TITLE: Peripheral manifestations in spondyloarthritis and their impact: an ancillary analysis of the ASAS-COMOSPA study.

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Running head: Peripheral manifestations in Spondyloarthritis.

ABSTRACT

Objective: a) to determine the factors associated with the presence of peripheral manifestations in patients with spondyloarthritis (SpA) from the ASAS-COMOSPA study, b) to evaluate the impact of these symptoms on treatment and Patient Reported Outcomes (PROs).

Methods: All patients from the ASAS-COMOSPA study were included. All patients had a SpA diagnosis according to the rheumatologist. Patients and disease characteristics associated with the presence of these peripheral manifestations (peripheral arthritis, peripheral enthesitis or dactylitis) were explored by univariate and multivariate logistic regression. Patients who reported peripheral manifestations were divided into three categories: current, past history and no history. The impact of peripheral involvement on PROs was evaluated through the use of one-factor ANOVA.

Results: Out of the 3984 patients included in ASAS-COMOSPA, 2562 (64.3%) reported at least one peripheral manifestation, with a prevalence of 51.5%, 37.8% and 15.6% for peripheral arthritis, peripheral enthesitis and dactylitis, respectively.

South American patients, history of uveitis, current or past history of psoriasis, and the absence of HLAB27 were associated with higher prevalence of peripheral manifestations. Patients with peripheral involvement showed greater use of drugs, and those with "current" peripheral manifestations showed higher levels in all PROs, in contrast to those with past or no history.

Conclusion: Peripheral manifestations appear in 64% of patients with SpA. Psoriasis and the absence of HLAB27 are associated with the development of peripheral symptoms. The presence of any peripheral symptom at the time of the visit was associated with higher scores in all PROs.

Keywords: Spondyloarthritis, peripheral manifestations

Significance and innovations: This study evaluate peripheral manifestations in a large sample of patients with Spondyloarthritis (SpA). It is one of the first to evaluate peripheral manifestations not only in axial SpA but also in the whole group of SpA in a world-wide population.

In this study, we show that more than 64.3% of patients with SpA report at least one peripheral manifestation. Also, we demonstrate that exists a high probability of the occurrence of these manifestations over time after axial symptoms onset.

INTRODUCTION

Spondyloarthritis (SpA) is a chronic inflammatory rheumatic disease that mainly affect the axial skeleton and sacroiliac joints. Within the clinical picture, SpA patients may also experience peripheral symptoms such as arthritis, enthesitis and dactylitis, as well as extra-rheumatological manifestations (psoriasis, uveitis and inflammatory bowel disease) [1].

The prevalence of these peripheral manifestations is rather unclear and varies depending on the subtype of SpA (e.g. Ankylosing Spondylitis –AS-, Psoriatic Arthritis –PsA-, IBD-associated SpA, reactive arthritis and undifferentiated SpA) and the disease stage. In addition, most studies about peripheral manifestations are focused on axial SpA, and not on peripheral phenotypes. In 2011, the Assessment in SpondyloArthritis international Society (ASAS) group published the classification criteria for peripheral SpA [2,3]. In this study, the most frequent single peripheral manifestation was peripheral arthritis, observed in 46.6% of patients, followed by enthesitis (9.8%) and dactylitis (1.9%). A recently published meta-analysis [4] showed that this prevalence varies depending on the disease stage; that is, the prevalence of peripheral manifestations was different between AS and non-radiographic axial SpA (nr-axSpA).

The above data suggest that there is variability in the frequency of peripheral manifestations with regard to the phenotype of SpA. In addition, there is a lack of knowledge about factors associated with the presence of these symptoms, and their impact on treatment and quality of life.

These preliminary remarks prompted us to conduct this study aiming a) to describe the prevalence (current or ever) of peripheral manifestations in patients with SpA; b) to determine the factors associated with the presence of peripheral manifestations

in these patients; c) to evaluate the impact of these symptoms on treatment and Patient Reported Outcomes (PROs).

MATERIALS AND METHODS

Study design

This is an ancillary analysis of the ASAS-COMOSPA study. ASAS-COMOSPA is an observational, cross-sectional, multicentre and international study, with 22 participating countries from 4 continents (Africa, America, Asia and Europe), performed under the umbrella of the ASAS society. This worldwide study was described in detail elsewhere [5].

