

Differential Features Between Primary Ankylosing Spondylitis and Spondylitis Associated with Psoriasis and Inflammatory Bowel Disease

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ABSTRACT. Objective. To describe differential characteristics of axial involvement in ankylosing spondylitis (AS) as compared with that seen in psoriatic arthritis (PsA) and inflammatory bowel disease (IBD) in a cohort of Ibero-American patients.

Methods. This study included 2044 consecutive patients with spondyloarthritis (SpA; ESSG criteria). Demographic, clinical, disease activity, functional ability, quality of life, work status, radiologic, and therapeutic data were evaluated and collected by RESPONDIA members from different Ibero-American countries between June and December 2006. Patients selected for analysis met modified New York criteria (mNY) for AS.

Results. A total of 1264 patients met the New York criteria for AS: 1072 had primary AS, 147 had psoriatic, and 45 had IBD-associated spondylitis. Median disease duration was comparable among the 3 patient groups. Patients with primary AS were significantly younger ($p = 0.01$) and presented a higher frequency of males ($p = 0.01$) than the other 2 groups. Axial manifestations such as inflammatory back pain and sacroiliac pain were significantly more frequent in patients with primary AS ($p = 0.05$) versus other groups, whereas frequency of dactylitis, enthesitis, and peripheral arthritis was more common in patients with psoriatic spondylitis ($p = 0.05$). Spinal mobility was significantly more limited in patients with primary AS versus the other 2 groups ($p = 0.0001$). Radiologic changes according to BASRI total score were equally significant in primary AS. Disease activity (BASDAI), functional ability (BASFI), and quality of life (ASQoL) scores were comparable in the 3 groups.

Conclusion. Patients with primary AS had more severe axial involvement than those with spondylitis associated with psoriasis or IBD. Functional capacity, disease activity, and quality of life were comparable among the groups studied. (First Release June 1 2011; *J Rheumatol* 2011;38:1656–60; doi:10.3899/jrheum.101049)

Key Indexing Terms:

ANKYLOSING SPONDYLITIS
INFLAMMATORY BOWEL DISEASE

PSORIASIS
AXIAL INVOLVEMENT

Involvement of the axial skeleton, a characteristic feature of ankylosing spondylitis (AS), may also be present in patients

with psoriatic arthritis (PsA) and inflammatory bowel disease (IBD). The initial descriptions by Wright¹ and Wright and

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Moll² identified the presence of inflammatory low back pain as a form of clinical presentation of these diseases. To date, there is no accepted definition for axial involvement in PsA³. Different definitions have been advanced, from isolated radiologic changes of unilateral sacroiliitis or presence of syndesmophytes to use of the New York modified classification criteria for AS^{4,5}. Studies have evaluated clinical and radiologic differences between primary AS and spondylitis associated with psoriasis and IBD, and have shown that psoriatic spondylitis is generally less severe regarding clinical manifestations, mobility impairments, and radiologic features^{6,7,8,9}.

The aim of this study was to describe differential features between patients diagnosed with primary AS and patients with PsA and IBD (ulcerative colitis and Crohn's disease) with axial involvement, from a large Ibero-American cohort with spondyloarthritis (SpA).

Our results derive from a cross-sectional analysis of data gathered from the point of entry into the database.

MATERIALS AND METHODS

A total of 2044 consecutive patients with SpA according to the European Spondylarthropathy Study Group (ESSG) classification criteria¹⁰ were included into the database. Demographic and clinical data were collected during a 6-month period in 2006 in a multinational, multicenter cohort designated as the RESPONDIA (Registro Iberoamericano de Espondiloartropatías). RESPONDIA includes 100 rheumatologists from Argentina, Brazil, Costa Rica, Chile, Ecuador, Mexico, Peru, Uruguay, and Venezuela for Latin America, and Portugal. The RESPONDIA database is supported by the Spanish Society of Rheumatology and included around 2000 Latin American patients with SpA¹¹.

