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The ASAS Health Index: A New Era for Health Impact Assessment in Spondyloarthritis

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ABSTRACT. Spondyloarthritis (SpA) encompasses a group of inflammatory rheumatic diseases that share clinical and imaging characteristics as well as a common genetic basis. These diseases can affect 0.20–1.6% of the general population, limiting functioning and affecting the quality of life of patients. Considering the patient perspective in the management of the disease and ensuring patients are sufficiently prepared to participate in decision making is critical to treatment success, as well as for optimal health outcomes. The overall picture of impairments, limitations, and restrictions in activities or social participation for patients with SpA is not adequately assessed in SpA-specific instruments. Therefore, it is important to measure the broader range of impairments that can affect patients with SpA and integrate these into a single measure of overall functioning in daily life. The Assessment of SpondyloArthritis international Society Health Index (ASAS HI) is a recently introduced health instrument for evaluating SpA based on the International Classification of Functioning, Disability and Health (ICF) that could cover a good part of the health metric needs in SpA. This review addresses its origins, measurement properties, and use in routine clinical practice, as well as its prospects for future use.

Key Indexing Terms: ASAS Health Index, axial spondyloarthritis, impact of disease, patient-reported outcomes measures, spondyloarthritis

Disease burden in spondyloarthritis: The need for new health metrics

The term *spondyloarthritis* (SpA) refers to a series of inflammatory rheumatic diseases that share clinical and imaging characteristics as well as a common genetic basis. This conceptual umbrella includes diseases such as ankylosing spondylitis (AS) and nonradiographic (nr-) axial SpA (axSpA), as well as predominantly peripheral forms.[1] The 2009 Assessment of SpondyloArthritis international Society (ASAS) classification criteria have greatly contributed to providing a cohesive view of these diseases that has facilitated their study from multiple standpoints.[2]

AxSpA is characterized by inflammatory spinal pain and spinal stiffness and includes AS (radiographic axSpA) and nr-axSpA.[2] A previous metaanalysis reported a global prevalence of these conditions that ranges from 0.20% in Southeast Asia to 1.61% in Arctic circumpolar areas.[3] As these conditions usually start in young individuals, when many are starting their working lives, SpA may hinder patients' professional prospects. The inability of these patients to continue working affects their social lives considerably, and has economic repercussions for both the individuals and society.[4] When compared to rheumatoid arthritis (RA), patients with axSpA and psoriatic arthritis (PsA) experience more pain and fatigue, and patients with axSpA have more overall and nocturnal spinal pain than those with PsA and RA.[5] A previous study showed that the global unemployment rate in axSpA is 25%, wherein 20.6% was due to the disease itself and risk factors included female sex, low educational level, living in rural areas, and high rates of disease activity.[6]

Symptoms of pain, stiffness, and fatigue associated with progressive bony fusion of the spine are major contributors to disease burden and limit physical functioning, including the ability to perform daily activities.[7,8,9,10,11] Many patients with axSpA also experience sexual dysfunction, depression, anxiety, and sleep alterations.[11] Therefore, patients with axSpA show significantly lower health-related (HR-) quality of life (QOL) compared with the general population, and physical components of HRQOL tend to be more affected than psychological ones in both sexes.[11,12,13]

The European Map of Axial Spondyloarthritis (EMAS) has been the largest survey carried out to date for people with axSpA, with 2846 respondents from 13 European countries.[14] The EMAS's focus was on understanding the patient perspective through a holistic approach and utilizing a questionnaire designed for patients by patients. As such, EMAS collected not only clinical characteristics of the disease but also the effect it had on patients' psychological health, daily activities, and working and social lives, as well as how the disease related to their hopes and fears, all of which are considered important aspects for patients with axSpA.[14] The final patient questionnaire included

