EPIDEMIOLOGICAL SCIENCE

Isolated axial disease in psoriatic arthritis and ankylosing spondylitis with psoriasis

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ABSTRACT

Objectives To compare isolated axial psoriatic arthritis (PsA), axial PsA with peripheral involvement and isolated axial ankylosing spondylitis (AS) with psoriasis. To evaluate predictors for developing peripheral disease from isolated axial PsA over time.

Methods Two PsA and AS cohorts identified patients with PsA with axial disease and isolated axial patients with AS with psoriasis. Logistic regression compared isolated axial PsA to axial PsA with peripheral involvement and isolated axial AS with psoriasis. Cox proportional hazards model evaluated predictors for developing peripheral disease from isolated axial PsA.

Results Of 1576 patients with PsA, 2.03% had isolated axial disease and 29.38% had axial and peripheral disease. human leucocyte antigen HLA-B*27 positivity (OR 25.00, 95% CI 3.03 to 206.11) and lower Health Assessment Questionnaire scores (OR 0.004, 95% CI 0.00 to 0.28) were associated with isolated axial disease. HLA-B*27 also predicted peripheral disease development over time (HR 7.54, 95% CI 1.79 to 31.77). Of 1688 patients with AS, 4.86% had isolated axial disease with psoriasis. Isolated axial patients with PsA were older at diagnosis (OR 1.06, 95% CI 1.01 to 1.13), more likely to have nail lesions (OR 12.37, 95% CI 2.22 to 69.07) and less likely to have inflammatory back pain (OR 0.12, 95% CI 0.02 to 0.61) compared with patients with isolated axial AS with psoriasis.

Conclusions Isolated axial PsA and AS with psoriasis are uncommon. HLA-B*27 positivity is associated with isolated axial PsA and may identify those who develop peripheral disease over time. Isolated axial PsA is associated with better functional status. Isolated axial PsA appears clinically distinct from isolated axial AS with psoriasis.

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT?

⇒ Pure axial disease is uncommon in psoriatic arthritis (PsA), comprising <5% of patients, while the remainder have concomitant peripheral involvement.

WHAT DOES THIS STUDY ADD?

⇒ Isolated axial patients with PsA may have better functional status when compared with those with concomitant peripheral disease. human leucocyte antigen-B*27 predicted the development of peripheral involvement from isolated axial PsA over clinic follow-up.

⇒ Isolated axial PsA appears distinct from isolated axial AS with psoriasis.

HOW MIGHT THIS IMPACT ON CLINICAL PRACTICE OR FUTURE DEVELOPMENTS?

⇒ Isolated axial PsA and isolated axial ankylosing spondylitis with psoriasis may be two distinct clinical phenotypes and may warrant different treatment approaches.

INTRODUCTION

Psoriatic arthritis (PsA) is a multisystem disease characterised by psoriasis and musculoskeletal manifestations.[1] The presentation of PsA can involve five distinct disease domains, including peripheral disease, axial disease, enthesitis, dactylitis, skin and nail disease.[2] Given the considerable clinical overlap between ankylosing spondylitis (AS) and PsA within the spondyloarthritis (SpA) family, cross-sectional studies in the past have sought to better delineate their associated disease features and clinical outcomes. Epidemiological studies have aimed to study their genetics, clinical features, imaging findings, prognosis and optimal treatment modalities.[3] Within the PsA disease entity, patients with axial only disease pose an area of research interest, given its similarities to AS. Pure axial involvement exists in less than 5% of all patients with PsA, while the majority of patients have concomitant peripheral involvement.[4] A recent longitudinal study concluded that axial PsA appears to be distinct clinically from AS and is associated with worse peripheral arthritis and less back pain.[5]

A cross-sectional study performed in 2017 found that patients with AS without psoriasis, those with axial PsA and those with peripheral PsA all had similar disease activity as measured by composite clinical indices, namely, the Ankylosing Spondylitis Disease Activity Score, metrology and disability scores as measured by the Health Assessment Questionnaire Disability Index.[6] A subsequent registry-based study has demonstrated a higher proportion of moderate/severe psoriasis, higher disease activity and lower quality of life among patients with PsA with axial disease.[7] However, the PsA population with isolated axial disease without peripheral involvement has not been exclusively studied. Furthermore, it is unknown at this time which clinical variables increase the chance of developing peripheral disease among patients with PsA with isolated axial disease at initial presentation. This is also clinically significant, as patients with axial disease have distinct disease characteristics that

