BMJ Open

Cross-sectional study of patients with axial spondyloarthritis fulfilling imaging arm of ASAS classification criteria: baseline clinical characteristics and subset differences in a single-centre cohort

Kristyna Bubová,[1] Šárka Forejtová,[1] Kateřina Zegzulková,[1] Monika Gregová,[1] Markéta Hušáková,[1] Mária Filková,[1] Jana Hořínková,[1] Jindřiška Gatterová,[1] Michal Tomčík,[1] Lenka Szczuková,[2] Karel Pavelka,[1] Ladislav Šenolt[1]

To cite: Bubová K, Forejtová Š, Zegzulková K, *et al*. Cross-sectional study of patients with axial spondyloarthritis fulfilling imaging arm of ASAS classification criteria: baseline clinical characteristics and subset differences in a single-centre cohort. *BMJ Open* 2019;**9**:e024713. doi:10.1136/bmjopen-2018-024713

Received 20 June 2018
Revised 1 December 2018
Accepted 22 January 2019

[1]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic
[2]Institute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno, Czech Republic

Correspondence to
Ladislav Šenolt;
senolt@revma.cz

ABSTRACT

Objective This study compared demographic, clinical and laboratory characteristics between patients with radiographic and non-radiographic axial spondyloarthritis (axSpA).

Methods In this single-centre cross-sectional study, a total of 246 patients with axSpA fulfilling the imaging arm of Assessment of SpondyloArthritis International Society classification criteria were recruited. A total of 140 patients were diagnosed as non-radiographic axial spondyloarthritis (nr-axSpA), and 106 patients had ankylosing spondylitis (AS). Sociodemographic characteristics, disease manifestations, clinical and laboratory disease activity and their differences between subsets were analysed. P values below 0.05 with CI 95% were considered statistically significant.

Results More nr-axSpA patients were women (61.4%) compared with 24.7% of AS patients. First symptoms developed earlier in AS patients compared with nr-axSpA (23.0 (IQR 17.5–30.0) vs 27.8 (IQR 21.0–33.7) years, p=0.001). Disease manifestations did not differ, but patients with nr-axSpA experienced peripheral arthritis more frequently (35.7% vs 17.0%, p=0.001) with less hip involvement (8.6% vs 18.9%, p=0.022) compared with patients with AS. Patients with AS exhibited worse spinal mobility and physical function compared with nr-axSpA. AS Disease Activity Scores and CRP levels were significantly higher in patients with AS compared with nr-axSpA (2.4 (IQR 1.7–2.8) vs 2.0 (IQR 1.1–2.3), p=0.022 and 7.1 (IQR 2.6–14.9) vs 2.5 (IQR 0.8–8.2) mg/L, p<0.001, respectively).

Conclusions Our data demonstrated some known and also novel differences between the two imaging arm fulfilling axSpA subgroups. Non-radiographic patients were mostly women who had experienced shorter disease duration, milder disease activity and better functional status with less hip involvement but more peripheral arthritis compared with patients with AS.

Strengths and limitations of this study

- A strength of this study is the large sample size.
- This is the first study investigating the differences between axial spondyloarthritis patients in the Czech Republic.
- We included only patients fulfilling imaging arm of Assessment of SpondyloArthritis International Society classification criteria (ankylosing spondylitis and non-radiographic axial spondyloarthritis), patients fulfilling only clinical arm were not included.
- One of the limitations was that the MRI was performed in several imaging centres.

INTRODUCTION

Spondyloarthritis (SpA) is a frequent chronic inflammatory disease that primarily affects the axial skeleton and causes a typical lower back pain. SpA is a heterogeneous group of disorders that share common clinical features, including peripheral arthritis, enthesitis and extra-articular manifestations, such as uveitis, inflammatory bowel disease (IBD) or psoriasis.[1] SpA is divided into predominantly axial or predominantly peripheral disease based on the sites of inflammation.[2] Ankylosing spondylitis (AS) is a prototype of axial spondyloarthritis (axSpA). The prevalence of axSpA is approximately 0.7%–1.4% in the general population.[3] Patients generally develop signs of inflammatory back pain that correspond to sacroiliitis (or spondylitis) as detected by imaging. AS is a slowly progressive disease that is defined using modified New York classification criteria, in which conventional radiographs of the sacroiliac (SI) joints exhibit definite structural changes.[4]