For the purpose of our analysis, patients with primary AS (New York modified criteria)¹², PsA (Moll and Wright)², and IBD were included only if they met the modified New York criteria for AS. The variables analyzed in this study were disease duration, tender and swollen joint count, and visual analog scales (VAS) for pain and disease activity (patient and physician). Present indications or history of peripheral arthritis were recorded and 68 tender and 66 swollen joint counts were assessed in each patient. Laboratory tests included erythrocyte sedimentation rate (ESR, Westergren) and C-reactive protein (CRP, by different methods); clinimetric evaluations included the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)¹³, Functional Index (BASFI)¹⁴, and Metrology Index (BASMI)¹⁵; spinal mobility measurements included the occiput-to-wall distance, thoracic expansion, finger-to-floor distance, modified Schober's test, and lateral spinal flexion. For enthesitis, the Maastricht Ankylosing Spondylitis Enthesitis Score¹⁶ was used. Health related quality of life assessment was carried out with the ASQoL questionnaire¹⁷. All questionnaire evaluations were carried out with cross-culturally adapted instruments for each country. For radiologic evaluation we used the Bath Ankylosing Spondylitis Radiographic Index (BASRI) for the spine (BASRI-spine), which includes the lumbar and cervical spine and sacroiliac joints, BASRI for the hips (BASRI-hips), and BASRI-total (BASRI-spine plus BASRI-hips)¹⁸. Cervical spine involvement was determined by means of the goniometric measurement of cervical rotation (defined as < 20°, 20°–70°, and > 70°). Shoulder involvement was evaluated by the presence of pain and/or limitation of motion. Hip involvement was also assessed by clinical (presence of pain and/or limitation) and radiologic evaluations (classified as normal, suspicious, mild, moderate, or severe) regarding BASRI-hips. Radiography studies were performed in all patients at entry to the study or within 6 months prior to entry.

Special training and reliability exercise workshops for clinimetric, radiologic, and protocol procedures were performed by site investigators at a national or regional level, and were coordinated by the same 2 experts (EC-E

and JV-M). Radiography studies of sacroiliac joints were performed according to routine techniques, but radiograph reading was not centralized. Consensus about radiograph reading was reached during the training workshops, prior to onset of the study. Degree of skin and nail involvement was not specifically evaluated in the psoriatic patients. Goniometers were not standardized across sites and countries.

Definitions of variables were as specified in the ESSG criteria¹⁰. Work disability was assessed by direct questioning of patients and was graded into 3 broad categories: absent, and if present as partial or total.

Statistical analysis. Categorical variables were compared by chi-square and Fisher's exact test, and continuous variables by ANOVA or Kruskal-Wallis tests. Post hoc analyses were performed using Tukey test or Games-Howell test, depending on variance distributions. Analysis of data was adjusted for age, sex, and disease duration in order to compare clinical features between patient groups using multivariate linear regression models. A value of $p < 0.05$ was considered significant. SPSS version 15 was used for the analysis.

RESULTS

From a total of 2044 patients selected according to the ESSG criteria (including 403 with PsA and 87 with IBD-associated arthritis), a total of 1264 patients met the New York criteria for AS. Specifically, 1072 (84.8%) had primary AS, 147 (11.6%) had psoriatic spondylitis, and 45 (3.6%) had IBD-associated spondylitis. In the primary AS cohort, there was a significant predominance of male sex, 817 (76%) compared to 85 (58%) in psoriatic spondylitis and 22 (49%) in IBD ($p = 0.01$). Median age was significantly higher in the IBD cohort, 49 years [interquartile range (IQR) 40–57], and in psoriatic spondylitis 48 years (IQR 40–58) compared to 42 years (IQR 33–50) in patients with primary AS ($p = 0.01$).

