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Evaluation of Clinical Diagnosis of Axial Psoriatic Arthritis (PsA) or Elevated Patient-reported Spine Pain in CorEvitas' PsA/Spondyloarthritis Registry

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ABSTRACT. ***Objective***. To determine the presence of axial symptoms in patients with psoriatic arthritis (PsA) and examine differences between those with or without a diagnosis of axial PsA (axPsA).

Methods. Patients with PsA at their Corevitas' (formerly Corrona) Psoriatic Arthritis/Spondyloarthritis Registry enrollment visit were stratified into 4 mutually exclusive groups based on axial manifestations: physician-diagnosed axPsA only (Dx^+Sx^-), patient-reported elevated spine symptoms only (Dx^-Sx^+; defined as Bath Ankylosing Spondylitis Disease Activity Index ≥ 4 and spine pain visual analog scale ≥ 40), physician-diagnosed and patient-reported manifestations (Dx^+Sx^+), and no axial manifestations (Dx^-Sx^-). Patient characteristics, disease activity, and patient-reported outcomes (PROs) at enrollment in each axial manifestation group were compared with the Dx^-Sx^- group. Associations of patient characteristics with the odds of having axial manifestations were estimated using multinomial logistic regression (reference: Dx^-Sx^-).

Results. Of 3393 patients included, 226 (6.7%) had Dx^+Sx^-, 698 (20.6%) had Dx^-Sx^+, 165 (4.9%) had Dx^+Sx^+, and 2304 (67.9%) had Dx^-Sx^-. Patients with Dx^-Sx^+ or Dx^+Sx^+ were more frequently women and had a history of depression and fibromyalgia (FM) vs patients who had Dx^-Sx^-. Patients with Dx^+Sx^- or Dx^+Sx^+ were more frequently HLA-B27 positive than those with Dx^-Sx^-. FM was significantly associated with increased odds of Dx^+Sx^- or Dx^+Sx^+. Disease activity and PROs were worse in patients with Dx^-Sx^+ or Dx^+Sx^+ than in those with Dx^-Sx^-.

Conclusion. Patients who had self-reported elevated spine symptoms, with or without physician-diagnosed axPsA, had worse quality of life and higher disease activity overall than patients without axial manifestations, suggesting an unmet need in this patient population.

Key Indexing Terms: epidemiology, psoriatic arthritis, registry, spondyloarthropathy

Psoriatic arthritis (PsA) is a chronic, systemic inflammatory disease with heterogeneous symptoms and presentations.[1,2] The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recognizes 6 key disease domains that may present alone or in combination: skin disease, peripheral arthritis, nail psoriasis (PsO), enthesitis, dactylitis, and axial disease.[1] Depending on axial disease definition and study methodology, axial disease due to inflammation occurs in 25–70% of patients with PsA.[3,4] Clinical signs and symptoms of axial PsA (axPsA) include inflammatory back pain, reduced spinal mobility, and sacroiliitis, which is often asymmetrical.[3,5,6,7,8] If untreated, patients with axPsA can experience significantly reduced spinal

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mobility; nearly 40% of patients without sacroiliitis have developed grade ≥ 2 sacroiliitis at 5-year follow-up.[4] A previous study in Corevitas' (formerly Corrona) PsA/Spondyloarthritis (SpA) Registry showed that patients who had axPsA had higher disease activity, reduced quality of life (QOL), and more impaired physical function and work productivity than those without axial involvement.[9] Thus, prompt identification and treatment of axPsA are important to prevent increasing structural damage, maintain mobility, and improve QOL.

The diagnosis of axPsA is generally based on patient history, physical examination, imaging, and laboratory testing.[5,10] However, no consensus currently exists on criteria to define axPsA. Back pain is highly prevalent in the general population and can result from numerous causes, including injury, occupational conditions, chronic pain disorders, or other conditions that affect the spine.[11] Additionally, up to 30% of patients with PsA with visible structural damage on imaging have no axial symptoms.[4,12,13,14] Together, these factors can result in missed or delayed diagnosis of axial disease in patients with PsA. The lack of validated classification criteria for axPsA also limits consistent evaluation and meaningful comparison of treatment efficacies for patients with axPsA in clinical research. A randomized controlled trial assessing the efficacy of secukinumab in patients with axPsA (MAXIMISE) used the following inclusion criteria for axPsA: patients had to meet the ClASsification criteria for Psoriatic ARthritis, have a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥ 4 (suggesting the presence of active axial manifestations), and have a patient-reported spine pain score ≥ 40 on a visual analog scale (VAS).[15] Efforts are currently underway by GRAPPA and the Assessment of SpondyloArthritis international Society to better define axPsA.[16] Our study evaluated characteristics of patients with PsA and physician-diagnosed axPsA, and of patients with PsA who had active elevated spine symptoms as assessed by BASDAI and patient-reported spine pain.

METHODS

Data source. Corevitas' PsA/SpA Registry is a large, independent, prospective, observational cohort of patients with rheumatologist-diagnosed PsA or SpA. The registry includes patients recruited by 67 participating rheumatologists from 64 private and academic practice sites across 40 US states. As of January 1, 2021, the registry included data on approximately 4683 patients with PsA/SpA from 20,230 patient visits. Corevitas' PsA/SpA Registry and its investigators have been reviewed and approved by a central institutional review board (IRB; New England Independent Review Board No. 120160070). For academic investigative sites that did not receive a waiver to use the central IRB, approval was obtained from the respective governing IRB. All participating investigators were required to obtain full board approval for conducting noninterventional research with a limited dataset involving human participants. Registry participants were required to provide written informed consent and authorization prior to participating. All research was conducted in compliance with the current (2013) Declaration of Helsinki.

Study design and patient population. This cross-sectional study included patients aged ≥ 18 years with PsA enrolled in the registry between March 2013 and November 2019. Patients were assessed for the presence of physician-diagnosed axPsA and elevated spine symptoms at registry enrollment. Physicians identified the subset of patients with axPsA based on history, physical examination, imaging, and laboratory workup. All patients completed a BASDAI questionnaire and spine pain VAS (0–100) at enrollment; the criteria for patient-reported elevated spine symptoms were a BASDAI ≥ 4 (indicating active axial manifestations) and a spine pain VAS ≥ 40. Patients were stratified into mutually exclusive groups based on axial manifestations: physician diagnosis of axPsA only (Dx^+Sx^-), patient-reported elevated spine symptoms only (Dx^-Sx^+), both physician diagnosis of axPsA and patient-reported elevated spine symptoms (Dx^+Sx^+), and patients without physician diagnosis of axPsA or patient-reported elevated spine symptoms (Dx^-Sx^-; Supplementary Figure 1, available with the online version of this article).

Data collection and definitions. Data were collected at registry enrollment using questionnaires from patients and their treating rheumatologists that were completed at routine office visits. Data collected included patient demographics, clinical characteristics, history of comorbidities, prior and current treatment use, disease activity and patient-reported outcomes (PROs), and work productivity and activity impairment. Disease activity measures included tender joint count (TJC) in 68 joints, swollen joint count (SJC) in 66 joints, physician global assessment (PGA) VAS, Disease Activity Index in Psoriatic Arthritis (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), and minimal disease activity (MDA). MDA was defined as meeting 5 of the 7 following criteria: TJC ≤ 1, SJC ≤ 1, PsO-affected body surface area (BSA) < 3%, patient-reported pain VAS ≤ 15, patient global assessment (PtGA) VAS ≤ 20, Health Assessment Questionnaire–Disability Index (HAQ-DI) ≤ 0.5, and tender entheseal points ≤ 1 using the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index.[17] PROs included BASDAI, spine pain VAS, patient-reported pain and fatigue VAS, PtGA VAS, morning stiffness VAS, EuroQol VAS (EQ VAS), HAQ-DI, and the HAQ for the Spondyloarthropathies (HAQ-S). Work productivity was assessed using the Work Productivity and Activity Impairment (WPAI) questionnaire.

