ASSOCIATION OF ANXIETY, DEPRESSION AND RESILIENCE WITH OVERALL HEALTH AND FUNCTIONING IN AXIAL SPONDYLOARTHRITIS (axSpA): A CROSS-SECTIONAL STUDY

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ABSTRACT

Objectives To evaluate the association between anxiety, depression and resilience with overall health and functioning in axial spondyloarthritis (axSpA).

Design Cross-sectional evaluation of baseline data from a prospective cohort study, with recruitment from January 2018 to March 2021.

Setting Outpatient clinic in a tertiary hospital in Singapore.

Participants Patients aged 21 years and above who were diagnosed with axSpA.

Outcome measures The Hospital Anxiety and Depression Scale (HADS) was used for assessing anxiety and depression, 10-item Connor Davidson Resilience Scale (CD-RISC-10) for resilience, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for disease activity, Bath Ankylosing Spondylitis Functional Index (BASFI) for functional limitation and Assessment of SpondyloArthritis International Society Health Index (ASASHI) for overall health and functioning. Univariable and multivariable linear regression analyses were performed to assess the association between anxiety, depression and resilience with health and functioning.

Results We included 296 patients in this study. The median (IQR) score for HADS-Anxiety was 5.0 (2.0–8.0), with 13.5% and 13.9% having borderline abnormal and abnormal anxiety, respectively. The median (IQR) score for HADS-Depression was 3.0 (1.0–7.0), with 12.8% and 8.4% having borderline abnormal and abnormal depression, respectively. The median (IQR) CD-RISC-10 score was 29.0 (23.0–32.0) while the median (IQR) ASAS HI score was 4.0 (2.0–7.0). Apart from BASDAI, BASFI and disease duration, anxiety and depression were associated with overall health and functioning (β: 0.12, 95% CI 0.03, 0.20; β: 0.20, 95% CI 0.09, 0.31) in the multivariable linear regression. Level of resilience was not associated with health and functioning. Clinicians could consider routinely screening for anxiety and depression in their patients, especially in patients with more severe symptoms.

INTRODUCTION

Axial spondyloarthritis (axSpA) is an inflammatory disease marked by chronic low back pain, stiffness and fatigue, which are potentially disabling and greatly affect a patient’s function and overall health.1 2 3 The understanding of gender disparities in axSpA is gradually shifting internationally, from being a male predominant disease to affecting both men and women equally, especially for nr-axSpA.3 4 Health and functioning is a novel concept in axSpA, and was included as a core domain in the 2021 Assessment of SpondyloArthritis International Society-Outcomes Measures in Rheumatology.4 ‘Functioning’ was adapted from the International Classification of Functioning, Disability and Health (ICF) framework, which was conceptualised based on the biopsychosocial model, and encompasses disease-specific constructs (eg, pain, physical function) as well as the impact on contextual factors (eg, social function, personal factors), both of which are normally inter-related.4–7 The Assessment of SpondyloArthritis International Society Health Index (ASAS HI) was developed with the aim...
of having a comprehensive questionnaire to assess health and functioning in axSpA.5 8

Mental health issues such as depression and anxiety are significant in patients with axSpA, with the prevalence of depression ranging from 15% to 52%, depending on the screening tools used and demographic factors.9 Patients afflicted with mental health issues have worse disease activity, functionality and work performance.9–12 Other studies have shown that fatigue, pain and disease activity of axSpA affect patients in multiple domains including their work productivity, ability to drive and sexual functioning,26 27 few studies have explored the role of psychological factors such as anxiety, depression and resilience on patients’ health and functioning. Therefore, we aimed to evaluate the association of depression, anxiety and resilience with overall health and functioning in axSpA. We hypothesise that more severe depression and anxiety are associated with poorer health and functioning, while increased resilience is associated with better health and functioning.