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108 items related to 12 different areas: sociodemographic and anthropometric characteristics, disability assessment, work life, daily life, lifestyle habits, diagnostic journey, healthcare resource use, treatment, comorbidities (including extraarticular manifestations), psychological health, disease outcomes, and patient disease-related attitudes and treatment goals.[14] Data from this survey indicated important unmet needs in axSpA, including long diagnostic delay, deterioration of QOL, and high burden of disease for patients. Mean diagnostic delay was calculated as > 7 years, confirming similar results drawn from other studies.[15] The results of EMAS showed a high burden of disease for patients. Most participants reported moderate to severe limitation during disease flares, which was especially evident while performing daily activities including physical exercise, cleaning, getting out of bed, or getting dressed.[14] The EMAS sample showed a high prevalence of mental health difficulties. Thus, 61.5% of patients were at risk for psychological distress, with 33.8% and 38.6% reporting depression and anxiety, respectively. Participants also reported the difficulties finding a job due to their condition (74.1%), the influence of the disease on their job choice (45.7%), and workplace adaptation that was required (43.9%).[14]

The factors positively associated with poorer HRQOL in patients with SpA include inflammatory activity, axial mobility, and physical function. QOL instruments, both generic and specific, usually capture the impact of these factors; however, there are contextual and social factors as well as specific disease aspects (such as fatigue or sexuality) that are not included in these tools. On the other hand, concepts such as QOL, HRQOL, or disease impact are not entirely synonymous since the measurement dimensions and the construct content of these approximations are not the same.[16] Therefore, there is a growing need for instruments that address the well-being and overall health of these patients in a more holistic way.[16]

Development of the ASAS Health Index

The International Classification of Functioning, Disability and Health (ICF) is an instrument developed by the World Health Organization (WHO) to provide a standard language and framework for the description of health and health-related states.[17] In ICF, the term *functioning* refers to all body functions, activities, and participation, whereas *disability* is similarly an umbrella term for impairments, activity limitations, and participation restrictions. ICF also lists environmental factors that interact with all these components.[17] This more holistic model of disability might be called the biopsychosocial model of disease. In this proposal, disability is viewed as a complex phenomenon that affects a person at both the medical and the social level. Therefore, disability is always an interaction between features of the person and features of the overall context in which the person lives; however, some aspects of disability are almost entirely internal to the person, whereas other aspects are almost entirely external. In other words, the biopsychosocial model integrates disability as a feature of the person, directly caused by a disease, trauma, or other health condition that requires medical care provided in the form of individual treatment by professionals, as well as disability as a socially created problem that requires a political response, since the problem is created by an unaccommodating physical environment brought about by attitudes and other features of the social environment. Therefore, ICF provides a coherent view of different perspectives of health: biological, individual, and social.[17]

Figure 1 shows the 3 levels of human functioning classified by ICF: functioning at the level of body or body part, the whole person, and the whole person in a social context. Disability therefore involves alterations at ≥ 1 of the following levels: impairments, activity limitations, and participation restrictions.[17]

The overall picture of impairments, limitations, and restrictions in activities or social participation of patients with SpA is not adequately assessed in SpA-specific instruments.[18] Moreover, the concepts used to create most of the existing questionnaires are not clearly defined in the original publications. To overcome this, the ASAS group developed an instrument to assess health as defined by the ICF according to ICF categories of functioning.[19] The comprehensive ICF Core Set for AS is a disease-specific selection of the ICF factors that are typical and relevant for patients; this core set served as the underlying construct of the Assessment of SpondyloArthritis international Society Health Index (ASAS HI) since the whole range of functioning, disability, and health of patients with AS was captured.[20] The ASAS HI is a linear composite measure containing 17 items with dichotomous response options ("I agree" or "I do not agree") that cover most of the ICF core set (Table 1). The item selection was carried out based on the Rasch model. Each positive answer is scored as 1, whereas a negative answer is scored as 0. The result is the sum of individual items. Higher values reflect a major degree of impairments, limitations, and restrictions.[18,19] Five phases were used to develop the questionnaire and to achieve an index for functioning and health that is easy to administer, easy to fill in, and applicable to patients worldwide. The items incorporated into the final questionnaire originated from a 251-item pool, which had been developed by linking items from existing questionnaires (either disease-specific or generic instruments) to 44 categories of the comprehensive ICF Core Set for AS related to the components of body function, activities, and participation. A total of 76 items covered the 23 ICF categories from the body functions component, 122 items covered the 24 categories from the activities and participation component, and 53 items covered the 14 categories of environmental factors (EFs).[18,19] The final 17 items cover a wide range of ICF factors including pain, emotional function, sleep, sexual function, mobility, self-care, and community life. The ASAS HI was originally developed in parallel in English speaking countries (Australia, Canada, Ireland, UK, US), but was later translated and cross-culturally adapted into 19 languages worldwide.[19,21]