Many patients develop similar axial symptoms but lack the typical changes on radiographs, which potentially causes delayed or missed diagnosis.[5] MRI is used to visualise the radio,graphic changes that typically occur several years after SI joint inflammation. MRI is also included in the new Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axSpA to enable the diagnosis of non-radiographic axSpA (nr-axSpA).[6] Nr-axSpA may be a prestage of AS; however, not all of these patients develop the destructive joint changes that are typical of long-standing disease. Only approximately 10%–20% of patients with nr-axSpA develop structural changes and AS over in the subsequent 2 years, and approximately half of the patients exhibit radiographic sacroiliitis after 5 years of the disease.[7]

Some recent studies investigated differences between these two subgroups.[8–10] These studies varied in male-to-female ratios, the proportion of patients with objective signs of inflammation (such as bone marrow oedema), and the proportion of patients with increased levels of C-reactive protein (CRP), all of which are higher in patients with AS.[8–10] Clinical characteristics such as disease activity, physical impairment and quality of life were comparable between these two subgroups.[11 12] However, some inconsistencies exist. Therefore, our study described the baseline demographic, clinical and laboratory characteristics of axSpA patients and examined differences between AS and nr-axSpA subgroups fulfilling the imaging arm of ASAS classification criteria.

Patients and methods

This study is a descriptive, single-centre, cross-sectional, ongoing study of the Prague Spondyloarthritis Cohort (PRASPAC), which included 246 patients who fulfilled the ASAS classification criteria for axSpA.[13] Patients with a suspicion of SpA were referred to our specialised early-SpA centre in the outpatient department of the Institute of Rheumatology mostly by general practitioners/ophthalmologists/rheumatologists (minority of patients by other specialists) from the central region of the Czech Republic. Patients were further classified as AS or nr-axSpA based on radiographic findings, and irrespective of the presence of psoriasis or IBD. Patients were classified as nr-axSpA if radiographic changes in the SI joints of at least grade II bilaterally or grade III or IV unilaterally were lacking, and positive MRI (ie, characteristic bone marrow oedema) was present with at least one SpA feature. Patients were classified as AS according to New York classification criteria.[4] Patients who fulfilled only clinical arm of ASAS classification criteria were included in the PRASPAC and underwent the same examination protocol. However, these patients were not included in our analyses. No restrictions for disease duration or treatment protocol were used at inclusion.

All patients were recruited from October 2012 to March 2016 at the outpatient rheumatology department of the Institute of Rheumatology in Prague and were followed every 6 months for the first 2 years. Trained rheumatologists obtained data related to the disease status according to recommended standardised methodologies: metrology (modified Schober, occiput to wall, chin–chest distance and chest expansion), Maastricht Ankylosing Spondylitis Enthesitis Score,[14] swollen joint count and tender joint count (SJC and TJC), physician global assessment (MDGAS), Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP),[15] Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[16] and Bath Ankylosing Spondylitis Functional Index (BASFI).[17] Laboratory parameters (CRP and erythrocyte sedimentation rate [ESR]) were analysed from blood samples at each visit. Additional data related to the diagnosis were obtained at the recruitment visit, including age at the onset of first symptoms, type of first symptom (eg, back pain, peripheral arthritis and extra-articular manifestations), age at diagnosis, family history (AS, IBD and psoriasis), inflammatory back pain, occurrence of peripheral or hip arthritis and extra-articular manifestations, previous and current medications (non-steroidal anti-inflammatory drugs [NSAIDs], conventional synthetic disease-modifying antirheumatic drugs [csDMARDs], glucocorticoids, biological treatment [bDMARDs]), HLA-B27 positivity and sociodemographic data (age, gender, Body Mass Index [BMI]), current/ex/non-smoker). Both axSpA subsets were treated according to the EULAR recommendations for the management of SpA. Patients with mild disease were treated with NSAIDs on demand. Most of the patients with previously developed peripheral arthritis were treated with csDMARDs. Patients with severe disease were treated with bDMARDs. The study was initiated before anti-TNF treatment was approved for nr-axSpA by local authorities. Data presented in this study were collected from the recruitment visit.