The proportion of patients with Dx^+Sx^-, Dx^-Sx^+, Dx^+Sx^+, and Dx^-Sx^- was determined in the overall population and in patients initiating a biologic at registry enrollment to reduce confounding in the assessment of disease activity in patients who were already receiving treatment at enrollment. The frequencies of other PsA manifestations (enthesitis [SPARCC Enthesitis Index count > 0], dactylitis [dactylitis count > 0], peripheral arthritis [TJC and/or SJC > 0], nail PsO [global nail PsO VAS > 0], and skin disease [affected BSA > 0%]) were reported in each axial manifestation group separately in both the overall and bioinitiator populations.

Statistical analysis. The proportion of patients with Dx^+Sx^-, Dx^-Sx^+, and other active PsA manifestations at enrollment was summarized descriptively. Patient characteristics, disease activity, and PROs at enrollment were compared between patients with Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ and those with Dx^-Sx^- using 2-sample *t* tests for continuous variables and chi-square or Fisher exact tests for categorical variables. Significance testing was not adjusted for multiple comparisons due to the descriptive nature of this study. Complete case analyses were used, with no imputation for missing data.

A multinomial logistic regression model was used to calculate odds ratios (ORs) estimating the associations of patient characteristics with having Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ at enrollment (reference: Dx^-Sx^-). Covariates chosen a priori included age, sex, race, time since diagnosis, and BMI, as well as current and prior biologic, conventional synthetic disease-modifying antirheumatic drug (csDMARD), and prednisone use. Harrell's list of relevant covariate types was used to determine other candidate covariates,[18] which were tested for collinearity (correlation coefficient $\rho \geq 0.6$) and nonlinearity ($\rho < 0.6$). Additional covariates identified for inclusion were fibromyalgia (FM; included as the surrogate measure TJC/SJC ratio ≥ 7),[19,20] depression, clinical DAPSA (cDAPSA) score, and EuroQol 5-dimensions (EQ-5D) questionnaire score. HAQ-S was excluded from the final model due to its multicollinearity with cDAPSA and EQ-5D. Time since diagnosis and cDAPSA had nonlinear associations with the outcome measures and were therefore included in the model as 4-knot restricted cubic splines.

The associations of Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ with disease activity and PRO measures were analyzed using multivariable linear or logistic regression

models with Dx^-Sx^- as the reference group (Supplementary Table 1, available with the online version of this article). Models were adjusted for age, sex, race, BMI, time since diagnosis, FM (TJC/SJC ratio ≥ 7), depression, cDAPSA score, EQ-5D score, and prior and current biologic, csDMARD, and prednisone use. All statistical analyses were performed using Stata 15.1 (StataCorp).

RESULTS

Frequency of axial and other PsA manifestations. Of 3393 patients with PsA enrolled in the registry, 226 (6.7%) had Dx^+Sx^-, 698 (20.6%) had Dx^-Sx^+, and 165 (4.9%) had Dx^+Sx^+ (Figure 1A); 2304 patients (67.9%) were Dx^-Sx^-. Of the 769 patients who initiated a biologic at registry enrollment, 55 (7.2%) had Dx^+Sx^-, 216 (28.1%) had Dx^-Sx^+, and 54 (7.0%) had Dx^+Sx^+ (Figure 1B); 444 biologic initiators (57.7%) were Dx^-Sx^-.

The frequency of coexisting PsA manifestations was higher in patients with Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ than in those with Dx^-Sx^- in both the overall population and in patients initiating a biologic at registry enrollment, except for dactylitis, which was reported less often in patients with Dx^+Sx^- than in those with Dx^-Sx^- (Figure 2). Most patients across all study groups had active skin disease and peripheral arthritis at registry enrollment, with the highest frequency in patients with Dx^-Sx^+ (skin disease: overall, 76.8%; bioinitiators, 82.9%; peripheral arthritis: overall, 78.1%; bioinitiators, 88.4%). The frequency of active nail PsO, enthesitis, and dactylitis was highest in patients with Dx^+Sx^+, with more than half having active nail PsO (overall, 56.4%; bioinitiators, 55.6%) and enthesitis (overall, 50.3%; bioinitiators, 51.9%).

Patient demographics and clinical characteristics at enrollment. Higher proportions of patients with Dx^-Sx^+ (64.3%) or Dx^+Sx^+ (61.0%) were female compared with patients with Dx^-Sx^- (50.6%; both $P < 0.05$; Table 1). Patients with Dx^-Sx^+ or Dx^+Sx^+ had a higher prevalence of depression (22.1% and 28.5%, respectively), and FM (both 13.3%) compared with patients with Dx^-Sx^- (depression, 13.1%; FM, 3.2%; both $P < 0.05$). Patients with Dx^-Sx^+ had a higher prevalence of hypertension, metabolic syndrome, diabetes mellitus, and cardiovascular disease than those with Dx^-Sx^-. Patients with Dx^+Sx^- or Dx^+Sx^+ were more likely to be HLA-B27 positive (among those with available HLA-B27 test results) than patients with Dx^-Sx^- (Dx^+Sx^-, 34.3%; Dx^+Sx^+, 39.2%; Dx^-Sx^-, 20.2%; $P < 0.05$).

Higher proportions of patients with Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ had prior biologic experience compared with patients with Dx^-Sx^- (all $P < 0.05$; Table 1). The proportion of patients currently using biologics was higher in the Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ groups compared with the Dx^-Sx^- group, although the difference only reached statistical significance in the Dx^+Sx^+ group (71.5% vs 63.8%; $P < 0.05$). Prior and current tsDMARD and prednisone use were more frequent among patients with Dx^-Sx^+ than among those with Dx^-Sx^- (all $P < 0.05$). Fewer patients with Dx^+Sx^- or Dx^-Sx^+ were currently receiving csDMARDs compared with patients with Dx^-Sx^- (both $P < 0.05$).

Disease activity, PROs, and work productivity at enrollment. Patients with Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ had higher PGA scores than those with Dx^-Sx^- (all $P < 0.01$; Figure 3). Additionally, patients with Dx^-Sx^+ or Dx^+Sx^+ had higher TJC and SJC, worse DAPSA and PASDAS scores, and were less likely to be in MDA at enrollment than those with Dx^-Sx^- (all $P < 0.01$). Patients with Dx^-Sx^+ or Dx^+Sx^+ also had worse PRO scores than those with Dx^-Sx^-, including pain, fatigue, PtGA, morning stiffness, spine pain, EQ VAS, HAQ-DI, HAQ-S, BASDAI, and WPAI (all $P < 0.01$; Figure 4). Results were generally consistent in multivariable adjusted regression models (Supplementary Table 1, available with the online version of this article).

