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ORIGINAL RESEARCH

# Characterising the axial phenotype of psoriatic arthritis: a study comparing axial psoriatic arthritis and ankylosing spondylitis with psoriasis from the REGISPONSER registry

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## ABSTRACT

**Aims** To explore the clinical and radiographical characteristics of axial psoriatic arthritis (PsA) and to compare it with ankylosing spondylitis (AS) with psoriasis.

**Methods** Cross-sectional study from the national multicentre registry REGISPONSER where participants fulfilled the European Spondyloarthropathy Study Group spondyloarthritis criteria at entry. Clinical, laboratory and radiographical characteristics between patients classified as axial PsA and AS with psoriasis by their rheumatologist are compared according to HLA-B27 status.

**Results** Of 2367 patients on REGISPONSER, n=405 had PsA, of whom 27% (n=109) had axial involvement as per the treating rheumatologist. 30% (n=26/86) of axial PsA were HLA-B27 positive. In the AS group, 9% (127/1422) had a history of psoriasis and were more frequently male, with longer diagnostic delay and more anterior uveitis than those with axial PsA who had more peripheral involvement and nail disease. Patients with HLA-B27-negative axial PsA reported less inflammatory pain and structural damage compared with AS with psoriasis. By contrast, HLA-B27-positive axial PsA shared clinical characteristics similar to AS and psoriasis although with a lower BASRI score. In the multivariable analysis, patients with AS and psoriasis were independently associated with HLA-B27 positivity (OR 3.34, 95% CI 1.42 to 7.85) and lumbar structural damage scored by BASRI (OR 2.14, 95% CI 1.4 to 3.19).

**Conclusion** The more prevalent axial PsA phenotype is predominantly HLA-B27 negative and presents different clinical and radiological manifestations when compared with AS with psoriasis. There is great heterogeneity in what rheumatologists consider axial PsA from a clinical and imaging perspective, highlighting the need for research into possible genetic drivers and a consensus definition.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is great heterogeneity in what is considered axial psoriatic arthritis (PsA) with a prevalence range varying between 11% and 78%.
⇒ Research in axial PsA is hampered by the lack of a definition of what is axial PsA.

### WHAT THIS STUDY ADDS

⇒ Axial PsA has different clinical and radiographical characteristics when compared with ankylosing spondylitis (AS)/r-axSpA (radiographic-axSpA) with and without psoriasis.
⇒ Axial PsA is largely independent of HLA-B27 and presents different clinical and radiographical manifestations when compared with AS/r-axSpA with psoriasis.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There is a need for identifying genetic drivers underpinning axial PsA to better understand its differential characteristics when compared with axial spondyloarthritis.

## INTRODUCTION

Inflammatory disease of the axial skeleton is a hallmark of spondyloarthritis (SpA) and one of the clinical phenotypes of psoriatic arthritis (PsA).[1] Indeed, when Moll *et al* described the SpA concept in 1974, they included PsA within the overall SpA group based on the high prevalence of sacroiliac and spine involvement, which they estimated at 22.9% at that time.[2] Historically, research in PsA has focused on the more prevalent peripheral arthritis phenotype with efforts to characterise axial involvement in PsA being hampered by the lack of a definition of axial PsA leading to a great heterogeneity on prevalence (varying between 11% and 78%), clinical and radiographical findings being described in the literature.[3]

At the clinical level, the challenge remains as to whether axial PsA represents a distinct entity or the coexistence of psoriasis and axial spondyloarthritis (axSpA).[4] There are few studies comparing axial PsA with axSpA reporting significant differences in prevalence of sex, body mass index (BMI), HLA-B27 positivity, peripheral arthritis, nail involvement, dactylitis and extramusculoskeletal manifestations.[5–8] To our knowledge, only one study to date fully characterised and compared the radiographical findings including the spine with complete ankylosis of the sacroiliac joints (SIJs) and bridging syndesmophytes seen more likely in the radiographical form of axSpA (ankylosing spondylitis (AS)) when compared with axial PsA.[7] Further, a single study compared axial PsA with the AS subset with a history of psoriasis finding more back pain at presentation in the AS with psoriasis group as well as a higher grade of sacroiliitis, worse metrology and worse Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) compared with axial PsA.[9] No comparison dividing axial PsA according to HLA-B27 status was performed in these studies, and only one report by Queiro *et al* described the differences between HLA-B27-negative and HLA-B27-positive patients in an axial PsA cohort.[10] Taking into account that HLA-B27 prevalence is as low as ~20% in PsA compared with 80%–90% in axSpA,[11 12] the main question is whether HLA-B27-positive axial PsA is more similar to AS with psoriasis, suggesting that the axial PsA phenotype may be driven by other genetic factors different from HLA-B27. Thus, the aims of this study were to explore the axial phenotype of PsA regarding its clinical and radiographical characteristics and to compare it with AS with psoriasis with a further subanalysis according to HLA-B27 status.