Measurement properties

To review the metrological properties of the ASAS HI in patients with SpA, we searched all the articles referring to this instrument in PubMed from its original publication until March 2021. Additionally, some references were obtained from the databases of the European Alliance of Associations for Rheumatology

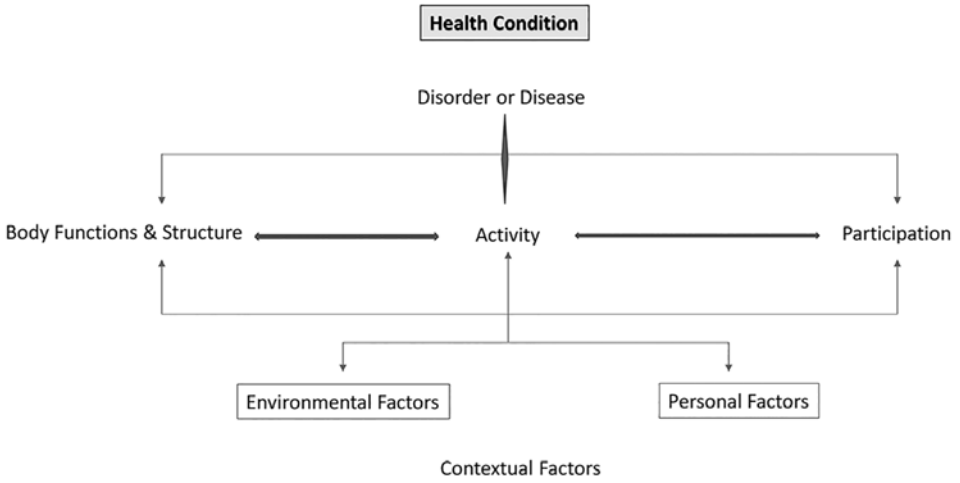

Figure 1. The biopsychosocial model of disease based on the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization (WHO). The model is based on 3 levels of human functioning: functioning at the level of body or body part, the whole person, and the whole person in a social context. Disability therefore involves alterations at ≥ 1 of these same levels: impairments, activity limitations, and participation restrictions.

Table 1. The 17 items of the ASAS Health Index.[18]

Item		Category
1	Pain sometimes disrupts my normal activities.	Pain
2	I find it hard to stand for long.	Maintaining body position
3	I have problems running.	Moving around
4	I have problems using toilet facilities.	Toileting
5	I am often exhausted.	Energy and drive
6	I am less motivated to do anything that requires physical effort.	Motivation
7	I have lost interest in sex.	Sexual functions
8	I have difficulty operating the pedals in my car.	Driving
9	I am finding it hard to make contact with people.	Community life
10	I am not able to walk outdoors on flat ground.	Moving around
11	I find it hard to concentrate.	Handling stress
12	I am restricted in traveling because of my mobility.	Recreation and leisure
13	I often get frustrated.	Emotional functions
14	I find it difficult to wash my hair.	Washing oneself
15	I have experienced financial changes because of my rheumatic disease.	Economic self-sufficiency
16	I sleep badly at night.	Sleep
17	I cannot overcome my difficulties.	Handling stress

ASAS: Assessment of SpondyloArthritis international Society.

and American College of Rheumatology congresses, avoiding duplications.

Interpretability. The ASAS HI is a linear composite measure, with higher values reflecting a major degree of impairments, limitations, and restrictions.[19] The most important study carried out so far to validate the clinimetric properties of the ASAS HI was a 2018 cross-sectional international observational study that included 1548 patients from 23 countries.[22] The ASAS HI was provided in 19 languages and proved to be a valid, interpretable, reliable, and responsive questionnaire to assess overall functioning and health in this global international validation study.[22] The mean total score on the ASAS HI ranged from 3.2 to 8.37.[19,23–33]

