

Dactylitis Is Associated With More Severe Axial Joint Damage and Higher Disease Activity in Axial Psoriatic Arthritis

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ABSTRACT. *Objective.* To investigate the association of dactylitis with disease activity and the severity of damage detected by radiography in patients with axial psoriatic arthritis (axPsA).

Methods. Patients with axPsA who met the Classification Criteria for Psoriatic Arthritis were recruited. Clinical data, radiographic changes, and disease activity in patients with axPsA with or without dactylitis were compared using *t* tests, Mann-Whitney *U* tests, or Kruskal-Wallis tests for continuous variables. Chi-square or Fisher exact tests were used for categorical variables, and logistic regression analysis was performed to evaluate the association between dactylitis and damage detected by radiography.

Results. A total of 186 patients with axPsA were analyzed and dichotomized according to the presence or absence of dactylitis. Patients with dactylitis, as compared to those without dactylitis, had higher C-reactive protein ($P = 0.004$), erythrocyte sedimentation rate ($P = 0.006$), neutrophil-to-lymphocyte ratio ($P = 0.04$), and platelet-to-lymphocyte ratio ($P = 0.02$). In addition, patients with dactylitic axPsA, as compared to patients with nondactylitic axPsA, had higher tender joint counts, swollen joint counts, Disease Activity Index for Psoriatic Arthritis (DAPSA) scores, and Health Assessment Questionnaire scores ($P < 0.001$). Patients with axPsA who had dactylitis, as compared to those who did not, also had higher values for the Disease Activity Score in 28 joints, Ankylosing Spondylitis Disease Activity Score, Bath Ankylosing Spondylitis Functional Index, and Bath Ankylosing Spondylitis Disease Activity Index ($P < 0.05$), while fewer of these patients met the criteria for minimal disease activity and low disease activity ($P < 0.05$). Consistently, they had more severe damage as detected by radiography ($P < 0.05$), higher sacroiliac scores (odds ratio [OR] 2.08, 95% CI 1.14-3.79; $P = 0.02$), and a more significant reduction in bone mass density (OR 2.42, 95% CI 1.34-4.37; $P = 0.003$). No statistical differences were observed regarding HLA-B27 and the Leeds Enthesitis Index between these 2 groups of patients. Notably, only half of the patients with dactylitic axPsA had inflammatory back pain.

Conclusion. Our study demonstrated that patients with axPsA who had dactylitis had higher disease activity and more severe joint damage compared to those without dactylitis. Careful examination and proper management of axial involvement are recommended.

Key Indexing Terms: dactylitis, axial, disease activity index, psoriatic arthritis, radiographic damage

Psoriatic arthritis (PsA), an inflammatory disease associated with psoriasis (PsO), may have skeletal involvement at both peripheral and axial sites.¹ Clinical manifestations may vary at different stages of the disease. Articular and extraarticular manifestations may present in PsA, including axial or peripheral joint disease, nail lesions, enthesitis, and dactylitis.² Previous studies have shown that axial involvement occurs in over 40% of patients with PsA who have severe skin lesions and high disease activity.^{3,4}

Dactylitis is a characteristic feature of PsA and manifests as diffuse swelling of the fingers or toes. Its incidence in PsA is

about 33% to 45%.^{5,6} Dactylitis is associated with severe joint destruction as evidenced by prominent synovitis detected by ultrasound, a greater degree of structural damage seen on digital radiographs (DRs), higher swollen joint counts (SJs), higher levels of C-reactive protein (CRP), and poorer functional status.^{7,8} However, very few studies have been conducted to elucidate the differences in clinical characteristics between patients with axial psoriatic arthritis (axPsA) who have dactylitis and those without. As such, the relationship between dactylitis and axial joint damage remains elusive.

We aimed to compare demographic and clinical characteristics to unveil the potential differences in characteristic features and disease activity between patients with axPsA who have dactylitis and those without, and to explore the correlation between dactylitis and the severity of axial joint damage.

METHODS

Study design. A total of 313 patients who fully met the Classification Criteria for Psoriatic Arthritis for PsA⁹ were enrolled in this prospective, cross-sectional, observational study. All patients were newly diagnosed, and the study was conducted at the First Affiliated Hospital of Zhengzhou

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University, China, between January 2019 and October 2021. Patients with other autoimmune rheumatic diseases, infections, malignancies, and serious concomitant diseases were excluded. Among the included 313 patients, 186 (59.4%) were diagnosed with axPsA based on the highest sacroiliitis grade scores and/or the presence of syndesmophytes on all DRs, as follows:

1. Radiographic criteria according to the modified New York (mNY) criteria¹⁰: at least bilateral grade 2 or unilateral grade 3 or 4 sacroiliitis.

2. Magnetic resonance imaging (MRI) abnormalities¹¹: bone marrow edema on short-tau inversion recovery (STIR) images or structural changes, including bone erosion, fat deposition, osteophytes, or ankylosis on T1-weighted images.

