British Society for Rheumatology

RHEUMATOLOGY
ADVANCES IN PRACTICE

OXFORD

Clinical science

Comparing clinical profiles in spondyloarthritis with Crohn's disease or ulcerative colitis: insights from the ASAS-PerSpA study

Valeria Rios Rodriguez [1,*], **Tugba Izci Duran** [2], **Murat Torgutalp**[1],
Clementina López-Medina [3], **Maxime Dougados**[4,5], **Mitsumasa Kishimoto** [6], **Keisuke Ono** [6],
Mikhail Protopopov [1], **Hildrun Haibel** [1], **Judith Rademacher**[1], **Denis Poddubnyy** [1,7,‡],
Fabian Proft [1,‡]

[1]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany
[2]Clinic of Rheumatology, Denizli State Hospital, Denizli, Turkey
[3]Department of Rheumatology, Reina Sofia Hospital, IMIBIC, University of Cordoba, Cordoba, Spain
[4]Department of Rheumatology, Université de Paris., Hôpital Cochin, Assistance Publique, Hôpitaux de Paris, Paris, France
[5]INSERM (U1153): Clinical Epidemiology and Biostatistics, PRES Sorbonne Paris-Cité, Paris, France
[6]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan
[7]Epidemiology Unit, German Rheumatism Research Centre, Berlin, Germany

*Correspondence to: Valeria Rios Rodriguez, Department of Gastroenterology, Infectious Diseases and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Hindenburgdamm 30, 12203 Berlin, Germany. E-mail: valeria.rios-rodriguez@charite.de

‡D.P. and F.P. contributed equally.

Abstract

Objectives: Assuming SpA manifestations may vary among patients with different inflammatory bowel disease (IBD) subtypes, we explored the clinical characteristics associated with the presence of Crohn's disease (CD) or ulcerative colitis (UC) in patients with spondyloarthritis (SpA).

Methods: We included 3152 patients of ASAS-PerSpA study diagnosed with either axial SpA or peripheral SpA, according to their treating rheumatologist. Of these, 146 (4.6%) had confirmed IBD by endoscopy and were categorized into CD or UC groups. Demographics, clinical characteristics, treatments and patient-reported outcomes were compared between the two subgroups.

Results: From 146 patients included in the current analysis, 87 (59.6%) had CD [75 (86.2%) axial SpA and 12 (13.8%) peripheral SpA], and 39 (26.7%) had UC [34 (87.2%) axial SpA and 5 (12.8%) peripheral SpA]. CD and UC groups had similar age with average of 44.9 (13.5) *vs* 44.0 (13.0) years, respectively, and a slight male predominance in CD (63.2%) compared with UC (51.3%). Diagnostic delay for SpA was 7.0 (6.9) years for CD and 8.8 (8.1) years for UC. Chronic back pain was the most reported symptom present in 95.4% of CD patients and 89.7% of UC patients. Both groups had similar musculoskeletal phenotyping, with higher frequency of psoriasis (15.4%) and uveitis 28.2% in UC; and higher tendency to be HLA-B27 positive in CD (51.9% in CD *vs*.s 39.4% in UC).

Conclusion: In our analysis patients with SpA and concurrent CD or UC had mainly similar musculoskeletal phenotypes. However, they differ slightly in extra-musculoskeletal manifestations and HLA-B27 prevalence.

Lay Summary

What does this mean for patients?

Spondyloarthritis (SpA) refers to a group of chronic inflammatory rheumatic diseases that share clinical and genetic features and develop primarily as arthritis of the spine and other joints. It often occurs at the same time as other inflammatory conditions such as Crohn's disease (CD) and ulcerative colitis (UC), which are types of inflammatory bowel disease (IBD). In our study, doctors and researchers looked at the health characteristics of more than 3000 patients with SpA included in the ASAS-PerSpA study, focusing on those who also had either CD or UC. We found that both groups of patients had similar symptoms, with small differences. For example, patients with CD were slightly more likely to test positive for HLA-B27, a genetic marker often associated with SpA, although this finding will require further research to better understand its meaning. The main take-home message from our study is that the type of IBD—whether CD or UC—does not really change the way that SpA affects a person. However, the distinction between CD and UC remains crucial in tailoring treatment strategies. This will ensure that patients diagnosed with SpA are receiving appropriate treatment, taking into account their specific type of IBD.

Keywords: spondyloarthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis.

Key messages
- Patients with SpA and concomitant CD or UC have largely similar musculoskeletal profiles.
- Differentiating CD and UC is vital to adjust treatment strategies for effective SpA management.

Introduction

Spondyloarthritis (SpA) includes a group of chronic immune-mediated diseases primarily affecting the axial skeleton, named axial SpA, and the peripheral joints, peripheral SpA. While the main manifestation lies in the musculoskeletal system, SpA also shares significant associations with other inflammatory conditions, including inflammatory bowel diseases (IBD) such as Crohn's disease (CD and ulcerative colitis (UC); anterior acute uveitis and psoriasis.

The co-occurrence of SpA and IBD has been extensively documented, reflecting shared pathogenic mechanisms that result in shared treatment targets, such as biologic agents—anti-tumor necrosis factor (TNF) agents, and small molecules such as JAK inhibitors. Studies have reported a higher prevalence of IBD among patients with SpA and vice versa, with rates ranging from 6% to 14% [1–3]. When subclinical microscopic gastrointestinal inflammation is considered, the prevalence of IBD in SpA raises as high as 66% [4, 5]. This strong association has led to the inclusion of IBD as a clinical feature for the classification of SpA, encompassing both axial and peripheral forms, as defined by the Assessment of SpondyloArthritis international Society (ASAS) criteria [6, 7].

