

Prevalence of Comorbidities and Risk Factors for Comorbidities in Patients with Spondyloarthritis in Latin America: A Comparative Study with the General Population and Data from the ASAS-COMOSPA Study

Wilson Bautista-Molano, Robert Landewé, Rubén Burgos-Vargas, José Maldonado-Cocco, Anna Moltó, Filip van den Bosch, Rafael Valle-Oñate, Maxime Dougados, and Désirée van der Heijde

ABSTRACT. Objective. Increased risk of comorbidities has been reported in spondyloarthritis (SpA). The objective of this study was to determine the prevalence and risk of developing comorbidities in patients with SpA in 3 Latin American (LA) countries, and to compare that prevalence with the general population. **Methods.** Data were analyzed from 390 patients with SpA enrolled in the Assessment of SpondyloArthritis international Society of Comorbidities in SpA study from Argentina, Colombia, and Mexico. Age- and sex-standardized prevalence (95% CI) was estimated for arterial hypertension (AHT), tuberculosis (TB), and malignancies. Age- and sex-specific data from the general population were obtained from the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study for AHT, the Global TB report, and the GLOBOCAN project for malignancies. Data analyzed for AHT were confined to Colombia and Mexico. The prevalence in patients with SpA was compared with the prevalence in the general population per age- and sex-specific stratum, resulting in standardized risk ratios (SRR).

Results. In total, 64% of the patients with SpA were male, with a mean age of 45 years (SD 14.7). The most common comorbidities in the 3 LA countries were AHT (25.3%, 95% CI 21.2–30.0), hypercholesterolemia (21.5%, 95% CI 17.6–26.0), and osteoporosis (9.4%, 95% CI 6.8–12.9). AHT prevalence in Colombia and Mexico was 21.4% (95% CI 15.4–28.9) and was higher than the general population (12.5%, 95% CI 11.4–13.7), resulting in an SRR of 1.5. TB prevalence in the 3 LA countries was 3.3% (95% CI 1.8–5.7), which was significantly higher than in the general population (0.32%), leading to an SRR of 10.3. The prevalence of malignancies was not increased.

Conclusion. Patients with SpA in LA are at increased risk of AHT and TB in comparison to the general population. While this sample of patients may not be entirely representative of the patient population in each country, a systematic evaluation of these comorbidities in all patients with SpA still may help to monitor these conditions better. (First Release December 15 2017; J Rheumatol 2018;45:206–12; doi:10.3899/jrheum.170520)

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From the Rheumatology Department, Leiden University Medical Center, Leiden, the Netherlands; School of Medicine, Universidad Militar Nueva Granada and Rheumatology Department, Hospital Militar, Bogotá, Colombia; Amsterdam Rheumatology and Clinical Immunology Center, Amsterdam; Zuyderland Medical Center Heerlen, Heerlen, the Netherlands; Servicio de Reumatología, Hospital General de México and Universidad Nacional Autónoma de México, Mexico City, Mexico; School of Medicine, Buenos Aires University and Argentine Rheumatologic Foundation Dr. Osvaldo Garcia Morteo, Buenos Aires, Argentina; Rheumatology B Department, Paris Descartes University, Cochin Hospital, AP-HP; INSERM (U1153): Clinical epidemiology and biostatistics, PRES Sorbonne Paris-Cité, Paris, France; Department of Rheumatology, Ghent University Hospital, Ghent, Belgium.

W. Bautista-Molano, MD, Rheumatology Department, Leiden University Medical Center, and School of Medicine, Universidad Militar Nueva Granada and Rheumatology Department, Hospital Militar; R. Landewé, MD, PhD, Amsterdam Rheumatology and Clinical Immunology Center, and Zuyderland Medical Center Heerlen; R. Burgos-Vargas, MD, Servicio

de Reumatología, Hospital General de México and Universidad Nacional Autónoma de México; J. Maldonado-Cocco, MD, School of Medicine, Buenos Aires University and Argentine Rheumatologic Foundation Dr. Osvaldo Garcia Morteo; A. Moltó, MD, PhD, Rheumatology B Department, Paris Descartes University, Cochin Hospital, AP-HP, and INSERM (U1153): Clinical epidemiology and biostatistics, PRES Sorbonne Paris-Cité; F. van den Bosch, MD, PhD, Department of Rheumatology, Ghent University Hospital; R. Valle-Oñate, MD, School of Medicine, Universidad Militar Nueva Granada and Rheumatology Department, Hospital Militar; M. Dougados, MD, Rheumatology B Department, Paris Descartes University, Cochin Hospital, AP-HP, and INSERM (U1153): Clinical epidemiology and biostatistics, PRES Sorbonne Paris-Cité; D. van der Heijde, MD, PhD, Rheumatology Department, Leiden University Medical Center.