There were no significant differences among groups regarding family history of SpA and work disability. It is noteworthy that median disease duration since clinical diagnosis was comparable among the groups — median 6 years in primary AS and psoriatic spondylitis and 4 years in IBD ($p =$ non-significant). However, disease duration since first symptoms was significantly greater between primary AS patients and those with psoriatic and IBD-associated spondylitis ($p < 0.01$; Table 1). Evaluating clinimetric data, there was a significantly higher limitation on the different measures of BASMI in patients with primary AS, reflecting greater involvement of the axial skeleton in such patients. Modified Schober test data were significantly lower in primary AS patients than in the other groups; whereas occiput-to-wall and finger-to-floor distances were greater and BASRI-total and BASRI-spine scores were significantly higher in patients with primary AS (Table 2).

The percentage of patients with cervical rotation greater than 70° was lower (28%) in the primary AS group compared to psoriatic and IBD spondylitis (47% and 49%, respectively; $p = 0.001$). Similarly, the frequency and severity of hip involvement in patients with primary AS were significantly greater than in the other groups (Table 3). There were no significant differences of shoulder involvement among groups.

Overall, patients with primary AS had higher frequencies of axial and sacroiliac joint pain than the other groups; and patients with psoriatic spondylitis more frequently had upper and lower limb arthritis, dactylitis, and enthesitis (Figure 1).

Table 1. Sociodemographic features of patients with axial involvement from the RESPONDIA group.

Variables	AS, n = 1072	Psoriatic Spondylitis, n = 147	IBD Spondylitis, n = 45	p
Male, n (%)	817 (76)	85 (58)	22 (49)	0.01
Age, yrs, median (IQR)	42 (33–50)	48 (40–58)	49 (40–57)	0.01
Disease duration at diagnosis, yrs, median (IQR)	6 (2–12)	6 (2–11)	4 (2–8)	NS
Disease duration at first symptom, yrs, median (IQR)	14 (7–23)	10.5 (5–17)	7 (4–15)	0.01
SpA family history, n (%)	199 (19)	25 (17)	5 (11.1)	NS
Work disability, n (%)	67 (6.3)	10 (6.8)	0	NS

AS: ankylosing spondylitis; IBD: inflammatory bowel disease; SpA: spondyloarthropathy; IQR: interquartile range; NS: nonsignificant.

Table 2. Spinal mobility and radiological damage in patients with axial involvement from the RESPONDIA Group. All variables were adjusted for disease duration.

Variables	AS, n = 1072	Psoriatic Spondylitis, n = 147	IBD Spondylitis, n = 45	ANOVA p
Schober test, cm, mean ± SD	2.7 ± 2	3.8 ± 1.8	3.9 ± 2.1	0.001
Occiput-to-wall, cm, mean ± SD	6.5 ± 7.6	2.9 ± 5.2	3.8 ± 6.7	0.001
Finger-to-floor, cm, mean ± SD	28.2 ± 20	20 ± 20	21 ± 19	0.001
BASRI-total, mean ± SD	8.2 ± 4	6.1 ± 4	5.6 ± 4.4	0.001
BASRI-spine, mean ± SD	7 ± 3.2	5.2 ± 3.1	4.8 ± 3.7	0.001

BASRI: Bath Ankylosing Spondylitis Radiographic Index; other definitions given in Table 1.

Table 3. Cervical and hip involvement in patients with axial involvement from the RESPONDIA Group. All variables adjusted for disease duration.

Variables	AS, n = 1072	Psoriatic Spondylitis, n = 147	IBD Spondylitis, n = 45	p
Cervical rotation < 20°, n (%)	228 (21)	20 (14)	8 (18)	0.001
Cervical rotation 20°–70°, n (%)	459 (43)	46 (31)	15 (33)	0.001
Cervical rotation > 70°, n (%)	303 (28)	69 (47)	22 (49)	0.001
Hip involvement, n (%)	473 (44)	43 (29)	12 (27)	0.001

Definitions as in Table 1.

