

## Performance of the ASAS health index for the evaluation of spondyloarthritis in daily practice

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## Abstract

**Background and aims:** The Assessment of SpondyloArthritis international Society-Health Index (ASAS-HI) is a tool designed to assess disease impact in spondyloarthritis (SpA), but its clinical performance is barely known. We aimed to test the clinimetric properties of ASAS HI in a real clinical scenario.

**Methods:** This cross-sectional study included 111 consecutive SpA patients. The measurement properties of ASAS HI were tested against conventional assessment measures. Convergent validity was assessed by Spearman's rho correlations, while discriminative validity was analyzed through ROC curves. A multivariate regression analysis was designed to identify ASAS HI items associated with active disease.

**Results:** The average ASAS-HI was  $5.4 \pm 3.8$  (IQR: 3-8). ASAS HI showed high convergent validity against other SpA measures ( $\rho \geq 0.70$ ,  $p < 0.0005$ ). The optimal criterion for detecting high / very high disease activity ASDAS categories was an ASAS-HI score  $> 6$ , area under the ROC curve 0.86 (95%CI: 0.78-0.92), +LR 7.3 (95%CI: 3.1-17.1),  $p < 0.0001$ . The ASAS-HI items significantly associated with BASDAI active disease were, "I often get frustrated" [OR 9.2 (95%CI: 1.2-69.4),  $p = 0.032$ ], and, "I sleep badly at night" [OR 7.7 (95%CI: 1.4-41.6),  $p = 0.018$ ]. As for ASDAS, it was, "pain sometimes disrupts my normal activities" [OR 8.7 (95%CI: 1.7-45.2),  $p = 0.010$ ].

**Conclusions:** The ASAS HI is a useful and simple instrument for its application in daily practice. Given its good clinimetric properties it could be used as an additional instrument to evaluate SpA.

## Introduction

The spondyloarthritis (SpA) are a group of related conditions that share a common genetic basis through HLA-B27, but also clinical and radiographic features (1). Axial spondyloarthritis (axSpA) include diseases with predominantly axial involvement, such as ankylosing spondylitis (AS) and non-radiographic axial SpA (nr-axSpA) which share as key symptoms both inflammatory back pain and morning axial stiffness (1,2). On the other hand, psoriatic arthritis (PsA) is mostly a peripheral SpA with less axial component (1,2). In addition, in both peripheral and axial SpA, enthesitis or dactylitis may occur with some frequency, which makes the general clinical picture of these entities very heterogeneous (1).

For decades, different tools have been available to assess the activity (BASDAI / ASDAS), physical function (BASFI), movement metrics (BASMI) and structural damage (BASRI / mSASSS) of SpA (1,3). Most of these indices are important for clinical and therapeutic decision-making, however, these tools were designed based on the experience of clinicians who were very familiar with these entities. Therefore, although most of these instruments also contain patient-reported outcome measures (PROM), mostly the information they provide is oriented to decision-making based on the doctor's vision. In different rheumatic diseases, including SpA, it is a recognized fact that patients' perceptions about what their disease means in their daily lives (disease impact) do not always coincide with the results derived from the different disease assessment instruments (4). As a consequence, discrepancy between patient's and physician's ratings of general health status is not unusual in these diseases (5). The consequence of such a discordant viewpoint is that decisions are often prone to not being shared between patients and physicians. The patients' own perspectives of their health status

should be an important additional measure to assess disease activity as well as its impact and therefore for clinical and therapeutic decision-making.

At present, there is a growing tendency to use instruments that capture, in the best possible way, the impact that SpA generate on patients' lives. For that purpose, tools such as the Psoriatic Arthritis Impact of Disease (PsAID), for PsA, and the Assessment of SpondyloArthritis international Society-Health Index (ASAS-HI), for SpA, have been recently developed and validated (6,7). ASAS-HI was developed to assess health in patients with AS according to the International Classification of Functioning, Disability and Health (ICF) categories. The 17 statements of ASAS HI were obtained from a pool of 251 items originating from questionnaires already in use for patients with axSpA or from questionnaires linked to the ICF (7). The ASAS HI contains items addressing categories of pain, emotional functions, sleep, sexual function, mobility, selfcare, and community life (7). Therefore, ASAS-HI could provide information on the full range of difficulties that patients with SpA face in their daily lives.