Address correspondence to Dr. W. Bautista-Molano, School of Medicine, Universidad Militar Nueva Granada, Transversal 3 No. 49-00, Bogotá, Colombia. E-mail: wilson.bautista@gmail.com

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Comorbidities are frequently associated with inflammatory rheumatic diseases such as ankylosing spondylitis (AS), psoriatic arthritis (PsA), and rheumatoid arthritis (RA). In addition to the musculoskeletal manifestations for spondyloarthritis (SpA) and SpA-related extraarticular features [psoriasis, uveitis, inflammatory bowel disease (IBD)], patients may also have an increased risk of cardiovascular (CV) events, metabolic syndrome, malignancies, and infections^{1,2,3}. These comorbidities may result in premature death⁴.

The risk of developing comorbid conditions seems to be higher in patients with SpA than in the general population⁵, and these comorbidities may manifest shortly after the onset of initial symptoms⁶. CV events occur more frequently in patients with AS, likely because of an increased prevalence of traditional risk factors [e.g., metabolic syndrome, arterial hypertension (AHT)]^{7,8,9} and to the medications used for the treatment of SpA [e.g., nonsteroidal antiinflammatory drugs (NSAID)]. The increased risk of tuberculosis (TB) may be due to immune disturbances by the disease itself and by pharmacological immunosuppression¹⁰. Additionally, the risk of developing malignancies may be related to chronic inflammation and autoimmunity, although epidemiological evidence that AS is associated with the development of malignancy is lacking¹¹.

The Assessment of SpondyloArthritis international Society of COMorbidities in SpA (ASAS-COMOSPA) study is a cross-sectional observational study to assess comorbidities and their risk factors in SpA. This initiative included 3 Latin American (LA) countries, and provides an opportunity to analyze the association of these comorbidities with SpA. While there are data in the literature on comorbid conditions in SpA in other regions, this information is limited in LA countries.

The objectives of this study were (1) to determine the prevalence of and the risks to present comorbidities as assessed in the ASAS-COMOSPA study (used as a reference group) in patients with SpA in 3 LA countries; and (2) to compare the prevalence of these with the information in the general population, to find out whether the prevalence and the risk of these comorbidities has increased.

MATERIALS AND METHODS

Study design and patient recruitment. This was a cross-sectional study that used data from the worldwide ASAS-COMOSPA study¹². Briefly, the ASAS-COMOSPA study was an observational, multicenter, and international study (22 countries from 4 continents) that included consecutive adult patients who fulfilled the ASAS SpA criteria (axial or peripheral). The patients in the ASAS-COMOSPA study enrolled from Argentina, Colombia, and Mexico (1 academic center in each country) were selected and analyzed for our present study. Additionally, 47 Colombian patients with data that made them eligible for ASAS-COMOSPA, but that were offered after the electronic database for the international study had been locked were included in this analysis. The results from the Global ASAS-COMOSPA study data reported here include the data from the LA countries. The study was approved by the Ethics and Research Committee of the Hospital Militar

(No.C-2014-027) and was conducted according to the guidelines for good clinical practice. All patients signed the informed consent forms.

Data collection. Details of the data collection methods have been published previously¹². A case report form was used in the study to collect the data, including patient demographics, SpA disease characteristics, and extra-articular manifestations (uveitis, psoriasis, and IBD). Information about past and current medications [NSAID, corticosteroids, conventional synthetic and biologic disease-modifying antirheumatic drugs (DMARD)] was also collected.

The following comorbidities and risk factors for comorbidities were collected: AHT (defined as a history of AHT or use of antihypertensive therapy or a blood pressure at the study visit > 140/90); TB (defined as a history or currently active TB); and cancer [defined as a history of neoplasia in the colon, skin (melanoma and basocellular carcinoma), lymphoma (Hodgkin and non-Hodgkin disease), breast, cervix, and prostate]. All data were collected by a study investigator by interview and were completed by reviewing medical records. The information was collected and registered in a centralized electronic case report form.

