Performance of the Assessment in Spondyloarthritis International Society Classification for Axial and Peripheral Spondyloarthritis in an Established Clinical Cohort: Comparison with Criteria Sets of Amor and the European Spondylarthropathy Study Group

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ABSTRACT. ***Objective.*** To evaluate the performance of the Assessment in Spondyloarthritis International Society (ASAS) criteria (axial or peripheral) against the Amor and European Spondylarthropathy Study Group criteria in established spondyloarthritis (SpA).

Methods. Rheumatologist-diagnosed patients with SpA were retrospectively classified according to the different criteria sets. Clinical characteristics of patients fulfilling all 3 criteria were compared with those who did not, by nonparametric statistics.

Results. ASAS classified 90% of the 231 patients, with 169 (73%) fulfilling all 3 criteria sets. Multivariate analysis showed the 62 patients not fulfilling all criteria sets were older at symptom onset ($p < 0.001$) and less likely to have inflammatory back pain ($p < 0.001$), peripheral arthritis ($p < 0.001$), or elevated C-reactive protein levels ($p = 0.034$).

Conclusion. ASAS criteria can be used in established disease. (J Rheumatol First Release Feb 15 2012; doi:10.3899/jrheum.111088)

Key Indexing Terms:
SPONDYLOARTHRITIS CRITERIA ANKYLOSING SPONDYLITIS
CLASSIFICATION CLINICAL PRACTICE

Different sets of classification criteria such as the Amor and the European Spondylarthropathy Study Group (ESSG) criteria have been developed for spondyloarthritis (SpA)[1,2]. The Assessment in Spondyloarthritis International Society (ASAS) group has recently proposed 2 sets of criteria (covering axial and peripheral presentations), which incorporate sacroiliitis confirmed by magnetic resonance imaging (MRI), to improve the classification of SpA[3,4,5]. Although these criteria were derived by an international group of experts according to recent methodological standards[6], initially for early and late SpA, they still require external validation against the Amor or ESSG criteria for established SpA in clinical practice. Our objective was to evaluate the ASAS criteria against the Amor and ESSG in the setting of an established SpA cohort, looking in particular at effects of disease duration and the specific components in the criteria that differentiate its performance.

MATERIALS AND METHODS

A retrospective single-center study of unselected patients having rheumatologist-diagnosed SpA was conducted between January and July 2010: the COSPA (COchin SpondyloArthritis) study[7]. Patients were assessed for all characteristics included in the ASAS, ESSG, and Amor criteria outlined in Table 1[1,2,3,4,5]. Baseline disease characteristics were collected such as age, disease duration (from first symptom onset), anti-tumor necrosis factor (TNF) exposure, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and Bath Ankylosing Spondylitis Functional Index (BASFI; scale 0–100 mm)[8,9]. Each patient was retrospectively classified according to Amor and ESSG, modified Amor, and modified ESSG (which included the possibility of using MRI to diagnose sacroiliitis), and either the axial or peripheral ASAS criteria based on the predominant clinical manifestations of the patient. For patients who had simultaneous axial and peripheral involvement, the physician had made a decision on which was the more predominant manifestation based on history and examination. Patients with insufficient data to allow application of the axial classification criteria, which rely on knowledge of

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Table 1. Characteristics included in ASAS, Amor, and ESSG criteria.

ASAS (axial)[†]: Sacroiliitis on imaging plus ≥ 1 SpA feature, or HLA-B27 plus ≥ 2 SpA features:	
Inflammatory back pain*	
Arthritis	
Enthesitis (heel)	
Uveitis	
Dactylitis	
Psoriasis	
IBD	
Good response to NSAID	
Family history for SpA	
HLA-B27	
Elevated CRP	
ASAS (peripheral)[†]: Arthritis or enthesitis or dactylitis plus either ≥ 1 SpA feature, or ≥ 2 SpA features	
≥ 1 SpA features:	≥ 2 SpA features:
Uveitis	Arthritis
Psoriasis	Enthesitis
IBD	Dactylitis
Preceding infection	IBP ever
HLA-B27	Family history for SpA
Sacroiliitis on imaging	
Amor: Clinical symptoms or history of	
Lumbar or dorsal pain during the night, or morning stiffness of lumbar or dorsal spine	
Asymmetric oligoarthritis	
Buttock pain, if affecting alternately the right or the left buttock	
Dactylitis	
Heel pain or any other well defined enthesopathy (enthesitis)	
Iritis	
Nongonoccal urethritis or cervicitis accompanying, or within 1 month before, the onset of arthritis	
Presence or history of psoriasis, banalitis, or IBD	
Radiological findings	
Sacroiliitis	
Genetic background	
HLA-B27 or family history of SpA	
Response to treatment	
Good response to NSAID in < 48 h	
ESSG	
Inflammatory spinal pain or synovitis (asymmetric or predominantly in the lower limbs), and ≥ 1 SpA feature:	
Positive family history	
Psoriasis	
IBD	
Urethritis, cervicitis, or acute diarrhea within 1 month before arthritis	
Alternating buttock pain	
Enthesopathy	
Sacroiliitis	