While research has traditionally focused on the concomitance of IBD as a whole in SpA, it is important to recognize that inside IBD are distinct entities with their own unique clinical features. CD is characterized by patchy transmural inflammation that can affect any part of the gastrointestinal tract, while UC primarily involves continuous inflammation of the colon and rectum, with inflammation limited to the mucosal layer [8]. These differences in the location and extent of the inflammation contribute to variations in symptoms, disease complications, and treatment strategies. Consequently, variations in the manifestations of SpA may exist among patients with these different IBD subtypes. Our manuscript seeks to explore whether there are differences in SpA characteristics and outcomes within the context of a main diagnosis of CD or UC in patients with SpA.

Methods

Study design and patient selection

The ASAS-PerSpA is a cross-sectional multicentre observational study conducted in a total of 24 countries. Patients with a diagnosis of SpA ($n = 4465$) were included in the study. Local rheumatologists were asked to specify the diagnosis into axial SpA, peripheral SpA, psoriatic arthritis, reactive arthritis, IBD-associated SpA, juvenile SpA, or other type of SpA. Details of the study design and description of the overall study population have been previously reported elsewhere [9].

For the present ancillary analysis, we included 3152 patients whose primary diagnosis was axial SpA or peripheral SpA, and we excluded those with the primary diagnosis of psoriatic arthritis, reactive arthritis, IBD-associated SpA, juvenile SpA, or other type of SpA (Fig. 1).
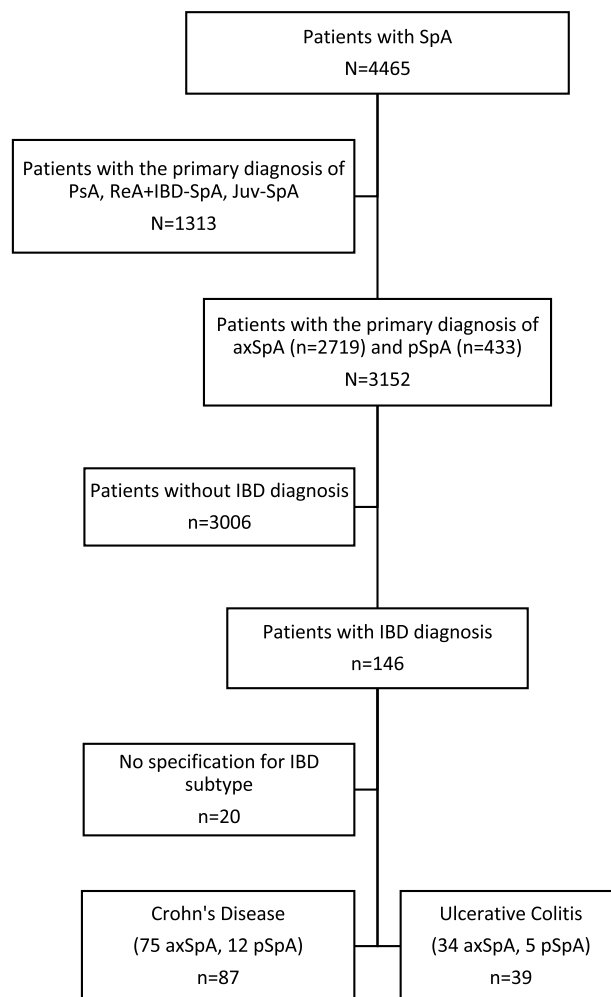
Figure 1. Flowchart showing the selection of patients from the PerSpA Study included in the analysis

The ASAS-PerSpA was performed in accordance with the guidelines for Good Clinical Practice. Informed consent was obtained from all participants before their enrolment in the study, and the study protocol received approval from the ethical committees of all participating countries. This analysis represents an ancillary study to the primary project and, as such, did not require independent ethical approval.

Collected variables

Data was collected by rheumatologists at each centre during a single routine patient visit using a standardized case report form. The data collected included:

- Sociodemographic information: age, sex, body mass index (BMI, kg/m^2), smoking and alcohol consumption, and country of residence.

- Clinical characteristics: symptom duration since symptom onset, diagnostic delay. Musculoskeletal manifestations included axial and peripheral involvement. This information was detailed collected as: chronic back pain; HLA-B27 status; information on sacroiliitis based on radiographs and magnetic resonance imaging (MRI); peripheral articular disease ever; presence of objective signs of synovitis (ie, physical examination by a rheumatologist or confirmed by ultrasonography), and localization; midfoot arthritis (tarsitis) ever; 'root-joint' (ie, shoulder and hip) involvement ever; enthesitis ever confirmed by specific tests (ie, sonography, radiographs, MRI or bone scintigraphy); and information about dactylitis ever and localization of dactylitis (fingers or toes). Extramusculoskeletal involvement was defined as uveitis; IBD confirmed by endoscopy and subtypes of IBD (Crohn's disease, ulcerative colitis, unspecific); and psoriasis confirmed by a physician.
- Disease activity, functional status and patient-reported outcomes (PROs): Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [10], Bath Ankylosing Spondylitis Functional Index (BASFI) [11], Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP) [12], tender joint count (TJC), 66 swollen joint count (SJC) [13], Mander enthesitis index (MEI) [14], Leeds Enthesitis Index (LEI) [15], Spondyloarthritis Research Consortium of Canada enthesitis score (SPARCC) [16], ASAS Health Index (ASAS-HI) [17], Patient Global Assessment of Well-being (PGA) (0–10), Euro quality of life (QoL)-5D (EQ-5D) [18], and the self-reported Fibromyalgia Rapid Screening Tool (FiRST) [19].
- Laboratory information: detection of C-reactive protein (CRP) levels and rheumatoid factor.
- Treatment information (current and ever): nonsteroidal anti-inflammatory drugs (NSAIDs), local and systemic corticosteroids, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and biological DMARDs (bDMARDs).

