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ORIGINAL ARTICLES

Zone-specific analysis of radiographic pelvic enthesitis in axial spondyloarthritis: identification and associations with mobility, function, and disease activity

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ABSTRACT

Objectives: To evaluate the frequency of radiographic pelvic enthesitis in patients with axial spondyloarthritis (axSpA), focusing on zone-specific entheseal sites and their associations with disease activity, mobility, and functional outcomes.

Methods: This prospective cross-sectional study included 100 patients with radiographic axial spondyloarthritis (r-axSpA) and 100 patients with non-radiographic axial spondyloarthritis (nr-axSpA), who were consecutively admitted to a tertiary hospital's rheumatology outpatient clinic. Pelvic enthesitis was evaluated in three zones using anteroposterior pelvic X-rays, guided by the recently introduced Radiographic Enthesis Index (REI). Disease activity, spinal mobility, and functionality were assessed using ASDAS-CRP, BASDAI, BASMI, and BASFI.

Results: Radiographic enthesitis in the pelvic region was found in 128 patients (64% of the total), comprising 72 (72%) in the r-axSpA group and 56 (56%) in the nr-axSpA group ($p = 0.018$). Zone 3 (ischiopubic ramus) enthesitis was the most common (59.5%) and was significantly correlated with impaired spinal mobility (BASMI), reduced lumbar lateral flexion, cervical rotation, and modified Schober test scores ($p < 0.001$). Zone 2 (pubic symphysis) enthesitis was associated with higher disease activity (BASDAI, $p = 0.026$). Patients with pelvic enthesitis also experienced longer symptom duration ($p < 0.001$).

Conclusions: Pelvic enthesitis detected by AP pelvic radiography is frequent and clinically significant in axSpA. Our findings highlight novel associations with increased disease activity (particularly at the Zone 2) and reduced spinal mobility (notably at the Zone 3).

Keywords: Axial spondyloarthritis; Enthesopathy; Functional Status; Inflammation; Pelvic Bones; Radiography.

KEY MESSAGES

- Radiographic pelvic enthesitis is highly prevalent in axial spondyloarthritis, particularly in the radiographic subtype.
- Zone-specific analysis links pubic-symphysis enthesitis to higher disease activity and ischiopubic enthesitis to impaired spinal mobility.
- A simple anteroposterior pelvic X-ray offers a practical tool for targeted enthesitis assessment in everyday rheumatology practice.

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INTRODUCTION

Axial spondyloarthritis (axSpA) is a long-term chronic rheumatic disease, it is characterized by the inflammation of the sacroiliac joints, the spine, and notably the entheses[1]. Entheses are anatomical structures representing the points of attachment of tendons, ligaments, joint capsules and fascias to bone. These junctions play a pivotal role in the biomechanical transfer of muscular force to the skeletal system, especially facilitating movement and ensuring structural stability.

From a pathophysiological perspective, enthesitis related to spondyloarthritis (SpA) is characterized as an atypical reaction to biomechanical stress, triggering the activation of an innate inflammatory response[2, 3]. This condition is believed to stem from disruptions in the cytokine cascade[2]. These cytokines not only orchestrate the inflammatory response but also play a pivotal role in the pathological overgrowth of bone and fibrous tissue, a defining feature of axSpA that leads to the characteristic structural deformities observed in the condition. Furthermore, this inflammatory cascade can extend be-

yond the entheses, influencing adjacent bone and soft tissues, thereby amplifying the structural damage.

Clinically, enthesitis is associated with higher disease activity, reduced spinal mobility, and impaired quality of life[2,4]. Real-world data suggest that it significantly affects daily activities, work productivity, and overall well-being. Peripheral enthesitis, in particular, has been identified as a predictor of spinal damage across different subtypes of SpA[5]. This finding highlights its role in disease progression and management[5]. However, most studies have relied on enthesitis indices rather than assessing specific types or locations of enthesitis, limiting a more detailed understanding of its clinical implications. Enthesitis exhibits a wide spectrum of symptoms. Superficial entheses, such as those in the Achilles tendon, patellar tendon, and lateral epicondyle, often present with visible soft tissue swelling. In contrast, deeper entheses, including those at the iliac crests, pubis, and ischial tuberosities, may manifest only as tenderness or palpable swelling[6]. In some cases, pain may be the sole symptom, necessitating confirmation through appropriate imaging[6]. Given its role in disease burden, accurate identification of enthesitis is essential for effective diagnosis and management.

Imaging plays a key role in detecting and evaluating enthesitis. Radiography remains a widely used diagnostic tool, particularly for assessing sacroiliac joint involvement and aiding in differential diagnosis. While ultrasonography and magnetic resonance imaging (MRI) offer more detailed visualization, their extensive time requirements often limit routine use in busy outpatient settings. As a result, despite its limitations in detecting early entheseal changes, radiography continues to be the most accessible and commonly employed imaging modality in clinical practice.

