Determinants of health-related quality of life and global functioning and health in axSpA, pSpA, and PsA: results from the ASAS-PerSpA study

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Abstract

Objectives

We aim to identify determinants of health-related quality of life (HRQoL) and global functioning and health (GH) in axial spondyloarthritis (axSpA), peripheral spondyloarthritis (pSpA), and psoriatic arthritis (PsA).

Methods

ASAS-perSpA study data were analyzed. Models for the three patient groups were performed separately to explore factors associated with HRQoL and GH, assessed by EQ-5D and ASAS-HI, respectively.

Results

The analyses included 4185 patients: 2719 with axSpA, 433 with pSpA, and 1033 with PsA.

In axSpA, disease activity (DA) (β=-0.061), physical function (β=-0.041), female sex (β=-0.019), and fibromyalgia (β=-0.068) were associated with worse HRQoL; age (β=0.001) and university education (β=0.014) with better HRQoL. In pSpA, DA (β=-0.04) and physical function (β=-0.054) were associated with worse HRQoL. In PsA, DA (β=-0.045), physical function (β=-0.053), axial disease (β=-0.041), and female sex (β=-0.028) were associated with worse HRQoL.

In axSpA, DA (β=0.889), physical function (β=0.887), peripheral disease (β=0.564), female sex (β=0.812) and fibromyalgia (β=1.639) were associated with worse GH; age (β=-0.013) and university education (β=-0.274) with better GH. In pSpA, physical function (β=1.142), and female sex (β=1.060) were associated with worse GH; university education (β=-0.611) with better GH. In PsA, DA (β=0.703), physical function (β=1.025), axial involvement (β=0.659), female sex (β=0.924), and fibromyalgia (β=1.387) were associated with worse GH; age (β=-0.024) and university education (β=-0.856) with better GH.

Conclusions

DA and physical function are major HRQoL and GH determinants across spondyloarthritis types, and clinical characteristics and sociodemographic factors play an important role, highlighting the importance of a holistic approach for individual patients.

Key words

determinants; quality-of-life; EQ-5D; global-health; ASAS-HI**;** spondyloarthritis; psoriatic arthritis; outcomes; PerSpA; burden

Rheumatology key messages

- Disease activity and physical function are major determinants of HRQoL and GH in spondyloarthritis.
- Clinical characteristics and sociodemographic factors have an important influence on HRQoL and GH in spondyloarthritis.
- Identifying factors associated with HRQoL and GH may promote personalized treatment strategies.

Introduction

Spondyloarthritis is a group of phenotypically related but distinct disorders that can affect the axial skeleton (spine and sacroiliac joints), enthesis, and peripheral joints and may occur with extra-musculoskeletal manifestations, such as uveitis, psoriasis, and inflammatory bowel disease [1]. According to the Assessment of SpondyloArthritis International Society (ASAS) classification criteria, the cardinal manifestation of axial spondyloarthritis (axSpA) is back pain [2], and the cardinal manifestations of peripheral spondyloarthritis (pSpA) are arthritis, enthesitis, and dactylitis [3].

It is unclear whether the axial and peripheral forms of the disease require different approaches. Although the concept of axSpA and pSpA is generally accepted, only a minority of epidemiological and clinical studies address pSpA as a separate disease entity. However, the heterogeneity of clinical manifestations in pSpA (arthritis, enthesitis, dactylitis, skin and nail psoriasis, uveitis, and inflammatory bowel disease) [4], the existence of separate classification criteria for psoriatic arthritis (PsA) (e.g., CASPAR classification criteria), and the relatively high prevalence of peripheral manifestations in axSpA [4] contribute to increased difficulty in understanding the features distinguishing axSpA, pSpA, and PsA.

In the three spondyloarthritis phenotypes, the regular evaluation of the level of disease activity (considering signs, symptoms and inflammatory markers) and physical function (patient's ability to perform activities of daily living and engage in social, work, and recreational activities) is current practice. In addition to assessing the direct consequences of the disease, it is becoming increasingly important to assess the overall impact on individual well-being using validated scores, namely, to assess health-related quality of life (HRQoL) and global functioning and health and (GH).

HRQoL is a subjective and multidimensional concept that can be defined as an individual's experience with their general health status, including physical, social, and mental well-being [5]. AxSpA and pSpA are potentially disabling conditions, as the resulting inflammation and structural damage lead to pain and stiffness that can impair several domains of HRQoL[6–8]. Moreover, the disease course of PsA is highly variable, with some patients experiencing mild symptoms while others develop severe and debilitating disease[9]. Both musculoskeletal (with pain, stiffness and swelling) and skin manifestations can have a substantial impact on HRQoL[10], leading to significant impairment in its physical, emotional, and social domains[11]. More recently, the ASAS Health Index (ASAS-HI) [12] has been developed as a measure of GH in patients with spondyloarthritis to define and compare the impact of the disease and its health effects in this patient group. It was developed based on the biopsychosocial model of disease, aiming to comprehensively encompass the entire spectrum of functioning, disability, and health

among these patients. This approach provides a more precise representation of the disease impact. On the contrary, HRQoL assessment gives a more general patient's perspective[13].

As axSpA, pSpA, and PsA may affect physical, social, and mental dimensions differently, the assessment and comparison of factors associated with HRQoL and GH in these three entities can help identify unrecognized needs and promote personalized treatment strategies. Therefore, it is clinically relevant to understand whether HRQoL and GH determinants differ in axSpA, pSpA, and PsA.

Patients and Methods

Population

This study used data from the ASAS Peripheral Involvement in SpondyloArthritis (perSpA) cohort, a multinational observational cross-sectional study involving 24 participating countries worldwide. The study recruited patients from July 2018 to February 2020.

