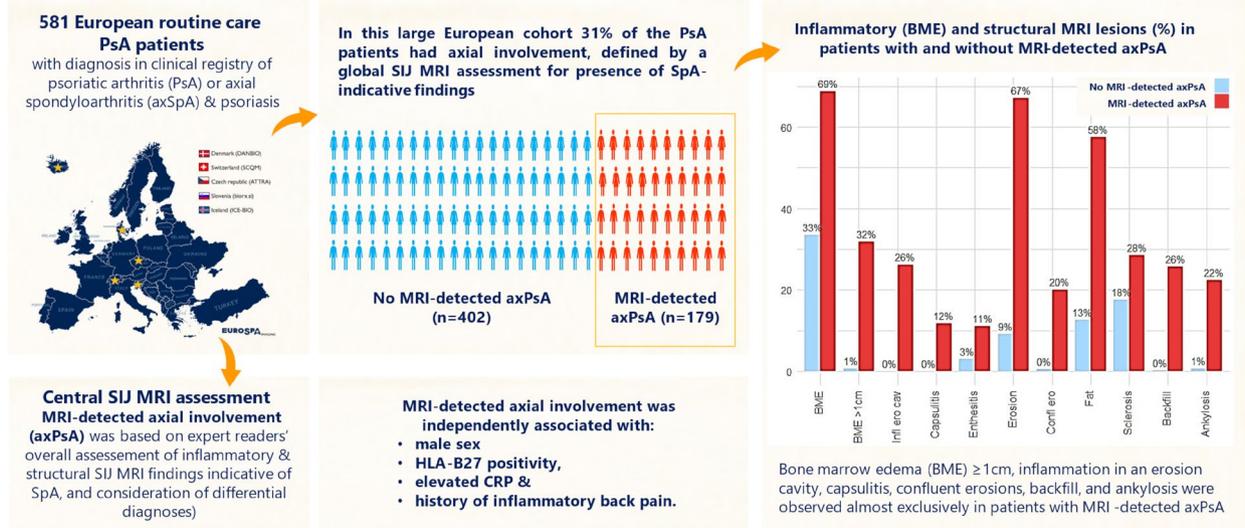
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Graphical Abstract

Sacroiliac joint involvement in psoriatic arthritis: MRI-detected axial involvement is present in one-in-three European routine care patients



Highlights

- **What is already known on this topic.**
- Axial involvement in psoriatic arthritis (axPsA) is associated with worse disease outcomes and reduced quality of life; yet a generally accepted definition is lacking, complicating both diagnosis and treatment.
- **What this study adds.**
- In a large European cohort of 581 PsA patients, one third had MRI-defined axial involvement based on central assessment of sacroiliac joint MRIs and pelvic radiographs, documenting its prevalence in routine care. Key MRI findings included bilateral BME, erosions, and fat lesions, which were strongly associated with male sex, HLA-B27 positivity, elevated CRP, and a history of inflammatory back pain, but not current BASDAI back pain. Clinical and radiographic definitions of axial involvement in PsA did not fully overlap with MRI-based classification, underscoring the need for a comprehensive approach.
- **How this study might affect research, practice or policy.**
- Understanding patterns of axial involvement in PsA and integrating MRI into future axPsA definition may lead to earlier detection and diagnosis and guide relevant treatment choices in clinical practice.

Keywords Axial spondyloarthritis, Axial psoriatic arthritis, Imaging, Magnetic resonance imaging

Introduction

Spondyloarthritis (SpA), encompassing psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA), is a group of complex immune-mediated inflammatory disorders that share genetic, clinical, and imaging characteristics [1]. AxSpA predominantly presents with axial inflammation of the sacroiliac joints (SIJs) and spine, with primary clinical manifestations including inflammatory back pain, stiffness, and reduced spinal mobility [2]. Although PsA is typically characterized by peripheral arthritis, enthesitis, dactylitis, and skin and nail psoriasis, it may also involve the SIJs and spine [3–5].

The reported prevalence of axial involvement in PsA varies widely, ranging from 5 to 28% in early disease to 25–70% in longstanding PsA, depending on the definitions applied [6–9]. Although axial disease in PsA is common, a universally accepted definition of axial PsA (axPsA) is still lacking, complicating both diagnosis and treatment [10]. In both clinical trials and routine practice, different criteria for axPsA have been used, ranging from clinical back pain (e.g., inflammatory back pain (IBP) or a BASDAI score above a certain threshold), through MRI-detected sacroiliitis, or fulfilment of radiographic criteria

such as the modified New York criteria (mNYc) for ankylosing spondylitis (AS) [11].

Accurately identifying axial involvement in PsA patients is crucial, as it is associated with worse disease outcomes and reduced quality of life compared to PsA with isolated peripheral disease [12, 13]. Moreover, certain biological therapies (e.g., IL-23 and IL-12/23 inhibitors) show differing efficacy in axPsA and axSpA, suggesting potential differences in the nature of axial disease between these conditions [14], highlighting the importance of precise detection to guide optimal management [4].

No imaging findings are considered pathognomonic for axPsA, even though a more asymmetrical pattern compared to AS is often described on radiographs [15–17]. Nevertheless, most knowledge on MRI findings in patients with axPsA derives from studies of a broader group of axSpA patients, in whom MRI is proven to be the most sensitive method to detect and monitor the axial disease [18–22].

To date, no studies of PsA patients in routine care settings have combined MRI and radiographic data to characterise axPsA [10]. Existing data come primarily from randomized controlled trials or small, research-centred clinical cohorts, with highly selected patient populations that are not generalizable to routine care where patients differ from trial participants in disease duration, severity, comorbidities, co-medications and treatment adherence [23].

Evaluating axial involvement on MRIs and radiographs in a large routine care PsA cohort is essential to understand the presence and pattern of axial involvement in real-world patients with PsA. This approach would enable the exploration of clinical, radiographic and composite axPsA definitions used in both clinical practice and research.

Thus, the aim of this study is to describe the occurrence and characteristics of MRI-detected inflammatory and structural lesions in the SIJs along with radiographic SIJ findings in routine care PsA patients, stratified by MRI-detected axial involvement, and to explore the association between MRI-detected axial involvement and various clinical characteristics.

Methods

Study design and population

This observational study of patients with PsA treated in routine care was conducted as a part of the European Spondyloarthritis Research Collaboration Network (EuroSpA), which includes 17 European registries collecting clinical data on patients with axSpA and PsA [24]. A EuroSpA imaging subgroup including five countries (Denmark (Danbio registry), Switzerland (SCQM), Czech Republic (ATTRA), Slovenia (biorx.si), Iceland (ICEBIO),

was established to integrate clinical registry data with linked imaging data (acquired in routine clinical practice) on a large cohort of patients (Supplementary Table S1).

The study included SIJ radiographs and MRIs performed from 2005 to 2022, linked to corresponding clinical registry data at the individual level. Inclusion criteria were: (1) adult patients registered with the clinical diagnoses of either PsA (clin-PsA group) or of axSpA with psoriasis (clin-axSpA + Pso group) in one of the participating registries (Fig. 1); (2) available SIJ MRI with short tau inversion recovery (STIR) or T2-weighted fat-saturated images for assessing inflammatory lesions and T1-weighted images for assessing structural lesions.

Collection of clinical data

Clinical data from the participating registries included patient demographics, disease characteristics, disease activity measures, and medication history (see Table 1).

Collection and assessment of images

Images were collected and pseudonymized in the local registries, and then transferred to the EuroSpA Coordinating Center in Copenhagen for quality checks and central reading preparation. Each MRI was independently assessed by two central readers, including an experienced musculoskeletal radiologist and an experienced reader (radiologist or rheumatologist) with more than 5 years' experience. They were trained and calibrated before scoring [25, 26]. Readers were blinded to other imaging and clinical information except for sex and age.

Readers performed a “global” assessment of the SIJ MRI to determine whether the overall findings were “indicative of SpA” (hereafter referred to as the MRI-AxPsA group) or not (MRI-noAxPsA group) [27–29]. Similarly, the readers separately evaluated for presence of inflammatory and structural lesions indicative of SpA and for fulfilment of the ASAS definition of a positive MRI (active sacroiliitis) in axSpA [29]. The reader's confidence for each of these four questions was rated on a scale from –5 (definitely no) to 5 (definitely yes).