Despite its clinical significance, enthesitis in axSpA is often underrecognized due to time constraints and high patient volumes in outpatient clinics. Additionally, conventional assessment methods typically evaluate enthesitis as a single entity, overlooking site-specific variations and their distinct contributions to disease progression. To address this limitation, developing a practical and effective method for differentiating enthesitis subtypes and assessing their associations with disease burden is essential. This is the subject of the present report. Given the clinical advantages of radiography, our method is based on X-ray imaging.

In this context, we found that the zone-specific analysis developed by Enrique et al. is the most suitable approach for evaluating pelvic enthesitis[7]. This method focuses on three distinct pelvic zones: the iliopubic ramus, pubic symphysis, and ischiopubic ramus. Although Enrique et al.'s study provided a clear anatomical classification of pelvic entheses and demonstrated their potential utility in aiding diagnosis, the association with clinical outcomes remains unexplored. To address this gap, this report aims to evaluate zone-specific pelvic enthesitis detected by AP pelvic radiography in patients with axSpA and to investigate its associations with mobility, function, and disease activity. Additionally, we will explore differences between radiographic and non-radiographic axSpA subtypes, contributing to a more comprehensive understanding of disease heterogeneity and its implications for patient outcomes.

PATIENTS AND METHODS

This cross-sectional study enrolled 200 adult patients (18-65 years) who fulfilled the Assessment of SpondyloArthritis International Society (ASAS) criteria for axSpA[1]. Of these, 100 patients had radiographic axSpA (r-axSpA) and 100 had non-radiographic axSpA (nr-axSpA). Participants were consecutively recruited from the outpatient clinic of Rheumatology at xxx University Faculty of Medicine and volunteered to participate in the study between June 2022 and November 2022. Patients were excluded if they had a history of malignancy, metabolic bone disorders, or pelvic fractures, were pregnant, had experienced acute infection, or declined to provide informed consent. Ethical approval was obtained from the local ethics committee (Approval No=2022/287), and all participants provided written informed consent after being fully informed about the study protocol.

A comprehensive questionnaire was administered to gather demographic and clinical data, including age, gender, height, weight, smoking status, systemic conditions, and use of anti-rheumatic drugs. Laboratory markers such as hemoglobin, creatinine, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and HLA-B27 status were recorded.

Measurement Tools for Clinical Outcomes

Disease activity was evaluated using the Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP), Ankylosing Spondylitis Disease Activity Score with ESR (ASDAS- ESR) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[8-10]. Disability was assessed using the Health Assessment Questionnaire (HAQ), and quality of life was evaluated through the EQ-5D-3L scale[11-13]. Functional status was measured using the Bath Ankylosing Spondylitis Functional Index (BASFI), and spinal mobility was assessed with the Bath Ankylosing Spondylitis Metrology Index (BASMI)[14-16].

Radiographic Evaluation

The radiographs were systematically analyzed to iden-

tify features of enthesitis and sacroiliitis. These images were evaluated by a rheumatologist (K.E.) with over fifteen years of experience in musculoskeletal diseases. The rheumatologist was blinded to the clinical details of the patients to ensure unbiased interpretation. As context, a previously published reliability study involving the present study's reader reported moderate-to-substantial intra-reader and moderate inter-reader agreement for pelvic radiograph grading in axSpA [17]. Pelvic enthesitis was evaluated using the Radiographic Enthesis Index (REI), a standardized scoring system applied to pelvic X-rays obtained in anteroposterior views with the coccyx and pubic symphysis aligned to the midline[7]. The evaluation focused on three specific zones: Zone I (iliopubic ramus), Zone II (pubic symphysis), and Zone III (ischiopubic ramus). Each zone was assessed for the presence or absence of enthesitis (yes/no) based on radiographic findings, including subcortical bone demineralization, periosteal whiskering, erosion, or sclerosis (Figure); per the REI, any grade ≥1 was classified as enthesitis (present), and grade 0 bilaterally as absent. For each zone, the right and left sides were assessed separately; for the primary analyses, zone-level enthesitis was defined as present if detected on at least one side (right and/or left). For outcome comparisons, zone-specific enthesitis was analyzed using three independent binary indicators (Zone 1, Zone 2, Zone 3: present vs absent); therefore, any patient with Zone 1 enthesitis was included in the Zone 1–positive group irrespective of Zone 2 or Zone 3 status, and analogous definitions were applied for the other zones.

The evaluation of sacroiliitis was based on the modified New York criteria and was graded by the same reader (K.E.). Definite sacroiliitis was identified as bilateral sacroiliitis of at least grade 2 severity or unilateral sacroiliitis of at least grade 3 severity, as visible on pelvic x-rays. Patients meeting these criteria were classified as having r-axSpA. Conversely, patients who did not meet these criteria were categorized as nr-axSpA.