Consecutive patients considered to have axSpA, pSpA, or PsA by their treating rheumatologist (determined with the question "In your opinion which is the disease that better describes your patient?") and who were able to complete the questionnaires were enrolled.

The study was approved by the ethical committees of all participating centers, and written informed consent was obtained from all subjects.

Outcomes

The main outcomes of this study were HRQoL and GH assessed by the three-level version of the EuroQoL five dimensions (EQ5D) and ASAS-HI, respectively. Validated versions of these tools in the native language of each participating country were used.

The EQ5D is a self-reported questionnaire comprising a descriptive health component and a visual analog scale (VAS). The descriptive component evaluates five dimensions describing different aspects of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and extreme problems (labeled 1–3, respectively). Scores from the three items can be used to derive a single utility score. The descriptive system is converted into a summary index score ranging from −1 (states worse than death, with 0 equivalent to death) to 1 (full health). The EuroQoL VAS (EQ VAS) is a 20-centimeter vertical scale of 0–100 points, where scores of 0 and 100 correspond to the "worst imaginable health state" and the "best imaginable health state," respectively[14].

The ASAS-HI questionnaire comprises 17 dichotomous items, evaluating functioning, disability and health in spondyloarthritis patients. ASAS-HI is a self-reported questionnaire addressing pain, emotional function, sleep, sexual function, mobility, self-care, and social participation. The

score is linear, ranging from 0 to 17, with higher scores reflecting greater impairment. The ASAS-HI questionnaire has been validated for the entire spectrum of spondyloarthritis (radiographic axSpA, non-radiographic axSpA, and pSpA), including PsA[12].

Independent variables

For the three groups of participants, we collected data regarding:

- Sociodemographic characteristics: age, sex, region (Latin America, Europe, and North America, Asia, Middle East, and North Africa), marital status, and education level;
- Lifestyle habits: alcohol intake and smoking (the term "ever" alcohol was used to defined alcohol consumption as either a current or previous history of daily intake; similarly, "ever" smoking was defined as a current or previous history of smoking habits);
- Anthropometric data: body mass index (BMI);
- Clinical characteristics: age at symptom onset, diagnostic delay, the presence of sacroiliitis on pelvic x-ray (defined as at least grade II bilateral or grade III unilateral), sacroiliitis on magnetic resonance imaging (ASAS definition), HLA-B27 status, history of uveitis confirmed by an ophthalmologist, history of inflammatory bowel disease (IBD) confirmed by endoscopy, history of psoriasis confirmed by a dermatologist, c-reactive protein (CRP) levels, the patient's global assessment (PGA), and the number of tender (Ritchie articular index) and swollen (66 Joint Count) joints. Axial and peripheral joint involvement was defined according to rheumatologist opinion: axial involvement (determined with the question "Do you consider that this patient has ever suffered from axial involvement of SpA?") for patients with pSpA and PsA, peripheral involvement for patients with axSpA (determined with the question "Do you consider that this patient has ever suffered from peripheral joint disease?"). Disease activity in axSpA was assessed by the Ankylosing Spondylitis Disease Activity Score–c-reactive protein (ASDAS-CRP) and in pSpA and PsA by the 44-joint Disease Activity Score-CPR (DAS44-CRP). Physical function was assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) in all groups. Regarding therapy, we investigated current therapy with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), biologic disease-modifying anti-rheumatic drugs (bDMARDs), targeted synthetic disease-modifying anti-rheumatic drugs (tsDMARDs), and glucocorticoids. Non-steroidal anti-inflammatory drugs (NSAIDs) use was calculated using the NSAIDs intake score (NSAIDs-IS). Finally, data on the presence of fibromyalgia, as indicated by the rheumatologist's opinion, were collected.

Statistical analysis

Patients were stratified into three groups according to their diagnosis (axSpA, pSpA, and PsA). A descriptive analysis of sociodemographic characteristics, lifestyle factors, anthropometric data, and clinical characteristics was conducted for each group using frequencies/proportions for categorical variables and mean/standard deviation for continuous variables.

Univariable and multivariable linear regression models were used to investigate the factors associated with HRQoL and GH in participants with axSpA, pSpA, and PsA. Univariable analyses were performed first, and variables with a *p*-value <0.2 were assessed using the multivariable model. Age was forced into the models for participants with PsA and pSpA. As the BASDAI, ASDAS, and DAS44-CRP are disease activity indices, we selected the ASDAS-CRP for participants with axSpA and DAS44-CRP for participants with PsA and pSpA to avoid collinearity. For the same reason (collinearity), PGA was not considered in the models.

Dependent variables were the EQ5D score for HRQoL and the ASAS-HI score for GH. As sacroiliitis on MRI and HLA-B27-positive variables exhibited a high percentage of missing data, multiple imputations were performed for these variables using the *mice* package. Estimates for these associations are shown as standardized beta coefficients (standardized β). The significance level was set at 0.05. The descriptive analysis was performed using STATA V16.1, and the remaining analyses was performed using RStudio software V.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki, and approval was granted by the Ethics Committee of NOVA Medical School (nº123/2020/CEFCM).

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Results

A total of 4185 participants were eligible for the study analyses — 2719 with axSpA, 433 with pSpA, and 1033 with PsA.

Sociodemographic, lifestyle, and anthropometric data characteristics

The mean age (SD) of axSpA patients was 42.0 (13.0) years; that of pSpA patients was 44.2 (14.4) years, and that of PsA patients was 51.8 (13.0) years. The proportion of female axSpA, pSpA, and PsA patients was 31.7%, 53.1%, and 51.5%, respectively (Table 1).