## METHODS

We performed a cross-sectional study from the national, multicentre (31 centres) Spanish REGISPONSER registry recruiting between March 2004 and March 2007. Eligibility for study entry was fulfilment of the European Spondyloarthropathy Study Group criteria. For the current analysis, we included patients who had a primary diagnosis of PsA or AS as confirmed by the treating rheumatologist. Specifics of the REGISPONSER registry have been previously published.[13]

### Data collected

Clinical, laboratory and imaging data were systematically collected in all patients. Demographic characteristics included age, sex, time to diagnosis (defined as time from symptom onset to diagnosis), BMI and family history of spondyloarthritis (SpA). In addition, past or present (ever) history of cervical pain, inflammatory back pain (fulfilling the Calin criteria[14]), alternating buttock pain, anterior uveitis, inflammatory bowel disease, dactylitis, enthesitis, peripheral arthritis, skin psoriasis and psoriatic nail disease were collected. In patients with skin psoriasis, SpA onset before or after psoriasis was determined using PsA/AS and psoriasis time of diagnosis. Laboratory tests included HLA-B27, C reactive protein (CRP) and erythrocyte sedimentation rate. Rheumatoid factor and hand/foot plain X-rays were not systematically collected in this study, which predates the development and publication of the Classification for Psoriatic Arthritis (CASPAR) classification criteria for PsA.[15]

Radiographs of the cervical, lumbar and pelvic X-rays, including SIJs, were performed in all participants. Images were scored using the Bath Ankylosing Spondylitis Radiology Index (BASRI) by the local reader, who was in all cases a rheumatologist with an interest in SpA. Additionally, the following patient-reported outcomes (PROs) were gathered irrespective of diagnosis: BASDAI, Bath Ankylosing Spondylitis Functional Index, Ankylosing Spondylitis Disease Activity Score-CRP.

### Group definition

The axial PsA group included patients with a primary diagnosis of PsA and axial involvement as defined by the treating rheumatologist who had access to the full set of clinical, laboratory and imaging data. The AS group included patients with a rheumatologist diagnosis of AS and current or history of psoriasis as recorded during the study visit. Modified New York Criteria (mNYc) for Ankylosing Spondylitis, ASAS (Assessment of Spondyloarthritis International Society) classification criteria for axSpA and CASPAR were retrospectively applied to the study population.

### Analysis

Descriptive statistics are shown as proportions/percentages for categorical variables and mean/SD or median/IQR as appropriate. Demographic, clinical and radiological characteristics were compared between the two groups (axial PsA and AS with psoriasis). A further sensitivity analysis was performed including all patients with PsA with definite radiographical sacroiliitis according to the local reader. Student's t-test or Mann-Whitney U tests for continuous variables and $\chi^2$ for categorical variables were used. Same statistics were used for further subgroup comparisons and sensitivity analysis. Associations between possible relevant demographic, clinical and radiological predictors, and disease groups (axial PsA vs AS with psoriasis) were explored with univariable and multivariable logistic regression. A non-automated model selection methodology was used including variables with a p value of <0.1 in the univariable analysis as well as plausible relevant variables considered by the investigators. Variable collinearity was assessed and the more clinically relevant variable was included in the model. All analyses were conducted using Stata V.16.1.

## RESULTS

A total of 405 patients with a primary diagnosis of PsA and 1422 patients with a primary diagnosis of AS were analysed. Twenty-seven per cent (n=109) of the patients with PsA had axial involvement as per the treating

rheumatologist, and 9% (n=127) of patients with AS had current or a history of skin psoriasis (online supplemental figure 1). Ninety-six per cent (1369/1422) of patients with a primary diagnosis of AS and 100% of AS with psoriasis patients fulfilled the mNYc for AS and the ASAS classification criteria (imaging arm) for axSpA when applied retrospectively. 60% (244/405) patients with a primary diagnosis of PsA fulfilled the CASPAR criteria for PsA when applied retrospectively with variables other than rheumatoid factor and imaging data which were not collected systematically. CASPAR criteria were applied taking into account the following variables: inflammatory back pain, peripheral disease or enthesitis as entry criterion and current or history of psoriasis, family history of psoriasis, dactylitis and nail disease as major and minor criteria. A sensitivity analysis comparing relevant characteristics (excluding variables used for the classification criteria) did not show significant differences between patients with CASPAR-positive and CASPAR-negative PsA (online supplemental table 1).