Data from the general population. Total and sex- and age-group specific prevalence data for AHT of general population were obtained from the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study. This is a population-based observational study (n = 11,550)^{13,14} assessing the prevalence of CV risk factors in 7 LA cities including Buenos Aires, Bogotá, and Mexico City. The analyses of data of the general population for AHT were confined to Colombia and Mexico. We found a huge intercountry variability regarding the AHT prevalence in the region, especially the data reported in Argentina. Whereas the AHT prevalence in the general population in Colombia and Mexico was comparable (13% and 11%, respectively), in Argentina the reported prevalence was 29%. Because of this discrepancy, which can be explained by genetic, ethnic, and demographic differences among the countries in the region, the analyses for AHT were limited only to Colombia and Mexico for comparison with the general population.

Prevalence data obtained from the general population of Argentina, Colombia, and Mexico were standardized for TB and malignancies. Specific prevalence data for TB stratified for sex and age categories have been obtained for the 3 countries using the 2015 Global Tuberculosis report¹⁵. This report is an initiative of the World Health Organization (WHO) that provides comprehensive information on the status of the disease at global and country levels. Regarding malignancies, sex- and age-group specific prevalence data have been obtained for the 3 countries using the 2012 GLOBOCAN project^{16,17}. This initiative provides prevalence estimates for the major types of cancer worldwide.

Statistical analyses. Descriptive statistics were used for the demographic data, disease characteristics, disease activity, risk factors, and the comorbidities of the patients included in the analyses. Data are presented as numbers (%) for qualitative variables and as the mean (SD) for continuous variables. The data were stratified for age categories and for males and females separately by comparing expected (general population) versus observed (LA) frequencies. Data from the Global ASAS-COMOSPA study were included for comparison with LA countries. In addition, 95% CI were estimated using the method described by Wilson¹⁸, which is considered an accurate and precise method for calculating CI¹⁹. Standardized risk ratios (SRR) were determined to compare event rates (in our study, comorbidities and risk factors) in patients with SpA versus the general population. SPSS Statistics 22 was used to perform the statistical analyses.

RESULTS

In total, all 390 patients from the 3 countries (Argentina, n = 236; Colombia, n = 85; and Mexico, n = 69) participating in the ASAS-COMOSPA study were included in the analysis. Patient characteristics including demographic and disease characteristics by country, for the LA countries combined,

and the global study population (which includes information for the LA countries), are presented in Table 1. In the LA countries, 64% were male, with a mean age of 45 (15) years and a mean disease duration since symptom onset of 7.0 (8.1) years. The proportion of patients with arthritis, enthesitis, and dactylitis was higher in the 3 LA countries (74%, 63%, and 24%, respectively) as compared with all patients (n = 3984) in the ASAS-COMOSPA study (56%, 38%, and 16%, respectively). The usage of NSAID and DMARD (particularly methotrexate) was higher in LA countries than in the entire ASAS-COMOSPA study (72% and 68%, respectively, for NSAID, and 48% and 33%, respectively, for DMARD), whereas biological therapy was less frequently used (34% vs 44%, respectively). The most common comorbidities and risk factors in all 3 LA countries were AHT (25.3%, 95% CI 21.2–30.0), hypercholesterolemia (21.5%, 95% CI 17.6–26.0), osteoporosis (9.4%, 95% CI 6.8–12.9), and gastrointestinal ulcer (7.7%, 95% CI 5.3–10.9).

Prevalence of comorbidities and risk factors. The prevalence of AHT limited to patients with SpA in Colombia and Mexico was higher (21.4%, 95% CI 15.4–28.9) compared to the general population (12.5%, 95% CI 11.4–13.7) in these 2 countries. The prevalence of AHT was higher in men than in women, especially in the age stratum of 55–64 years (57% vs 11%, respectively) and also in patients ≥ 65 years (70% vs 25%, respectively), in whom CV risk is expected to be more similar in both sexes. Additionally, in young patients (25–44 yrs), the prevalence of AHT was consistently increased

in both sexes compared to the general population. All the findings were consistent with the prevalence data of the global ASAS-COMOSPA study. The total AHT risk of patients with SpA in Colombia and Mexico between 24 and 64 years was increased (SRR 1.5) compared to the general population. This risk was increased in women and in men (1.5 and 1.4, respectively) and consistent across different age groups, except in the stratum of 55–64 years, in which the risk in women was lower. Detailed data on the prevalence of AHT compared to the general population are shown in Table 2.