Statistical analysis

Our main analysis focused on comparing the clinical characteristics, disease impact and treatment modalities among patients with SpA, first divided into two groups based on the presence or absence of IBD, as confirmed by endoscopy; and then divided into groups based on the presence of CD, UC, or other forms of IBD.

Descriptive data are presented in two ways: continuous variables are presented as means with standard deviations, and categorical variables are presented as frequencies and percentages. For the univariate pairwise comparison of these variables Chi-square test was used for categorical variables, while the Mann–Whitney test and Kruskal–Wallis test were used for continuous variables. The Benjamini–Hochberg method was applied to adjust for multiple comparisons.

All data was processed and analyzed using SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA). For all analyses, *p*-value less than 0.05 indicated statistical significance.

Results

Among the 3152 patients with axial and peripheral spondyloarthritis from the ASAS Per-SpA cohort, 146 (4.6%) had IBD, as confirmed by endoscopy. The mean (SD) age of patients in the study cohort was 42.3 (13.3) years, with a higher proportion of men in the total population (65.4%) as well as in the IBD subgroup (58.2%). Body mass index (BMI) and lifestyle factors such as smoking and alcohol consumption were similar between the groups. However, the geographic distribution differed significantly, with a larger number of patients with IBD in Europe, North America, followed by the Middle East and North Africa. Asia presented significantly fewer patients with SpA and IBD than SpA without IBD (1.4% *vs*.s 24.8%). Patients with IBD had longer symptom duration and diagnostic delay for SpA compared with those without IBD [17.0 (10.1) *vs* 13.6 (11.0) years and 8.1 (7.6) *vs* 5.5 (7.6) years, respectively] as well as lower positivity of HLA-B27 (44.8% *vs* 78.1%, respectively). However, there were no significant differences between the two groups in terms of prevalence of peripheral arthritis, enthesitis or dactylitis. Patients with IBD had a higher prevalence of psoriasis and were more likely to be treated with systemic corticoids and DMARDs (conventional and biologic). Table 1 shows the sociodemographic, disease characteristics and treatment modalities of the total study population and of the subgroups with and without IBD.

We performed a comparative analysis between the groups SpA and IBD and an expanded IBD group including patients diagnosed with IBD-arthritis (group excluded from the main analysis) to identify any clinical differences that the inclusion of the IBD-arthritis diagnosis might reveal in the context of SpA. This additional analysis revealed no major differences in the clinical profiles between the two groups (see Supplementary Table S1, available at *Rheumatology Advances in Practice* online).

Demographic characteristics within CD and UC subgroups

Among the 146 patients diagnosed with IBD and confirmed with endoscopy, 87 (59.6%) patients were classified into CD and 39 (26.7%) patients into UC; 20 (13.7%) remaining patients with IBD were classified as "no specification for IBD subtype". Age and BMI were similar across the three groups, with a mean (SD) age of 44.9 (13.5) years for CD, 44.0 (13.0) for UC and 44.7 (12.8) for other IBDs; and BMI between 25 and 27, stating that in average, patients were overweighted according to the WHO classification for BMI [20]. Similarly to the whole cohort, male were more predominant in both groups (63.2% in CD group and 51.3% in UC group). Smoking history was similar across the groups (41.4% CD, 48.7% UC and 50% other IBD) while alcohol consumption varied with higher prevalence by the CD group (43.7% CD, 25.6% UC and 15% other IBD). Regarding geographical distribution, UC was more prevalent in Latin America and there were nearly no patients in Asia with any of the three forms of IBD (see Table 2).

Musculoskeletal manifestations within CD and UC subgroups

In general, SpA patients with CD or UC did not differ in their musculoskeletal phenotyping. Among patients with CD, 75 patients had a diagnosis of axial SpA and 12 of peripheral SpA by their local rheumatologist. Patients with UC presented a similar ratio between SpA classification, with 34 patients with axial SpA and 5 with peripheral SpA (see Fig. 1). The diagnostic delay for SpA was 7.0 (6.9) years for

Table 1. Socio-demographics and clinical characteristics, disease activity, and treatment of patients with SpA stratified according to the presence or absence of inflammatory bowel disease

	Total $N = 3152$	Patients with IBD $N = 146$	Patients without IBD $N = 3006$	B-H Adj. P
Demographics				
Age, years, mean (SD)	42.3 (13.3)	44.6 (13.2)	42.2 (13.2)	0.247
Sex, men, n/N (%)	2061/3152 (65.4)	85/146 (58.2)	1976/3006 (65.7)	0.350
BMI, kg/m^2, mean (SD)	25.9 (5.2)	26.3 (4.9)	25.9 (5.2)	0.557
Ever smoker, n/N (%)	1313/3149 (41.7)	65/146 (44.5)	1248/3003 (41.6)	0.694
Ever alcohol, n/N (%)	1268/3150 (40.3)	51/146 (34.9)	1217/3004 (40.5)	0.529
Symptom duration of SpA, years, mean (SD)	13.8 (11.0)	17.0 (10.1)	13.6 (11.0)	0.023
Diagnosis delay of SpA, years, mean (SD)	5.6 (7.6)	8.1 (7.6)	5.5 (7.6)	0.023
Extramusculoskeletal involvement				
Psoriasis ever, diagnosed by a physician n/N (%)	238/3152 (7.6)	21/146 (14.4)	217/3006 (7.2)	0.023
Uveitis ever, n/N (%)	663/3152 (21.0)	31/146 (21.2)	632/3006 (21.0)	0.975
Musculoskeletal involvement				
Peripheral arthritis ever, n/N (%)	1388/3152 (44.0)	75/146 (51.4)	1313/3006 (43.7)	0.356
Enthesitis ever, n/N (%)	1361/3152 (43.2)	51/146 (34.9)	1310/3006 (43.6)	0.275
Dactylitis ever, n/N (%)	264/3152 (8.4)	6/146 (4.1)	258/3006 (8.6)	0.337
Axial involvement ever according to the rheumatologist, n/N (%)	2889/3152 (91.7)	136/146 (93.2)	2753/3006 (91.6)	0.707
Back pain, n/N (%)	3002/3152 (95.2)	141/146 (96.6)	2861/3006 (95.2)	0.678
Laboratory assessment				
HLA-B27 positive, n/N (%)	1906/2484 (76.7)	47/105 (44.8)	1859/2379 (78.1)	0.023
CRP mg/l, mean (SD)	12.0 (26.4)	15.1 (41.2)	11.8 (25.5)	0.578
Treatment				
NSAIDs, n/N (%)	2978/3152 (94.4)	135/146 (92.5)	2841/3006 (94.5)	0.610
Systemic glucocorticoids ever, n/N (%)	638/641 (99.5)	87/90 (96.7)	551/551 (100.0)	0.023
csDMARDs ever, n/N (%)	1786/3152 (56.7)	123/146 (84.2)	1663/3006 (55.3)	0.023
bDMARDs ever, n/N (%)	1836/3152 (58.2)	120/146 (82.2)	1716/3006 (57.1)	0.023

