RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Comparison of the ASAS Health Index in patients classified as radiographic axial spondyloarthritis (axSpA) or non-radiographic axSpA in the ASAS Health Index international validation study

Warren Fong ,[1,2] Ting Hui Woon,[1] Yu Heng Kwan,[1,3] Jürgen Braun ,[4] Désirée van der Heijde ,[5] Annelies Boonen ,[6] Uta Kiltz [4,7]

To cite: Fong W, Woon TH, Kwan YH, *et al*. Comparison of the ASAS Health Index in patients classified as radiographic axial spondyloarthritis (axSpA) or non-radiographic axSpA in the ASAS Health Index international validation study. *RMD Open* 2024;**10**:e003794. doi:10.1136/rmdopen-2023-003794

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/rmdopen-2023-003794).

Received 6 October 2023
Accepted 21 December 2023

For numbered affiliations see end of article.

Correspondence to
Dr Warren Fong;
gmsfwsw@nus.edu.sg

ABSTRACT

Objectives To determine if there were differences in the Assessment of SpondyloArthritis international Society Health Index (ASAS HI) scores between patients classified as radiographic axial spondyloarthritis (r-axSpA) and non-radiographic axSpA (nr-axSpA), and to identify factors associated with higher ASAS HI scores in both disease phenotypes.

Methods This study was an ancillary analysis of the ASAS HI international validation project performed in 23 countries. Patients were included if they were ≥18 years of age and diagnosed with axSpA. Univariable and multivariable analysis were performed to determine if ASAS HI scores differed between the axSpA phenotypes, and to identify other variables associated with ASAS HI scores. We also tested for potential interactions between the axSpA phenotype and significant variables identified through the multivariable regression.

Results A total of 976 patients were included, with 703 having r-axSpA and 273 nr-axSpA. Patients with r-axSpA reported higher (worse) ASAS HI scores compared with those with nr-axSpA (6.8 (4.4) vs 6.0 (4.0), p=0.02), but the axSpA phenotype was not associated with ASAS HI scores in the multivariable regression (β: −0.19, 95% CI: −0.56 to 0.19). Female gender, having worse physical function (Bath Ankylosing Spondylitis Functional Index), disease activity (Ankylosing Spondylitis Disease Activity Score) and anxiety and depressive symptoms (Hospital Anxiety and Depression Scale) were associated with higher ASAS HI scores. No interactions were found to be significant.

Conclusion Overall health and functioning are similarly affected in patients with r-axSpA and nr-axSpA. Female patients, having worse physical function, disease activity, anxiety and depressive symptoms were independently associated with higher ASAS HI scores.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Prior studies reported conflicting results regarding the differences in Assessment of SpondyloArthritis international Society Health Index (ASAS HI) scores between radiographic axial spondyloarthritis (r-axSpA) and non-radiographic axSpA (nr-axSpA).

WHAT THIS STUDY ADDS

⇒ Using data from an international study, we observed that patients with r-axSpA and nr-axSpA had similar overall health and functioning.

⇒ Gender (being female), having worse physical function, disease activity, anxiety and depressive symptoms were independently associated with higher ASAS HI scores in all patients.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study highlights that the overall health and function are similarly affected in both patients with r-axSpA and nr-axSpA.

⇒ Modifiable factors such as physical function, disease activity, anxiety and depressive symptoms could be optimised in the care of patients with axSpA to improve overall health and function.

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic disease, which is typically characterised by inflammation in the sacroiliac joints and causes symptoms such as low back pain and stiffness.[1 2] If untreated, it can lead to new bone formation in the axial skeleton and entheses, and fusion of the spine.[3] Patient-reported outcome measures (PROMs) are self-reported outcomes that assess patients' perceptions of their health and are used in the clinical management of patients with axSpA.[4] However, most available PROMs focus on specific aspects of the disease such as fatigue, pain, stiffness or functional limitation.[5 6] In order to have a more comprehensive and disease-specific questionnaire that

could best reflect the patients' overall state of health, the Assessment of SpondyloArthritis international Society (ASAS) Health Index (ASAS HI) was developed to assess 'overall health and functioning' in axSpA.[7 8] The concept of 'overall health and functioning' has been included in the 2021 update of the ASAS-Outcomes Measures in Rheumatology core domain set, with the ASAS HI as the self-reported measurement instrument.[5 9]

There are two subtypes of axSpA: radiographic axSpA (r-axSpA), where radiographic damage is present in the sacroiliac joints, and non-radiographic axSpA (nr-axSpA), where inflammation in the sacroiliac joints may be present on MRI but radiographic damage is not detected.[10 11] There has been debate about whether a differential disease impact exists between r-axSpA and nr-axSpA. A systematic review showed that patients with r-axSpA and nr-axSpA had similar levels of functional limitations, disease activity and health-related quality of life, despite patients with r-axSpA having higher levels of C reactive protein (CRP) and more structural damage in the sacroiliac joints.[12] In contrast, the COAST-V and COAST-X studies which recruited patients with r-axSpA and nr-axSpA, respectively, who had active disease and were naïve to biological disease-modifying antirheumatic drugs (bDMARDs) showed that patients with nr-axSpA had slightly higher mean (SD) ASAS HI scores at baseline ((9.1 (3.6) vs 8.1 (3.6)).[13 14] However, these were two separate studies, which makes the comparison challenging. A study performed in USA, however, reported similar mean ASAS HI scores in both disease subtypes.[15] Factors associated with poorer overall health and functioning were also inconsistent, with different studies showing that higher disease activities, functional limitation, radiographic progression, intake of non-steroidal anti-inflammatory drugs (NSAIDs) and being of female gender were associated with reduced overall health and functioning.[15–18]