METHODS

Study design

This study was a cross-sectional evaluation of baseline data from a prospective cohort study. Consecutive patients were recruited from an outpatient clinic in Singapore General Hospital, a tertiary hospital in Singapore, from January 2018 to March 2021. Informed consent was obtained from all participants. Inclusion criteria included being 21 years and above and being diagnosed with axSpA by a rheumatologist. All patients fulfilled the 2009 Assessment of SpondyloArthritis International Society criteria.27 28 None of the patients were clinically diagnosed with fibromyalgia, anxiety or depression prior to diagnosis of axSpA. Three hundred and twenty patients were assessed for enrolment and eight patients who did not provide consent were not enrolled. Out of the 314 patients enrolled, 18 patients were not included in the analysis as 13 did not complete the questionnaires at baseline and 5 had incomplete data for Hospital Anxiety and Depression Scale (HADS) and/or 10-item Connor Davidson Resilience Scale (CD-RISC-10) (figure 1). This study was reported in line with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.29

Measurements

Sociodemographic and clinical variables

Sociodemographic and clinical variables collected include: age, sex, ethnicity, level of education, body mass index, human leukocyte antigen (HLA-B27) results, disease duration, history of peripheral arthritis and extramuscloskeletal symptoms such as psoriasis, uveitis and inflammatory bowel disease, current medication use and comorbid conditions.

Assessment of anxiety, depression and resilience

Anxiety and depression were measured using the HADS, which was developed to assess states of anxiety and depression in non-psychiatric patients.30 31 It contains two subscales (HADS-A and HADS-D) that measure anxiety and depression, respectively.32 Each subscale contains seven questions, with each question having a score from 0 to 3, and total scores ranging from 0 to 21. A normal level of anxiety or depression was defined as having scores <8, a borderline level of anxiety or depression as having scores ≥8 and <11 and an abnormal level of anxiety or depression as having scores ≥11 and <21.33 These cut-offs have been used in Singaporean patients previously.34–36 Resilience was measured using the CD-RISC-10. Each question is scored from 0 to 4, with higher scores indicating greater resilience.41 42 CD-RISC-10 has been validated in Singapore and is reliable in the measure of resilience in axSpA.42

Assessment of health and functioning

Health and functioning was assessed using the ASAS HI, which has been validated in patients with axSpA.5 43 It was conceptualised based on the ICF framework and contains 17 questions related to the biopsychosocial model of health, which range from disease-specific aspects such as physical mobility, to other aspects such as self-care and community life.8 Questions use dichotomous response options, where agreeing with the statement will equate to a score of 1, and disagreeing with the statement will equate to a score of 0. Scores range from 0 to 17 and higher scores indicate poorer health and functioning. Scores ≤5 were considered as having good health and functioning, scores >5 and <12 were considered as moderate health and functioning and scores ≥12 were considered as poor health and functioning.

Assessment of disease activity and functional limitation

Disease activity was measured using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), a 6-item validated patient-reported outcome, which contains questions related to fatigue, spinal pain, joint pain, enthesitis, duration and severity of morning stiffness.44 45 Each question is scored on a numerical rating scale from 0 (no symptoms) to 10 (very severe symptoms or having morning stiffness lasting for ≥2 hours). The BASDAI sum score ranges between 0 and 10, with higher scores indicating higher disease activities, and a score of 4 or
more suggesting suboptimal disease control. Functional limitation was assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI), which contains 10 questions—eight that assess the amount of functional limitation for activities such as bending and reaching, as well as two that assess how well patients cope with everyday life. Each question is scored on a numerical rating scale from 0 (easy to perform the activity) to 10 (impossible to perform the activity). Total scores range from 0 to 10 and higher scores indicate greater functional impairment.