Patient characteristics associated with axial manifestations. In the multinomial logistic regression model, age was not significantly associated with having Dx^+Sx^- or Dx^-Sx^+; however, for each 1-year increase in age, a patient's odds of having Dx^+Sx^+ decreased relative to the presence of Dx^-Sx^- (OR 0.98, 95% CI 0.96–0.99, $P < 0.01$; Figure 5). The odds of having Dx^-Sx^+ were comparable between Black and White patients; however, relative to White

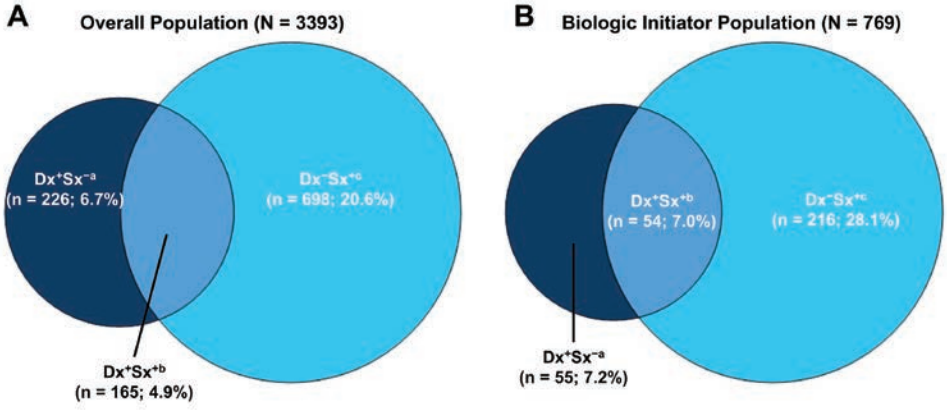

Figure 1. Frequency of axial manifestations in (A) the overall population of patients with PsA, and (B) patients with PsA who initiated a biologic at registry enrollment. [a] Patients with physician-diagnosed axPsA only based on clinical assessments, imaging, and laboratory examinations. [b] Patients who had both a physician diagnosis of axPsA and elevated spine symptoms. [c] Patients with elevated spine symptoms (BASDAI ≥ 4 and spine pain VAS ≥ 40) only. axPsA: axial psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; Dx: diagnosis; PsA: psoriatic arthritis; Sx: symptoms; VAS: visual analog scale.

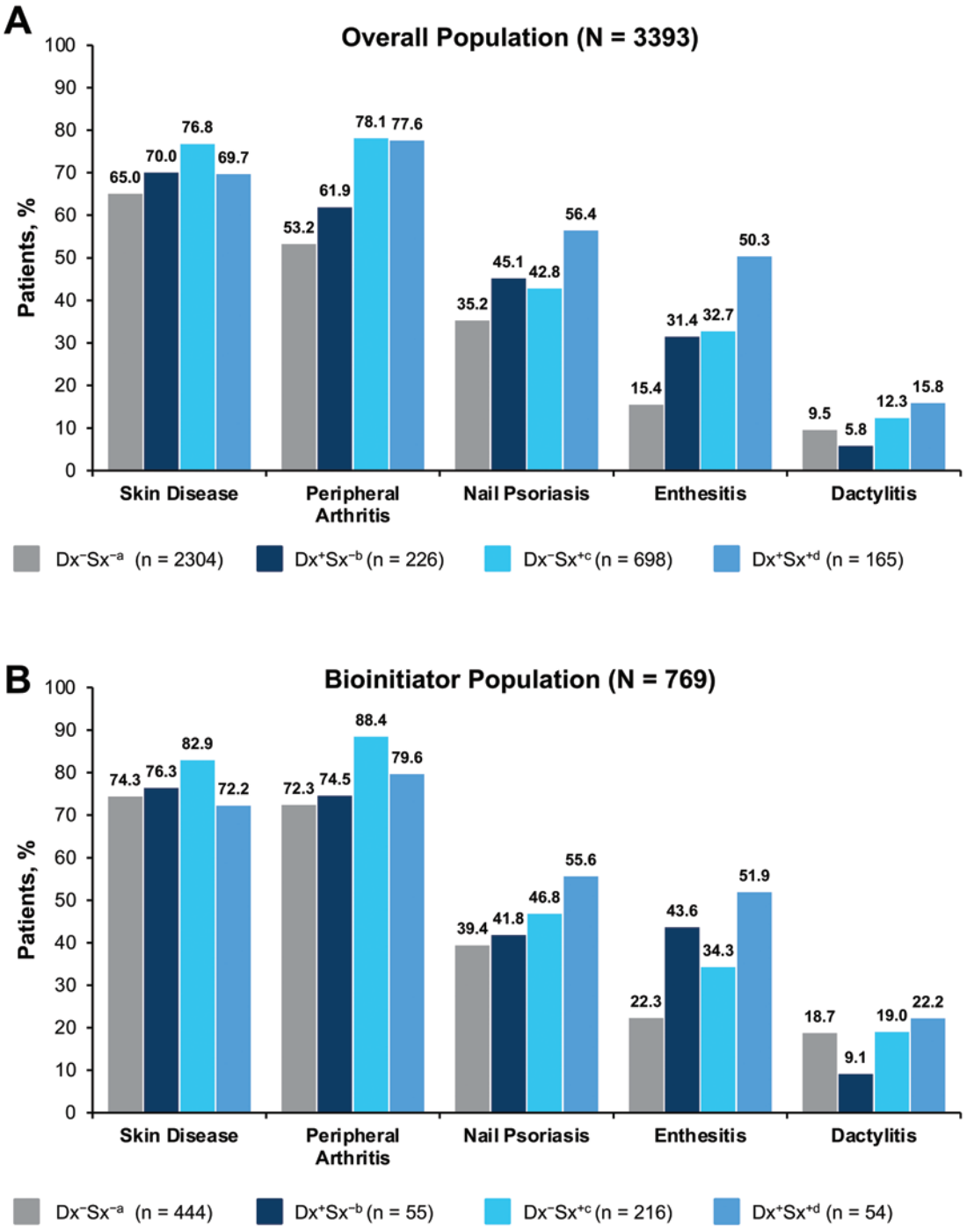

Figure 2. Frequency of other active PsA manifestations by study group in the (A) overall population of patients with PsA, and (B) patients with PsA who initiated a biologic at registry enrollment. [a] Patients who did not have a physician diagnosis of axPsA or elevated spine symptoms. [b] Patients with physician-diagnosed axPsA only based on clinical assessments, imaging, and laboratory examinations.[c] Patients with elevated spine symptoms (BASDAI ≥ 4 and spine pain VAS ≥ 40) only. [d] Patients who had both a physician diagnosis of axPsA and elevated spine symptoms. axPsA: axial psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; Dx: diagnosis; PsA: psoriatic arthritis; Sx: symptoms; VAS: visual analog scale.

patients, patients of other races had higher odds of reporting Dx^-Sx^+ (OR 1.75, 95% CI 1.11–2.74, $P = 0.02$) compared with Dx^-Sx^-. BMI was not associated with having Dx^-Sx^+ or Dx^+Sx^+, but the odds of having Dx^+Sx^- decreased for each unit increase in BMI (OR 0.96, 95% CI 0.94–0.98, $P < 0.01$) relative to Dx^-Sx^-. Patients with FM had significantly higher odds of having Dx^+Sx^- (OR 2.20, 95% CI 1.24–3.91, $P < 0.01$) or Dx^+Sx^+ (OR 2.35, 95% CI 1.44–3.85, $P < 0.01$). Prior csDMARD and