To date, very few studies have been published assessing the applicability of ASAS-HI under conditions of routine clinical practice (8-11). It would be interesting to find out whether the ASAS-HI correlates well with other standard measuring instruments used in SpA, and above all, whether it is able to discriminate the states of disease activity against the inactive ones. This information would give a great boost to this tool for its dissemination in the clinical routine of rheumatologists attending patients with SpA. For this purpose, the present study has been carried out.

### **Patients and methods**

This cross-sectional study included 111 consecutive axSpA patients who were classified according to ASAS criteria (2). Study population was recruited from a SpA monographic

unit from a university hospital in northern Spain. The study period extended from May to October 2019. Patients were informed about the objectives of the study and their written informed consent was obtained. The clinical research ethics committee of our hospital approved the study (HUCA ref EO 12/19).

For this study, sociodemographic, clinical, analytical and imaging variables were collected. All patients were adults of both sexes. The educational level, disease duration, the family history of SpA and other rheumatic diseases, as well as the presence of comorbidities, especially of the cardiometabolic type, were collected. Within the analytical parameters, ESR (mm/h), C-reactive protein (mg/dl), rheumatoid factor, antinuclear antibodies, and HLA-B27, were included among others. The presence of psoriasis (or personal/family history), enthesitis, dactylitis, uveitis, and inflammatory bowel disease, was also included in the study protocol. In all patients, pelvis radiographs were performed in anteroposterior projection, as well as anteroposterior and lateral views of the cervical and lumbar spine. No specific reading method was used for the radiographic study, but the degree of involvement of the sacroiliac joints was assessed by the New York criteria (12). In patients with suspected SpA, but with normal radiographs, an MRI study was ordered to detect the presence of sacroiliitis (SI) following the definition for this purpose included in the ASAS criteria for axSpA (2).

As for assessment measures, ASDAS-CRP and BASDAI for disease activity, and BASFI for physical function were included as standard assessment measures. Although some metrics of axial skeleton movement were collected (Schober test, tragus to wall distance, chest expansion, finger to floor distance), the BASMI was not determined in this study.

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For the assessment of disease impact on patients' lives we used the ASAS HI questionnaire (7). This instrument is composed by 17 items, expressed in the first person and in present tense, with a dichotomous response option: "I agree" or "I do not agree". Each positive answer is scored 1 while a negative answer is scored 0. The final result is the sum of individual items (7). Higher values reflect a major degree of impairments, limitations and restrictions. All patients filled out the questionnaire only once, therefore a test-retest study was not done. However, coefficients of agreement between ASAS HI scores on first and second administrations tend to be excellent (8,10).

#### *Statistical methodology*

A descriptive statistical analysis of all the variables was performed, including central tendency and dispersion measures for continuous variables, and absolute and relative frequencies for categorical variables. Student's t-test, Mann-Whitney-U test or Kruskal Wallis H test were used to compare quantitative variables and Pearson's chi-square or Fisher's exact tests for qualitative variables. We examined construct convergent validity by correlating the scores of the ASAS HI with ASDAS, BASDAI and BASFI. Spearman's rho correlation coefficients were obtained to quantify these relationships. Correlations were interpreted as follow: very high ( $>0.90$ ), high ( $0.70-0.89$ ), moderate ( $0.50-0.69$ ), low ( $0.26-0.49$ ), and poor or almost nil ( $\leq 0.25$ ). We also calculated the coefficient of variation (CV) as a measure of the extent of variability of ASAS-HI in relation to the mean of it. If the CV is less than or equal to 80%, it means that the arithmetic mean is representative of the data set, therefore the data set is homogeneous. In order to distinguish patients with active and non-active disease (discriminant validity) and to assess their respective cut off point values, the receiver operating characteristic (ROC) curve analysis was used. A logistic regression was made to determine the ASAS-HI items

with greater capability to discriminate active versus inactive disease. Data were analyzed using SPSS V19.0 statistical software (IBM Corp. NY, USA).

