The Effect of Axial Spondyloarthritis on Mental Health: Results from the Atlas

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ABSTRACT. ***Objective.*** To assess the risk of mental disorders in patients with axial spondyloarthritis (axSpA) and to examine the factors associated with this.

Methods. In 2016, a sample of 680 patients with axSpA were interviewed as part of the development process for the Atlas of Axial Spondyloarthritis in Spain. The risk of mental disorders in these patients was assessed using the 12-item General Health Questionnaire scale. Additionally, the variables associated with the risk of mental disorders were investigated, including sociodemographic characteristics (age, sex, relationship, patient association membership, job status, and educational level), disease status (Bath Ankylosing Spondylitis Disease Activity Index, spinal stiffness, and functional limitation), and previous diagnosis of mental disorders (depression and anxiety). Bivariate correlation analyses were performed, followed by multiple hierarchical and stepwise regression analysis.

Results. A total of 45.6% patients were at risk of mental disorders. All variables except educational level and thoracic stiffness significantly correlated with risk of mental disorders. Nevertheless, disease activity, functional limitation, and age showed the highest coefficient ($r = 0.543$, $p \leq 0.001$; $r = 0.378$, $p \leq 0.001$; $r = -0.174$, $p \leq 0.001$, respectively). In the stepwise regression analysis, 4 variables (disease activity, functional limitation, patient association membership, and cervical stiffness) explained the majority of the variance for the risk of mental disorders. Disease activity displayed the highest explanatory degree ($R^2 = 0.875$, $p < 0.001$).

Conclusion. In patients with axSpA, the prevalence of risk of mental disorders is high. Combined with a certain sociodemographic profile, high disease activity is a good indicator of the risk for mental disorders. (First Release July 15 2019; J Rheumatol 2019;46:1284–9; doi:10.3899/jrheum.180868)

Key Indexing Terms:
AXIAL SPONDYLOARTHRITIS BASDAI SPINAL STIFFNESS
FUNCTIONAL LIMITATION DEPRESSION GENERAL HEALTH QUESTIONNAIRE

Axial spondyloarthritis (axSpA) manifestations, such as loss of mobility, chronic pain, and fatigue, affect a patient's daily functioning and quality of life[1]. However, the same number and degree of manifestations do not always have the same effect on all patients. On the one hand, increasing evidence published during the last 10 years has demonstrated the importance of psychosocial factors for patients adjusting to their physical limitations and chronic pain stemming from the disease[2,3,4]. Mental disorders, such as depression and anxiety, can worsen functioning and adherence to treatment[5]. A longitudinal study carried out over 1 year in patients with ankylosing spondylitis showed that depression is a mediating factor between the disease activity degree and functional limitation[6]. On the other hand, previous data suggest that the psychological health status of patients with axSpA may be influenced by the level of disease activity experienced, although these findings have not been confirmed[7].

A recent systematic review and metaanalysis reported that the prevalence of depression in patients with axSpA ranges from 11% to 64%[8]. This wide estimation in previous studies reflects the very heterogeneous definitions and assessments of depression used in these studies. In addition, most of these studies mainly included male patients with a very long disease duration and substantial radiographic damage, and therefore their results are difficult to apply to all patients across the entire spectrum of axSpA.

The Spanish Atlas of Axial Spondyloarthritis[9] is a national

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initiative that seeks to better understand the current state of people with axSpA. It uses an integrative approach based on scientific evidence, expert knowledge, and patient opinion. The Atlas population represents the entire spectrum of axSpA and is equally distributed in terms of sex. Additionally, the risk of mental disorders was assessed by using the 12-item General Health Questionnaire (GHQ-12). This is a validated screening tool for identifying minor psychiatric disorders in the general population within nonpsychiatric clinical settings such as primary care or general medical outpatient facilities. Therefore, the Atlas 2017 provides an opportunity to further examine the effect of disease outcomes on mental health in patients with axSpA. Moreover, the screening tool can shed light on the influence of explanatory variables related to mental disorders in these patients.

The objective of our present study was to determine the extent of risk of mental disorders in patients with axSpA and any associated factors. Our hypothesis was that greater disease activity is associated with a higher risk of having mental disorders.