3. At least 1 marginal or paramarginal syndesmophyte of the cervical and/or lumbar spine.³

Patients with axPsA were further dichotomized by the presence or absence of dactylitis: (1) axPsA with dactylitis (ie, dactylitic axPsA); and (2) axPsA without dactylitis (ie, nondactylitic axPsA). The dichotomy was used to record dactylitis of each digit with or without tenderness. Basic demographic data, clinical features, and radiographic patterns were collected.

Laboratory and radiographic results evaluation. Dactylitis was defined as diffuse swelling of the digits. Both acute (with painful inflammatory changes) and chronic (swollen but painless) dactylitis were included in this study.⁵ Radiographic examination of the hands, feet, spine, and sacroiliac joints (SIJs) was performed at baseline. MRI was performed only when axial involvement was suspected but could not be confirmed by DR.

Routine laboratory tests included complete blood count, CRP, erythrocyte sedimentation rate (ESR), and HLA-B genotyping. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were also calculated. Radiographic abnormalities in the axial joints (ie, pelvis and cervical, thoracic, and lumbar spine) and peripheral joints (ie, hands and feet) were evaluated independently by 2 radiologists with expertise in the musculoskeletal system. The severity of sacroiliitis was scored using the mNY criteria, ranging from 0 to 4.¹⁰ In SIJs or the spine, inflammatory changes such as bone marrow edema on STIR images, or structural changes such as bone erosion, fat deposition, osteophytes, or ankylosis on T1-weighted images, were defined as MRI abnormalities.¹¹ Spinal osteophytes, degeneration in intervertebral discs or endplates, and inflammatory syndesmophytes were recorded. Radiographic findings were interpreted independently by 3 experienced rheumatologists. A previous study confirmed the reliability of the assessment methods for axial involvement.¹² If possible axial involvement could not be confirmed, we would perform MRI examination. Bone mass density (BMD) was measured to confirm the presence of osteoporosis or osteopenia.¹³

Clinical examination and assessments. Clinical manifestations in patients with axPsA, including inflammatory joint disease, dactylitis, enthesitis, and uveitis, were collected and assessed by an experienced rheumatologist.

At the time of enrollment, current spinal or buttock pain, SJC in 66 joints, and tender joint counts (TJCs) in 68 joints were also recorded. The patients completed the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)¹⁴ and the Bath Ankylosing Spondylitis Functional Index (BASFI).¹⁵ Axial and peripheral arthritis disease activity and function were evaluated with the Ankylosing Spondylitis Disease Activity Score (ASDAS) using CRP (ASDAS-CRP) and ESR (ASDAS-ESR),¹⁶ as well as the Disease Activity Score in 28 joints (DAS28) using CRP (DAS28-CRP) and ESR (DAS28-ESR).¹⁷ In addition, the Psoriasis Area and Severity Index (PASI) was used to represent the severity of PsO,¹⁸ and the Leeds Enthesitis Index (LEI) was used to measure the level of enthesitis.¹⁹ Pain and patient global assessment (PtGA) of disease activity were rated on a 100-mm visual analog scale (VAS). The Dermatology Life Quality Index (DLQI) and the Health Assessment Questionnaire (HAQ) were used to evaluate quality of life (QOL) and physical function. Disease Activity Index for Psoriatic Arthritis (DAPSA) assessments were done after completing data collection,

with scores of 4 or lower designated as remission (REM) and scores ranging from > 4 to 14 as low disease activity (LDA).^{20,21} Minimal disease activity (MDA) was defined as the achievement of at least 5 of the following 7 clinical outcomes: TJC \leq 1, SJC \leq 1, PASI \leq 1, pain VAS \leq 15, PtGA VAS \leq 20, HAQ score \leq 0.5, and tender enthesal points \leq 1, with a maximum value of 13.²²

Statistical analyses. To compare the differences between patients with axPsA who have dactylitis and those without, *t* tests, Mann-Whitney *U* tests, and Kruskal-Wallis tests were used for descriptive analysis. Pearson chi-square, correction for continuity, or Fisher exact tests were used for categorical variables. Odds ratios (OR) with 95% CIs were calculated by logistic regression analysis to evaluate the risk factors and correlations between 2 groups. *P* \leq 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp).

Ethics approval and consent to participate. The Ethics Committee of the First Affiliated Hospital of Zhengzhou University approved this study in accordance with the Declaration of Helsinki (2019-KY-199). All patients provided written informed consent.

RESULTS

Among 313 patients with PsA, 131 (41.9%) had dactylitis, 186 (59.4%) had axial involvement, and 69 (22.0%) had both dactylitis and sacroiliitis.

Sociodemographic and laboratory characteristics. A total of 186 patients with axPsA were enrolled in this cross-sectional study, including 69 (37.1%) patients with dactylitic axPsA and 117 (62.9%) patients with nondactylitic axPsA. Compared to patients with nondactylitic axPsA, patients with dactylitic axPsA had similar ages of onset of arthritis (mean 37.71, SD 12.02 yrs vs mean 35.09, SD 13.55 yrs) and longer duration of PsO (*P* = 0.002). No significant difference was found in the disease course of arthritis; however, patients with dactylitis had higher values (mean 5.24, SD 6.34 yrs vs mean 3.95, SD 5.61 years; *P* = 0.06). Other sociodemographic data, including percentage of current PsO and family history of PsO, were similar (Table 1).