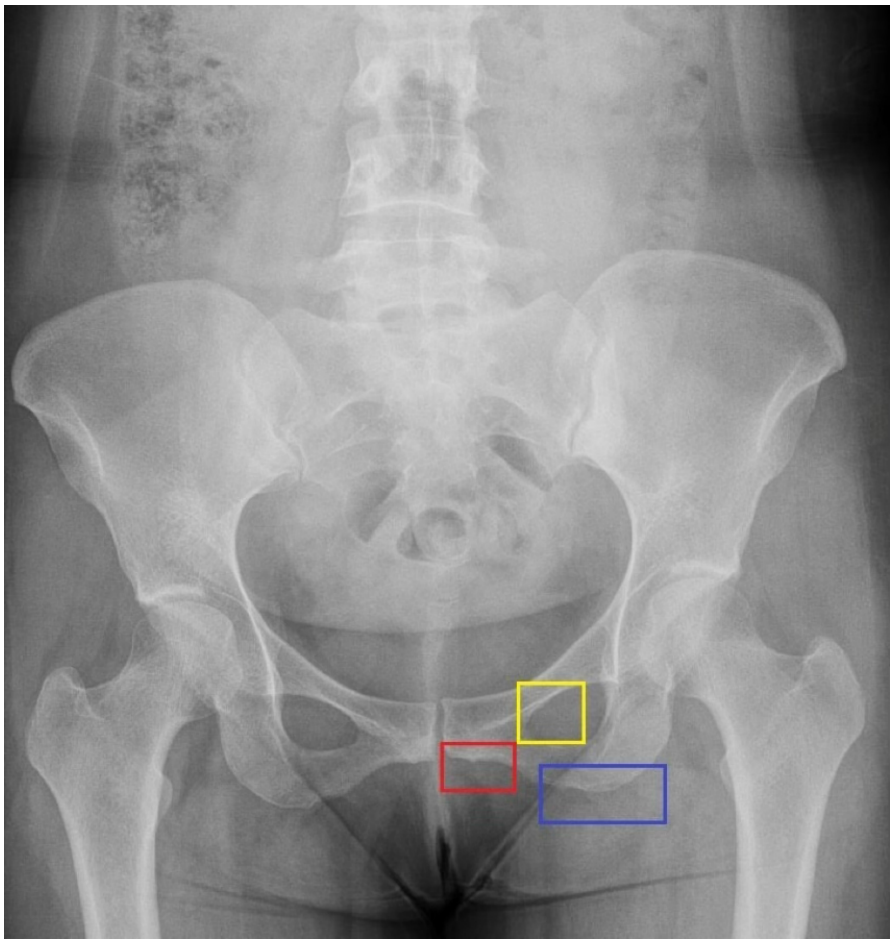

Figure 1. Pelvic radiograph of a 35-year-old female patient with axial spondyloarthritis, showing three distinct zones delineated with colored outlines along the anatomical margins: Zone I (ZI, yellow) corresponds to the iliopubic ramus; Zone II (ZII, red) denotes the pubic symphysis; and Zone III (ZIII, blue) represents the ischiopubic ramus.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Discrete variables were presented as frequencies and percentages, while continuous variables were described using means and standard deviations or medians and interquartile ranges [25th–75th percentiles], as appropriate based on data distribution. The Shapiro-Wilk test was employed to assess the normality of the data distributions. For discrete variables, differences between groups were analyzed using the Chi-square test. Continuous variables that followed a normal distribution were compared using the Student's t-test, whereas the Mann-Whitney U test was utilized for those variables not meeting the criteria for normality. All tests were two-sided, and a p-value of less than 0.05 was considered to indicate statistical significance.

RESULTS

In this cross-sectional study, we evaluated 200 patients with axSpA, assessing enthesitis radiographically in regions where patient consent was obtained. The median age of the cohort was 39 years (interquartile range: 30, 47), with males comprising 53% of the participants.

From the outset, the study population consisted of two groups: 100 patients with nr-axSpA and 100 with r-axSpA. A statistical analysis of gender distribution between these groups revealed differences; 38% of the r-axSpA group and 56% of the nr-axSpA group were female (p = 0.011). Comprehensive demographic and clinical data are detailed in Table I.

Zone-specific evaluation of enthesitis revealed that Zone 3 (ischiopubic ramus) alone was affected in 75 patients (37.5%). Zone 1 (iliopubic ramus) alone showed enthesitis in only 1 patient (0.5%), while Zone 2 (pubic symphysis) alone was affected in 6 patients (3.0%). Combined involvement of multiple zones was observed as follows: Zones 1 and 3 were affected in 23 patients (11.5%), Zones 1, 2, and 3 in 9 patients (4.5%), Zones 1 and 2 in 2 patients (1%), and Zones 2 and 3 in 12 patients (6%).

