EXTENDED REPORT

Validity of the Ankylosing Spondylitis Disease Activity Score (ASDAS) in patients with early spondyloarthritis from the Esperanza programme

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ABSTRACT

Objectives To evaluate the validity of the Ankylosing Spondylitis Disease Activity Score (ASDAS) in early spondyloarthritis (SpA) in comparison with conventional clinical measures of disease activity.

Methods Six hundred and seventy-six incident cases of early SpA from the Esperanza programme were included. Patients were categorised into high and low disease activity states based on patient and physician global assessment scores and on the physician's decision to start treatment with a disease-modifying antirheumatic drug or tumour necrosis factor blocker. The discriminant ability of ASDAS-C-reactive protein (CRP) and ASDAS-erythrocyte sedimentation rate (ESR) was tested using standardised mean differences between patients with high and low disease activity. Convergent validity was tested by Pearson correlation between ASDAS versions and other measures of disease activity.

Results ASDAS-ESR and ASDAS-CRP showed good correlation with BASDAI (r=0.79 and 0.74, respectively). Both indices correlated well with the patient global assessment (r=0.70 in both indices) and moderately with the physician global score (r=0.46 and 0.47, respectively). CRP and ESR showed poor correlation with patient- and physician-derived measures. ASDAS performed similarly across the global SpA sample, ankylosing spondylitis (AS), non-radiographic axial SpA and peripheral SpA.

Conclusions ASDAS performed as a valid activity score even being slightly better than the Bath Ankylosing Spondylitis Disease Activity Index in its ability to discriminate between high and low disease activity in early SpA. ASDAS performed similarly in AS, early forms of SpA, non-radiographic axial SpA and peripheral SpA.

INTRODUCTION

The field of rheumatology requires a constant evaluation of results. Continuous measurement of disease activity facilitates an understanding of the patient's disease process, evaluation of treatment effectiveness and the development of better disease management and control strategies. Evaluating disease activity in patients with spondyloarthritis (SpA) is complicated as indicated by the number of years spent on this topic by expert networks, such as Outcome Measures in Rheumatology (OMERACT) or Assessment of SpondyloArthritis international Society (ASAS). Unfortunately, disease activity remains a difficult concept to define in SpA owing to a lack of measures that comfortably pass the OMERACT filter of truth, discrimination and feasibility.[1] Inadequate measurement of SpA disease activity is a result, in part, of the multifactorial causes of disease activity.[2] Subjective measures are the most commonly used. These are based on patient's perceptions, such as patient global assessment, spinal pain and morning stiffness, or composite scores such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) which, like previous indices, shares the limitation of including the patient's perspective only.

The Ankylosing Spondylitis Disease Activity Score (ASDAS) has been statistically developed in a similar fashion to the Disease Activity Score for rheumatoid arthritis. It is the first validated activity score for ankylosing spondylitis (AS) that combines acute phase reactants with patient-reported outcome measures.[2] Further, the inclusion of inflammatory biomarkers increases construct validity by incorporating an objective measure of disease activity. Compared with BASDAI in patients with AS, ASDAS showed good correlation with other disease activity measures and greater discriminant ability in differentiating patients with varying levels of disease activity and patients with different levels of change.[2] Thus, it may be a tool better suited than those already available for measuring disease activity in these patients. However, ASDAS was recently evaluated in patients with psoriatic arthritis, and the results were similar, but no better, than results obtained with BASDAI.[3] These inconsistencies illustrate the need to test ASDAS validity in other disease subgroups such as patients with early SpA, who remain to be evaluated. Our objective was to fill this gap with an in-depth study of the validity and discriminant ability of ASDAS in a cohort of patients diagnosed with early SpA.[4 5]

METHODS

Study population

The study is based on a sample of patients diagnosed with early SpA by their rheumatologist and treated and recruited at the Esperanza programme between April 2008 and June 2011 (for a description of the programme see Muñoz-Fernández *et al*[4]). The programme had the following referral criteria: (1) age <45 years; (2) symptom duration