Table 1 Clinical parameters between patients with PsA isolated axial disease versus those with concomitant peripheral disease at first presentation of axial disease

Variable	Isolated axial group (N=32)	Axial and peripheral group (N=463)	P value
Demographics			
Age	43.09 (14.06)	45.54 (13.22)	0.346
Male (%)	71.88	63.28	0.431
Caucasian (%)	87.50	85.53	0.963
Age at diagnosis of PsA in years	37.44 (12.36)	35.06 (13.36)	0.302
Age at diagnosis of psoriasis in years	25.78 (17.31)	27.32 (14.31)	0.627
Smoker (%)	59.38	46.65	0.226
Clinical features			
Sacroiliitis grade*	2.75 (0.67)	2.59 (0.69)	0.189
Enthesitis† (%)	3.13	14.90	0.068
Elevated ESR (%)	39.29	46.71	0.560
PASI	6.06 (8.00)	7.29 (9.61)	0.517
BSA	10.13 (18.30)	9.79 (18.01)	0.946
Nail lesion (%)	53.13	74.95	0.013
Uveitis (%)	18.75	9.72	0.185
Inflammatory bowel disease† (%)	6.25	7.78	1.000
Inflammatory back pain‡ (%)	50.00	33.96	0.172
Back metrology§			
Neck rotation (degrees)	67.81 (22.80)	71.84 (20.81)	0.506
Lateral flexion, Domjan method (degrees)	15.03 (5.78)	15.58 (4.54)	0.709
Schober test (cm)	4.07 (1.65)	4.52 (1.31)	0.263
Chest expansion (cm)	5.67 (2.76)	5.35 (2.65)	0.551
Comorbidities			
BMI	26.61 (6.08)	29.26 (6.61)	0.101
Cardiovascular disease† (%)	12.50	18.36	0.485
Diabetes† (%)	7.41	7.19	1.000
Patient-reported outcomes			
BASDAI	1.97 (1.73)	4.65 (2.58)	<0.001
Fatigue	2.90 (2.51)	5.32 (2.87)	0.015
Spinal pain	1.50 (1.90)	4.45 (3.20)	<0.001
Joint pain/swelling	1.30 (1.49)	4.61 (2.84)	<0.001
Areas of localised tenderness	1.40 (1.84)	4.41 (2.99)	<0.001
Morning stiffness severity	2.70 (2.58)	4.35 (3.11)	0.084
Morning stiffness duration	2.80 (3.16)	3.60 (3.02)	0.462
HAQ	0.16 (0.29)	0.68 (0.61)	<0.001
SF-36 physical	46.75 (10.36)	36.61 (12.07)	0.009
SF-36 mental	52.68 (8.66)	46.50 (12.11)	0.042
Human leucocyte antigen (HLA) types			
HLA-B†27 (%)	34.62	21.46	0.188
HLA-B†38† (%)	15.38	15.66	1
HLA-B†39† (%)	0	8.84	0.152
HLA-B†8† (%)	11.54	19.95	0.442
HLA-B†13 (%)	11.54	7.32	0.435
HLA-B†40† (%)	0	1.52	1
HLA-C†6 (%)	23.08	25.38	0.977
Medications			
NSAIDs (%)	50.00	69.98	0.031
DMARDs (%)	28.13	47.30	0.055
Biologics (%)	18.75	13.39	0.558

Continued

Table 1 Continued

Variable	Isolated axial group (N=32)	Axial and peripheral group (N=463)	P value

Where applicable, figures reported as mean (SD); % denotes percentage of patients in the respective groups;
*The sacroiliac joint with the highest grade was used preferentially for analysis.
†Fisher's exact test used due to low sample size in each sub-group.
‡Low back pain or neck pain and stiffness for more than 3 months that improves with exercise but is not relieved by rest.
§The side with the lowest numeric value was used preferentially for analysis, where applicable.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; BSA, body surface area of psoriasis; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; NSAID, nonsteroidal anti-inflammatory drug; PASI, psoriasis area and severity index; PsA, psoriatic arthritis; SF-36, Short Form Health Survey.

may warrant and subsequently respond to different treatment approaches.[8–13]

Our previous study looked at all patients with PsA with axial disease.[5] The primary objective of this study was to compare patients with PsA with isolated axial disease (ie, do not have peripheral arthritis at presentation to the PsA clinic) to those with axial and peripheral disease. We also aimed to delineate predictors for developing peripheral disease in patients with PsA who present with isolated axial disease. Finally, we described the subset of patients with AS with axial disease with psoriasis who do not have peripheral disease (isolated axial disease) and compared their clinical features to patients with isolated axial PsA.