When considering each region independently, enthesitis was present in 17.5% of cases in the iliopubic ramus (Zone 1; 35 out of 200 cases) and 14.5% in the pubic symphysis (Zone 2; 29 out of 200 cases). The ischiopubic ramus (Zone 3; 119 out of 200 cases) showed the highest prevalence of enthesitis, with 59.5% of cases affected. Among patients with zone-specific enthesitis, the proportion with bilateral disease was 68.6% (24/35) in Zone 1, 86.2% (25/29) in Zone 2, and 95.8% (114/119) in Zone 3. Overall, the incidence of pelvic enthesitis among axSpA patients was observed to be 64% (128 out of 200 patients).

The prevalence of enthesitis varied significantly be-

TABLE I. Demographic, clinic and laboratory findings of patients

	r-axSpA (n=100)	nr-axSpA (n=100)	P value
Age, median (25^{th}-75^{th}), years	40 (32.25, 47)	39 (28, 47.75)	0.228
Gender, male, n (Positive/total, %)	62 (62/100, 62%)	44 (44/100, 44%)	0.011
BMI, median (25^{th}-75^{th}), kg/ m^2	28.28 (24.89, 32.02)	26.98 (23.5, 30.98)	0.123
Smokers, n (Positive/total, %)	44 (44/97, 45.4%)	28 (28/94, 29.79%)	0.026
Psoriasis, n (Positive/total, %)	6 (6/99, 6%)	4 (4/95, 4.2%)	0.748
IBD, n (Positive/total, %)	2 (2/99, 2%)	0 (0/95, 0%)	0.498
HLA B27, n (Positive/total, %)	41 (44/78, 56.41%)	25 (25/88, 28.4%)	0.002
Biological DMARD, n (Positive/total %)	27 (27/98, 27.55%)	6 (6/99, 6%)	<0.001
Hb, median (25^{th}-75^{th})	14.3 (13, 15.55)	14.1 (12.9, 15.7)	0.890
Creatinine, median (25^{th}-75^{th})	0.77 (0.67, 0.9)	0.74 (0.65, 0.88)	0.495
ESR, median (25^{th}-75^{th}), (mm/h)	8 (4, 14)	5 (2, 8.25)	<0.001
CRP, median (25^{th}-75^{th}), (mg/l)	6.03 (3.3, 13)	3.34 (2.4, 6.05)	<0.001
ASDAS-CRP, mean (SD)	2.93 (0.88)	2.72 (0.77)	0.073
ASDAS-ESR, median (25^{th}-75^{th})	2.4 (1.95, 3)	2.3 (1.88, 3)	0.273
BASDAI, (0-10), median (25^{th}-75^{th})	3.9 (3.4, 5.9)	4.25 (3.5, 6.53)	0.321
BASFI, (0-10), median (25^{th}-75^{th})	2.7 (1.25, 4.75)	2.7 (1.28, 4.6)	0.794
BASMI, (0-10), median (25^{th}-75^{th})	2 (1.3, 3)	1.5 (0.8, 2.4)	0.001

axSpA, axial spondyloarthritis; nr-axSpA, non-radiographic axial spondyloarthritis; r-axSpA, radiographic axial spondyloarthritis; BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; 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; IBD, Inflammatory bowel disease*

TABLE II. The relationship between Zone 1, 2,3 enthesitis and patients' demographic, clinical and laboratory data

	Zone 1enthesitis (n=200)			Zone 2 enthesitis (n=200)			Zone 3 enthesitis (n=200)		
	Positive (n=35)	Negative (n=165)	P value	Positive (n=29)	Negative (n=171)	P value	Positive (n=119)	Negative (n=81)	P value
Age, median (25th-75th), years	46 (38, 50)	38 (28, 46)	0.001	45 (36, 49.5)	39 (29, 46)	0.026	43 (36, 49)	30 (23.5, 43)	<0.001
Gender, male, n (male/ total, %)	17 (17/35, 48.57%)	89 (89/165, 53.94%)	0.695	6 (6/29, 20.69%)	100 (100/171, 58.48%)	<0.001	68 (68/119, 57.14%)	38 (38/81, 46.91%)	0.155
BMI, median (25th-75th), kg/ m²	27.73 (24.35, 30.85)	27.45 (24.24, 31.61)	0.743	29.55 (26.57, 33.58)	27.18 (24.22, 30.86)	0.021	27.47 (24.65, 30.9)	27.84 (23.85, 31.97)	0.916
Smokers, n (Positive/ total, %)	10 (10/35, 28.57%)	62 (62/156, 39.74%)	0.299	6 (6/28, 21.43%)	66 (66/163, 40.49%)	0.087	44 (44/113, 38.94%)	28 (28/78, 35.9%)	0.670
HLA B27, n (Positive/ total, %)	10 (10/30, 33.33%)	56 (56/136, 41.18%)	0.556	8 (8/25, 32%)	58 (58/141, 41.13%)	0.523	39 (39/93, 41.94%)	27 (27/73, 36.99%)	0.518
ESR, median (25th-75th), (mm/h)	8 (2, 12)	6 (2, 12)	0.464	8 (4.5, 12.5)	6 (2, 12)	0.094	7 (2, 12)	5 (2, 10)	0.084
CRP, median (25th-75th), (mg/l)	4.38 (2.83, 12.2)	4.27 (3.05, 8.2)	0.438	5.06 (2.69, 9.7)	4.29 (3.07, 8.62)	0.791	4.29 (2.97, 11.4)	4.44 (3.17, 7.43)	0.460
ASDAS-CRP, mean (SD)	2.95 (0.93)	2.8 (0.81)	0.351	3 (0.82)	2.8 (0.83)	0.224	2.83 (0.9)	2.82 (0.72)	0.946
ASDAS-ESR, median (25th-75th)	2.3 (2, 3.1)	2.4 (1.9, 3)	0.556	2.6 (2.2, 3.38)	2.3 (1.9, 3)	0.051	2.3 (1.9, 3)	2.4 (1.9, 3)	0.851
BASDAI, median (25th-75th)	4 (3.5, 6.9)	4.15 (3.4, 6.08)	0.416	5 (3.73, 7.13)	4 (3.4, 5.9)	0.036	4 (3.4, 6.35)	4.2 (3.5, 6.23)	0.736
BASFI, median (25th-75th)	2.7 (1.5, 4.4)	2.7 (1.2, 4.78)	0.672	3.2 (1.55, 5.03)	2.7 (1.2, 4.7)	0.479	27 (1.2, 5.05)	2.55 (1.5, 4.5)	0.914
BASMI, median (25th-75th)	2 (1.2, 2.8)	1.8 (1, 2.4)	0.220	1.8 (1.2, 2.4)	1.8 (1, 2.6)	0.827	2 (1.3, 2.9)	1.4 (0.8, 2.1)	<0.001