Cognitive debriefing studies have shown that items of the ASAS HI and EF Item Set are clear, relevant, and comprehensive. All translated versions were accepted with minor modifications with respect to item wording and response options. In these studies, only the wording of 3 items (#7 ["I have lost interest in sex"] and #8 ["I have difficulty operating the pedals in my car"] of ASAS HI, and #6 of the EF Item Set ["Treatment of my rheumatic disease is taking up time"]) had to be adapted to improve clarity. As a result of cognitive debriefing, a new response option, "not applicable," was added to 2 items of the ASAS HI to improve appropriateness.[21]

Content validity. ASAS HI construct validity by Spearman correlation coefficient ranged from low (absenteeism: 0.23) to high (Bath Ankylosing Spondylitis Functional Index [BASFI] 0.71 or 36-item Short Form Health Survey physical component summary score 0.73). Of note, the correlations between ASAS HI and age ($\rho = 0.10$) and symptom duration were weak. Bath Ankylosing Spondylitis Disease Activity Index [BASDAI], BASFI, and Ankylosing Spondylitis Disease Activity Score [ASDAS] correlations with ASAS HI were high, with values reported in various studies of 0.51–0.77, 0.62–0.80, and 0.51–0.70, respectively.[19,22–25,27–29,31–33]

In the study by Min et al,[27] multivariable regression analysis of the axSpA group showed that high nonsteroidal antiinflammatory drug (NSAID) intake and higher modified Stoke Ankylosing Spondylitis Spine Score were positively associated with ASAS HI, whereas higher economic status and higher alcohol consumption were negatively associated with ASAS HI. Results were consistent in the AS group on subgroup analysis, whereas alcohol consumption was the only factor significantly

Table 2. Main worldwide studies carried out to date with the ASAS HI.

Author, Yr	N	SpA Type, n	Treatment	BASDAI Correlation, ρ	BASFI Correlation, ρ	ASDAS Correlation, ρ	ASAS HI Average Score, mean (SD)	Activity Discrimination Score, mean ± SD	Internal Consistency, Cronbach α	Reliability, ICC (95% CI)	SDC	SRM (95% CI)	Floor/ Ceiling Effects, %	Test Completion Time, mean
Choi, 2014[29]	43	13 nr-axSpA; 30 AS	ND	0.63	0.69	ND	5.3 (4.2)	ND	ND	0.97 (0.95–0.98)	ND	ND	ND	75.4 ± 31.7 s
Kiltz, 2015[19]	1754	AS	ND	0.60	0.70	ND	8.37 (3.9)	5.0 ± 3.2 for BASDAI < 4	ND	ND	ND	ND	ND	ND
Kiltz, 2016[21]	215	140 AS; 75 nr-axSpA	ND	ND	ND	ND	7.1 (4.4)	ND	ND	ND	ND	ND	ND	ND
Di Carlo, 2016[25]	140	98 AS; 42 nr-axSpA	70.7% TNFi, all with NSAID on demand	0.56	0.67	0.56	7.6 (3.9)	4	ND	0.98 (0.97–0.98)	ND	ND	ND	1.92 ± 0.76 min (range 0.8–3.5)
Cruz, 2017[26]	10	6 AS; 4 nr-axSpA	ND	ND	ND	ND	5.1 (4.0)	ND	ND	ND	ND	ND	ND	2.2 ± 0.4 min (range 1.2–3.2)
Di Carlo, 2017[34]	140	93 AS; 47 nr-axSpA	70.7%TNFi, all with NSAID on demand	ND	ND	ND	ND	4	ND	ND	ND	ND	ND	ND
Bautista-Molano, 2018[24]	50	30 AS; 14 nr-axSpA; 6 pSpA	ND	0.66	0.62	0.65	8.2 (5.1)	5.9 ± 3.0 for ASDAS low activity	0.91	0.84 (0.71–0.93)	ND	TNFi: 2.94 (2.13–4.24); NSAID or DMARD: 2.22 (1.23–3.21)	ND	ND
Kiltz, 2018[22]	1548	1292 axSpA (375 nr-axSpA; 917 AS); 256 pSpA	64.2% NSAID 26.2% DMARD 38.2% TNFi	0.70	0.71	0.61	6.7 (4.3)	5	0.93 AS; 0.94 nr-axSpA; 0.91 pSpA	0.87 (0.84–0.89)	3	−0.44 NSAIDs; −0.69 csDMARDs; −0.85 TNFi	6.9/0.8	ND
Kiltz, 2019[23]	171	90 AS, 44 nr-axSpA, 37 pSpA	76.6% NSAID 21.6% DMARD 30.4% TNFi	0.71	0.74	0.52	7.3 (4.1)	4.8 ± 3.2 for ASDAS moderate activity	0.83	0.94 (0.90–0.96)	3	−0.27	ND	ND
Kwan, 2019[28]	108	axSpA	70.2% NSAID 16.4% DMARD 14.7% biologics	0.61	0.62	ND	3.2 (range 0–15)	ND	0.83	Week 1: 0.96 (0.93–0.98); Week 2: 0.95 (0.91–0.98)	1.02	ND	ND	1.2 min
Essers, 2019[30]	199	130 AS, 69 nr-axSpA	ND	ND	ND	ND	7.2 (4.5)	ND	ND	ND	ND	ND	ND	ND
Min, 2019[27]	357	261 AS, 96 nr-axSpA	54.6 % NSAID 34.3% SSZ 47.8% TNFi	0.58	0.65	0.56	3.5 (3.4)	5	ND	ND	ND	ND	ND	ND
Alonso-Castro, 2020[31]	111	74 AS, 37 nr-axSpA	80.2% NSAID 60.3% biologics	0.77	0.80	0.70	5.4 (3.8)	6	ND	ND	ND	ND	ND	ND
Akgul, 2020[32]	991	851 AS, 140 nr-axSpA	ND	0.50	0.57	0.51	6.16 (4.37)	4	0.84	ND	ND	ND	9.2/1.9	ND
Rodrigues-Manica, 2020[33]	91	63 axSpA (49 AS and 14 nr-axSpA); 28 pSpA	74% NSAID; 44% csDMARD 18% TNFi	0.77	0.76	0.66	6.4 (3.6)	4.5 (2.0) for ASDAS low activity	0.88; AS 0.90; nr-axSpA 0.86; pSpA 0.50	0.76 (0.09–0.91)	3	−0.53	0/1.1	ND