All results are presented as mean and SD and percentages for continuous and categorical variables, respectively.
bDMARDs: biological disease-modifying antirheumatic drugs; B-H Adj. P: Benjamini-Hochberg adjusted P-value; BMI: body mass index; CRP: C reactive protein; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; IBD: inflammatory bowel disease; NSAIDs: non-steroidal anti-inflammatory drugs.

CD and 8.8 (8.1) years for UC group. The most common symptom was chronic back pain (95.4% in CD and 89.7% in UC), defined as back pain longer than 3 months. The presence of peripheral arthritis, enthesitis, and dactylitis was similar among the groups. The distribution of the arthritis was predominantly oligoarthritis with preference on the hands (see Table 2 for details). A third of patients reported history of enthesitis with a clear dominance of the heel enthesitis, present during the study in 3.4% of patients with CD and in 12.8% of patients with UC. CD patients showed a higher tendency to be HLA-B27 positive (51.9% in CD vs.s 39.4% in UC), but this did not reach statistical significance. In terms of extra-musculoskeletal involvement other than IBD, UC patients showed a higher frequency of psoriasis and uveitis diagnosis compared with CD patients (15.4% vs 10.3% for psoriasis and 28.2% vs 19.5% for uveitis; respectively), although this was not statistically significant. Regarding SpA disease activity, such as ASDAS, BASDAI, BASFI and CRP, there were no major differences between patients with CD or UC—see Table 2.

We did a sub-analysis stratifying patients between their predominant SpA form: axial and peripheral and investigated if their phenotyping between those with CD and UC were similar (see Supplementary Table S2, available at *Rheumatology Advances in Practice* online). Patients with axial SpA and CD were more predominantly males than UC (66.7% vs.s 52.9%); instead, patients with peripheral SpA were less predominantly male in both IBD forms (41.7% from CD and 40% for UC). Symptom duration, diagnosis delay for SpA

and musculoskeletal manifestations were similar in CD and UC patients independently of the form of SpA that they suffered. Psoriasis was more common in CD with axial SpA and, uveitis in patients with UC and peripheral SpA. HLA-B27 positivity was more prevalent in CD patients than in UC patients (58.7% vs 41.9% in the axial SpA group; and 12.5% vs 0% in the peripheral SpA) – See Supplementary Table S2, available at *Rheumatology Advances in Practice* online.

Discussion

While the SpA as a whole spectrum has long been in the scientific focus, we investigated a clinical angle that has not been well explored: the similarities and differences in patients with SpA and a parallel diagnosis of CD or UC. Our findings from the ASAS-PerSpA cohort suggest an overall resemblance in demographic characteristics and clinical presentation among SpA patients with either CD or UC.

The comparison of demographics between patients with CD and UC showed no differences, supporting the existing literature that suggests a similar demographic profile among patients diagnosed with either condition [21, 22]. However, we observed a slightly increased prevalence of male patients in the CD group compared with UC. This finding aligns with the mixed results from various studies, showing no definitive consensus on whether sex differences exist between CD and UC [23, 24].

Our study found no differences between CD and UC in relation to musculoskeletal manifestations, with chronic back pain

Table 2. Socio-demographics and clinical characteristics, disease activity and treatment of patients with SpA stratified by presence of Crohn's disease or ulcerative colitis