**Statistical analysis**

Continuous variables were reported in mean and SD if normally distributed, or median and IQR if otherwise. Categorical variables were expressed as frequencies and percentages. Univariable linear regression analyses were used to determine the association between each variable and the ASAS HI score. Variables were selected based on previous literature. Variables with p<0.1 in the univariable analyses were then included in a multivariable analysis, and was considered to be significant if p<0.05. As some variables might be correlated, we used the variance inflation factor to determine if multicollinearity was present, with a value of 5 as the threshold. The potential of resilience modifying the association between anxiety, depression and ASAS HI scores was tested, where effect modification was considered to be significant if the p value of the interaction term was <0.05. A post-hoc non-parametric equality-of-mediants test was conducted to determine if there were differences in the BASDAI, BASFI, HADS-Anxiety, HADS-Depression scores between patients with longer as compared with shorter disease durations. Disease duration was categorised as long if it was 10 years and above. Data analyses were conducted using Stata SE V.15 (StataCorp).

**RESULTS**

**Patient demographics and characteristics**

A total of 296 patients were included in the study. Patient demographics and characteristics are shown in [Table 1](#). Patients had a median (IQR) age of 41.0 (29.5–53.0) years. Majority of the patients were men (n=225, 76.0%), Chinese (n=274, 92.6%), diagnosed with radiographic axSpA (n=224, 75.7%) and positive for HLA-B27 (n=246, 85.4%). The median (IQR) disease duration was 9.0 (4.0–14.5) years. The median BASDAI and BASFI scores were 2.2 (1.3–3.9) and 1.1 (0.2–3.0), respectively. The proportion of patients who used non-steroidal anti-inflammatory drugs (NSAIDs) was the...
Table 1 Patient demographics and characteristics (N=296)

<table>
<thead>
<tr>
<th>Demographics and characteristics</th>
<th>Asian ethnicity, n (%)</th>
<th>Male sex, n (%)</th>
<th>Chinese ethnicity, n (%)</th>
<th>BMI, kg/m², median (IQR)‡</th>
<th>Completion of secondary education (10 years and above), n (%)</th>
<th>Occupation status</th>
<th>Comorbidities</th>
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<tbody>
<tr>
<td>Age, years, median (IQR)</td>
<td>41.0 (29.5–53.0)</td>
<td>225 (76.0)</td>
<td>274 (92.6)</td>
<td>24.9 (21.8–28.4)</td>
<td>273 (92.2)</td>
<td>Employed and national service personnel, n (%)</td>
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<td>Unemployed, n (%)</td>
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<td>Full-time students, n (%)</td>
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<td>Housewife, n (%)</td>
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<td>Retiree, n (%)</td>
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<td>Radiographic-axial spondyloarthritis</td>
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<td>HLA-B27, n (%)*</td>
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<td>History of extramusculoskeletal symptoms</td>
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<td>Psoriasis, n (%)</td>
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<td>Uveitis, n (%)</td>
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<td>Inflammatory bowel disease, n (%)</td>
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<td>History of peripheral arthritis, n (%)</td>
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<td>Current use of csDMARDs and immunosuppressants, n (%)</td>
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<td>Hypertension, n (%)</td>
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<td>Diabetes mellitus, n (%)</td>
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<td>Dyslipidaemia, n (%)</td>
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<td>Cerebrovascular accident, n (%)</td>
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<td>Ischaemic heart disease, n (%)</td>
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<td>Chronic kidney disease, n (%)</td>
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<td>BASFI, median (IQR)</td>
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<td>HADS-Anxiety, median (IQR)†</td>
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<td>HADS-Depression, median (IQR)‡</td>
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<td>Normal</td>
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<td>CD-RISC-10, median (IQR)</td>
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<td>ASAS HI, median (IQR)§</td>
<td>4.0 (2.0–7.0)</td>
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Continued

Table 1 Continued

<table>
<thead>
<tr>
<th>Good functioning</th>
<th>176 (59.5)</th>
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<tr>
<td>Moderate functioning</td>
<td>102 (34.5)</td>
</tr>
<tr>
<td>Poor functioning</td>
<td>18 (6.1)</td>
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</tbody>
</table>

*Data on the status of HLA-B27 was unavailable for eight patients. †A normal level of anxiety was defined as having scores <8, a borderline level of anxiety as having scores ≥8 and <11 and an abnormal level of anxiety as having scores ≥11 and <21. §A normal level of depression was defined as having scores <8, a borderline level of depression as having scores ≥8 and <11 and an abnormal level of depression as having scores ≥11 and ≤21. Good functioning was defined as having ASAS HI scores ≤5, moderate functioning as having scores >5 and ≤12, while poor functioning as having scores ≥12.