AS: ankylosing spondylitis; ASAS HI: Assessment of SpondyloArthritis international Society Health Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial SpA; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; DMARD: disease-modifying antirheumatic drug; ICC: intraclass correlation coefficient; ND: not described; NSAID: nonsteroidal antiinflammatory drugs; nr-axSpA: nonradiographic axial SpA; pSpA: peripheral SpA; SSZ: sulfasalazine; SDC: smallest detectable change; SpA: spondyloarthritis; SRM: standardized response mean; TNFi: tumor necrosis factor-α inhibitor.

Table 3. Defined health status groups according to the ASAS HI.[22]

External Equivalents	Good Health Status (≤ 5)	Moderate Health Status (> 5 to < 12)	Poor Health Status (≥ 12)
ASAS HI	2.1 (1.5)	7.8 (2.0)	13.7 (1.5)
BASFI	1.2 (1.5)	3.8 (2.5)	6.3 (2.3)
BASDAI	2.1 (1.6)	4.8 (2.1)	6.6 (1.9)
ASDAS	1.7 (0.9)	2.6 (2.1)	3.7 (1.1)
SF-36 PCS	47.6 (7.1)	35.7 (8.8)	28.7 (6.6)
EQ-5D	0.8 (0.1)	0.6 (0.2)	0.4 (0.2)

The 3 defined health status groups within ASAS HI discriminate with respect to disease activity (BASDAI, ASDAS), functioning (BASFI), and QOL measures (SF-36, EQ-5D). Modified from reference 22. Values are means (SD). ASAS HI: Assessment of SpondyloArthritis international Society Health Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; PCS: physical component summary score; SF-36: 36-item Short Form Health Survey; QOL: quality of life.

associated with ASAS HI in the nr-axSpA group. In short, in this cohort study,[27] patients with AS had poorer health status than those with nr-axSpA.

