

# Prevalence of Nonradiographic Sacroiliitis in Patients With Psoriatic Arthritis: A Real-life Observational Study

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ABSTRACT. Objective. To establish the prevalence of nonradiographic sacroiliitis within a real-life sample of patients with psoriatic arthritis (PsA), using pelvic radiographs and magnetic resonance imaging (MRI) of sacroiliac joints (SIJs).

> Methods. This cross-sectional study included 107 consecutive adults with PsA (Classification Criteria for Psoriatic Arthritis criteria). Participants completed clinical and laboratory evaluation, pelvic radiographs scored for radiographic sacroiliitis according to the modified New York (mNY) criteria, and noncontrast MRI of SIJs, scored by the Berlin score and categorized into active sacroiliitis using the 2016 Assessment of Spondyloarthritis international Society (ASAS) criteria and the presence of structural sacroiliitis.

> Results. Radiographic sacroiliitis/mNY criteria were detected in 28.7% (n = 29), confirmed by MRI-detected structural lesions in 72.4% (n = 21). Active sacroilitis was detected by MRI in 26% (n = 28) of patients, with 11% (n = 11) qualifying for nonradiographic sacroilitis. Patients with radiographic and nonradiographic sacroiliitis had similar clinical characteristics, except for a longer duration of psoriasis (PsO) and PsA in the radiographic subgroup (PsO:  $23.8 \pm 12.5$  vs  $14.1 \pm 11.7$  yrs, P = 0.03; PsA:  $12.3 \pm 9.8$  vs  $4.7 \pm 4.5$  yrs, P = 0.02, respectively). Inflammatory back pain (IBP) was reported in 46.4% (n = 13) with active sacroiliitis and 27% (n = 3) with nonradiographic sacroiliitis. The sensitivity of IBP for detection of nonradiographic sacroiliitis was low (27%) and moderate for radiographic sacroiliitis (52%), whereas specificity ranged from 72% to 79% for radiographic and nonradiographic sacroiliitis, respectively.

> Conclusion. The prevalence of active sacroiliitis among a real-life population of patients with PsA was 26%. However, the prevalence of nonradiographic sacroilitis was low (11%) compared to the radiographic sacroiliitis (28.7%) seen in patients with longer disease duration. IBP was not a sensitive indicator for the presence of early-stage sacroiliitis that was commonly asymptomatic.

Key Indexing Terms: MRI, psoriatic arthritis, sacroiliitis, spondyloarthropathy

Psoriatic arthritis (PsA) is a multidomain inflammatory disease involving peripheral joints, entheses, and the axial skeleton. Prolonged disease duration, severe peripheral joint disease, and

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presence of HLA-B27 have been associated with axial disease development in PsA.<sup>1,2</sup> The reported prevalence of axial disease in PsA widely varies between 25-75%, based on disease duration (early vs long-term disease) and the definition of axial disease (clinical or radiographic). 3,4,5,6,7 Previous studies conducted in the PsA population have used mainly conventional radiographs of sacroiliac joints (SIJs) for the detection of structural lesions (e.g., erosions and ankylosis) and the diagnosis of radiographic sacroiliitis, applying the 1984 modified New York (mNY) criteria developed for ankylosing spondylitis (AS).8 While this method of assessment is broadly available, it has only moderate reliability and validity for the diagnosis of axial spondyloarthritis (axSpA), especially in the early stages of the disease. Over the last decade, magnetic resonance imaging (MRI) has evolved as an important imaging modality for the detection of early inflammatory disease of SIJs prior to the development of structural damage, which is apparent on conventional radiographs. According to the current terminology introduced by the Assessment of Spondyloarthritis international Society (ASAS), axSpA encompasses both radiographic and nonradiographic forms of sacroiliitis, differentiated by the presence or absence of structural lesions on pelvic radiographs, respectively.10 Nonradiographic sacroiliitis is defined by

the presence of active inflammation (subchondral bone marrow edema [BME]) of SIJs depicted on MRI, in the absence of corresponding radiographic sacroiliitis.<sup>11</sup>

The clinical course of axial PsA (axPsA) can be highly heterogeneous, ranging from asymptomatic disease<sup>5,12,13</sup> to severe inflammatory back pain (IBP). Lack of IBP in patients with PsA commonly leads to a late diagnosis of the axial disease.<sup>5,12,14</sup> Early detection of axPsA is thus important for monitoring disease activity and appropriate treatment initiation, as reflected in the international guidelines for the treatment of nonradiographic axSpA,<sup>15</sup> underlining an ongoing need for investigating early axial disease in PsA.

