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Spondyloarthritis on the move: Thrilling developments

OP0031

ARE THE MODIFIED NEW YORK AND ASAS AXIAL SPONDYLOARTHRITIS CRITERIA INTERCHANGEABLE IN THE CLASSIFICATION OF SPONDYLOARTHRITIS PATIENTS WITH RADIOGRAPHIC SACROILIITIS: COMPARISON IN 8 COHORTS?

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Background: Axial spondyloarthritis (axSpA) patients with radiographic sacroiliitis may be classified using the modified New York (mNY) criteria and the more recent ASAS criteria. In the mNY criteria these patients are referred to as ankylosing spondylitis (AS) patients and in the ASAS criteria as radiographic axSpA (r-axSpA) patients. In both the mNY and the ASAS r-axSpA classification sets the radiographic criterion is the same but the additionally required features differ (figure), for example patients with age at onset of back pain ≥ 45 cannot fulfil the ASAS criteria. This raises the question whether the two sets can be used interchangeably in the classification of axSpA patients with radiographic sacroiliitis.

Modified New York criteria for the classification of AS	ASAS criteria for the classification of radiographic axSpA
1. Low back pain and stiffness for at least 3 months, which improves with exercise and is not relieved by rest 2. Limitation of lumbar spine motion in the sagittal and frontal planes 3. Decreased chest expansion, compared to age- and sex-matched controls 4a. Unilateral sacroiliitis grade 2 or 4 4b. Bilateral sacroiliitis grade 2 or 4	1. Back pain 3 months 2. Age at onset ≥ 45 years 3. Sacroiliitis on imaging* 4. 2/3 SpA features: - Inflammatory back pain - Ankyritis - Enthesitis - Uveitis - Dactylitis - Psoriasis - Crohn's/colitis - Good response to NSAIDs - Family history for SpA - HLA-B27 positive - Elevated CRP (or ESR)
Definite AS if sacroiliitis as described in 4a or 4b and any of the clinical symptoms (1-3).	*Definite radiographic sacroiliitis according to mNY criteria Definite r-axSpA if fulfillment of 1 and 2, sacroiliitis as described in 3 and at least one of the clinical SpA features as described in 4.

Figure 1. mNY and ASAS r-axSpA criteria for the classification of patients with axSpA and radiographic sacroiliitis.

Objectives: To investigate to what degree patients with axSpA and radiographic sacroiliitis who fulfil the mNY criteria also fulfil the ASAS criteria for r-axSpA and vice-versa.

Methods: Patients diagnosed with axSpA who had back pain longer than 3 months and definite radiographic sacroiliitis (i.e. common and mandatory features for both classification criteria sets (figure)) were selected from several cohorts (ASAS, Esperanza, GESPIC, OASIS, Reuma.pt, SCQM, SPACE, and UCSF). Subsequently we calculated how many patients fulfil the mNY criteria and/or the ASAS r-axSpA criteria. For the Esperanza and OASIS cohorts specific information on the individual items of the mNY criteria was unavailable, which restricted data analysis for these cohorts.

Results: Of the 3882 patients fulfilling the mNY criteria, 93% also fulfilled the ASAS r-axSpA criteria. Inversely, of the 3434 patients fulfilling the ASAS r-axSpA criteria, 96% also fulfilled the mNY criteria (table). In total, 89% (3607/4041) of patients with axSpA and radiographic sacroiliitis fulfilled both criteria sets; 7% only the mNY criteria; 3% only the ASAS criteria and 1% neither set.

Table 1. Percentage of patients fulfilling ASAS r-axSpA within subgroup fulfilling mNY criteria and vice-versa (per cohort and overall)

	ASAS within mNY subgroup	mNY within ASAS subgroup
ASAS	93% (3607/3882)	96% (3300/3434)
Esperanza	97% (106/109)	NA
GESPIC	95% (78/89)	93% (78/84)
OASIS	95% (201/211)	NA
Reuma.pt	93% (1156/1249)	95% (1156/1211)
SCQM	93% (161/171)	95% (161/165)
SPACE	100% (77/77)	84% (77/92)
UCSF	96% (129/138)	95% (129/138)
Total	93% (3607/3882)	96% (3300/3434)

The main difference between the two criteria sets was caused by reported age at onset of back pain. Out of 275 mNY+ patients not fulfilling the ASAS criteria (7% of all included patients), 265 (96%) cases were due to the age criterion and 10 (4%) due to the absence of SpA features. Of the 3434 ASAS+ patients, 90% fulfilled the mNY criteria because they had IBP, another 6% despite not having IBP fulfilled the mNY criteria due to a mobility restriction; and the remainder 4% had neither but fulfilled the ASAS criteria because of other SpA features.