Common differential diagnoses, including degenerative disease, were also registered (for details see Table 2 and Supplementary Table S2 - Questionnaire to the central readers).

Furthermore, SIJ MRIs were evaluated for the presence of pre-defined inflammatory and structural lesions in each part of the SIJs (right ilium, right sacrum, left sacrum and left ilium), as defined by the ASAS working group [27–29]. A complete list of lesions is presented in Table 2.

SIJ radiographs were evaluated by two experienced readers, calibrated before scoring [26]. Each SIJ was graded 0–4, according to the mNYc definitions and

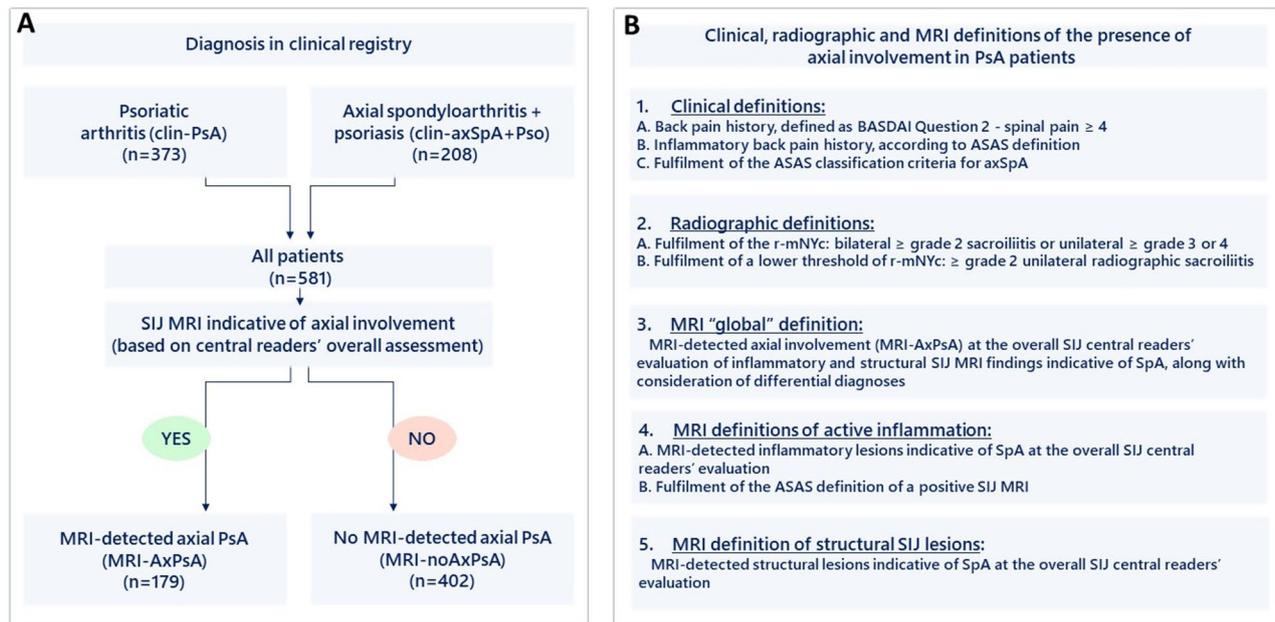


Fig. 1 Patient groups and definitions of axial involvement. **A**) Routine care patients with a clinical diagnosis of either psoriatic arthritis (clin-PsA) or axial spondyloarthritis with psoriasis (clin-axSpA + Pso) in one of the five EuroSpA registries and an available SIJ MRI were included. SIJ MRIs were required to include T1-weighted images for assessing structural lesions and short tau inversion recovery (STIR) or T2-weighted fat saturated images for assessing inflammatory lesions. Subsequently, a centralized global evaluation of SIJ MRIs were performed. Study patients with overall MRI findings indicative of SpA (see MRI "global" definition) were categorised as having MRI-detected axPsA (MRI-AxPsA) and those without such findings as not having it (MRI-noAxPsA). **B**) Various definitions of axial involvement were applied; clinical definitions were based on registry records, radiographic and MRI definitions on central reading ASAS: Assessment of SpondyloArthritis International Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; r-mNYc: Radiographic part of the modified New York criteria for ankylosing spondylitis

fulfilment of the radiographic part of the mNYc (r-mNYc) was determined [30].

MRIs were adjudicated when the primary readers disagreed on (1) whether the MRI was indicative of SpA; (2) whether the MRI fulfilled the ASAS definition for a positive MRI; and/or (3) when certain differential diagnoses (fracture, neoplasia or infection) were indicated. SIJ radiographs were adjudicated if readers disagreed on fulfilment of the r-mNYc [30]. The adjudicator was an expert musculoskeletal radiologist (member of the ASAS MRI group) who was blinded to the assessments by previous readers.

Definitions of axial PsA

Different clinical, radiographic and MRI definitions of the presence of axial involvement in PsA patients were applied (see Fig. 1b; Table 3).

Statistical analysis

Descriptive statistical analyses were performed on demographic, clinical, and imaging variables. Continuous variables were reported as means (SD), and categorical variables as numbers and percentages. Group comparisons utilised the Kruskal-Wallis and Wilcoxon rank-sum tests for continuous variables, and the Chi-squared test or Fisher's exact test for categorical variables. Spearman's

rank correlation was used for correlation analysis. A two-sided significance level of 0.05 was applied to all analyses.

Additionally, associations between MRI-AxPsA and selected demographic, clinical and laboratory variables (see Table 3) were assessed using logistic regression. Missing clinical data were imputed via multiple imputations with chained equations (20 datasets). Backward selection identified factors associated with the MRI findings indicative of SpA. Country was forced into all multivariable models as an adjustment factor. Results were presented as odds ratios (OR) with 95% CI and Wald test *p*-value.

All statistical analyses were carried out using R v.4.2.1.

Results

Patient characteristics

We included 581 patients with clinical diagnoses of peripheral PsA (clin-PsA, $n = 373$) or axSpA with concomitant skin or nail psoriasis (clin-axSpA + Pso) ($n = 208$) (Table 1). The patients had a mean age of 44.6 years, and 47% were male. Patient characteristics are shown in Table 1.

At the timepoint of MRI, 76% of the patients were bio-naïve, however 70% of these patients received biologics later in the disease course (Table 1).