Higher levels of CRP (median 45.06 [IQR 18.52-89.80] mg/L vs 26.68 [IQR 10.81-66.65] mg/L; *P* = 0.004) and ESR (median 70.00 [IQR 26.50-95.00] mm/h vs 43.00 [IQR 10.50-81.50] mm/h; *P* = 0.006) were observed in patients with dactylitis. The median NLR and median PLR were also higher in patients with dactylitic axPsA (NLR: *P* = 0.04; PLR: *P* = 0.02; Table 1).

Clinical examination and evaluation. Patients with dactylitic axPsA had a higher proportion of polyarthritis (*P* < 0.001) and significantly greater medians of TJC (median 7.0, IQR 5.0-9.0 vs median 3.0, IQR 1.0-5.5; *P* < 0.001) and SJC (median 1.0, IQR 0.0-2.0 vs median 4.0, IQR 3.0-5.0; *P* < 0.001). On the contrary, oligoarthritis was more common in patients with nondactylitic axPsA (113/117, 96.6%; *P* < 0.001; Table 1). After excluding the joints affected by dactylitis, the TJCs and SJC were still higher in patients with dactylitis (total TJCs: 404 joints in 69 patients with dactylitis vs 402 joints in 117 patients without dactylitis, *P* < 0.001; total SJC: 183 joints in 69 patients with dactylitis vs 148 joints in 117 patients without dactylitis, *P* < 0.001).

No significant difference was detected in the prevalence of uveitis and enthesitis between patients with dactylitic axPsA

Table 1. Sociodemographic, laboratory, and clinical evaluation of patients with nondactylitic AxPsA and dactylitic AxPsA (n = 186).

	Nondactylitic AxPsA	Dactylitic AxPsA	P
Patients, n (%)	117 (62.9)	69 (37.1)	–
Age at arthritis onset, yrs	35.09 (13.55)	37.71 (12.02)	0.14
Duration of arthritis, yrs	3.95 (5.61)	5.24 (6.34)	0.06
Age at arthritis diagnosis, yrs	39.03 (13.49)	42.96 (11.53)	0.03
Age at psoriasis onset, yrs	31.98 (12.60)	32.29 (10.72)	0.65
Duration of psoriasis, yrs	7.06 (7.43)	10.67 (8.30)	0.002
Male, n (%)	73 (62.4)	41 (59.4)	0.69
Current psoriasis, n (%)	108 (92.3)	58 (84.1)	0.08
Family history of psoriasis, n (%)	53 (45.3)	30 (43.5)	0.81
Laboratory markers			
NLR	2.42 (1.91-3.44)	2.80 (2.11-4.61)	0.04
PLR	163.57 (128.33-240.65)	209.21 (145.00-284.36)	0.02
CRP, mg/L	26.68 (10.81-66.65)	45.06 (18.52-89.80)	0.004
ESR, mm/hour	43.00 (10.50-81.50)	70.00 (26.50-95.00)	0.006
Clinical examination and evaluation			
TJC68	3.0 (1.0-5.5)	7.0 (5.0-9.0)	< 0.001
SJC66	1.0 (0.0-2.0)	4.0 (3.0-5.0)	< 0.001
TJC68 (excluding dactylitis)	3.0 (1.0-5.5)	5.0 (3.0-8.0)	< 0.001
SJC66 (excluding dactylitis)	1.0 (0.0-2.0)	2.0 (3.0-4.0)	< 0.001
DAS28-CRP	3.51 (2.51-4.15)	4.43 (4.01-4.79)	< 0.001
DAS28-ESR	3.81 (2.86-4.71)	4.87 (4.17-5.52)	< 0.001
Uveitis, n (%)	5 (4.3)	3 (4.3)	> 0.99
Clinical enthesitis, n (%)	62 (53.0)	37 (53.6)	0.93
LEI	1.0 (0.0-2.0)	1.0 (0.0-2.0)	0.81
PASI	2.2 (1.2-3.3)	2.6 (0.6-4.3)	0.28
DLQI	4.0 (2.0-7.0)	5.0 (2.0-7.0)	0.93
HAQ	0.5 (0.1-0.75)	0.75 (0.5-1.0)	< 0.001
Disease phenotype			
Oligoarthritis ^a , n (%)	113 (96.6)	40 (58.0)	< 0.001
Disease activity–composite outcomes			
DAPSA score	16.09 (10.56-24.22)	26.10 (22.08-31.08)	< 0.001
DAPSA-LDA, n (%)	47 (40.2)	1 (1.4)	< 0.001
MDA, n (%)	15 (12.8)	2 (2.9)	0.03

Values are expressed as mean (SD) or median (IQR) unless indicated otherwise. ^a Oligoarthritis defined by SJC66 < 5. AxPsA: axial psoriatic arthritis; CRP: C-reactive protein; DAPSA: Disease Activity Index for Psoriatic Arthritis; DAS28-CRP: Disease Activity Score in 28 joints using C-reactive protein; DAS28-ESR: Disease Activity Score in 28 joints using erythrocyte sedimentation rate; DLQI: Dermatology Life Quality Index; ESR: erythrocyte sedimentation rate; LEI: Leeds Enthesitis Index; HAQ: Health Assessment Questionnaire; LDA: low disease activity; MDA: minimal disease activity; NLR: neutrophil-to-lymphocyte ratio; PASI: Psoriasis Area and Severity Index; PLR: platelet-to-lymphocyte ratio; SJC66: swollen joint count in 66 joints; TJC: tender joint count in 68 joints.