To our knowledge, only limited data on the prevalence of MRI-detected sacroilitis in patients with PsA are available. A Brazilian study reported the prevalence of active inflammatory lesions of SIJs detected by MRI in 37.8% out of 45 patients with PsA. <sup>16</sup> In this study, the prevalence of nonradiographic sacroilitis was not reported. Further, little is known about the difference in clinical phenotypes of nonradiographic vs radiographic sacroilitis in PsA. Herein, we conducted a cross-sectional observational study based on consecutively recruited patients with PsA, aiming to establish the prevalence of nonradiographic sacroilitis (primary outcome) within a real-life clinic sample. We further compared the clinical characteristics associated with nonradiographic vs radiographic sacroilitis and investigated the correlation between the clinical indices of axial disease and MRI findings of SIJs (secondary outcome).

## **METHODS**

*Ethical considerations*. Our study was conducted according to the guidelines of the Declaration of Helsinki and the approval of the institute's review board (0352-13-TLV). All patients signed informed consent upon enrollment into the study.

Patients. Adult consecutive patients (≥ 18 yrs) with PsA according to the Classification Criteria for Psoriatic Arthritis<sup>17</sup> attending the rheumatology clinic of the Tel Aviv Medical Center, Tel Aviv, Israel, between the years of 2016 and 2018 were eligible to participate in the study. Exclusion criteria included refusal to sign the written informed consent, as well as pertinent exclusion criteria for a standard radiographic/MRI examination, such as pregnancy, claustrophobia, metallic foreign body (stent, coils, filters), implanted pacemaker or defibrillator, cochlear implants, or insulin pump.

Study design and clinical variables. We conducted a cross-sectional observational study. The following patient information was obtained: age, height, weight, psoriasis (PsO) and PsA duration, comorbidities, and history of previous and present medical treatments. A detailed history regarding the presence of back pain, including location, intensity, and duration of pain, was collected. Assessment of IBP using ASAS criteria was considered positive in patients with chronic back pain (duration > 3 months) with 4 out of 5 variables present (age at onset < 40 yrs, insidious onset, improvement with exercise, no improvement with rest, and nocturnal pain).<sup>18</sup> A comprehensive physical examination of PsA domains included the following measures/ indices: tender joint count in 68 joints (TJC), swollen joint count in 66 joints (SJC), Leeds Enthesitis Index,19 Maastricht AS Enthesitis Score,20 and Bath Ankylosing Spondylitis Metrology Index (BASMI).21 Participants completed patient-reported outcome measures validated for use in axPsA: Health Assessment Questionnaire (HAQ),<sup>22</sup> Bath Ankylosing Spondylitis Disease Activity Index (BASDAI),<sup>23</sup> Bath Ankylosing Spondylitis Functional Index (BASFI),24 and patient global assessments of pain and disease activity measured using 1–100 visual analog scales (VAS). AS Disease Activity Score (ASDAS)<sup>25</sup> was also calculated. The disease activity of PsA was assessed by the Disease Activity Index for PsA (DAPSA) score.<sup>26</sup> This index is a composite measure comprising SJC and TJC, patient global and pain assessments, and an acute-phase reactant<sup>26</sup> that corresponds with joint damage and disability in PsA.<sup>27</sup> Peripheral PsA disease activity was defined based on the DAPSA score: remission (0–4), low (5–14), moderate (15–28), and high (> 28). Physician global assessment of disease activity was measured using 1–100 VAS. The severity of skin disease was defined based on the PsO Area and Severity Index (PASI).<sup>28</sup>

Laboratory assessment. All patients underwent HLA-B27 testing and measurement of C-reactive protein (CRP) levels.