Patient and public involvement

The patients and/or public were not involved in the design, recruitment or conduct of the study.

Imaging

Radiographs of the SI joints and lumbar and cervical spine from all patients were obtained prior to recruitment, and a trained rheumatologist and/or central radiologist scored the radiographs for the initial disease classification. Radiographic sacroiliitis was scored from grade 0 (normal) to grade 4 (ankylosis) according to the Bennett scoring system.[18] Cervical and lumbar spines were scored according to the modified Stoke AS Spine Score.[19] A trained rheumatologist scored MRI images from nr-axSpA patients obtained at recruitment.

Laboratory analysis

Fasting blood samples were collected from all patients on the same day as the clinical examination. CRP levels were measured using turbidimetry (Beckman Coulter, Pasadena, CA, USA), and ESR was measured according to the Fahraeus Westergren method in a routine clinical laboratory. HLA-B27 was detected using flow cytometry

kits (IOTest HLA-B27-FITC/HLA-B7-PE, Beckman Coulter—Immunotech SAS, Marseille, France) and BDTM HLA-B27 Kit (BD Bioscience, San Jose, CA, USA) according to the manufacturer's protocol.

Statistical analysis

Statistical analysis was performed using GraphPad Prism 5.1. A Kolmogorov-Smirnov test of normality was performed for all variables. Categorical variables were compared between groups using Fisher's exact test. Data for continuous variables are presented as the median with IQR, and variables were compared using Mann-Whitney tests if not stated otherwise. P values below 0.05 with CI 95% were considered statistically significant for all statistical evaluations.

RESULTS

Demographic data

A total of 246 patients who fulfilled ASAS classification criteria for axSpA were included in this study. Table 1 shows patients' demographic data. The entire group consisted of 106 patients with AS (43.1%) and 140 patients with nr-axSpA (56.9%). There was no gender predominance in the entire group (male-to-female ratio: 53.3% vs 46.7%). However, most of the nr-axSpA patients were women compared with the AS patients (p<0.001). There were no significant differences in age, BMI or smoking history between AS and nr-axSpA patients.

Mean age at the diagnosis was 33.2 years, and the disease duration from first symptoms was 7.8 years for the entire axSpA group. The first clinical symptoms developed earlier in patients with AS compared with patients with nr-axSpA (p=0.001). AS patients were younger at the time of diagnosis than nr-axSpA patients (p=0.023).

Clinical parameters

Disease activity as determined by ASDAS-CRP was 2.2 in the entire axSpA group, and it was significantly higher in AS patients compared with nr-axSpA patients (p=0.022). The mean BASDAI was 2.6 in the entire axSpA group, but it did not significantly differ between AS and nr-axSpA subgroups. AS patients exhibited significantly worse spinal mobility compared with nr-axSpA patients. AS patients exhibited worse BASFI compared with nr-axSpA patients (p=0.030).

Peripheral arthritis and hip arthritis were present in 27.6% and 13.0% of all axSpA patients, respectively. Patients with nr-axSpA exhibited peripheral arthritis more frequently and hip arthritis less frequently compared with AS patients (p=0.001 and p=0.022, respectively). SJC and TJC were significantly higher in nr-axSpA patients compared with AS patients (p=0.021 and p=0.015, respectively). There were no significant differences in the first symptoms of the disease, extra-articular manifestations, or current and previous medications. Division of axSpA according to gender to compare joint variables (peripheral arthritis, hip arthritis, SJC and TJC) revealed a significant difference only in hip arthritis that was more frequent in male patients compared with female patients (p<0.001). Tables 1 and 2 present all clinical parameters.

Laboratory parameters

CRP serum levels (p<0.001) and ESR (p=0.007) were significantly higher in AS patients than nr-axSpA patients. HLA-B27 was found in most of the patients in this study (87.4%), and the prevalence of HLA-B27 was not significantly higher in AS patients than nr-axSpA patients. Tables 1 and 2 show all of the laboratory parameters.

DISCUSSION

This study investigated similarities and differences between AS and nr-axSpA subgroups fulfilling the imaging arm of ASAS classification criteria in a single-centre axSpA cohort in Prague.