The distribution of TB prevalence and risk is presented in Table 3. Overall, the observed prevalence of TB infection in LA patients with SpA in the 3 countries was 3.3% (95% CI 1.8–5.7), which was much higher than in the general population (0.32%) in these 3 LA countries and also higher than the prevalence data of the global ASAS-COMOSPA study (2.5%, 95% CI 2.0–3.0). TB prevalence in LA was lower in men than in women (2.8% vs 4.2%, respectively), in contrast to the global study in which the prevalence was higher in men (3.0% vs 1.6%, respectively). Cases of TB in LA were observed after the age of 35 and homogeneously distributed among all age groups regardless of sex (in total, 7 cases of TB in men and 6 cases in women). Seven of these cases were reported in Argentina and 6 in Colombia. In contrast, in the ASAS-COMOSPA study, TB cases were reported as early as age 25 and were more frequent in men (78 men and 23 women). The average risk of TB was 10.3 times higher in patients with SpA than in the general

Table 1. Demographic, disease characteristics, and comorbidities of the Latin America countries and the global ASAS-COMOSPA study. All values are %, except for n (%) for categorical or mean (SD) for continuous variables.

Characteristics	ASAS-COMOSPA	Latin America	Argentina	Colombia	Mexico
No. patients	3984	390	236	85	69
Male	65.0	63.8	61.9	60.0	75.4
Age, yrs	44 (14)	44.6 (14.7)	45.4 (14.5)	44.1 (13.9)	42.6 (16.3)
Education level, university	42.4	42.6	34.7	50.6	59.4
Smoking status, current	23.0	16.7	22.0	10.6	5.8
Disease duration, yrs	8.2 (9.4)	7.0 (8.1)	6.7 (8.3)	5.2 (5.6)	9.3 (8.7)
Disease symptoms					
Axial involvement	88.7	84.2	78.3	92.9	94.0
Arthritis	56.4	73.9	77.0	70.6	67.2
Enthesitis	38.0	62.5	57.9	77.6	59.7
Dactylitis	15.6	23.8	25.5	24.7	16.4
Uveitis	20.3	15.8	14.9	11.8	23.9
Psoriasis	22.5	23.0	33.2	4.7	10.4
IBD	5.2	3.3	3.4	3.5	3.0
ASDAS-CRP	2.0 (1.1)	1.9 (1.1)	1.8 (1.1)	2.0 (1.0)	1.8 (1.4)
BASFI	3.0 (2.7)	3.4 (2.8)	3.1 (2.8)	4.3 (2.2)	3.7 (3.0)
NSAID use, last 3 mos	67.8	71.8	71.9	68.2	76.1
Methotrexate, ever	32.7	47.6	48.7	42.3	50.7
Sulfasalazine, ever	43.9	43.5	25.4	70.2	87
Biological (TNFi), ever	43.9	34.1	35.6	36.4	26.1

ASAS-COMOSPA: Assessment of SpondyloArthritis international Society of COMOrbidities in SpA; SpA: spondyloarthritis; IBD: inflammatory bowel disease; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score–C-reactive protein; BASFI: Bath Ankylosing Spondylitis Functional Index; NSAID: nonsteroidal antiinflammatory drug; TNFi: tumor necrosis factor inhibitor.

Table 2. Observed prevalence of AHT in the ASAS-COMOSPA study (Latin America) compared with the expected prevalence in the general population and the prevalence of Global ASAS-COMOSPA for reference.

Sex	Age, yrs	Observed LA ASAS-COMOSPA		Expected General Population Prevalence (%)	SRR (CI 95%)	Global ASAS-COMOSPA	
		n	(%)			n	(%)
Men	≤ 24	0	0	NA	—	3	2.65
	25–34	4	12.5	3.6	3.4	49	8.47
	35–44	2	8.7	7.8	1.1	152	24.4
	45–54	6	28.5	14.6	1.9	247	43.3
	55–64	4	57.1	30.9	1.8	240	61.1
	≥ 65	7	70.0	NA	—	201	84.1
	Total	23	22.3	12.9	1.4 (0.9–2.2)	892	34.4
Women	≤ 24	0	0	NA	—	0	0
	25–34	1	8.3	0.9	9.2	17	7.4
	35–44	2	15.3	3.8	4.0	61	16.8
	45–54	5	41.6	17.0	2.4	132	36.8
	55–64	1	11.1	34.3	0.3	104	45.6
	≥ 65	1	25.0	NA	—	102	68.6
	Total	10	19.6	12.1	1.5 (0.8–2.8)	416	29.8
Total (men/women)		33	21.4	12.5	1.5 (1.0–2.1)	1308	33.1