Axial radiographic assessment. Axial disease was assessed in all study participants by an anterior-posterior pelvic radiograph of SIJs and semicoronal T1-weighted and short-TI inversion recovery MRI sequences of SIJ, without contrast material. All MRI examinations were performed on a 1.5T unit (Optima 450W-70cm, GE Healthcare). The spines of these patients were also imaged by MRI for further evaluation.

The pelvic radiograph of each patient was independently interpreted by 2 separate experienced musculoskeletal radiologists (GF, ID), blinded to clinical data and MRI findings. Radiographic sacroiliitis was determined based on the 1984 mNY criteria, considered positive in cases of unilateral grade  $\geq 3$  or bilateral grade  $\geq 2$  sacroiliitis on pelvic radiographs. The final score was the average of the 2 readers. Interreader agreement ( $\kappa$ ) between both readers was calculated and found to be good ( $\kappa = 0.73$ ).

MRI images were interpreted by a third experienced musculoskeletal radiologist (IE), blinded to the radiographs' findings and to clinical data. The intrareader reliability was calculated as the intraclass correlation coefficient (ICC), based on the repeated reading of 20 randomly selected MRI scans with an interval of 1 month between the readings. Intrareader ICC for the reliability of MRI assessment of SIJs was good for erosions (0.71) and BME (0.70), moderate for fat metaplasia (0.64), and poor for sclerosis (0.36), consistent with a limited ability of MRI to detect sclerosis of SIJ (data not shown).<sup>29</sup>

SIJs on MRI were evaluated for the presence of active inflammatory lesions according to the 2016 ASAS criteria. The presence of BME highly suggestive of sacroiliitis was defined as active sacroiliitis/ASAS criteria, 11 and the presence of structural lesions, such as erosions, fat metaplasia, subchondral sclerosis, and ankylosis, was defined as structural sacroiliitis.<sup>30</sup> SIJs were evaluated using a validated and accepted scoring method, the Berlin score, as follows: Each joint was divided into 4 quadrants. Each quadrant was scored for osteitis/BME as follows: 0 = absent (no osteitis); 1 = < 33% of quadrant area; 2 = 23% to < 66% of quadrant area; 3 = 266% of quadrant area with a maximum score of  $24.^{31}$  Subchondral sclerosis was scored in the same way. Erosions were scored as follows: 0 = normal joint margin; 1 = 1-2 erosions; 2 = 3-5 erosions; 3 = > 5 erosions. Fatty lesions and ankylosis were allocated binary scores: 0 = absent; 1 = present. Nonradiographic sacroiliitis was defined by the presence of active sacroiliitis/ASAS criteria of SIJs on MRI in the absence of corresponding radiographic sacroilitis on pelvic radiographs.11

Statistical analysis. Descriptive statistics included means and SDs for continuous variables and frequency tables for categorical variables. When applicable, continuous variables were compared using independent sample t tests for 2 samples and 1-way ANOVA for more than 2 independent groups (with posthoc tests when needed), and categorical variables were compared using chi-square test of independence. The interreader agreement was determined by calculating kappa coefficient ( $\kappa$ ).<sup>32</sup> To assess the diagnostic value of IBP for detecting radiographic sacroiliitis defined by radiograph and sacroiliitis defined by MRI (active or structural lesions in SIJs), sensitivity, specificity, and negative and positive likelihood ratios, along with their respective 95% CIs, were calculated. Two-sided P value < 0.05 was considered significant. All analyses were performed using RStudio version 1.1.383 (RStudio Team).

#### **RESULTS**

Characteristics of the study population. Our study included a total of 107 White patients with PsA, aged 49.7  $\pm$  12.5 years, with a nearly equal representation of both sexes (53 males, 54 females). The demographics and clinical characteristics of the study population are summarized in Table 1. The majority of patients had long-standing (≥ 5 yrs) PsO and PsA (83.2% [n = 82] and 62% [n = 65], respectively). Peripheral joint disease, assessed by DAPSA, was well controlled in 58% of the study population, with remission in 21% (n = 22) and low disease activity in 37% (n = 40). A third of patients (31%, n = 33) had moderate disease activity, and a minority (11%, n = 12) had high disease activity. The severity of PsO, assessed by PASI, was mild (PASI < 7) in 93% (n = 99) of patients.