METHODS

Setting

This longitudinal study was conducted at the University of Toronto Psoriatic Arthritis Clinic, which is an observational cohort of patients with PsA and the University of Toronto Ankylosing Spondylitis Clinic, which is an observational cohort of patients with AS. At both clinics, patients are followed prospectively at 6–12 month intervals by a rheumatologist according to a standard protocol. All patients with PsA included in this study fulfilled the 2006 CASPAR criteria and have axial and/or peripheral inflammatory arthritis in the presence of psoriasis.[14] Patients in the AS cohort fulfilled the modified New York AS criteria.[15] The protocols recorded information on clinical, laboratory and radiographic variables at initial consultation and at each follow-up visit. At the time of analysis, 1576 patients were followed in the PsA cohort, while 1688 patients were followed in the AS cohort.

Patient selection and case definitions

The longitudinal single-centre PsA and AS cohorts were analysed to identify patients from cohort inception in January 1978 to October 2020 inclusive for the PsA cohort and July 2003 to November 2019 inclusive for the AS cohort. In general, patients with psoriasis and predominant peripheral symptoms are referred to the PsA clinic while those with predominant lower back symptoms are referred to the AS clinic for assessment. Patients with axial disease were identified from the database according to the presence of sacroiliitis on prior imaging. In this study, axial disease was defined as having features of ≥grade 2 sacroiliitis bilaterally or ≥grade 3 sacroiliitis unilaterally on radiographs of the sacroiliac joint, according to the modified New York criteria, and as interpreted by a radiologist with additional expertise in

Table 2 Clinical parameters between patients with PsA isolated axial disease versus those with isolated axial AS with psoriasis at first presentation of axial disease

Variable	Isolated axial PsA (N=32)	Isolated axial AS with psoriasis (N=82)	P value
Demographics			
Age	43.09 (14.06)	36.92 (12.57)	0.035
Male (%)	71.88	73.17	1
Caucasian (%)	87.50	76.83	0.362
Age at diagnosis of PsA/AS in years	37.44 (12.36)	29.65 (11.25)	0.003
Smoker (%)	59.38	39.02	0.079
Clinical features			
Enthesitis* (%)	3.13	7.32	0.671
Elevated ESR (%)	39.29	25.00	0.256
PASI	6.06 (8.00)	1.72 (2.08)	0.030
BSA	10.13 (18.30)	4.61 (9.03)	0.328
Nail lesion (%)	53.13	6.06	<0.001
Uveitis (%)	18.75	34.15	0.166
Inflammatory bowel disease* (%)	6.25	18.29	0.146
Inflammatory back pain† (%)	50.00	77.33	0.021
Back metrology‡			
Neck rotation (degrees)	67.81 (22.80)	66.57 (22.96)	0.849
Lateral flexion, Domjan method (degrees)	15.03 (5.78)	13.49 (5.95)	0.344
Schober test (cm)	4.07 (1.65)	4.00 (1.61)	0.870
Chest expansion (cm)	5.67 (2.76)	4.99 (2.04)	0.230
Comorbidities			
BMI	26.61 (6.08)	25.96 (4.50)	0.696
Cardiovascular disease* (%)	12.50	6.10	0.265
Diabetes* (%)	7.41	3.70	0.597
Patient reported outcomes			
BASDAI	1.97 (1.73)	4.23 (2.59)	0.002
Fatigue	2.90 (2.51)	5.05 (2.82)	0.027
Spinal pain	1.50 (1.90)	4.92 (3.04)	<0.001
Joint pain/swelling	1.30 (1.49)	2.93 (2.86)	0.011
Areas of localised tenderness	1.40 (1.84)	3.86 (3.29)	0.002
Morning stiffness severity	2.70 (2.58)	4.67 (3.15)	0.047
Morning stiffness duration	2.80 (3.16)	4.08 (3.45)	0.256
HAQ	0.16 (0.29)	0.59 (0.58)	<0.001
SF-36 physical	46.75 (10.36)	39.14 (10.47)	0.041
SF-36 mental	52.68 (8.66)	45.33 (12.53)	0.027
Human leucocyte antigen (HLA) types			
HLA-B*27 (%)	34.62	75.95	<0.001
Medications			
NSAIDs (%)	50.00	60.98	0.392
DMARDs (%)	28.13	10.98	0.049
Biologics (%)	18.75	59.76	<0.001