and patients with nondactylitic axPsA; in addition, the LEI was similar among patient groups ($P = 0.81$). However, the severity of peripheral arthritis measured using the DAS28, disease activity assessed using the DAPSA, and physical function assessed using the HAQ were greater in patients with dactylitic axPsA than in those with nondactylitic axPsA (DAS28-CRP: median 4.43 [IQR 4.01-4.79] vs 3.51 [IQR 2.51-4.15], $P < 0.001$; DAPSA: median 26.10 [IQR 22.08-31.08] vs 16.09 [IQR 10.56-24.22], $P < 0.001$; HAQ: median 0.75 [IQR 0.5-1.0] vs 0.5 [IQR 0.1-0.75], $P < 0.001$). The same was true for patients' self-rated PtGA (median 45 [IQR 40-60] vs 50 [IQR 40-60]; $P = 0.04$). Of note, only 1 and 2 patients with dactylitic axPsA were assessed as LDA and MDA, respectively, as measured by the DAPSA

(LDA: $P < 0.001$; MDA: $P = 0.03$), and none were classified as REM. Results from the PASI, to measure skin lesions; the DLQI; and the pain VAS did not reveal significant differences between the 2 groups (PASI: $P = 0.28$; DLQI: $P = 0.93$; pain VAS: $P = 0.10$; Table 1).

Axial symptoms and metrology. Inflammatory axial symptoms were present in 69 out of 117 (59.0%) patients with nondactylitic axPsA and 35 out of 69 (50.7%) patients with dactylitic axPsA (OR 0.72, 95% CI 0.39-1.30; $P = 0.27$; Table 2). Spine and buttock pain were the most common initial symptoms, and a slight difference was found between patients with dactylitis and those without (34.8% vs 54.7%, $P < 0.001$; Figure). No significant difference was detected between the 2 groups with

Table 2. Axial-associated examination indicators and radiographic characteristics in patients with nondactylitic AxPsA and dactylitic AxPsA.

	Nondactylitic AxPsA, n = 117	Dactylitic AxPsA, n = 69	P	OR (95% CI)
HLA-B27 presence, n (%)	59 (50.4)	30 (43.5)	0.36	0.76 (0.42-1.38)
Current axial symptoms, n (%)	69 (59.0)	35 (50.7)	0.27	0.72 (0.39-1.30)
BMD, n (%)			0.003	2.42 (1.34-4.37)**
Osteopenia	26 (22.2)	28 (40.6)		
Osteoporosis	11 (9.4)	10 (14.5)		
Clinical examination indices				
ASDAS-CRP, median (IQR)	3.1 (2.4-3.8)	3.4 (3.0-4.1)	0.004	
ASDAS-ESR, median (IQR)	2.9 (1.9-4.0)	3.6 (2.6-4.3)	0.004	
BASFI, mean (SD)	3.4 (0.73)	3.7 (0.69)	0.008	
BASDAI, median (IQR)	3.6 (3.0-4.2)	4.2 (3.4-4.6)	0.001	
Radiographic evaluation				
Bilateral sacroiliitis pattern	94 (80.3)	54 (78.3)	0.73	0.88 (0.42-1.83)
Sacroiliac joint morphology, n (%)			0.02	2.08 (1.14-3.79)*
Grade 1	11 (9.4)	5 (7.2)		
Grade 2	80 (68.4)	35 (50.7)		
Grade 3	20 (17.1)	27 (39.1)		
Grade 4	6 (5.1)	2 (2.9)		
Vertebral morphology, n (%)			0.46	1.25 (0.69-2.25)
Nonbridging syndesmophyte	41 (35.0)	30 (43.5)		
Bridging syndesmophyte	7 (6.0)	3 (4.3)		

Values in bold are statistically significant. * $P \leq 0.05$. ** $P \leq 0.01$. ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score using C-reactive protein; ASDAS-ESR: Ankylosing Spondylitis Disease Activity Score using erythrocyte sedimentation rate; axPsA: axial psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BMD: bone mass density; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; OR: odds ratio.

regard to HLA-B27 allele (30/69, 43.5% vs 59/117, 50.4%; $P = 0.36$; Table 2).