Table 1. Patients' characteristics (n = 107).

	Values
Age, yrs	49.7 (12.5)
Sex, M:F	53:54
Tender joint count	5.5 (8.5)
Swollen joint count	1.1 (2.8)
CRP, mg/L	6 (7)
DAPSA	15.3 (12.1)
LEI	1 (1.2)
MASES	1.4 (2.5)
Dactylitis, n (%)	16 (15)
PASI	3.8 (8.5)
Low back prevalence, n (%)	68 (63.5)
IBP prevalence, n (%)	31 (29)
Back pain intensity (patient VAS 0-10)	3.3 (3.3)
BASDAI	3.9 (2.4)
ASDAS-CRP	0.9 (2.2)
BASMI	2.7 (1.2)
BASFI	2.9 (2.3)
Current medication use, n (%)	, ,
sDMARD	51 (47.7)
Apremilast	1 (0.9)
Biologics	41 (38.3)
Anti-TNF	35 (32.7)
Anti–IL-17	1 (0.9)
Anti-IL-12/23	3 (2.8)
MRI SIJ scores	
Total Berlin score	6.9 (10.7)
Osteitis/BME (0–24)	1.6 (3.3)
Fat infiltration score (0–24)	1.3 (3.5)
Erosion score (0–24)	3.4 (5.8)
Sclerosis score (0–8)	0.4 (1.2)
Ankylosis score (0–8)	0.3 (1.4)

Values are expressed as mean (SD) unless otherwise stated. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BME: bone marrow edema; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; IBP: inflammatory back pain; IL: interleukin; LEI: Leeds Enthesitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MRI: magnetic resonance imaging; PASI: Psoriasis Area and Severity Index; sDMARD; synthetic disease-modifying antirheumatic drug; SIJ: sacroiliac joint; TNF: tumor necrosis factor; VAS: visual analog scale.

A history of general back pain was present in 69% (n = 74), predominantly in the lumbar region (55%, n = 59). A history of IBP (ASAS criteria) was reported in a third of patients (29%, n = 31; Table 1), mainly in the lumbar area. Axial disease activity, assessed by ASDAS-CRP, was inactive in 26.4% (n = 28), low in 17.9% (n = 19), high in 47.2% (n = 50), and very high in 8.5% (n = 9) of patients. Only 4 patients (3.7%) were HLA-B27 carriers, with 2 of them diagnosed with radiographic (n = 1) and nonradiographic (n = 1) sacroillitis. Concomitant fibromyalgia (FM) was detected in 10% patients (n = 11), contributing to higher scores of disease activity indices and patient-reported outcomes in this subgroup.

About half of patients (48%, n = 51) were treated with synthetic disease-modifying antirheumatic drugs (sDMARDs), with methotrexate being the most prevalent sDMARD (38%, n = 41), followed by leflunomide (8%, n = 9). A total of 38% (n = 41) of patients were treated with biologics at the time of enrollment into the study. Tumor necrosis factor (TNF) inhibitors constituted the most prevalent biologic treatment (33%, n = 35), followed by ustekinumab (4%, n = 4), and secukinumab (2%, n = 2). Exposure to any biologic treatment in the past or present was reported in 47% (n = 50) of patients.

Radiographic and MRI outcomes. Imaging outcomes of SIJ imaging are presented in Figure 1. Active sacroilitis/ASAS was detected in 26% (n = 28) of patients. Among the cases with active sacroilitis, 39% (n = 11; 11% of the entire study population) qualified for nonradiographic sacroilitis. Only 46.4% (n = 13) of patients with active sacroilitis and 27.3% (n = 3) of patients with nonradiographic sacroilitis reported IBP (Table 2).