To our knowledge, there has been no multisite study across different countries, which included both patients with r-axSpA and nr-axSpA. Therefore, we aimed to determine if there were differences in ASAS HI scores between patients with r-axSpA and nr-axSpA, and factors associated with ASAS HI scores in both subtypes of axSpA.

METHODS

Study design

This study was an ancillary analysis of the ASAS HI international validation study which was performed in 23 countries from 2014 to 2015.[19] A representative sample of patients diagnosed with spondyloarthritis (SpA) by a rheumatologist and also fulfilled the 2009 ASAS classification criteria for axSpA or peripheral SpA were included in the original study.[11 20 21] Patients with severe concomitant disease and who were cognitively unable to understand the questionnaires were excluded. Informed consent was obtained prior to participation. In this ancillary analysis, only patients diagnosed with axSpA were included. The proportion of patients with r-axSpA and nr-axSpA was estimated to be around 60% and 40%, respectively, for each site.

Data collection

Demographics collected included: age, gender, educational status, marital status and employment status. Clinical variables collected included: disease, symptom duration, human leucocyte antigen-B27 (HLA-B27) status, presence of musculoskeletal and extramusculoskeletal features as assessed by the treating rheumatologist, levels of CRP, medication use and comorbidities.

Overall health and functioning were measured using the ASAS HI,[8] which has been validated in various countries in patients with axSpA.[19 22 23] The ASAS HI consists of 17 questions. Each question is scored 1 if participants agree with the statement and 0 if they disagree. Participants were allowed to select 'not applicable' for two specific questions and scores would not be awarded. A maximum of three missing item scores were allowed. To obtain the total ASAS HI score, the item summation score (obtained by summing the scores of all items) should be divided by the total number of non-missing items and multiplied by 17. Participants with scores of ≤5 were considered to have good health and functioning, while participants with scores between 6 and 11 had moderate health and functioning, and participants with scores ≥12 were classified as having poor health and functioning.

The Bath Ankylosing Spondylitis (AS) Disease Activity Index (BASDAI) and Bath AS Functional Index (BASFI) were collected to assess self-reported disease activity and physical function, respectively.[24] The BASDAI has six items that assess for factors such as fatigue, pain in the spine and peripheral joints, intensity and duration of morning stiffness and areas of localised tenderness. Each item is scored from 0 to 10 and higher scores indicate greater levels of symptoms.[25] The BASFI has 10 questions that assess disease-related impairments in physical function, with scores ranging from 0 to 10 and higher scores indicating worse physical function.[26–28] Additionally, the Ankylosing Spondylitis Disease Activity Score assessment (ASDAS) was calculated based on the severity of back pain, severity of peripheral pain and swelling and duration of morning stiffness obtained through BASDAI, as well as patient global scores and CRP levels.[29] ASDAS scores <1.3 are considered as having an inactive disease, scores ≥1.3 and <2.1 as low disease activity, scores ≥2.1 and ≤3.5 as high disease activity and scores >3.5 as very high disease activity.[30]

The Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety and depression in a general population of patients with medical problems, is widely used in the primary care and hospital and has been validated in many languages and countries. The HADS is a 14-item self-reported questionnaire consisting of 2 subscales, HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D), which assess for possible/probable anxiety and depression in non-psychiatric patients, respectively.[31 32] Items were scored from 0 to 3, with

higher scores indicating a more severe problem for each item. Scores are interpreted as having mild (≥8 and ≤10), moderate (≥11 and ≤14) or severe (≥15 and ≤21) levels of anxiety or depression.[33]

The 36-item Short Form Survey (SF-36) is a self-administered questionnaire that is used to measure health status of adults and allows for objective measurement of quality of life. The questionnaire consists of 36 individual questions covering 8 subscales in the areas of physical functioning, role limitation due to physical problem, bodily pain, general health, vitality, social functioning, role limitation due to emotional problem and mental health. The SF-36 Physical Component Summary and SF-36 Mental Component Summary were obtained by norm-based scoring of the eight subscales and were used to assess for physical and mental health status, respectively.[34]

Statistical analysis

Continuous variables were reported in means and SD while categorical variables were expressed as frequencies and percentages. Univariable and multivariable linear regression analyses were used to identify factors associated with ASAS HI scores. ASAS HI scores were selected as the dependent variables. Independent variables were selected from the sociodemographics, clinical variables and patient-reported outcomes. We selected disease-specific PROMs instead of generic PROM to be included in the regression for similar constructs. The variance inflation factor (VIF) was used to assess for multicollinearity, with a value of 5 as the threshold.[35] Variables with a p≤0.1 from the univariable analysis were included into the multivariable analysis. To identify potential interactions between the axSpA phenotype and significant variables (gender, BASFI, ASDAS, HADS-A and HADS-D) identified through the multivariable analysis, interaction terms were tested, where effect modification was considered significant if the p value of the interaction term was <0.05. Data analyses were conducted by using Stata SE V.15 (StataCorp).