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3–24 months and (3) at least one of the following: (a) inflammatory back pain (defined as two of the following: insidious onset, spinal morning stiffness for ≥30 min, improvement with exercise but not with rest); (b) asymmetrical arthritis, especially in the lower limbs; (c) the presence of spinal or joint pain plus at least one of the following: psoriasis, inflammatory bowel disease, anterior uveitis, radiographic sacroiliitis, human leucocyte antigen B27 (HLA-B27) positivity, or a family history of spondylitis, psoriasis, inflammatory bowel disease or anterior uveitis.

Variables

Several disease activity measures are collected as part of the Esperanza protocol: patient global assessment score (disease activity rated by the patient at the time of the assessment), physician global assessment score (disease activity rated by the physician) and BASDAI's six individual questions: (1) fatigue; (2) spinal pain; (3) pain and swelling of peripheral joints; (4) pain at entheseal sites; (5) severity of morning stiffness and (6) duration of morning stiffness. All scores are recorded on a visual analogue scale (VAS) from 0 to 10 cm or on a numerical rating scale, also from 0 to 10, with 10 as the highest score possible. Erythrocyte sedimentation rate (ESR) (mm/h), C-reactive protein (CRP) (mg/l), Bath Ankylosing Spondylitis Functional Index (BASFI) and the number of swollen joints are also collected. Patients were classified as presenting sacroiliitis (x-ray/MRI) if they had radiographic sacroiliitis either by standard x-ray examination (New York criteria) or by MRI based on ASAS criteria.

Table 1 Demographic and clinical characteristics of the study population (n=676)

Variables	Parameter
Age*	33±7
Men	414 (61)
Time from symptoms onset (months)*	12±7
HLA-B27	356 (56)
Psoriasis	106 (16)
Uveitis	35 (5)
Inflammatory back pain	339 (50)
Number of swollen joints*	0.93±2.39
Arthritis	247 (37)
Dactylitis	63 (9)
Enthesitis	322 (48)
Inflammatory bowel disease	36 (5)
Family history	218 (32)
Radiographic sacroiliitis (x-ray/MRI)	206 (30)
CRP	65 (27)
Raised ESR	139 (25)
Good response to NSAIDs	403 (60)
Taking NSAIDs	560 (83)
DMARDs/anti-TNF therapy	141 (21)
ESR* (mm/h)	17.1±17.5
CRP* (mg/l)	10.8±26.9
Patient global assessment*	5.22±2.53
Physician global assessment*	3.92±2.14
ASDAS-ESR*	2.60±0.99
ASDAS-CRP*	2.60±1.06
BASDAI*	4.47±2.24
ASQoL	6.94±4.86
BASFI*	2.65±2.22

Results are reported as number (percentage over those tested) unless otherwise specified.
*Mean±SD.
ASDAS, Ankylosing Spondylitis Disease Activity score; ASQoL, Ankylosing Spondylitis Quality of Life; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; DMARDs, disease-modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate; NSAIDs, non-steroidal anti-inflammatory drugs; TNF, tumour necrosis factor.

Calculation of ASDAS

The ASAS has developed four different formulae for ASDAS. For this study we evaluated the formulae recommended by ASAS that include ESR (ASDAS B=0.08×back pain+0.07×duration of morning stiffness+0.11×patient global+0.09×peripheral pain/swelling+0.29×$\sqrt{}$(ESR)) and CRP (ASDAS C=0.12×back pain +0.06×duration of morning stiffness+0.11×patient global +0.07×peripheral pain/swelling+0.58×ln(CRP+1)).[2] The two ASDAS formulae were calculated from the measures routinely collected in Esperanza.

Definition of high/low disease activity states

To reproduce the original ASDAS discriminant validation study in our population, we used three approaches to classify patients into two extreme categories: high vs low disease activity.[6]

Patient global score: a high disease activity state was defined as a score >6 out of 10 cm (>6/10) from one VAS. A VAS <4/10 was defined as a low disease activity state. Patients with scores from 4 to 6 were excluded.