## Results

Seventy-four men and 37 women were included, mean age  $43.3 \pm 10.6$  years (IQR: 36-50), average disease duration of  $7.6 \pm 6.8$  years (IQR: 4-10). Out of 111 patients, 74 (66.7%) had AS (male/female ratio 2.5:1), while the rest met axSpA criteria. Eighteen out of 111 patients (16.2%) had peripheral arthritis (mostly asymmetric arthritis of the lower limbs). As for other manifestations of SpA, 8 (7.2%), 14 (12.6%), and 6 (5.4%) patients presented enthesitis, anterior uveitis and inflammatory bowel disease, respectively. Sixteen patients (14.4%) showed family history of SpA. Of the study population, 43 (38.7%) patients had primary education, 34 (30.6%) secondary education, and another 34 (30.6%) had a university degree.

The average value of ESR was  $7.2 \pm 8.2$  mm/h (IQR: 2-8), that of CRP  $0.37 \pm 0.45$  mg/dl (IQR: 0.10-0.40), while HLA-B27 testing was positive in 88 patients (79.3%). Women had significantly higher ESR values ( $9.6 \pm 11.2$  mm/h) than men ( $6.03 \pm 5.9$  mm/h),  $p= 0.03$ .

Regarding cardiometabolic risk factors, 44 (39.6%) patients were smokers, 18 (16.2%) were obese, 14 (12.6%) were hypertensive, 6 (5.4%) were diabetic, 26 (23.4%) had high lipid levels, and one patient (0.9%) had suffered a myocardial infarction.

Regarding radiographic manifestations, the majority of patients presented bilateral SI (the most frequent grade being grade III). In the patients undergoing MRI study (n: 25), in most of them (18/25), the bone marrow oedema (BMO) indicative of active SI was bilateral. Other classic signs of spondylitis found in this study were squaring and

syndesmophytes, in 19.8% and 18.9%, respectively. More men (87.8%) than women (59.5%) presented bilateral SI,  $p = 0.002$ . Also, more men (24.3%) than women (8.1%) showed syndesmophytes,  $p = 0.040$ .

Regarding the treatments received by the patients at the study visit, only 6 patients were under conventional DMARDs, the majority (80.2%) took NSAIDs on demand, and 67/111 were under biological treatment (mostly anti-TNF $\alpha$ ). Of the patients under biological therapy, 44 (65.7%) had received only one biological, 15 (22.4%) had received two, 5 (7.5%) three, 2 (3%) four, and one had received 5 of these therapies. The median number of biological therapies received by men was 1 (IQR: 0-1) against 0 (IQR: 0-1) in women,  $p = 0.02$ . Table 1 summarizes the main sociodemographic and clinical features of the study population.

The average value of BASDAI was  $3.4 \pm 2.3$ , for ASDAS-CRP it was  $2.1 \pm 0.84$ , while for BASFI it was  $2.95 \pm 2.32$ . Thirty-five (31.5%) of the 111 patients were in BASDAI remission, while 17/111 (15.3%) were in the ASDAS inactive disease category. The average score for ASAS-HI was  $5.4 \pm 3.8$  (IQR: 3-8). The CV of the ASAS-HI was 70.2%. Mean ASAS-HI score in men was  $5.12 \pm 3.94$ , while for women it was  $6.08 \pm 3.54$ ,  $p = 0.21$ . HLA-B27 negative patients had a significantly higher average ASAS-HI value ( $7.65 \pm 4.47$ ) than that HLA-B27 positives ( $4.86 \pm 3.43$ ),  $p = 0.002$ . The only ASAS-HI item with a significantly higher affirmative statement among women (89.2%) respect to men (70.3%) was item # 1 ("pain sometimes disrupts my normal activities"),  $p = 0.027$ . There were no significant differences between genders in relation to the affirmative answers given to the other ASAS-HI items. Figure 1 illustrates the distribution of the different affirmative items of ASAS-HI in the total population as well as in men and women.



The correlations (Spearman's rho) were high between BASDAI, BASFI and ASDAS-CRP (Table 2),  $p < 0.0005$ . Construct convergent validity was high for ASAS-HI, both against BASDAI (rho: 0.77,  $p < 0.0005$ ) and ASDAS (rho: 0.70,  $p < 0.0005$ ) (Figure 2).