Internal consistency. Numerous studies show a high internal consistency of the ASAS HI with a Cronbach α, ranging from 0.83 to 0.93.[22,23,24,28,32,33] Moreover, internal consistency did not vary across different disease groups (0.93 for AS, 0.94 for nr-axSpA, and 0.91 for peripheral SpA; Table 2).[22]

Reliability and measurement error. Reliability was excellent in all the studies analyzed with intraclass correlation coefficient (ICC), with minimum values of 0.84 (95% CI 0.71–0.93, $P < 0.001$) and maximum values of 0.97 (95% CI 0.95–0.98; $P < 0.001$).[22,23,24,25,28,29,33]

Also, ICCs (95% CIs) were comparably high in all disease subtypes: AS 0.87 (0.84–0.89) and 0.94 (0.86–0.97); nr-axSpA 0.89 (0.85–0.93) and 0.97 (0.89–0.99); peripheral SpA 0.83 (0.75–0.88) and 0.92 (0.79–0.97).[22,23]

Bland-Altman plot showed good agreement between ASAS HI sum score at first and second assessments.[22,23,25] The smallest detectable change (SDC) was calculated as 3.0, which corresponds to the minimum change beyond measurement error that can be detected in an individual patient over time.[22,23,33] However, Kwan et al showed a lower SDC calculated as 1.02.[28]

Responsiveness. Several studies analyzed sensitivity to change of ASAS HI in patients who initiated therapy or changed from their original therapy. The standardized response mean (SRM) varied across different studies between –0.27 (low) and 2.58 (large). In general, the SRM was higher in patients whose intervention was a tumor necrosis factor (TNF)-α blocker than in those starting an NSAID or conventional synthetic (cs-) disease-modifying antirheumatic drug (DMARD).[22,23,24,33]

Discriminant ability. ASAS HI discriminated well between patients with different disease activity states (measured by ASDAS and BASDAI) and function (measured by BASFI). The groups with greater disease activity and more impaired functioning had higher mean ASAS HI scores than those with lower disease activity and functional scores. Moreover, ASAS HI was able to differentiate between different stages of disease activity and physical functioning in patients with SpA. Patients with high disease activity and limited physical function had poorer global functional capacity as measured by the sum score of ASAS HI.[22,23,24,33]

The following is a summary of the main ASAS HI cut-off points that discriminate disease activity:

(A) 5.0 ± 3.2 as a cut-off point for identifying low disease activity measured by BASDAI < 4.[19]

(B) 2.9 ± 3.1 as an inactive disease identifier measured by ASDAS and 2.8 ± 2.9 as an identifier of BASDAI remission.[22]

(C) 4.8 ± 3.2 as a moderate activity identifier measured by ASDAS.[23]

(D) 5.9 ± 3.0 as a low activity identifier measured by ASDAS.[24]

(E) 4.0 as a cut-off point to define the inactive disease, with respect to ASDAS–C-reactive protein (CRP)[34] and simplified ASDAS.[25]

(F) ≤ 6.0 aligned well with the states of remission–low activity of ASDAS.[31]

(G) 4.5 ± 2.0 as a low activity identifier measured by ASDAS.[33]

With respect to ASAS HI scores related to physical function, we found the following cut-off points:

(A) 3.7 ± 3.1 as a threshold, < 2 measured by BASFI.[22]

(B) 3.5 ± 2.9 as a threshold, < 2 measured by BASFI.[23]

(C) 4.1 ± 3.4 as a threshold, < 2 measured by BASFI.[32]

Thresholds of meaning and cut-off values. There are few studies that have determined specific ASAS HI cut-off points that discriminate health states. The following figures have been proposed as cut-off points to define health status (Table 3):

(A) Kiltz et al[22] designed a threshold for evaluating the discriminant ability of the ASAS HI by calculating the mean ASAS HI scores for predefined status groups (ASDAS status groups: inactive, moderate, high, and very high; BASDAI and BASFI thresholds: < 2.0, 2.0–3.99, 4.0–5.99, ≥ 6.0) by ANOVA. To distinguish between relevant health states (an additional relevant aspect of interpretability), 2 different methods were applied: fixed 90% specificity and the closest point to 0.1. They used the patient global assessment (PtGA) at predefined levels (6 on numerical rating scale and cut-off between "good" and "poor" on Likert scale) as external constructs for poor, moderate, and good health status. They used a global rating of change questionnaire (Likert scale) as an external construct to assess change perceived by the patient. A cut-off between "improved" vs "no change" or "worse" was used to determine minimal clinically important improvement. In order to balance sensitivity and specificity, a threshold of ASAS HI, which differentiated patients with good/very good health from those with moderate health state, was identified as being 5.0. In contrast, the 90% specificity criterion was considered to be the most clinically relevant threshold of ASAS HI for moderate vs poor/very poor health identified as a score ≥ 12.0.[22]

