

Editorial

ASAS Health Index: The “All in One” for Spondyloarthritis Evaluation?



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The assessment of multifaceted disease processes is a key element in the management of chronic inflammatory rheumatic diseases such as axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS). The evaluation includes not only patients' history and clinical symptoms but also the assessment of disease activity, function, structural damage, and comorbidities. The management of patients with axSpA is especially challenging in this regard, because this complex disease entity has a wide variability of clinical signs and symptoms^{1,2}. Within the variable course of SpA, adding to the burden of the disease are axial involvement, peripheral arthritis, enthesitis, and extramusculoskeletal involvement in other organs such as the eye, the skin, and the gut. The most prominent health problems in addition to inflammatory back pain are spinal stiffness, mobility limitations, fatigue, and sleep problems that are associated with significant restrictions in activities of daily living in patients with axSpA³.

The evaluation of the current state of health of a patient with axSpA includes the assessment of several aspects of the disease with a focus on disease activity, because the degree of inflammatory activity is the main driver of pain, stiffness, and radiographic progression⁴. Therefore, the reduction of disease activity is of major importance and a central target for intervention, with remission as the main objective of treat-to-target (T2T) strategies⁵. However, assessment of disease activity alone cannot sufficiently characterize the entire effect of the disease on the patient³. This is especially relevant when evaluating impairments in phys-

ical function and spinal mobility in patients with axSpA, because it has been clearly shown that associated limitations depend on both inflammatory and structural changes⁶.

A variety of validated tools for the assessment of axSpA, evaluating different aspects of the disease, is available and frequently used in clinical trials, registries, and cohorts⁷. For the assessment of disease activity, the Bath ASDisease Activity Index (BASDAI), a pure patient-reported outcome, and the AS Disease Activity Score (ASDAS), which includes C-reactive protein (CRP), are used. Assessment of functioning usually concentrates on physical functioning by use of a questionnaire, the Bath AS Functional Index (BASFI), or by a physical examination investigating range of motion by the Bath AS Metrology Index. Further, performance tests such as the AS Physical Performance Index are now increasingly used^{8,9}. New bone formation or structural spinal damage in axSpA is mainly assessed by the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), but it covers only parts of the spine¹⁰.

Functioning is increasingly taken into account not only when assessing the effect of a chronic disease on individual patients, but also when quantifying the efficacy of an intervention in clinical studies. However, it is important to realize that the assessment of function is often limited to physical function, thus ignoring the complexity of global functioning. The term “functioning and health” has been proposed as part of a broader concept that was conceptualized in the International Classification of Functioning, Disability, and Health (ICF). The ICF, published by the World Health Organization more than 2 decades ago, refers to health impairments, limitations, and disabilities that patients experience because of a disease¹¹. The ICF framework adheres to the bio-psycho-social model of disease and recognizes that functioning and health results from a complex interplay of the “functioning and disability components,” body functions and body structures, and activities and participation, with “contextual factors” that consist of environmental and personal factors (Figure 1). This means for daily practice that aspects of physical

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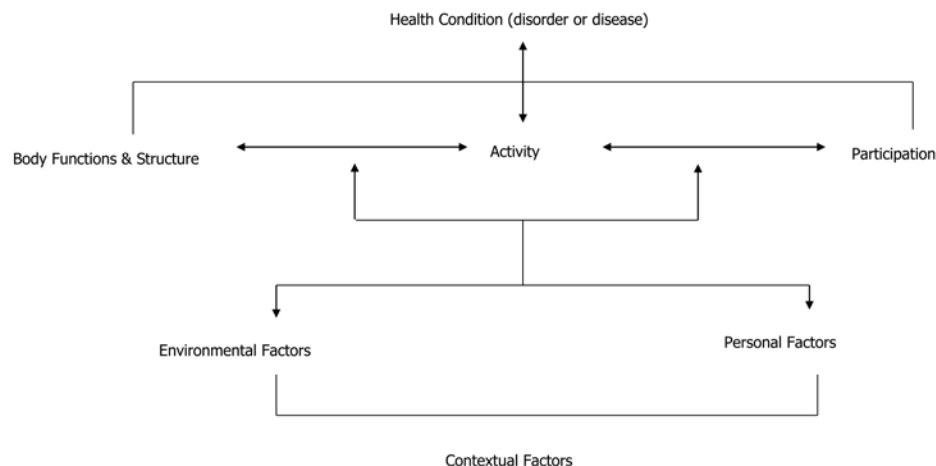


Figure 1. The bio-psycho-social framework of health of the World Health Organization that is the basis for the International Classification of Functioning, Disability and Health. (Used with permission of the World Health Organization.)

functioning are differentiated from emotional and social functioning as well as environmental factors. Indeed, the burden of disease is explained not only by disease activity or structural damage but by general health, and the actual state of disease is also potentially influenced by depression and anxiety or lack of social activity and participation¹².