Patients

All participants belonging to the ASAS-COMOSPA were included in this analysis (3984 patients). The inclusion criteria were adult patients fulfilling the ASAS criteria for peripheral SpA (pSpA) or axial SpA (axSpA) [2]. All participants gave written informed consent and local ethics committees (North East-Newcastle/North Tyneside 2 Research Ethics committee 12/Ne/0417, the 14th/12/2012) approved the ASAS-COMOSPA study protocol.

Collected data

A case report form was used to collect the following data during a face-to-face patient interview at each centre. Information about symptoms occurred before the study visit were collected retrospectively asking patients or checking their medical records.

Socio-demographic variables included age, gender, obesity (body mass index $\geq$ 30 kg/m^2), smoking status, alcohol intake, university education and country of residence.

Regarding disease characteristics, chronic inflammatory back pain (IBP) (as well as date of onset), uveitis, personal and family history of psoriasis, HLA-B27 status and inflammatory bowel disease (IBD) were collected. Regarding peripheral manifestations (current or ever), peripheral arthritis was considered only in case of objective signs of synovitis demonstrated on clinical exam by a doctor or by imaging (MRI, ultrasonography). Enthesitis was considered not only at the heel level but also in other locations. History of dactylitis was collected. However, specific locations of these three peripheral manifestations were not collected in the CRF. Date of onset of these three peripheral manifestations (i.e. peripheral arthritis, peripheral enthesitis and dactylitis) were collected.

Data regarding intake of NSAIDs, prednisone, csDMARDs and bDMARDs were also collected. PROs collected were: Patient Global assessment (by Numerical Rate Scale, NRS), Bath Ankylosing Spondylitis Functional Index (BASFI) [6], Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [7], and Work Productivity and Activity Impairment Questionnaire (WPAI) [8].

Missing data was considered as negative (e.g. in case of missing data on history of dactylitis, the patient was considered as not having ever presented dactylitis).

Classification criteria

Patients included in the ASAS-COMOSPA study had to fulfil the ASAS criteria according to the rheumatologist; however, the fulfilment of these criteria was not verified before the recruitment. For this reason, the fulfilment of ASAS (pSpA or axSpA) and CASPAR criteria was recalculated in this analysis [9].

To evaluate ASAS criteria, we first selected patients with “current” inflammatory back pain (IBP). In this group, only axial ASAS criteria could be applied [2]; thus, in

these patients, we confirmed the presence of back pain for at least 3 months AND age at onset below 45 years old, and if they were positive, we confirmed the fulfilment of any of the two arms (imaging or clinical arm). In patients with X-ray or MRI sacroiliitis, only one SpA feature was required in order to fulfil the imaging arm. Patients without positive imaging but with HLA-B27 positive antigen needed at least two other additional SpA features to be classified as axSpA according to the clinical arm. In patients without "current" IBP, peripheral ASAS criteria could only be applied in patients with "current" peripheral manifestations (i.e., peripheral arthritis, peripheral enthesitis or dactylitis) [10]. These patients were required to have another SpA feature if this was a specific SpA feature or at least two SpA features for less specific features in order to be classified as pSpA [2]. Finally, in patients with neither "current" IBP nor "current" peripheral manifestations, ASAS criteria for axSpA were applied in case of presence of back pain for at least 3 months AND age at onset below 45 years old.

Regardless of the fulfilment of ASAS criteria, all patients were evaluated for CASPAR criteria fulfilment [9]. In this criteria set, the entry criterion is the presence of inflammatory articular disease (joint, spine or entheseal) and a score ≥ 3 points based on the presence of psoriasis, psoriatic nail dystrophy, negative test result for rheumatoid factor, dactylitis and radiologic evidence of juxta-articular new bone formation (each characteristic is assigned a specific number of points).

Statistical analysis

First, a description of the prevalence of the three peripheral manifestations, both in the entire cohort and with regard to different sets of criteria, was performed.

To evaluate the time of occurrence of peripheral manifestations regarding axial disease (i.e., IBP), we evaluated date of onset of each symptom. In this way, patients were divided into three groups: before, concomitantly or after axial symptoms.

Factors associated with the presence of each peripheral manifestation was explored first by univariate analysis, and thereafter by multivariate logistic regression, including in the model variables selected by the univariate analysis (when $p \leq 0.15$). Interactions, confounding factors and collinearity were tested, and all comparisons were bilateral considering $p \leq 0.05$ as a significant result.