Hypertension defined as a history of hypertension or antihypertensive therapy use or blood pressure $\geq 140/90$ mm Hg at the study visit. LA: Latin America (data confined to patients from Colombia and Mexico); SRR: standardized risk ratio (ratio calculated for the age of 25–64 yrs); n: number with a diagnosis of arterial hypertension (AHT) in each sex and age group; ASAS-COMOSPA: Assessment of SpondyloArthritis international Society of COMOrbidities in SpA; SpA: spondyloarthritis; NA: not available.

Table 3. Observed prevalence of TB in the ASAS-COMOSPA study (Latin America) compared with the expected prevalence in the general population and the prevalence of Global ASAS-COMOSPA for reference.

Sex	Age, yrs	Observed LA ASAS-COMOSPA		Expected General Population Prevalence (%)	SRR (CI 95%)	Global ASAS-COMOSPA	
		n	(%)			n	(%)
Men	20–24	0	0	0.29	—	0	0
	25–34	0	0	0.21	—	16	2.7
	35–44	2	3.3	0.23	14.3	15	2.4
	45–54	2	4.3	0.40	10.7	18	3.1
	55–64	2	7.4	0.73	10.1	12	3.1
	≥ 65	1	4.0	1.14	3.5	17	7.1
	Total men	7	2.8	0.41	6.8 (3.2–13.9)	78	3.0
Women	20–24	0	0	0.22	—	0	0
	25–34	0	0	0.13	—	1	0.4
	35–44	2	5.6	0.15	37.3	4	1.1
	45–54	1	2.8	0.19	14.7	6	1.7
	55–64	2	7.4	0.37	20.0	11	4.8
	≥ 65	1	7.1	0.41	17.3	1	0.7
	Total women	6	4.2	0.23	18.2 (8.5–40.6)	23	1.6
Total (men/women)	13	3.3	0.32	10.3 (6.1–17.8)	101	2.5	

LA: Latin America; TB: tuberculosis; SRR: standardized risk ratio; ASAS-COMOSPA: Assessment of SpondyloArthritis international Society of COMOrbidities in SpA; SpA: spondyloarthritis.

population. The risk was more increased in women than in men (18.2% vs 6.8%, respectively) and was found in all age categories except in patients ≥ 65 years, in whom the risk declined in both sexes.

The malignancies found in male patients with SpA were prostate cancer (n = 2), skin cancer (n = 2), and colon cancer (n = 1); and in women were cervical cancer (n = 2), breast cancer (n = 2), and skin cancer (n = 2). The majority of cases

had been reported in patients ≥ 50 years of both sexes (7 cases in Argentina, 3 in Colombia, and 1 in Mexico). The overall prevalence of malignancies observed in the 3 LA countries was 2.8% (95% CI 1.4–5.1), which was slightly lower than the prevalence in the global ASAS-COMOSPA study (3.2%, 95% CI 2.6–3.8) and not significantly increased in comparison to the general population (2.6%; p = 0.5). The SRR for malignancies was 1.0. There was not a significant

increase in the prevalence and the risk to develop malignancies in patients with SpA compared with the general population (Table 4).

DISCUSSION

The results of our study show that the prevalence and the risk of AHT and TB is increased in patients with SpA if compared to the age- and sex-adjusted general population in LA. Of note, the prevalence and the risk of developing malignancies were not significantly increased in patients with SpA in comparison to the reference population.

Studies assessing the prevalence of AHT in patients with AS have yielded different results. These discrepancies could be explained by the heterogeneity of the study populations investigated²⁰. A cross-sectional US analysis²¹ of the risk factors of CV disease showed an increased prevalence ratio of AHT in AS (1.3, 95% CI 1.1–1.4) compared with control subjects (27% vs 22%). Similar rates were observed in patients with PsA in our study. In a Dutch study, a higher prevalence of AHT, stratified by age and sex, was observed in patients with AS (41%) than in the general population (31%)²². Further, a Canadian study has shown that AHT was more common in patients with AS (23%) than in matched controls without AS (18%)²³. Our results are consistent with these studies, reporting a higher AHT prevalence in patients with SpA compared to a reference population of non-SpA individuals. In contrast, a Swedish study did not find a substantial difference between patients with AS and controls regarding AHT (32% vs 29%, respectively)²⁴. While chronic

inflammation may have had a detrimental effect on endothelial function and may have accelerated the progression of atherosclerosis, the common use of NSAID that we found in our current study (72%) is a more likely explanation for the increased prevalence of AHT.