Continued

Table 2 Continued

Where applicable, figures reported as mean (SD); % denotes percentage of patients in the respective groups.
*Fisher's exact test used due to low sample size in each sub-group.
†Low back pain or neck pain and stiffness for more than 3 months that improves with exercise but is not relieved by rest.
‡The side with the lowest numeric value was used preferentially for analysis, where applicable.
§The sacroiliac joint with the highest grade was used preferentially for analysis.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; BSA, body surface area of psoriasis; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; NSAID, nonsteroidal anti-inflammatory drug; PASI, psoriasis area and severity index; PsA, psoriatic arthritis; SF-36, Short Form Health Survey.

musculoskeletal imaging.[15 16] Furthermore, those with isolated axial disease were characterised by the absence of inflammatory peripheral arthritis, damaged joints and/or dactylitis documented on clinical examination or imaging at any point in the patient's clinical course, leading up to the initial presentation of axial disease, whereas those with axial PsA and peripheral disease were characterised as having inflammatory peripheral joint involvement, damaged joints and/or dactylitis along with axial disease, at any point prior to first presentation of axial disease. For patients in the AS cohort, the presence of psoriasis was defined as at least one documented occurrence of psoriasis from initial consultation to most recent follow-up, or any previous history of psoriasis as diagnosed by a rheumatologist or dermatologist. Hence, the presence of isolated axial AS with psoriasis is defined as patients with AS and psoriasis but without peripheral involvement, which is likewise defined as the absence of inflammatory peripheral arthritis, damaged joints and/or dactylitis.

Data collection

For the PsA cohort, variables on demographics, clinical features, comorbidities, patient-reported outcomes, human leucocyte antigen (HLA) types and treatments at first presentation of axial disease in addition to each subsequent follow-up visit for those with isolated axial disease and for those with concomitant peripheral disease were retrieved for analysis, if collected and available in the database. For the AS cohort, clinical features were collected at the baseline clinic visit only.

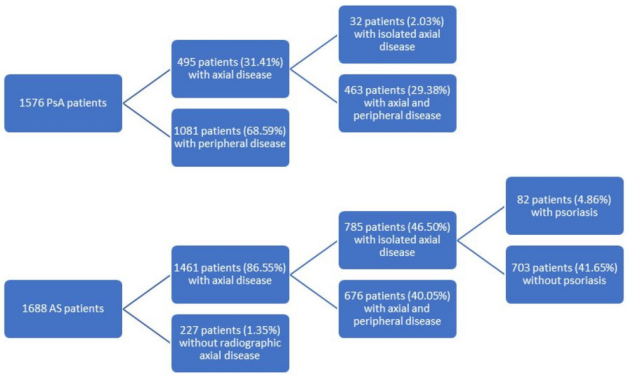

Figure 1 Flow diagram of the patients among the PsA and AS cohorts at baseline visit. AS, ankylosing spondylitis; PsA, psoriatic arthritis.