The proportion of axSpA, pSpA, and PsA patients with a university-level education was 43.4%, 45.5%, and 51.8%, respectively; 63.8%, 61.7%, and 72.6% of the axSpA, pSpA, and PsA patients were married, respectively. The diagnosis distribution according to regions is shown in Table 1. Regarding lifestyle habits, smoking (past or present) was reported by 43.6% of axSpA, 29.6% of pSpA, and 47.9% of PsA participants, and alcohol ingestion (past or present) by 40.1%, 41.4%, and 43.7%. The mean (SD) BMI of AxSpA patients was 25.9 (5.1) Kg/m2, that of pSpA patients was 26.3 (5.4) Kg/m2, and that of PsA patients was 28.0 (5.9) Kg/m2.

Clinical characteristics, quality of life, and global health and functioning

The mean disease duration was highest in PsA patients (16.6 (11.9) years), followed by axSpA (14.4 (11.1) years) and pSpA (10.1 (9.5) years) patients. The same trend was observed regarding the diagnostic delay (9.1 (11.1) years in PsA patients, 5.8 (7.7) in axSpA patients, and 4.3 (6.6) in pSpA patients). Seventy-five percent of axSpA patients had radiographic sacroiliitis, which was present in 20.5% of pSpA patients and 33.7% of PsA patients. Positivity for HLA-B27 was observed in 78.8% of axSpA patients, 62.3% of pSpA patients, and 18.1% of PsA patients. As expected, axSpA patients had more axial than peripheral joint involvement (97.5% *vs.* 36.0%, respectively), and the opposite was observed in pSpA and PsA (55.0% *vs.* 94.7% and 35.5% *vs.* 90.8%, respectively). Fibromyalgia, determined according to the rheumatologist's opinion, was present in 7.8% of axSpA patients, 11.1% of pSpA patients, and 11.6% of PsA patients. The mean BASFI, CRP, and PGA values were similar across the three groups (Table 1). Disease activity in axSpA patients was evaluated using the ASDAS-CRP, with a mean value of 2.6 (1.1); DAS44-CRP was used for pSpA and PsA patients, with a mean value of 1.8 (0.9) in both. BASDAI values were also collected for the three groups (mean BASDAI 3.7 (2.4), 4.0 (2.4), 4.3 (2.5), in the axSpA, pSpA, and PsA groups, respectively). Current therapies and NSAIDs-IS are summarized in Table 1.

The HRQoL and GH results stratified by diagnosis and evaluated by the EQ-5D and ASAS-HI, respectively, are summarized in Table 2.

Determinants of HRQoL in axSpA, pSpA, and PsA

In the multivariable analysis, higher disease activity (β=-0.061; p-value<0.001), worse physical function (β=-0.041; p-value<0.001), female sex (β=-0.019; p-value=0.007), and fibromyalgia (β=-0.068; p-value<0.001) were associated with worse HRQoL in axSpA patients; older age (β=0.001; p-value=0.035), university education (β=0.014; p-value=0.037), and positivity for HLA-B27 (β=0.023; p-value=0.021) was associated with better HRQoL.

In pSpA patients, higher disease activity (β=-0.04; p-value<0.001), worse physical function (β=-0.054; p-value<0.001) and higher NSAIDs-IS scores (β=-0.009; p-value<0.001) were associated with worse HRQoL; older age (β=0.002; p-value=0.048) was associated with better HRQoL.

Regarding PsA, worse HRQoL higher disease activity (β=-0.045; p-value<0.001), worse physical function (β=-0.053; p-value<0.001), female sex (β=-0.028; p-value=0.017), axial involvement (β=-0.041; p-value=0.003), and glucocorticoid therapy (β=-0.030; p-value=0.035) were associated with worse HRQoL; biologic therapy (β=0.025; p-value=0.021) was associated with better HRQoL (Table 3).

Our models explain over 50% of the HRQoL across spondyloarthritis subtypes (53.6% in axSpA, 52.0% in pSpA, and 55.1% in PsA) (Table 3).

Determinants of GH in axSpA, pSpA, and PsA

In axSpA patients, higher disease activity (β=0.889; p-value<0.001), worse physical function (β=0.887; p-value<0.001), female sex (β=0.703; p-value<0.001), fibromyalgia (β=1.639; p-value<0.001), and peripheral disease (β=0.564; p-value<0.001) were associated with worse GH; older age (β=-0.013; p-value=0.041), university education (β=-0.274; p-value=0.031), higher BMI (β=-0.039; p-value=0.002), and higher NSAIDs-IS scores (β=-0.034; p-value=0.006) were associated with better GH.

In pSpA patients, worse physical function (β=1.142; p-value<0.001), female sex (β=1.060; p-value<0.001), inflammatory bowel disease (β=1.707; p-value=0.025), treatment with csDMARDs (β=0.956; p-value=0.002), and higher NSAIDs-IS scores (β=0.083; p-value=0.028) were associated with worse GH; a university education (β=-0.611; p-value=0.044) was associated with better GH.

Regarding PsA patients, female sex (β=0.924; p-value<0.001), alcohol intake (β=0.465; p-value=0.035), fibromyalgia (β=1.387; p-value<0.001), axial involvement (β=0.659; p-value<0.001), higher disease activity (β=0.703; p-value<0.001) and worse physical function (β=1.025; p-value<0.001) were associated with worse GH; older age (β=-0.024; p-value=0.003) and a university education (β=-0.856; p-value<0.001) were associated with better GH (Table 4).

Our models explain over 50% of the GH across spondyloarthritis subtypes (52.9% in axSpA, 54.5% in pSpA, and 56.0% in PsA) (Table 4).

Discussion

In this study, we analyzed the determinants of HRQoL and GH in axSpA, pSpA, and PsA.