Compared to patients with nondactylitic axPsA, axial metrology assessed with the ASDAS, BASFI, and BASDAI was

much higher in patients with dactylitic axPsA (ASDAS-CRP: median 3.4 [IQR 3.0-4.1] vs 3.1 [IQR 2.4-3.8]; $P = 0.04$; BASFI: mean 3.7 [SD 0.69] vs 3.4 [SD 0.73]; $P = 0.008$; BASDAI: median 4.2 [IQR 3.4-4.6] vs 3.6, [IQR 3.0-4.2];

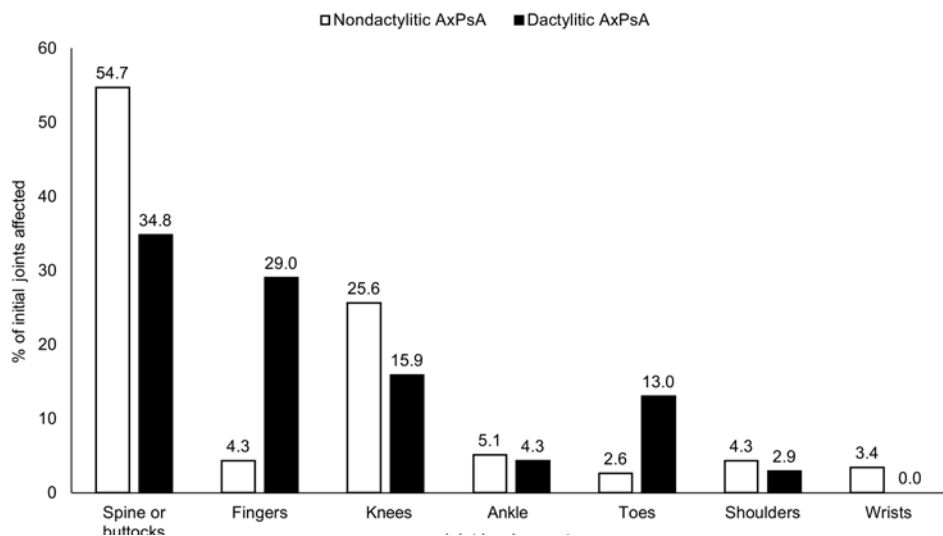


Figure 1. Comparison of initial symptoms in patients with dactylitic axPsA and those with nondactylitic axPsA. There were statistical differences in initial symptoms caused by joint involvement ($P < 0.001$). Pain in the back or buttocks was the most common initial symptom, but only in 34.8% of patients with dactylitic axPsA, which was less frequent than in patients without dactylitis. Fingers (29.0%) and knees (25.6%) were also commonly afflicted sites based on the presence or absence of dactylitis. axPsA: axial psoriatic arthritis.

$P = 0.001$). Notably, patients with dactylitic axPsA had more significant decreases in BMD. Over half of the patients with dactylitis (38/69, 55.1%) had a reduction in BMD. The incidence of osteopenia was 28 out of 69 (40.6%), and that of osteoporosis was 10 out of 69 (14.5%; OR 2.42, 95% CI 1.34 to 4.37; $P = 0.003$; Table 2).

Axial radiographic comparison. Bilateral sacroiliitis was the predominant pattern, which presented in 54 out of 69 (78.3%) patients with dactylitic axPsA and 94 out of 117 (80.3%) patients with nondactylitic axPsA, with no statistical differences ($P = 0.73$). Similarly, no significant difference was detected between these 2 groups in spinal radiography assessments, especially regarding vertebral syndesmophytes (OR 1.25, 95% CI 0.69-2.25; $P = 0.46$). Nevertheless, the sacroiliitis grades seemed higher in patients with dactylitis than in those without (OR 2.08, 95% CI 1.14-3.79; $P = 0.02$; Table 2).

Characteristics of dactylitis. Dactylitis was asymmetrically distributed and was present in 58 out of 69 (84.1%) patients with dactylitic axPsA. The commonly afflicted digits included hands (22/69, 31.9%), feet (38/69, 55.1%), or both (9/69, 13.0%). A total of 111 digits were affected by dactylitis; among them, 22 (19.8%) did not have tenderness and 89 (80.2%) did have tenderness. In addition, 36 out of 69 (52.2%) patients with dactylitis had multiple digit involvement. The presence of dactylitis in toes (69/111, 62.2%) was dominant; the fourth toe (27/111, 24.3%) was most frequently involved, whereas dactylitis appeared most frequently in the second finger (17/111, 15.3%).

Peripheral articular characteristics. Radiological examination was performed to detect structural damage in small joints in the hands and feet. Joint destruction was more common in the hands (41/69, 59.4%) than in the feet (27/69, 39.1%) in patients with dactylitis, although dactylitis was less frequent in the hands (31/69, 44.9%). In addition, patients with dactylitic axPsA seemed to have an increased risk of severe structural damage in the digital joints, including interphalangeal, metatarsophalangeal, and wrist joints (OR 2.12, 95% CI 1.05-4.29; $P = 0.03$). However, excluding the hands and feet, other peripheral articular symptoms were not detected statistical significance (Table 3).

DISCUSSION

Dactylitis and axial involvement are the hallmarks of PsA. Previous studies have demonstrated that PsA patients with dactylitis or axial involvement had significantly higher disease activity.^{23,24} To the best of our knowledge, this is the first study to have demonstrated the differences in clinical characteristics, disease activity, and damage detected by radiography of both axial and peripheral arthritis in patients with axPsA based on the presence or absence of dactylitis. Our study confirms that patients with axPsA who have dactylitis have a more severe disease burden than those without dactylitis. They tend to have higher TJC_s, SJC_s, CRP levels, and ESRs, consistent with a recent report.⁷ Our study shows that the incidence of dactylitis was lower in patients with PsA who have axial involvements than in those who do not. Consistent with a previous report,²⁵ the

number of swollen small joints increased and the risk of axial involvement decreased with disease progression. The mechanisms responsible for this dissociation are not fully understood.