Physician global score: a high disease activity state was defined as a physician's score >6. A VAS <4 was defined as low disease activity state. Patients with scores from 4 to 6 were excluded.

Treatment course: a rheumatologist's decision to start treatment with disease-modifying antirheumatic drugs (DMARDs) or tumour necrosis factor (TNF) blockers was used as an external construct of high disease activity.

Statistical analyses

First, we performed descriptive analyses on the data—that is, we ran frequency analyses and calculated means and SDs or median and IQR, depending on the variable type. We then tested

Table 2 Correlations (r coefficients) between ASDAS-ESR and CRP scores and other disease activity measures included in the Esperanza programme database

Disease activity variables	ASDAS-ESR	ASDAS-CRP
BASDAI 1: fatigue	0.59	0.53
BASDAI 2: spinal pain	0.59	0.63
BASDAI 3: pain/swelling peripheral joints	0.57	0.50
BASDAI 4: pain at entheseal sites	0.54	0.49
BASDAI 5: severity of morning stiffness	0.55	0.54
BASDAI 6: duration of morning stiffness	0.56	0.53
BASDAI	0.79	0.74
Physician global assessment score	0.46	0.47
Patient global assessment score	0.70	0.70
BASFI	0.66	0.63
CRP	0.36	0.63
ESR	0.62	0.40
Number of swollen joints	0.22	0.16

All p values are<0.01.
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Table 3 Correlation (r coefficients) between ASDAS, BASDAI and inflammatory biomarkers and patient and physician global assessments of disease activity at baseline

	Patient global assessment score	Physician global assessment score
ASDAS-ESR	0.70	0.46
ASDAS-CRP	0.70	0.47
BASDAI	0.71	0.44
Physician global assessment score	0.47	–
BASDAI 1: fatigue	0.60	0.32
BASDAI 2: spinal pain	0.67	0.33
BASDAI 3: pain/swelling peripheral joints	0.32	0.27
BASDAI 4: pain at entheseal sites	0.53	0.35
BASDAI 5: severity of morning stiffness	0.55	0.34
BASDAI 6: duration of morning stiffness	0.42	0.33
ESR	0.14	0.16
CRP	0.11	0.17

All p values are p<0.01.
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

differences and performed group comparisons using Student t tests. Further, to examine associations between quantitative variables we calculated Pearson's correlation coefficients for normally distributed variables and Spearman's correlation coefficients otherwise.

To test the validity of ASDAS-ESR and ASDAS-CRP, we analysed their correlation with the disease activity measures collected as part of the routine protocol (see 'Variables' section). Finally, to assess the indices' ability to discriminate between patients with high and low disease activity states, across the three different approaches described above, we calculated the standardised mean difference of the indices between states (difference of the group means divided by the pooled SD of the group means). Tests results with a p value ≤0.05 were considered statistically significant. The statistical package Stata10 was used for all data analyses.

RESULTS

Table 1 shows the clinical and demographic characteristics of the 676 patients with a clinical diagnosis of SpA (either axial, peripheral or AS), included in Esperanza programme as of 7 July 2011.

Correlation with disease activity

Table 2 shows r coefficients for the correlations between ASDAS-ESR and ASDAS-CRP and the various disease activity measures. Both indices showed good correlations (r>0.60) with BASDAI (0.79 and 0.74, respectively; p<0.001) and with patient's global score (0.70, p<0.001). They also showed a good correlation with physical functioning as measured by BASFI (0.66 and 0.63, p<0.001) and a moderate correlation with the physician global score (0.46 and 0.47, p<0.001). The degree of correlation of ASDAS versions with the individual components of BASDAI was satisfactory. ASDAS-ESR had the highest correlation with BASDAI 1: fatigue (0.59, p<0.001) and BASDAI 2: spinal pain (0.59, p<0.001), whereas ASDAS-CRP correlated best with BASDAI 2: spinal pain (0.63, p<0.001). The lowest correlation coefficients for both indices were the