### Clinical and radiographical axial characteristics of the whole PsA cohort

Of the whole PsA cohort, 127/405 (31.5%) reported a history of inflammatory back pain or alternating buttock pain. Cervical pain was present in 20/405 (5%) of the whole PsA cohort. Pelvic X-rays were available in 395/405 (98%) of patients with PsA with 63% of patients (n=249) having normal SIJ as scored by the local reader (BASRI=0). A total of 91/395 (23%) had definite sacroiliitis (BASRI ≥2) with 8%, and 4% scored as BASRI grade III and IV, respectively. Complete sets of spine X-rays (ie, cervical and lumbar spine) were available in 385/405 (95%), of which 296 patients (76%) were scored as having a normal lumbar spine and 295 patients (76%) had a normal cervical spine. BASRI of ≥2 was reported in 12% of lumbar radiographs and in 11% of cervical radiographs. Cervical spine abnormalities were scored in 5/39 (13%) of subjects with definite sacroiliitis and no changes in the lumbar spine. In patients who reported a history of inflammatory back pain or alternating buttock pain (127/405), 59/127 (46.5%) had definite sacroiliitis (BASRI≥2) of whom 26/59 (44%) had associated spondylitic changes (BASRI ≥2). Isolated spondylitis was identified in 21 patients with PsA (6%). Six patients were classified as axial PsA in the absence of IBP, radiographical sacroiliitis or radiographical spondylitis. Of these, three had a history of cervical pain and the other three had low-grade sacroiliitis (grade 1).

### Comparison of clinical and radiographical characteristics of axial PsA and AS with psoriasis

Of the 109 patients classified as axial PsA (27% of the whole PsA cohort), 86.2% (94/109) had a mixed (peripheral+axial) and 13.8% (15/109) a pure axial phenotype. Demographic, clinical and radiographical variables comparing axial PsA and AS with psoriasis are presented in table 1. Patients with axial PsA were more frequently women (37.6% vs 21.3%, p=0.006) and had a shorter disease duration (7 vs 9 years, p=0.04) and diagnostic delay (1.0 vs 3.5 years, p=0.005) when compared with patients with AS with psoriasis. Inflammatory back pain (93.7% vs 78.9%, p<0.001), alternating buttock pain (63.2% vs 38%, p<0.001) and uveitis (12.8% vs 2.8%, p=0.005) were more frequently reported in the AS with psoriasis group, while peripheral arthritis (78.0% vs 58.1%, p=0.001) and nail involvement (43.1% vs 25.8%, p=0.005) were more frequently found in the axial PsA population. BASRI scores in SIJs, lumbar and cervical spine were higher in the AS with psoriasis group when compared with the axial PsA group (p<0.001). A sensitivity analysis using a radiographical definition of axial PsA (PsA diagnosis and definite SIJ involvement in pelvic X-rays) showed the same results when compared with AS with psoriasis (online supplemental table 2).

### Effect of psoriasis in patients with AS compared with axial PsA

Participants with a primary diagnosis of AS were then divided according to personal history of psoriasis. Clinical, demographic, laboratory and radiographical findings from patients with AS with psoriasis (n=127), AS with absent history of psoriasis (n=1289) and axial PsA (n=109) are presented in online supplemental table 3. Psoriasis in patients with AS conferred a higher BMI (27.8 vs 26.6, p=0.012) as well as higher likelihood of presenting with dactylitis (24.6% vs 3.3%, p<0.001), peripheral arthritis (58.1% vs 30.4%, p<0.001) and nail disease (25.8% vs 0.4%, p<0.001). HLA-B27 positivity was higher in the AS group with no psoriasis (84.7% vs 66.7%, p<0.001). Differences between axial PsA compared with AS with no psoriasis were consistent with previous comparison (axial PsA vs AS with psoriasis) and shown in online supplemental table 2,3.