Of note, we found that patients with dactylitis had a higher degree of damage detected by radiography compared to those without dactylitis, adding more evidence to previous observations that patients with PsA who have dactylitis have a poor prognosis.^{26,27} In contrast to previous studies, further evaluation of disease activity in peripheral arthritis was performed in our study. At the same time, clinical manifestations and imaging features in axial joints were carefully assessed. We demonstrated that increased DAS28 was associated with peripheral joint activity. In addition, these scores correlated with more severe structural damage on radiographic examination of SIJs in patients with dactylitic axPsA compared with patients with nondactylitic axPsA. Previous studies have shown that elevated CRP levels and ESRs are poor predictors of radiographic outcomes.^{25,28} Based on the findings from other groups, we posit that polyarticular disease at onset (SJC ≥ 5) is strongly associated with erosive lesions.²⁹ In addition, pain- and function-related subjective disease scores were also higher, including the ASDAS, BASFI, and BASDAI for axial metrology and measures of disease activity. These results lend novel insight into the formation of axial involvement in patients with PsA who have dactylitis. Somewhat surprisingly, only about half of the patients with dactylitic axPsA (35/69, 50.7%) had inflammatory axial symptoms. Further, spine and buttock pain was the first symptom in only 34.8% of patients with dactylitic axPsA, implying a disassociation of radiographic results and clinical manifestations. We cannot exclude the possibility that some patients took over-the-counter medicines to relieve pain before they visited our clinic. As no guidelines for standard imaging screening of PsA are currently available, axial involvement may be overlooked in patients with PsA who have dactylitis, particularly when subtle; this could lead to delayed diagnosis of axial arthritis and more aggressive disease.³⁰ It is imperative to develop sensitive screening tools for accurate and prompt diagnosis of early joint damage.

Two other indicators, PLR and NLR, were calculated in our study, and the results showed that both were higher in patients with dactylitic axPsA. These indicators represent the magnitude of inflammatory response and immune function, and they have better reliability and consistency than CRP and ESR.³¹ A previous report showed that elevated PLR and NLR are correlated with the severity of PsO and PsA.³² The results from the evaluations of the DAPSA, DAPSA-LDA, MDA, and HAQ suggest that patients with dactylitic axPsA have more severe disease activity and worse QOL, although statistical differences in PASI and DLQI results were not detected. We postulate that a higher proportion of patients with dactylitic PsA are less likely to have currently existing skin lesions; instead, they may have a family history of PsO. In some cases, dactylitis is the only initial manifestation, and skin disease may appear many years after diagnosis.⁶ In addition, previous studies have demonstrated that elevated inflammatory markers and higher disease activity contribute to the destruction of joints,^{27,33} which may

Table 3. Radiological damage in hands and feet and peripheral articular symptoms characteristics in nondactylitic vs dactylitic AxPsA.

	Nondactylitic AxPsA, n = 117	Dactylitic AxPsA, n = 69	P	OR (95% CI)
Radiological damage				
MCP joints	15 (12.8)	23 (33.3)	0.001	3.40 (1.63-7.11)***
PIP joints	11 (9.4)	20 (29.0)	0.001	3.93 (1.75-8.84)***
DIP joints	12 (10.3)	21 (30.4)	0.001	3.83 (1.74-8.41)***
Wrist	20 (17.1)	21 (30.4)	0.03	2.12 (1.05-4.29)*
MTP joints	17 (14.5)	19 (27.5)	0.03	2.24 (1.07-4.67)*
First IP joints	10 (8.5)	17 (24.6)	0.003	3.50 (1.50-8.17)**
Inflammatory peripheral articular symptoms				
Shoulder	35 (29.9)	22 (31.9)	0.78	1.10 (0.58-2.09)
Elbow	15 (12.8)	10 (14.5)	0.75	1.15 (0.49-2.73)
Knee	62 (53.0)	39 (56.5)	0.64	1.15 (0.63-2.10)
Ankle	32 (27.4)	20 (29.0)	0.81	1.08 (0.56-2.10)
Temporomandibular joints	2 (1.7)	2 (2.9)	0.63	1.72 (0.24-12.47)
Sternoclavicular joints	6 (5.1)	3 (4.3)	> 0.99	0.84 (0.20-3.48)

Values are expressed as n (%). * $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.001$. AxPsA: axial psoriatic arthritis; DIP: distal interphalangeal; IP: interphalangeal; MCP: metacarpophalangeal; MTP: metatarsophalangeal; OR: odds ratio; PIP: proximal interphalangeal.

partly explain the more severe damage, as detected by radiography, seen in patients with dactylitis.