	Crohn's disease $N = 87$	Ulcerative colitis $N = 39$	B-H Adj. P^a	Other IBDs $N = 20$	B-H Adj. P^b
Demographics					
Age, years, mean (SD)	44.9 (13.5)	44.0 (13.0)	0.802	44.7 (12.8)	0.0586
Sex, men, n/N (%)	55/87 (63.2)	20/39 (51.3)	0.553	10/20 (50.0)	0.610
BMI, kg/m^2, mean (SD)	26.9 (5.3)	25.6 (4.6)	0.553	25.1 (2.7)	0.794
Ever smoker, n/N (%)	36/87 (41.4)	19/39 (48.7)	0.682	10/20 (50.0)	0.795
Ever alcohol, n/N (%)	38/87 (43.7)	10/39 (25.6)	0.327	3/20 (15.0)	0.151
Region, n/N (%)			0.089		0.438
Latin America	2/87 (2.3)	6/39 (15.4)		3/20 (15.0)	
Europe and North America	43/87 (49.4)	20/39 (51.3)		10/20 (50.0)	
Asia	0/87 (0.0)	1/39 (2.6)		1/20 (5.0)	
Middle East and North Africa	42/87 (48.3)	12/39 (30.8)		6/20 (30.0)	
Symptom duration of SpA, years, mean (SD)	16.7 (9.4)	16.4 (10.4)	0.790	19.7 (12.6)	0.675
Diagnosis delay of SpA, years, mean (SD)	7.0 (6.9)	8.8 (8.1)	0.653	11.0 (9.1)	0.618
Extramusculoskeletal involvement					
Psoriasis ever, diagnosed by a physician, n/N(%)	9/87 (10.3)	6/39 (15.4)	0.698	6/20 (30.0)	0.532
Uveitis ever, n/N (%)	17/87 (19.5)	11/39 (28.2)	0.591	3/20 (15.0)	0.679
Musculoskeletal involvement					
Peripheral arthritis ever, n/N (%)	42/87 (48.3)	18/39 (46.2)	0.890	15/20 (75.0)	0.357
Enthesitis ever, n/N (%)	26/87 (29.9)	14/39 (35.9)	0.710	11/20 (55.0)	0.433
Dactylitis ever, n/N (%)	3/87 (3.4)	1/39 (2.6)	0.873	2/20 (10.0)	0.646
Axial involvement ever according to the rheumatologist, n/N (%)	79/87 (90.8)	37/39 (94.9)	0.678	20/20 (100.0)	0.607
Back pain, n/N (%)	84/87 (96.6)	37/39 (94.9)	0.794	20/20 (100.0)	0.770
Sacroiliitis on X-ray, n/N (%)	64/87 (73.6)	26/39 (66.7)	0.540	7/20 (35.0)	0.089
Sacroiliitis on MRI, n/N (%)	46/60 (76.7)	22/32 (68.8)	0.676	12/14 (85.7)	0.681
Laboratory assessment					
HLA-B27 positive, n/N (%)	28/54 (51.9)	13/33 (39.4)	0.570	6/18 (33.3)	0.611
Rheumatoid factor positive, n/N (%)	2/57 (3.5)	2/32 (6.3)	0.742	1/18 (5.6)	0.890
CRP mg/l, mean (SD)	11.1 (33.8)	15.3 (30.1)	0.459	32.0 (74.8)	0.457
Disease activity, function, pros					
ASDAS-CRP, mean (SD)	2.4 (1.0)	2.4 (1.1)	0.896	2.9 (1.3)	0.501
BASDAI, mean (SD)	3.7 (2.3)	3.2 (2.1)	0.581	4.8 (2.1)	0.790
PGA, mean (SD)	4.3 (2.7)	3.9 (2.6)	0.706	5.0 (2.6)	0.694
BASFI, mean (SD)	3.3 (2.6)	2.2 (2.1)	0.131	4.5 (2.8)	0.871
ASAS-HI, mean (SD)	7.0 (4.5)	5.7 (4.6)	0.443	8.8 (4.4)	0.926
EQ-5D, mean (SD)	0.7 (0.2)	0.7 (0.2)	0.618	0.5 (0.3)	0.828
Fibromyalgia (according to FiRST score), n/N (%)	20/85 (23.5)	6/37 (16.2)	0.658	5/18 (27.8)	0.741
Treatment					
NSAIDs, n/N (%)	79/87 (90.8)	36/39 (92.3)	0.867	20/20 (100.0)	0.656
Systemic glucocorticoids ever, n/N (%)	47/49 (95.9)	23/24 (95.8)	0.990	17/17 (100.0)	0.801
csDMARDs ever, n/N (%)	71/87 (81.6)	35/39 (89.7)	0.578	17/20 (85.0)	0.706
bDMARDs ever, n/N (%)	72/87 (82.8)	33/39 (84.6)	0.871	15/20 (75.0)	0.793

All results are presented as mean and SD and percentages for continuous and categorical variables, respectively.
ASAS-HI: ASAS Health Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; bDMARDs: biological disease-modifying antirheumatic drugs; B-H Adj. *P*: Benjamini-Hochberg adjusted *P*-value; BMI: body mass index; CRP: C reactive protein; csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; IBD: inflammatory bowel disease; NSAIDs: non-steroidal anti-inflammatory drugs; PGA: Patient's Global Assessment.
[a] Compare with Crohn's disease and ulcerative colitis.
[b] Compare with Crohn's disease and ulcerative colitis and Other IBDs.

being the predominant symptom in both entities. This similarity in musculoskeletal phenotyping suggests that the presence of CD or UC may not impact the musculoskeletal presentation of SpA. In addition, the distribution of peripheral arthritis, enthesitis, and dactylitis was similar between patients diagnosed with CD or UC, reinforcing the perception of comparable musculoskeletal involvement. Although no prior studies have specifically investigated how IBD might influence SpA's presentation, our results are in sync with studies that explored the presence of musculoskeletal involvement in patients with IBD. In this area, several studies showed no substantial differences in the articular manifestations based on whether the patients were classified under CD or CU [25–29].

Regarding other extra-musculoskeletal manifestations, our data suggested higher prevalence of both uveitis and psoriasis in the UC group compared with the CD group, although it was not statistically significant. While anterior acute uveitis, an inflammatory eye condition, is recognized as the most common extra-musculoskeletal manifestation in SpA with a prevalence of up to 33% [30], the differential prevalence between CD and UC within the context of SpA claims for deeper exploration. Existing literature presents unconclusive data, with more recent studies describing a higher prevalence in CD over UC [31–34]. These differences might be related to heterogeneity in their methodology and that they are based on single populations, whereas our study is a worldwide cohort.