(B) Min et al, using the health states proposed by Kiltz et al,[22] found that most patients analyzed were in a good health status (75.9%). Among patients with nr-axSpA, 84.4% were in a good health status compared to 72.8% of patients with AS.[27]

(C) Akgul et al performed a receiver-operating characteristic curve analysis to calculate health status thresholds. Based on ASDAS-CRP and PtGA as external anchors, they established ASAS HI ≤ 4 to distinguish good health status from moderate health status, and ≥ 12 to identify poor health status.[32]

Therefore, ASAS HI sum score ≤ 5 may be a good cut-off for discriminating good vs other health statuses and sum score between 4 and 6 may be a good discriminator for disease activity status.

Score (floor/ceiling effects). Floor (percentage of the respondents who had the lowest possible [total] score) or ceiling (percentage of the respondents who had the highest possible [total] score) effects of the ASAS HI were acceptable (0–9.2% and 0.8–1.2%, respectively).[22,32,33]

Use in clinical trials. The effects of ixekizumab (IXE) on functioning and health were assessed using the ASAS HI for the 303 patients with nr-axSpA enrolled in the COAST-X trial.[35] An improvement of ≥ 3 from baseline in ASAS HI represented a clinically meaningful change and attaining a good health status was defined by score of ≤ 5. Baseline mean (SD) scores were 9.1 (3.6) for ASAS HI. Patients treated with IXE every 2 weeks (Q2W) reported significant improvements in ASAS HI at Week 16 (−2.74 for IXE Q2W vs −1.76 for placebo, $P = 0.02$), with numerically greater improvements in ASAS HI changes from baseline in both IXE groups compared with placebo through Week 52.[35]

COAST-V and COAST-W are phase III, multicenter, placebo-controlled randomized trials, evaluating the efficacy and safety of IXE in patients with radiographic axSpA. Participants in COAST-V were biologic (b-) DMARD-naïve, whereas in the COAST-W trial participants had failed at least 1 and no more than 2 TNF inhibitor (TNFi) treatments.[36] At Week 16, bDMARD-naïve patients receiving IXE reported a significantly larger improvement from baseline on ASAS HI vs placebo (−2.36 for Q4W [$P = 0.01$], −2.74 for Q2W). IXE Q4W bDMARD-naïve patients achieved numerically similar ASAS HI mean change from baseline compared with patients who received IXE Q2W (−2.7 vs −3.3 at Week 52). Patients treated with the active reference adalimumab (ADA) also showed consistent significant improvement in ASAS HI mean change from baseline throughout 16 weeks. Patients who received ADA or placebo during the blinded treatment dosing period and switched to IXE at Week 16 demonstrated continued numeric improvements in ASAS HI through Week 52. Both IXE regimens (Q2W and Q4W) sustained similar improvements through Week 52. Patients in the bDMARD-naïve arm experienced a numerically greater improvement of ASAS HI mean change vs TNFi-experienced patients when treated with IXE Q4W (−2.4 vs −1.9 at Week 16 and −2.7 vs −2.3 at Week 52) or IXE Q2W (−2.7 vs −1.6 at Week 16 and −3.3 vs −2.5 at Week 52). The proportion of patients treated with IXE achieving improvement in ASAS HI ≥ 3 throughout the 52 weeks were 53.2% at Q2W and 43.0% at Q4W for bDMARD-naïve patients, and 43.3% and 36.8%, respectively, for TNFi-experienced patients.

Finally, the recently published TICOSPA study evaluated the benefit of a tight control strategy compared to usual practice in patients with axSpA.[37] One hundred sixty patients were randomized (1:1) to the tight control arm (strategy was prespecified by the scientific committee, based on current axSpA recommendations, visits every 4 weeks, and targeted [ASDAS < 2.1]) or usual practice arm (treatment decisions were made at the discretion of the rheumatologist, with visits every 12 weeks). The percentage of patients with a significant improvement (> 30%) in ASAS HI score during 1-year follow-up was the primary outcome of this study. Although 47.3% and 36.1% of patients in the strict control and usual practice arms, respectively, achieved a significant improvement in ASAS HI at the 1-year visit, the difference was not statistically significant. Table 2 summarizes the psychometric properties of ASAS HI discussed above.