Table 1. Demographics, clinical characteristics, and treatment profiles at enrollment of patients with psoriatic arthritis with vs without axial manifestations (unadjusted).[a]

	Axial Manifestation Category at Enrollment			
	$Dx^{-}Sx^{-}$[b], n = 2304	$Dx^{+}Sx^{-}$[c], n = 226	$Dx^{-}Sx^{+}$[d], n = 698	$Dx^{+}Sx^{+}$[e], n = 165
Age, yrs, mean (SD)	54.1 (13.3)	51.7 (13.9)*	53.5 (12.2)	50.2 (12.6)*
Female, n (%)	1157 (50.6)	113 (50.7)	448 (64.3)*	100 (61.0)*
Race, n (%)				
White	2132 (94.8)	205 (94.5)	627 (91.1)**	150 (92.6)
Black	16 (0.7)	0	10 (1.5)**	0
Other	102 (4.5)	12 (5.5)	51 (7.4)**	12 (7.4)
Work status, n (%)				
Full time	1324 (58.0)	123 (55.4)	290 (41.8)**	71 (43.6)**
Part time	192 (8.4)	27 (12.2)	57 (8.2)**	15 (9.2)**
Disabled	132 (5.8)	16 (7.2)	150 (21.6)**	30 (18.4)**
Retired	492 (21.6)	42 (18.9)	136 (19.6)**	28 (17.2)**
Other	143 (6.3)	14 (6.3)	60 (8.7)**	19 (11.7)**
BMI, kg/m^2, mean (SD)	31.6 (7.4)	29.8 (6.8)*	33.4 (7.9)*	31.7 (7.1)
BMI category, kg/m^2, n (%)				
Normal/underweight (< 25)	394 (17.5)	49 (22.3)	85 (12.3)**	26 (16.0)
Overweight (25 to < 30)	672 (30.0)	72 (32.7)	169 (24.5)**	46 (28.2)
Obese (≥ 30)	1185 (52.6)	99 (45.0)	435 (63.1)**	91 (55.8)
HLA-B27 positive, n/N (%)[f]	100/496 (20.2)	37/108 (34.3)*	47/187 (25.1)	31/79 (39.2)*
Symptom duration, yrs, mean (SD)	10.8 (10.1)	12.4 (11.2)*	10.3 (9.9)	11.7 (11.6)
Time since diagnosis, yrs, mean (SD)	8.0 (8.7)	7.5 (8.8)	6.6 (7.6)*	6.4 (9.0)*
History of comorbidities, n (%)				
Hypertension	859 (37.2)	70 (31.0)	298 (42.7)*	57 (34.5)
Hyperlipidemia	520 (22.6)	51 (22.6)	168 (24.1)	34 (20.6)
Metabolic syndrome	333 (14.5)	20 (8.8)*	130 (18.6)*	29 (17.6)
Diabetes mellitus	315 (13.7)	25 (11.1)	119 (17.0)*	25 (15.2)
Depression	301 (13.1)	32 (14.2)	154 (22.1)*	47 (28.5)*
Cardiovascular disease	246 (10.7)	23 (10.2)	94 (13.5)*	24 (14.5)
Any cancer (excluding NMSC)	179 (7.8)	19 (8.4)	43 (6.2)	16 (9.7)
Serious infections	133 (5.8)	14 (6.2)	53 (7.6)	13 (7.9)
Anxiety	91 (3.9)	11 (4.9)	70 (10.0)*	16 (9.7)*
Fibromyalgia	74 (3.2)	10 (4.4)	93 (13.3)*	22 (13.3)*
Uveitis	23 (1.0)	10 (4.4)*	17 (2.4)*	8 (4.8)*
Crohn disease	20 (0.9)	1 (0.4)	10 (1.4)	3 (1.8)
Ulcerative colitis	19 (0.8)	4 (1.8)	8 (1.1)	0 (0.0)
Prior medication use, n (%)				
Biologic	694 (30.1)	88 (38.9)*	274 (39.3)*	62 (37.6)*
tsDMARD	120 (5.2)	18 (8.0)	60 (8.6)*	10 (6.1)
csDMARD	671 (29.1)	74 (32.7)	230 (33.0)	47 (28.5)
Prednisone	330 (14.3)	20 (8.8)*	130 (18.6)*	19 (11.5)
Current medication use, n (%)				
Biologic	1469 (63.8)	157 (69.5)	452 (64.8)	118 (71.5)*
tsDMARD	157 (6.8)	18 (8.0)	68 (9.7)*	10 (6.1)
csDMARD	1204 (52.3)	94 (41.6)*	331 (47.4)*	74 (44.8)
Prednisone	172 (7.5)	11 (4.9)	87 (12.5)*	15 (9.1)

[a] All values were calculated based on available data and had < 10% missing data, except HLA-B27 (n = 870). [b] Patients who did not have a physician diagnosis of axPsA or elevated spine symptoms. [c] Patients with physician-diagnosed axPsA only based on clinical assessments, imaging, and laboratory examinations. [d] Patients with elevated spine symptoms (BASDAI ≥ 4 and spine pain VAS ≥ 40) only. [e] Patients who had both a physician diagnosis of axPsA and elevated spine symptoms. [f] Number of patients with positive test result (n) among those with known test result (N). * $P < 0.05$ for comparison with the $Dx^{-}Sx^{-}$ group. *P* values were calculated using 2-sample *t* tests for continuous variables and chi-square or Fisher exact tests for categorical variables. ** $P < 0.05$ for distribution across categories compared with the $Dx^{-}Sx^{-}$ group. *P* values were calculated using chi-square or Fisher exact tests. axPsA: axial psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; csDMARD: conventional synthetic disease-modifying antirheumatic drug; Dx: diagnosis; NMSC: nonmelanoma skin cancer; Sx: symptoms; tsDMARD: targeted synthetic disease-modifying antirheumatic drug; VAS: visual analog scale.

prednisone use was associated with decreased odds of having $Dx^{+}Sx^{+}$ (csDMARDs, OR 0.61, 95% CI 0.41–0.91; prednisone, OR 0.40, 95% CI 0.19–0.84; both $P < 0.05$) compared with $Dx^{-}Sx^{-}$.

DISCUSSION

Approximately one-third of patients in this real-world PsA population had axial manifestations. The proportion of patients reporting elevated spine symptoms ($Dx^{-}Sx^{+}$ and $Dx^{+}Sx^{+}$