Interestingly, patients with nondactylitic axPsA were younger and had shorter durations of PsO; however, the duration of arthritis was longer in patients with dactylitic axPsA. This finding is inconsistent with a previous report that found that patients with PsA who have dactylitis have a shorter disease duration and an earlier diagnosis.⁷ One explanation for joint damage in patients with dactylitis is that increased ESR is associated with an increased risk of developing axial disease at an early stage of PsA,²⁵ and joint damage is a slowly progressive process. Moreover, prolonged PsO may affect the pace of articular destruction through a yet unknown mechanism. Clinical variables for spinal involvement in patients with PsA, such as prolonged disease course, may also affect joint function.³⁴ Taking these factors into consideration, we postulate that a more significant decrease in BMD in patients with dactylitic axPsA may result from a longer duration of articular involvement and more severe joint destruction. However, no significant difference was found between these 2 groups of patients after morphological examination of the whole spine. Similarly, no difference was detected in enthesitis as assessed by the LEI, in accordance with the results of ultrasound-verified pathology assessments in another study.³⁵

Moreover, our study did not reveal significant differences in HLA-B27 alleles and other peripheral manifestations. In contrast, a higher frequency of the HLA-B27:05:02 allele has proven to be associated with dactylitis in another study.³⁶ Unfortunately, we do not routinely perform sequencing of this allele owing to many issues. The specific features of dactylitis were evaluated as well, in accordance with previous studies.^{7,26} However, most patients were only examined by radiograph, and a more precise procedure, such as ultrasound, was not performed in order to detect dactylitis in a large majority of patients.

Further, not all other peripheral joints were subjected to radiologic examination because of the cost. Selective examination of the most afflicted joints may have caused incomplete collection of data from asymptomatic joints and, therefore, selection bias. Assessment of health status, such as through use of the Psoriatic Arthritis Disease Activity Score, may help us obtain a more specific activity score, but this is not performed routinely in our hospital owing to several issues.

The treat-to-target strategy, a common strategy used for other types of autoimmune rheumatic diseases, can also be applied to PsA (eg, REM or LDA). In our study, very few patients with dactylitis met LDA and MDA criteria, and none of them could be defined as REM. Given the heterogeneity and complexity of PsA, each patient may have different domains of the clinical spectrum, such as axial arthritis, peripheral arthritis, and dactylitis, and the levels of disease activity may vary across different domains. To date, limited treatment recommendations have been proposed based on previous observations about complicated disease manifestations. Very few of them have been compared regarding the across-domain effect in a head-to-head study, although some biosimilars show promising potential in this respect.³⁷ The decision-making process for individualized therapeutic regimens poses a tremendous challenge for clinicians with regard to the assessment of the treatment outcomes for patients with dactylitic axPsA and other types of PsA. We speculate that it may be easier for patients without dactylitis to achieve sustained REM or very low disease activity. Clinical trials are necessary to determine differences in prognosis and to find the drugs that are effective for patients with dactylitic axPsA as well as patients with other types of PsA. Early diagnosis, prompt treatment, regular evaluation, and needs-based adjustments of treatment may help achieve maximal effects, including optimal functional status, improved QOL, and minimal structural damage.

We are confident about the reliability of our study, as it is a collaborative effort from experienced rheumatologists and radiologists to determine subtle differences in disease activity and axial involvement in patients with dactylitic axPsA. In addition, all patients had complete clinical and radiological data, in particular, quantitative radiographic scores and morphological analyses. One of the disadvantages in a cross-sectional study is that patients may be at different stages of axPsA, although all of them were already diagnosed. A prospective, multicenter, longitudinal study to monitor axial progression with dactylitis, the efficacy of treatment, and prognosis is warranted. More importantly, great endeavors are needed to establish standardized assessment tools for axPsA to facilitate accurate identification and effective management of axPsA.

In conclusion, our study was the first to demonstrate that patients with dactylitic axPsA have higher disease activity, as evidenced by higher CRP levels, ESRs, PLRs, and NLRs, as well as more significant structural damage. The assessments of axial involvement—in particular, the function-related disease index and imaging of SIJs—show that the disease is more severe in patients with dactylitis. Therefore, we recommend that imaging screening of axial joints be performed in all patients to improve prognosis, even when there are no axial symptoms.