There were no differences regarding frequency of tarsal involvement (tarsitis) among the groups ($p = 0.228$).

ESR evaluated in 1081 patients showed a median value of 20 mm/h in the 3 groups of patients; determination of CRP was not analyzed due to the small number of patients tested and different methods used for measurement.

Of note, there were no significant differences in BASFI, BASDAI, and ASQoL scores among groups (Table 4).

Regarding treatment, patients with psoriatic spondylitis used disease-modifying antirheumatic drugs with more frequency (mostly methotrexate and leflunomide), IBD patients used sulfasalazine, and patients with primary AS used nonsteroidal anti-inflammatory drugs. Only 5.7% of patients of this cohort received treatment with tumor necrosis factor- α inhibitors.

DISCUSSION

Spondyloarthritides comprise a group of heterogeneous diseases that share certain clinical, radiologic, and serologic fea-

tures. Inflammatory axial involvement, a characteristic feature of AS, may also be present in patients with PsA and IBD.

Although there are different opinions regarding the definition of axial involvement in PsA¹⁹, many authors have shown their interest towards this issue from the initial descriptions reported by Wright and Moll². Axial involvement in PsA patients presents certain characteristics that clearly differentiate it from involvement in AS. These characteristics were first described by Porrini, *et al*²⁰ and later by McEwen, *et al*²¹, who proved that patients with AS and spondylitis associated with IBD presented clinical and radiologic features that differed from those of patients with PsA and reactive arthritis. Gladman, *et al*⁶ and Helliwell, *et al*⁷ confirmed those findings, mainly in regard to the asymmetric involvement and the presence of syndesmophytes of axial disease in PsA, together with the less severe clinical and radiologic involvement in these patients in comparison to patients with primary AS. Recently, Fernández-Sueiro, *et al*²² observed a significant difference

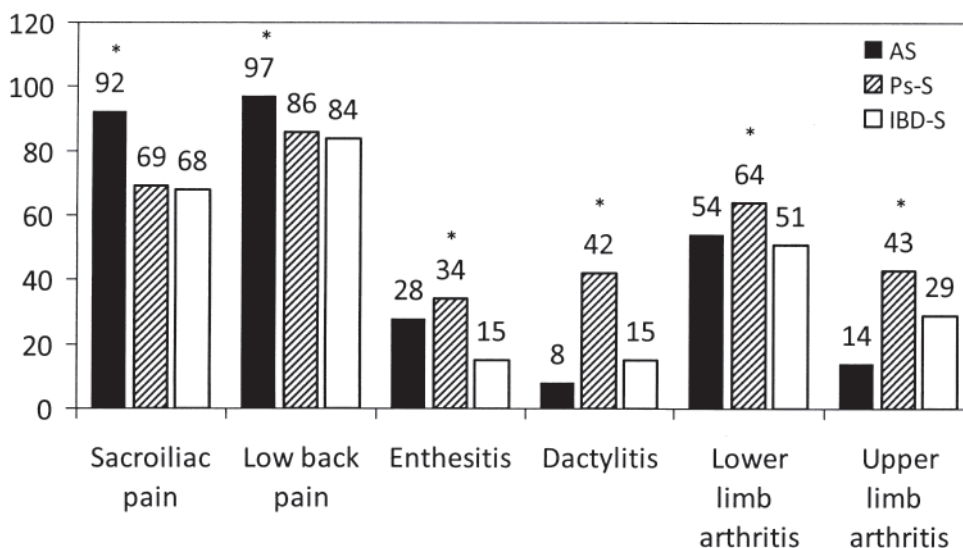


Figure 1. Clinical manifestations in patients with axial involvement from the RESPONDIA group. AS: ankylosing spondylitis; Ps-S: psoriatic spondylitis; IBD-S: inflammatory bowel disease spondylitis. * $p < 0.05$.

Table 4. Disease activity, functional capacity, and quality of life in patients with axial involvement from the RESPONDIA Group. All variables were adjusted for disease duration.