Except for GH in pSpA, both outcomes were primarily determined by disease activity and physical function across the three phenotypes of spondyloarthritis.

When we examine the connection between disease activity and HRQoL in spondyloarthritis, it becomes evident that the severity of symptoms directly influences various aspects of a patient's daily functioning and overall health. High disease activity, characterized by high levels of inflammation and pain, exert a profound impact, leading to physical limitations, reduced mobility, and hindered the execution of routine tasks. Moreover, compromised joint functionality introduce challenges in professional endeavors, social interactions, and participation in recreational activities, thereby influencing HRQoL.

Central to the pathogenesis of spondyloarthritis, pivotal cytokines play a crucial role in driving disease activity, exhibiting a robust correlation with symptom severity and joint damage. As such, interventions targeting these inflammatory pathways have demonstrated significant improvements in both disease activity and HRQoL[15,16].

This underscores a direct link between biological mechanisms and the overall state of well-being, reinforcing the profound influence of underlying physiological processes on patients' HRQoL.

Determinants of HRQoL

As mentioned, disease activity was significantly related to worse HRQoL, consistent with previous studies of patients with axSpA [6,17–19] and PsA [20]. In a prospective study, van Lunteren et al. [17] reported that in patients with axSpA, an increase in disease activity (evaluated by ASDAS) was associated with a decline in physical HRQoL over time but not mental HRQoL. Moreover, in a *post hoc* analysis of the EMBARK study, a decrease in disease activity was associated with improved HRQoL [21]. Few data exist regarding the association between disease activity and HRQoL in pSpA patients [22–24]. Mease et al. [22] showed that a decrease in disease activity after adalimumab treatment was associated with an improvement in HRQoL in patients with non-psoriatic peripheral spondyloarthritis. Navarini et al.[23] recently studied a group of PsA patients and found an inverse relationship between disease activity and HRQoL domains.

Our study showed that a worse physical function also negatively influences HRQoL. In line with our results, physical functioning has been shown to be associated with physical and mental HRQoL by other authors [18,25,26]. Moreover, in the model proposed by Dean et al. [27] in Ankylosing Spondylitis patients, physical function was most strongly associated with poor HRQoL. Carvalho et al. [28] recently obtained similar results in a cohort of peripheral and axial spondyloarthritis patients; physical function was found to be the main contributor to HRQoL in both phenotypes. Patients with PsA also experience a substantial burden of physical impairment

resulting from joint involvement and other disease manifestations, including enthesitis, dactylitis, axial disease, and psoriasis [9,29]. Previous studies corroborate our results, showing that physical impairment negatively affects HRQoL in PsA patients [20,30].

Beyond disease activity and physical function, it is also important to analyze the effect of sociodemographic factors, clinical characteristics and therapeutics on HRQoL.

We found older age to be associated with better HRQoL in axSpA and pSpA. With aging, the accumulation of comorbidities is natural during the course of the disease[31], increasing significantly the burden of disease and reducing quality of life[32]. However, although aging can lead to cognitive and physical declines, research also suggests that well-being may not necessarily decrease in older individuals when compared to younger individuals[33]. One possible explanation cold be that older individuals may develop better coping mechanisms and resilience to deal with health challenges. Moreover, as people age, their priorities and expectations might shift, leading to a different perspective on what constitutes good HRQoL. Additionally, it is possible that older patients had successfully managed their chronic health condition, leading to a higher perceived HRQoL despite the presence of certain limitations.

It is known that the disease phenotype and burden may differ between men and women in spondyloarthritis [34]. In our cohort, female sex was associated with worse HRQoL in axSpA and PsA. Several studies have shown that women are more likely to report worse HRQoL [35,36]; however, others did not confirm this finding [37,38].

Among clinical characteristics, the association between the presence of HLA-B27 and better HRQoL in axSpA patients is intriguing. One possible explanation for this finding could be that patients who are HLA-B27 positive often receive and earlier diagnosis, leading to timely treatment interventions and, subsequently, an improvement in HRQoL. However, it´s essential to note that our study is purely observational and does not establish causation. There may be confounding factors or interactions between variables that were not accounted for in the analysis, which could influence the observed relationship.

The influence of peripheral involvement on HRQoL in axSpA has rarely been addressed. A recent longitudinal study including patients from the DESIR cohort revealed that peripheral joint pain is associated with worse well-being in early axSpA [39]; however, in our cohort this association was only significant in the univariable analysis. In PsA, axial involvement remains poorly understood and is still debated. In our cohort, axial involvement was associated with a poorer HRQoL, in line with previous data from the Corrona PsA/SpA Registry [40]. Wervers et al. [41] also found that back pain was independently associated with worse HRQoL in a cohort of early PsA regardless of whether the patients' back pain fulfilled the ASAS inflammatory back pain criteria. These results suggest that HRQoL is influence by the overall patient's impairments and

burden of the disease, rather than being solely determined by the specific spondyloarthritis phenotype.

Fibromyalgia is a frequent comorbid condition in spondyloarthritis, and its identification is challenging due to the possibility of misdiagnosis, especially in non-radiographic axSpA and PsA with predominant enthesitis manifestations. Fibromyalgia concomitant with rheumatic conditions, namely spondyloarthritis, has been associated with worse outcomes by several authors [42]. In our cohort, the diagnosis of fibromyalgia was associated with a worse HRQoL in axSpA patients. Macfarlane et al.[6] also identified fibromyalgia diagnosis as an independent predictor for worse HRQoL in axSpA patients. In our study, no association was observed between fibromyalgia and HRQoL in pSpA patients. To the best of our knowledge, no previous studies have investigated the relationship between pSpA and fibromyalgia. While fibromyalgia has been linked to lower HRQoL in patients with PsA [43], we did not observe a statistically significant association in our cohort.