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REFERENCES

1. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. *Lancet* 2018;391:2273-84.
2. FitzGerald O, Ogdie A, Chandran V, et al. Psoriatic arthritis. *Nat Rev Dis Primers* 2021;7:59.
3. Jadon DR, Sengupta R, Nightingale A, et al. Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis. *Ann Rheum Dis* 2017;76:701-7.
4. Helliwell PS. Axial disease in psoriatic arthritis. *Rheumatology* 2020;59:1193-5.
5. Kaeley GS, Eder L, Aydin SZ, Gutierrez M, Bakewell C. Dactylitis: a hallmark of psoriatic arthritis. *Semin Arthritis Rheum* 2018; 48:263-73.
6. McGonagle D, Tan AL, Watad A, Helliwell P. Pathophysiology, assessment and treatment of psoriatic dactylitis. *Nat Rev Rheumatol* 2019;15:113-22.
7. Dubash S, Alabas OA, Michelena X, et al. Dactylitis is an indicator of a more severe phenotype independently associated with greater SJC, CRP, ultrasound synovitis and erosive damage in DMARD-naive early psoriatic arthritis. *Ann Rheum Dis* 2021;81:490-5.
8. Mease PJ, Karki C, Palmer JB, et al. Clinical characteristics, disease activity, and patient-reported outcomes in psoriatic arthritis patients with dactylitis or enthesitis: results from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry. *Arthritis Care Res* 2017;69:1692-9.
9. Taylor W, Gladman D, Helliwell P, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* 2006;54:2665-73.
10. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984;27:361-8.
11. Rudwaleit M, van der Heijde D, Landewé, R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777-83.
12. Biagioni BJ, Gladman DD, Cook RJ, et al. Reliability of radiographic scoring methods in axial psoriatic arthritis. *Arthritis Care Res* 2014;66:1417-22.
13. Compston JE, McClung MR, Leslie WD. Osteoporosis. *Lancet* 2019;393:364-76.
14. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994;21:2286-91.
15. Fernández-Sueiro JL, Willisch A, Pértega-Díaz S, et al. Evaluation of ankylosing spondylitis spinal mobility measurements in the assessment of spinal involvement in psoriatic arthritis. *Arthritis Rheum* 2009;61:386-92.
16. Lukas C, Landewé R, Sieper J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. *Ann Rheum Dis* 2009;68:18-24.
17. Prevoo ML, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995;38:44-8.
18. Fredriksson T, Pettersson U. Severe psoriasis--oral therapy with a new retinoid. *Dermatologica* 1978;157:238-44.
19. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures and development of an instrument specific to psoriatic arthritis. *Arthritis Rheum* 2008;59:686-91.
20. Schoels M, Aletaha D, Funovits J, Kavanaugh A, Baker D, Smolen JS. Application of the DAREA/DAPSA score for assessment of disease activity in psoriatic arthritis. *Ann Rheum Dis* 2010; 69:1441-7.
21. Schoels MM, Aletaha D, Alasti F, Smolen JS. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. *Ann Rheum Dis* 2016;75:811-8.
22. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. *Ann Rheum Dis* 2010;69:48-53.
23. Girolimetto N, Giovannini I, Crepaldi G, et al. Psoriatic dactylitis: current perspectives and new insights in ultrasonography and magnetic resonance imaging. *J Clin Med* 2021;10:2604.
24. Ogdie A, Blachley T, Lakin PR, et al. Evaluation of clinical diagnosis of axial psoriatic arthritis or elevated patient-reported spine pain in CorEvitas' Psoriatic Arthritis/Spondyloarthritis Registry. *J Rheumatol* 2022;49: 281-90.
25. Chandran V, Tolusso DC, Cook RJ, Gladman DD. Risk factors for axial inflammatory arthritis in patients with psoriatic arthritis. *J Rheumatol* 2010;37:809-15.
26. Brockbank JE, Stein M, Schentag CT, Gladman DD. Dactylitis in psoriatic arthritis: a marker for disease severity? *Ann Rheum Dis* 2005;64:188-90.
27. Geijer M, Lindqvist U, Husmark T, et al. The Swedish Early Psoriatic Arthritis Registry 5-year followup: substantial radiographic progression mainly in men with high disease activity and development of dactylitis. *J Rheumatol* 2015;42:2110-7.
28. van der Heijde D, Gladman DD, FitzGerald O, et al. Radiographic progression according to baseline C-reactive protein levels and

- other risk factors in psoriatic arthritis treated with tofacitinib or adalimumab. *J Rheumatol* 2019;46:1089-96.
29. Queiro-Silva R, Torre-Alonso JC, Tinturé-Eguren T, López-Lagunas I. A polyarticular onset predicts erosive and deforming disease in psoriatic arthritis. *Ann Rheum Dis* 2003;62:68-70.
 30. Haroon M, Gallagher P, FitzGerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann Rheum Dis* 2015;74:1045-50.
 31. Qin B, Ma N, Tang Q, et al. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. *Mod Rheumatol* 2016;26:372-6.
 32. Kim DS, Shin D, Lee MS, et al. Assessments of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in Korean patients with psoriasis vulgaris and psoriatic arthritis. *J Dermatol* 2016;43:305-10.
 33. Gladman DD, Mease PJ, Choy EHS, Ritchlin CT, Perdok RJ, Sasso EH. Risk factors for radiographic progression in psoriatic arthritis: subanalysis of the randomized controlled trial ADEPT. *Arthritis Res Ther* 2010;12:R113.
 34. Jenkinson T, Armas J, Evison G, Cohen M, Lovell C, McHugh NJ. The cervical spine in psoriatic arthritis: a clinical and radiological study. *Br J Rheumatol* 1994;33:255-9.
 35. Husic R, Greter J, Felber A, et al. Disparity between ultrasound and clinical findings in psoriatic arthritis. *Ann Rheum Dis* 2014;73:1529-36.
 36. Haroon M, Winchester R, Giles JT, Heffernan E, FitzGerald O. Certain class I HLA alleles and haplotypes implicated in susceptibility play a role in determining specific features of the psoriatic arthritis phenotype. *Ann Rheum Dis* 2016;75:155-62.
 37. Kavanaugh A, Coates LC, van der Windt DA, Corp N, Soriano ER. GRAPPA treatment recommendations: updates and methods. *J Rheumatol Suppl* 2020;96:41-5.