Interestingly, we observed a trend towards a higher frequency of HLA-B27 positivity among patients with CD compared with UC. In any case, our observation should be interpreted with caution and it needs further analysis to confirm this association. In an extension arm of the German Spondyloarthritis Inception Cohort (GESPIC) the prevalence of HLA-B27 in patients with CD was similar to healthy population [35], but to our knowledge, the most of the studies have explored HLA-B27 status in the conjunction of IBD [28, 36, 37]. Only one study [38] has previously described an HLA-B27 comparison, where 33.3% of patients with CD were HLA-B27 positive compared with 25% of patients with UC; however, the HLA-B27 positivity in those patients was much higher than the general population, bringing some controversy to the literature. HLA-B27 is a genetic marker that has been strongly associated with the development of SpA, meaning a strong genetic component to the disease's aetiology [39, 40]. Specific interactions between the HLA-B27 gene and other genetic or environmental factors might predispose individuals with CD to develop SpA more than those with UC. For example, the HLA-B27 expression might interact with the gut microbiota associated with CD, leading to aberrant immune responses that could contribute to SpA [41, 42]. If future research confirms our findings and demonstrates a higher frequency of HLA-B27 positivity in patients with CD compared with UC and the development of SpA, it could indicate a distinct genetic or immunological connection between CD, HLA-B27 and SpA. This would not only strengthen our understanding of the pathophysiology of the diseases but also potentially facilitate the diagnosis of the concomitant diseases and the development of more targeted and effective therapeutic strategies.

This study presents several strengths and limitations that should be considered when interpreting the results. A key strength is the international scope of the study, which was conducted in 24 countries, enabling the collection of diverse population and at the same time bringing generalizability of the results to different populations. However, the cross-sectional nature of the study is a limiting factor, leading to interpret the observed associations as correlations rather than causal relationships. The use of endoscopy-based criteria for CD or UC diagnosis, while robust, could potentially overlook patients and it left 20 patients out of the classification due to inconclusive or missing data. Although ASAS-PerSpA study included over 3000 patients, making it a large cohort, the small sample size with patients with concomitant CD and UC may have reduced the statistical power to detect differences between the two IBD entities, and could be an explanation why trends, such as higher prevalence of HLA-B27 among patients with CD did not reach statistical significance.

Our study explored how clinical manifestations presented in patients with SpA and concomitant CD or UC, finding no major phenotypic discrepancies. Although this may not impact the initial diagnosis of SpA, it is essential in the management and treatment of patients with SpA, as each IBD entity requires distinct therapeutic approaches. Further research is needed to optimize patient care and develop more personalized treatment strategies, along with deeper understanding of the shared pathogenetic mechanisms between these conditions. This study contributes to the body of knowledge in rheumatology and gastroenterology, highlighting the crucial role of interdisciplinary approach in managing patients with concurrent SpA and IBD.

Supplementary material

Supplementary material is available at *Rheumatology Advances in Practice* online.

Data availability

The data supporting the results of this study are available from the corresponding author (VRR) upon reasonable request.