Radiographic sacroiliitis based on the mNY criteria was detected in 28.7% of patients (n = 29), confirmed by the presence of structural sacroiliitis by MRI in the majority of cases (72.4%, n = 21). Six patients (5.6%) presented with isolated structural lesions of SIJs by MRI in the absence of corresponding radiographic structural changes. IBP symptoms were present in 41.4% (n = 12) of patients with radiographic sacroiliitis. Notably, 8 patients with radiographic sacroiliitis had no evidence of active or structural sacroiliitis by MRI. The majority of this positive radiograph/negative MRI subgroup (75%, n = 6) reported general back pain, which was consistent with IBP in only 1 patient. All were HLA-B27-negative. In comparison to the rest of the sample, positive radiograph/negative MRI patients had significantly worse functional limitation measured by BASFI  $(4.6 \pm 1.7 \text{ vs } 2.9 \pm 1.7, \text{ respectively}; P = 0.04; \text{ data not})$ shown).

The comparisons between the clinical characteristics of patients with nonradiographic and radiographic sacroiliitis are shown in Table 2. Both subgroups had a similar sex distribution, age, BMI, and history of comorbidities. Patients with radiographic sacroiliitis had a significantly longer duration of PsO and PsA compared to nonradiographic sacroiliitis subgroup (PsO:  $23.8 \pm 12.5$  vs  $14.1 \pm 11.7$  yrs, respectively [P = 0.03]; PsA:  $12.3 \pm 9.8$  vs  $4.7 \pm 4.5$  yrs, respectively [P = 0.02]). There was no significant difference in the prevalence of IBP between both subgroups (46.4% in radiographic vs 27% in nonradiographic subgroup, P = 0.65). Spinal mobility was lower in

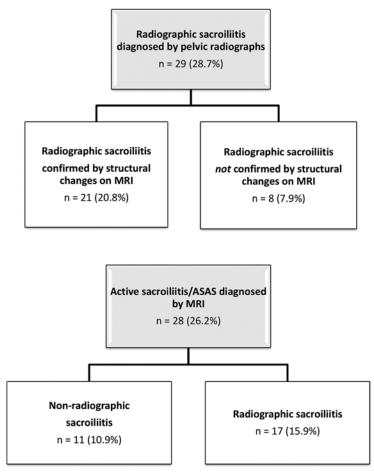


Figure 1. Sacroiliitis prevalence based on pelvic radiographs and MRI in patients with psoriatic arthritis (n = 107). Radiographic sacroiliitis was determined based on the 1984 modified New York criteria, considered positive in case of unilateral grade  $\geq$  3 or bilateral grade  $\geq$  2 sacroiliitis on pelvic radiographs. Active sacroiliitis detected by MRI was defined based on the 2016 ASAS criteria. Nonradiographic sacroiliitis was defined by the presence of active sacroiliitis/ASAS criteria of SIJs on MRI in the absence of corresponding radiographic sacroiliitis on pelvic radiographs. Percentage is calculated in relation to the total study population. ASAS: Assessment of Spondyloarthritis international Society; MRI: magnetic resonance imaging; SIJ: sacroiliac joint.

the radiographic sacroiliitis subgroup, as reflected by higher BASMI scores (mean  $\pm$  SD:  $3.2 \pm 1.4$  vs  $2.2 \pm 0.9$ , respectively; P = 0.046). Treatment patterns with sDMARDs and biologics were similar between both subgroups. Patients with radiographic sacroiliitis had an overall higher exposure rate to biologic treatments: 58.6% vs 18%, respectively (P = 0.05). Patients with nonradiographic sacroiliitis and patients without radiographic or nonradiographic sacroiliitis had similar demographic, clinical, and treatment characteristics and patterns.

Notably, a small number of patients (5.6%, n = 6) demonstrated structural sacroiliitis on MRI only, in the presence of normal pelvic radiograph. Comparisons between this subgroup and patients with radiographic sacroiliitis showed similar demographic, clinical, and patient-reported outcome profiles.

We further explored the clinical phenotype of back pain, axial disease indices, and prevalence of the radiographic phenotype based on sex difference (females: n = 54; males: n = 53).