### Effect of HLA-B27 in axial PsA

Clinical, demographic, laboratory and radiographical findings from patients with axial PsA subdivided by HLA-B27 status are presented in table 2. The only significant differences between HLA-B27-positive and HLA-B27-negative axial PsA were the presence of family history of SpA (27% vs 9%, p=0.022) and a higher percentage of patients with a diagnosis of skin psoriasis made before the SpA diagnosis in the HLA-B27-negative subgroup (95% vs 63%, p=0.002). When comparing axial PsA divided by HLA-B27 with AS with psoriasis, patients with HLA-B27-negative axial PsA reported less inflammatory pain (78% vs 93.7%, p=0.002), were more likely to present with psoriasis before SpA onset (95% vs 77%, p=0.02) and had less structural damage compared with AS with psoriasis. By contrast, HLA-B27-positive axial PsA shared similar clinical characteristics with AS and psoriasis patients although a lower BASRI score when evaluating structural damage. Additional analysis were performed comparing HLA-B27-negative axial PsA versus HLA-B27-negative AS with psoriasis and HLA-B27-positive axial PsA versus HLA-B27-positive AS with psoriasis (online supplemental table 4), which showed less inflammatory back pain/

**Table 1** Comparison of demographic, clinical and radiographical characteristics between axial PsA and AS with psoriasis

| Variable | Axial PsA N=109 | AS with psoriasis N=127 | P value |
|---|---|---|---|
| Demographic characteristics | | | |
| Age (years), mean (SD) | 50.1 (12.9) | 49.9 (12.6) | 0.89 |
| Age at diagnosis (years), mean (SD) | 42.2 (13.9) | 37.9 (12.8) | 0.016 |
| Sex (female), n (%) | 41 (37.6) | 27 (21.3) | 0.006 |
| Disease duration (years), median (IQR), mean (SD) | 7.0 (2.5–13.0) | 9.0 (5.0–18.0) | 0.040 |
| Diagnostic delay (years),* median (IQR), mean (SD) | 1.0 (0.0–5.0), 4.7 (8.0) | 3.5 (0.0–11.0), 7.2 (8.4) | 0.005 |
| BMI, mean (SD) | 27.8 (5.6) | 27.8 (5.3) | 0.99 |
| Family history of SpA, n (%) | 14/97 (14.4) | 19/113 (16.8) | 0.64 |
| Clinical characteristics, n (%) | | | |
| Cervical pain | 12/109 (11.0) | 21/127 (16.5) | 0.22 |
| Inflammatory back pain | 92/109 (84.4) | 121/127 (95.3) | 0.005 |
| Alternating buttock pain | 41/108 (38.0) | 79/125 (63.2) | <0.001 |
| Anterior uveitis | 3/109 (2.8) | 16/125 (12.8) | 0.005 |
| Inflammatory bowel disease | 1/108 (0.9) | 5/127 (3.9) | 0.14 |
| Dactylitis | 37/109 (33.9) | 31/126 (24.6) | 0.12 |
| Enthesitis | 38/108 (35.2) | 49/125 (39.2) | 0.53 |
| Peripheral arthritis | 85/109 (78.0) | 72/124 (58.1) | 0.001 |
| Nail disease | 47/109 (43.1) | 32/124 (25.8) | 0.005 |
| Psoriasis before SpA onset | 60/68 (88) | 64/83 (77) | 0.076 |
| Laboratory findings | | | |
| HLA-B27, n (%) | 26/86 (30) | 62/93 (67) | <0.001 |
| CRP (mg/L), median (IQR) | 9.3 (16.0) | 9.3 (15.9) | 0.99 |
| ESR (mm/hour), median (IQR) | 16.6 (17.3) | 19.1 (16.4) | 0.26 |
| Radiographical findings | | | |
| Definite sacroiliitis (BASRI ≥2), n (%) | 60/109 (55.0) | 122/122 (100.0) | <0.001 |
| Isolated spondylitis (no sacroiliitis), n (%) | 11/104 (10.6) | 0 (0) | <0.001 |
| Any radiographical finding, n (%) | 71/104 (68.3) | 122/122 (100.0) | <0.001 |
| BASRI sacroiliac joint, median (IQR) | 2.0 (0.0–3.0) | 3.0 (2.0–4.0) | <0.001 |
| BASRI lumbar, median (IQR) | 0.0 (0.0–2.0) | 2.0 (1.0–3.0) | <0.001 |
| BASRI cervical, median (IQR) | 0.0 (0.0–1.0) | 1.0 (0.0–3.0) | <0.001 |
| PROs | | | |
| BASDAI, median (IQR) | 4.2 (2.2–6.4) | 4.1 (2.4–6.4) | 0.77 |
| BASFI, median (IQR) | 3.2 (1.1–5.4) | 3.8 (1.7–6.6) | 0.12 |
| ASDAS-CRP, median (IQR) | 2.4 (1.6–3.3) | 2.7 (1.9–3.5) | 0.28 |