[†] Patient age at onset < 45 yrs and ≥ 3 months' back pain (for axial predominant disease). * Four out of 5 of the following measures present: (1) age at onset < 40 yrs, (2) insidious onset, (3) improvement with exercise, (4) no improvement with rest, and (5) pain at night (with improvement upon getting up). ASAS: Assessment in Spondyloarthritis International Society; ESSG: European Spondylarthropathy Study Group; SpA: spondyloarthritis; NSAID: nonsteroidal antiinflammatory drugs; CRP: C-reactive protein; IBD: inflammatory bowel disease; IBP: inflammatory back pain.

sacroiliitis, were not included. For those patients, sacroiliitis could not be ascertained on plain radiographs (absence of sacroiliitis, n = 27, or unavailable sacroiliac radiographs, n = 17) and MRI was not available.

Statistical analysis. Statistical analysis was carried out using SPSS 18 (SPSS, Chicago, IL, USA). Venn diagrams illustrated the proportion of patients fulfilling the 3 criteria; the classification rate was defined as the proportion of patients fulfilling the particular criteria set. To explore disagreements, patients who fulfilled all 3 criteria (concordant group) were compared to those who did not (discordant group) by nonparametric statistics. A stepwise multivariate logistic regression analysis was performed to look at variables predictive of criteria disagreements. The same analysis was performed on patients with disease duration ≤ 10 years. Sensitivities, specificities, and positive likelihood ratios (LR) with 95% CI were calculated: ASAS criteria were tested against either Amor or ESSG as the "gold standard," for example, LR > 1 indicated an increased probability that the "target" (i.e., Amor or ESSG criteria) is fulfilled as well.

Imputation analysis was performed to examine the potential selection bias of excluding patients without sacroiliac MRI. Of the 44 patients initially excluded, the ASAS criteria were retested against the Amor and ESSG criteria on the hypothesis that "all" those patients had MRI evidence of sacroiliitis (best-case scenario), versus the hypothesis that "all" those patients had no MRI evidence of sacroiliitis (worst-case scenario).

RESULTS

Of the 275 patients in COSPA, 231 were included, 63% were men, 77% had HLA-B27, with median age of 44 years; 82% had radiographic sacroiliitis (Table 2) and 59% had MRI of the sacroiliac joints. Although disease duration was long (median 16 years, Q1: 8, Q3: 27, range 2–52 yrs), 75 patients had SpA ≤ 10 years. Activity of disease was low to moderate with a median BASDAI of 28 and BASFI of 23; 62% had previous or concomitant anti-TNF treatment. A majority of patients were diagnosed with ankylosing spondylitis (n = 178, 77%), followed by psoriatic arthritis (n = 21, 9%), undifferentiated SpA (n = 16, 7%), SpA related to inflammatory bowel disease (n = 9, 4%), juvenile onset SpA (n = 5, 2%), and reactive arthritis (n = 2, < 1%).

The highest classification rate was found with the Amor criteria (96%), followed by the ASAS criteria (90%, 196 predominantly axial and 11 predominantly peripheral), then the ESSG criteria (83%). Figure 1 shows the number of patients fulfilling the 3 different criteria sets for SpA. Overall, 169 patients (73%) fulfilled the 3 criteria sets (concordant group). Of the remaining 62 patients (27%) in the discordant group, 50 fulfilled 2 criteria sets, 11 fulfilled 1, and 1 fulfilled neither.

Of the 75 patients with disease duration ≤ 10 years (Figure 1B), 46 (61%) fulfilled 3 criteria sets. However, even in these patients, ASAS criteria sets had the lowest classification rate (76%).

When compared to the Amor and ESSG criteria as "gold standards," the ASAS criteria had a high sensitivity, between 0.90 and 0.92 (95% CI 0.87–0.95) (95% CI 0.85–0.93), respectively (Table 3). However, the specificity of ASAS versus ESSG was markedly lower than versus Amor. Performance of ASAS was similar compared to the modified Amor and ESSG. An imputational analysis for missing results of MRI indicated robust results (Table 3).