Table 4 Discriminant ability: standardised mean differences between patients requiring/not requiring DMARDs or anti-TNF therapy

	DMARDs/anti-TNF (n=141) Mean (SD)	No DMARDs/anti-TNF (n=535) Mean (SD)	Standardised mean difference
ASDAS-ESR	2.91 (1.03)	2.50 (0.96)	0.42
ASDAS-CRP	2.98 (1.13)	2.50 (1.02)	0.46
BASDAI	4.98 (2.18)	4.33 (2.24)	0.29
Ln (CRP+1)	2.18 (1.24)	1.5 (1.07)	0.57
CRP (mg/l),* median (range)	9.5 (2–22.9)	3 (1–8)	
√(ESR)	4.27 (2.12)	3.50 (1.80)	0.41
ESR* median (range)	15.5 (7–32)	10 (5–20)	
Ln (number of swollen joints +1)	0.95 (0.85)	0.19 (0.48)	1.32
Number of swollen joints,* median (range)	2 (0–4)	0 (0–0)	
√(Number of tender entheseal points)	0.68 (0.76)	0.51 (0.78)	0.22
Number of tender entheseal points,* median (range)	0 (0–2)	0 (0–1)	
Physician global assessment score	4.69 (2.13)	3.72 (2.10)	0.46
Patient global assessment score	5.29 (2.34)	5.21 (2.58)	0.03
Night-time spinal pain	3.66 (3.05)	4.66 (2.94)	−0.34
BASFI	2.94 (2.17)	2.57 (2.22)	0.16
BASDAI question 1 (fatigue)	4.77 (2.83)	4.78 (2.89)	−0.004
BASDAI question 2 (spinal pain)	4.42 (3.14)	5.45 (2.80)	−0.36
BASDAI question 3 (pain/swelling peripheral joints)	5.67 (2.92)	2.73 (3.10)	0.96
BASDAI question 6 (duration of morning stiffness)	4.14 (3.11)	3.91 (3.05)	0.08

The standardised mean difference was calculated only for variables with a normal distribution, which is why logarithms are used for some of the measures.
*Only for information purposes, actual values.
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; DMARDs, disease-modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate.

Table 5 Discriminant ability. Standardised mean differences between patient global score of disease activity based on VAS: high (>6/10) versus low (<4/10)

	Patient global assessment score >6/10 (n=211)Mean (SD)	Patient global assessment score <4/10 (n=163) Mean (SD)	Standardised mean difference
ASDAS-ESR	3.34 (0.80)	1.66 (0.74)	2.18
ASDAS-CRP	3.41 (0.87)	1.61 (0.78)	2.18
BASDAI	6.21 (1.58)	2.23 (1.78)	2.38
Ln (CRP+1)	1.90 (1.29)	1.53 (1.00)	0.32
CRP (mg/l),* median (range)	3.9 (1–21.2)	3 (1.18–7.7)	
$\sqrt{}$(ESR)	4.01 (2.09)	3.37 (1.76)	0.33
ESR* median (range)	12 (5–31)	9 (5–18)	
Ln (number of swollen joints +1)	0.36 (0.68)	0.32 (0.65)	0.06
Number of swollen joints,* median (range)	0 (0–1)	0 (0–0)	
BASFI	4.33 (2.15)	0.87 (1.16)	1.94
BASDAI question 1 (fatigue)	6.65 (2.41)	2.45 (2.34)	1.77
BASDAI question 2 (spinal pain)	7.24 (2.25)	2.55 (2.37)	2.03
BASDAI question 3 (pain/swelling peripheral joints)	4.57 (3.58)	1.79 (2.57)	0.88
BASDAI question 6 (duration of morning stiffness)	5.33 (3.04)	1.99 (2.22)	1.24

The standardised mean difference was calculated only for variables with a normal distribution, which is why logarithms are used for some of the measures.
*Only for information purposes, actual values.
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; VAS, visual analogue scale.

ones involving the count of swollen joints (0.22 and 0.16, p<0.001, respectively).