*Time from symptom onset to diagnosis.
AS, ankylosing spondylitis; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASRI, Bath Ankylosing Spondylitis Radiology Index; BMI, body mass index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; PRO, patient-reported outcome; PsA, psoriatic arthritis; SpA, spondyloarthritis.

alternating back pain and radiographical damage in axial PsA regardless of HLA-B27 status when compared with the axSpA population with psoriasis. HLA-B27-negative AS with patients with psoriasis had more cervical pain, dactylitis and presented more frequently with psoriasis before the axSpA diagnosis compared with HLA-B27-positive AS with psoriasis.

### Demographic, clinical and radiographical factors associated with a clinician diagnosis of AS with psoriasis (rather than axial PsA)

Univariable associations are shown in online supplemental table 5. In the multivariable analysis, patients with AS and psoriasis were independently associated with HLA-B27 positivity (OR 3.34, 95% CI 1.42 to 7.85) and

**Table 2** Comparison of demographic, clinical and radiographical characteristics between axial PsA subdivided by HLA-B27 status and AS with psoriasis

| Variable | Axial PsA B27 positive N=26 | Axial PsA B27 negative N=60 | P value | AS with psoriasis N=127 | Axial PsA B27 positive versus AS with psoriasis *P value* | Axial PsA B27 neg versus AS with psoriasis *P value* |
|---|---|---|---|---|---|---|
| Demographic characteristics | | | | | | |
| Age, mean (SD) | 45.1 (11.6) | 49.7 (12.2) | 0.11 | 49.9 (12.6) | 0.075 | 0.92 |
| Age at diagnosis, mean (SD) | 35.6 (11.1) | 42.6 (13.6) | 0.024 | 37.9 (12.8) | 0.40 | 0.025 |
| Sex (female), n (%) | 11/26 (42) | 25 (43) | 0.93 | 27 (21.3) | 0.024 | 0.002 |
| Disease duration, median (IQR) | 7.0 (2.0–15.0) | 7.0 (2.0–15.0) | 0.66 | 9.0 (5.0–18.0) | 0.36 | 0.025 |
| Diagnostic delay, median (IQR) | 1.0 (0.0, 4.0) | 1.0 (0.0, 4.0) | 0.91 | 3.5 (0.0, 11.0) | 0.081 | 0.047 |
| BMI, mean (SD) | 28.6 (6.3) | 26.5 (5.2) | 0.17 | 27.8 (5.3) | 0.27 | 0.44 |
| Family history of SpA, n (%) | 6/26 (27) | 5/60 (9) | 0.022 | 19/113 (16.8) | 0.16 | 0.18 |
| Clinical characteristics, n (%) | | | | | | |
| Cervical pain | 3/26 (12) | 6/60 (10) | 0.83 | 21/127 (16.5) | 0.52 | 0.24 |
| Inflammatory back pain | 24/26 (92.3) | 47/60 (78) | 0.27 | 121/127 (95.3) | 0.54 | 0.002 |
| Alternating buttock pain | 12/26 (46) | 20/60 (33) | 0.26 | 79/125 (63.2) | 0.11 | <0.001 |
| Anterior uveitis | 2/26 (8) | 1/60 (2) | 0.16 | 16/125 (12.8) | 0.46 | 0.014 |
| Inflammatory bowel disease | 1/26 (4) | 0/60 (0) | 0.13 | 5/127 (3.9) | 0.98 | 0.12 |
| Dactylitis | 5/26 (19) | 22/60 (37) | 0.11 | 31/126 (24.6) | 0.56 | 0.088 |
| Enthesitis | 10/26 (38) | 20/60 (33) | 0.65 | 49/125 (39.2) | 0.94 | 0.44 |
| Peripheral arthritis | 18/26 (69) | 47/60 (78) | 0.37 | 72/124 (58.1) | 0.29 | 0.007 |
| Nail disease | 9/26 (35) | 27/60 (45) | 0.37 | 32/124 (25.8) | 0.36 | 0.009 |
| Psoriasis before SpA onset | 10/16 (63) | 36/38 (95) | 0.002 | 64/83 (77) | 0.16 | 0.020 |
| Laboratory findings | | | | | | |
| CRP (mg/L), median (IQR) | 10.5 (17.5) | 9.7 (17.5) | 0.85 | 9.3 (15.9) | 0.73 | 0.87 |
| ESR (mm/hour), median (IQR) | 19.4 (23.5) | 16.5 (16.4) | 0.53 | 19.1 (16.4) | 0.95 | 0.33 |
| Radiographical findings, n (%) | | | | | | |
| Definite sacroiliitis (BASRI ≥2) | 15/26 (58) | 31/60 (52) | 0.61 | 122/122 (100.0) | <0.001 | <0.001 |
| Isolated spondylitis (no sacroiliitis) | 3/6 (50) | 6/18 (33) | 0.47 | 0 (0) | <0.001 | <0.001 |
| Any radiographical finding, n (%) | 18/25 (72) | 37/56 (66) | 0.60 | 122/122 (100.0) | <0.001 | <0.001 |
| BASRI sacroiliac joint, median (IQR) | 2.0 (1.0–3.0) | 2.0 (0.0–3.0) | 0.55 | 3.0 (2.0–4.0) | <0.001 | <0.001 |