Comparison of disease characteristics between the concordant and discordant group is presented in Table 2. In multivariate analysis, the discordant group was older at first onset of symptoms ($p < 0.001$) and less likely to fulfill the ASAS definition of inflammatory back pain[3] ($p < 0.001$). In addition, they were less likely to have a history of synovitis or peripheral arthritis ($p < 0.001$) and elevated C-reactive protein (CRP) levels ($p = 0.034$). Similar differences were observed in the discordant group with early disease (≤ 10 years; Table 4), with the same variables being predictive in multivariate analysis; i.e., older at first symptom onset ($p = 0.002$) and less likely to have ASAS-defined inflammatory back pain ($p = 0.002$), synovitis/peripheral arthritis ($p = 0.04$), and elevated CRP ($p = 0.04$).

Table 2. Baseline disease characteristics with comparison of patients with full concordance with criteria sets and patients with discordance. Results are n (%) or median with interquartile ranges (Q1:Q3).

Characteristic	All Patients, n = 231	Concordance**, n = 169	Discordance**, n = 62	p*
HLA-B27†	176 (76.2)	137 (86.2)	39 (70.9)	0.014
Sex (men)	145 (62.8)	107 (63.3)	38 (61.3)	0.878
Radiographic sacroiliitis†	190 (82.3)	147 (88.6)	43 (71.7)	0.004
Sacroiliitis MRI†	66 (28.6)	46 (49.5)	20 (46.5)	0.854
IBP ASAS definition	154 (66.7)	139 (82.2)	15 (24.2)	< 0.001
Synovitis	103 (44.6)	88 (52.4)	15 (24.2)	< 0.001
Psoriasis	64 (27.7)	46 (27.4)	18 (29.0)	0.869
Raised CRP†	150 (64.9)	114 (75.0)	36 (64.3)	0.163
Uveitis	69 (29.9)	55 (32.7)	14 (22.6)	0.148
Hip involvement	44 (19.0)	36 (21.0)	8 (12.9)	0.187
IBD	21 (9.1)	17 (10.1)	4 (6.5)	0.606
Family history	97 (42.0)	76 (45.5)	21 (35)	0.173
Anti-TNF to exposure	143 (61.9)	114 (67.5)	29 (46.8)	0.006
Response to NSAID	192 (83.1)	144 (85.7)	48 (80.0)	0.307
Enthesitis (heel)	117 (50.6)	88 (52.1)	29 (46.8)	0.553
Dactylitis	47 (20.3)	38 (22.5)	9 (14.5)	0.202
Disease duration, yrs	16 (8, 27)	18 (10, 27)	11 (6, 20)	0.002
Age, yrs	44 (35, 55)	42 (39, 50)	51 (39, 59)	0.001
Age at first symptom, yrs	24 (18, 32)	22 (17, 27)	33 (23, 49)	< 0.001
BASDAI, mm	28 (15, 44)	27 (14, 43)	31 (15, 45)	0.549
BASFI, mm	23 (6, 42)	22 (5, 39)	26 (7, 52)	0.148

† On the number of available data. * Comparing the concordant with the discordant group. ** Concordance defined as a patient fulfilling the 3 criteria, discordance defined as a patient that did not fulfill all 3 criteria. MRI: magnetic resonance imaging; ASAS: Assessment in Spondyloarthritis International Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CRP: C-reactive protein; IBD: inflammatory bowel disease; IBP: inflammatory back pain; NSAID: nonsteroidal anti-inflammatory drugs; TNF: tumor necrosis factor.