Treatment modalities were compared in patients with/without each of the peripheral manifestations by using the Chi-square and T-test for qualitative and quantitative variables, respectively.

Patients reported outcomes (PROs) were compared across patients with past history/ current/ never peripheral manifestations by one-factor ANOVA test.

All of these analyses were performed for peripheral arthritis, enthesitis and dactylitis individually, and considering "any" peripheral manifestation (peripheral arthritis OR peripheral enthesitis OR dactylitis).

Data were analysed using the software SPSS 20.0 version.

RESULTS

Prevalence

Regarding the total COMOSPA database, 2777 (69.7%) patients fulfilled the axial ASAS criteria, 558 (14.0%) the peripheral ASAS criteria, and 894 (22.4%) the CASPAR criteria, while 431 (10.8%) patients did not fulfil any classification set. 322 (8.1%) patients fulfilled both the peripheral ASAS and CASPAR criteria.

A total of 2562 (64.3%) patients reported at least one peripheral manifestation during their disease course. The most prevalent peripheral manifestation was peripheral arthritis (51.5%). Among patients who fulfilled both the peripheral ASAS and CASPAR criteria, this figure increased to 98.4% (Figure 1). Peripheral enthesitis was reported in 37.8% of patients. Among those who fulfilled the peripheral ASAS criteria, this prevalence was 62.7% and 50.5% in the CASPAR criteria group. Finally, the prevalence of dactylitis was 15.6% and was more frequent among patients who fulfilled both the peripheral ASAS and CASPAR criteria (52.8%). Among the group of patients who did not fulfil any classification set (n=431), 57.5% reported at least one peripheral manifestation (44.5%, 35.3% and 11.4% reported peripheral arthritis, peripheral enthesitis and dactylitis, respectively). The prevalence of other SpA features in each subgroup of patients is showed in Supplementary Table 1. Among patients who reported current peripheral arthritis at the time of the study (n=1333), the presentation was more frequently oligoarticular (40.2% showed between 1 and 3 swollen joints) than polyarticular (16% of patients showed between 4 and 10 swollen joints) (Supplementary Figure 1).

De distribution of peripheral manifestations across continents (Supplementary Table 2) showed that these are more frequent among patients from South American countries.

Among the 2562 (64.3%) patients who presented at least one peripheral manifestations (i.e. either peripheral arthritis, enthesitis or dactylitis), a total of 1875 patients (47.1% from the entire cohort) had also suffered axial involvement. Among these, 489 (26.1%) showed at least one peripheral manifestation before axial symptoms, 518 (27.6%) concomitantly, and 1149 (61.3%) after axial involvement, respectively. Analysing each peripheral manifestation individually, the three appeared more frequently

after axial symptoms onset (47.4%, 58.3% and 60.8% for peripheral arthritis, peripheral enthesitis and dactylitis, respectively) (Supplementary Figure 2).

Factors associated

Peripheral manifestations (Table 1) were more frequent among older patients (≥43 years old –which corresponds to the median age on the ASAS-COMOSPA population-) [OR 1.64 (95%CI 1.42-1.90)], females [OR 1.42 (95%CI 1.21-1.66)] from South American countries [OR 3.23 (95%CI 2.40-4.37)], HLAB27 negatives [OR 1.32 (95%CI 1.14-1.54)], with absence of chronic IBP [OR 1.56 (95%CI 1.27-1.91)], with uveitis [OR 1.32 (95%CI 1.10-1.57)], with psoriasis [OR 5.45 (95%CI 3.98-7.46)], with family history of psoriasis [OR 1.61 (95%CI 1.26-2.07)], and among those who have never smoked [OR 1.34 (95%CI 1.15-1.50)] and who have never drank alcohol [OR 1.32 (95%CI 1.14-1.53)].

Peripheral arthritis, specifically, (Table 2) was associated with age ≥43 years [OR 1.44 (95%CI 1.24-1.67)], residence in South American countries [OR 1.97 (95%CI, 1.51-2.58)], HLAB27 negatives [OR 1.29 (95%CI 1.11-1.50)], absence of chronic IBP [OR 1.89 (95% CI 1.55-2.33)], peripheral enthesitis [OR 2.48 (95%CI, 2.13-2.88)], dactylitis [OR 6.62 (95%CI, 4.90-8.84)], psoriasis [OR 4.20 (95%CI 3.22-5.50)], family history of psoriasis [OR 1.44 (95%CI 1.13-1.82)], never smoking [OR 1.41 (95%CI 1.21-1.64)] and never alcohol intake [OR 1.36 (95%CI 1.17-1.58)].