axSpA, axial spondyloarthritis; nr-axSpA, non-radiographic axial spondyloarthritis; r-axSpA, radiographic axial spondyloarthritis; BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; 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; IBD, Inflammatory bowel disease

tween patients with r-axSpA and nr-axSpA in specific anatomical regions. Higher rates of enthesitis were observed in patients with r-axSpA (72%, 56%, p=0.018). In the iliopubic ramus (Zone 1), enthesitis was detected in 24% of r-axSpA cases compared to 11% of nr-axSpA cases, demonstrating a statistically significant difference (p = 0.026). In the pubic symphysis (Zone 2), enthesitis was observed in 19% of nr-axSpA cases and 10% of r-axSpA cases, although this difference was not statistically significant (p = 0.108). In the ischiopubic ramus (Zone 3), enthesitis was significantly more frequent in r-axSpA cases (71%) compared to nr-axSpA cases (48%) (p = 0.001).

The analysis of the relationship between enthesitis in Zones 1, 2, and 3 and patients' demographic, clinical, and laboratory characteristics demonstrated significant findings. Patients with enthesitis in all zones were notably older, with the most pronounced difference observed in Zone 3. Additionally, male gender was significantly less prevalent among patients with Zone 2 enthesitis, and a higher BMI was found to be associated with Zone 2 enthesitis. Disease activity, as assessed by BASDAI, was notably higher in patients with Zone 2 enthesitis, while spinal mobility impairment, measured by BASMI, was significantly greater in those with Zone 3 enthesitis. No statistically significant associations were observed between enthesitis and smoking status, HLA-B27 positivity, or inflammatory markers, including ESR and CRP. These findings are detailed in Table II. Evaluation of fatigue using Question 1 of the BASDAI revealed no significant association with enthesitis at the zone 1 (p = 0.980), zone 2 (p = 0.260), or zone 3 (p = 0.460).

In our comparative analysis, significant differences

were observed in mobility and flexibility measures between patients with and without enthesitis in Zone 3, while no significant differences were found in Zones 1 and 2. Specifically, patients with Zone 3 enthesitis exhibited reduced lumbar lateral flexion (mean [SD]: 15.52 [4.55] cm vs. 18.14 [4.51] cm; $p < 0.001$), decreased cervical rotation (median [25th- 75th percentile]: 80° [70–90°] vs. 87.5° [80–90°]; $p < 0.001$), and lower Modified Schober test scores (median [25th- 75th percentile]: 21 cm [20–22 cm] vs. 21 cm [20.88–22.13 cm]; $p = 0.009$) compared to those without enthesitis. No significant differences were observed in occiput wall distance, intermalleolar distance, tragus wall distance, or chest expansion across any zones. These findings indicate that enthesitis in Zone 3 is associated with decreased spinal mobility and flexibility, as detailed in Table III.

HAQ scores did not differ significantly between patients with and without enthesitis across all zones: Zone 1 (0.25 [0–0.75] vs. 0.25 [0–0.5], $p = 0.935$), Zone 2 (0.19 [0.03–0.5] vs. 0.25 [0–0.5], $p = 0.973$), and Zone 3 (0.25 [0–0.62] vs. 0.25 [0–0.5], $p = 0.778$). Similarly, EQ-5D-3L scores showed no significant differences: Zone 1 (7 [6–9] vs. 8 [6–9], $p = 0.725$), Zone 2 (8 [6–9] vs. 8 [6–9], $p = 0.719$), and Zone 3 (8 [6–9] vs. 8 [6–9], $p = 0.896$).