Applications, potential uses, and use in clinical practice

The ASAS HI effectively gathers all measurement properties for its use in routine clinical practice as it captures not only aspects related to the activity of the disease or functional limitations, but also those related to the individual and their social environment.

Quality-adjusted life-years (QALYs) play an important role in reimbursement decisions when one of the criteria is the cost effectiveness of the health technology. While many generic QALYs (e.g., based on the EQ-5D) are viewed as the gold standard, there has been a considerable increase in interest in using condition-specific data to generate QALYs.[38] Therefore, using patient-reported measures as a basis for indirect health utility valuation may not accurately reflect the effect of interventions on specific impairments and limitations typically experienced by patients with SpA.[30] The ASAS HI offers an interesting starting point to develop a disease-specific utility index, as it was developed with the specific aim to reflect common aspects of health that are important to patients with axSpA, and to a lesser extent for peripheral SpA.[30] Essers et al[30] developed 1 generic and 6 country-specific algorithms that are now available to convert scores of the ASAS HI into a utility from the societal cost perspective. This makes it possible to use disease-specific utilities and QALYs in decision-making processes when comparing treatment strategies among patients with SpA.[30]

The best–worst scaling (BWS) method is widely used to measure health preferences. Kiltz et al conducted a BWS exercise in patients with axSpA from 20 countries worldwide.[39] The study was completed by 199 patients. The highest relative importance was assigned to pain, sleep, exhaustion, standing, and motivation to do anything that requires physical effort. The lowest relative importance was assigned to sexual relationships, toileting, contact with people, driving, and washing hair.[39] As authors concluded, this information may help to align clinical care with patients' needs.

In the most important validation study carried out to date, ASAS HI was found to be applicable in all patients with SpA regardless of the disease subgroup (83.5% with axSpA and 16.5% with peripheral SpA). However, the proportion of patients with concomitant psoriasis did not exceed 10%, so the representativeness of patients with PsA was presumably very low in this validation exercise. Morante et al evaluated the performance of the ASAS HI in 90 Spanish patients with PsA. Mean ASAS HI

was 5.8 ± 4.3. Convergent validity was high, both against the Disease Activity Index for Psoriatic Arthritis (DAPSA) and the Psoriatic Arthritis Impact of Disease questionnaires. ASAS HI also showed a high discriminant capacity against DAPSA categories of disease activity. The ASAS HI items significantly associated with DAPSA active disease were: "I find it hard to stand for long" (β 4.48, $P < 0.0001$), "I find it hard to concentrate" (β 2.94, $P = 0.04$), and "I sleep badly at night" (β 1.86, $P = 0.04$). These results suggest that ASAS HI could be a valid instrument to assess overall functioning and health in PsA.[40] Also, recently, the usefulness of ASAS HI has been proven to analyze some differentiating aspects of QOL between patients with PsA and axSpA.[41,42]

Gaps and future research

Although it is a fast, simple, and accessible tool in clinical practice, we have observed that the dissemination of ASAS HI in clinical practice is still very limited.[43] More evidence is also needed to determine cut-off points that better discriminate between states of health. Moreover, more information is needed regarding ASAS HI as a potential discriminator of disease activity in SpA. Finally, we also do not know to what extent other concomitant conditions (e.g., fibromyalgia) may influence the ASAS HI sum score.[44] In short, it is necessary to expand the studies in real clinical practice with this new instrument.

Conclusion

The ASAS HI is a new SpA-related instrument based on the WHO ICF categories. Its measurement properties make it a suitable tool for assessing health and functioning in patients with different SpA phenotypes in routine clinical practice, cohort studies, and clinical trials. In future, it could be a valid questionnaire for the evaluation of other entities such as PsA, and for planning health policies from a societal cost perspective. Finally, since SpA is frequently accompanied by other conditions that affect the ways in which patients cope with their day-to-day lives, it would be beneficial to determine whether ASAS HI can capture the effects associated with these other SpA-related manifestations.[45,46]

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