Table 1 Patient characteristics

	n	All patients (n = 581)		Clinical diagnosis in the registry		MRI assessment		p	MRI-noAxPsA (n = 402)	p	
		n	clin-PsA (n = 373)	n	clin-axSpA + Pso (n = 208)	n	MRI-AxPsA ¹ (n = 179)				n
Patient characteristics											
Age, mean (SD)	581	45 (13)	373	46 (13)	208	42 (12)	179	41 (13)	402	46 (12)	0.01
Sex, male	581	271(47%)	373	162(44%)	208	109(52%)	158	125(70%)	342	146(36%)	0.01
Smoking (Current/previous/never)	500	138(28%) 247(49%) 115(23%)	305	66(22%) 173(57%) 66(22%)	195	72(37%) 74(38%) 49(22%)	158	53(34%) 36(23%) 69(44%)	342	85(25%) 79(23%) 178(52%)	0.11
BMI, mean (SD)	442	26.7 (4.9)	286	27.2 (5.2)	156	25.7 (4.2)	134	26.1 (4.6)	308	26.9 (5.1)	0.13
Participating countries	581	188(32%) 57(10%) 260(45%) 15(3%) 61(11%)	373	124(33%) 38(10%) 140(38%) 15(4%) 56(15%)	208	64(31%) 19(9%) 120(58%) 0 5(2%)	179	50(28%) 23(13%) 85(48%) 2(1%) 19(11%)	402	138(34%) 34(9%) 175(44%) 13(3%) 42(10%)	0.2
Disease characteristics											
Time of MRI	413	114(28%) 84(20%) 51(12%) 164(40%)	274	68(25%) 60(22%) 34(12%) 112(41%)	139	46(33%) 24(17%) 17(12%) 52(37%)	128	42(33%) 23(18%) 16(13%) 47(36%)	285	72(25%) 61(21%) 35(12%) 117(41%)	0.6
Before diagnosis											
0–2 years after diagnosis											
2–5 years after diagnosis											
> 5 years after diagnosis											
Peripheral arthritis and enthesitis (current)	277	219(79%)	190	159(84%)	200	60(69%)	69	52(75%)	208	167(80%)	0.4
≥ 1 tender joint	289	170(59%)	176	126(72%)	113	44(39%)	84	41(49%)	205	129(63%)	0.03
≥ 1 swollen joint	498	379(76%)	316	226(72%)	182	153(84%)	154	109(71%)	344	270(79%)	0.06
≥ 1 tender entheses											
Axial symptoms											
Inflammatory back pain (ASAS definition, ever)	479	263(55%)	299	127(43%)	180	136(76%)	145	102(70%)	334	161(48%)	0.01
BASDAI back pain ≥ 4 (current)	262	214(81%)	111	90(81%)	151	124(82%)	106	83(78%)	156	131(84%)	0.2
Extraarticular manifestations (ever)											
Skin psoriasis	559	545(98%)	352	341(95%)	207	204(99%)	176	173(98%)	383	372(97%)	0.2
Nail psoriasis	399	189(47%)	331	177(54%)	68	12(18%)	99	31(31%)	300	158(53%)	0.01
Dactylitis	547	196(36%)	350	160(46%)	197	36(18%)	169	46(27%)	378	150(40%)	0.01
Uveitis	527	46(9%)	350	16(5%)	189	30(16%)	165	22(13%)	363	24(7%)	0.01
IBD	535	28(5%)	341	16(5%)	194	12(6%)	165	8(5%)	366	20(6%)	0.7
Arthritis	556	493(89%)	362	347(96%)	194	146(75%)	168	131(89%)	388	362(93%)	0.01
Heel enthesitis	507	330(65%)	321	200(62%)	186	130(70%)	158	93(59%)	349	237(68%)	0.2
HLA-B27 positivity	410	151(37%)	224	57(25%)	186	94(51%)	145	80(55%)	265	71(27%)	0.01
Family history of SpA	438	174(40%)	284	116(41%)	154	58(38%)	134	48(36%)	304	126(41%)	0.4
Family history of psoriasis	352	129(37%)	242	97(40%)	110	32(29%)	94	28(30%)	258	101(39%)	0.11
Disease activity (current), mean (SD)											
DAPSA	284	18 (11)	137	21 (11)	146	16 (9)	105	16 (10)	169	20 (11)	0.02

Table 1 (continued)

	n	All patients (n = 581)	Clinical diagnosis in the registry		p	Central MRI assessment			p	
			clin-PsA (n = 373)	clin-axSpA + Pso (n = 208)		n	MRI-AxPsA ¹ (n = 179)	MRI-noAxPsA (n = 402)		
BASDAI	263	6 (2)	113	150	0.9	107	5 (2)	156	6 (2)	0.2
ASDAS-CRP	242	3 (1)	100	142	0.6	97	3 (1)	145	3 (1)	0.4
C-reactive protein mg/L	368	9 (14)	210	158	0.01	123	13 (16)	245	7 (12)	0.01
BASFI	259	4 (3)	132	147	0.4	104	4 (3)	155	4 (3)	0.2
HAQ	216	0.9 (0.7)	140	76	0.2	66	1 (0.6)	150	0.8 (0.7)	0.06
Medication (current)										
No previous b/tsDMARD	581	442 (76%)	373	270 (72%)	0.01	179	134 (75%)	402	309 (77%)	0.6
Current b/tsDMARD ¹	88	68 (78%)	60	44 (73%)	-	22	18 (82%)	66	50 (77%)	-
TNF inhibitor		12 (14%)		11 (18%)			3 (14%)		9 (14%)	
IL-17 inhibitor		2 (2%)		1 (2%)			0		2 (3%)	
IL-6 receptor blocker		5 (6%)		4 (7%)			1 (4%)		4 (6%)	
IL-12/23 inhibitor		1 (1%)		1 (2%)			1 (4%)		0	
JAK inhibitor										
b/tsDMARD received later ²	443	304 (70%)	270	67 (23%)	0.01	134	102 (72%)	309	202 (65%)	0.13
Criteria fulfilment (as reported by the registries)										
ASAS class. crit. for axSpA	452	206 (46%)	277	73 (26%)	0.01	142	108 (76%)	310	98 (32%)	0.01
r-mNY criteria for AS	111	52 (47%)	29	4 (14%)	0.01	53	32 (60%)	58	20 (35%)	0.01
CASPAR criteria for PsA	444	434 (98%)	347	337 (97%)	0.13	109	106 (97%)	335	328 (98%)	0.7

P-value <0.05 is considered significant, Chi-squared test or Fisher's test are used for categorical variables, t-test or Wilcoxon rank-sum test for continuous variables. All variables are presented as n (%) unless indicated. For each variable, available data (n) are presented in separate column (n) for all patients and for each subgroup

¹b/tsDMARD: b/tsDMARD received prior to or at the time of MRI examination; ²b/tsDMARD received later: refers to patients who had not received b/tsDMARD therapy at the timepoint of the MRI examination and initiated such treatment at some point after the MRI examination

Clinical diagnosis in the registries: clin-axSpA + Pso: axial spondyloarthritis and psoriasis; clin-PsA: psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; DAPSA: Disease activity in PsA; CRP: C-reactive protein; HLA-B27: human leucocyte antigen-B27; DMARD: Disease modifying antirheumatic drug; cs: conventional synthetic; b: biological; ts: targeted synthetic; DMARD, TNFi: Tumour necrosis factor inhibitor, IL: Interleukin; JAK: Janus kinase; ASAS: Assessment of SpondyloArthritis International Society classifications criteria for axSpA, r-mNY criteria for AS; Radiographic part of the modified New York criteria for ankylosing spondylitis, CASPAR: Classification criteria for Psoriatic Arthritis

Table 2 MRI findings in the sacroiliac joints of patients with PsA and AxSpA with psoriasis for all patients and subgroups