The median symptom duration was significantly longer in patients with pelvic enthesitis (11 years [6–19]) compared to those without (5 years [2–8.5], $p < 0.001$). Similarly, the median time since diagnosis was 2 years [0–10] in patients with pelvic enthesitis, compared to 1 year [0–2] in those without ($p = 0.040$). These findings suggest that pelvic enthesitis is linked to a longer symptom duration and a more prolonged disease course.

DISCUSSION

In this prospective cross-sectional study, we evaluated 200 patients with axSpA, comprising 100 patients with nr-axSpA and 100 with r-axSpA. Radiographic pelvic enthesitis was observed in 64% of the cohort, with a higher prevalence in patients with r-axSpA. The ischiopubic ramus (Zone 3) was the most commonly affected region, with enthesitis present in 59.5% of cases. Notably, Zone 3 enthesitis was strongly associated with reduced spinal mobility and flexibility, as evidenced by decreases in lumbar lateral flexion, cervical rotation, Modified Schober test scores, and BASMI scores. Additionally, enthesitis in the pubic symphysis (Zone 2) was linked to higher disease activity, as measured by the BASDAI. Beyond these zone-specific observations, any pelvic enthesitis—defined as positivity in at least one of the three REI zones—was frequent (64%) and was associated with longer symptom duration and longer time since diagnosis, underscoring the overall clinical burden.

Enthesitis is a key pathological feature of axSpA,

TABLE III. Comparison of Mobility and Flexibility Measures by Enthesitis Status Across Zones

	Zone 1enthesitis (n=200)			Zone 2 enthesitis (n=200)			Zone 3 enthesitis (n=200)		
	Positive (n=35)	Negative (n=165)	P value	Positive (n=29)	Negative (n=171)	P value	Positive (n=119)	Negative (n=81)	P value
Lumbar lateral flexion (cm); mean (SD)	16.04 (5.38)	16.72(4.54)	0.445	17.34 (4.12)	16.47 (4.79)	0.365	15.52 (4.55)	18.14(4.51)	<0.001
Cervical rotation (°); median (25th, 75th percentile)	82.5 (75, 87.5)	85 (75, 90)	0.349	82.5 (72.5, 89.38)	85 (75, 90)	0.478	80 (70, 90)	87.5 (80, 90)	<0.001
Modified Schober test (cm); median (25th, 75th percentile)	21 (20, 22)	21 (20, 22)	0.068	21 (20.25, 22)	21 (20, 22)	0.333	21 (20, 22)	21 (20.88, 22.13)	0.009
Occiput wall distance (cm); median (25th, 75th percentile)	0 (0, 7.5)	0 (0, 3.75)	0.124	0 (0, 6)	0 (0, 4)	0.945	0 (0, 5.75)	0 (0, 2)	0.079
Intermalleolar distance (cm); median (25th, 75th percentile)	100 (92, 108)	103.5 (86, 116.75)	0.596	100 (87.5, 110.75)	104 (88, 117)	0.495	102 (88.5, 116)	104.5 (87.5, 116)	0.746
Tragus wall distance (cm); median (25th, 75th percentile)	13 (11.5, 17)	12.5 (11.5, 14.38)	0.503	12.75 (11.5, 14.75)	12.5 (11.5, 14.5)	0.970	12.5 (11.5, 15)	12.5 (11.38, 14)	0.329
Chest expansion (cm); median (25th, 75th percentile)	6 (5, 7)	6 (5, 7)	0.694	6 (6, 7)	6 (5, 7)	0.753	6 (5, 7)	6 (5, 7)	0.185

though its reported prevalence varies across studies. A meta-analysis by de Winter et al. found enthesitis in 35.4% of nr-axSpA and 28.8% of ankylosing spondylitis patients[18]. A Danish cohort study reported a prevalence of 39%, while a Brazilian study involving 1,505 SpA patients observed a higher rate of 54%[19,20]. Nadon et al. found enthesitis in 55.8% of patients at baseline, increasing to 71% over five years, whereas Mease et al. reported a lower prevalence of 25.4% in axSpA[4,21]. These discrepancies likely result from differences in assessment methods and enthesitis definitions. Our study, using AP pelvic radiography, found a higher prevalence (64%) in the pelvic region, underscoring the significant burden of enthesitis in axSpA. By focusing on specific pelvic sites, our findings enhance understanding of enthesitis distribution and its clinical implications, providing insights often overlooked in broader studies.