Table 3 Logistic regression analysis for factors associated with isolated axial PsA at first presentation of axial disease adjusted for sex and age at PsA diagnosis (N=495)

Sex (male)				0.588	(0.097, 3.570)	0.564
Age at diagnosis of PsA in years				1.061	(0.990, 1.138)	0.095
Sacroiliitis grade*	1.332	(0.811, 2.188)	0.257	2.021	(0.698, 5.852)	0.195
Enthesitis	0.176	(0.024, 1.312)	0.090	0.000	(0.000, ∞)	0.995
Elevated ESR	0.689	(0.312, 1.521)	0.357	3.298	(0.599, 18.173)	0.170
Nail lesion	0.357	(0.171, 0.745)	0.006	0.445	(0.075, 2.633)	0.372
HLA-B*27	2.013	(0.848, 4.779)	0.113	25.000	(3.033, 206.114)	0.003
Uveitis	2.195	(0.854, 5.644)	0.103	0.859	(0.040, 18.311)	0.922
HAQ	0.063	(0.008, 0.502)	0.009	0.004	(0.000, 0.284)	0.010
SF-36 PCS	1.080	(1.014, 1.151)	0.017	0.919	(0.817, 1.034)	0.161

*The sacroiliac joint with the highest grade was used preferentially for analysis.
ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; PsA, psoriatic arthritis; SF-36 PCS, Short Form Health Survey Physical Health.

Statistical analyses

Descriptive statistics determined the percentages of patients with isolated axial and axial with peripheral disease among the PsA cohort, in addition to the percentage of patients with isolated axial disease with psoriasis in the AS cohort. Student's two sample t tests determined differences between baseline continuous variables and χ^2 tests or Fisher's exact tests for baseline categorical variables, all at first presentation of axial disease between the two groups. Univariate and multivariate logistic regression models, adjusted for sex and age at PsA diagnosis, was performed to calculate ORs for presenting with isolated axial disease, when compared with patients with concomitant axial and peripheral disease at initial presentation of axial disease. Subsequently, survival analysis was performed to determine covariates that predicted the development of concomitant peripheral disease over time, in patients with PsA with isolated axial disease at presentation. This was done using Cox proportional hazards models using baseline and time-dependent covariates. Patients with axial disease who did not develop peripheral disease during the entire follow-up period were right censored at their last clinic visit. Survival models were adjusted for sex and age at PsA diagnosis. Time to the event of developing peripheral disease was measured from time of first radiographic evidence of axial disease. Finally, univariate and multivariate logistic regression models, adjusted for sex and age at PsA/AS diagnosis, were performed to compare clinical features associated with patients with isolated axial patients with PsA versus AS with isolated axial disease with psoriasis.

For all models, missing data were imputed from the closest previous clinic visit data point, if available. All statistically significant thresholds were set at $p<0.05$. Statistical analysis was performed using R V.4.0.5. Informed consent was obtained for the patients who participated in the cohort and the study was approved by the University Health Network Research Ethics Board (REB 18–5538).

RESULTS

Patients in the PsA cohort were compared with those in the AS cohort (tables 1 and 2). Of the 1576 patients with PsA in the cohort, 495 (31.41%) had axial disease at presentation to the clinic. Of those, 32 patients (2.03%) had isolated axial disease and 463 patients (29.38%) had axial with peripheral disease (figure 1). At first presentation of axial disease, significantly fewer patients with isolated axial disease had nail lesions or used non-steroidal anti-inflammatory drugs. Furthermore, those with

Table 4 Cox proportional regression for the development of peripheral disease among PsA patients who presented with isolated axial disease at first presentation of axial disease adjusted by sex and age at diagnosis of PsA (N=32)

	Univariate model		
Variable	HR	95% CI	P value
Sex (male)			
Age at diagnosis of PsA in years			
Sacroiliitis grade*	0.899	(0.466 to 1.733)	0.751
Enthesitis	0.940	(0.121 to 7.342)	0.953
Elevated ESR	0.626	(0.230 to 1.708)	0.360
Nail lesion	0.826	(0.319 to 2.141)	0.694
PASI	1.030	(0.960 to 1.106)	0.408
Uveitis	2.130	(0.786 to 5.769)	0.137
HLA-B*27	1.069	(0.394 to 2.901)	0.896
NSAIDS	1.009	(0.434 to 2.346)	0.983
DMARDS	0.825	(0.341 to 1.993)	0.669
Biologics	1.137	(0.381 to 3.392)	0.818

*The sacroiliac joint with the highest grade was used preferentially for analysis.
DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; NSAID, non-steroidal anti-inflammatory drug; PASI, psoriasis area and severity index; PsA, psoriatic arthritis.