As HASI, Assessment of Spondyloarthritis International Society Health Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying antirheumatic drugs; BMI, body mass index; CD-RISC-10, 10-item Connor Davidson Resilience Scale; csDMARDs, conventional synthetic disease-modifying antirheumatic drug; HADS, Hospital Anxiety and Depression Scale; HLA-B27, human leukocyte antigen B27; NSAIDs, non-steroidal anti-inflammatory drugs; tsDMARDs, targeted synthetic disease-modifying antirheumatic drugs.

The median (IQR) score for HADS anxiety was 5.0 (2.0–8.0), with 40 (13.5%) and 41 (13.9%) patients having borderline abnormal and abnormal scores for anxiety, respectively. The median (IQR) score for HADS depression was 3.0 (1.0–7.0), with 38 (12.8%) and 25 (8.4%) patients having borderline abnormal and abnormal scores for depression, respectively. The median (IQR) score for CD-RISC-10 and ASAS HI were 29.0 (23.0–32.0) and 4.0 (2.0–7.0), respectively. Most of the patients in this study had good functioning (n=176, 59.5%), while only 18 (6.1%) had poor functioning.

When stratified by the level of overall health and functioning, patients with poor functioning had the highest median (IQR) BASDAI scores of 6.0 (4.5–6.7), while those with good functioning had the lowest scores of 1.8 (1.0–2.6) (p<0.01). Similarly, median (IQR) BASFI scores were the highest in patients with poor functioning and lowest in those with good functioning (6.4 (4.9–6.8), 0.5 (0.0–1.4) p<0.01). For psychological factors, patients with poor functioning had the highest anxiety and depression scores. As reflected by the median (IQR) CD-RISC-10 scores, patients with poor functioning had the lowest resilience (19.5 (16.0–28.0)) compared with those of moderate functioning (26.0 (20.0–30.0)) and good functioning (30.0 (27.0–35.0)) (p<0.01) (table 2).
Factors associated with health and functioning

The univariable analysis showed that being women, having higher BASDAI, BASFI, HADS-Anxiety and HADS-Depression scores were associated with higher ASAS HI scores. Higher CD-RISC-10 scores and longer disease duration were associated with lower ASAS HI scores (table 3). In the multivariable analysis, higher anxiety and depression scores were associated with higher ASAS HI scores, as shown by HADS-Anxiety ($\beta$: 0.12, 95% CI 0.03, 0.20) and HADS-Depression ($\beta$: 0.20, 95% CI 0.09, 0.31). The level of resilience as measured by CD-RISC-10 was not associated with ASAS HI scores ($\beta$: −0.02, 95% CI −0.06, 0.03) (table 3). Interaction terms between resilience and anxiety, and resilience and depression were non-significant (p=0.796 and p=0.934, respectively, data not shown).

Higher disease activities and functional limitation were also associated with higher ASAS HI scores, as reflected by BASDAI ($\beta$: 0.41, 95% CI 0.22, 0.60) and BASFI ($\beta$: 0.71, 95% CI 0.54, 0.88). Having a longer disease duration was associated with having lower ASAS HI scores ($\beta$: −0.04,
95% CI −0.07 to −0.01). The post-hoc analysis showed that patients with a longer disease duration (≥10 years) had lower median (IQR) BASDAI scores of 1.9 (1.1–3.3) than patients with a shorter disease duration, whose median (IQR) BASDAI scores were 2.6 (1.5–4.4) (p<0.01). Differences for BASFI, HADS-Anxiety and HADS-Depression scores were non-significant (online supplemental file 1).