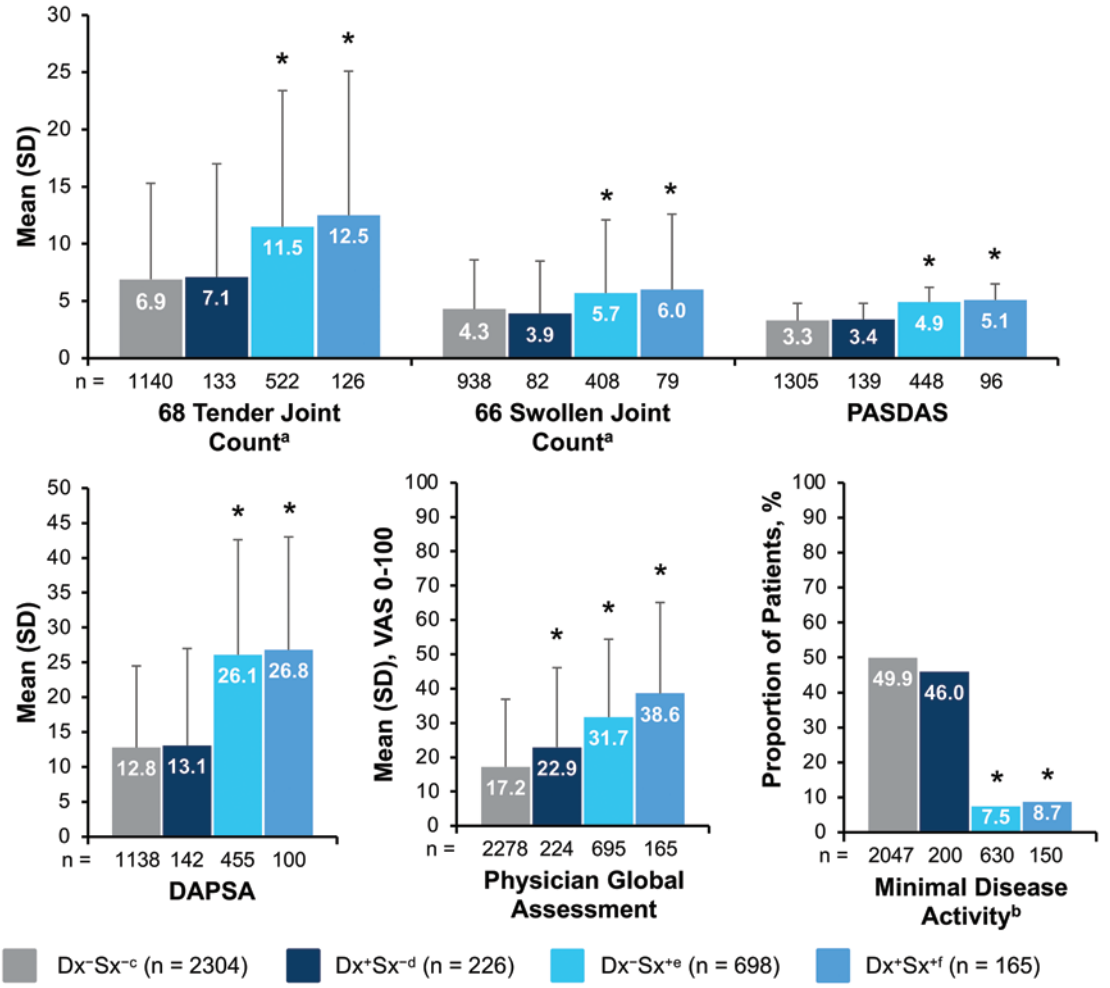

Figure 3. Unadjusted mean disease activity measures at enrollment in mutually exclusive axial manifestation groups. [a] In patients with ≥ 1 tender/swollen joint. [b] Minimal disease activity was defined as meeting 5 of the 7 following criteria: tender joint count ≤ 1, swollen joint count ≤ 1, psoriasis-affected body surface area < 3%, patient-reported pain VAS ≤ 15, patient global assessment VAS ≤ 20, Health Assessment Questionnaire–Disability Index ≤ 0.5, and tender entheseal points ≤ 1 using the Spondyloarthritis Research Consortium of Canada Enthesitis Index. [c] Patients who did not have a physician diagnosis of axPsA or elevated spine symptoms. [d] Patients with physician-diagnosed axPsA only based on clinical assessments, imaging, and laboratory examinations. [e] Patients with elevated spine symptoms (BASDAI ≥ 4 and spine pain VAS ≥ 40) only. [f] Patients who had both a physician diagnosis of axPsA and elevated spine symptoms. * $P < 0.01$ for comparison with the $Dx^{-}Sx^{-}$ group. axPsA: axial psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; DAPSA: Disease Activity Index in Psoriatic Arthritis; Dx: diagnosis; PASDAS: Psoriatic Arthritis Disease Activity Score; Sx: symptoms; VAS: visual analog scale.

combined) was higher than those who had a physician diagnosis of axPsA ($Dx^{+}Sx^{-}$ and $Dx^{+}Sx^{+}$ combined). Patients with $Dx^{-}Sx^{+}$ or $Dx^{+}Sx^{+}$ had higher unadjusted disease activity and worse PRO scores than patients with $Dx^{-}Sx^{-}$, whereas disease activity and PRO scores were generally comparable in patients with $Dx^{+}Sx^{-}$ and those with $Dx^{-}Sx^{-}$. These results suggest that managing spine symptoms is important for improving patient QOL and disease outcomes.

The proportion of patients with a physician diagnosis of axPsA ($Dx^{+}Sx^{-}$ or $Dx^{+}Sx^{+}$) in Corevitas' PsA/SpA Registry was 11.5%, which is lower than that observed in other real-world studies. Estimates of the prevalence of axPsA among patients with PsA generally range from 5% to 28% for patients with early disease[6,21–27] and 25–70% in patients with established PsA.[3,8,12] Additionally, > 50% of patients in our study population with physician-diagnosed axPsA did not have patient-reported elevated spine symptoms (ie, were $Dx^{+}Sx^{-}$), although most were currently on therapy at the time of sampling. It is possible that some of these patients may have been asymptomatic despite having imaging evidence of axPsA and may have been switching therapies for control of other disease manifestations at the time of registry enrollment. Additionally, treating physicians may not take into account other more objectively measured characteristics in their diagnosis of axPsA; for example, increases in BMI were associated with decreased presence of $Dx^{+}Sx^{-}$ relative to $Dx^{-}Sx^{-}$. Previous studies indicate that 20–30% of patients with PsA with visible structural damage on imaging have no axial symptoms.[4,12,13,14] In contrast, nearly one-quarter of patients in our study had patient-reported elevated spine symptoms, of whom only 19% also had physician-diagnosed axPsA. Many of the