Demographic characteristics were comparable in both axSpA subgroups, except the male-to-female ratio, which was higher in AS patients than nr-axSpA patients, which is consistent with previous studies.[8–11] The nr-axSpA subgroup consisted of more female patients than the AS subgroup. Our data also demonstrated that nr-axSpA patients presented first symptoms of the disease later than AS patients, which is also consistent with some previous studies.[20 21] Male gender and early onset of the disease in AS were proposed prognostic factors for severe radiographic damage,[22 23] and female gender was associated with milder disease and later onset.[24] Female predominance and later disease onset in nr-axSpA may underlie the lower percentage of nr-axSpA female patients progressing to AS.[11]

Positive family history is a common finding in SpA. For example, siblings of HLA-B27-positive AS patients exhibit a 50-fold increased risk of developing AS compared with the general population.[25] Many patients, especially HLA-B27-positive patients, have a positive family history of SpA or related diseases. More than one-third of all cases had first-degree relatives with AS, psoriasis or IBD in our study. Furthermore, recent findings even suggest that a substantial proportion of healthy first-degree relatives of HLA-B27-positive AS patients exhibit clinical and/or imaging abnormalities suggestive of SpA, and almost 33% may be classified as SpA especially as nr-axSpA.[26] Comparison of first-degree relatives across gender did not reveal any differences, but a significantly greater frequency of positive family history was previously described in women.[27 28] This result contrasts one study of the occurrence of SpA in first-degree relatives of patients in which no gender differences were demonstrated.[29]

The disease activity of axSpA patients, using ASDAS score and CRP levels, differed between subgroups but remained similar when BASDAI was used in the present study. AS patients exhibited significantly higher disease activity as determined by ASDAS and acute phase reactants compared with nr-axSpA patients, which is consistent with previous studies.[11 30] Elevated CRP may predict the

Table 1 Baseline characteristics: demographic and clinical features of spondyloarthritis

Characteristic		SpA	nr-axSpA	AS	M-W/FET p value
Age (years), median (IQR)		34.7 (29.3–43.5)	36.9 (29.2–46.9)	36.0 (29.3–44.1)	**0.551**
Gender	Male number (%)	131 (53.3)	54 (38.6)	77 (72.6)	**<0.001**
BMI (kg/m^2), median (IQR)		24.3 (21.7–27.4)	24.8 (21.6–28.2)	24.2 (22.6–26.6)	0.946
History of smoking					
	Ever-smoker, number (%)	107 (43.7)	52 (37.1)	55 (52.4)	0.138
HLA-B27 positive, number (%)		215 (87.4)	117 (83.6)	98 (92.5)	0.051
Disease duration, years (IQR)		7.8 (3.1–14.5)	5.6 (2.6–12.2)	10.2 (5.1–15.5)	**0.001**
First symptom					0.086
	Back pain, number (%)	195 (79.3)	104 (74.3)	91 (85.8)	
	Peripheral arthritis, number (%)	27 (11.0)	19 (13.6)	8 (7.5)	
	Extra-articular manifestations, number (%)	24 (9.8)	17 (12.1)	7 (6.6)	
Family history					
	First-degree relatives, number (%)	86 (35.0)	38 (27.1)	24 (22.6)	0.460
	Second-degree relatives, number (%)	28 (11.4)	18 (12.9)	10 (9.4)	0.426
History of					
	Peripheral arthritis, number (%)	68 (27.6)	50 (35.7)	18 (17)	**0.001**
	Hip arthritis, number (%)	32 (13.0)	12 (8.6)	20 (18.9)	**0.022**
	Uveitis, number (%)	63 (25.6)	39 (27.9)	24 (22.6)	0.379
	IBD, number (%)	13 (5.3)	9 (6.4)	4 (3.8)	
	Psoriasis, number (%)	1 (0.4)	0 (0)	1 (0.9)	
	Other, number (%)	3 (1.2)	1 (0.7)	2 (1.9)	
Current symptoms					
	MASES, median (IQR)	0.0 (0.0–2.0)	0.0 (0.0–2.0)	0.0 (0.0–1.3)	0.289
	SJC, mean (±SD)	0.4 (1.4)	0.5 (1.5)	0.3 (1.4)	**0.021**
	TJC, mean (±SD)	0.4 (1.4)	0.5 (1.4)	0.3 (1.7)	**0.015**
Current medication					
	NSAIDs, number (%)	126 (51.2)	71 (50.7)	55 (51.9)	**0.898**
	CsDMARDs, number (%)	39 (15.9)	26 (18.6)	13 (12.3)	**0.218**
	Corticosteroids, number (%)	5 (2)	2 (1.4)	3 (2.8)	
	BoDMARDs/bsDMARDs, number (%)*	6 (2.4)	2 (1.4)	4 (3.8)	