General lumbar back pain was significantly more prevalent in females compared to males (females: 68.5%, n = 37; males: 41.5%, n = 22; P = 0.009). The prevalence of IBP (females: 33.3%, n = 18; males: 24.5%, n = 13; P = 0.43) and radiographic outcomes (i.e., radiographic and nonradiographic sacroiliitis) was similar between females and males. Despite similar prevalence of sacroiliitis, females presented significantly higher indices of axial disease activity (mean  $\pm$  SD), including BASDAI (4.4  $\pm$  2.6 in females vs  $3.4 \pm 2.0$  in males, P = 0.03), ASDAS-CRP ( $2.4 \pm 1.1$ in females vs 2.0  $\pm$  0.9 in males, P = 0.049), BASFI (3.4  $\pm$  2.4 in females vs  $2.4 \pm 2.1$  in males, P = 0.032), and HAQ (0.9 ± 0.7 in females vs  $0.5 \pm 0.6$  in males, P = 0.012). This observation may be explained by a high prevalence of FM among female patients (20.4%, n = 11) compared to none among male patients in this cohort (P = 0.002). The treatment pattern was similar between both groups.

An additional subanalysis of the study population based on

Table 2. Comparison between patients wih PsA with radiographic and nonradiographic sacroiliitis.

	Radiographic Sacroiliitis	Nonradiographic Sacroiliitis	P
Patients, n	29	11	_
Sex, female, n (%)	10 (34.5)	4 (36)	> 0.999
Age, yrs	52.5 (12.2)	47.6 (9.9)	0.25
BMI, kg/m <sup>2</sup>	25.9 (5.8)	26.3 (5.4)	0.84
Active smoking status, n (%)	1 (3.4)	1 (9.1)	0.62
Fibromyalgia, n (%)	2 (6.9)	0 (0.0)	0.94
PsO duration, yrs	23.8 (12.5)	14.1 (11.7)	0.03
PsA duration, yrs	12.3 (9.8)	4.7 (4.5)	0.02
Tender joint count	5.6 (8.9)	3.6 (4.7)	0.47
Swollen joint count	0.9 (1.6)	0.9 (1.5)	0.93
CRP, mg/L	8.7 (9.4)	7.1 (7.8)	0.62
DAPSA	15.1 (12.5)	14.2 (7.2)	0.84
LEI	0.7 (0.9)	0.6 (0.8)	0.56
MASES	0.9 (1.9)	0.3 (0.7)	0.39
Dactylitis, n (%)	6 (20.7)	3 (27.2)	0.74
PASI	8.2 (14.3)	2 (2.6)	0.17
Low back prevalence, n (%)	21 (72.4)	8 (72.7)	> 0.999
IBP prevalence, n (%)	13 (46.4)	3 (27.3)	0.52
Back pain intensity (patient VAS 0-10)	3.0 (3.0)	2.5 (3.1)	0.59
BASDAI	3.5 (2.5)	4.3 (1.9)	0.34
ASDAS-CRP	2.1 (1.1)	2.3 (0.8)	0.71
BASMI	3.2 (1.4)	2.2 (0.9)	0.05
BASFI	2.9 (2.3)	2.4 (2.1)	0.52
Current medication use, n (%)			
Current sDMARD treatment	8 (27.6)	6 (54.5)	0.22
Current biologic treatment	14 (48.3)	2 (18.2)	0.17
MRI SIJ scores			
Total Berlin score	17.5 (13.1)	8.5 (7.7)	0.04
Osteitis/BME (0–24)	3.7 (4.7)	4.2 (3.3)	0.75
Fat infiltration score (0–24)	4 (5.5)	0.1 (0.3)	0.02
Erosion score (0–24)	7.9 (7.8)	3.5 (3.6)	0.08
Sclerosis score (0–8)	0.8 (1.6)	0.8 (1.6)	0.48
Ankylosis score (0–8)	1.1 (2.6)	0 (0)	0.09