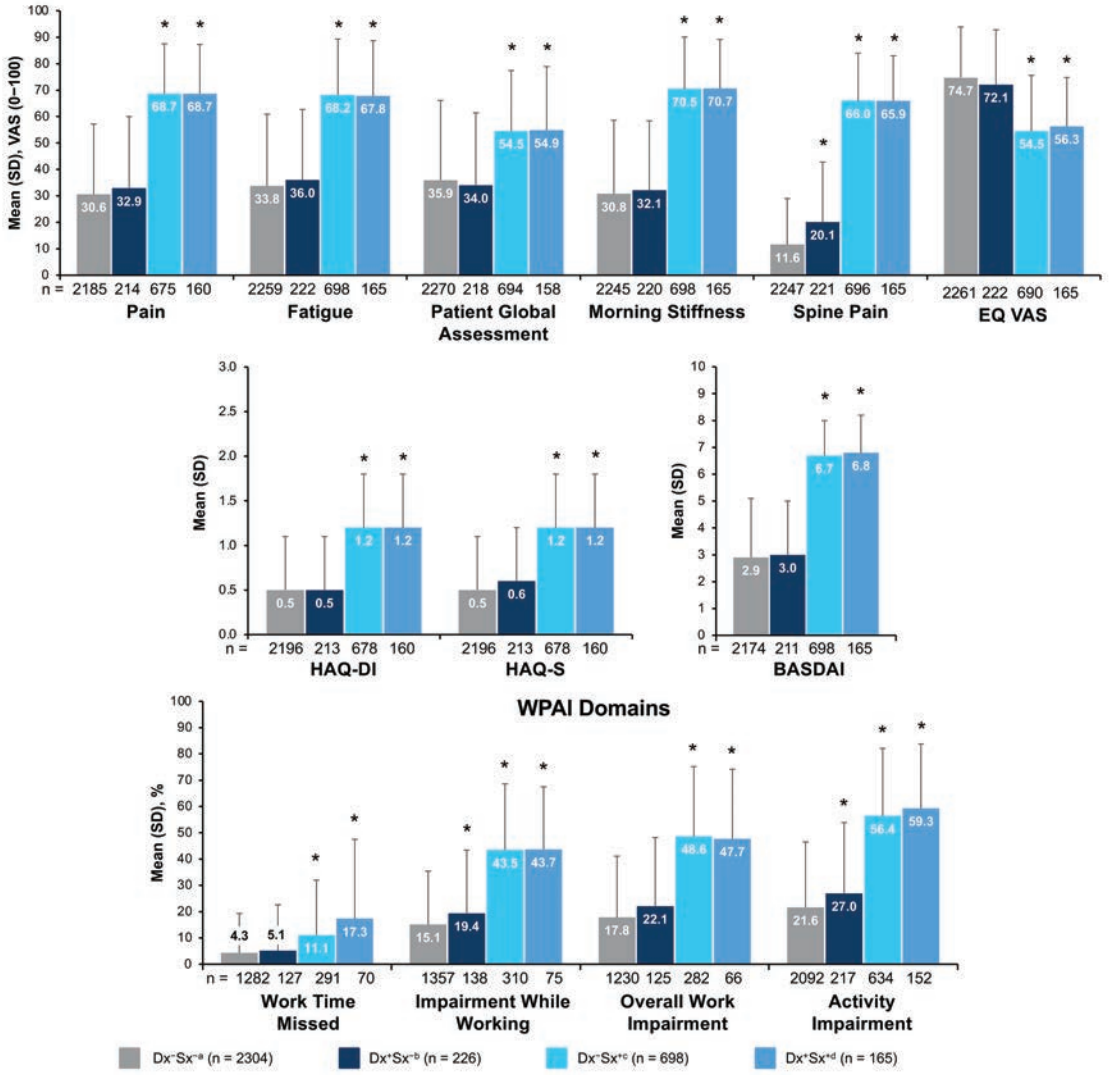

Figure 4. Unadjusted mean patient-reported outcome measures at enrollment in mutually exclusive axial manifestation groups. [a] Patients who did not have a physician diagnosis of axPsA or elevated spine symptoms. [b] Patients with physician-diagnosed axPsA only based on clinical assessments, imaging, and laboratory examinations. [c] Patients with elevated spine symptoms (BASDAI ≥ 4 and spine pain VAS ≥ 40) only. [d] Patients who had both a physician diagnosis of axPsA and elevated spine symptoms. * $P < 0.01$ for comparison with the Dx^-Sx^- group. axPsA: axial psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; Dx: diagnosis; EQ VAS: EuroQol visual analog scale; HAQ-S: Health Assessment Questionnaire for the Spondyloarthropathies; Sx: symptoms; WPAI: Work Productivity and Activity Impairment questionnaire.

previous studies investigating the prevalence of axPsA required imaging confirmation. There are no clear guidelines to suggest that rheumatologists always obtain imaging in the workup of PsA. As such, there was no imaging requirement in the registry; the presence of a physician diagnosis of axPsA was based on the judgment of the treating physician. The diagnosis of axPsA may have been missed in some patients with patient-reported elevated spine symptoms, contributing to the relatively low prevalence of axial disease in our cohort. This study emphasizes the need to establish a clinically relevant set of criteria defining axPsA and to develop sensitive screening tools that allow accurate diagnosis of the underlying conditions causing patients' back pain.

Among those with available HLA-B27 status, the proportion of HLA-B27–positive patients was significantly higher in patients with Dx^+Sx^- (34.3%) or Dx^+Sx^+ (39.2%) than in those with Dx^-Sx^- (20.2%), and numerically higher than in those with Dx^-Sx^+ (25.1%; statistical comparisons not performed). HLA-B27 positivity has been associated with a higher prevalence of axPsA among patients with PsA.[14,28] Approximately 20% of patients with PsA overall are HLA-B27 positive,[29] but the prevalence of HLA-B27 is substantially higher in those with vs without axial involvement (23–40% vs 7–17%, respectively).[8,9,14,28] Although HLA-B27 testing is not recommended for all patients with suspected PsA, it may be helpful in diagnosing axial disease due to PsA among patients with PsA.

Some patients classified as having Dx^-Sx^+ may have also had physician-diagnosed axPsA (and could have been in the Dx^+Sx^+ group); however, many may have had back pain due to other underlying conditions. Back pain is highly prevalent in the general population. The lifetime prevalence of spinal pain is