RESULTS

Patient demographics and characteristics

Patient demographics and characteristics are shown in table 1. A total of 976 patients with a diagnosis of axSpA were included in the study, of which, 703 (72.0%) were classified as r-axSpA and 273 (28.0%) as nr-axSpA. Mean (SD) age was 41.3 (13.4) years and patients with r-axSpA were older than patients with nr-axSpA (43.4 (13.6) years vs 36.0 (11.5) years, p<0.01). Six hundred and sixty-five (68.1%) were males and the proportion of males in r-axSpA was higher as compared with nr-axSpA (73.5% vs 54.2%, p<0.01). Similarly, the proportion of patients positive for HLA-B27 was also higher in r-axSpA than nr-axSpA, respectively (83.2% vs 72.6%, p<0.01). Mean (SD) disease and symptom duration among all patients were 8.5 (9.2) years and 15.2 (11.6) years, respectively. Patients with r-axSpA had a significantly longer disease (10.1 (9.9) years vs 4.3 (5.3) years, p<0.01) and symptom duration (17.5 (11.8) years vs 9.4 (8.9) years, p<0.01) compared with patients with nr-axSpA.

The most common musculoskeletal and extramusculoskeletal symptoms (current or past) were enthesitis (n=495, 50.7%) and uveitis (n=268, 27.5%), respectively. Six hundred and eighteen (63.3%) patients were currently on NSAIDs, 205 (21.0%) on conventional synthetic DMARDs and 361 (37.0%) on bDMARDs.

PROMs and clinical assessments

In table 2, mean (SD) ASAS HI score was 6.6 (4.3), and patients with r-axSpA reported poorer scores compared with patients with nr-axSpA (6.8 (4.4) vs 6.0 (4.0), p=0.02). A higher proportion of patients with r-axSpA had poor ASAS HI scores compared with patients with nr-axSpA (16.6% vs 9.9%). ASAS HI scores did not differ between regions (online supplemental file 1). Scores of HADS-A and HADS-D did not differ between both subtypes. One hundred and eighty-four (18.9%) patients were scored as having mild anxiety and 174 (17.8%) patients as moderate to severe anxiety, while 162 (16.6%) had mild depressive symptoms and 137 (14.0%) had moderate to severe depressive symptoms.

Mean (SD) BASFI score was 3.3 (2.8) and higher in patients with r-axSpA than those with nr-axSpA (3.5 (2.9) vs 2.7 (2.6), p<0.01). Mean (SD) BASDAI score for all patients was 4.1 (2.5) and did not differ between both groups (p=0.46). Although patients with r-axSpA had higher CRP levels than nr-axSpA (11.2 (17.5) vs 6.8 (12.0), p<0.01), mean (SD) ASDAS was 2.5 (1.2) and did not differ between groups (p=0.11). When classified based on ASDAS, over half of the patients (n=570, 58.4%) had high and very high disease activity, while 192 (19.7%) had inactive disease (table 2).

Factors associated with poorer ASAS HI scores

The axSpA phenotype, age, gender, current or past dactylitis or enthesitis, BASFI, ASDAS, HADS-A and HADS-D scores had a p<0.10 in the univariable regression. In the multivariable regression, the axSpA phenotype was not associated with ASAS HI scores (β: −0.19, 95% CI: −0.56 to 0.19). Females were associated with having higher ASAS HI scores (β: 0.67, 95% CI: 0.32 to 1.03). Performing worse on physical function and having higher disease activity as shown by the BASFI (β: 0.59, 95% CI: 0.50 to 0.67) and ASDAS (β: 0.54, 95% CI: 0.35 to 0.72) scores, respectively, were associated with higher ASAS HI scores. Higher HADS-A (β: 0.14, 95% CI: 0.09 to 0.20) and HADS-D scores (β: 0.30, 95% CI: 0.24 to 0.35) which reflected greater anxiety and depression were also positively associated with ASAS HI scores (table 3). Multicollinearity was not noted as VIF was less than 5 for variables in the multivariable linear regression. No interactions between the axSpA phenotype and variables were found to be significant (online supplemental file 2).