Table 3 shows correlation results between BASDAI, its individual components, ASDAS and inflammatory biomarkers and the measures of disease activity—that is, patient and physician global scores. The correlation coefficient between physician and patient global scores was 0.47 (p<0.001). Both BASDAI and ASDAS correlated well with disease activity as measured by the patient global score (BASDAI r=0.71, ASDAS B r=0.70, ASDAS C r=0.70, p<0.001). Correlations between ASDAS indices and physician global scores were modest, still quite similar across indices, though slightly higher for ASDAS (BASDAI r=0.44, ASDAS-ESR r=0.46, ASDAS-CRP r=0.47; p<0.001). BASDAI individual components also had a higher

Table 6 Discriminant ability. Standardised mean differences between patients with high and low disease activity based on physician's global assessment (VAS) high (>6/10) versus low (<4/10)

	Physician global assessment score >6/10 (n=96)Mean (SD)	Physician global assessment score <4/10 (n=291)Mean(SD)	Standardised mean difference
ASDAS-ESR	3.29 (1.02)	2.18 (0.91)	1.19
ASDAS-CRP	3.36 (1.10)	2.16 (0.92)	1.25
BASDAI	5.78 (2.03)	3.59 (2.20)	1.01
Ln (CRP+1)	2.12 (1.41)	1.47 (0.95)	0.59
CRP (mg/l),* median (range)	6.4 (1.3–22.3)	3 (1–6.3)	
$\sqrt{}$(ESR)	4.36 (2.30)	3.31 (1.69)	0.56
ESR* median (range)	14 (8–33)	9 (4–18)	
Ln (number of swollen joints +1)	0.62 (0.81)	0.25 (0.57)	0.58
Number of swollen joints,* median (range)	0 (0–2)	0 (0–0)	
Patient global assessment score	6.72 (2.40)	4.15 (2.50)	1.04
BASFI	3.92 (2.33)	1.75 (1.83)	1.10
BASDAI question 1 (fatigue)	6.10 (2.76)	3.97 (2.93)	0.74
BASDAI question 2 (spinal pain)	6.21 (2.87)	4.39 (2.93)	0.63
BASDAI question 3 (pain/swelling peripheral joints)	4.92 (3.80)	2.53 (2.86)	0.77
BASDAI question 6 (duration of morning stiffness)	4.76 (3.19)	3.06 (2.97)	0.56

The standardised mean difference was calculated only for variables with a normal distribution, which is why logarithms are used for some of the measures.
*Only for information purposes, actual values.
ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; VAS, visual analogue scale.

correlation with patient global assessment than with physician global assessment. Peripheral joint pain showed the weakest correlation (BASDAI 3, r=0.32 and 0.27, p<0.001, respectively) while spinal pain (BASDAI 2) showed the strongest correlation with patient global assessment. BASDAI 2 correlated with patient global score almost as well (0.67, p<0.001) as BASDAI total with patient global score (0.71, p<0.001). In contrast, BASDAI 4 (pain at entheseal sites) correlated the best and only moderately, with physician global score (0.35, p<0.001). Finally, ESR and CRP showed poor correlation with the physician global score (0.16 and 0.17, p<0.001, respectively) and patient global score (0.11 for CRP, p<0.01; and 0.14 for ESR, p<0.001).

Discrimination between high and low disease activity states

We compared the discriminant ability of ASDAS-ESR and CRP with the BASDAI indices and other measures (tables 4–6). Table 4 shows discrimination results when patients were differentiated according to those receiving DMARDs and/or TNF-blockers (n=141; 21%) and the rest (n=535; 79%). The standardised mean differences between states show that the discriminant abilities of ASDAS-ESR and ASDAS-CRP were similar and moderate, but still greater than those of BASDAI (ASDAS-ESR: 0.42; ASDAS-CRP: 0.46, p<0.001; BASDAI: 0.29, p=0.003). The variables that discriminated the best, in addition to ASDAS, were the physician global assessment (0.46, p<0.001), ASDAS-CRP (0.57, p<0.001), ASDAS-ESR (0.41, p<0.001), BASDAI 3: pain and swelling of peripheral joints (0.96, p<0.001) and number of swollen joints (1.32, p<0.001).