Peripheral enthesitis (Table 3), was frequent among South American patients [OR 2.29 (95%CI 1.81-2.90)], obese patients [OR 1.22 (95%CI 1.03-1.45)], with peripheral arthritis [OR 2.58 (95%CI 2.23-3.00)], dactylitis [OR 2.33 (95%CI 1.91-2.84)], uveitis [OR 1.50 (95%CI 1.27-1.78)] and family history of psoriasis [OR 1.25 (95%CI 1.02-1.53)].

Finally, dactylitis (Supplementary Table 3) was more frequent in older patients (age ≥43 years) [OR 1.33 (95%CI 1.08-1.63)], high socioeducational level [OR 1.49 (95%CI 1.22-1.84)], HLAB27 negatives [OR 1.48 (95%CI 1.19-1.84)], absence of chronic IBP [OR 1.81 (95%CI 1.45-2.27)] peripheral arthritis [OR 6.95 (95%CI 5.16-9.36)], peripheral enthesitis [OR 2.51 (95%CI 2.05-3.06)], psoriasis [OR 2.08 (95%CI 1.64-2.64)], family history of psoriasis [OR 1.60 (95%CI 1.25-2.03)] and non smokers [OR 1.44 (95%CI 1.18-1.76)].

Impact on treatment and PROs

Evaluation of the impact of peripheral manifestations on treatment (Table 4) yielded that the presence of any of the three peripheral manifestations was associated ($p<0.001$) with a greater use of drugs such as NSAIDs [2326 (90.8%) vs. 1222 (85.9%)], csDMARDs [1825 (71.2%) vs. 546 (38.4%)], bDMARDs [1236 (48.2%) vs. 506 (35.6%)] and corticosteroids [1223 (47.7%) vs. 300 (21.1%)], compared to patients without history of these symptoms. The same results were obtained when we analysed the impact of each peripheral manifestation individually (Supplementary Table 4).

PROs were compared in patients divided into three groups depending on the presence of the peripheral manifestation at the time of the study ("current"), before the study ("past history") or not at all ("never"). Patient global NRS (4.6 vs. 3.3 vs. 3.9), BASDAI (4.5 vs. 2.9 vs. 3.4), BASFI (38.2 vs. 24.9 vs. 26.6), Work impairment (34.7 vs. 21.0 vs. 26.6) and Activity impairment (39.4 vs. 24.9 vs. 29.5) (both from the WPAI questionnaire) showed statistically significant higher numbers in patients with "current" peripheral arthritis compared to patients classified as "past history" or "never", respectively (Supplementary Figure 3). Similar results were obtained for peripheral enthesitis and dactylitis (Supplementary Figures 4-5).

DISCUSSION

To our knowledge, this is one of the first studies to attempt to evaluate peripheral manifestations not only in axSpA but also in the whole group of SpA. Our study shows that more than 64.3% of patients with SpA, regardless the initial presentation, report at least one peripheral manifestation at some point during the course of the disease. This study confirms the high prevalence of peripheral rheumatological manifestations in the past history of patients presenting axial symptoms, emphasizing the importance to check for those clinical features in order to facilitate the diagnosis of SpA. Moreover, the high probability of the occurrence of these preripheral manifestations over time after the occurrence of axial symptoms, emphasizing also the importance of a systematic iterative check of these clinical features during the monitoring of these patients.

The most frequent peripheral manifestation in this study was peripheral arthritis (51.5%). This manifestation was found to be more prevalent among patients fulfilling concomitantly the CASPAR criteria for Psoriatic Arthritis. These results are in line with those reported in studies focused on pSpA and PsA, where peripheral arthritis was reported in approximately 46% and 51% of patients, respectively [2,11]. Cases of peripheral arthritis were more frequently oligoarticular than polyarticular, and only 16% of patients showed polyarticular involvement (who are most likely patients with the psoriatic subtype). These data confirm the suitability of including peripheral arthritis as a SpA feature in the Amor, ESSG and ASAS criteria [12,13,2], allowing to cover the whole spectrum of the SpA, in contrast to New York criteria [14].