Continued

**Table 2** Continued

| Variable | Axial PsA B27 positive N=26 | Axial PsA B27 negative N=60 | P value | AS with psoriasis N=127 | Axial PsA B27 positive versus AS with psoriasis *P value* | Axial PsA B27 neg versus AS with psoriasis *P value* |
|---|---|---|---|---|---|---|
| BASRI lumbar, median (IQR) | 0.0 (0.0–1.0) | 0.0 (0.0–1.0) | 0.55 | 2.0 (1.0–3.0) | <0.001 | <0.001 |
| BASRI cervical, median (IQR) | 0.0 (0.0–0.0) | 0.0 (0.0–1.0) | 0.19 | 1.0 (0.0–3.0) | <0.001 | <0.001 |
| PROs | | | | | | |
| BASDAI, median (IQR) | 4.6 (2.2–6.4) | 4.4 (2.3–6.4) | 0.91 | 4.1 (2.4–6.4) | 0.92 | 0.99 |
| BASFI, median (IQR) | 2.0 (1.0–4.8) | 2.3 (1.1–5.4) | 0.46 | 3.8 (1.7–6.6) | 0.086 | 0.16 |
| ASDAS-CRP, median (IQR) | 2.6 (2.0–3.2) | 2.3 (1.5–3.5) | 0.60 | 2.7 (1.9–3.5) | 0.77 | 0.27 |

AS, ankylosing spondylitis; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASRI, Bath Ankylosing Spondylitis Radiology Index; BMI, body mass index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; PRO, patient-reported outcome; PsA, psoriatic arthritis.

lumbar structural damage scored by BASRI (OR 2.14, 95% CI 1.4 to 3.19) (figure 1).

## DISCUSSION

This study explored the axial phenotype of a historic multicentre SpA cohort including patients with AS/r–axSpA and PsA. Our results show that there is an heterogenous understanding of axial involvement in PsA with a combination of clinical and radiographical findings in the SIJs and lumbar/cervical spine found in what rheumatologists consider axial PsA, which underscores the need for a unifying definition. Rheumatologists have often wondered whether axial PsA is part of the axSpA spectrum, where 10% of the population is reported to have concomitant skin psoriasis, or whether it represents a distinct PsA subset. When comparing the axial PsA population with that of patients with AS who have concomitant psoriasis in this study, significant differences were seen in clinical presentation with more severe radiographical findings seen in the AS with psoriasis group. Further, when subdividing the axial PsA population according to HLA-B27 status, the clinical and imaging characteristics of HLA-B27-positive axial PsA appeared to be more similar to that of patients with AS with psoriasis although with significantly higher levels of structural damage seen in the latter. These findings suggest that axial PsA as understood by clinicians appears to be overall and regardless of HLA-B27 status associated with less radiographical progression than AS. Interestingly, no differences in PROs were seen in the respective group comparisons.