Thus, a comprehensive and standardized assessment for patients with axSpA is needed to identify modifiable factors that can be addressed by the treatment modality and strategy chosen. The Assessment of SpondyloArthritis international Society (ASAS), an international group of experts in the field of SpA, is currently working on an update of the axSpA core set of tools for the assessment of the response to medical and physical therapies — for both clinical studies and clinical record keeping¹³. According to the recently published ASAS quality standards, patients need a timely diagnostic examination to ensure correct diagnosis and to achieve better longterm outcomes and improve the health-related quality of life (HRQOL)^{7,14}.

However, none of those above-mentioned ASAS tools has been able to assess global functioning and health in patients with axSpA based on the Comprehensive ICF Core Set¹⁵, and severity of the disease could not be assessed in a standardized manner. Indeed, several rounds of expert discussions within ASAS revealed that it was virtually impossible to agree on a definition of severe disease, because the intensity and duration of reversible changes such as pain and associated symptoms such as fatigue, and irreversible changes such as radiographic progression, seemed to be incompatible. Therefore, ASAS decided to develop the ASAS Health Index (ASAS HI) to allow assessment and comparison of the severity of axSpA by assessing the overall global functioning and health including impairments, limitations, and restrictions in activities of daily living and social participation of patients with axSpA on the group level. The ASAS HI⁸ is the first disease-specific instru-

ment to be developed that is based on the ICF concept. The whole process including validation followed a rigorous methodology that turned out to be a major effort lasting several years because of its international approach (countries representing 5 continents included more than 3300 patients) and its broad engagement of different patient populations. One result of patients' input was the integration of new items into ASAS HI that had never been part of any SpA instrument available to date. The 4 items address "pain during normal activities," "exhausting," "sexual functions," and "operating pedals in the car." The main calculation for the ASAS HI was based on the Rasch analysis technique to permit a unidimensional scale that can provide a sum score representing all different levels of functioning¹⁶.

The ASAS HI consists of a 17-question self-questionnaire with a binary agree/do not agree and a score range from 0 to 17, with 0 indicating the best state of health. The 17 questions of this self-report questionnaire cover different ICF domains (pain, emotion, sleep, sexual function, mobility, self-care, social life). ASAS has published favorable psychometric properties of the ASAS HI for internal consistency, construct validity, discriminant ability, and sensitivity to change as well as data-driven thresholds to discriminate different health states of patients with axSpA¹⁷. Construct validity was shown for disease activity and physical functioning as well as emotional and social functioning. Finally, it is a simple tool, easily understood by patients, and is not time-consuming.

In this issue of *The Journal*, Alonso-Castro, *et al*¹⁸ tested the performance of the ASAS HI in daily practice in a monocentric cross-sectional study with > 100 patients with axSpA who had peripheral involvement (16%), were smokers (39%), and/or were obese (16%); the prevalence of fibromyalgia was rather low (2.7%). A strength of this study is that the prevalences of extraarticular manifestations and comorbidities are explicitly

presented. On the other hand, almost no data about the severity of the disease state and no data on emotional factors or social participation are provided to characterize this cohort with relatively low disease activity [mean (SD): BASDAI 3.4 (2.3)], good physical function [BASFI 2.95 (2.32)], and health [ASAS HI 5.4 (3.8)]. The authors confirm a good correlation between the ASAS HI and the established indices for disease activity and physical function, and they report thresholds for interpreting different health states quite similar to those of the original publication of the ASAS HI as well as to those of other cohorts. However, neither the sample size nor the methods used to calculate such thresholds are comparable^{17,19}. Some ASAS HI items were associated with high disease activity in the study, namely “feelings of frustration” and “sleep disorders” — both determinants of impaired HRQOL in axSpA²⁰. The study also confirms data on the construct validity of the ASAS HI^{17,21}. However, the relatively small sample size resulting in too few patients in subpopulations and the lack of assessments outside the domain of physical functioning in this cohort make generalization difficult. The finding and confirmation of a correlation between the ASAS HI and disease activity as well as functional measures was expected; nevertheless, it is always important to show that clinical trial data also hold true in a real-life setting.