Table 1 Patient demographics and characteristics

Characteristics	All (N=976)	r-axSpA (n=703, 72.0%)	nr-axSpA (n=273, 28.0%)	P value*
Age, year, mean (SD)	41.3 (13.4)	43.4 (13.6)	36.0 (11.5)	<0.01
Male sex, n (%)	665 (68.1)	517 (73.5)	148 (54.2)	<0.01
Education				<0.01
Primary school and below, n (%)	94 (9.6)	80 (11.4)	14 (5.1)	
Secondary school, n (%)	439 (45.0)	324 (46.1)	115 (42.1)	
University and above, n (%)	443 (45.4)	299 (42.5)	144 (52.7)	
Marital status				0.11
Single, n (%)	314 (32.2)	211 (30.0)	103 (37.7)	
Married, n (%)	592 (60.7)	437 (62.2)	155 (56.8)	
Divorced, n (%)	53 (5.4)	42 (6.0)	11 (4.0)	
Widow, n (%)	17 (1.7)	13 (1.8)	4 (1.5)	
Employment status				
Employed, n (%)	612 (62.7)	433 (61.6)	179 (65.6)	0.25
Unemployed, n (%)	62 (6.4)	49 (7.0)	13 (4.8)	0.20
Disabled, n (%)	80 (8.2)	70 (10.0)	10 (3.7)	<0.01
Homemaker, n (%)	65 (6.7)	39 (5.5)	26 (9.5)	0.03
Disease duration, year, mean (SD)	8.5 (9.2)	10.1 (9.9)	4.3 (5.3)	<0.01
Symptom duration, year, mean (SD)	15.2 (11.6)	17.5 (11.8)	9.4 (8.9)	<0.01
HLA-B27 positive†, n (%)	647 (79.9)	464 (83.2)	183 (72.6)	<0.01
SpA-related conditions				
Arthritis, current or past, n (%)	472 (48.4)	337 (47.9)	135 (49.5)	0.67
Dactylitis, current or past, n (%)	129 (13.2)	82 (11.7)	47 (17.2)	0.02
Enthesitis, current or past, n (%)	495 (50.7)	352 (50.1)	143 (52.4)	0.52
Uveitis, current or past, n (%)	268 (27.5)	210 (29.9)	58 (21.2)	0.01
Psoriasis, current or past, n (%)	77 (7.9)	53 (7.5)	24 (8.8)	0.52
IBD, current or past, n (%)	78 (8.0)	56 (8.0)	22 (8.1)	0.96
Current use of NSAIDs, n (%)	618 (63.3)	422 (60.0)	196 (71.8)	<0.01
Current use of csDMARDs, n (%)	205 (21.0)	159 (22.6)	46 (16.8)	0.05
Current use of bDMARDs, n (%)	361 (37.0)	291 (41.4)	70 (25.6)	<0.01
Comorbidities				
Heart disease, n (%)	60 (6.1)	45 (6.4)	15 (5.5)	0.60
Hypertension, n (%)	195 (20.0)	158 (22.5)	37 (13.6)	<0.01
Lung disease, n (%)	42 (4.3)	30 (4.3)	12 (4.4)	0.93
Diabetes, n (%)	40 (4.1)	33 (4.7)	7 (2.6)	0.13
Ulcer or stomach disease, n (%)	127 (13.0)	88 (12.5)	39 (14.3)	0.46
Kidney disease, n (%)	38 (3.9)	27 (3.8)	11 (4.0)	0.89
Liver disease, n (%)	31 (3.2)	23 (3.3)	8 (2.9)	0.79
Cancer, n (%)	5 (0.5)	5 (0.7)	0 (0)	0.33
Osteoporosis, n (%)	73 (7.5)	59 (8.4)	14 (5.1)	0.08
Fracture, n (%)	43 (4.4)	31 (4.4)	12 (4.4)	0.99

*Comparison between r-axSpA and nr-axSpA.
†HLA-B27 status was 'unknown' for 166 patients in total, of which 145 were patients with r-axSpA and 21 were patients with nr-axSpA.
bDMARDs, biological disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic DMARDs; HLA-B27, human leucocyte antigen B27; IBD, inflammatory bowel disease; nr-axSpA, non-radiographic axial spondyloarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; r-axSpA, radiographic axSpA; SpA, spondyloarthritis.

DISCUSSION

This study aimed to determine if there were differences in ASAS HI scores between patients with r-axSpA and nr-axSpA, as well as to investigate factors associated the scores between both subtypes of axSpA. To the best of our knowledge, this is the first multisite study conducted across different countries to explore this aim.

In our study, the level of overall health and functioning did not differ between patients with r-axSpA and nr-axSpA. This complements the study by Akgul *et al*,