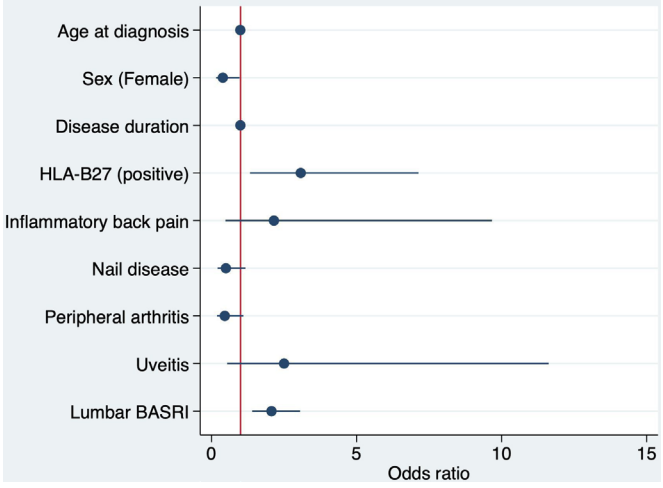


**Figure 1** Final multivariable model with factors associated with ankylosing spondylitis with psoriasis versus axial psoriatic arthritis (ref). BASRI, Bath Ankylosing Spondylitis Radiology Index.

The main weakness of our study is the lack of a standardised definition of axial PsA. Yet, a number of studies have also compared cohorts of axial PsA with axSpA, using different definitions that must be taken into account when interpreting their results. In the Toronto study,[9] axial PsA was defined as all patients with PsA that had SIJ radiographical changes fulfilling the mNYc. Jadon *et al* used the same definition but also included spine syndesmophytes as criteria to classify patients as axial PsA[7]; however, they did not differentiate axial PsA from AS with psoriasis. Fragoulis *et al* used a combination of inflammatory axial symptoms and imaging findings (SIJ/lumbar spine X-ray or MRI).[6] A recent study by Benavent *et al*[5] used a similar approach to our study, basing the classification of axial PsA on the opinion of the treating rheumatologist. However, the main difference and a strength of our study is the complete characterisation of

our cohort with availability of clinical data together with pelvic, lumbar and cervical X-ray data for all patients, including those not classified as axial PsA. Interestingly, and despite a different axial PsA definition used in the Toronto study,[9] we found similar results when comparing axial PsA and AS with psoriasis in our study population. In both studies, male prevalence, younger age, positive HLA-B27, presence of inflammatory back pain, higher SIJ radiographical scores and uveitis were more frequently reported in the AS with psoriasis cohort, as expected in a primary AS/r-axSpA population. In addition, we report higher BASRI scores in the lumbar and cervical spine in those patients with AS and psoriasis. Although these data were not available in the Toronto study, the authors reported a higher BASMI in patients with AS with psoriasis, which is known to correlate well with radiographical damage.[16]

When looking at HLA-B27, a higher prevalence was found in the AS group (with and without psoriasis) when compared with the PsA group, as expected. Further subanalysis showed that HLA-B27 was found more often in patients with AS without psoriasis compared with those with a history of psoriasis contrary to findings reported in the Toronto cohort where a similar prevalence of HLA-B27 was seen between the groups, although we note that no pairwise comparison was reported in that study.[9] This difference between the two studies could be related to the different inclusion criteria used, or to possible misclassification in both studies. Additionally, we found that the subgroup of patients with AS and psoriasis resembled that of axial PsA with a higher BMI compared with AS without psoriasis (not reported in the Toronto study). Likewise, the presence of skin psoriasis in AS seems to modify the clinical phenotype with more peripheral disease, dactylitis and nail disease seen in this subgroup, likely driven by genetic factors other than HLA-B27 as shown by its lower prevalence when compared with AS with no skin psoriasis. Another interesting observation is that patients with HLA-B27-negative AS and axial PsA were more likely to present with skin psoriasis before the onset of articular symptoms, resembling the presentation of peripheral PsA as compared with AS/r-axSpA. Similarly, patients with HLA-B27-positive axial PsA reported an onset of articular symptoms before that of skin psoriasis as seen in axial SpA or AS. Further, patients with HLA-B27-negative AS presented with more dactylitis and cervical pain compared with patients with HLA-B27-positive AS suggesting a more similar phenotype to PsA.