	All patients (n = 581)	Clinical diagnosis in the registry			Central MRI assessment		
		Clin-PsA (n = 373)	Clin-axS- pA + Pso (n = 208)	p	MRI-AxPsA (n = 179)	MRI- noAxPsA (n = 402)	p
MRI global assessment of SIJs¹							
Overall findings indicative of SpA¹	179(31%)	60(16%)	119(57%)	0.01	179(100%)	0	-
Inflammatory lesions indicative of SpA ²	121(21%)	41(11%)	80(39%)	0.01	114(64%)	7(2%)	0.01
ASAS-positive MRI ³	107(18%)	34(9%)	73(35%)	0.01	104(58%)	3(0.7%)	0.01
Structural lesions indicative of SpA ⁴	165(28%)	56(15%)	109(52%)	0.01	155(87%)	10(3%)	0.01
Inflammatory lesions							
Subchondral BME	258(44%)	133(36%)	125(60%)	0.01	123(69%)	135(34%)	0.01
Deep subchondral BME (> 1 cm in depth)	60(10%)	18(5%)	42(20%)	0.01	57(32%)	3(0.7%)	0.01
Inflammation in an erosion cavity	47(8%)	17(5%)	30(14%)	0.01	47(26%)	0	0.01
Enthesitis	32(6%)	14(4%)	18(9%)	0.01	20(11%)	12(3%)	0.01
Capsulitis	21(4%)	11(3%)	10(5%)	0.2	21(12%)	0	0.01
Joint space fluid	43(7%)	19(5%)	24(12%)	0.01	31(17%)	12(3%)	0.01
Structural lesions							
Sclerosis (> 5 mm in depth)	122(21%)	62(17%)	60(29%)	0.01	51(29%)	71(18%)	0.01
Erosion	157(27%)	72(19%)	85(41%)	0.01	120(67%)	37(9%)	0.01
Erosion confluent (> 2 cm in extent)	38(7%)	13(4%)	25(12%)	0.01	36(20%)	2(0.5%)	0.01
Fat lesion	154(27%)	69(19%)	85(41%)	0.01	103(58%)	51(13%)	0.01
Deep fat lesion (> 1 cm in depth)	78(13%)	31(8%)	47(23%)	0.01	61(34%)	17(4%)	0.01
Backfill	47(8%)	14(4%)	33(16%)	0.01	46(26%)	1(0.2%)	0.01
Ankylosis	43(7%)	11(3%)	32(15%)	0.01	40(22%)	3(0.7%)	0.01
Differential diagnostic findings/conditions							
Any differential diagnosis	241(42%)	178(74%)	63(26%)	0.01	21(9%)	158(47%)	0.01
Fluid-filled bone cyst	22(4%)	20(5%)	2(1.0%)	0.01	2(1%)	20(5%)	0.02
Vascular signal mimicking BME	24(4%)	17(5%)	7(3%)	0.5	1(0.6%)	23(6%)	0.01
SIJ normal variation that may be misinterpreted as SpA-indicative lesion	27(5%)	17(5%)	10(5%)	0.9	4(2%)	23(6%)	0.06
BME, probably strain related	61(11%)	38(10%)	23(11%)	0.7	4(2%)	57(14%)	0.01
Osteitis condensans ilii	46(8%)	31(8%)	15(7%)	0.6	1(0.6%)	45(11%)	0.01
Lumbosacral transitional anomaly	24(4%)	19(5%)	5(2%)	0	8(6%)	16(4%)	0.8
Osteoarthritis/degeneration	95(16%)	70(19%)	25(12%)	0.03	3(2%)	92(23%)	0.01
DISH SIJ lesions	9(2%)	9(2%)	0	0.03	2(1%)	7(2%)	0.7
Fracture/stress fracture	1(0.2%)	1(0.3%)	0	0.9	1(0.6%)	0	0.3
Infection	0	0	0	-	0	0	0
Neoplasia (not including haemangioma and lipoma)	1(0%)	1(0%)	0	0.9	0	1(0.2%)	0.9
Other	13(2%)	8(2%)	5(2%)	0.9	0	13(3%)	0.01
Normal MRI							
MRI without any SpA related lesions	189(47%)	156(42%)	33(16%)	0.01	0	189(47%)	0.01
MRI without any SpA related lesions and/or diff. diagnoses	139(35%)	119(32%)	20(10%)	0.01	0	139(35%)	0.01
ASAS criteria for axSpA fulfilment							
Fulfilment of ASAS criteria for axSpA ⁵	196(34%)	72(19%)	124(60%)	0.01	179(100%)	17(4%)	0.01
Radiographic findings							
Fulfilment of r-mNY criteria	(n = 259)	(n = 141)	(n = 114)		(n = 97)	(n = 162)	
	74(29%)	24(17%)	50(43%)	0.01	57(59%)	17(11%)	0.01

P-value < 0.05 is considered significant. Fisher's exact test and Pearson's Chi-squared test were used. All data are presented as numbers (%)

BME: Bone marrow oedema; Clin-axSpA+Pso: Psoriasis and axial spondyloarthritis; PsA: psoriatic arthritis

¹Overall MRI findings of the SIJs that were indicative of SpA (expert evaluation based on the presence of both inflammation and structural lesions)

²Inflammatory lesions: The presence of active inflammatory lesions typical of axial SpA in the SIJs (per expert opinion)

³MRI fulfilling the ASAS definition of a positive MRI for active sacroiliitis, requiring the presence of bone marrow edema (BME) "in a typical anatomical area (subchondral bone)" and that the "MRI appearance must be highly suggestive of axSpA"

⁴Structural lesions: The presence of structural lesions typical of axial SpA in the sacroiliac joints such as erosion, fat lesions, sclerosis, backfill or ankylosis (per expert opinion)

⁵Fulfilment of Assessment of SpondyloArthritis International Society (ASAS) criteria for axial spondyloarthritis (axSpA); imaging arm (sacroiliitis per MRI) and/or radiographic sacroiliitis as per Radiographic part of the modified New York criteria for ankylosing spondylitis (r-mNY criteria for AS)

Table 3 Fulfilment of various definitions of axial psoriatic arthritis in all patients and in patients with/ without SIJ MRI findings indicative of SpA

Various definitions of axPsA	Central MRI assessment						
	All patients (n = 581)		MRI-AxPsA (n = 179)		MRI-noAxPsA (n = 402)		p
	n		n		n		
1. Clinical definitions (as reported by the registries):							
A. BASDAI Question 2 (spinal pain ≥ 4)	262	214(82%)	106	83(78%)	156	131(84%)	0.2
B. Inflammatory back pain (by ASAS criteria)	479	263(55%)	145	102(70%)	334	161(48%)	0.01
C. Fulfilment of ASAS classification criteria for axSpA	452	206(46%)	142	108(76%)	310	98(32%)	0.01
2. Radiographic definitions (central reading):							
A. Fulfilment of the radiographic part of mNY criteria	259	74(29%)	95	57(59%)	160	17(11%)	0.01
B. At least grade 2 unilateral radiographic sacroiliitis	259	84(32%)	95	58(60%)	160	26(16%)	0.01
3. MRI "global" definition (central reading):							
Overall MRI findings indicative of SpA	581	179(31%)	179	100%	402	0	-
4. MRI definitions of active inflammation (central reading):							
A. ASAS-positive MRI	581	107(18%)	179	104(58%)	402	3(1%)	0.01
B. Inflammatory lesions indicative of axSpA	581	121(29%)	179	114(64%)	402	7(2%)	0.01
5. MRI definition of structural lesions (central reading):							
Structural lesions indicative of axSpA	581	165(28%)	179	155(87%)	402	10(2.5%)	0.01

P-value < 0.05 is considered significant. Fisher's exact test and Pearson's Chi-squared test were used. All data are presented as numbers (%). MRI-AxPsA: patients with SIJ MRI findings indicative of SpA at the global SIJ MRI assessment; MRI-noAxPsA: patients without SIJ MRI findings indicative of SpA at the global SIJ MRI assessment. ASAS: Assessment of SpondyloArthritis International Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; mNY criteria: Modified New York criteria for ankylosing spondylitis

MRI characteristics

In the overall population, 31% of patients (16% of clin-PsA and 57% of clin-axSpA + Pso) had axial involvement, i.e. MRI findings indicative of SpA based on SIJ global assessment, while 69% did not (Fig. 1).

Inflammatory lesions indicative of SpA were present in 21% of patients, while "BME in general" (including all detected BME lesions, i.e. both those indicative of SpA and the non-specific) was present in 44% of patients [bilateral: 20%]. Other inflammatory lesions were identified, including inflammation in erosion cavity (8%), enthesitis (5.5%), capsulitis (4%), and joint space fluid (7%) (Table 2).

Structural SIJ MRI lesions indicative of SpA were observed in 28% of patients. The most common structural lesions were erosions (27%, [bilateral in 15%]), fat lesions (26%, [bilateral: 18%]), and sclerosis (21%, [bilateral: 11%]), followed by backfill (8%, [bilateral: 4%]) and ankylosis (7%, [bilateral: 6%]).

MRI without any SpA-related lesions was observed in 47% of patients and a normal MRI, showing neither SpA-related lesions nor differential diagnoses, was found in 35% of patients (Table 2).

Figure 2 shows the frequency of inflammatory and structural MRI lesions in patients with and without MRI-AxPsA. Among MRI-AxPsA patients, MRI findings were generally similar in the two clinical cohorts (clin-PsA and clin-axSpA + Pso), except for a higher frequency of ankylosis in clin-axSpA + Pso patients (see Supplementary Table S3).

In the MRI-AxPsA group, BME was more often bilateral than unilateral (44% vs. 25%) across the entire SIJ as well as in both the ilium and sacrum. In contrast, in the MRI-noAxPsA group BME was predominantly seen unilaterally. Certain lesion types, such as deep BME (≥ 1 cm), inflammation in an erosion cavity, capsulitis, backfill and ankylosis were found almost exclusively in MRI-AxPsA patients. Sclerosis was most frequently observed on the iliac side of the SIJ, occurring equally often unilaterally and bilaterally in both patient groups (Fig. 3). Erosions were also frequent on the iliac side. They tended to be bilateral in MRI-AxPsA patients and unilateral in MRI-noAxPsA patients. Fat lesions were commonly bilateral in both groups, and ankylosis was typically bilateral. Backfill occurred equally often unilaterally and bilaterally in MRI-AxPsA patients.