Table 2 Patient-reported outcomes and disease activities

	All (N=976)	r-axSpA (n=703, 72.0%)	nr-axSpA (n=273, 28.0%)	P value*
Spinal pain NRS, mean (SD)	3.9 (3.1)	3.9 (3.0)	4.0 (3.1)	0.74
Physician global, mean (SD)	3.6 (2.4)	3.6 (2.4)	3.8 (2.3)	0.05
Patient global, mean (SD)	4.4 (2.8)	4.4 (2.8)	4.5 (2.8)	0.46
BASDAI, mean (SD)	4.1 (2.5)	4.0 (2.5)	4.2 (2.6)	0.46
BASDAI disease activity level†				0.34
Low, n (%)	510 (52.3)	374 (53.2)	136 (49.8)	
High, n (%)	466 (47.7)	329 (46.8)	137 (50.2)	
BASFI, mean (SD)	3.3 (2.8)	3.5 (2.9)	2.7 (2.6)	<0.01
CRP, mean (SD)	10.0 (16.3)	11.2 (17.5)	6.8 (12.0)	<0.01
ASDAS, mean (SD)	2.5 (1.2)	2.6 (1.3)	2.4 (1.2)	0.11
ASDAS disease activity level‡				0.59
Inactive, n (%)	192 (19.7)	133 (18.9)	59 (21.6)	
Low, n (%)	214 (21.9)	150 (21.3)	64 (23.4)	
High, n (%)	352 (36.1)	259 (36.8)	93 (34.1)	
Very high, n (%)	218 (22.3)	161 (22.9)	57 (20.9)	
ASAS HI, mean (SD)	6.6 (4.3)	6.8 (4.4)	6.0 (4.0)	0.02
Level of overall health and functioning§				0.02
Good, n (%)	419 (42.9)	289 (41.1)	130 (47.6)	
Moderate, n (%)	413 (42.3)	297 (42.2)	116 (42.5)	
Poor, n (%)	144 (14.8)	117 (16.6)	27 (9.9)	
HADS-A, mean (SD)	6.6 (4.3)	6.7 (4.3)	6.5 (4.1)	0.71
Level of anxiety¶				0.40
Normal, n (%)	618 (63.3)	439 (62.4)	179 (65.6)	
Mild anxiety, n (%)	184 (18.9)	140 (19.9)	44 (16.1)	
Moderate to severe anxiety, n (%)	174 (17.8)	124 (17.6)	50 (18.3)	
HADS-D, mean (SD)	5.6 (4.2)	5.8 (4.3)	5.1 (4.0)	0.05
Level of depression¶				0.06
Normal, n (%)	677 (69.4)	473 (67.3)	204 (74.7)	
Mild depression, n (%)	162 (16.6)	122 (17.4)	40 (14.7)	
Moderate to severe depression, n (%)	137 (14.0)	108 (15.4)	29 (10.6)	
SF36 PCS, mean (SD)	39.4 (10.6)	39.1 (10.5)	40.2 (10.8)	0.19
SF36 MCS, mean (SD)	47.2 (11.2)	47.1 (11.5)	47.6 (10.6)	0.79
SF36 item scales				
Physical functioning, mean (SD)	66.5 (26.6)	65.0 (26.9)	70.3 (25.6)	<0.01
Role limitations due to physical health, mean (SD)	51.7 (43.6)	51.3 (43.5)	52.9 (44.0)	0.80
Role limitations due to emotional problems, mean (SD)	64.9 (42.8)	63.9 (43.0)	67.5 (42.1)	0.26
Energy/fatigue, mean (SD)	52.7 (22.6)	52.5 (23.2)	53.2 (21.0)	0.58
Emotional well-being, mean (SD)	66.8 (20.3)	66.4 (21.0)	67.7 (18.3)	0.65
Social functioning, mean (SD)	70.8 (25.5)	70.2 (25.6)	72.1 (25.2)	0.27
Pain, mean (SD)	55.6 (25.3)	55.4 (25.6)	56.2 (24.6)	0.64
General health, mean (SD)	47.9 (20.5)	47.3 (20.7)	49.3 (19.9)	0.15

*Comparison between r-axSpA and nr-axSpA.
†BASDAI scores of <4 was considered as having low disease activity and scores ≥4 as high disease activity.
‡ASDAS scores of <1.3 was considered as having inactive disease, scores ≥1.3 and <2.1 as low disease activity, scores ≥2.1 and ≤3.5 as high disease activity and scores >3.5 as very high disease activity.
§ASAS HI scores of ≤5 was considered as good health and functioning, scores >5 and <12 as moderate health and functioning, and scores ≥12 as poor health and functioning.
¶For each subscale in HADS, scores ≥8 and ≤10 indicated borderline anxiety or depression, while scores ≥11 indicated moderate or severe levels of depression or anxiety.
ASAS HI, Assessment of SpondyloArthritis international Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score assessment ; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C reactive protein; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, HADS-Depression; nr-axSpA, non-radiographic axial spondyloarthritis; NRS, Numerical Rating Scale; PCS, Physical Component Summary; r-axSpA, radiographic axSpA; SF36 MCS, 36-item Short Form survey Mental Component Summary.

Table 3 Univariable and multivariable linear regression to identify factors associated with ASAS HI

	Total axSpA (n=976)					
	Univariable			Multivariable*		
	β	95% CI	P value	β	95% CI	P value
axSpA phenotype						
r-axSpA	Ref			Ref		
nr-axSpA	−0.75	−1.35 to to 0.15	0.01	−0.19	−0.56 to 0.19	0.33
Age	0.03	0.01 to 0.05	<0.01	−0.01	−0.02 to 0.00	0.08
Female gender	1.18	0.61 to 1.75	<0.01	0.67	0.32 to 1.03	<0.01
Disease duration	0.00	−0.03 to 0.03	0.83			
Current or past arthritis	0.23	−0.31 to 0.77	0.40			
Current or past dactylitis	1.32	0.52 to 2.11	<0.01	0.15	−0.34 to 0.64	0.54
Current or past enthesitis	0.93	0.39 to 1.46	<0.01	−0.10	−0.43 to 0.23	0.54
Current or past uveitis	−0.17	−0.78 to 0.43	0.57			
Current or past psoriasis	0.04	−0.96 to 1.04	0.93			
Current or past IBD	−0.46	−1.45 to 0.54	0.37			
BASFI	1.06	0.99 to 1.13	<0.01	0.59	0.50 to 0.67	<0.01
ASDAS	2.14	1.97 to 2.31	<0.01	0.54	0.35 to 0.72	<0.01
HADS-A	0.60	0.54 to 0.65	<0.01	0.14	0.09 to 0.20	<0.01
HADS-D	0.68	0.64 to 0.73	<0.01	0.30	0.24 to 0.35	<0.01