In our study, considering patients who only fulfil the axial ASAS criteria, the percentage of peripheral arthritis decreased to 37.2%, slightly higher than that reported in axial SpA (20%-30%) [4,11]. This can be explained by the great heterogeneity of

COMOSPA participants, which include South American patients, who are more likely to develop peripheral manifestations. The second most prevalent peripheral manifestation was enthesitis (37.8%), followed by dactylitis (15.6%). In axSpA, these manifestations appeared more frequently after axial symptom onset; that is, patients with axial forms can develop peripheral manifestations at any time during the follow-up.

Peripheral manifestations were more frequent among older patients. This can be explained by the fact that the cumulative probability of appearance of these symptoms is higher in old patients. They are also more frequent among patients from South American countries, which confirms previous studies reporting a greater prevalence of peripheral arthritis and enthesitis in Latin Americans compared with European patients [15]. This finding can be explained by the lower prevalence of the HLA-B27 antigen in Latin populations [16], which is classically associated with axial SpA, particularly AS [17]. Psoriasis and family history of psoriasis are also two independent factors associated with the development of these symptoms. These results are expected since 96% of PsA patients have peripheral joints affected and only 50% have axial involvement [18].

In our study, peripheral arthritis and dactylitis were less prevalent among HLA-B27 positive patients, patients with chronic IBP and smokers. It is well known that smoking can be associated with radiographic severity in axSpA [19,20]; however, the relationship between smoking and peripheral manifestation is not so known. Our results are in line with a recent work, which has demonstrated a lower prevalence of arthritis among current smokers in comparison to patients who have never smoked [21]. On the other hand, peripheral enthesitis was more prevalent among patients with chronic IBP and was not associated with either HLA-B27 nor tobacco. This study also confirms results from the ESPeranza cohort in Spain, in which Dactylitis has been found to be associated with peripheral arthritis, enthesitis and psoriasis [22]. Finally, we have shown that the

presence of any of the three peripheral manifestations (arthritis, enthesitis or dactylitis) acts are associated with the development of other peripheral symptoms.

The evaluation of the impact of peripheral manifestations on treatment showed that the presence of any of the three peripheral manifestations was associated with a greater use of any drug. As expected, corticosteroids and csDMARDs were more frequent among patients with arthritis, peripheral enthesitis or dactylitis. Interestingly, bDMARDs were also more frequently used among patients with these peripheral symptoms as compared to those without peripheral manifestations.

Regarding PROs, the presence of any peripheral manifestation at the time of the study visit resulted in higher levels on all questionnaires compared to those patients with a past history or who had never suffered these symptoms.

Our study had some limitations but also several strengths. A limitation was the cross-sectional nature of the study, which hampers our ability to collect information about symptoms occurred before the study visit, and to determine whether the appearance of peripheral manifestations are causes or consequences of other clinical characteristics. However, the availability of the timing of each manifestation provided us the possibility to determine the natural course of the disease in each patient. The second limitation was that no systematic assessment and scoring of peripheral manifestations was performed (i.e. 44SJC, MASES, etc). Finally, the proportion of axSpA patients is larger than the other two groups, which could lead to an underestimation of peripheral symptoms. However, this proportion is in line with clinical practice, in which axSpA patients are more prevalent than pSpA.

The mains strengths of our study are the large sample of SpA patients covering the whole spectrum, and that it is the first to evaluate peripheral manifestations not only in axSpA but also in the whole group of SpA in a world-wide population.

Because the majority of studies evaluating peripheral manifestations have been conducted in patients with axSpA, other studies focused in pSpA patients are required. This will enable us to better precise the relationship existing between these clinical manifestations and psoriasis and also to better analyse this clinical presentation and treatment possibilities.

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Figure legends

Figure 1. Venn diagram from the total of COMOSPA database (3984 patients), which represents the distribution of peripheral manifestations regarding the different classification set.

Footnote:

*431 patients fulfil neither axial ASAS, nor peripheral ASAS, nor CASPAR criteria. (P.A. 44.5%, Ent. 35.3%, Dac. 11.4%).
P.A.: Peripheral Arthritis. *Ent.:* Enthesitis. *Dac.:* Dactylitis.

Figure 1.