Determinants of GH in axSpA, pSpA, and PsA

In the three spondyloarthritis phenotypes, as for HRQoL, disease characteristics such as disease activity (except in pSpA) and physical function were also determinants of worse GH. In addition, peripheral involvement in axSpA and axial involvement in PsA appeared to be relevant determinants for GH.

We found a direct relationship between the ASAS-HI score and higher disease activity. Previous studies also found this relationship in axSpa and pSpA patients [44,45]. Morante et al. [46] evaluated the clinimetric properties of the ASAS-HI in PsA patients and found an association between ASAS-HI and disease activity according to the DAPSA categories. We did not find this association in pSpA patients, which was surprising. A potential explanation might be related to the methodology used to evaluate disease activity, a composite score for peripheral disease (DAS44-CRP). As pSpA is a heterogeneous disease, this score may not fully capture disease activity across the disease spectrum; for example, entheseal and axial involvement. Thus, we speculate whether we are using instruments that fully capture disease activity in pSpA since very few studies have been conducted in comparison with the number of axSpA and PsA studies.

Physical function is one of the most important outcomes in rheumatic and musculoskeletal diseases. The negative impact of spondyloarthritis on physical function is well-known [47,48]; thus, it was unsurprising that a worse physical function was associated with a worse GH in all spondyloarthritis phenotypes. Other studies also found this association in the radiographic and non-radiographic subtypes of axSpA [44]. Puche-Larrubia et al. [49] found the same result in a

mixed cohort of patients with axial and peripheral forms of spondyloarthritis; however, no studies addressing factors associated with GH specifically in pSpA and PsA have been conducted. In our study, female sex predicted a worse GH across the three groups. Chen et al. [50] specifically addressed this issue in ankylosing spondylitis patients and found that higher ASAS-HI scores were significantly associated with female sex ; however, no data are available for pSpA and PsA.

Fibromyalgia, characterized by widespread chronic pain, fatigue, sleep disturbances and impaired cognition [42], was found to be associated with worse GH in axSpA and PsA patients. Similarly, Puche-Larrubia et al. [49] showed that spondyloarthritis patients with fibromyalgia have significantly worse GH than those without.

Another relevant finding was the association of a better GH with a university education across the three groups. Min et al. [44] previously found no association between ASAS-HI scores and education level; however, they observed an association with economic status.

In summary, in our study, GH was determined by both disease characteristics and sociodemographic factors, while sociodemographic characteristics appeared to affect HRQoL to a lesser extent. EQ5D captured the impact of disease activity, axial mobility, and physical function in HRQoL; however, contextual, social, and disease-specific aspects (like fatigue or sexuality) exist that are not captured by this questionnaire or other more disease-specific quality-of-life questionnaires but are captured by the ASAS-HI. This fact could explain our findings regarding sociodemographic factors in association with GH that were not observed in HRQoL and support the notion that GH is not fully explained by the disease itself and is also affected by sociodemographic factors that should be considered for a global patient approach.

Health-related quality of life and global functioning and health comparison across disease phenotypes

While HRQoL and GH diverge in their conceptualization, our study unveils comparable associations among certain determinants across the three disease phenotypes. Notably, disease activity and physical function consistently correlated with both inferior HRQoL and poorer GH across all spondyloarthritis phenotypes. Similarly, female sex consistently links to reduced HRQoL and diminished GH within all three groups. Moreover, peripheral disease in axSpA and axial disease in PsA emerge as factors contributing to worsened HRQoL and GH, underscoring the pivotal role of disease manifestations in influencing these outcomes. Furthermore, older age consistently showed associations with improved HRQoL and GH, while university education was linked to enhanced GH across all disease phenotypes. Notably, the association of university education primarily with GH suggests that education may primarily affect individuals'

perceptions on their general health and daily functioning. In contrast, HRQoL encompasses a subjective assessment of a patient's well-being, potentially influenced by various factors beyond educational attainment.

In conclusion, despite the conceptual disparities between HRQoL and GH, our findings highlight a striking similarity in the factors influencing these outcomes across the three phenotypes. However, the notable discrepancy lies in the impact of university education, predominantly influencing patient's overall perception of functioning and health, with a less consistent influence on HRQoL.

Strengths and limitations

This study has several strengths and limitations. The strengths include the large sample size analyzed, including patients from 24 participating countries, reflecting daily clinical practice using multiple validated outcomes and disease activity assessments commonly employed in clinical studies and recommended or endorsed by ASAS. In addition, the use of DAS44-CRP (a more extensive joint count) to evaluate activity in peripheral involvement represents a strength. Finally, this is the first study to evaluate the determinants of HRQoL and GH in the three phenotypes of spondyloarthritis.

The main limitation is the cross-sectional study design, which prevents drawing conclusions regarding a causal effect relationship. Additionally, the sample size was small in some countries, and the possibility of a selection bias must be considered. Also, other variables that can impact our outcomes, such as the presence of other comorbidities, were not analyzed. Finally, the diagnosis of axSpA, pSpA and PsA hinged upon the evaluation conducted by the treating rheumatologist. While this approach mirrors real-world clinical practice, we acknowledge that it could introduce some level of subjectivity and potential bias, stemming from its dependence on the rheumatologist's individual experience.

Conclusions

Considering that the primary goal of treating patients with spondyloarthritis is to maximize long-term HRQoL and GH and that patients with spondyloarthritis have been reported to lose most of their physical function within the first 10 years after disease onset, tight control of disease activity might provide substantial HRQoL and GH benefits.