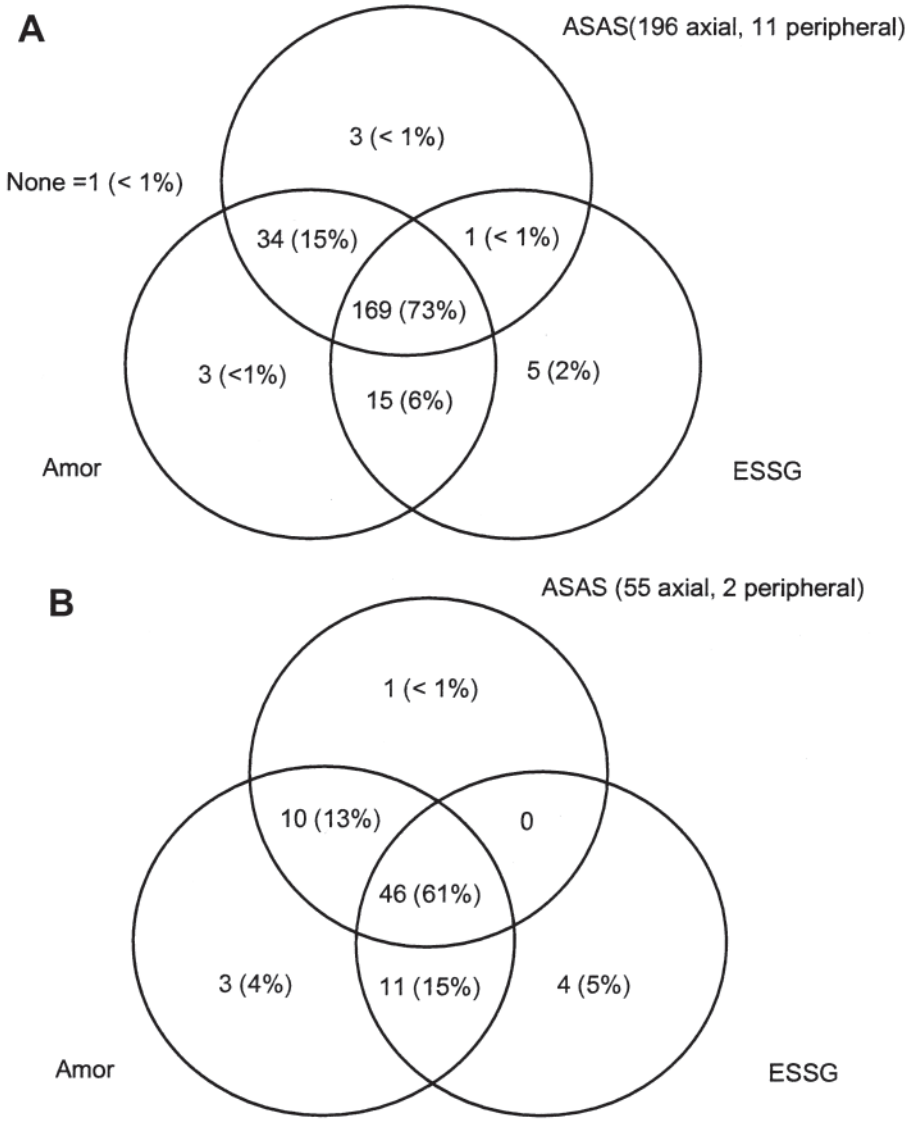

Figure 1. Numbers of patients meeting the criteria of ASAS, Amor, and ESSG. A. Total cohort analyzed (n = 231); results are number (percentage of total cohort) fulfilling each set of criteria. B. Patients with disease duration ≤ 10 years (n = 75); results are number (percentage) fulfilling each set of criteria. ASAS: Assessment in Spondyloarthritis International Society; ESSG: European Spondylarthropathy Study Group.

DISCUSSION

Our study has demonstrated that in established SpA, the ASAS criteria did not perform better than the Amor or ESSG criteria in classification of patients considered to have SpA, according to rheumatologists. The results show that ASAS criteria may be used in such a population but may continue to lead to misclassification when compared to the Amor or ESSG criteria. Further, patients who failed to fulfill all 3 criteria sets were less likely to have inflammatory back pain defined by ASAS, peripheral arthritis, or elevated CRP, and were more likely to be older at first symptom onset. This was irrespective of disease duration.

Although the ASAS criteria were initially developed for both early and late disease, particularly for patients with nonradiographic SpA, our study has shown that they can be applied to the majority of patients with established SpA in the clinical setting. Reports in early SpA cohorts have illustrated potential problems of the "entry" requirement, particularly in a predominantly HLA-B27-negative population[10,11]. Potential problems may occur in classification of patients when initial onset of symptoms may be more than the "entry" criterion of age younger than 45 years[12]. Further studies of ASAS criteria on different cohorts are required.

A significant strength and also limitation of our study was

Table 3. Sensitivity, specificity, and agreement of ASAS criteria compared to either Amor or ESSG criteria as the "gold standard."

Criteria	Sensitivity	95% CI	Specificity	95% CI	Positive Likelihood Ratio	95% CI
Amor	0.92	0.87, 0.95	0.56	0.27, 0.81	2.07	0.99, 4.30
ESSG	0.90	0.85, 0.93	0.10	0.04, 0.23	1.00	0.89, 1.11
mAmor*	0.91	0.87, 0.94	0.57	0.25, 0.84	2.14	0.91, 5.03
mESSG*	0.89	0.84, 0.93	0.05	0.01, 0.17	0.94	0.86, 1.03
Analysis by imputation of ASAS criteria compared to either Amor or ESSG criteria:						
Amor†	0.93	0.89, 0.95	0.56	0.27, 0.81	2.09	1.0, 4.33
Amor††	0.88	0.84, 0.91	0.56	0.27, 0.81	1.98	0.95, 4.12
ESSG†	0.91	0.87, 0.94	0.11	0.05, 0.23	1.03	0.92, 1.14
ESSG††	0.91	0.85, 0.93	0.13	0.06, 0.25	1.03	0.92, 1.16