*Adalimumab two patients; certolizumab one patient; golimumab two patients; infliximab one patient.
AS, ankylosing spondylitis; BMI, Body Mass Index; BoDMARDs, biological original disease modifying antirheumatic drugs; bsDMARDs, biosimilar disease modifying antirheumatic drugs; csDMARDs, conventional synthetic disease modifying antirheumatic drugs; IBD, inflammatory bowel disease; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; M-W/FETp, Mann-Whitney/Fisher exact test p value; nr-axSpA, non-radiographic axial spondyloarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; SJC, swollen joint count; SpA, spondyloarthritis; TJC, tender joint count.

development of radiographic changes.[8] However, recent findings demonstrated similar disease activity as determined by the BASDAI index between AS and nr-axSpA subgroups.[8] The BASDAI may not be a reliable index for evaluating disease activity in axSpA because it reflects subjective perceptions of the disease. Spinal mobility measures and BASFI reflecting movement functions were significantly worse in the AS patients, which is consistent with the results of the German Spondyloarthritis Inception cohort.[11] These results are most likely due to advanced structural changes in the spine of AS patients.

A recent meta-analysis found that arthritis and extra-articular manifestations were equally prevalent in AS and nr-axSpA subgroups, except uveitis, which is slightly more

Table 2 Baseline characteristics: activity and metrology

Characteristic	SpA	nr-axSpA	AS	M-W/FET p value
ASDAS-CRP, median (IQR)	2.2 (1.4–2.8)	2.0 (1.1–2.3)	2.4 (1.7–2.8)	**0.022**
BASDAI, median (IQR)	2.6 (1.2–4.7)	2.7 (1.0–4.9)	2.4 (1.2–3.7)	0.362
CRP (mg/L)	4.3 (1.2–12.0)	2.5 (0.8–8.2)	7.1 (2.6–14.9)	**<0.001**
ESR (mm/h)	8.0 (4.0–17.8)	7.0 (3.0–16.0)	12.0 (4.4–22.0)	**0.007**
BASFI, median (IQR)	1.4 (0.5–2.1)	1.1 (0.3–2.9)	1.8 (0.7–3.3)	**0.030**
Metrology				
Modified Schober (cm), median (IQR)	4.0 (3.0–5.0)	4.5 (3.5–5.5)	4.0 (3.0–5.0)	**<0.001**
Occiput to wall (cm), median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	**<0.001**
Chin–chest distance (cm), median (IQR)	1.5 (0.0–3.0)	1.0 (0.0–2.0)	2.0 (0.0–3.0)	**0.008**
Chest expansion (cm), median (IQR)	4.0 (3.0–6.0)	4.0 (3.0–6.0)	3.8 (2.0–6.0)	0.136

AS, ankylosing spondylitis; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score based on CRP; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; M-W/FETp, Mann-Whitney/Fisher exact test p value; nr-axSpA, non-radiographic axial spondyloarthritis; SpA, spondyloarthritis.

prevalent in AS patients.[12] However, our study demonstrated a significant difference between the occurrence of peripheral arthritis, which was more frequent in the nr-axSpA than AS subgroup. A large SpA cohort recently demonstrated more peripheral involvement in women,[27] which may explain the higher prevalence of peripheral arthritis in nr-axSpA with the larger female predominance, at least in the present study. Hip involvement was more frequent in AS patients than the nr-axSpA patients in our cohort. Hip involvement is more prevalent in patients with a younger disease onset, which may be associated with more severe axial disease, and it represents a prognostic factor for severe outcome.[23 31]