Understanding the determinant factors of HRQoL and GH in different phenotypes of spondyloarthritis and whether these determinants differ between spondyloarthritis phenotypes can help rheumatologists improve personalized care. These outcomes are important for medical

decision-making and predicting treatment success; thus, the outcomes can be critical for planning therapeutic and other interventions focused on the needs of each patient.

Data Availability

Data is owned by a third party. The data underlying this article were provided by Assessment of Spondyloarthritis international Society (ASAS) by permission. Data will be shared on request to the corresponding author with permission of the ASAS-PerSpA steering committee.

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Table 1 – Sociodemographic, lifestyle, anthropometric data, and clinical characteristics stratified by diagnosis

	axSpA n=2719	**pSpA n=433**	**PsA n=1033**
Female sex, n (%)	861 (31.7%)	230 (53.1%)	532 (51.5%)
Age years (mean ± sd)	42.0 ± 13	44.2 ± 14.4	51.8 ± 13
University education	1178 (43.4%)	197 (45.5%)	320 (31.0%)
Married (yes)	1735 (63.8%)	267 (61.7%)	748 (72.6%)
Region			
Latin America	276 (10.2%)	35 (8.1%)	176 (17.0%)
Europe and North America	1012 (37.2%)	102 (23.5%)	489 (47.3%)
Asia	610 (22.4%)	138 (31.9%)	165 (16.0%)
Middle East and North Africa	821 (30.2%)	158 (36.6%)	203 (19.7%)
BMI kg/m² (mean ± sd)	25.9 ± 5.1	26.3 ± 5.4	28.0± 5.9
Ever smoker	1185 (43.6%)	128 (29.6%)	494 (47.9%)
Ever alcohol	1089 (40.1%)	179 (41.4%)	451 (43.7%)
Disease duration, years (mean ± sd)	14.4 ± 11.1	10.1 ± 9.5	16.8 ± 11.9
Age at first symptoms, years (mean ± sd)	27.8 ± 10.7	34.2 ± 14.7	35.2 ± 14.9
Diagnostic delay, years (mean ± sd)	5.8 ± 7.7	4.3 ± 6.6	9.1 ± 11.1
Sacroiliitis on X-ray	2042 (75.1%)	146 (33.7%)	212 (20.5%)
HLA-B27 positive	1709 (78.8%)	197 (62.3%)	86 (18.1)
Uveitis	588 (21.6%)	75 (17.3%)	27 (2.6%)
Psoriasis*	154 (5.7%)	53 (12.2%)	894 (86.5%)
Inflammatory bowel disease**	127 (4.7%)	19 (4.4%)	5 (0.5%)
Axial disease (according to the rheumatologist)	2651 (97.5%)	238 (55.0%)	367 (35.5%)
Peripheral joint disease (according to the rheumatologist)	978 (36.0%)	410 (94.7%)	938 (90.8%)
Fibromyalgia			
FiRST	427 (17.2%)	69 (17.6%)	245 (24.9%)
Rheumatologist's opinion	212 (7.8%)	48 (11.1%)	120 (11.6%)
Number swollen joints (mean ± sd)	0.3 ± 2.0	1.2 ± 2.9	1.9 ± 4.8
Number tender joints (mean ± sd)	1.5 ± 4.4	3.3 ± 6.2	4.8 ± 8.7
Number dactylitis (mean ± sd)	1.7 ± 3.4	2.4 ± 4.1	2.2 ± 4.3
CRP mg/L (mean ± sd)	12.0 ± 32.0	13.9 ± 23.4	12.6 ± 45.2
Patient's Global Assessment (mean ± sd)	4.3 ± 2.7	4.5 ± 2.7	4.6 ± 2.7
BASDAI (mean ± sd)	3.7 ± 2.4	4.0 ± 2.4	4.3 ± 2.5
ASDAS-CRP (mean ± sd)	2.6 ± 1.1	-	-
DAS44-CRP (mean ± sd)	-	1.78±0.86	1.81±0.92
BASFI (mean ± sd)	3.0 ± 2.6	2.8 ± 2.6	3.1 ± 2.8
Current csDMARD	629 (23.1%)	230 (53.1%)	616 (59.6%)
Current bDMARD	1281 (47.1 %)	148 (34.2 %)	471 (45.6%)
Current tsDMARD	16 (0.6%)	10 (2.3 %)	51 (4.9 %)
Current Corticosteroids			
n (%)	172 (6.4%)	89 (20.5%)	192 (18.7%)
Dose (mg/daily), (mean ± sd)	8.8 ± 9.6	6.3 ± 4.9	6.5 ± 3.8
NSAIDs intake score (mean ± sd)	5.9 ± 0.1	6.1 ± 3.8	4.7 ± 4.0

*confirmed by a dermatologist; **confirmed by endoscopy

axSpA – axial spondyloarthritis; pSpA - peripheral spondyloarthritis; PsA – psoriatic arthritis; BMI - Body Mass Index; CRP – C-Reactive Protein; FiRST – Fibromyalgia Rapid Screening Tool; BASDAI – Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP - Ankylosing Spondylitis Disease Activity Score-CRP; DAS44-CRP - Disease Activity Score 44-CPR; BASFI – Bath Ankylosing Spondylitis Disease Functional Index, csDMARDs - conventional synthetic Disease-Modifying Anti-Rheumatic Drug, bDMARDs – biologic Disease-Modifying Anti-Rheumatic Drug; tsDMARDs – target synthetic Disease-Modifying Anti-Rheumatic Drug; NSAIDs - non-steroidal anti-inflammatory drugs