From an imaging viewpoint, patients with axial PsA had less radiographical damage than AS with psoriasis regardless of HLA-B27 status, suggesting again the presence of other genetic drivers. Coates *et al* reported the association of HLA-B27 and radiographical expression of axSpA (including both AS and axial PsA) with more severe radiographical damage including higher grades of sacroiliitis and more marginal syndesmophytes and symmetry seen in HLA-B27-positive patients (regardless of clinical diagnosis of axSpA or PsA).[17] However, no difference was seen in the prevalence of SIJ symmetry and non-marginal syndesmophytes considered typical radiographical findings of axial PsA, suggesting the existence of factors other than HLA-B27 driving this latter phenotype.

To our knowledge, this is the largest study benefitting from a complete imaging data set comprising cervical, lumbar and pelvic X-rays for all patients of a PsA cohort independent from their clinical phenotype (peripheral or axial) and comparing it with AS with psoriasis. Also, we have further divided the axial PsA cohort by HLA-B27 status shown in previous reports to be relevant in the radiographical and clinical phenotype.[10 17] The main limitation of our study is its cross-sectional nature and, as mentioned before, the fact that the primary diagnoses were based on physician assessment as the study predates the publication of the ASAS[18] or CASPAR classification criteria.[15] In common with other studies, however, and reflecting the lack of validated definitions and criteria, axial involvement was defined by the rheumatologist. Another limitation is the fact that our study compares the 'full spectrum' of axial PsA with the axSpA radiographical population (AS). Ideally, a population comprising the full spectrum of axSpA, including non-radiographical disease, would have been desirable but this were not included in REGISPONSER, which predates the publication of the ASAS classification criteria.[18] In the absence of a clinical or imaging definition of axial PsA, we decided to use the rheumatologist definition rather than focus on the presence of radiographical sacroiliitis in order to also encompass those patients with axial PsA, which may have an isolated lumbar/cervical involvement without sacroiliitis.[7] Our approach was validated by a subsequent sensitivity analysis using radiographical sacroiliitis (BASRI ≥2) as defining criteria which did not show significant differences between the groups when compared with clinician definition. Another limitation is the lack of central reading of the radiographs with multiple readers involved. Yet, it is important to note that the local readers participating in the REGISPONSER registry are rheumatologists with an interest in SpA, members of the Spanish Spondyloarthropathies Study Group of the Spanish Society of Rheumatology, who underwent a 2 -day training in the study processes, well versed in the reading of spinal and SIJ radiographs both in clinical practice and in research settings, and as such represent a highly specialised group of clinicians.[13] This in itself could be considered a strength as it reflects clinical practice in a specialist setting and allows us to encompass the whole spectrum of clinical and radiographical findings described in axial PsA.[3] In this line, as X-rays were scored using BASRI, we do not have details on the morphology of syndesmophytes or posterior element involvement, which has been shown as a difference in radiological presentation between AS and axial PsA.[19]

Finally, HLA-B27 data were limited with 23 (21%) missing values in the axial PsA group, similar to the AS with psoriasis group (n=34, 27%) reflecting clinical practice where HLA-B27 testing is not universal in PsA

cohorts. Nevertheless, we found significant results when subdividing the cohort according to HLA-B27 despite reduced numbers suggesting that HLA-B27 modulates the clinical phenotype and imaging morphotype of axial PsA. This is in accordance with a previous MRI study where HLA-B27-positive axial PsA subjects with active inflammatory back pain had more bone marrow oedema findings than the HLA-B27-negative group, although less than axSpA.[20] Similarly, the presence of psoriasis appears to modulate an AS subgroup, more likely to be HLA-B27 negative and with clinical characteristics more akin to those of PsA. Whether these findings represent a misclassification of the study population or a true phenotypical difference will only be answered by a systematic evaluation of the genotype underpinning these cohorts. Currently available Genome-Wide Association studies in PsA lack fully detailed radiographical and clinical data that could bring light to a better definition of axial PsA, and future research efforts should be aimed to address this crucial question.[21 22]

In conclusion, axial PsA appears to be a distinct phenotype within the PsA disease spectrum with different clinical and radiographical characteristics when compared with AS/r-axSpA with and without psoriasis. Axial PsA is largely independent of HLA-B27 and presents different clinical and radiographical manifestations when compared with AS with psoriasis, highlighting the need for a better understanding of other genetic drivers to define specific classification criteria for this entity in order to allow for better management of these patients.

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