*VIF for the multivariable regression was 1.59.
ASAS HI, Assessment of SpondyloArthritis international Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score assessment with CRP; axSpA, axial spondyloarthritis; BASFI, Bath Ankylosing Spondylitis Functional Index; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, HADS-Depression; nr-axSpA, non-radiographic axSpA; r-axSpA, radiographic axSpA; VIF, variance inflation factor.

which also found that the mean (SD) ASAS HI score did not differ between patients with r-axSpA and nr-axSpA (6.1 (4.3) vs 6.4 (4.9), p=0.721).[17] In two systematic reviews, patients with r-axSpA and nr-axSpA also had similar disease burden and health-related quality of life, though objective markers of inflammation such as CRP and spinal inflammation on MRI were higher in r-axSpA.[12 36] A study by Hunter *et al* conducted in the USA also reported similar mean ASAS HI scores for r-axSpA and nr-axSpA after adjusting for confounding variables (5.7 vs 5.3, p=0.295).[15] However, Min *et al* found that patients with r-axSpA in Korea had higher ASAS HI scores than those with nr-axSpA (3.8 (3.5) vs 2.7 (2.8), p=0.003).[18] A possible reason for this difference might be that patients with r-axSpA were taking more NSAIDs compared with nr-axSpA in the study by Min *et al*,[18] with high NSAID intake being associated with worse ASAS HI scores, but this was the reverse in our study.

Next, we found that females had poorer ASAS HI scores than males, which was similar to other studies.[17 37 38] A possible reason for this might be that females have been known to have larger impairments in physical function, fatigue, sleep and sexual activity compared with males,[38–40] and these categories are represented in the ASAS HI.[8]

As expected, having greater functional limitation, disease activity and higher levels of anxiety and depression (as reflected by the BASFI, ASDAS and HADS, respectively) were associated with ASAS HI in all patients. These aspects were explicit parts of the ASAS HI and our analyses confirm the relative importance of these to the overall score of the ASAS HI. Prior studies have also shown physical function and disease activity to be correlated to ASAS HI scores.[18 19 41] Having more anxiety and depressive symptoms based on the HADS were also associated with increased disease activity scores[42 43] and also poorer health and functioning.[19 41 44] Having possible anxiety and depression at treatment initiation was also associated with poorer treatment outcomes,[45 46] and this could also affect overall health and function.

There are limitations of our study, which should be mentioned. First, the cross-sectional design prevents assessment of a causal relationship. Classification of r-axSpA and nr-axSpA was based on the judgement of local readers of the radiograph in local centres and central reading of the images to confirm radiographic damage in the sacroiliac joints was not performed. Confounding factors such as smoking and the presence of fibromyalgia were not collected as part of the study.

CONCLUSION

In summary, our study demonstrated that the overall health and functioning are similarly affected in patients

with r-axSpA and nr-axSpA. Gender (being female), having more anxiety and depressive symptoms, greater functional limitation and disease activity were associated with higher ASAS HI scores in all patients.

Author affiliations
[1]Department of Rheumatology and Immunology, Singapore General Hospital, Singapore
[2]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[3]Program in Health Services and Systems Research, Duke-NUS Graduate Medical School, Singapore
[4]Ruhr University Bochum, Bochum, Germany
[5]Rheumatology, LUMC, Leiden, The Netherlands
[6]Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Center, and the Caphri Research Institute Maastricht University, Maastricht, The Netherlands
[7]Rheumazentrum Ruhrgebiet, Herne, Germany

Acknowledgements We would like to thank the late Dr Tan Chuen Seng from National University of Singapore Saw Swee Hock School of Public Health for his advice in conducting the statistical analysis.

Contributors JB, DvdH, AB and UK conceptualised the study design and acquired the data. WF, YHK and THW analysed the data. WF and THW wrote the first manuscript draft. All authors critically revised the article for important intellectual content and approved of the final manuscript. WF is the guarantor for this manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and this is an ancillary study. All centres in the original study received approval from their local ethics committee. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information.