MATERIALS AND METHODS

Study design and population. As part of the Atlas of Axial Spondyloarthritis in Spain project[9], 680 patients diagnosed with axSpA were interviewed between May 1 and August 15, 2016. The Atlas seeks to promote early diagnosis, improved care, and the use of effective treatments in patients with axSpA. The anonymous questionnaire included a series of items related to disease status [disease activity as measured by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) self-administered questionnaire, spinal stiffness, and functional limitation] and psychological aspects related to coping with the disease. All the methodologies upon which the Atlas is based have been previously published in detail. This specific study includes data from 474 patients with recorded information about risk for mental disorders using the GHQ-12.

Disease activity. Disease activity was measured using the BASDAI with a range between 0 and 10[10].

Spinal stiffness. In addition, spinal stiffness levels in the 3 areas of the vertebral column (cervical, dorsal, and lumbar) were collected, measured on a scale from lower to higher levels using an ordinal variable (1 = without limitation, 2 = mild limitation, 3 = moderate limitation, and 4 = severe limitation). Using this information, an index of spinal stiffness was created by adding, but without weighting, the degree of stiffness in each of the 3 areas. The resulting values ranged between 3 and 12. The Cronbach's alpha coefficient of this scale was 0.85, which attests to its consistency for assessing general stiffness.

Functional limitations in daily activities. To determine the degree of functional limitation, a composite index was used and included the sum of recorded limitation in 18 daily activities (dressing, grooming, bathing, tying shoelaces, moving about the home, walking up and down stairs, getting into/out of bed, using the toilet, shopping, preparing meals, eating, housework, walking, using public transportation, going to the doctor, driving, physical exercise, and sexual relations) using an ordinal variable (0 = none, 1 = little, 2 = some, and 3 = moderate). The resulting values oscillate between 0 and 54; thus, a value of 0–18 was set as a low limitation, 18–36 as a medium limitation, and 36–54 as an indication of high limitation. The Cronbach's alpha coefficient of this scale was 0.964, guaranteeing its reliability as a means for assessing limitation.

Sociodemographic aspects. The following demographic aspects were also collected: sex, age, living as a couple, education level, employment status, and whether the individual belonged to a patient association.

Comorbidity of mental health. Finally, patients were queried about any previous mental health diagnosis (made by psychologist or psychiatrist), including anxiety or depression. Such diagnoses of depression and/or anxiety referred to some point(s) in the past and patients were asked to provide a positive answer only when said diagnosis had been made by a psychologist/psychiatrist based on clinical criteria.

Risk of mental disorders. The risk of mental disorders was determined by using the GHQ-12[11], which consists of 12 items, each one assessing the severity of a mental health problem during the previous 4 weeks using a Likert scale (0–3). Thus, a maximum score of 36 was obtained; higher scores reflected an increased risk of psychiatric morbidity. However, to determine the risk of patients with poor mental health, these scores were transferred to a GHQ scale, where 0 or 1 = 0, and 2 or 3 = 1. Following this methodology, the majority of studies found that scores ≥ 3 indicated a high risk of poor mental health; therefore, we used this cutoff point for the present study[12]. The GHQ-12 offers reliability in studies developed within the Spanish population, resulting in a Cronbach's alpha coefficient that oscillated between 0.76 and 0.90[11,13]. In our study, a Cronbach's alpha coefficient of 0.934 was obtained, which supported the reliability hypothesis of this scale.

Statistical analysis. The statistical analysis was conducted in 3 stages. The first step focused on the descriptive statistics for the sample and the study variables. The second step consisted of bivariate regression analyses of each predictor regarding the risk of poor mental health (GHQ-12). Here, nonparametric contrasts were made because the GHQ-12 values obtained did not follow a normal distribution pattern. For quantitative variables, Mann-Whitney U tests for 2 categories, and Kruskal-Wallis tests for more than 2 categories were performed. For categorical variables, chi-square independence test or Fisher's exact test was used. In addition, the Spearman correlation coefficient was used to assess whether there was a relationship between mental health status (GHQ-12) and the different quantitative factors, such as the level of disease activity as measured by BASDAI.