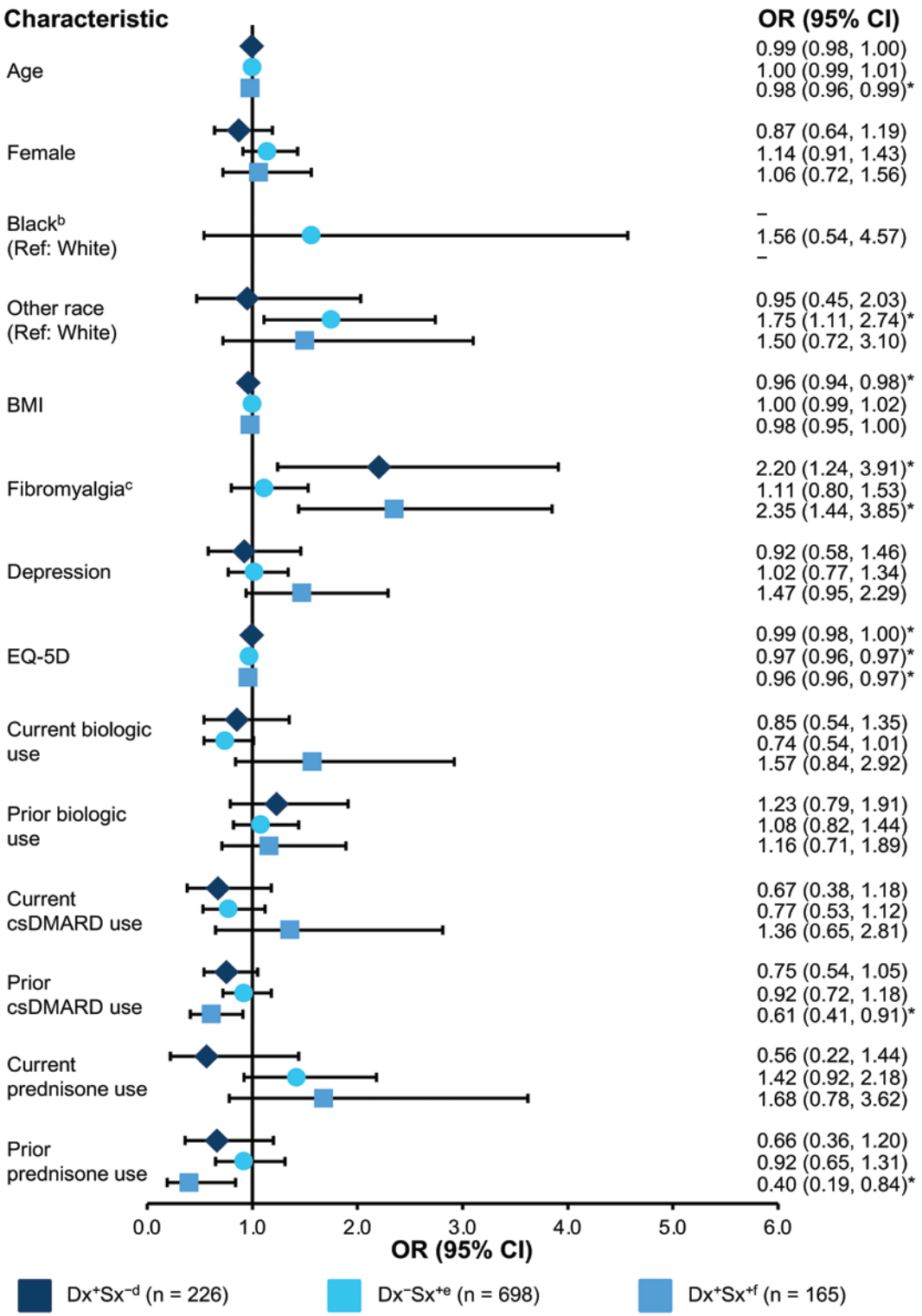

Figure 5. Adjusted ORs estimating the association of patient characteristics with having Dx^+Sx^-, Dx^-Sx^+, or Dx^+Sx^+ relative to Dx^-Sx^- [a], at enrollment. [a] Multivariable logistic regression model with Dx^-Sx^- as the reference group. Model included age, sex, race, time since diagnosis, BMI, fibromyalgia, depression, cDAPSA, EQ-5D score, and current and prior biologic, csDMARD, and prednisone use. [b] Effects on Dx^+Sx^- or Dx^+Sx^+ could not be estimated due to separation of data. [c] Defined as tender/swollen joint count ratio ≥ 7. [d] Patients with physician-diagnosed axPsA only based on clinical assessments, imaging, and laboratory examinations. [e] Patients with elevated spine symptoms (BASDAI ≥ 4 and spine pain VAS ≥ 40) only. [f] Patients who had both a physician diagnosis of axPsA and elevated spine symptoms. * $P < 0.05$. axPsA: axial psoriatic arthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; cDAPSA: Clinical Disease Activity Index in Psoriatic Arthritis; csDMARD: conventional synthetic disease-modifying antirheumatic drug; Dx: diagnosis; EQ-5D: EuroQol 5-dimensions questionnaire; Sx: symptoms; VAS: visual analog scale.

estimated to be 54–80%, and 25–60% of patients with low back or neck pain experience pain lasting ≥ 1 year.[11] There are many causes of chronic back pain, including degenerative spine disease, injury, occupational conditions, and chronic pain disorders such as FM.[11] Causes of chronic back pain are not mutually exclusive; patients may have a combination of conditions, such as degenerative spine disease and axPsA. The presence of other conditions that cause chronic back pain in patients with PsA could result in increased spine pain VAS scores, regardless of the presence of axPsA.

The BASDAI assesses both axial symptoms and symptoms consistent with those of peripheral PsA, including pain and swelling in other joints, areas tender to touch or pressure (eg, enthesitis), fatigue, and morning stiffness.[30] Patients with $Dx^{-}Sx^{+}$ in our study population had higher TJC, SJC, and fatigue and morning stiffness VAS scores than those with $Dx^{+}Sx^{-}$ or $Dx^{-}Sx^{-}$. Patients with a greater burden of peripheral symptoms and higher overall disease activity may have had higher BASDAI scores and thus were eligible for inclusion in the $Dx^{-}Sx^{+}$ group, despite the absence of true axPsA. Together with the frequency of chronic back pain in the general population, the potential effect of peripheral symptoms on BASDAI scores may have contributed to the higher frequency of $Dx^{-}Sx^{+}$ compared with $Dx^{+}Sx^{-}$ or $Dx^{+}Sx^{+}$. Establishing consensus criteria to identify axPsA and the development of screening tools to more easily differentiate between axPsA and other causes of back pain are important to ensure accurate diagnosis and appropriate management of the underlying cause of patients' back pain.

The higher frequency of $Dx^{-}Sx^{+}$ may also have been influenced by the presence of central sensitization, a hypersensitivity to painful or inflammatory stimuli caused by dysregulation of the central nervous system.[31] Central sensitization can lead to chronic pain, perceived pain intensity disproportionate to the intensity of the stimulus, or pain perceived in areas where injury or inflammation has not occurred.[32] Central sensitization contributes to the pain hypersensitivity characteristic of several disorders including FM, which is characterized by chronic widespread pain, fatigue, sleep disturbance, and cognitive disfunction.[33] FM is more common in women than in men and is more prevalent in patients with rheumatic disease than in the general population.[34,35] Patients with PsA and comorbid FM have worse disease activity when assessed using measures with subjective or patient-reported components, including DAPSA, Leeds Enthesitis Index, BASDAI, HAQ, pain, and fatigue scores.[31,36,37] In our study cohort, history of FM was significantly associated with a patient's odds of having axial manifestations by either definition, which may support the difficulty in differentiating FM from axial symptoms in PsA. However, patients with $Dx^{-}Sx^{+}$ were more likely to be female and had higher TJC and worse BASDAI, pain, and fatigue scores than patients with $Dx^{+}Sx^{-}$ or $Dx^{-}Sx^{-}$. The presence of central sensitization in some patients in our study population may have increased their pain and fatigue, resulting in higher BASDAI and spine pain scores and contributing to their eligibility for the $Dx^{-}Sx^{+}$ cohort in the absence of axPsA. To better identify FM in future analyses, Corevitas' PsA/SpA Registry is currently incorporating the Widespread Pain Index and Symptom Severity Scale, a validated, quantitative measure of central sensitization[38,39] to better identify FM in future analyses..

Our study has several strengths. The observational design of Corevitas' PsA/SpA Registry captures real-world practice patterns and data on patients seen in routine clinical practice, and thus may provide information more representative of the general population of patients with PsA than the stringent protocols and patient populations in clinical trials. Additionally, the registry collects an extensive number of demographic, clinical, and PRO variables, allowing a detailed characterization of the registry's patient population. The sample size of patients with PsA was large enough to allow adjustment for confounding variables. We collected PRO data on axial symptoms in patients without a clinical diagnosis of axPsA, providing a broader view of the effect of axial symptoms on QOL in patients with PsA, regardless of the presence of axPsA.

Our study also has some limitations. Active PsA disease manifestations at the time of registry enrollment were physician reported and may not reflect all PsA presentations experienced by patients throughout the course of their disease. As laboratory tests (eg, HLA-B27) are not required at all visits and are reported only when collected, these missing data may reflect practice patterns of the enrolling providers. Although used as an assessment of axial involvement in clinical trials of PsA, the BASDAI has not been validated as a disease activity measure in patients with PsA without clearly defined axial disease. $Dx^{+}Sx^{-}$ was physician reported and patients may have been misclassified. For example, imaging prior to enrollment in the registry may not have been adequately recorded or preserved, particularly if the imaging was conducted long before enrollment. Additionally, because imaging confirmation of axPsA was not required, this could have led to overestimation (patients with $Dx^{+}Sx^{-}$ who would not have had imaging findings) or underestimation (missed axPsA in patients with $Dx^{-}Sx^{+}$) of the prevalence of axPsA.