ORCID iDs
Warren Fong http://orcid.org/0000-0003-1891-1892
Jürgen Braun http://orcid.org/0000-0002-9156-5095
Désirée van der Heijde http://orcid.org/0000-0002-5781-158X
Annelies Boonen http://orcid.org/0000-0003-0682-9533
Uta Kiltz http://orcid.org/0000-0001-5668-4497

REFERENCES

1 Sieper J, Poddubnyy D. Axial Spondyloarthritis. *Lancet* 2017;390:73–84.
2 Strand V, Singh JA. Patient burden of axial Spondyloarthritis. *J Clin Rheumatol* 2017;23:383–91.
3 Navarro-Compán V, Sepriano A, El-Zorkany B, *et al*. Axial Spondyloarthritis. *Ann Rheum Dis* 2021;80:1511–21.
4 Cella D, Hahn EA, Jensen SE, *et al*. Types of patient-reported outcomes. In: *Patient-Reported Outcomes in Performance Measurement. Research Triangle Park (NC)*. RTI Press, 2015.
5 Navarro-Compán V, Boel A, Boonen A, *et al*. Instrument selection for the ASAS core outcome set for axial Spondyloarthritis. *Ann Rheum Dis* 2023;82:763–72.
6 Png K, Kwan YH, Leung YY, *et al*. Measurement properties of patient reported outcome measures for Spondyloarthritis: A systematic review. *Semin Arthritis Rheum* 2018;48:274–82.
7 Kiltz U, van der Heijde D, Boonen A, *et al*. The ASAS health index (ASAS HI) - A new tool to assess the health status of patients with Spondyloarthritis. *Clin Exp Rheumatol* 2014;32:S–105.
8 Kiltz U, van der Heijde D, Boonen A, *et al*. Development of a health index in patients with Ankylosing Spondylitis (ASAS HI): final result of a global initiative based on the ICF guided by ASAS. *Ann Rheum Dis* 2015;74:830–5.
9 Navarro-Compán V, Boel A, Boonen A, *et al*. The ASAS-OMERACT core domain set for axial Spondyloarthritis. *Semin Arthritis Rheum* 2021;51:1342–9.
10 Rudwaleit M, Haibel H, Baraliakos X, *et al*. The early disease stage in axial Spondylarthritis results from the German Spondyloarthritis inception cohort. *Arthritis Rheum* 2009;60:717–27.
11 Rudwaleit M, van der Heijde D, Landewé R, *et al*. The development of assessment of Spondyloarthritis International society classification criteria for axial Spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777–83.
12 López-Medina C, Ramiro S, van der Heijde D, *et al*. Characteristics and burden of disease in patients with radiographic and non-radiographic axial Spondyloarthritis: a comparison by systematic literature review and meta-analysis. *RMD Open* 2019;5:e001108.
13 Walsh JA, Magrey MN, Baraliakos X, *et al*. Improvement of functioning and health with Ixekizumab in the treatment of active Nonradiographic axial Spondyloarthritis in a 52-week, randomized . *Arthritis Care & Research* 2022;74:451–60. 10.1002/acr.24482 Available: https://acrjournals.onlinelibrary.wiley.com/toc/21514658/74/3
14 Kiltz U, van der Heijde D, Boonen A, *et al*. Clinimetric validation of the assessment of Spondyloarthritis International society health index in patients with radiographic axial Spondyloarthritis in Ixekizumab trials. *J Rheumatol* 2023;50:754–62.
15 Hunter T, Sandoval D, Booth N, *et al*. Comparing symptoms, treatment patterns, and quality of life of Ankylosing Spondylitis and non-radiographic axial Spondyloarthritis patients in the USA: findings from a patient and Rheumatologist survey. *Clin Rheumatol* 2021;40:3161–7.
16 Di Carlo M, Lato V, Carotti M, *et al*. Clinimetric properties of the ASAS health index in a cohort of Italian patients with axial Spondyloarthritis. *Health Qual Life Outcomes* 2016;14:78.
17 Akgul O, Bodur H, Ataman S, *et al*. Clinical performance of ASAS health index in patients with Ankylosing Spondylitis and non-radiographic axial Spondyloarthritis: real-world evidence from multicenter nationwide Registry. *Rheumatol Int* 2020;40:1793–801.
18 Min HK, Lee J, Ju JH, *et al*. Predictors of assessment of Spondyloarthritis International society (ASAS) health index in axial Spondyloarthritis and comparison of ASAS health index between Ankylosing Spondylitis and Nonradiographic axial Spondyloarthritis: data from the Catholic axial. *J Clin Med* 2019;8:467.
19 Kiltz U, van der Heijde D, Boonen A, *et al*. Measurement properties of the ASAS health index: results of a global study in patients with axial and peripheral Spondyloarthritis. *Ann Rheum Dis* 2018;77:1311–7.
20 Rudwaleit M, Landewé R, van der Heijde D, *et al*. The development of assessment of Spondyloarthritis International society classification criteria for axial Spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. *Ann Rheum Dis* 2009;68:770–6.
21 Rudwaleit M, van der Heijde D, Landewé R, *et al*. The assessment of Spondyloarthritis International society classification criteria for peripheral Spondyloarthritis and for Spondyloarthritis in general. *Ann Rheum Dis* 2011;70:25–31.
22 Kiltz U, van der Heijde D, Boonen A, *et al*. Measuring impairments of functioning and health in patients with axial Spondyloarthritis by using the ASAS health index and the environmental item set: translation and cross-cultural adaptation into 15 languages. *RMD Open* 2016;2:e000311.
23 Kwan YH, Aw FF, Fong W, *et al*. Validity and reliability of the assessment of Spondyloarthritis International society health index in English-speaking patients with axial Spondyloarthritis in Singapore. *Int J Rheum Dis* 2019;22:1644–51.
24 Zochling J. Measures of symptoms and disease status in Ankylosing Spondylitis: Ankylosing Spondylitis disease activity score (ASDAS),