MRI findings in different subgroups

Sex (females vs. males)

In the overall population, male patients had a higher frequency of MRI findings indicative of SpA, and a higher frequency of all types of inflammatory and structural lesions, except for sclerosis, which was more prevalent in females. Notably, while "BME in general" occurred equally in both sexes, whereas SpA-indicative inflammatory lesions and ASAS-positive MRIs were significantly more frequent in males (Fig. 2b).

In the subgroup of MRI-AxPsA patients, the lesion frequency did not differ by sex, except for sclerosis and

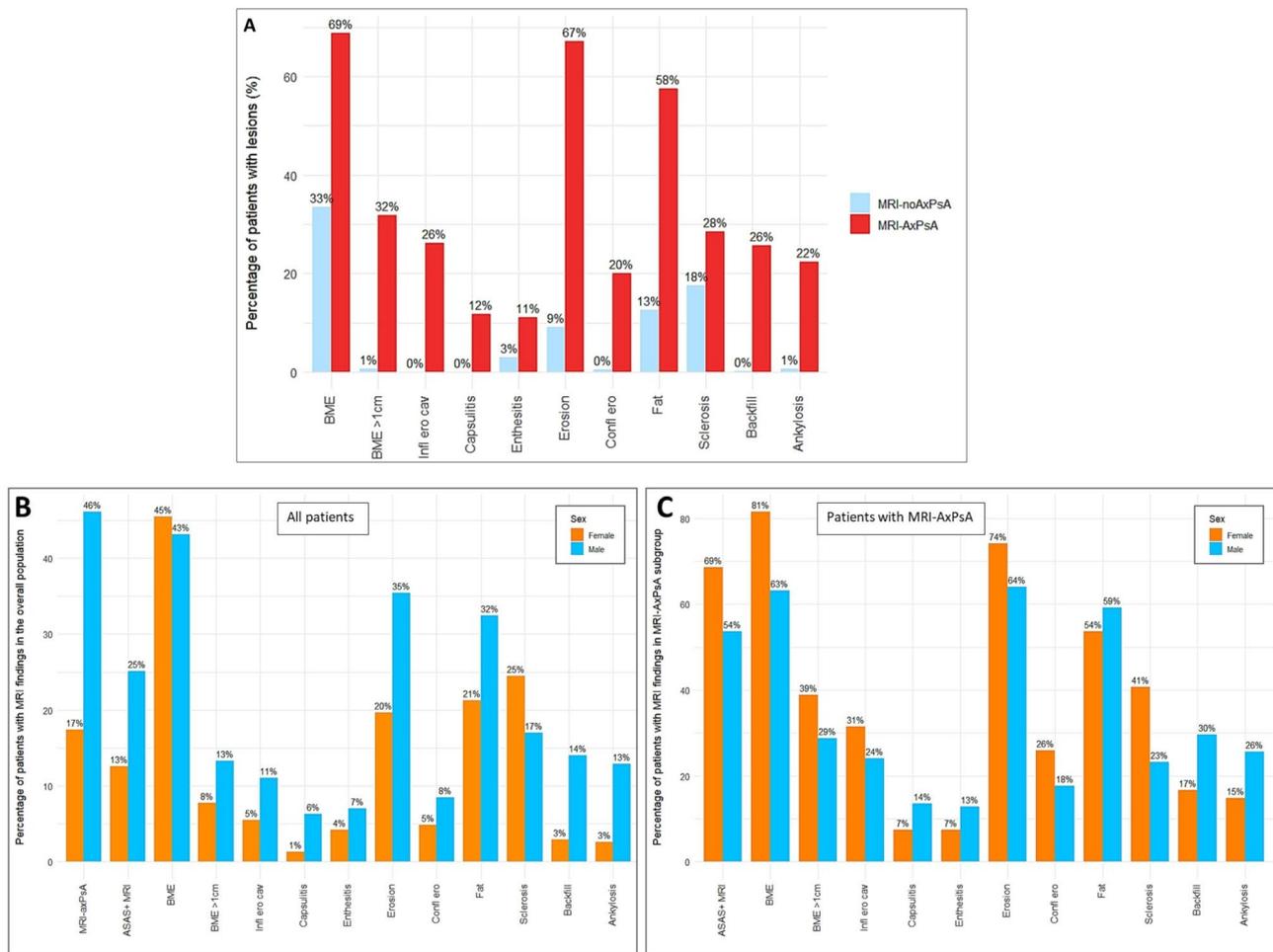


Fig. 2 Inflammatory and structural MRI lesions in (A) patients with and without MRI-AxPsA and stratified by sex in (B) all patients and in (C) patients with MRI-AxPsA. MRI-AxPsA: patients with SIJ MRI findings indicative of SpA at the global SIJ MRI assessment; MRI-noAxPsA: patients without SIJ MRI findings indicative of SpA at the global SIJ MRI assessment. BME, bone marrow edema; Infl ero cav, inflammation in an erosion cavity; Confl ero, confluent erosion; Fat, fat lesion

BME, which remained significantly more frequent in female patients (Fig. 2c).

HLA-B27 positivity

In the overall study population, HLA-B27 positive patients more frequently exhibited MRI findings indicative of SpA than HLA-B27 negative patients (53% vs. 23%, respectively, $p = 0.01$). Both inflammatory and structural lesions were significantly more frequent in HLA-B27 positive patients across all lesion types, except for “BME in general” and sclerosis.

In the subgroup of MRI-AxPsA patients, no significant differences were observed between HLA-B27 positive and negative patients, except for ankylosis, which was more prevalent among HLA-B27 positive patients (31% vs. 12%, $p = 0.01$). Mean age and sex distribution did not differ between the groups.

For details see Supplementary Tables S4-7.

Differential diagnoses

Degenerative changes in the SIJs were the most common differential diagnostic finding, observed in 95(16%) of all patients. Strain-related BME (10.5%) and osteitis condensans ilii (8%) were equally prevalent in both clinical cohorts. Relatively rare findings were fluid-filled bone cysts (4%) and DISH lesions (1.5%), as well as normal variations of the SIJ anatomy (5%) and lumbosacral anomalies (4%). In the MRI-AxPsA patient group, strain-related BME, osteitis condensans ilii and degenerative SIJ changes were less prevalent than in the MRI-noAxPsA group (Table 2).

Radiographic findings

Radiographs of the SIJ were available for 259 patients. Of these, 29% met the r-mNYc (Table 2) and 38% had an MRI indicative of SpA (MRI-AxPsA). The radiographic SIJ involvement of those who fulfilled the mNYc was predominantly bilateral (90.5%). Figure 4 shows the