* Inclusion of MRI for diagnosis of sacroiliitis into the original criteria. † Imputational analysis if all the 44 patients excluded from the analysis had sacroiliitis. †† Imputational analysis if all the 44 patients excluded from the analysis did not have sacroiliitis. ASAS: Assessment in Spondyloarthritis International Society; mAmor: modified Amor; mESSG: modified European Spondylarthropathy Study Group.

Table 4. Baseline disease characteristics of patients (≤ 10 years' disease duration) with full concordance between the criteria sets and patients with discordance. Results are n (%) or median with interquartile ranges (Q1:Q3).

Characteristic	All patients, n = 75	Concordance**, n = 46	Discordance**, n = 29	p*
HLA-B27†	54 (72.0)	35 (81.4)	19 (73.1)	0.548
Sex (men)	44 (58.7)	29 (63.0)	15 (51.7)	0.348
Radiographic sacroiliitis†	52 (69.3)	37 (80.4)	15 (53.6)	0.019
Sacroiliitis MRI†	28 (37.3)	17 (51.5)	11 (44.0)	0.606
IBP ASAS definition	46 (61.3)	37 (80.4)	9 (31.0)	< 0.001
Synovitis	33 (44.0)	23 (50.0)	10 (34.5)	0.235
Psoriasis	22 (29.3)	12 (26.1)	10 (34.5)	0.449
Raised CRP†	47 (62.7)	31 (73.3)	16 (27.3)	0.211
Uveitis	10 (13.3)	5 (10.9)	5 (17.2)	0.496
Hip involvement	6 (8.0)	4 (8.7)	2 (6.9)	1.000
IBD	8 (10.7)	5 (10.9)	3 (10.3)	1.000
Family history	27 (36.0)	17 (37.8)	10 (35.7)	1.000
Anti-TNF exposure	35 (46.1)	24 (52.2)	11 (37.9)	0.246
Response NSAID	60 (80.0)	53 (84.1)	7 (63.6)	0.203
Enthesitis (heel)	40 (53.3)	22 (47.8)	18 (62.1)	0.246
Dactylitis	15 (20.0)	10 (21.7)	5 (17.2)	0.770
Disease Duration, yrs	6 (4, 8)	7 (3, 8)	6 (4, 8)	0.734
Age, yrs	35 (28, 46)	31 (27, 39)	48 (35, 56)	< 0.001
Age at first symptom, yrs	28 (22, 42)	24 (21, 31)	42 (28, 52)	< 0.001
BASDAI, mm	25 (12, 45)	23 (13, 41)	31 (11, 50)	0.475
BASFI, mm	14 (3, 39)	23 (6, 42)	13 (4, 32)	0.417

† On the number of available data. *Comparing the concordant with the discordant group. ** Concordance defined as a patient fulfilling the 3 criteria, discordance defined as a patient that did not fulfill all 3 criteria. MRI: magnetic resonance imaging; ASAS: Assessment in Spondyloarthritis International Society; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CRP: C-reactive protein; IBD: inflammatory bowel disease; IBP: inflammatory back pain; NSAID: nonsteroidal anti-inflammatory drugs; TNF: tumor necrosis factor.

that inclusion was based on expert opinion from the rheumatologist concerning diagnosis of SpA. This allowed comparison of the different sets of criteria, but historically the unit is used to refer to Amor's criteria, which may explain the high classification rate for Amor. Another limitation is that our cohort was more representative of patients with axial SpA. The selection bias of the patients excluded from the analysis due to missing data (MRI or radiographs), which precluded an absolute exclusion of sacroiliitis, may have contributed to such bias. However, analysis by imputation confirmed the current results to be robust.

Having a widely accepted international classification crite-

ria set is useful both for usual care and for research and teaching[13]. Showing that these internationally derived sets of criteria are usable in an established cohort is important in terms of its feasibility. However, there is no added value of the ASAS criteria in established cohorts where there is already a high proportion of patients with radiographic sacroiliitis. Not surprisingly, the ASAS criteria did not perform better when compared against the modified Amor or modified ESSG criteria.

In an established cohort of patients with SpA, the ASAS criteria are comparable to other criteria sets with no added value in the presence of radiographic sacroiliitis, with the "entry" requirements restricting classification in a minority of patients. Further validation is therefore required.

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