Conclusion: AxSpA patients classified as AS according to mNY criteria and those classified as r-axSpA according to ASAS criteria are mostly the same: 93% of mNY positive patients also fulfil the ASAS r-axSpA criteria while 96% of ASAS r-axSpA positive patients also fulfil the mNY criteria. These findings support the interchangeable use of the terms r-axSpA and AS, which was also approved by a vote of ASAS members at the 2019 annual workshop in Amsterdam.

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OP0032

LOCALIZATION AND MORPHOLOGY OF MAGNETIC RESONANCE IMAGING FEATURES OF PATHOLOGIC CHANGES IN THE SACROILIAC JOINTS SUGGESTIVE OF AXIAL SPONDYLOARTHRITIS – A SYSTEMATIC COMPARISON OF PATIENTS AND CONTROLS WITH CHRONIC BACK PAIN

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Background: Bone marrow edema (BME), fat metaplasia (FL) and erosions have been identified as relevant for magnetic resonance imaging (MRI) changes in the sacroiliac joints (SIJ) of patients with axial spondyloarthritis (axSpA). However, a high prevalence of MRI changes has recently also been reported in subjects with no evidence of axSpA (1,2).

Objectives: To map the MRI lesions suspicious of axSpA in patients diagnosed with axSpA and compare them to those in patients with chronic back pain (cBP, non-SpA).

Methods: Consecutive patients with cBP < 45 years were included if they had at least one pathologic lesion of any type in the SIJ-MRI performed at the time point of cBP symptoms. AxSpA patients diagnosed by 2 experienced rheumatologists in consensus also had to fulfil ASAS classification criteria. Two experienced readers, blinded for diagnosis and patient's demographics, evaluated all MRIs independently. Lesions were only counted as positive if both readers were in agreement and mean values of both readers were calculated for the final analysis. Both the coronal (assessing the upper and lower sacral and iliac SIJ part) and axial (assessing the ventral, middle and retroauricular as well as the upper and lower sacral and iliac SIJ part) MRI orientations were analyzed for the localization of BME, FL, sclerosis and erosions. In addition, length and width were digitally measured for BME, FL and sclerosis, and signal intensity was measured electronically in each individual patient in comparison to the cerebrospinal fluid signal for BME and the subcutaneous fat for FL (no units).

Comparisons were calculated by Mann-Whitney-U-test for patients classified as positive by both readers for the respective lesions.

Results: A total of 200 consecutive patients (100 axSpA, 100 non-SpA), mean age 36.1 $\pm$ 11.3 and 40.3 $\pm$ 11.0 years, respectively, were analyzed. BME was found in 85% vs. 80% of patients, while 80% vs. 69% had FL, 54% vs. 40% had sclerosis and 64% vs. 12% had erosions, respectively. The largest surface area covered by BME in axSpA vs. non-SpA was found in the lower and dorsal SIJ: 60 $\pm$ 10.1 mm³ in the iliac and 47.3 $\pm$ 9.4 mm³ in the sacral part vs. the upper and ventral SIJ: 18.7 $\pm$ 3.4 mm³ in the sacral and 5.2 $\pm$ 0.1 mm³ in the iliac part.

Patients with axSpA showed a larger surface area covered by FL was found in the upper and anterior sacral SIJ (305.5 $\pm$ 56.3 mm³), whereas patients with non-SpA showed larger FL areas in the lower and posterior sacral SIJ (197.9 $\pm$ 1.2 mm³). Regarding sclerosis, the upper and anterior iliac part had more surface involvement in both SpA (139.3 $\pm$ 11.6 mm³) and non-SpA (81.8 $\pm$ 2.8 mm³) patients.

The mean signal intensity of all lesions and MRI planes differed between axSpA (102.385 units?) and non-SpA (48.995) patients for BME ($p<0.001$) but not for FL. Overall, axSpA patients also had significantly more SIJ quadrants with pathologic changes, except for BME and sclerosis in the ventral and fat located in the retroauricular part of the SIJ. The occurrence of erosions in the mid (61 vs. 7) and the ventral (51 vs. 8) part of the SIJ could discriminate best between axSpA and non-SpA (both $p<0.001$).

Conclusion: These data show that although all types of lesions may be found in both patient groups, the anatomic pattern of SIJ involvement can still distinguish axSpA from non-SpA. The localization and morphological appearance of SIJ-MRI features suggestive of axSpA may serve as an additional feature in the definition of a 'positive' MRI both for diagnosis and classification.