Enrique *et al.* were the first to define these pelvic zones in the literature, making a significant contribution to the evaluation of enthesitis[7]. As in their study, we used these zones to assess enthesitis. Their cohort included axSpA (39.6%), peripheral SpA (47.7%), and unclassified SpA (12.7%), reporting enthesitis in 42.3% of the iliopubic ramus (Zone 1), whereas our axSpA-exclusive study found a lower prevalence (17.5%). Pubic symphysis (Zone 2) findings were similar (17.1% vs. 14.5%). For the ischiopubic ramus (Zone 3), Enrique et al. reported 74.7% prevalence, compared to 59.5% in our study. This discrepancy may be attributed to the inclusion of peripheral SpA patients in their cohort, further highlighting the distinct entheseal involvement patterns between axial and peripheral SpA. Furthermore, while *Enrique et al.'s* study introduced the Radiographic Enthesis Index (REI) and demonstrated its diagnostic utility—particularly for SpA patients without sacroiliitis on standard imaging—it did not evaluate how pelvic enthesitis in these specific zones correlates with clinical measures such as disease activity or mobility. This distinction underscores the unique contribution of our study in addressing these critical clinical aspects.

In 2016, de Winter *et al.* conducted a meta-analysis and found no statistically significant difference in the prevalence of clinical enthesitis between nr-axSpA and AS[18]. More recently, Mease et al. reported a higher prevalence of clinical enthesitis in nr-axSpA compared to r-axSpA[4]. In contrast, our study demonstrated a higher frequency of radiographic pelvic enthesitis in patients with r-axSpA. This discrepancy may stem from the regional focus of our study and the specific use of anteroposterior pelvic radiography, which can influence both the detection and interpretation of enthesitis. Differences in methodologies, including imaging techniques and assessment criteria, may further explain these variations. While our study employed radiographic diagnosis, other investigations relied predominantly on clinical assessments rather than imaging-based methods. Additional research using more sensitive imaging modalities is necessary to better characterize enthesitis subtypes, but our findings nonetheless highlight the regional specificity of pelvic enthesitis, particularly in patients with r-axSpA.

In our study examining the relationship between HLA-B27 and pelvic enthesitis, we observed similar rates of HLA-B27 positivity in patients with and without enthesitis. This finding contrasts with the variability reported in previous studies. For example, de Winter *et al.* noted reduced HLA-B27 positivity among axSpA patients with peripheral involvement, although the difference was not statistically significant[22]. Similarly, Nadon *et al.* and Mathew *et al.* reported an association between the absence of HLA-B27 and peripheral enthesitis[19,21]. Conversely, some studies on peripheral spondyloarthritis have described a higher prevalence of enthesitis in HLA-B27 positive patients[23]. These divergent findings may reflect differences in the anatomical sites of enthesitis examined, as HLA-B27 associations could vary depending on the enthesis involved. Additionally, variations in patient populations, study designs, and the lack of subtype differentiation for HLA-B27 might contribute to these inconsistencies. Beyond these findings, the overall prevalence of HLA-B27 itself differs markedly by region, ranging from 26.2% to 91% in axial SpA populations, with lower rates reported in Japan and the Middle East (41–84%) compared to Western countries[24-26]. Consistent with our geographic setting, HLA-B27 positivity was identified in 56.4% of patients with radiographic axSpA and 28.4% of those with non-radiographic axSpA. Taken together, our results underscore the need for further research to clarify the variability in HLA-B27's role across diverse entheses and its broader implications for both axial and peripheral disease features. Our results highlight the need for further research to investigate the potential variability in HLA-B27's role across different entheses and its impact on axial and peripheral disease features.

The relationship between enthesitis and disease activity is a critical area of investigation in rheumatology, with previous studies consistently demonstrating a correlation between enthesitis and elevated disease activity[4,19,20,27-32]. Our study provides a unique perspective by examining site-specific associations, revealing that while iliopubic and ischiopubic enthesitis were not linked to disease activity, pubic symphysis enthesitis was significantly correlated with higher BASDAI scores. A review of the literature identified only one comparable study by Slouma *et al.*, which assessed heel enthesitis via ultrasound and reported increased disease activ-

ity[33]. By focusing on distinct pelvic enthesitis sites, our study expands current knowledge on the heterogeneity of enthesitis in axSpA.

The relationship between enthesitis and inflammatory markers, such as ESR and CRP, has been widely debated in the literature, with mixed findings. While one study has suggested a potential association, the majority have not demonstrated a significant correlation[4,19,20,27-30,34]. In our study, we did not observe any relationship between pelvic enthesitis and levels of ESR or CRP. This aligns with the findings of several previous studies that also reported no significant link between enthesitis and systemic inflammatory markers. The lack of a consistent association in the literature may be attributable to variations in study populations, the anatomical sites of enthesitis examined, and the diagnostic techniques employed. Given that our study focused on enthesitis detected using AP radiography, it is more likely to identify chronic changes, making its correlation with acute inflammatory parameters less probable.