The ASAS-HI also showed a high discriminative capacity, both for BASDAI remission [optimal criterion  $\leq 2$ , area under the ROC curve 0.88 (95%CI: 0.81-0.94), sensitivity 66%, specificity 96%,  $p < 0.0001$ ], and for ASDAS-CRP inactive disease [optimal criterion  $\leq 0$ , area under the ROC curve 0.87 (95%CI: 0.80-0.93), sensitivity 59%, specificity 95%,  $p < 0.0001$ ]. The ASAS-HI also demonstrated a high discriminative capacity between the remission / low activity categories versus the high / very high activity categories of the ASDAS-CRP. Thus, the optimal criterion for detecting the high / very high disease activity ASDAS-CRP categories was an ASAS-HI score  $> 6$ , area under the ROC curve 0.86 (95%CI: 0.78-0.92), +LR 7.3 (95%CI: 3.1-17.1),  $p < 0.0001$  (Figure 3).

In the multivariate regression model developed to weight ASAS-HI items associated with active disease according to both BASDAI and ASDAS-CRP, the only two ASAS-HI items significantly associated with BASDAI active disease were, "I often get frustrated" [OR 9.2 (95%CI: 1.2-69.4),  $p = 0.032$ ], and "I sleep badly at night" [OR 7.7 (95%CI: 1.4-41.6),  $p = 0.018$ ]. As for ASDAS-CRP, the only item significantly associated with active disease was "pain sometimes disrupts my normal activities" [OR 8.7 (95%CI: 1.7-45.2),  $p = 0.010$ ].

## Discussion

In this study we were able to verify that the ASAS-HI, a disease impact measurement instrument, has a good convergent and discriminative validity, with respect to the main evaluation instruments used in SpA. Thus, we found high correlations between ASAS HI, BASDAI, BASFI and ASDAS-CRP, while an ASAS HI cut-off point of 6, marked an adequate

boundary to discriminate between the states of high-very high disease activity, as opposed to the low activity and remission categories. On the other hand, ASDAS-CRP and BASDAI had a high correlation, which supports the use of any of these instruments in the daily evaluation of disease activity in these patients.

In recent years we are witnessing an intense search for instruments that adequately, simply and reliably, capture the limitations and restrictions that patients with rheumatic diseases face in their daily lives (6,7). This need has arisen from the finding that in many cases there is a notable disagreement or discrepancy between the results of conventional activity measures and PROM (4,13,14). For example, in the field of PsA, there is certain mismatch between the results of activity measures (DAPSA) or that of treatment targets (MDA), and the results of disease impact tools such as the PsAID (15). The factors that seem to explain this misalignment seem more psychological than physical (14). On the other hand, the doctors' own perceptions of the states of remission or low activity of the disease do not usually coincide with these same perceptions, when they come from the patients themselves (5). In short, these mismatches between the visions of doctors and patients are not a minor issue, insofar as they can also lead to mismatches in therapeutic orientation. In a recent PsA study, it was found that one third of patients in a clinically acceptable condition according to the evaluating physician, did not reach the MDA response, so that if a treat to target strategy had been applied, these patients should have received a therapeutic intensification (16). Therefore, we need to balance the information from conventional activity measures, with those reflecting patient's perceptions, in order to make clinical and therapeutic decision making that conform to current disease management recommendations (17,18). In our study, however, the results of the ASDAS-CRP or BASDAI correlated well with those of the

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ASAS-HI, which gives great value to this latter instrument in the general assessment of this entity.

In the most important validation study carried out to date to define the measurement properties of ASAS-HI, values  $\leq 5$  had balanced specificity to distinguish good health as opposed to moderate health, and values  $\geq 12$  were specific to represent poor health as opposed to moderate health (10). In our study we verified that a value  $\leq 6$  aligned well with the states of remission-low activity of ASDAS, and therefore this cut-off point would represent the limit to define a good health state in our SpA population. However, other researchers, such as Di Carlo et al, using ASDAS-CRP as gold standard, have defined cut points slightly different from ours, so our results require other corroborative studies (8,19). These data are extremely interesting because they would have a place, both in therapeutic and clinical decision making, and when planning treatment goals in these populations. In addition, several studies show that ASAS-HI is a simple instrument for patients, with good test-retest ability, adequate convergent and discriminant validity, as well as good sensitivity to change (8-11,19). In sum, it gathers all the properties for its use in clinical routine, even it could be the only instrument for SpA assessment in clinics with too busy agendas.

In our study, ASAS-HI score tended to be higher in women than in men, although these differences were only statistically significant with respect to item #1. This latter is not particularly striking as item #1 refers to pain, a PROM that women tend to score higher than men in SpA as well as in other rheumatic conditions (20,21).