Ankylosing Spondylitis quality of life scale (Asqol), Bath Ankylosing Spondylitis disease activity index (BASDAI), Bath Ankylosing SP. 2011;63:S47–58.
25 Garrett S, Jenkinson T, Kennedy LG, *et al*. A new approach to defining disease status in Ankylosing Spondylitis: the bath Ankylosing Spondylitis disease activity index. *J Rheumatol* 1994;21:2286–91.
26 Spoorenberg A, van der Heijde D, de Klerk E, *et al*. A comparative study of the usefulness of the bath Ankylosing Spondylitis functional index and the Dougados functional index in the assessment of Ankylosing Spondylitis. *J Rheumatol* 1999;26:961–5.
27 Eyres S, Tennant A, Kay L, *et al*. Measuring disability in Ankylosing Spondylitis: comparison of Bath Ankylosing Spondylitis functional index with revised Leeds disability questionnaire. *J Rheumatol* 2002;29:979–86.
28 Calin A, Garrett S, Whitelock H, *et al*. A new approach to defining functional ability in Ankylosing Spondylitis: the development of the bath Ankylosing Spondylitis functional index. *J Rheumatol* 1994;21:2281–5.
29 Lukas C, Landewé R, Sieper J, *et al*. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with Ankylosing Spondylitis. *Ann Rheum Dis* 2009;68:18–24.
30 Machado P, Landewé R, Lie E, *et al*. Ankylosing Spondylitis disease activity score (ASDAS): defining cut-off values for disease activity States and improvement scores. *Ann Rheum Dis* 2011;70:47–53.
31 Djukanovic I, Carlsson J, Årestedt K. Is the hospital anxiety and depression scale (HADS) a valid measure in a general population 65–80 years old? A Psychometric evaluation study. *Health Qual Life Outcomes* 2017;15:193.
32 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–70.
33 Snaith RP. The hospital anxiety and depression scale. *Health Qual Life Outcomes* 2003;1:29.
34 Ware JE. SF-36 health survey update. *Spine (Phila Pa 1976)* 2000;25:3130–9.
35 Samprit C, Jeffrey SS. *Handbook of Regression Analysis*. New York: Wiley, 2003.
36 Sieper J, Hu X, Black CM, *et al*. Systematic review of clinical, humanistic, and economic outcome comparisons between radiographic and non-radiographic axial Spondyloarthritis. *Semin Arthritis Rheum* 2017;46:746–53.
37 Benavent D, Capelusnik D, Ramiro S, *et al*. Does gender influence outcome measures similarly in patients with Spondyloarthritis? results from the ASAS-perSpA study. *RMD Open* 2022;8:e002514.
38 Chen H-H, Chen Y-M, Lai K-L, *et al*. Gender difference in ASAS HI among patients with Ankylosing Spondylitis. *PLoS One* 2020;15:e0235678.
39 Roussou E, Sultana S. Spondyloarthritis in women: differences in disease onset, clinical presentation, and Bath Ankylosing Spondylitis disease activity and functional indices (BASDAI and BASFI) between men and women with Spondyloarthritides. *Clin Rheumatol* 2011;30:121–7.
40 Mease PJ, McLean RR, Dube B, *et al*. Comparison of men and women with axial Spondyloarthritis in the US-based Corrona Psoriatic arthritis/Spondyloarthritis Registry. *J Rheumatol* 2021;48:1528–36.
41 Kiltz U, Wiatr T, Redeker I, *et al*. Effects of patient and disease characteristics on global functioning in patients with axial Spondyloarthritis in routine care. *Semin Arthritis Rheum* 2022;55:S0049-0172(22)00057-9.
42 Zhao S, Thong D, Miller N, *et al*. The prevalence of depression in axial Spondyloarthritis and its association with disease activity: a systematic review and meta-analysis. *Arthritis Res Ther* 2018;20:140.
43 Martindale J, Smith J, Sutton CJ, *et al*. Disease and psychological status in Ankylosing Spondylitis. *Rheumatology (Oxford)* 2006;45:1288–93.
44 Chung DXY, Loo YE, Kwan YH, *et al*. Association of anxiety, depression and resilience with overall health and functioning in axial Spondyloarthritis (axSpA): a cross-sectional study. *BMJ Open* 2023;13:e071944.
45 Zhao SS, Jones GT, Hughes DM, *et al*. Depression and anxiety symptoms at TNF inhibitor initiation are associated with impaired treatment response in axial Spondyloarthritis. *Rheumatology (Oxford)* 2021;60:5734–42.
46 Maguire S, Gallagher P, O'Shea F. Undiagnosed depression in axial Spondyloarthropathy and the negative impact on patient outcomes: results of a screening study. *Arthritis Rheum* 2021;73.