However, the ASAS HI has recently also been used as an important outcome measure in a clinical trial, the TICOSPA study presented at the European League Against Rheumatism 2020 meeting²². Indeed, in this first T2T trial in axSpA, a 30% improvement of ASAS HI was used as primary endpoint, which was reached by 47.3% of patients treated on the predefined T2T basis versus 6.1% in the control arm (usual care). The mean ASDAS-CRP at baseline had been 3.0 ± 0.7 and the mean ASAS HI, 8.6 ± 3.7 . One of the reasons to use the ASAS HI as primary endpoint was to avoid circular reasoning (using the same items for inclusion and outcome).

The original intention behind developing the ASAS HI was to define severity, to be able to measure global functioning and health on a group level in patients with axSpA. The ICF has proposed the term *functioning and health* to refer to health impairments and limitations as a consequence of disease. In this respect, the term *overall/global functioning and health* is used in parallel to *HRQOL*. Different HRQOL instruments are used in clinical trials, but many instruments lack a theoretical framework and do not represent the perspective of different people involved. The ASAS HI, in contrast, uses the theoretical framework of the ICF, and patients have played an important role in its development. Therefore, the ASAS HI has recently been used in clinical trials for recording global functioning and health²³. Transferring this assumption to real life requires that next to the ASAS HI itself, the full range of possible impairments of global functioning, health, and social participation in a cohort should be reported. The article by Alonso-Castro, *et al* limits the report solely to variables of disease activity and physical functioning. Structural damage, another relevant factor not assessed in the

study, has been studied in the Catholic axSpA Cohort, where it was shown that structural impairment (high mSASSS scores), heavy use of nonsteroidal antiinflammatory drugs, alcohol consumption, and socioeconomic factors are predictive of high ASAS HI scores¹⁸.

Alonso, *et al* argue that the ASAS HI could be used in routine care to assess disease activity. We disagree with this idea that BASDAI and ASDAS can be substituted by the ASAS HI because these tools — also combinations of different items — clearly measure something different and it was never planned to use the ASAS HI for that purpose. Instead, it gathers the whole range of functioning, disability, and health represented by the Comprehensive ICF Core Set for AS. The items of the ASAS HI cover a large variety of items representing different domains: pain, maintaining a body position, moving around, toileting, washing oneself, energy and drive, motivation, sexual functions, driving, community life, handling stress, recreation and leisure, emotional functions, economic self-sufficiency, and sleep — many factors other than disease activity. This list illustrates the multidimensional structure of the ASAS HI with many items that could also be influenced by completely different domains from disease activity but which may be very relevant for the patient.

Clearly, disease activity and physical function are important aspects of global health, but are only part of it. Thus, measurement of an association between disease activity and global health ignores the influence of structural damage on global functioning, a practice that may lead to erroneous interpretations of the study results. Further, the unidimensional construct of the ASAS HI makes it difficult to analyze associations between items of the ASAS HI. Therefore, it is questionable whether the reported association between ASAS HI items and high disease activity has any effect on the evaluation of a disease state.

The correlation with metrologic and radiographic scores, or the effect of extraarticular manifestations (uveitis, psoriasis, inflammatory bowel disease) and/or other comorbidities, and the level of education, or manual work and physical activity, are of major interest — leaving us with a long research agenda. Further, prospective longitudinal data to confirm the sensitivity to change of the ASAS HI and its predictive value on longterm outcome are needed. Such studies could test the usefulness of the ASAS HI as a tool for supporting therapeutic decisions and for assessing the response to therapy. Especially, longitudinal data of the ASAS HI in different cohorts would be very helpful to better understand the longterm variability of global functioning and health in different populations as well as responsiveness of global functioning and health in different therapeutic scenarios.

Once more information on these issues is provided, the ASAS HI could be used as a tool for assessment and monitoring by patients and rheumatologists in daily care. Its simplicity could enable self-monitoring and integration into a more general approach to health care, and be a step forward in the management of patients with axSpA.

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