The third step evaluated the independent influence of disease outcomes on mental health by using a hierarchical multiple regression analysis with those variables or disease outcomes that had shown a significant relationship with mental health status in the bivariate analyses conducted during the second step. For the hierarchical regression analysis, variables were grouped into 3 conceptual categories: (1) sociodemographic variables, (2) comorbidities, and (3) physical variables. This analysis introduced the variables of each category in a step-by-step fashion, thereby allowing for model comparison by building several regression models. Each model added variables to the previous one at each step; later models always included smaller models in their previous steps. In this case, our interest was to determine whether newly added conceptual categories of variables showed a significant improvement in R^2 (the proportion of explained variance in GHQ-12 by the model). Finally, a stepwise forward regression multivariable analysis was carried out, which included the variables that passed an F test, to ascertain the best associated factors.

All contrasts were bilateral and considered statistically significant when the p value was < 0.05. The data were analyzed using SPSS software, version 24 for 64 bits (IBM Corp.).

RESULTS

Characteristics of the study participants. A total of 838 patients with axSpA anonymously accessed the online questionnaire between May 1 and August 15, 2016. After validation and normalization of the information, the sample consisted of 680 patients who responded to the majority of the questionnaire (the completion rate exceeded 75%) and made up the total valid sample of the Spanish Atlas of Axial Spondyloarthritis[9]. From these, a total of 474 patients had valid data for the GHQ-12 and comprised the group under evaluation for this study; characteristics of the sample are summarized in Table 1. The characteristics of this subgroup

Table 1. Sociodemographic data, disease outcomes, and comorbidity sample characteristics.

Variables	Values
Sociodemographic	
Age, yrs	45.4 ± 10.7
Sex, male	233 (49.1)
Having a partner, n = 444	386 (86.9)
Education level, university	185 (39.0)
Job status, employee	234 (49.4)
Patient association membership	227 (47.8)
Disease outcomes	
BASDAI (0–10), n = 442	5.4 ± 2.1
Spinal stiffness, moderate or severe	
Cervical (1–4), n = 447	201 (44.9)
Thoracic (1–4), n = 435	186 (42.7)
Lumbar (1–4), n = 458	288 (62.8)
Functional limitations in daily activities (0–54), n = 473	27.5 ± 12.7
Treatment	
NSAID	363 (76.6)
sDMARD	181 (38.2)
bDMARD	240 (50.3)
Comorbidity	
Self-reported depression diagnostic	99 (20.8)
Self-reported anxiety diagnostic	134 (28.2)
GHQ-12 score (0–36)	18.3 ± 8.0

N = 474 unless otherwise specified. Results are expressed as mean ± SD or n (%). BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; NSAID: nonsteroidal antiinflammatory drug; sDMARD: synthetic disease-modifying antirheumatic drug; bDMARD: biological DMARD; GHQ-12: 12-item General Health Questionnaire.

were similar compared with the entire population, with the exception of more frequently having a relationship with a partner. In the studied population, the mean GHQ-12 score was 18.3 ± 8.0. Further, 310 (65.4%) patients were classified as having risk of mental disorders, while 164 (34.6%) had no risk of mental disorders.

Bivariate analyses. Table 2, Table 3, and Table 4 depict the results for the bivariate analyses. Mental health showed a statistically significant association with the following variables: older age, male sex, no relationship with a partner, unemployment, no patient association membership, anxiety and/or depression diagnosis, high level of disease activity (BASDAI), high degree of spinal stiffness (cervical and lumbar), and worse functional limitations in daily activities.

Table 2. Bivariate analysis of sociodemographic factors associated with the risk of mental disorders measured by GHQ-12.

Sociodemographic Factors	Homogeneity Test: Kruskal-Wallis or Mann-Whitney	Chi-square
Age, yrs	0.001* (Spearman = –0.174)	
Sex	0.013†	0.025
Having a partner	0.009†	0.021
Education level	0.607*	0.43
Job status	≤ 0.001*	≤ 0.001
Patient association membership	0.001†	0.001

* Kruskal-Wallis test. † Mann-Whitney test. GHQ-12: 12-item General Health Questionnaire.

Table 3. Bivariate analysis for comorbidity factors associated with risk of mental disorders measured by GHQ-12.

Comorbidity Factors	Homogeneity Test: Kruskal-Wallis or Mann-Whitney	Chi-square
Self-reported depression diagnostic	≤ 0.00†	≤ 0.001
Self-reported anxiety diagnostic	≤ 0.001†	≤ 0.001

† Mann-Whitney test. GHQ-12: 12-item General Health Questionnaire.