When the ASAS HI items associated with active disease were analyzed, both by BASDAI and ASDAS-CRP, these items were different in the two contexts of active disease

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definition. Therefore, despite the good correlation between ASDAS-CRP and BASDAI, the differences we found could imply the existence of subtle discriminative capacities between both tools in terms of detecting a good state of health. However, deciding which of the two instruments would be better to capture the health status of patients with SpA is beyond the scope of this study. In any case, this issue should be addressed in future studies.

This study of course has limitations. Among others, for example, not all SpA phenotypes were included. Also, the weight of structural damage measured by validated indices such as BASRI or mSASSS has not been assessed either. However, in our study men had more SI and syndesmophytes than women, but they did not score higher in ASAS HI. Nor did our study include other outcome measures such as BASMI. Furthermore, due to the cross-sectional nature of the study, it was also not possible to provide information on the sensitivity to change of this questionnaire. However, our results seem to align well, in terms of convergent and discriminant validity, with other recently published studies, which ultimately gives consistency to the results drawn from the present study.

### **Conclusions**

We have verified a good clinimetric alignment between ASAS HI and other standard outcome measures in SpA. A cut-off point  $\leq 6$  seems to set the limit for a good state of health in our population with SpA. ASAS HI is a simple instrument that could be used as a single measure for the evaluation of these patients in consultations with busy agendas. Regardless, we must keep in mind that the ASAS-HI and the BASDAI/ASDAS are instruments that were designed for different tasks therefore these measures are not

interchangeable, and both should be incorporated into the routine evaluation of these patients.

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**Figure 1 legend.**

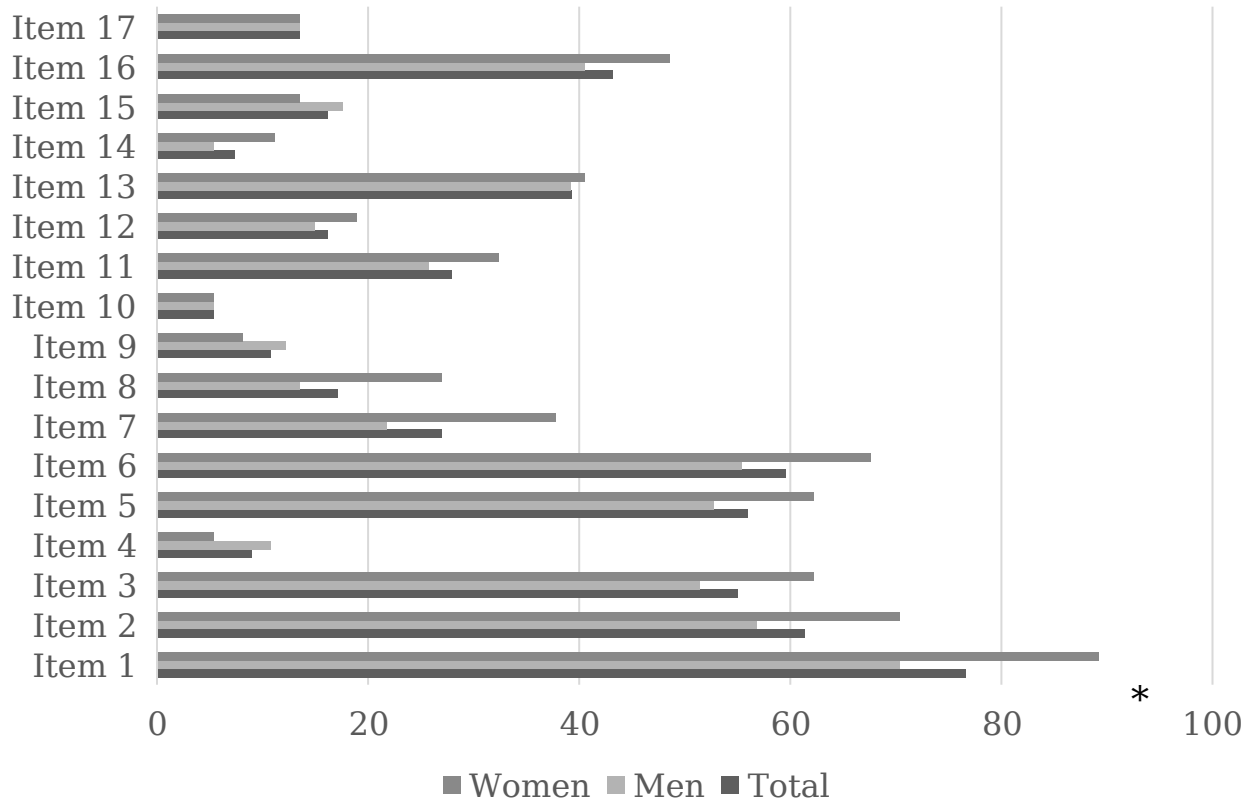
Distribution of ASAS-HI affirmative items. Item 1: Pain sometimes disrupts my normal activities; Item 2: I find it hard to stand for long; Item 3: I have problems running; Item 4: I have problems using toilet facilities; Item 5: I am often exhausted; Item 6: I am less motivated to do anything that requires physical effort; Item 7: I have lost interest in sex; Item 8: I have difficulty operating the pedals in my car; Item 9: I am finding it hard to make contact with people; Item 10: I am not able to walk outdoors on flat ground; Item 11: I find it hard to concentrate; Item 12: I am restricted in traveling because of my mobility; Item 13: I often get frustrated; Item 14: I find it difficult to wash my hair; Item 15: I have experienced financial changes because of my rheumatic disease; Item 16: I sleep badly at night; Item 17: I cannot overcome my difficulties.