Our study has some limitations. First, four assessors examined the patients, which may cause possible inter-rater variability. Second, MRI was performed in several centres, and two MRI sequences were not available for reassessment at the time of data analysis. Therefore, we followed the written report from the MRI examination to divide the patients into AS or nr-axSpA subgroups. We have tried to reduce possible bias by excluding patients fulfilling only the clinical arm of ASAS classification criteria and included only patients with sacroiliitis confirmed by MR (nr-axSpA) or conventional X-ray (AS). Patients fulfilling only the clinical arm had lower participation in the study and fulfilling only clinical arm of ASAS classification criteria provide relatively low sensitivity and specificity and sometimes causing questionable or borderline diagnosis.

CONCLUSIONS

In summary, although disease activity, as determined by ASDAS and acute phase reactants, and functional limitations are worse in AS compared with nr-axSpA patients fulfilling the imaging arm of ASAS classification criteria, we confirmed that patients with nr-axSpA and patients with AS share some similar disease manifestations. However, they differ in gender ratio where women are more prevalent in nr-axSpA than in AS subset and surprisingly, peripheral arthritis, unlike hip joint involvement, was more prevalent in nr-axSpA compared with AS subset. To conclude, patients with nr-axSpA and AS exhibited many similarities despite the issue of classification, which suggests a common therapeutic approach.

Acknowledgements The authors would like to thank nurse Jana Gistrová and nurse Jiřina Kvítková for assistance during the patients examinations. Furthermore, the authors would like to thank the Department of molecular biology and immunogenetics for technical assistance during the laboratory analyses.

Contributors MH, KB, LS and KP designed the study. MH, KB, SF, KZ, MG, JH, MF, MT, KP and LS prepared the clinical database or took clinical care of axSpA patients in the PRASPAC cohort. KB, MT and LS did the data analysis. KB, MT and LS drafted the manuscript. KB and JG determined the radiographic and MRI scores. All authors contributed to and approved the final manuscript.

Funding This study has been supported by the Project for Conceptual Development for the institution of Ministry of Health Czech Republic—Institute of Rheumatology (number 023728), by SVV for LF1 UK (number 260373) and grant MHCR (number 17-33127A).

Competing interests None declared.

Patient consent for publication Obtained.

Ethics approval The local ethics committee (Mgr. Ivana Půtova) of the Institute of Rheumatology in Prague approved this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available. All data from the PRASPAC cohort are available to all qualified researchers/research groups on request.

REFERENCES

1. Sieper J, Poddubnyy D. Axial spondyloarthritis. *Lancet* 2017;390:73–84.
2. Taurog JD, Chhabra A, Colbert RA. Ankylosing spondylitis and axial spondyloarthritis. *N Engl J Med* 2016;375:2563–74.