A significantly higher prevalence and risk of developing TB in patients with SpA was found. Genetic factors favoring disease reactivation from latent TB or progression of the infection in addition to conventional risk factors for TB (e.g., age, sex, socioeconomic status, and occupation) may explain this finding. Additionally, it is also challenging to relate the increased prevalence of TB to the immune disturbances caused by the disease itself, which may also contribute to the risk of developing TB. This increased rate of TB has been observed previously in the early stages of disease in patients with SpA⁶ and was expected to also be present in patients with longer disease duration (and longer exposure to inflammation), as in our current study (mean disease duration of 7.0 yrs). Previous studies in patients with RA who were naive to antitumor necrosis factor (TNF) have shown an increased risk of developing TB (ranging from a 4-fold to a 7-fold increase) compared with the general population¹⁰, suggesting that uncontrolled and chronic inflammation predisposes to TB.

Although some studies have reported that the overall prevalence of TB is lower in women, plausible reasons that explain such a differential effect remain obscure. Factors such as differences in the progression from infection to clinically manifest disease, differences in immune system responsivity, and biological differences in disease presentation may be part

Table 4. Observed prevalence of all malignancies in the ASAS-COMOSPA study (Latin America) compared with the expected prevalence in the general population and prevalence of Global ASAS-COMOSPA for reference.

Sex	Age, yrs	Observed LA ASAS-COMOSPA		Expected General Population Prevalence (%)	SRR (CI 95%)	Global ASAS-COMOSPA	
		n	(%)			n	(%)
Men	20–39	0	0	0.41	—	4	0.3
	40–44	0	0	0.76	—	2	0.6
	45–49	0	0	1.29	—	5	1.6
	50–54	1	5.0	2.39	2.0	8	3.0
	55–59	1	7.6	4.11	1.8	9	3.9
	60–64	1	7.1	6.49	1.0	9	5.4
	65–70	1	8.3	9.28	0.8	13	11.3
	≥ 70	1	7.6	15.17	0.5	27	21.9
	Total men	5	2.0	2.41	0.8 (0.3–1.9)	77	2.9
	Women	20–39	0	0	0.54	—	6
40–44		0	0	1.91	—	3	1.6
45–49		1	4.3	2.70	1.5	4	2.2
50–54		2	15.3	3.53	4.3	11	6.0
55–59		2	13.3	4.49	2.9	6	4.6
60–64		1	8.3	5.90	1.4	10	10.0
65–70		0	0	6.98	—	4	4.8
≥ 70		0	0	9.57	—	7	10.7
Total women		6	4.2	2.67	1.5 (0.7–3.4)	51	3.6
Total (men/women)		11	2.8	2.6	1.0 (0.6–1.9)	128	3.2

LA: Latin America; n: number with a diagnosis of malignancies in each sex and age group; ASAS-COMOSPA: Assessment of SpondyloArthritis international Society of COMOrbidities in SpA; SpA: spondyloarthritis; SRR: standardized risk ratio.

of the explanation²⁵. Although the incidence of TB in LA has declined in the last 2 decades, the region is still considered an endemic area for TB, mainly owing to the presence of social factors that predispose to the disease²⁶. In general, these factors increase the exposure to TB bacilli.

The risk of developing a malignancy was not significantly increased in patients with SpA in comparison to the general population. This finding is consistent with previous studies reporting that the overall risk of malignancies was not significantly higher in patients with AS and PsA, including those treated with DMARD or TNF inhibitors²⁷. While malignancies are not rare in patients with AS, there is not a biologically plausible reason to expect a higher risk of cancer in these patients¹².