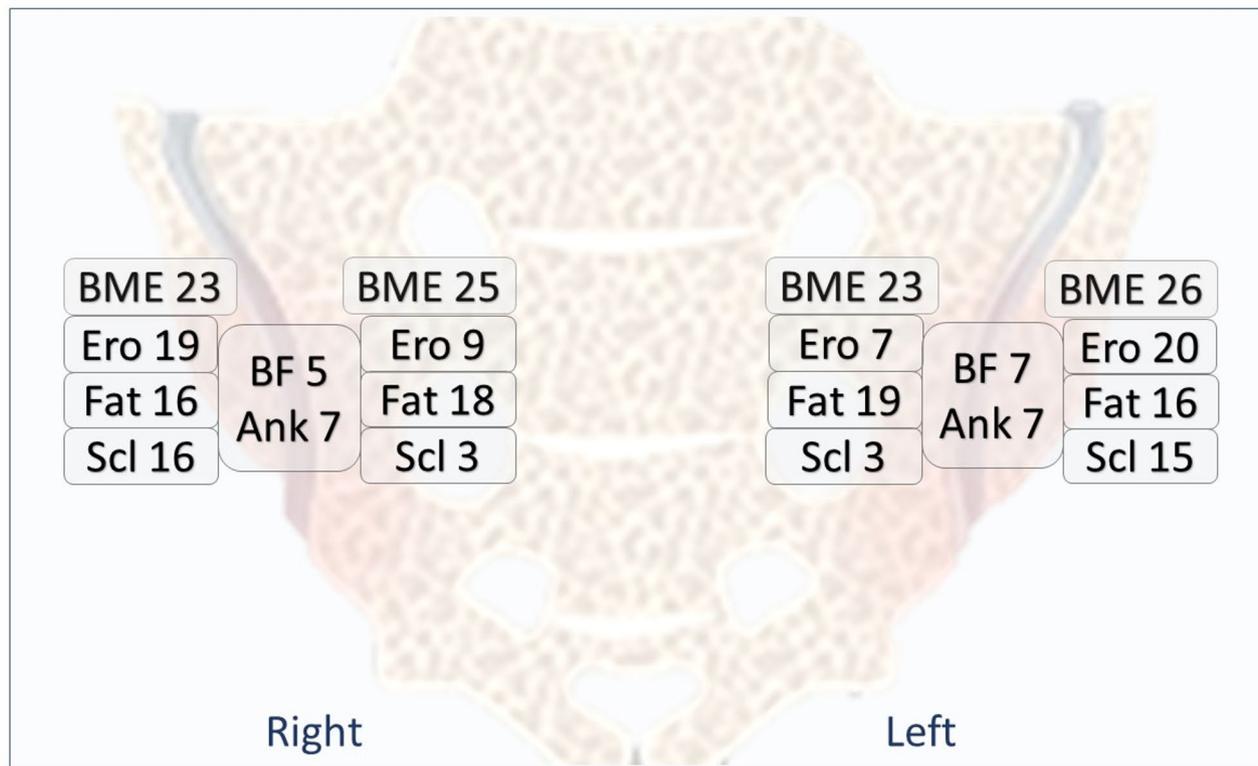


Fig. 3 Distribution (%) of the most common MRI-detected inflammatory and structural SIJ lesions in patients with MRI findings indicative of SpA (MRI-AxPsA). Values are percentages of patients with inflammatory and structural lesions present in each sacroiliac joint (backfill and ankylosis) or in the different sides (ilium/sacrum) of each sacroiliac joint (BME, erosion, fat and sclerosis). BME: bone marrow oedema; Ero: erosion; Fat: fat lesion; Scl: sclerosis; BF: backfill; Ank: ankylosis

pattern of radiographic sacroiliitis as by the r-mNY criteria grades.

Clinical characteristics associated with axial involvement (MRI-AxPsA)

The MRI-AxPsA patients showed distinct clinical characteristics compared to those without such findings (Table 1, Supplementary table S3). In the univariate analysis, younger age, male sex, HLA-B27 positivity, history of IBP, uveitis and elevated CRP were associated with higher odds of MRI-AxPsA. Conversely, nail psoriasis, peripheral arthritis, enthesitis and dactylitis were associated with lower odds (Table 4). In the multivariable analysis, male sex, HLA-B27 positivity, history of IBP and elevated CRP remained independently, positively associated with MRI-AxPsA, whereas peripheral arthritis continued to show a negative association.

MRI findings in PsA patients fulfilling various definitions of axpsa

Various clinical, radiographic and MRI-based definitions of axial involvement in PsA were applied and compared (Table 3; Fig. 5).

Three clinical definitions of axPsA were applied (Table 3, definition 1 A-C). First, “BASDAI back pain ≥ 4 ,”

was met by 82% of patients with available data ($n = 262$), with similar proportions in MRI-AxPsA (78%) and MRI-noAxPsA (84%) patients. The second clinical definition “inflammatory back pain” ($n = 479$) was met by 55% of patients including 70% of those with and 48% without MRI-AxPsA. The third definition, “ASAS axSpA criteria fulfilment” (registry-reported, $n = 452$), was met in 46% of cases. Notably, many patients without MRI-AxPsA still had BASDAI pain ≥ 4 (84%), IBP (48%), or fulfilled the ASAS criteria for axSpA (32%).

Two radiographic definitions were applied (Table 3, definition 2 A-B). First, “r-mNYc fulfilment” was achieved by 29% of all patients with radiographic data ($n = 259$), including 59% of those with and 11% of those without MRI-AxPsA. The “Unilateral radiographic sacroiliitis \geq grade 2” definition was met by 32% of patients.

Four MRI-based definitions were applied (Table 3, definition 3–5).

The “MRI-global” definition, based on overall SIJ MRI findings indicative of SpA, was met by 31% of patients (MRI-AxPsA group).

The “MRI-inflammatory lesions” definition was met by 20% of the overall population, and 64% of MRI-AxPsA patients. The “ASAS definition of a positive MRI” was met by 18% of all patients and 58% of MRI-AxPsA patients.

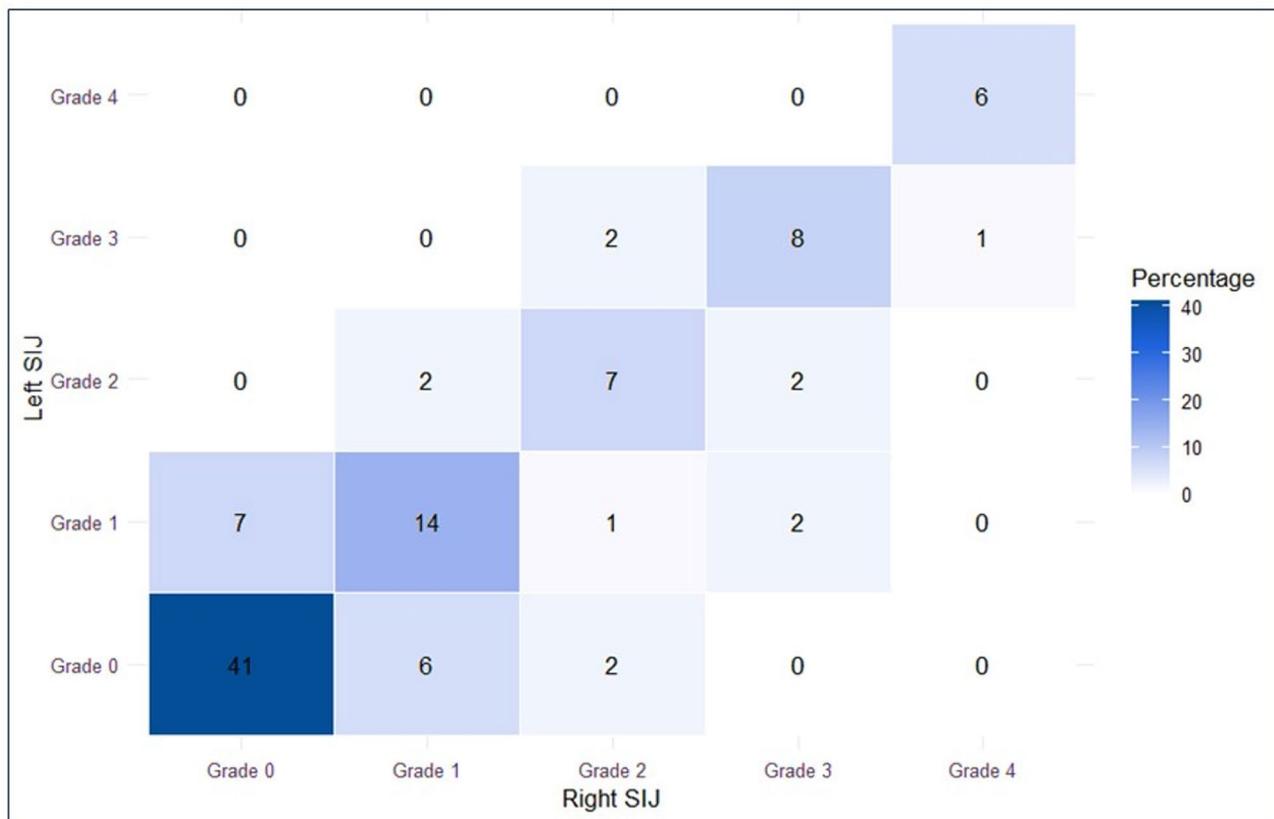


Fig. 4 Distribution in percentages of different grades of radiographic sacroiliitis as by the radiographic part of the modified New York criteria for ankylosing spondylitis (r-mNYC) in all patients in the left and right sacroiliac joint (SIJ)

Finally, the “MRI structural lesions” definition was fulfilled by 28% of all patients, and 87% of MRI-AxPsA patients. These MRI definitions were met by only 1-2.5% of MRI-noAxPsA patients.