DISCUSSION

This study aimed to determine the association between anxiety, depression and resilience with health and functioning in patients with axSpA. To our knowledge, few studies have assessed the role of psychological factors and this is the first study assessing the association between anxiety and resilience with overall health and functioning. Validated scales were also used for the rating of anxiety, depression and resilience. Psychological symptoms are often under-recognised and the use of self-reported outcomes instead of formal diagnoses might be more relevant.54 55

As expected, higher disease activities and functional limitation as reflected by the BASDAI and BASFI scores were positively associated with poorer overall health and functioning, similar to prior studies.24 43  The ASAS HI was developed with the aim of having an all-encompassing tool for assessing the disease impact of axSpA, by mapping items from existing tools (including BASDAI and BASFI) to the ICF categories.28  Apart from disease activities and functional limitation, we found that anxiety and depression were associated with poorer overall health and functioning in our population, while the level of resilience was not. Previous studies have reported that patients with axSpA had higher levels of depression and anxiety as compared with the general population.53 In our study, 27.4% had possible anxiety (HADS-A≥8), which was lower than previous studies (32%–63%).52 54 55 while 21.2% had possible depression (HADS-D≥8), which was consistent with previous reports (14%–56%).9 44 Though often comorbid, anxiety often develops prior to depression, and symptoms could have been more reflective of depression at the point of data collection, hence causing the lower prevalence of anxiety.56 57 Apart from disease activity and functional limitation, levels of anxiety and depression were associated with poorer health and functioning in our study population. This could be explained by the fact that factors such as pain, fatigue and functional impairment were also identified as major drivers and correlated to psychological issues including anxiety and depression.53 58 59 Anxiety and depression were also found to impair treatment responses,52 which might imply reciprocal effects between anxiety and depression with disease activity. Given the association between anxiety and depression with poorer overall health and functioning, it further emphasises that clinicians should be aware of and screen for anxiety and depression in their patients with axSpA.60 61 especially in patients with more severe symptoms. Clinicians should also factor in possible anxiety and depression when interpreting disease activities.

Our study did not find a significant association between resilience and higher overall health and functioning in axSpA. This is similar to a previous study which showed that levels of resilience did not contribute to patients’ perception of their disease activities for axSpA, though direct comparisons cannot be drawn as different resilience scales were used.92 Our observation could possibly be explained by various reasons. Resilience is a multi-dimensional concept, which not only depends on an individual’s disposition during adversities, but also the strength of interpersonal ties, the resources available in an individual’s community and family that can be used to facilitate resilience, biological factors, stressors, as well as an individual’s level of self-awareness.63–67 Having experienced past traumas as well as higher levels of education and income were also related to the level of resilience.66 67 Although the CD-RISC-10 is one of the most widely used and reliable scales,68 it mainly focuses on resilience at the level of the individual and does not account for other aspects.61 62 There is currently no gold standard for the measurement of resilience and out of the available scales, only the Resilience Scale for Adults covered both intrapersonal and interpersonal aspects of resilience.63 69 but this scale has neither been validated in the axSpA cohort nor in Singapore. Limited studies related to resilience have been conducted in patients with axSpA, and future research could focus on validating alternative resilience scales in axSpA. Despite resilience not being associated with higher overall health and functioning in our study, previous studies have shown that higher levels of resilience were associated with positive outcomes, such as experiencing less fatigue, better medication adherence and a better quality of life in patients with primary Sjögren’s syndrome, systemic lupus erythematosus and chronic kidney disease, respectively.78–72 Resilience was found to moderate the effect of disease activity on mental HRQoL (assessed by the 36-item Short-Form Health Survey Mental Component Summary) in patients with rheumatoid arthritis.73 In patients with fibromyalgia, apart from pain intensity, having a higher resilience was associated with lower pain catastrophisation and disease burden.74 75 When examined in geriatric populations, greater resilience was associated with more successful ageing, fewer depressive symptoms as well as lower mortality.76 77 Contextual factors such as helplessness have been shown to be associated with a poorer quality of life in axSpA and improving resilience might contribute to better health and functioning in these patients.78