Table 5 Time-dependent univariate Cox proportional regression for the development of peripheral disease among PsA patients who presented with isolated axial disease, adjusted by sex and age at diagnosis of PsA (N=32)

Variable	HR	95% CI	P value
Sex (male)			
Age at diagnosis of PsA in years			
Sacroiliitis grade*	1.302	(0.497 to 3.406)	0.591
Enthesitis	0.000	(0.000 to ∞)	0.998
Elevated ESR	1.292	(0.454 to 3.672)	0.631
Nail lesion	0.984	(0.388 to 2.500)	0.974
PASI	1.039	(0.984 to 1.098)	0.167
Uveitis	2.752	(0.883 to 8.572)	0.081
HLA-B*27	7.544	(1.792 to 31.769)	0.006
NSAIDS	0.924	(0.322 to 2.655)	0.884
DMARDS	1.454	(0.570 to 3.710)	0.434
Biologics	1.086	(0.335 to 3.515)	0.891

*The sacroiliac joint with the highest grade was used preferentially for analysis.
DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; NSAID, nonsteroidal anti-inflammatory drug; PASI, psoriasis area and severity index; PsA, psoriatic arthritis.

Table 6 Logistic regression analysis for factors associated with isolated axial PsA at first presentation of axial disease adjusted for sex and age at psa/as diagnosis among the isolated axial PsA and isolated axial AS with psoriasis cohorts (N=114)

	Univariate model			Multivariate model		
Variable	OR	95% CI	P value	OR	95% CI	P value
Sex (male)				0.638	(0.131 to 3.106)	0.578
Age at diagnosis of PsA or AS in years				1.063	(1.002 to 1.129)	0.043
Nail lesion	17.295	(4.923 to 60.760)	<0.001	12.370	(2.215 to 69.073)	0.004
Inflammatory back pain	0.170	(0.054 to 0.537)	0.003	0.116	(0.074 to 1.320)	0.011
HLA-B*27	0.200	(0.074 to 0.540)	0.001	0.312	(0.074 to 1.320)	0.113
Biologics	0.125	(0.043 to 0.368)	<0.001	0.319	(0.074 to 1.380)	0.126

AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HAQ, Health Assessment Questionnaire; PsA, psoriatic arthritis.

isolated axial disease also had significantly lower Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Health Assessment Questionnaire (HAQ) scores but higher short form health survey (SF-36) physical and mental scores, when compared with patients with axial and peripheral disease (table 1). Of note, the lower BASDAI scores associated with patients with isolated axial disease were across all individual components with fatigue, spinal pain, joint pain/swelling and areas of localised tenderness reaching statistical significance. In the AS cohort, 82 (4.86%) of the 1688 patients had isolated axial disease with psoriasis (figure 1). When compared with patients with AS with isolated axial disease with psoriasis at first presentation of axial disease, those with isolated axial PsA were older, had a later age of diagnosis, had higher Psoriasis Area Severity Index scores, a higher chance of having psoriatic nail lesions but a lower chance of having inflammatory back pain, a lower chance of HLA-B*27 positivity as well as were less likely to be on biologics but more likely to be on a disease-modifying antirheumatic drug. From a functional perspective, they had lower BASDAI, HAQ scores and higher SF-36 physical and mental scores (table 2). The lower BASDAI scores associated with patients with isolated axial PsA were across all individual components with fatigue, spinal pain, joint pain/swelling, areas of localised tenderness and morning stiffness severity reaching statistical significance.

In univariate logistic regression analysis for the 495 patients with PsA with axial disease irrespective of peripheral involvement, isolated axial disease was significantly associated with a lower probability of having nail lesions (OR 0.357, 95% CI 0.171 to 0.745, p<0.006), lower HAQ scores (OR 0.063, 95% CI 0.008 to 0.502, p<0.009) and higher SF-36 PCS scores (OR 1.080, 95% CI 1.014 to 1.151, p<0.017) at first presentation of axial disease, when adjusted for sex and age at PsA diagnosis, when compared with patients with concomitant axial and peripheral disease. Full protocol data were available for 237 patients to perform multivariate logistic regression analysis. In the multivariate model, HLA-B*27 positivity (OR, 25.000, 95% CI 3.033 to 206.114, p<0.003) and lower HAQ scores (OR 0.004, 95% CI 0.000 to 0.284, p<0.010) were significantly associated with isolated axial disease when compared with patients with concomitant axial and peripheral disease (table 3).