Values are expressed as mean (SD) unless otherwise stated. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BME: bone marrow edema; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; IBP: inflammatory back pain; IL: interleukin; LEI: Leeds Enthesitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MRI: magnetic resonance imaging; PASI: Psoriasis Area and Severity Index; PsA: psoriatic arthritis; PsO: psoriasis; sDMARD: synthetic disease-modifying antirheumatic drug; SIJ: sacroiliac joint; VAS: visual analog scale.

the exposure to any biologic treatment in the past or present revealed a trend toward a higher prevalence of nonradiographic sacroiliitis among patients not exposed to biologics (17.3% [n=9] vs 4.1% [n=2], respectively; P=0.07; data not shown). The prevalence of radiographic sacroiliitis was similar in both groups.

Finally, we calculated the sensitivity and specificity of the IBP symptoms for the detection of sacroilitis by radiograph and MRI, using imaging as the gold standard for the diagnosis of sacroilitis (Table 3). Overall, the sensitivity of IBP was very low for a nonradiographic sacroilitis detected by MRI (range 17–27%), increasing to 52% for radiographic sacroilitis, whereas specificity ranged from 72% to 79% for nonradiographic and radiographic sacroilitis. By comparing the positive likelihood

ratios (LRs), IBP performed the best to identify radiographic sacroiliitis based on the mNY criteria (LR 2.46). By comparing the negative LRs, IBP performed the best for ruling out non-radiographic ASAS sacroiliitis (LR 0.35).

### **DISCUSSION**

To our knowledge, this is the first study using concurrent imaging of SIJs by pelvic radiograph and MRI to determine the prevalence of nonradiographic sacroiliitis conducted in a large, real-life, clinical PsA sample. Detection of axial involvement in patients with PsA is important, as axial involvement is associated with worse outcomes and worse quality of life compared to patients with peripheral disease alone. <sup>1,33</sup> Our findings indicate a low prevalence (11%) of nonradiographic sacroiliitis compared

Table 3. Sensitivity, specificity, and LRs of IBP defined by ASAS criteria in detecting sacroiliitis by various imaging methods and criteria.<sup>2</sup>

Imaging Outcome	Sensitivity (%)	Specificity (%)	LR+	LR-
Radiographic sacroiliitis, mNY criteria MRI sacroiliitis, ASAS	52	79 77	2.46	0.6 0.69
MRI nonradiographic sacroiliitis, ASAS	46 27	72	0.98	0.69
MRI nonradiographic structural sacroiliitis	17	72	0.59	1.16

<sup>&</sup>lt;sup>a</sup> Sacroiliitis defined by radiograph or MRI is considered the gold standard. ASAS: Assessment of Spondyloarthritis international Society; IBP: inflammatory back pain; LR: likelihood ratio; mNY: modified New York; MRI: magnetic resonance imaging.

to radiographic sacroiliitis, detected by pelvic radiographs and MRI, in about one-third of the study population. This low prevalence of nonradiographic sacroiliitis, indicating an early stage of axial disease, may be explained by the fact that the majority of patients had long-standing PsO and PsA. While data on the prevalence of nonradiographic sacroiliitis among patients with PsA is limited, the prevalence of radiographic sacroiliitis in our study is consistent with a number of previous reports.<sup>3,7,34</sup> In addition, we evaluated the prevalence of structural lesions in SIJs in the absence of inflammation on MRI, defined as "structural-only nonradiographic sacroiliitis" (5.9%). The phenomenon of structural lesions, particularly erosions, present on MRI but not radiographs of SIJs, has been previously reported in axSpA and probably results from the reduced sensitivity and specificity of 2D pelvic radiographs compared to the 3D MRI.35 While the prognostic implication associated with structural lesions in axial PsA is presently unknown, detection of these lesions may potentially be important for patients' management and follow-up. Moreover, we identified a small group of patients (7.9%) qualifying for radiographic sacroiliitis defined by the mNY criteria8 in the absence of active/structural sacroiliitis on MRI, pointing to the low reliability of radiographic evaluation alone. 9,36