**Figure 2 legend.**

Correlations between ASAS HI and BASDAI ( $\rho: 0.77, p < 0.0005$ ), and between ASAS HI and ASDAS ( $\rho: 0.70, p < 0.0005$ ).

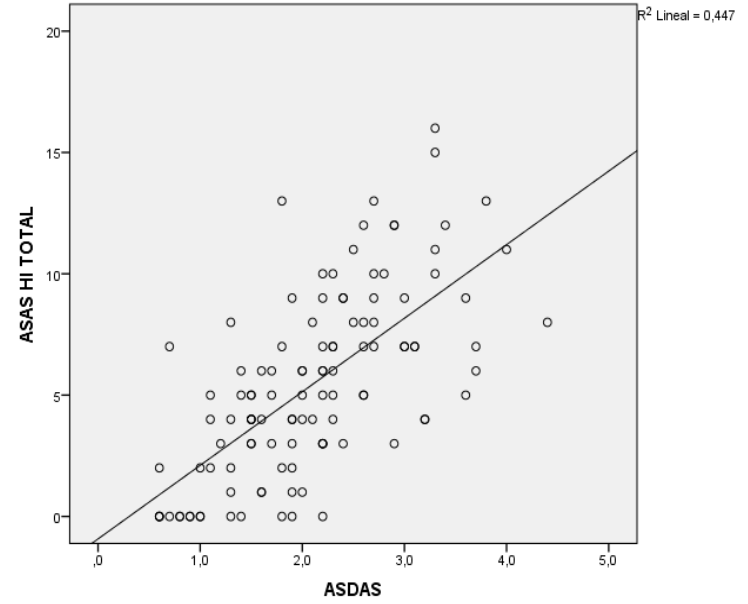
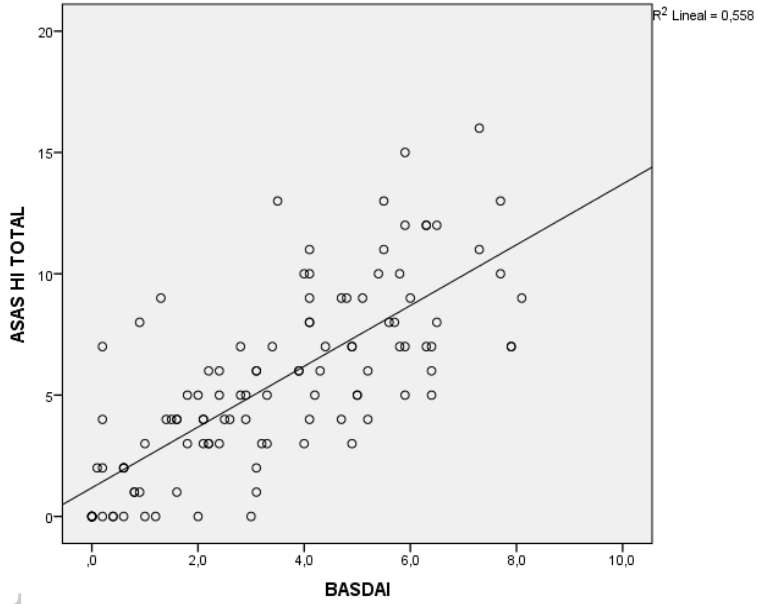
**Figure 3 legend.**

Area under the ROC curve (AUC) for discriminating between high-very high disease activity against remission-low disease activity categories of the ASDAS. Optimal criterion >6 (95%CI: 3-6), Sensitivity 66.1, Specificity 90.9.