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OP0033

WHAT IS AXIAL SPONDYLOARTHRITIS? A LATENT CLASS AND TRANSITION ANALYSIS IN THE SPACE AND DESIR COHORTS

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Background: Axial spondyloarthritis (axSpA) is a disease with a rather heterogeneous presentation that may be difficult to diagnose. Classification criteria, such as the ASAS criteria, which have been developed and validated against the gold-standard 'expert diagnosis', exist, but may suffer from inappropriate circularity because features deemed important by experts (e.g. sacroiliitis on MRI) may have easily got a too prominent, and therefore biased, role. If classification criteria are used inappropriately to confirm a diagnosis, overdiagnosis ('too much SpA') may be an unwarranted consequence.

Objectives: To gain an unbiased insight into the concept of axSpA, by circumventing expert opinion and investigating its 'latent constructs'. We examined the SpA-features' mutual statistical coherence, established the unbiased 'Gestalt' of SpA, and evaluated how well the ASAS axSpA classification criteria capture these 'latent constructs'.

Methods: Two independent cohorts of patients (pts) with early onset chronic back pain (SPACE cohort) and inflammatory back pain (IBP) (DESIR cohort) were included. Latent class analysis (LCA) (different than a cluster analysis) was used to estimate the latent (i.e. unobserved) 'Gestalt' of axSpA by modelling the covariance of the observed SpA features (without 'a priori' assumptions on their 'weights'). The selected best LCA model splits axSpA into a number of (clinically

meaningful) classes with best data fit. Each class was labelled by us and named according to most prominent features. The latent axSpA classes were then used as 'gold-standard' against which the ASAS axSpA, pSpA (ignoring IBP) and both (SpA criteria) were tested. Finally, 5-year follow-up data from DESIR were used to perform a latent transition analysis (LTA) in order to examine if patients change classes over 5-year time.

Table 1. Latent class analysis model in SPACE (N=465)

	'Axial' (P*=15.9%)	'IBP+Peripheral' (P*=20.0%)	'At risk' (P*=24.3%)	'No SpA' (P*=39.7%)
	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)
Inflammation on MRI-SIJ (ASAS)	0.74 (0.52; 0.88)	0.04 (0.01; 0.14)	0.00 (0.00; 1.00)	0.03 (0.01; 0.08)
Radiographic sacroiliitis (mNY)	0.32 (0.19; 0.49)	0.09 (0.04; 0.20)	0.01 (0.00; 0.32)	0.03 (0.01; 0.08)
Elevated CRP (≥ 6 mg/dl)	0.49 (0.32; 0.65)	0.22 (0.13; 0.34)	0.21 (0.13; 0.32)	0.20 (0.15; 0.28)
BME on MRI-Spine (≥ 5 lesions)	0.25 (0.14; 0.42)	0.02 (0.00; 0.18)	0.00 (0.00; 1.00)	0.00 (0.00; 0.11)
≥ 1 syndesmophyte on X-spine	0.03 (0.01; 0.11)	0.06 (0.03; 0.14)	0.00 (0.00; 1.00)	0.04 (0.02; 0.08)
Good response to NSAIDs (ever)	0.59 (0.41; 0.75)	0.85 (0.72; 0.93)	0.25 (0.14; 0.29)	0.20 (0.14; 0.29)
Peripheral arthritis (ever)	0.17 (0.09; 0.30)	0.44 (0.30; 0.58)	0.04 (0.01; 0.15)	0.10 (0.06; 0.17)
Dactylitis (ever)	0.02 (0.00; 0.17)	0.18 (0.11; 0.29)	0.00 (0.00; 1.00)	0.03 (0.01; 0.07)
Heel enthesitis (ever)	0.10 (0.04; 0.25)	0.66 (0.50; 0.79)	0.13 (0.06; 0.24)	0.04 (0.01; 0.11)
HLA-B27	0.84 (0.67; 0.93)	0.33 (0.23; 0.46)	0.69 (0.24; 0.94)	0.00 (0.00; 1.00)
Family history of SpA	0.38 (0.24; 0.54)	0.50 (0.38; 0.62)	0.71 (0.56; 0.82)	0.21 (0.10; 0.38)
Psoriasis (ever)	0.10 (0.04; 0.22)	0.31 (0.21; 0.43)	0.02 (0.00; 0.23)	0.08 (0.05; 0.14)
Uveitis (ever)	0.13 (0.06; 0.24)	0.07 (0.03; 0.17)	0.12 (0.06; 0.22)	0.02 (0.00; 0.11)
IBD (ever)	0.03 (0.01; 0.16)	0.15 (0.08; 0.25)	0.00 (0.00; 1.00)	0.10 (0.06; 0.17)
Inflammatory back pain	0.68 (0.55; 0.79)	1.00 (0.00; 1.00)	0.66 (0.53; 0.76)	0.09 (0.01; 0.59)

* Probability of the latent class. Values are the conditional probability (95% confidence interval) for each SpA feature positivity within each latent class (range: 0-1). Values in **bold** highlight dominant features between latent classes. Values in *italic* highlight dominant features (probability >50%) within each class. BME, bone marrow edema; IBD, inflammatory bowel disease.