Our study identifies the similar demographics, disease characteristics, and treatment patterns including exposure to biologic treatments in the past and in the present, among patients with nonradiographic and radiographic sacroiliitis, with the only significant difference being a shorter duration of PsO and PsA among the former subgroup. Indeed, in the Toronto PsA cohort, 15% of patients without axial involvement at presentation developed axial disease during 10 years of follow-up.1 Further, the clinical similarities between both subgroups are consistent with the observational data comparing patients with nonradiographic and radiographic axSpA. For instance, the United Statesbased Corrona registry of patients with AS showed that both subgroups had comparable disease burden and similar treatment patterns.<sup>37</sup> Other studies in axSpA also reported similar levels of disease activity, overall physical impairment, and health-related quality of life between these subgroups, while the patients with nonradiographic axSpA were more often female, had shorter mean disease duration, and displayed lower levels of acute-phase reactants. 38,39,40,41,42 Moreover, both subgroups had similar rates of persistence and response to treatment with anti-TNF therapy over time. 42 Our study did not show female predominance in the nonradiographic group, nor a significant difference in the level

of inflammatory markers in blood. Overall, preliminary data on axial disease in PsA is consistent with the accumulated data in AS/axSpA cohorts, implying that both nonradiographic and radiographic forms of sacroiliitis represent a spectrum of the same axial disease at different stages.

On clinical grounds, efficient screening for axial disease among patients with PsA is warranted. While the history of IBP is essential for the diagnosis of sacroiliitis, only 57.1% of patients with radiographic sacroilitis and 27.3% of patients with nonradiographic sacroiliitis reported a history of IBP in our study. These data are further supported by other studies reporting a high prevalence of asymptomatic axial disease and the transient nature of axial symptoms in PsA.5,7,12 A recent study reported the prevalence of MRI-detected acute sacroiliitis/ASAS in 37.8% of a clinical PsA sample (n = 45), with lower back pain reported in only 29.4% of patients with MRI-detected sacroiliitis.16 Further, clinical criteria for IBP developed for AS did not perform well when ascertaining axial involvement in PsA.<sup>43</sup> Thus, awareness of asymptomatic axial disease in patients with PsA is warranted, dictating the use of appropriate imaging for axial disease detection.

One of the unique features of our study is a very low prevalence of HLA-B27, confirming a similar observation reported in another PsA cohort in Israel.<sup>44</sup> The accumulated evidence supports the notion of HLA-B27 carriage being linked to susceptibility, extent, and severity of psoriatic axSpA, <sup>1,2,7,45,46,47</sup> with the exception of 1 study conducted in the United Kingdom that did not demonstrate a correlation between HLA-B27 and sacroiliitis diagnosed by MRI in patients with PsA.<sup>48</sup> Thus, other mechanisms seem to contribute to the pathogenesis of axial disease in our population.

Our study has a number of limitations. The cross-sectional design of the study precludes the observation of the development and clinical course of the radiographic findings. Inception cohort studies with a longitudinal follow-up are needed to address this issue. There is a potential selection bias in the recruitment of this study population, with patients suffering from any type of back pain inclined to participate, as opposed to asymptomatic patients. The study population is heterogeneous with variable disease duration and treatment exposures. Data on family history of SpA features are missing. Finally, the definition of active sacroilitis by MRI was based on the updated 2016 ASAS classification criteria for AS.<sup>11</sup> The most up-to-date definitions of other MRI SIJ lesions defined by the ASAS MRI Working Group in

2019 were not applied in our study protocol. Importantly, the definition of subchondral BME in the SIJ indicative of active sacroiliitis was not revised in 2019.

To conclude, our study indicates that the prevalence of non-radiographic sacroiliitis among a real-life population of patients with PsA is low (11%) compared to radiographic sacroiliitis, which is prevalent in about 30% of patients with longstanding disease. IBP is not a sensitive indicator for the detection of early-stage sacroiliitis, prompting the use of MRI for diagnosis of sacroiliitis. These results further contribute to the understanding of the axial disease pattern in PsA. Longitudinal follow-up studies are warranted to explore the rates and factors affecting the progression of sacroiliitis from nonradiographic to a radiographic stage.

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