In Corevitas' PsA/SpA Registry, a higher prevalence of $Dx^{-}Sx^{+}$ than $Dx^{+}Sx^{-}$ was observed. Patients with $Dx^{-}Sx^{+}$ or $Dx^{+}Sx^{+}$ had significantly higher disease activity and worse PRO scores than those with $Dx^{-}Sx^{-}$ and numerically worse scores than those with $Dx^{+}Sx^{-}$. Although patients with $Dx^{-}Sx^{+}$ may have had other reasons for back pain, such as degenerative spine disease or central sensitization, it is possible that axPsA was present in some of these patients, thus warranting further evaluation. These findings highlight the need to establish standardized assessment tools for axPsA to facilitate the accurate identification and effective management of axial disease in patients with PsA.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

REFERENCES

1. Coates LC, Kavanaugh A, Mease PJ, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis. Arthritis Rheumatol 2016;68:1060-71.
2. Coates LC, Helliwell PS. Psoriatic arthritis: state of the art review. Clin Med 2017;17:65-70.
3. Gladman DD. Axial disease in psoriatic arthritis. Curr Rheumatol Rep 2007;9:455-60.
4. Chandran V, Barrett J, Schentag CT, Farewell VT, Gladman DD. Axial psoriatic arthritis: update on a long-term prospective study. J Rheumatol 2009;36:2744-50.
5. Gottlieb A, Korman NJ, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol 2008;58:851-64.
6. Baraliakos X, Coates LC, Braun J. The involvement of the spine in psoriatic arthritis. Clin Exp Rheumatol 2015; 5 Suppl 93:S31-5.
7. Gladman DD. Clinical, radiological, and functional assessment in psoriatic arthritis: is it different from other inflammatory joint diseases? Ann Rheum Dis 2006;65 Suppl 3:iii22-4.
8. Haroon M, Winchester R, Giles JT, Heffernan E, FitzGerald O. Clinical and genetic associations of radiographic sacroiliitis and its different patterns in psoriatic arthritis. Clin Exp Rheumatol 2017;35:270-6.
9. Mease PJ, Palmer JB, Liu M, et al. Influence of axial involvement on clinical characteristics of psoriatic arthritis: analysis from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry. J Rheumatol 2018;45:1389-96.
10. Helliwell PS. Axial disease in psoriatic arthritis. Rheumatology 2020;59:1193-5.
11. Manchikanti L, Singh V, Datta S, Cohen SP, Hirsch JA; American Society of Interventional Pain Physicians. Comprehensive review of epidemiology, scope, and impact of spinal pain. Pain Physician 2009;12:E35-70.
12. Braga MV, de Oliveira SC, Vasconcelos AHC, et al. Prevalence of sacroiliitis and acute and structural changes on MRI in patients with psoriatic arthritis. Sci Rep 2020;10:11580.
13. Queiro R, Belzunegui J, González C, et al. Clinically asymptomatic axial disease in psoriatic spondyloarthropathy. A retrospective study. Clin Rheumatol 2002;21:10-3.
14. 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.
15. Baraliakos X, Coates LC, Gossec L, et al. Secukinumab improves axial manifestations in patients with psoriatic arthritis and inadequate response to NSAIDs: primary analysis of the MAXIMISE trial. Ann Rheum Dis 2019;78:195-6.
16. Goel N, Coates LC, De Marco G, et al. GRAPPA 2019 project report. J Rheumatol Suppl 2020;96:53-7.
17. 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.
18. Harrell FJ. Regression modeling strategies, with application to linear models, logistic and ordinal regression, and survival analysis. 2nd ed. Heidelberg: Springer; 2015.
19. Kristensen LE, Bliddal H, Christensen R, et al. Is swollen to tender joint count ratio a new and useful clinical marker for biologic drug response in rheumatoid arthritis? Results from a Swedish cohort. Arthritis Care Res 2014;66:173-9.
20. Pollard LC, Kingsley GH, Choy EH, Scott DL. Fibromyalgic rheumatoid arthritis and disease assessment. Rheumatology 2010;49:924-8.
21. Torre Alonso JC, Rodriguez Perez A, Arribas Castrillo JM, Ballina Garcia J, Riestra Noriega JL, Lopez Larrea C. Psoriatic arthritis (PA): a clinical, immunological and radiological study of 180 patients. Br J Rheumatol 1991;30:245-50.
22. Yang Q, Qu L, Tian H, et al. Prevalence and characteristics of psoriatic arthritis in Chinese patients with psoriasis. J Eur Acad Dermatol Venereol 2011;25:1409-14.
23. Moghaddassi M, Shahram F, Chams-Davatchi C, Najafizadeh SR, Davatchi F. Different aspects of psoriasis: analysis of 150 Iranian patients. Arch Iran Med 2009;12:279-83.
24. Coates LC, Conaghan PG, Emery P, et al. Sensitivity and specificity of the classification of psoriatic arthritis criteria in early psoriatic arthritis. Arthritis Rheum 2012;64:3150-5.
25. Niccoli L, Nannini C, Cassarà E, et al. Frequency of iridocyclitis in patients with early psoriatic arthritis: a prospective, follow up study. Int J Rheum Dis 2012;15:414-8.
26. Nossent JC, Gran JT. Epidemiological and clinical characteristics of psoriatic arthritis in northern Norway. Scand J Rheumatol 2009;38:251-5.
27. Papadavid E, Katsimbri P, Kapniari I, et al. Prevalence of psoriatic arthritis and its correlates among patients with psoriasis in Greece: results from a large retrospective study. J Eur Acad Dermatol Venereol 2016;30:1749-52.
28. 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.
29. Feld J, Chandran V, Haroon N, Inman R, Gladman D. Axial disease in psoriatic arthritis and ankylosing spondylitis: a critical comparison. Nat Rev Rheumatol 2018;14:363-71.
30. 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.
31. Mease PJ. Fibromyalgia, a missed comorbidity in spondyloarthritis: prevalence and impact on assessment and treatment. Curr Opin Rheumatol 2017;29:304-10.
32. Yunus MB. Central sensitivity syndromes: a new paradigm and group nosology for fibromyalgia and overlapping conditions, and the related issue of disease versus illness. Semin Arthritis Rheum 2008;37:339-52.
33. Clauw DJ. Fibromyalgia: a clinical review. JAMA 2014;311:1547-55.
34. Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. Br J Anaesth 2013;111:52-8.
35. Zhao SS, Duffield SJ, Goodson NJ. The prevalence and impact of comorbid fibromyalgia in inflammatory arthritis. Best Pract Res Clin Rheumatol 2019;33:101423.
36. Brikman S, Furer V, Wollman J, et al. The effect of the presence of fibromyalgia on common clinical disease activity indices in patients with psoriatic arthritis: a cross-sectional study. J Rheumatol 2016;43:1749-54.
37. Ulus Y, Akyol Y, Bilgici A, Kuru O. The impact of the presence of fibromyalgia on fatigue in patients with psoriatic arthritis: comparison with controls. Adv Rheumatol 2019;60:1.
38. Wolfe F, Clauw DJ, Fitzcharles MA, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum 2016;46:319-29.
39. Wolfe F, Butler SH, Fitzcharles M, et al. Revised chronic widespread pain criteria: development from and integration with fibromyalgia criteria. Scand J Pain 2019;20:77-86.