Table 2– Quality of life (EQ5D) and global health and functioning (ASAS-HI) stratified by diagnosis

	axSpA n=2719	pSpA n=433	PsA n=1033
EQ5D			
Mobility			
No problems	1504 (55.4%)	204 (47.1%)	506 (49.0%)
Some problems	1172 (43.2%)	214 (49.4%)	505 (48.9%)
Extreme problems	37 (1.4%)	15 (3.5%)	21 (2.0%)
Self-care			
No problems	2031 (74.9%)	309 (71.5%)	763 (74.1%)
Some problems	644 (23.7%)	117 (27.1%)	252 (24.5%)
Extreme problems	38 (1.4%)	6 (1.4%)	15 (1.5%)
Usual activities			
No problems	1333 (49.2%)	179 (41.4%)	458 (44.5%)
Some problems	1301 (48.0%)	230 (53.2%)	539 (52.4%)
Extreme problems	77 (2.8%)	23 (5.3%)	32 (3.1%)
Pain/discomfort			
No pain or discomfort	623 (23.0%)	74 (17.1%)	208 (20.2%)
Moderate pain or discomfort	1786 (65.9%)	308 (71.1%)	662 (64.2%)
Extreme pain or discomfort	303 (11.2%)	51 (11.8%)	161 (15.6%)
Anxiety/depression			
Not anxious or depressed	1550 (57.15%)	226 (52.19%)	509 (49.32%)
Moderately anxious or depressed	1008 (37.2%)	181 (41.8%)	425 (41.2%)
Extremely anxious or depression	154 (5.7%)	26 (6.0%)	98 (9.5%)
EQ5D score (mean ± sd)	0.67 ± 0.23	0.63 ± 0.23	0.63 ± 0.25
ASAS HI (mean ± sd)	6.3 ± 4.5	6.6 ± 4.4	7.2 ± 4.7

axSpA – axial spondyloarthritis; pSpA - peripheral spondyloarthritis; PsA – psoriatic arthritis; EQ5D – Euro quality of life 5 dimensions; ASAS-HI - Assessment of Spondyloarthritis International Society Health Index

Table 3 – Determinants of HRQoL (EQ5D) stratified by diagnosis (multivariable regression analysis)

	axSpA n=2697				pSpA n=418				PsA n=1016			
	β	CI 95%	Std. error	p-value	β	CI 95%	Std. error	p-value	β	CI 95%	Std. Error	p-value
Female Sex	-0.019	[-0.033; -0.005]	0.007	**0.007**	-0.025	[-0.059; 0.009]	0.017	0.146	-0.028	[-0.051; -0.005]	0.012	**0.017**
Age	0.001	[0.00001; 0.001]	0.0003	**0.035**	0.002	[0.00002; 0.004]	0.001	**0.048**	0.001	[-0.00002; 0.002]	0.0004	0.076
Education level (University)	0.014	[0.001; 0.026]	0.007	**0.037**					-0.002	[-0.025; 0.022]	0.012	0.875
BMI	0.001	[-0.001; 0.002]	0.001	0.224	0.003	[-0.001; 0.006]	0.002	0.116	-0.001	[-0.003; 0.001]	0.001	0.207
Ever smoker	-0.010	[-0.023; 0.003]	0.007	0.137								
Ever alcohol	-0.012	[-0.025; 0.002]	0.007	0.090					-0.003	[-0.026; 0.020]	0.012	0.796
Fibromyalgia (rheumatologist's opinion)	-0.068	[-0.092; -0.043]	0.013	**<0.001**	-0.020	[-0.074; 0.034]	0.028	0.473	-0.035	[-0.069; -0.0003]	0.018	0.052
Age of 1st symptoms (years)	0.0001	[-0.001; 0.001]	0.0004	0.840	-0.001	[-0.003; 0.001]	0.001	0.180				
Sacroiliitis on MRI	-0.004	[-0.02; 0.015]	0.009	0.602					0.016	[-0.020; 0.053]	0.018	0.362
HLA-B27 positive	0.023	[004; 0.042]	0.009	**0.021**	0.028	[-0.020; 0.075]	0.023	0.237				
Uveitis	0.015	[-0.001; 0.031]	0.008	0.051					-0.007	[-0.072; 0.058]	0.033	0.832
Psoriasis*	-0.004	[-0.030; 0.023]	0.014	0.795								
Inflammatory bowel disease**									-0.072	[-0.221; 0.076]	0.076	0.341
Axial disease					-0.003	[-0.038; 0.032]	0.018	0.867	-0.041	[-0.068; -0.014]	0.013	**0.003**
Peripheral joint disease	-0.013	[-0.027; 0.005]	0.007	0.059								
BASFI	-0.041	[-0.044; -0.037]	0.002	**<0.001**	-0.054	[-0.061; -0.047]	0.004	**<0.001**	-0.053	[-0.058; -0.049]	0.002	**<0.001**
ASDAS-CRP	-0.061	[-0.069; -0.054]	0.004	**<0.001**								
DAS44-CRP					-0.04	[-0.064; -0.022]	0.011	**<0.001**	-0.045	[-0.058; -0.031]	0.007	**<0.001**
Current csDMARD	0.016	[0.0004; 0.032]	0.008	**0.044**	0.005	[-0.032; 0.041]	0.019	0.796				
Current bDMARD	-0.003	[-0.015; 0.010]	0.007	0.690	-0.003	[-0.040; 0.035]	0.019	0.896	0.025	[0.004; 0.047]	0.011	**0.021**
Current Corticosteroids	-0.008	[-0.034; 0.018]	0.013	0.541	-0.0003	[-0.041; 0.040]	0.021	0.988	-0.030	[-0.058; -0.002]	0.014	**0.035**
NSAIDs intake score	-0.00002	[-0.001; 0.001]	0.001	0.976	-0.009	[-0.013; -0.005]	0.002	**<0.001**	0.001	[-0.002; 0.003]	0.001	0.659
Model fit		R^2=0.536				R^2=0.520				R^2=0.551		

*confirmed by a dermatologist; **confirmed by endoscopy

Bold text highlights significant values.