Previous studies in LA have assessed the prevalence rates of comorbid conditions, especially in RA. A systematic literature review evaluating CV risk factors in patients with RA²⁸ found that AHT was the most common finding in almost all studies performed in the region, with an overall prevalence of 28% (range 11.2–80.6%). In our study, we found a prevalence of AHT in patients with SpA of 25.3% in the 3 LA countries, which was higher than expected from the general population, but still lower than the prevalence reported in RA. This finding is consistent with the data observed in patients with AS, in whom CV risk factors are less manifest than in patients with RA⁸. Regarding TB data in LA, a prospective Brazilian study of patients with chronic inflammatory arthritis including AS, RA, and PsA has suggested that patients who start TNF blockers have a significantly higher rate of active TB than healthy controls (87 vs 36/100,000 person-yrs)²⁹.

Our study has limitations. First, the sample of patients may not be generalizable to the patient population in each country or the whole region. This cohort may not have been fully representative of all patients with SpA in the participating countries; moreover, the sample was rather small (especially for Colombia and Mexico) and limited to those patients who had access to specialized rheumatology care in academic centers. In particular, the higher educational status in Mexico and Colombia gives rise to the suggestion that the sample that was investigated may not be entirely representative of the population of patients with SpA in these countries. This should be taken into account when interpreting the results.

In addition, the patients in our study were from only 3 LA countries (those that participated in the international ASAS-COMOSPA study). Moreover, data for Argentina regarding AHT was not included in the analyses for comparison to general population and calculation of SRR. This was mainly due to a high intercountry variability of data in the general population as a result of ethnic and demographic differences; therefore, the AHT data were analyzed for only 2 countries (Colombia and Mexico). This limits the ability to extrapolate findings to the whole region. Second, the prevalence of some comorbidities might have

been underestimated, because patients may have been unable to participate as a result of clinically relevant conditions. On the other hand, comorbidities might have been overestimated because of investigation bias: SpA patients with comorbidities that are known to be associated with the disease may be overrepresented in this sample. Finally, it is important to mention an additional source of potential bias in relation to TB case ascertainment: While the global TB report had been based on comprehensive data reported at the national level according to guidelines by the WHO, in the ASAS-COMOSPA study, cases of TB had been ascertained by the patients and subsequent medical record review. These data do not necessarily yield the same results.

LA patients with SpA have an increased risk of developing AHT and TB compared with the general population. These findings illustrate the need for optimal detection and monitoring of these conditions in patients with SpA, and have implications for rheumatologists' health assessments, prevention, and treatment planning in LA countries.

REFERENCES

1. Ogdie A, Schwartzman S, Husni ME. Recognizing and managing comorbidities in psoriatic arthritis. *Curr Opin Rheumatol* 2015;27:118-26.
2. Sun LM, Muo CH, Liang JA, Chang SN, Sung FC, Kao CH. Increased risk of cancer for patients with ankylosing spondylitis: a nationwide population-based retrospective cohort study. *Scand J Rheumatol* 2014;43:301-6.
3. Germano V, Cattaruzza MS, Osborn J, Tarantino A, Di Rosa R, Salemi S, et al. Infection risk in rheumatoid arthritis and spondyloarthropathy patients under treatment with DMARDs, corticosteroids and TNF- α antagonists. *J Transl Med* 2014;12:77.
4. Prati C, Claudepierre P, Pham T, Wendling D. Mortality in spondyloarthritis. *Joint Bone Spine* 2011;78:466-70.
5. Bremander A, Petersson IF, Bergman S, Englund M. Population-based estimates of common comorbidities and cardiovascular disease in ankylosing spondylitis. *Arthritis Care Res* 2011;63:550-6.
6. Gherghe AM, Dougados M, Combe B, Landewé R, Mihai C, Berenbaum F, et al. Cardiovascular and selected comorbidities in early arthritis and early spondyloarthritis, a comparative study: results from the ESPOIR and DESIR cohorts. *RMD Open* 2015;1(1):e000128.
7. Mathieu S, Motreff P, Soubrier M. Spondyloarthropathies: an independent cardiovascular risk factor? *Joint Bone Spine* 2010;77:542-5.
8. McCarey D, Sturrock RD. Comparison of cardiovascular risk in ankylosing spondylitis and rheumatoid arthritis. *Clin Exp Rheumatol* 2009;27:S124-6.
9. Essers I, Stolwijk C, Boonen A, De Bruin ML, Bazelier MT, de Vries F, et al. Ankylosing spondylitis and risk of ischaemic heart disease: a population-based cohort study *Ann Rheum Dis* 2016;75:203-9.
10. Carmona L, Hernandez-Garcia C, Vadillo C, Pato E, Balsa A, Gonzalez-Alvaro I, et al. Increased risk of tuberculosis in patients with rheumatoid arthritis. *J Rheumatol* 2003;30:1436-9.
11. Franks AL, Slansky JE. Multiple associations between a broad spectrum of autoimmune diseases, chronic inflammatory diseases and cancer. *Anticancer Res* 2012;32:1119-36.
12. Molto A, Enchuto A, van der Heijde D, Landewe R, van den Bosch F, Bautista-Molano W, et al. Prevalence of comorbidities and

- evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study. *Ann Rheum Dis* 2016;75:1016-23.
13. Schargrofsky H, Hernandez-Hernandez R, Champagne BM, Silva H, Vinueza R, Silva Ayaquer LC, et al. CARMELA: assessment of cardiovascular risk in seven Latin American cities. *Am J Med* 2008;121:58-65.
 14. Hernandez-Hernandez R, Silva H, Velasco M, Pellegrini F, Macchia A, Escobedo J, et al. Hypertension in seven Latin American cities: the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study. *J Hypertens* 2010;28:24-34.
 15. Raviglione M. Global tuberculosis report 2015, World Health Organization. [Internet. Accessed November 9, 2017.] Available from: http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf
 16. Bray F, Ren JS, Masuyer E, Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. *Int J Cancer* 2013;132:1133-45.
 17. Ferlay J, Soerjomataram I, Ervik M, Forman D, Bray F, editors. GLOBOCAN 2012: Estimated cancer Incidence, Mortality and prevalence Worldwide in 2012. International Agency for Research on Cancer, World Health Organization. 2013. [Internet. Accessed November 9, 2017.] Available from: <http://globocan.iarc.fr>
 18. Wilson EB. Probable inference, the law of succession, and statistical inference. *J Am Stat Assoc* 1927;22:209-12.
 19. Wallis S. Binomial confidence intervals and contingency tests: mathematical fundamentals and the evaluation of alternative methods. *J Quant Linguist* 2013;20:178-208.
 20. Mathieu S, Gossec L, Dougados M, Soubrier M. Cardiovascular profile in ankylosing spondylitis: a systematic review and meta-analysis. *Arthritis Care Res* 2011;63:557-63.
 21. Han C, Robinson DW, Hackett MV, Paramore LC, Fraeman KH, Bala MV. Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. *J Rheumatol* 2006;33:2167-72.
 22. Heslinga SC, Van den Oever IA, Van Sijl AM, Peters MJ, Van der Horst-Bruinsma IE, Smulders YM, et al. Cardiovascular risk management in patients with active ankylosing spondylitis: a detailed evaluation. *BMC Musculoskelet Disord* 2015;16:80.
 23. Haroon NN, Paterson JM, Li P, Inman RD, Haroon N. Patients with ankylosing spondylitis have increased cardiovascular and cerebrovascular mortality a population-based study. *Ann Intern Med* 2015;163:409-16.
 24. Sundstrom B, Johansson G, Johansson I, Wallberg-Jonsson S. Modifiable cardiovascular risk factors in patients with ankylosing spondylitis. *Clin Rheumatol* 2014;33:111-7.
 25. Connolly M, Nunn P. Women and tuberculosis. *World Health Stat Q* 1996;49:115-9.
 26. Munayco CV, Mujica OJ, Leon FX, del Granado M, Espinal MA. Social determinants and inequalities in tuberculosis incidence in Latin America and the Caribbean. *Rev Panam Salud Publica* 2015;38:177-85.
 27. Fanto M, Peragallo MS, Pietrosanti M, Di Rosa R, Picchianti Diamanti A, Salemi S, et al. Risk of malignancy in patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis under immunosuppressive therapy: a single-center experience. *Intern Emerg Med* 2016;11:31-40.
 28. Sarmiento-Monroy JC, Amaya-Amaya J, Espinosa-Serna JS, Herrera-Diaz C, Anaya JM, Rojas-Villarraga A. Cardiovascular disease in rheumatoid arthritis: a systematic literature review in Latin America. *Arthritis* 2012;2012:371909.
 29. Gomes CM, Terreri MT, Moraes-Pinto MI, Barbosa C, Machado NP, Melo MR, et al. Incidence of active mycobacterial infections in Brazilian patients with chronic inflammatory arthritis and negative evaluation for latent tuberculosis infection at baseline - A longitudinal analysis after using TNFa blockers. *Mem Inst Oswaldo Cruz* 2015;110:921-8.