For the 32 patients with isolated axial disease, 25 ultimately developed peripheral disease by most recent clinic follow-up. Survival analysis using univariate Cox proportional-hazards models adjusted for sex and age of PsA diagnosis did not reveal any significant predictors for the development of peripheral disease, at first presentation of axial disease (table 4). However, with time-dependent variables over clinic follow-up, HLA-B*27 positivity was associated with the development of peripheral disease (HR 7.544, 95% CI 1.792 to 31.769, p<0.006) (table 5). The development of multivariate models was not possible due to the small sample size of the survival models (n=32).

In univariate logistic regression analysis for the 114 patients with isolated axial disease within both PsA and AS cohorts, those in the PsA cohort were more likely to have nail lesions (OR 17.295, 95% CI 4.923 to 60.760, p<0.001), but less likely to have inflammatory back pain (OR 0.170, 95% CI 0.054 to 0.537, p<0.003), to have HLA-B*27 positivity (OR 0.200, 95% CI 0.074 to 0540, p<0.001) and to be on biologics (OR 0.125, 95% CI 0.043 to 0.368, p<0.001) compared with the subset of AS patients with psoriasis. In the multivariate model, those in the PsA cohort were older (OR 1.063, 95% CI 1.002 to 1.129, p<0.043), more likely to have nail lesions (OR 12.370, 95% CI 2.215 to 69.073, p<0.004) and less likely to have inflammatory back pain (OR 0.116, 95% CI 0.022 to 0.606, p<0.011) (table 6).

DISCUSSION

In our PsA cohort, 2.03% patients had isolated axial disease at first presentation of axial disease, which is congruent with previously reported studies, citing a range between 2% and 5% of all patients with PsA.[16–18] While severe peripheral arthritis and HLA-B*27 positivity have been previously found to be risk factors for axial PsA, whether patients with PsA with isolated axial disease represent a distinct clinical phenotype has not been well studied thus far.[18] Our data suggest that those with isolated axial disease appear to have a milder form of PsA than those with axial and concurrent peripheral disease at baseline. The signal towards better patient-reported outcomes in the isolated axial group was reinforced in logistic regression analysis, with lower HAQ scores both in univariate and multivariate models compared with those patients with axial and peripheral disease.

Furthermore, in multivariate logistic regression, genetic factors appeared to influence the chances of presenting with isolated axial disease, as HLA-B*27 positivity was found to increase the odds by 25 times when compared with patients with PsA with concomitant axial and peripheral involvement, suggesting that HLA-B*27 may be used to identify patients with isolated axial disease at baseline. Patients with HLA-B*27 positivity were also found to have a higher likelihood of developing peripheral disease from isolated axial disease. In general, the impact of HLA risk alleles has been studied among patients with PsA of various clinical phenotypes. The association between HLA-B*27 and psoriatic spondylarthritis has been well established in prior cohort studies, but not within the subset of patients with PsA with isolated axial disease.[6] A 2012 study demonstrated an increase in HLA-B*39 prevalence positivity in patients with axial PsA compared with patients with psoriasis, while other studies

have previously linked HLA-B*27, HLA-B*08, HLA-Cw* 07:02 and HLA-B*38 to axial PsA.[19–21]

Additionally, we aimed to specifically study and compare the subset of patients with AS with isolated axial disease and psoriasis to patients with isolated axial PsA. While axial disease and psoriasis in AS have been evaluated before in the literature individually, isolated axial disease without peripheral involvement accompanied by concomitant psoriasis has not.[5 22–25] Compared with a recent study which found that 12% of patients with AS have concurrent psoriasis, our data indicate that 4.86% of patients with AS have isolated axial disease with psoriasis, which is higher than the 2.03% of patients with isolated axial disease in PsA.[5] As per our logistic regression analysis, isolated axial PsA appears to be a different clinical entity than isolated axial AS with psoriasis, with older age at diagnosis, a higher chance of nail lesions and lower odds of inflammatory back pain. This is congruent with a 2020 study, which compared the whole group of axial PsA, irrespective of peripheral involvement, to both AS as an umbrella group in addition to AS with psoriasis.[5] Hence, this study further solidifies the concept that axial PsA is indeed different from AS.