3. Paramarta JE, Baeten D. Spondyloarthritis: from unifying concepts to improved treatment. *Rheumatology* 2014;53:1547–59.
4. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984;27:361–8.
5. Dincer U, Cakar E, Kiralp MZ, *et al*. Diagnosis delay in patients with ankylosing spondylitis: possible reasons and proposals for new diagnostic criteria. *Clin Rheumatol* 2008;27:457–62.
6. Rudwaleit M, van der Heijde D, Landewé 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. Poddubnyy D, Sieper J. Radiographic progression in ankylosing spondylitis/axial spondyloarthritis: how fast and how clinically meaningful? *Curr Opin Rheumatol* 2012;24:363–9.
8. Poddubnyy D, Sieper J. Similarities and differences between nonradiographic and radiographic axial spondyloarthritis: a clinical, epidemiological and therapeutic assessment. *Curr Opin Rheumatol* 2014;26:377–83.
9. Kiltz U, Baraliakos X, Karakostas P, *et al*. Do patients with non-radiographic axial spondylarthritis differ from patients with ankylosing spondylitis? *Arthritis Care Res* 2012;64:1415–22.
10. Rudwaleit M, Haibel H, Baraliakos X, *et al*. The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. *Arthritis Rheum* 2009;60:717–27.
11. Baraliakos X, Braun J. Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences? *RMD Open* 2015;1:e000053.
12. de Winter JJ, van Mens LJ, van der Heijde D, *et al*. Prevalence of peripheral and extra-articular disease in ankylosing spondylitis versus non-radiographic axial spondyloarthritis: a meta-analysis. *Arthritis Res Ther* 2016;18:196.
13. Rudwaleit M, Braun J, Sieper J. [ASAS classification criteria for axial spondyloarthritis]. *Z Rheumatol* 2009;68:591–3.
14. Heuft-Dorenbosch L, Spoorenberg A, van Tubergen A, *et al*. Assessment of enthesitis in ankylosing spondylitis. *Ann Rheum Dis* 2003;62:127–32.
15. Lukas C, Landewé R, Sieper J, *et al*. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. *Ann Rheum Dis* 2009;68:18–24.
16. 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.
17. Jones SD, Calin A, Steiner A. An update on the Bath Ankylosing Spondylitis Disease Activity and Functional Indices (BASDAI, BASFI): excellent Cronbach's alpha scores. *J Rheumatol* 1996;23:407.
18. Bennett PH BT. *Population studies of the rheumatic diseases*. Amsterdam: Excerpta Medica Foundation, 1968.
19. Wanders AJ, Landewé RB, Spoorenberg A, *et al*. What is the most appropriate radiologic scoring method for ankylosing spondylitis? A comparison of the available methods based on the Outcome Measures in Rheumatology Clinical Trials filter. *Arthritis Rheum* 2004;50:2622–32.
20. Jeong H, Yoon JY, Park EJ, *et al*. Clinical characteristics of nonradiographic axial spondyloarthritis in Korea: a comparison with ankylosing spondylitis. *Int J Rheum Dis* 2015;18:661–8.
21. Wallis D, Haroon N, Ayearst R, *et al*. Ankylosing spondylitis and nonradiographic axial spondyloarthritis: part of a common spectrum or distinct diseases? *J Rheumatol* 2013;40:2038–41.
22. Lee W, Reveille JD, Davis JC, *et al*. Are there gender differences in severity of ankylosing spondylitis? Results from the PSOAS cohort. *Ann Rheum Dis* 2007;66:633–8.
23. Amor B, Santos RS, Nahal R, *et al*. Predictive factors for the longterm outcome of spondyloarthropathies. *J Rheumatol* 1994;21:1883–7.
24. Pradeep DJ, Keat A, Gaffney K. Predicting outcome in ankylosing spondylitis. *Rheumatology* 2008;47:942–5.
25. Carter N, Williamson L, Kennedy LG, *et al*. Susceptibility to ankylosing spondylitis. *Rheumatology* 2000;39:445.
26. Turina MC, de Winter JJ, Paramarta JE, *et al*. Clinical and Imaging Signs of Spondyloarthritis in First-Degree Relatives of HLA-B27-Positive Ankylosing Spondylitis Patients: The Pre-Spondyloarthritis (Pre-SpA) Cohort Study. *Arthritis Rheumatol* 2016;68:2444–55.
27. de Carvalho HM, Bortoluzzo AB, Gonçalves CR, *et al*. Gender characterization in a large series of Brazilian patients with spondyloarthritis. *Clin Rheumatol* 2012;31:687–95.
28. Will R, Edmunds L, Elswood J, *et al*. Is there sexual inequality in ankylosing spondylitis? A study of 498 women and 1202 men. *J Rheumatol* 1990;17:1649–52.
29. Dernis E, Said-Nahal R, D'Agostino MA, *et al*. Recurrence of spondylarthropathy among first-degree relatives of patients: a systematic cross-sectional study. *Ann Rheum Dis* 2009;68:502–7.
30. Wallman JK, Kapetanovic MC, Petersson IF, *et al*. Comparison of non-radiographic axial spondyloarthritis and ankylosing spondylitis patients-baseline characteristics, treatment adherence, and development of clinical variables during three years of anti-TNF therapy in clinical practice. *Arthritis Res Ther* 2015;17:378.
31. Vander Cruyssen B, Vastesaeger N, Collantes-Estévez E. Hip disease in ankylosing spondylitis. *Curr Opin Rheumatol* 2013;25:448–54.