Table 2. Latent class analysis model in DESIR (N=576)

	'Axial' (P*=18.8%)	'IBP+Peripheral' (P*=26.7%)	'At risk' (P*=54.5%)
	Estimated probability (95% CI)	Estimated probability (95% CI)	Estimated probability (95% CI)
Inflammation on MRI-SIJ (ASAS)	0.83 (0.69; 0.92)	0.22 (0.15; 0.30)	0.09 (0.06; 0.16)
Radiographic sacroiliitis (mNY)	0.58 (0.45; 0.70)	0.06 (0.02; 0.13)	0.02 (0.01; 0.08)
Elevated CRP (≥ 6 mg/dL)	0.56 (0.44; 0.67)	0.41 (0.32; 0.51)	0.14 (0.10; 0.20)
BME on MRI-Spine (≥ 5 lesions)	0.20 (0.13; 0.30)	0.00 (0.00; 1.00)	0.01 (0.00; 0.03)
≥ 1 syndesmophyte on X-spine	0.11 (0.06; 0.20)	0.05 (0.02; 0.11)	0.06 (0.04; 0.10)
Good response to NSAIDs (ever)	0.97 (0.90; 0.99)	0.84 (0.76; 0.90)	0.82 (0.77; 0.86)
Peripheral arthritis (ever)	0.09 (0.04; 0.20)	0.73 (0.49; 0.88)	0.00 (0.00; 1.00)
Dactylitis (ever)	0.03 (0.01; 0.15)	0.46 (0.36; 0.55)	0.01 (0.00; 0.31)
Heel enthesitis (ever)	0.26 (0.18; 0.37)	0.60 (0.51; 0.69)	0.45 (0.39; 0.51)
HLA-B27	0.90 (0.79; 0.96)	0.52 (0.43; 0.61)	0.53 (0.47; 0.59)
Family history of SpA	0.48 (0.37; 0.58)	0.44 (0.36; 0.53)	0.41 (0.36; 0.48)
Psoriasis (ever)	0.09 (0.04; 0.18)	0.29 (0.22; 0.38)	0.14 (0.10; 0.19)
Uveitis (ever)	0.08 (0.04; 0.18)	0.12 (0.07; 0.20)	0.08 (0.05; 0.12)
IBD (ever)	0.02 (0.00; 0.10)	0.05 (0.02; 0.11)	0.05 (0.03; 0.08)

* Probability of the latent class. Values are the conditional probability (95% confidence interval) for each SpA feature positivity within each latent class (range: 0-1). Values in **bold** highlight dominant features between latent classes. Values in *italic* highlight dominant features (probability >50%) within each class. BME, bone marrow edema; IBD, inflammatory bowel disease.

Results: In total, data of 465 (SPACE) and 576 (DESIR) pts were analyzed. SPACE yielded 4 latent classes (Table 1). The 'Axial' class characterized by highest likelihood on abnormal imaging and HLA-B27-positivity; the 'IBP+Peripheral' class had 100% likelihood of IBP in association with peripheral signs. The 'At risk' class is anchored on a positive family history and HLA-B27 positivity in association with IBP; and the 'No SpA' class had very low likelihoods for all SpA-features which were correlated. The independent analysis in DESIR (without 'no-SpA' patients) yielded identical latent classes ('Axial':19%; 'IBP+Peripheral':27% and 'At risk':55%) (Table 2). The ASAS axSpA criteria, tested in SPACE ('No SpA' absent in DESIR), captured 67% of the patients in the 'Axial' and 'IBP+Peripheral' classes ('latent gold-standard'), but sensitivity was better (87%) if axSpA and pSpA criteria were combined. Of note, the axSpA criteria captured only 4% of the patients from the 'No SpA' class. Importantly, the LTA suggests that transition between classes over time was highly unlikely. 'Axial' and 'IBP+Peripheral' patients did not switch and only 11% of 'At risk' pts had switched to 'IBP+Peripheral' after 5 years.

Conclusion: The 'Gestalt' of axial spondyloarthritis comprises three distinguishable clinical entities ('pure axial SpA', 'axial SpA with peripheral signs', and 'axial SpA at risk'). Patients keep their clinical entity over 5 years and transition is very rare. The 'Axial' and 'IBP+Peripheral' entities are best captured by combining the ASAS axSpA and pSpA criteria.

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