β - regression coefficient; CI 95% - confidence interval 95%; Std error – standard error; R^2 – Multiple R-squared.

axSpA – axial spondyloarthritis; pSpA - peripheral spondyloarthritis; PsA – psoriatic arthritis; EQ5D – Euro quality of life 5 dimensions; BMI - Body mass index; MRI - Magnetic resonance imaging; BASFI - Bath Ankylosing Spondylitis Disease Functional Index; ASDAS-CRP - Ankylosing Spondylitis Disease Activity Score C-Reactive Protein; DAS44-CRP – Disease Activity Score 44 C-Reactive Protein; csDMARDs - conventional synthetic Disease-Modifying Anti-Rheumatic Drug, bDMARDs – biologic Disease-Modifying Anti-Rheumatic Drug; NSAIDs - non-steroidal anti-inflammatory drugs.

Table 4 – Determinants of general health (ASAS-HI) stratified by diagnosis (multivariable regression analysis)

	axSpA n=2697				pSpA n=418				PsA n=1016			
	β	CI 95%	Std. error	p-value	β	CI 95%	Std. error	p-value	β	CI 95%	Std. Error	p-value
Female Sex	0.812	[0.549; 1.084]	0.139	**<0.001**	1.060	[0.427; 1.693]	0.322	**0.001**	0.924	[0.487; 1.361]	0.223	**<0.001**
Age	-0.013	[-0.025; -0.001]	0.006	**0.041**	-0.012	[-0.048; 0.023]	0.018	0.496	-0.024	[-0.040; -0.008]	0.008	**0.003**
Education level (University)	-0.274	[-0.523; -0.025]	0.127	**0.031**	-0.611	[-1.207; -0.016]	0.303	**0.044**	-0.856	[-1.296; -0.415]	0.224	**<0.001**
BMI	-0.039	[-0.063; -0.014]	0.012	**0.002**	0.203	[-0.447; 0.854]	0.331	0.539	-0.018	[-0.052; 0.017]	0.018	0.309
Ever smoker	0.155	[-0.104; 0.414]	0.132	0.241								
Ever alcohol	0.068	[-0.192; 0.329]	0.133	0.608					0.465	[0.032; 0.897]	0.220	**0.035**
Fibromyalgia	1.639	[1.175; 2.102]	0.237	**<0.001**	0.207	[-0.816; 1.129]	0.520	0.692	1.387	[0.736; 2.039]	0.332	**<0.001**
Age of 1st symptoms (years)	-0.003	[-0.017; 0.011]	0.007	0.345	-0.006	[-0.040; 0.028]	0.017	0.737				
Sacroiliitis on MRI	-0.163	[-0.502; 0.176]	0.172	0.338					-0.062	[-0.643; 0.519]	0.289	0.831
HLA-B27 positive	-0.156	[-0.478; 0.165]	0.163	0.345	-0.256	[-1.069; 0.557]	0.399	0.526				
Uveitis									-0.759	[-1.986; 0.468]	0.625	0.225
Psoriasis*									-0.357	[-0.935; 0.221]	0.295	0.226
Inflammatory bowel disease**					1.707	[0.220; 3.194]	0.756	**0.025**	-0.635	[-3.436; 2.166]	1.427	0.657
Axial disease									0.659	[0.192; 1.125]	0.237	**0.006**
Peripheral joint disease	0.564	[0.297; 0.831]	0.136	**<0.001**								
BASFI	0.887	[0.820; 0.953]	0.034	**<0.001**	1.142	[1.012; 1.273]	0.066	**<0.001**	1.025	[0.937; 1.112]	0.045	**<0.001**
ASDAS-CRP	0.889	[0.738; 1.040]	0.077	**<0.001**								
DAS44-CRP					0.188	[-0.206; 0.582]	0.200	0.349	0.703	[0.454; 0.953]	0.127	**<0.001**
Current csDMARD	0.076	[-0.228; 0.380]	0.155	0.624	0.956	[0.339; 1.574]	0.314	**0.002**				
Current bDMARD	-0.047	[-0.296; 0.201]	0.127	0.708								
Current Corticosteroids	-0.181	[-0.693; 0.331]	0.261	0.487	-0.097	[-0.861; 0.667]	0.389	0.803	0.063	[-0.460; 0.586]	0.267	0.814
NSAIDs intake score	-0.034	[-0.057; -0.010]	0.012	**0.006**	0.083	[0.009; 0.157]	0.038	**0.028**	0.011	[-0.041; 0.062]	0.026	0.685
Model fit		R^2=0.529				R^2=0.545				R^2=0.560		

*confirmed by a dermatologist; **confirmed by endoscopy

Bold text highlights significant values.

β - regression coefficient; CI 95% - confidence interval 95%; Std error – standard error; R^2 – Multiple R-squared.

axSpA – axial spondyloarthritis; pSpA - peripheral spondyloarthritis; PsA – psoriatic arthritis; ASAS-HI - Assessment of SpondylAarthritis International Society health index; BMI - Body mass index; MRI - Magnetic resonance imaging; BASFI - Bath Ankylosing Spondylitis Disease Functional Index; ASDAS-CRP - Ankylosing Spondylitis Disease Activity Score C-Reactive Protein; DAS44 CRP – Disease Activity Score 44 C-Reactive Protein; csDMARDs - conventional synthetic Disease-Modifying Anti-Rheumatic Drug, bDMARDs – biologic Disease-Modifying Anti-Rheumatic Drug; NSAIDs - non-steroidal anti-inflammatory drugs