The overlap between the clinical and imaging definitions is seen in Fig. 5.

No differences in axPsA definition fulfilment or patient characteristics were observed between those with and without BASDAI back pain ≥ 4 in the overall population or the MRI-AxPsA subgroup (Supplementary Table S9).

The prevalence of axPsA according to these definitions for the subgroup of patients with MRI findings indicative of SpA stratified by clinical diagnosis of clin-PsA and clin-axSpA + Pso, is presented in detail in Supplementary Table S10.

Discussion

This is the first study to assess axial involvement in a large cohort of routine care PsA patients using centrally evaluated SIJ MRIs for findings indicative of SpA. We evaluated 581 patients from five European countries, with one-third (31%) of patients demonstrating axial involvement (MRI-AxPsA), based on a global MRI assessment, with MRI lesions mainly distributed bilaterally. The most

common lesions were BME, erosions and fat lesions. Among the 259 patients with available SIJ radiographs, sacroiliitis meeting the r-mNYC was present in 29%, while 38% had MRI-AxPsA. Male sex, HLA-B27 positivity, elevated CRP and history of IBP were independently associated with MRI-AxPsA.

The lack of a consensus definition for axPsA leaves the diagnosis up to individual clinicians and researchers, leading to variability in definitions across clinical trials [6–8] and in registry studies [31–33], which complicates comparisons between studies. Consequently, reported axPsA prevalences vary depending on patient populations and applied criteria. For example, in registry cohorts, axial involvement, based on rheumatologist assessment, was reported in 27% of Spanish and 44% of Swiss patients, while a clinical and/or imaging-based definition identified axial involvement in 26% of German PsA patients [13, 31–33].

MRI-detected axial involvement in PsA has been examined in a few smaller studies, with reported rates comparable to our finding of MRI-detected sacroiliitis (31%) [18–20, 34, 35]. Williamson reported sacroiliitis in 38% of British ($n = 107$) PsA patients and Braga found sacroiliitis in 38% of Brazilian ($n = 45$) PsA patients, being bilateral in

Table 4 Clinical characteristics associated with axial involvement (MRI-AxPsA)

	Univariable analysis			Multivariable analysis		
	OR	CI	p-value	OR	CI	p-value
Age	0.97	(0.96–0.99)	<0.001			
Female sex	0.25	(0.17–0.36)	<0.001	0.24	(0.15–0.37)	<0.001
Ever smoker	1.44	(0.97–2.14)	0.072			
Body mass index	0.97	(0.93–1.01)	0.119			
Symptom duration (years)	1.01	(0.98–1.03)	0.623			
Diagnosis duration (years)	1.00	(0.97–1.02)	0.773			
Nail psoriasis	0.41	(0.24–0.70)	0.002			
Peripheral arthritis (swollen joints ever)	0.27	(0.16–0.46)	<0.001	0.45	(0.23–0.89)	0.022
Peripheral enthesitis	0.64	(0.41–0.98)	0.039			
Uveitis	1.96	(1.06–3.63)	0.032			
Dactylitis	0.57	(0.38–0.85)	0.006			
Inflammatory bowel disease	0.83	(0.36–1.91)	0.657			
HLA-B27 positivity	3.03	(1.96–4.68)	<0.001	2.31	(1.33–4.01)	0.003
Inflammatory back pain (acc. to ASAS criteria)	2.42	(1.62–3.62)	<0.001	1.66	(1.01–2.74)	0.046
BASDAI back pain ≥ 4	0.87	(0.51–1.50)	0.623			
BASDAI	0.96	(0.86–1.07)	0.444			
C-reactive protein > 5 mg/L	2.45	(1.56–3.84)	<0.001	2.16	(1.24–3.76)	0.007
Participating country: Czech Republic	1.87	(1.00–3.48)	0.177	2.03	(0.91–4.54)	0.096
Participating country: Denmark	1.34	(0.88–2.03)		1.13	(0.67–1.91)	
Participating country: Iceland	0.42	(0.09–1.95)		0.81	(0.15–4.54)	
Participating country: Slovenia	1.25	(0.66–2.35)		2.50	(1.16–5.39)	
Clinical diagnosis in the registry: clin-axSpA + Pso	6.98	(4.72–10.31)	<0.001	5.75	(3.42–9.67)	<0.001

Univariable and final multivariable logistic regression analyses models. Participating country is a forced variable in the model. clin-axSpA + Pso: Clinical diagnosis of axial spondyloarthritis with psoriasis; ASAS: Assessment of SpondyloArthritis International Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; OR: Odds ratio; CI: Confidence intervals

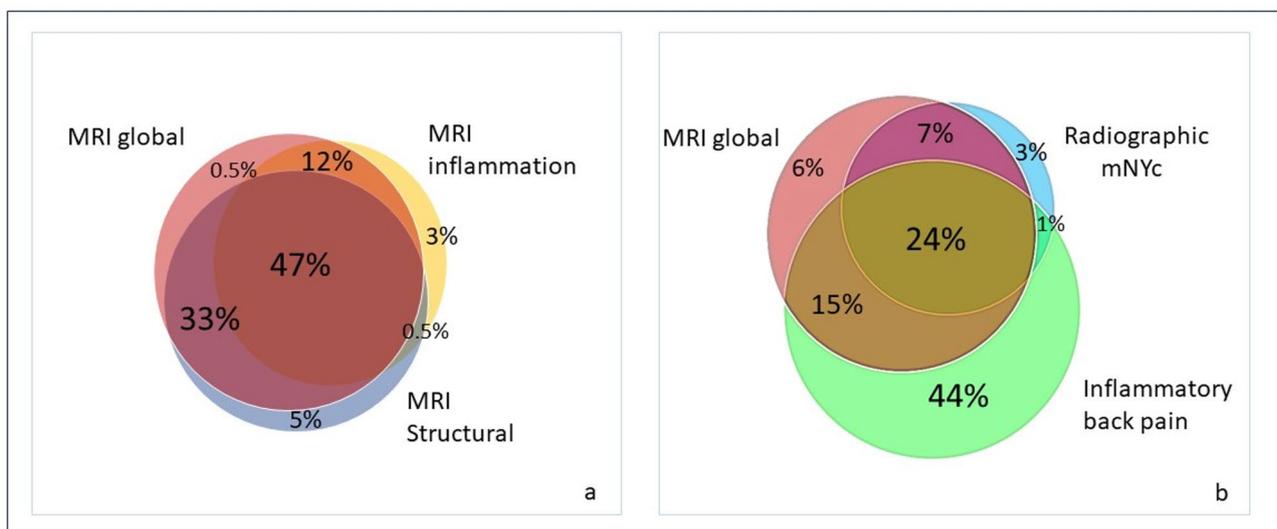


Fig. 5 Overlap between various definitions of axial PsA. Venn diagrams illustrating the overlap between fulfilment of various definitions of axial PsA. **(a)** Fulfilment of “MRI global definition” (overall MRI findings indicative of SpA, i.e., MRI-AxPsA), the “MRI inflammation definition” (inflammatory MRI lesions indicative of SpA) vs. the “MRI structural definition” (structural MRI lesions indicative of SpA). Here, the total number of patients with available data was $n=581$, of which 195 fulfilled one of the definitions; **(b)** Fulfilment of “MRI global definition” (overall MRI findings indicative of SpA), versus fulfilment of the “radiographic mNYc definition” (radiography positive for the radiographic part of the modified New York criteria) versus fulfilment of the “inflammatory back pain definition” (presence of inflammatory back pain, ASAS definition). Here, the total number of patients with available data was $n=204$, of which 148 fulfilled one of the definitions (MRI global, $n=79$; Radiographic mNYc, $n=54$; Inflammatory back pain, $n=128$)

53% cases [18, 34]. Furer found sacroiliitis in 26% of 107 Israeli patients [20]. In contrast, Diaz reported a lower prevalence (13%) in a Canadian cohort ($n=93$), probably related to a somewhat different population, including 65 PsA patients (with/without back pain) and 28 psoriasis patients with back pain and suspected PsA [19].