In this study, we identified a significant correlation between ischiopubic enthesitis and BASMI, particularly with lumbar lateral flexion, cervical rotation, and the Modified Schober test. These findings highlight the biomechanical relevance of the ischiopubic region. Notably, the ischial tuberosity—which forms part of the ischiopubic region—serves as the primary origin for the hamstring muscles (semimembranosus, semitendinosus, and the long head of the biceps femoris). Additionally, portions of the adductor magnus and other adductor muscles also attach along the ischiopubic ramus. Together, these muscle groups are essential for both pelvic stabilization and hip movement. During activities such as lateral trunk flexion or forward bending, they must act in concert with the lumbar paraspinal and abdominal musculature to maintain optimal lumbopelvic mechanics. Inflammation or structural changes at the ischiopubic entheseal sites can disrupt these coordinated movements—particularly those requiring simultaneous engagement of the lumbar spine and hip joints. In comparing our findings with previous work, Mease et al. also reported reduced spinal mobility—especially in lumbar lateral flexion—among patients with enthesitis, whereas data from the Danish national cohort linked enthesitis to higher BASMI scores in axSpA[4,19]. In contrast, Zahiroğlu *et al.* observed no significant BASMI differences, likely due to their use of the SPARCC enthesitis index, which excludes pelvic enthesitis[30]. Overall, these results underscore the importance of comprehensive enthesitis assessments, particularly in the ischiopubic region, to better understand the relationship between enthesitis, spinal mobility, and overall disease burden in axSpA.

Current research differs from several established studies in the literature, as we observed no significant differences in functionality or general health status between patients with and without radiographic pelvic enthesitis[4,19,20,28,30,32]. This discrepancy may be attributed to our focused examination of specific enthesitis types in the pelvic region and evaluated only by AP pelvic radiography. Contrasting evidence in the literature highlights the complexity of this issue. For example, Rezvani *et al.*, using the Maastricht Ankylosing Spondylitis Enthesitis Score, found no correlation between enthesitis scores and quality of life[27]. Similarly, Kaya *et al.,* employing the Stoke Enthesitis Index, which includes pelvic and spinal assessments, reported no association with BASFI scores[29]. Hamdi *et al.* also observed no link between radiographic evaluations of enthesitis and the Ankylosing Spondylitis Quality of Life index, this findings that align with our results[31]. Additionally, Mease et al. emphasized the role of fibromyalgia as a potential confounding factor influencing general health assessments in studies of enthesitis[4]. These varying outcomes underscore the need for further research to clarify the complex interactions between different types of enthesitis and their potential effects on general health and functionality.

Here, we also note that this study has some limitations that affect its interpretation and generalizability. First, the cross-sectional design restricts our ability to establish causal relationships between pelvic enthesitis and disease progression in axSpA. Second, relying solely on anteroposterior pelvic radiography—though practical—may underestimate enthesitis prevalence by failing to detect subclinical or early-stage changes that MRI or ultrasonography could reveal. This may disproportionately affect detection of enthesitis in nr-axSpA, potentially exaggerating differences between nr-axSpA and r-axSpA. In addition, because plain radiography predominantly depicts chronic structural change, degenerative features may mimic or coexist with entheseal abnormalities. Age and body mass index are known to influence spinal mobility and may contribute to the observed associations; these potential effects cannot be excluded on the basis of radiography alone and should be considered when interpreting the findings. Third, our exclusive focus on pelvic enthesitis limits applicability to other anatomical regions, and the single-center design introduces possible selection bias, as patients referred to tertiary centers often have more severe or complex disease profiles. Additionally, all pelvic radiographs were interpreted by a single, highly experienced rheumatologist with over fifteen years of musculoskeletal imaging expertise. While this approach promotes consistency in diagnosis, it also restricts external validation of our findings, as radiographic interpretations may vary in real-world settings or among less experienced

readers. Independent multi-reader validation was not performed in this study; external reproducibility should therefore be interpreted with appropriate caution. Future studies using multiple, blinded assessors would help confirm the reproducibility and generalizability of these results. Nevertheless, despite these limitations, the study's strengths are notable. The use of multiple validated indices for assessing disease activity, mobility, and function—such as ASDAS-CRP, BASDAI, BASFI, and BASMI—enhances the reliability and robustness of the findings. Moreover, our focused examination of specific entheseal sites in the pelvic region provides an in-depth analysis of the relationship between enthesitis and key disease metrics, offering valuable data not commonly explored in broader studies.

CONCLUSIONS

Our study demonstrates the high prevalence of radiographic pelvic enthesitis in axSpA, with notable differences between radiographic and non-radiographic subtypes. The findings highlight the importance of assessing specific entheseal sites, particularly in the pelvis, to better understand their relationship with disease activity, spinal mobility, and function. While ischiopubic enthesitis was associated with reduced mobility and pubic symphysis enthesitis with higher disease activity, no correlation was found with systemic inflammatory markers or overall health status. These results emphasize the complexity of enthesitis in axSpA. Future longitudinal studies with advanced imaging and comprehensive assessments are needed to clarify its role in disease progression and guide personalized treatment strategies.

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