To our knowledge, this is the first study in the literature to exclusively evaluate the prevalence of and factors associated with isolated axial disease within the general umbrella of axial PsA, differentiating patients with concomitant peripheral involvement. It is also the first study to exclusively study isolated axial AS with psoriasis. The advantages of our study include long-term follow-up data as well as the comprehensiveness of clinical parameters collected in our research protocol, facilitating analysis of two cohorts within the SpA family. Moreover, the weakness of small sample size in our PsA patient group with axial only disease (n=32) within our study can be attributed to the rarity of isolated axial PsA within the PsA clinical phenotypes, comprising only 2.03% of our cohort. As a result, despite our PsA cohort having 1576 patients at the time of data collection, only 32 patients had isolated axial disease. This low patient number limited our model development, precluding multivariate analysis. Moreover, a potentially non-modifiable limitation lies in the classification of patients with PsA as having isolated axial disease versus AS with psoriasis, as this is not based on existing classification criteria, leading to natural overlap. By using objective disease activity and characteristic markers present in our protocolised data within our two cohorts, referral bias to each individual clinic (PsA vs AS) can hopefully be minimised. Another limitation inherent to the retrospective cohort design of this study is that we are relying on radiographs in defining axial involvement. The lack of MRI data in our study population results in a potential underreporting of axial disease in our cohorts.

Recognising the importance of evaluating this important subset of patients with PsA, international efforts are being made to recruit patients for a multinational, multicentre study to better evaluate the impact of axial involvement in PsA via the Axial Involvement in Psoriatic Arthritis Cohort (AXIS).[26] The AXIS cohort will hopefully be able to address other risk factors for the development of peripheral disease over time, including further exploring the role of HLA-B*27 positivity, as our findings were unfortunately limited by the small sample size of patients presenting with isolated axial PsA.[27] From a methodological perspective, with the development of larger cohorts of patients with PsA with isolated axial disease, hopefully future analysis using multistate models can help determine predictors for transitions between axial and peripheral disease in this seldomly studied population.

Patients with isolated axial disease represent a small subset of total patients, and in PsA, accounts for 2.03% of patients in our cohort. Whether patients with PsA present with axial disease by coincidence versus real inflammatory back pain on presentation is an important area of focus for future study. Based on the clinical parameters in table 1, whereby only 50% of patients in the isolated axial group had inflammatory back pain symptoms, we would favour a large contributor being incidental axial disease picked up on imaging. As our data suggest, those with isolated axial PsA have a significantly higher chance of HLA-B*27 positivity, and better functional status as evidenced by improved HAQ scores at first presentation of axial disease, compared with those with concomitant peripheral involvement. Moreover, HLA-B*27 positivity appears to be a predictor for the development of peripheral disease among patients who present with isolated axial disease, though analysis was limited by small sample size. When isolated axial AS with psoriasis was evaluated in our study, this subset of patients comprised 4.86% of patients with AS in our cohort. Furthermore, isolated asial PsA patients were differentiated from isolated axial AS with psoriasis patients by an older age at diagnosis, a higher chance of having psoriatic nail lesions and lower chance of having inflammatory back pain.

While there may be different opinions regarding nomenclature of axial disease, and whether axial PsA is just axSpA our patients all fulfilled CASPAR criteria for PsA, and the majority accrued peripheral disease over time. If the group with isolated axPsA at presentation was the same as AS without peripheral arthritis, one would expect there to be no differences in clinical parameters between these groups. Our data indicate that the group with axial PsA was indeed different from the group with AS, supporting the validity of our findings and conclusions in the manuscript.

Given the paucity of studies focused on the uncommon clinical phenotype of isolated axial disease within the SpA family, more research is needed to further evaluate longitudinal clinical outcomes among those with isolated axial disease, including the possible use of multistate models to evaluate the impact of clinical changes such as peripheral involvement over time. Hopefully, with the upcoming recruitment for the AXIS cohort, and continued international collaboration, we may better understand the subgroup of patients with PsA with isolated axial disease. By extension, more longitudinal studies are required to study the subset of patients with AS with isolated axial disease with psoriasis, including associations for the development of peripheral disease over time as well as prognosis compared with those with peripheral disease.

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