Fabian Proft (Charité University, Berlin, Germany), Edit Toth (Flór Ferenc Hospital, Kistarcsa, Hungary), Katalin Nagy (Markhot Ferenc Hospital, Eger, Hungary), Attila Kovacs (MÁV Hospital, Szolnok, Hungary), Liza Rajasekhar (Nizam's Institute of Medical Sciences, Hyderabad, India), Sapan Pandya (Smt NHL Medical College and Sardar Vallabhbhai Patel Hospital and Vedanta Institute of Medical Sciences, Ahmedabad, India), Bhowmik Meghnathi (Sri Sai Siri Hospital and Prathima Institue of Medical Sciences, Karimnagar, India), Carlomaurizio Montecucco (Fondazione IRCCS Policlinico San Matteo, Pavia, Italia), Alessandro Biglia (Fondazione IRCCS Policlinico San Matteo, Pavia, Italia), Akihiko Asahina (The Jikei University School of Medicine, Japan), Masato Okada (St Luke's International University and Hospital, Japan), Tadashi Okano (Osaka City University, Japan), Yuko Kaneko (Keio University School of Medicine, Japan), Haruki Sawada (NTT Medical Center Tokyo, Japan), Yoshinori Taniguchi (Kochi University, Japan), Naoto Tamura (Juntendo University School of Medicine, Japan), Shigeyoshi Tsuji (National Hospital Organization Osaka Minami Medical Center, Japan), Yoichiro Haji (Daido Hospital, Japan), Ayako Hirata (Toho University, Japan), Akimichi Morita (Nagoya City University, Japan), Nelly Salloum (Saint-Joseph University, Beirut, Lebanon), Graciela Meza (CLIDITER), Julio Casasola-Vargas (Hospital General de Mexico, Mexico), César Pacheco-Tena (Hospital General Dr Salvador Zubirán, Chihuahua, Mexico), Greta Reyes-Cordero (Hospital General Dr Salvador Zubirán, Chihuahua, Mexico), César Ramos-Remus (Unidad de Investigación de Enfermedades Crónico Degenerativas, Jalisco, Mexico), J Dionisio Castillo (Unidad de Investigación de Enfermedades Crónico Degenerativas, Jalisco, Mexico), Laura González-López (Universidad de Guadalajara, Jalisco, Mexico), Iván Gámez-Nava (Unidad de Investigación Biomédica 02, Hospital de Especialidades, Centro Médico Nacional de Occidente, IMSS Guadalajara, Jalisco, Mexico), Fadoua Allali (University Mohammed V, CHU Ibn Sina, Rabat, Morocco), Hanan Rkain (University Mohammed V, CHU Ibn Sina, Rabat, Morocco), Lahcen Achemlal (University Mohammed V, CHU Ibn Sina, Rabat, Morocco), Taoufik Harzy (University Sidi Mohammed Benabdellah, CHU Hassan II, Fès, Morocco), Santiago Rodrigues-Manica (Universidade NOVA de Lisboa, Portugal), Agna Neto (Universidade NOVA de Lisboa, Portugal), Jose Marona (Universidade NOVA de Lisboa, Portugal), Ma Joao Gonçalves (Universidade NOVA de Lisboa, Portugal), Ana Filipa Mourao (Universidade NOVA de Lisboa, Portugal), Rita Pinheiro Torres (Universidade NOVA de Lisboa, Portugal), Simona Rednic (Iuliu Hatieganu University of Medicine, Cluj-Napoca, Romania), Siao-Pin Simon (Iuliu Hatieganu University of Medicine, Cluj-Napoca, Romania), Laura Muntean (Iuliu Hatieganu University of Medicine, Cluj-Napoca, Romania), Ileana Filipescu (Iuliu Hatieganu University of Medicine, Cluj-Napoca, Romania), Maria Tamas (Iuliu Hatieganu University of Medicine, Cluj-Napoca, Romania), Laura Damian (Iuliu Hatieganu University of Medicine, Cluj-Napoca, Romania), Ioana Felea (Iuliu Hatieganu University of Medicine, Cluj-Napoca, Romania), Dana Fodor (Second Medical Clinic, Emergency Conty Hospital, Cluj-Napoca, Romania), Hyun-Yi Kook (Chonnam National University Medical School and Hospital, South Korea), Hyun-Ju Jung (Chonnam National University Medical School and Hospital, South Korea), Tae-Hwan Kim (Hanyang University Hospital for Rheumatic Diseases, South Korea), Mireia Moreno (Hospital Parc Taulí, Barcelona, Spain), Eduardo Collantes-Estévez (Hospital Universitario Reina Sofía de Córdoba, Spain), M. Carmen Castro-Villegas (Hospital Universitario Reina Sofía, Córdoba, Spain), Cristina Fernández-Carballido (Hospital Universitario San Juan de Alicante, Alicante, Spain), Elizabeth Fernández (Hospital Universtario La Paz, Madrid, Spain), Marta Arévalo (Hospital Parc Taulí, Barcelona, Spain), Yeong-Jian Jan Wu (Chang Gung Memorial Hospital at Kee-Lung, Taiwan), Tian-Tsai Cheng (Chang Gung Memorial Hospital at Kao-Hsiung, Taiwan), Cheng-Chung Wei (Chung Sun Medical University, Taiwan), Servet Akar (Izmir Katip Çelebi University School of Medicine, Turkey), Ilhan Sezer (Akdeniz University School of Medicine), Umut Kalyoncu (Hacettepe University School of Medicine, Turkey), Sebnem Ataman (Ankara University School of Medicine, Turkey), Meltem Alkan Melikoglu (Erzurum Atatürk University School of Medicine, Turkey), Sami Hizmetli (Sivas Cumhuriyet University School of Medine, Turkey), Ozgur Akgul (Manisa Celal Bayar University School of Medicine, Turkey), Nilay Sahin (Balikesir University School of Medicine, Turkey), Erhan Capkin (Karadeniz Teknik University School of Medicine, Turkey), Fatima Gluçin Ural (Ankara Yildirim Beyazit University School of Medicine, Turkey), Figen Yilmaz (Istanbul Sisli Etfal Training and Research Hospital), Ilknur Aktas (Istanbul Fatih Sultan Mehmet Training and Research Hospital, Turkey), Anne Boel (Leiden University Medical Center, The Netherlands), Mirian Starmans-Kool (Zuyderland Medical Center, The Netherlands), Sofia Ramiro (Zuyderland Medical Center and Leiden University Medical Center, The Netherlands), Femke Hoekstra-Drost (Zuyderland Medical Center, The Netherlands), Maha Abdelkadir (Maasstad Hospital in Rotterdam, The Netherlands), Angelique Weel (Maasstad Hospital in Rotterdam, The Netherlands), Darerian Schueller (Cases Western Reserve University School of Medicine, Cleveland, Ohio, USA).

References

1. Stolwijk C, van Tubergen A, Castillo-Ortiz JD, Boonen A. Prevalence of extra-articular manifestations in patients with ankylosing spondylitis: a systematic review and meta-analysis. Ann Rheum Dis 2015;74:65–73.
2. Essers I, Ramiro S, Stolwijk C *et al.* Characteristics associated with the presence and development of extra-articular manifestations in ankylosing spondylitis: 12-year results from OASIS. Rheumatology (Oxford) 2015;54:633–40.
3. de Winter JJ, van Mens LJ, van der Heijde D, Landewé R, Baeten DL. Prevalence of peripheral and extra-articular disease in ankylosing spondylitis versus non-radiographic axial spondyloarthritis: a meta-analysis. Arthritis Res Ther 2016;18:196.
4. Kopylov U, Starr M, Watts C *et al.* Detection of Crohn Disease in Patients with Spondyloarthropathy: The SpACE Capsule Study. J Rheumatol 2018;45:498–505.
5. Van Praet L, Van den Bosch FE, Jacques P *et al.* Microscopic gut inflammation in axial spondyloarthritis: a multiparametric predictive model. Ann Rheum Dis 2013;72:414–7.
6. Rudwaleit M, van der Heijde D, Landewe R *et al.* The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 2009;68:777–83.

7. Rudwaleit M, van der Heijde D, Landewe R et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis 2011;70:25–31.

8. Abraham C, Cho JH. Inflammatory bowel disease. N Engl J Med 2009;361:2066–78.

9. López-Medina C, Molto A, Sieper J et al. Prevalence and distribution of peripheral musculoskeletal manifestations in spondyloarthritis including psoriatic arthritis: results of the worldwide, cross-sectional ASAS-PerSpA study. RMD open 2021;7:e001450.

10. Garrett S, Jenkinson T, Kennedy LG et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994; 21:2286–91.

11. Calin A, Garrett S, Whitelock H et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol 1994; 21:2281–5.

12. Lukas C, Landewé R, Sieper J, Assessment of SpondyloArthritis international Society et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis 2009;68:18–24.

13. Mainland D. A Seven-Day variability study of 499 patients with peripheral rheumatoid arthritis. Arthritis & Rheumatism 1965; 8:302–34.