\*

\* p = 0.027 ♀ vs. ♂



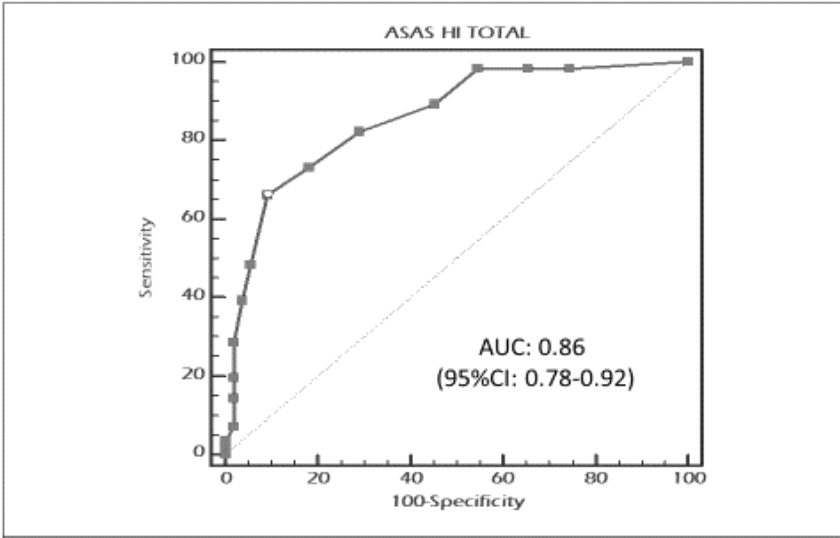


Table 1. Main disease features of the study population

Feature	N: 111
Age, yrs (mean $\pm$ SD)	43.3 $\pm$ 10.6
Disease duration, yrs (mean $\pm$ SD)	7.6 $\pm$ 6.8
Men, n (%)	74 (66.7)
Women, n (%)	37 (33.3)
AS, n (%)	74 (66.7)
Peripheral involvement, n (%)	18 (16.2)
Family history, n (%)	16 (14.4)
Educational level, n (%):	
-primary	43 (38.7)
-secondary	34 (30.6)
-university	34 (30.6)
Cardiovascular risk factors, n (%):	
-tobacco	44 (39.6)
-obesity	18 (16.2)
-hypertension	14 (12.6)
-diabetes	6 (5.4)
-dyslipidemia	26 (23.4)
Cardiovascular adverse events, n (%)	1 (0.9)
SpA-related conditions, n (%):	
-enthesitis	8 (7.2)
-anterior uveitis	14 (12.6)
-inflammatory bowel disease	6 (5.4)
Analytical parameters:	
ESR (mm/h)	7.2 $\pm$ 8.2
CRP (mg/dl)	0.4 $\pm$ 0.5
HLA-B27, n (%)	88 (79.3)
Other comorbidities, n (%):	
-fibromyalgia	3 (2.7)
-depression	8 (7.2)
-pneumonia	1 (0.9)
-neoplasms	1 (0.9)
-celiac disease	4 (3.6)
-obstructive sleep apnea	1 (0.9)

yrs: years, SD: standard deviation, n: numbers, AS: ankylosing spondylitis, SpA: spondyloarthritis, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, HLA: human leukocyte antigen.



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**Table 2. Correlations between main disease outcomes**

Parameter	BASDAI	BASFI	ASDAS	ASAS HI
<b>BASDAI</b>		rho: 0.86	rho: 0.89	rho: 0.77
<b>BASFI</b>	rho: 0.86		rho: 0.79	rho: 0.80
<b>ASDAS</b>	rho: 0.89	rho: 0.79		rho: 0.70
<b>ASAS HI</b>	rho: 0.77	rho: 0.80	rho: 0.70	

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, ASAS HI: Assessment of SpondyloArthritis international Society-Health Index.