Table 5 shows the discrimination results when patients were differentiated into high and low disease activity according to their VAS (VAS>6 n=211 (31%); VAS<4 n=163 (24%)). In this case, the discriminant abilities of the three indices were substantial and similar (ASDAS-ESR: 2.18; ASDAS-CRP: 2.18; BASDAI: 2.38, p<0.001), with BASDAI's discriminant power being slightly larger. These discrimination coefficients were higher than those of the acute phase reactants. Other variables that discriminated well between high and low disease activity were BASFI (1.94, p<0.001), the individual component of BASDAI 1 (1.77, p<0.001) and BASDAI 6 (1.24, p<0.001). BASDAI 2 deserves special mention, however, as its discriminant ability (2.03, p<0.001) was almost as high as that of ASDAS-ESR, ASDAS-CRP and BASDAI total.

In table 6, we differentiated between high and low disease activity according to physician's VAS (VAS>6, n=96/14%; VAS<4, n=291/43%). Based on this classification, ASDAS-CRP was the best discriminating index, though all three performed well (ASDAS-ESR: 1.19, ASDAS-CRP: 1.25; BASDAI: 1.01, p<0.001). Variables that also performed well included patient global score (1.04, p<0.001), BASFI's physical functioning measure (1.10, p<0.001) and BASDAI's questions 1 and 3 (0.74 and 0.77, respectively, p<0.001).

Validity in AS, axial SpA and peripheral SpA

To further examine the validity of these indices, we created a subset from our patients with early SpA including only those fulfilling the modified New York criteria (n=89). When we analysed the indices' correlation with activity measures and their discriminant performance in this subset, we found that results were similar to those reported for the total cohort, with ASDAS-CRP showing a slightly better performance for the three disease activity constructs (see online supplementary material, tables S1–S6). Additionally, we explored these relationships looking only at patients with non-radiographic axial SpA (n=362), excluding patients meeting ASAS criteria of peripheral SpA. In these results, we noticed an increase in the standardised mean difference in the BASDAI which then equalled that of ASDAS-ESR and CRP once we used DMARDs and/or anti TNF therapy to discriminate between high and low disease activity (see online supplementary material, tables S7–S12). Finally, we repeated these analyses with patients with peripheral SpA without axial disease (n=80) and, again, the results almost mirrored those for the total cohort (see online supplementary material, tables S13–S18).

DISCUSSION

As the BASDAI index is limited to the patient's perspective, the need for new indices of SpA disease activity is evident. ASDAS is a new composite index based on a continuous measurement scale, which aims at ascertaining the disease activity state at a specific moment. This is central to the decision-making for patient recruitment to clinical trials, support for treatment modifications and definition of therapeutic goals. Further, a recent publication defined the ASDAS cut-off values for disease activity states. These have proved to be valuable for the definition and monitoring of treatment goals.[6]

Nevertheless, before adopting a new index it is necessary to establish its validity in the populations for which it was originally developed and validated, and also in other populations and disease groups. Thus, the results of this study based on a population with early disease, ≤2 years since onset of symptoms and for the most part, meeting non-radiographic axial SpA criteria, are noteworthy.[7 8]

The correlation coefficients reported here between ASDAS-ESR and ASDAS-CRP with BASDAI, patient and physician global scores, BASFI, CRP and ESR in our population with early SpA were all similar to the correlation coefficients of ASDAS indices with these same variables from the two studies in which ASDAS was developed: International Study on Starting tumour necrosis factor blocking agents in Ankylosing Spondylitis (ISSAS) and Outcome in Ankylosing Spondylitis International Study (OASIS).[9] Both BASDAI and ASDAS showed good correlation with patient global assessment of disease activity but moderate correlation with the physician global assessment. These results suggest that both indices perform similarly in early SpA and are well suited for clinical use.