In addition, we also found longer disease duration to be associated with better health and functioning, which was unexpected as previous studies showed that having a longer symptom duration was associated with lower pain tolerance, more functional disabilities and poorer health and functioning.20 79 On further subgroup analysis, patients with a longer disease duration (≥10 years) had significantly better BASDAI scores, which
could possibly explain the higher overall health and functioning.

One limitation of our study was the cross-sectional design. Thus, a causal relationship could not be established. As anxiety, depression and resilience are dynamic and influenced by a multitude of factors, it might be more beneficial to observe changes over time and how this relates to overall health and functioning. Patients were recruited from a tertiary hospital where cases of axSpA might be more severe than those managed in the community. The median BASDAI score for our cohort was 2.2, which was slightly lower than that of other cohort studies and might limit the generalisability of the results, though other characteristics such as the proportion of males and HLA-B27 positivity were largely similar. Differences in the disease activity could be a reflection of country-level variation. Similarly, fewer patients in this study had possible anxiety as compared with other axSpA populations, which should be taken into consideration when interpreting results in other cohorts. Majority of the patients in this study were Chinese, and findings might not be similar in other ethnic populations. However, the racial proportion in this study is similar to other local studies, where majority of the patients are of Chinese ethnicity. Age and gender profiles were also similar to prior studies. Patient’s pain score could be a possible confounding factor for this study, but we had sought to mitigate this by including the BASDAI into the multivariate analysis, which includes a pain score for both the axial skeleton and peripheral joints, which are important manifestations of pain in patients with axSpA.

CONCLUSION

In summary, our study demonstrated that depression and anxiety were associated with poorer health and functioning in patients with axSpA, while resilience was not. Abnormal levels of anxiety and depression were found in 13.9% and 8.4% of patients, respectively. Hence, it would be beneficial for clinicians to screen for depression and anxiety in patients with axSpA, especially since mental health conditions are often under-detected.

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Contributors YHK, SA, WF conceptualised the study design. YHK, JKP, THW, WRG, SA, WF executed the study and acquired the data. JKP and THW analysed the data. DXYC and YEL wrote the first manuscript draft. WF is the content guarantor. All authors critically revised the article for important intellectual content and approved of the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by SingHealth Centralized Institutional Review Board (reference: 2017/2626). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets and statistical codes used are available from the corresponding author upon reasonable request.

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REFERENCES


Supplementary file 1. BASDAI, BASFI, HADS-Anxiety and HADS-Depression scores of participants, stratified by disease duration

<table>
<thead>
<tr>
<th></th>
<th>Short disease duration*</th>
<th>Long disease duration*</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI, median (IQR)</td>
<td>2.6 (1.5 – 4.4)</td>
<td>1.9 (1.1 – 3.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BASFI, median (IQR)</td>
<td>1.0 (0.2 – 3.1)</td>
<td>1.3 (0.2 – 2.9)</td>
<td>0.36</td>
</tr>
<tr>
<td>HADS-Anxiety, median (IQR)</td>
<td>5.0 (2.0 – 8.0)</td>
<td>5.0 (2.0 – 8.0)</td>
<td>0.64</td>
</tr>
<tr>
<td>HADS-Depression, median (IQR)</td>
<td>3.0 (1.0 – 7.0)</td>
<td>3.0 (1.0 – 6.0)</td>
<td>0.79</td>
</tr>
</tbody>
</table>

* Participants with a disease duration of ≥10 years were classified as having a long disease duration, while those <10 years were classified as having a short disease duration.

Legend:
BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, HADS: Hospital Anxiety and Depression Scale