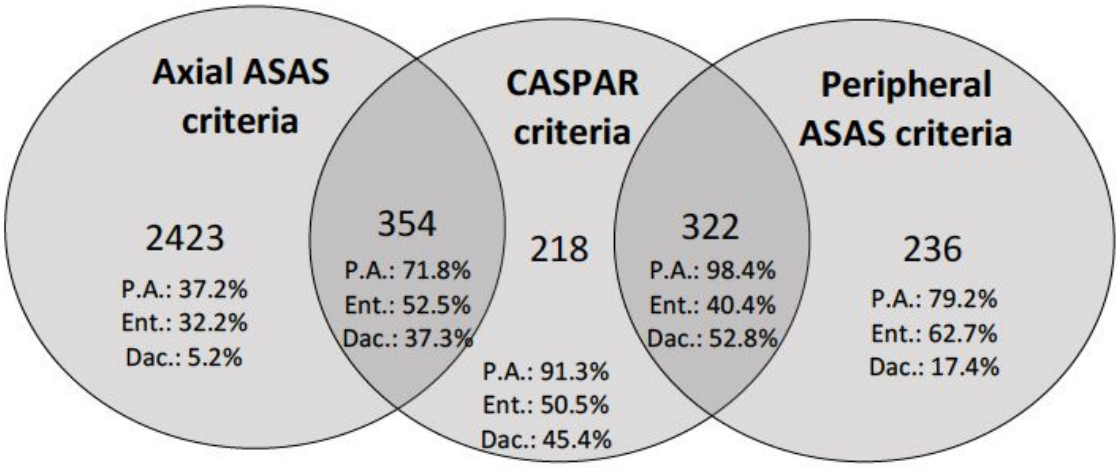

Table 1. Associated factors with the presence of any peripheral manifestation. Multivariate logistic regression.

Characteristic	Any peripheral manifestation n = 2562 (%)	No peripheral manifestation n = 1422 (%)	OR (95%CI)[1]	p-value
Age ≥ 43 years	1415 (55.2)	535 (37.6)	1.68 (1.45-1.94)	<0.001
Gender (female)	1016 (39.7)	378 (26.6)	1.42 (1.21-1.66)	<0.001
Socioeducational level (university)	1075 (42.0)	608 (42.8)		
South America	295 (11.5)	57 (4.0)	3.23 (2.40-4.37)	<0.001
Obese (BMI ≥ 30)	554 (21.6)	209 (14.7)		
HLA-B27 negative	1297 (50.6)	470 (33.1)	1.32 (1.14-1.54)	<0.001
Absence chronic IBP	592 (23.1)	167 (11.7)	1.56 (1.27-1.91)	<0.001
Uveitis	510 (19.9)	259 (18.2)	1.32 (1.10-1.57)	0.003
Psoriasis	584 (22.8)	50 (3.5)	5.45 (3.98-7.46)	<0.001
Family history of Psoriasis	443 (17.3)	101 (7.1)	1.61 (1.26-2.07)	<0.001
IBD	148 (5.8)	60 (4.2)		
Never smoking	1448 (56.5)	690 (48.5)	1.34 (1.15-1.50)	<0.001
Never alcohol intake	1289 (50.3)	630 (44.3)	1.32 (1.14-1.53)	<0.001

Hosmer-Lemeshow test: χ^2 square = 9.165, p=0.329

[1]OR (95%CI) for statistically significative variables which remain in the final model.

Percentages indicate number of patients with the covariate from the total number of patients in each column.

BMI: Body Mass Index; IBD: Inflammatory Bowel Disease; IBP: Inflammatory Back Pain.

Table 2. Associated factors with current or ever peripheral arthritis. Multivariate logistic regression.