Previous validity studies of the index ASDAS for patients with AS have made two important comments. First, the index reflects disease activity from both the patient's and the physician's perspective. Second, the high discriminant ability of ASDAS is greater than that of BASDAI for differentiating patients by disease activity levels and also between various levels of change.[2 10] In contrast, Eder *et al*[11] concluded that ASDAS and BASDAI indices have similar good-to-moderate discriminant ability and correlation coefficients with different constructs of disease activity in patients with axial psoriatic arthritis (AxPsA). Further, ASDAS does not improve on the ability of BASDAI to discriminate between high and low disease activity states in patients with AxPsA. Our results show that ASDAS-ESR and ASDAS-CRP correlate with BASDAI and with patient and physician global scores. However, discriminant ability between high and low disease activity based on DMARDs/anti-TNF therapy was moderate, although these indices still performed better than BASDAI. As one might expect, given that BASDAI is based on patient's opinions, it performed better when patient global assessment was the reference point. Conversely, when physician global scores were considered, ASDAS had higher discriminant

ability than BASDAI, though it is possible that clinical relevance is limited.

It is also worth noting that the indices performed similarly among patients meeting the modified New York AS criteria but in the non-radiographic axial SpA population, ASDAS-CRP was slightly better. Given that ESR and CRP show stronger correlation with peripheral arthritis, we considered it worth exploring the results when only axial variants were selected. Results of such analyses showed that the validity of ASDAS remained unchanged; this valuable information remained undetermined until now.

In addition, we examined the indices' performance on patients with peripheral SpA without axial disease. Surprisingly, the analyses confirmed that a tool designed for patients with axial disease was effective in evaluating patients with peripheral SpA. To our knowledge, this is the first study to examine this alternate use of the ASDAS instrument. Further research is needed to validate our results.

Pedersen *et al*[11] examined the different levels and changes of 10 inflammatory biomarkers in patients with axial SpA during treatment with TNF blockers. Based on their findings, they concluded that ASDAS had greater correlation with these biomarkers than BASDAI, thus better capturing the inflammatory process. Our results show a poor correlation between the inflammatory biomarkers available in our data (CRP and ESR) and disease activity measures, probably because only one-third of patients with early SpA had raised acute phase reactants, which might have affected our results.

In summary, ASDAS-ESR and ASDAS-CRP are indices with high validity for the assessment of patients with early SpA. This is based on their good correlation with BASDAI and their accurate depiction of the disease activity from both the patient's and the physician's perspective. ASDAS shows better correlation with the physician's opinion than BASDAI, which probably reflects the inclusion of data that improve on the patient's subjectivity. ASDAS also outperforms BASDAI, though only slightly, in discriminating patients requiring different treatments. Therefore, ASDAS indices are promising as useful monitoring tools for patients with early SpA in clinical practice. Our results show that the discriminant abilities of ASDAS-ESR, ASDAS-CRP and BASDAI were high-to-moderate with different disease activity constructs. Although in early SpA ASDAS shows a slightly better performance than BASDAI for discriminating between high and low disease activity states, its clinical relevance may not be substantial. In conclusion, in a population of patients with early SpA, ASDAS shows a good-to-moderate discriminant ability and correlation with different constructs of disease activity which are similar, though slightly better, than those of BASDAI. Further, ASDAS seems to display a similar construct validity in AS as in non-radiographic axial SpA and in peripheral SpA, although this finding may need further validation.

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Collaborators See online supplementary appendix.

Contributors LC and MG designed the programme and with EdM, CF-E, JM and EC-E, designed this specific analysis; MAD carried out all the analyses; MG cleaned up the data; ET and EL wrote the draft together with CF-E; LC, JM, EC-E, PZ and SM-F supervised and revised the manuscript.

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