14. Mander M, Simpson JM, McLellan A et al. Studies with an enthesis index as a method of clinical assessment in ankylosing spondylitis. Ann Rheum Dis 1987;46:197–202.

15. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures and development of an instrument specific to psoriatic arthritis. Arthritis Rheum 2008; 59:686–91.

16. Maksymowych WP, Mallon C, Morrow S et al. Development and validation of the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index. Ann Rheum Dis 2009; 68:948–53.

17. Kiltz U, van der Heijde D, Boonen A et al. Measurement properties of the ASAS Health Index: results of a global study in patients with axial and peripheral spondyloarthritis. Ann Rheum Dis 2018; 77:1311–7.

18. Gudex C. The descriptive system of the EuroQOL instrument. EQ-5D concepts and methods: a developmental history. The Netherlands: Springer, 2005: 19–27.

19. Perrot S, Bouhassira D, Fermanian J, CEDR (Cercle d'Etude de la Douleur en Rhumatologie). Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain 2010; 150:250–6.

20. de Onis M, Habicht JP. Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. Am J Clin Nutr 1996;64:650–8.

21. Cosnes J, Gower-Rousseau C, Seksik P, Cortot A. Epidemiology and natural history of inflammatory bowel diseases. Gastroenterology 2011;140:1785–94.

22. Loftus EV, Jr., Sandborn WJ. Epidemiology of inflammatory bowel disease. Gastroenterol Clin North Am 2002;31:1–20.

23. Loftus EV. Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology 2004;126:1504–17.

24. Weisman MH, Oleg S, Seok Kim H et al. Inflammatory bowel disease prevalence: surveillance data from the U.S. National Health and Nutrition Examination Survey. Prev Med Rep 2023; 33:102173.

25. van Erp SJ, Brakenhoff LK, van Gaalen FA et al. Classifying back pain and peripheral joint complaints in inflammatory bowel disease patients: a prospective longitudinal follow-up study. J Crohns Colitis 2016;10:166–75.

26. Vavricka SR, Brun L, Ballabeni P et al. Frequency and risk factors for extraintestinal manifestations in the Swiss inflammatory bowel disease cohort. Am J Gastroenterol 2011;106:110–9.

27. Ossum AM, Palm Ø, Cvancarova M et al. Peripheral arthritis in patients with long-term inflammatory bowel disease. Results from 20 years of follow-up in the IBSEN study. Scand J Gastroenterol 2018;53:1250–6.

28. Ossum AM, Palm Ø, Lunder AK, IBSEN Study Group et al. Ankylosing spondylitis and axial spondyloarthritis in patients with long-term inflammatory bowel disease: results from 20 years of follow-up in the IBSEN study. J Crohns Colitis 2018;12:96–104.

29. Karreman MC, Luime JJ, Hazes JMW, Weel A. The prevalence and incidence of axial and peripheral spondyloarthritis in inflammatory bowel disease: a systematic review and meta-analysis. J Crohns Colitis 2017;11:631–42.

30. Rademacher J, Poddubnyy D, Pleyer U. Uveitis in spondyloarthritis. Ther Adv Musculoskelet Dis 2020;12:1759720x20951733.

31. Karmiris K, Avgerinos A, Tavernaraki A et al. Prevalence and characteristics of extra-intestinal manifestations in a large cohort of Greek patients with inflammatory bowel disease. J Crohns Colitis 2016;10:429–36.

32. Bandyopadhyay D, Bandyopadhyay S, Ghosh P et al. Extraintestinal manifestations in inflammatory bowel disease: prevalence and predictors in Indian patients. Ind J Gastroenterol 2015;34:387–94.

33. Zippi M, Corrado C, Pica R et al. Extraintestinal manifestations in a large series of Italian inflammatory bowel disease patients. World J Gastroenterol 2014;20:17463–7.

34. Biedermann L, Renz L, Fournier N et al. Uveitis manifestations in patients of the Swiss Inflammatory Bowel Disease Cohort Study. Therap Adv Gastroenterol 2019;12:1756284819865142.

35. Rios Rodriguez V, Sonnenberg E, Proft F et al. Presence of spondyloarthritis associated to higher disease activity and HLA-B27 positivity in patients with early Crohn's disease: clinical and MRI results from a prospective inception cohort. Joint Bone Spine 2022;89:105367.

36. Palm O, Moum B, Ongre A, Gran JT. Prevalence of ankylosing spondylitis and other spondyloarthropathies among patients with inflammatory bowel disease: a population study (the IBSEN study). J Rheumatol 2002;29:511–5.

37. Salvarani C, Vlachonikolis IG, van der Heijde DM et al. Musculoskeletal manifestations in a population-based cohort of inflammatory bowel disease patients. Scand J Gastroenterol 2001; 36:1307–13.

38. Turkcapar N, Toruner M, Soykan I et al. The prevalence of extra-intestinal manifestations and HLA association in patients with inflammatory bowel disease. Rheumatol Int 2006;26:663–8.

39. Brown MA, Kennedy LG, MacGregor AJ et al. Susceptibility to ankylosing spondylitis in twins: the role of genes, HLA, and the environment. Arthritis Rheum 1997;40:1823–8.

40. Pedersen OB, Svendsen AJ, Ejstrup L et al. Ankylosing spondylitis in Danish and Norwegian twins: occurrence and the relative importance of genetic vs. environmental effectors in disease causation. Scand J Rheumatol 2008;37:120–6.

41. Asquith M, Sternes PR, Costello ME et al. HLA alleles associated with risk of ankylosing spondylitis and rheumatoid arthritis influence the gut microbiome. Arthritis Rheumatol 2019;71:1642–50.

42. Gill T, Asquith M, Brooks SR, Rosenbaum JT, Colbert RA. Effects of HLA-B27 on gut microbiota in experimental spondyloarthritis implicate an ecological model of dysbiosis. Arthritis Rheumatol 2018;70:555–65.