Variables	AS, n = 1072	Psoriatic Spondylitis, n = 147	IBD Spondylitis, n = 45	ANOVA p
BASDAI, mean \pm SD	4.3 \pm 2.3	4.7 \pm 2.5	4.5 \pm 2.5	NS
BASFI, mean \pm SD	4.7 \pm 2.8	4.1 \pm 2.9	4.3 \pm 2.8	NS
ASQoL, mean \pm SD	7.3 \pm 5.2	7.5 \pm 5.5	7.5 \pm 5.5	NS

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; ASQoL: Ankylosing Spondylitis Quality of Life Index; other definitions given in Table 1.

between primary AS and psoriatic spondylitis regarding structural damage evaluated by BASRI-spine and BASRI-total and BASMI measures (occiput-to-wall, thoracic expansion, and modified Schober test).

Different measures for evaluating spinal involvement in AS were developed and validated by different studies²³. The INSPIRE study (International Spondyloarthritis Inter-observer Reliability Exercise)²⁴ revealed that the use of these measures was reproducible in patients with psoriatic spondylitis, and they could be used to determine sensitivity to change in clinical trials of patients with psoriasis and axial involvement.

In our analysis the definition employed for axial involvement was that of the modified New York criteria¹², requiring radiologic sacroiliitis; therefore patients with PsA and cervical spine involvement but without sacroiliac changes could not be included in the analysis.

Even though disease duration since clinical diagnosis was not different between groups, disease duration since first symptoms was significantly longer in patients with primary AS, giving evidence for an important diagnostic delay in this disease.

In our study, patients diagnosed with primary AS presented significantly more severe involvement of axial skeleton,

demonstrated by clinical (measures of spinal mobility) and radiological evaluations (BASRI-spine and BASRI-total scores), as compared to patients with psoriasis and IBD spondylitis. Despite these findings, there were no significant differences of functional capacity, disease activity, and quality of life.

Cervical spine and hip involvement in different series of patients with SpA has been described, where presence of the latter was considered an indicator of a bad functional prognosis. In this study, patients with primary AS showed significantly greater limitation of cervical mobility, reflected by the lower percentage of patients who presented with cervical rotation $> 70^\circ$, compared to psoriatic and IBD spondylitis. Similarly, patients with primary AS presented significantly greater frequency and severity of hip involvement. Also, sacroiliac pain, inflammatory back pain, and alternating buttock pain, as a reflection of greater axial involvement, were more frequent in patients with pure AS.

As determination of HLA-B27 was not mandatory for registration into the database, few patients had such tests, precluding further analysis.

Our data show that patients with primary AS had more

severe axial involvement than the other 2 groups. Of interest, however, disease activity, functional studies, and quality of life did not differ between groups. These findings are in accord with recent reports that psoriatic axial involvement is as disabling as primary AS for 2 reasons: the disease progresses for a long time period, and it brings with it the burden of peripheral arthritis^{25,26}.

Although we used a centralized system of data collection for an international multicenter registry of SpA²⁷ and each investigator was specifically trained in an interobserver reliability exercise, our study has some limitations. Our analysis was based on a cross-sectional study, with patients seen only once. Reading of radiographic studies was not centralized. Axial involvement was radiographically defined by the presence of grade 2 or greater sacroiliitis, but we did not investigate the presence of other characteristic changes of spondylitis at different spinal levels, which in PsA may be present even in the absence of sacroiliac changes²⁸.

Our study is the first to investigate clinical and functional features in a large multicenter, multiethnic cohort. Overall, the data from the Ibero-American SpA cohort confirm the features reported in other series, showing that patients with primary AS present significantly more severe axial involvement, compared to patients with psoriasis and IBD spondylitis. However, there were no differences regarding the impact on functional capacity, disease activity, and quality of life in the different SpA with spinal involvement that were evaluated.

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