Characteristic	Peripheral arthritis n = 2051 (%)	No peripheral arthritis n = 1933 (%)	OR (95%CI)[1]	p-value
Age ≥ 43 years	1163 (56.7)	787 (40.7)	1.44 (1.24-1.67)	<0.001
Gender (female)	821 (40.0)	573 (29.6)		
Socioeducational level (university)	867 (42.3)	816 (42.2)		
South America	249 (12.1)	103 (5.3)	1.97 (1.51-2.58)	<0.001
Obese (BMI ≥ 30)	446 (21.7)	317 (16.4)		
HLA-B27 negative	1100 (53.6)	667 (34.5)	1.29 (1.11-1.50)	0.001
Absence chronic IBP	545 (26.6)	214 (11.1)	1.89 (1.55-2.33)	<0.001
Peripheral enthesitis	1021 (49.8)	485 (25.1)	2.48 (2.13-2.88)	<0.001
Dactylitis	563 (27.5)	55 (2.8)	6.56 (4.90-8.84)	<0.001
Uveitis	381 (18.6)	388 (20.1)		
Psoriasis	545 (26.6)	89 (4.6)	4.20 (3.22-5.50)	<0.001
Family history of Psoriasis	390 (19.0)	154 (8.0)	1.44 (1.13-1.82)	0.003
IBD	120 (5.9)	88 (4.6)		
Never smoking	1191 (58.1)	947 (49.0)	1.41 (1.21-1.64)	<0.001
Never alcohol intake	1046 (51.0)	873 (45.2)	1.36 (1.17-1.58)	<0.001

Hosmer-Lemeshow test: χ^2 square = 10.575; p = 0.227

[1]OR (95%CI) for statistically significative variables which remain in the final model.

Percentages indicate number of patients with the covariate from the total number of patients in each column.

BMI: Body Mass Index; IBD: Inflammatory Bowel Disease; IBP: Inflammatory Back Pain.

Table 3. Associated factors with current or ever peripheral enthesitis. Multivariate logistic regression.

Characteristic	Peripheral enthesitis n = 1506 (%)	No peripheral enthesitis n = 2478 (%)	OR (95%CI)[1]	p-value
Age ≥ 43 years	805 (53.5)	1145 (46.2)		
Gender (female)	582 (38.6)	812 (32.8)		
Socioeducational level (university)	654 (43.4)	1029 (41.5)		
South America	210 (13.9)	142 (5.7)	2.29 (1.81-2.90)	<0.001
Obese (BMI ≥ 30)	331 (22.0)	432 (17.4)	1.22 (1.03-1.45)	0.023
HLA-B27 negative	690 (45.8)	1077 (43.5)		
Absence chronic IBP	277 (18.4)	482 (19.5)	0.65 (0.54-0.78)	<0.001
Peripheral arthritis	1168 (77.6)	1211 (48.9)	2.58 (2.23-3.00)	<0.001
Dactylitis	378 (25.1)	240 (9.7)	2.33 (1.91-2.84)	<0.001
Uveitis	348 (23.1)	421 (17.0)	1.50 (1.27-1.78)	<0.001
Psoriasis	273 (18.1)	361 (14.6)	1.31 (1.07-1.61)	0.010
Family history of Psoriasis	255 (16.9)	289 (11.7)	1.25 (1.02-1.53)	0.031
IBD	92 (6.1)	116 (4.7)		
Never smoking	830 (55.1)	1380 (52.8)		
Never alcohol intake	765 (50.8)	1154 (46.6)		

Hosmer-Lemeshow test: χ^2 square = 9.166, p=0.241

[1]OR (95%CI) for statistically significative variables which remain in the final model.

Percentages indicate number of patients with the covariate from the total number of patients in each column.

BMI: Body Mass Index; IBD: Inflammatory Bowel Disease.

Table 4. Impact of any peripheral manifestation on the treatment.

	Total = 3984	ANY PERIPHERAL MANIFESTATION		
		Yes = 2562 n (%)	No = 1422 n (%)	p-value[1]
NSAIDs				
% of patients since the onset of SpA symptoms	3548 (89.0%)	2326 (90.8)	1222 (85.9)	**<0.001**
DMARDs INTAKE (PAST OR PRESENT)				
csDMARDs	2371(59.5)	1825 (71.2)	546 (38.4)	**<0.001**
bDMARDs	1742(43.7)	1236 (48.2)	506 (35.6)	**<0.001**
CORTICOSTEROIDS				
% of patients using corticosteroids	1523 (38.2)	1223 (47.7)	300 (21.1)	**<0.001**
Current prednisone intake (mg), mean(SD)	1.01 (4.18)	1.35 (4.82)	0.39 (2.53)	**<0.001**
Estimated total intake (mg), mean(SD)	1741(6901)	2388 (8047)	576 (3827)	**<0.001**

[1]Chi-square and T-test for qualitative and quantitative variables, respectively
Percentages indicate number of patients with the covariate from the total number of patients in each column.