In our MRI-AxPsA patients, the majority of inflammatory as well as structural SIJ MRI lesions were observed bilaterally, in accordance with Braga, whereas MRI-noAxPsA patients more commonly exhibited unilateral lesions [18, 34]. Conversely, some previous radiographic studies reported that axial involvement in PsA is predominantly asymmetric and often unilateral [15–17]. Our study confirmed BME, erosions and fat lesions as the most common axPsA pathologies, consistent with previous reports [6, 18–20, 34, 35]. Although small studies have reported SIJ involvement in axPsA, most SIJ MRI studies [6, 18–20, 34, 35] do not specify the location of lesions. In our study, erosions and sclerosis were mainly in the iliac bones, while BME, fat and other lesions were equally distributed between ilium and sacrum. Due to our more detailed evaluation, other types of lesions as defined by ASAS were also detected frequently, including BME ≥ 1 cm in depth, inflammation in an erosion cavity, capsulitis and backfill. These lesions were almost exclusively present in patients with MRI-AxPsA [28, 36].

Male sex and HLA-B27 positivity were positively associated with MRI-AxPsA, aligning with previous reports [12, 19, 37]. Although in the overall population both inflammatory and structural lesions were more frequent in males (except for sclerosis), among MRI-AxPsA patients the lesion frequency did not differ by sex, except for sclerosis and “BME in general”, which remained significantly more frequent in female patients. This indicates that in patients with objectively confirmed disease, there is no major difference in MRI findings between female and male patients. Additionally, structural lesions, particularly ankylosis were more common in HLA-B27-positive patients, reaffirming its link to more severe axial disease in PsA [12, 31, 37–39], parallel to findings in radiographic axSpA patients [1, 40].

Presence of BASDAI back pain ≥ 4 has previously been applied as an inclusion criterion in axPsA clinical trials (e.g. the MAXIMISE study) [6]. In our study current BASDAI back pain ≥ 4 was not associated with MRI-axPsA and was equally prevalent in both MRI-axPsA and MRI-noAxPsA groups. This may be explained by the common and non-specific nature of back pain, its fluctuating course, and the involvement of different pain mechanisms in PsA. Nevertheless, a history of IBP was independently associated with MRI-AxPsA, being reported by 70% of our MRI-AxPsA patients but also by nearly half of MRI-noAxPsA patients. These findings suggest that back pain measures alone cannot reliably

distinguish axial PsA from other causes of back pain, and therefore do not constitute a useful definition of axial PsA. This aligns with previous reports demonstrating low agreement between IBP and MRI-detected axPsA [19, 20, 37, 41–43].

Radiographic sacroiliitis, as defined by the mNYc, was present in 29% of our patients, while previous studies have reported axPsA rates using varying definitions [37, 44, 45]. For example, based on the r-mNYc, Feld identified axPsA in 37% of a large Canadian cohort, Jadon in 24% of British PsA patients, and Proft in 29% of German axPsA patients, comparable to our findings (29%). Another Canadian study introduced a lower threshold for radiographic axPsA (unilateral sacroiliitis \geq grade 2) and detected axial involvement in 45% of patients [16]. Using this approach, Proft reported a radiographic axPsA prevalence of 38% [45], while our study found a prevalence of 32%. However, among our patients meeting the r-mNYc, a fourth ($n=17$) did so in the absence of MRI findings indicative of SpA. Since MRI is considerably more sensitive, and equally specific, for structural SIJ changes than radiography, this likely reflects the low reliability of the radiographic assessment, consistent with previous reports [22, 46].

In this study, we applied a global MRI assessment for findings indicative of SpA as standard reference for axPsA, because MRI facilitates early detection of axial involvement before development of radiographic sacroiliitis, regardless of clinical symptoms [47, 48]. The central readers were aware, in agreement with recent publications [49, 50] that BME, sclerosis and fat lesions are not pathognomonic of axSpA, and can occur in other conditions [51]. BME, for example, was observed in 34% of MRI-noAxPsA patients, although it was observed in 69% of patients with MRI-AxPsA. The most commonly identified differential diagnoses were OCI, strain-related BME and degenerative disease, which are all known axSpA-mimickers [51]. Thus, in clinical practice it is important that differential diagnoses are considered, and that MRIs should be interpreted in the clinical context [29].

Summarising the various axPsA definitions applied in the study, both the clinical and the radiographic definitions of axPsA were far from identifying the same patients as the global MRI definition. Given that the MRI is accepted as the most accurate method for detecting sacroiliitis and that we used a fairly conservative MRI definition, our findings indicate that MRI should be part of the examination programme when axial involvement in PsA is suspected. Additionally, our data suggest that both inflammatory and structural lesions should be evaluated, as evaluating only one may lead to missed axPsA cases. This is also in line with current recommendations [29, 36].

A major strength of this large multicentre study is the high patient number and inclusion of a broad routine-care PsA population enhancing the generalizability of findings. Additionally, SIJ MRIs and radiographs were centrally evaluated by two independent experienced readers, with adjudication in case of disagreement, ensuring a rigorous and reliable assessment of findings indicative of SpA, individual lesions, and differential diagnoses based on current definitions and recommendations [29, 36]. However, some limitations should be considered. First, there is no universally accepted gold standard for axPsA. For the purpose of this study, we pooled patients registered with a clinical diagnosis of PsA and those with axSpA with psoriasis. Since both peripheral and axial arthritis are equally valid core requirements for CASPAR criteria fulfilment — defined as evidence of inflammatory articular disease involving joints, spine, or entheses — patients with axial spondyloarthritis and psoriasis (if accompanied by ≥ 1 additional feature) could therefore also be classified as PsA according to the CASPAR criteria. In addition, we stratified results by registry-based clinical diagnosis, allowing interpretation within both frameworks and facilitating comparison with future studies once a consensus definition of axPsA is established. Secondly, radiographs were unavailable for some patients. Thirdly, spine images were not available and since spine involvement in PsA can also occur without typical SIJ MRI lesions [52], some axPsA cases may have been missed. Besides, inclusion of spine imaging would have allowed a better assessment of the relationship between inflammatory back pain — which often affects the entire spine — and MRI findings that may be present not only in the SIJs but also, or exclusively, in the spine. Moreover, MRI was performed after initiation of biologics in few patients, which likely influenced the inflammatory MRI findings. Lastly, diagnoses in registries are based on clinicians' judgements and data on classification criteria fulfilment were not always available. Nevertheless, the investigated cohort truly represents patients treated under the diagnosis of PsA in European clinical practice.

In summary, axial involvement in PsA, defined by a global assessment of SIJ MRI findings was present in one-third (31%) of the routine care PsA patients in this large European cohort. Among those with available radiographs, 29% met the mNY criteria for radiographic sacroiliitis, while 38% had MRI-AxPsA. MRI-detected axial involvement was independently associated with male sex, HLA-B27 positivity, elevated CRP and a history of inflammatory back pain but not with current BASDAI back pain. MRI findings were predominantly bilateral, with common lesions including BME, erosions, and fat lesions. Neither the clinical nor radiographic axPsA definitions identified the same patients as the global MRI

evaluation. Assessing both inflammatory and structural lesions on SIJ MRI is essential to improve the detection of axial involvement in PsA. Our findings highlight the value of MRI in identifying SpA-indicative changes in a real-world PsA population. This study contributes to the ongoing discussion on defining axPsA and supports the integration of MRI-detected lesions into an axPsA definition. Early and accurate detection of axial involvement in PsA will contribute to optimal treatment and improved outcomes in routine care.

Supplementary Information

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Supplementary Material 1

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Author contributions

NV, MØ and SK: conception and design of the study; All authors: acquisition of data; NV, LØ, MØ: analysis and interpretation of data and drafting of the article; AH, RL, MN, TD, NV, MØ, ZS, IE, SK, AC, ISS, MdH, LØ contributed to revising the article critically for important intellectual content; All authors: final approval of the version to be submitted. No writing assistance or artificial intelligence was used to prepare the manuscript, including its data, figures, and tables.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval and informed consent were not applicable for this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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