Table 4. Bivariate analysis for disease activity and functional limitation factors associated with risk of mental health disorders measured by GHQ-12.

Factors	Spearman Correlation Coefficient	p
Disease activity		
BASDAI (0–10)	0.543	≤ 0.001
Spinal stiffness, moderate or severe, n (%)		
Cervical (1–4)	0.120	0.011
Thoracic (1–4)	0.073	0.130
Lumbar (1–4)	0.165	≤ 0.001
Limitations in daily activities (0–54)	0.378	≤ 0.001

GHQ-12: 12-item General Health Questionnaire; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

Hierarchical modeling with successive conceptual categories. To evaluate the independent influence of disease outcomes on mental health, a hierarchical multiple regression analysis with those variables that had shown a significant relationship with GHQ-12 in the bivariate analyses was performed (Table 5). This analysis demonstrated how, among sociodemographic variables, patient association membership had a significant regression coefficient while the rest did not.

In the first step, all sociodemographic attributes were included and established as control variables. That model explained patient mental health to a great extent (R^2 = 83.2%). In the second step, diagnoses of depression and anxiety were added to this model but the R^2 value increased by only 0.6% (p = 0.001) and yielded no significant regression coefficients (p values = 0.08 and 0.8, respectively). In the third step, disease activity (BASDAI and stiffness) and Functional Limitation Index were also included in the model, which added 5.5% (p < 0.001) to the variance of the GHQ-12 scores. However, of these last variables only BASDAI and functional limitations experienced in daily life had a coefficient significantly different from zero: 0.52, p < 0.001 and 0.14, p = 0.004, respectively. This means that once the sociodemographic characteristics and psychiatric/psychological comorbidity (depression and anxiety) were established, a change in BASDAI levels or functional limitation reflects a change in the GHQ-12.

Table 5. Hierarchical multivariate analyses of sociodemographic, comorbidity, and disease status factors in relation to the risk of mental disorders, measured by GHQ-12 (n = 474).

Step	Factors	β-Weights	95% CI	Standard β-Weights	p	R^2 (%), p+*	ΔR^2 (%), p+**
1	Sociodemographic					0.832	0.832
	Age, yrs	–0.137	–1.143, 0.870	–0.016	0.789		
	Sex	0.424	–0.953, 1.800	0.033	0.545		
	Being in a relationship	0.606	–0.548, 1.760	0.042	0.302		
	Job status	0.237	–0.083, 0.557	0.041	0.146		
	Patient association membership	2.113	0.770, 3.456	0.168	0.002		
2	Comorbidity					0.838	0.006
	Self-reported depression diagnostic	–1.705	–3.590, 0.181	–0.155	0.076		
	Self-reported anxiety diagnostic	–0.260	–2.020, 1.500	–0.023	0.772		
3	Disease outcomes					0.893	0.055
	BASDAI (0–10)	1.796	1.424, 2.167	0.527	< 0.001		
	Functional limitations in daily activities (0–54)	0.092	0.030, 0.154	0.140	0.004		
	Cervical stiffness (1–4)	0.392	–0.439, 1.224	0.051	0.354		
	Lumbar stiffness (1–4)	0.429	0.393, 1.250	0.063	0.306		

Only values that were statistically significant in the bivariate analysis (or marginally significant: $p < 0.09$) were included in this analysis. All β-weights, 95% CI, and p values for individual variables were estimates derived in the context of the full model (i.e., with all 3 conceptual blocks entered into the equation). * Overall R^2 (%) after adding each conceptual block and accompanying p value for the test of the overall R^2. ** Incremental R^2 change due to the addition of the conceptual block and accompanying p value for the test of the incremental R^2 change. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; GHQ-12: 12-item General Health Questionnaire.

Stepwise regression analysis without successive conceptual categories. Stepwise regression analysis resulted in the inclusion of 4 variables: BASDAI, functional limitations in daily activities, membership in a patient association, and cervical stiffness. All 4 of these variables contributed to a significant change in R^2 ($p < 0.001$ for BASDAI, belonging to a patient association, and functional limitations in daily activities, and $p = 0.03$ for cervical stiffness, where p is the p value for a change test in R^2). Out of these variables, BASDAI was found to have remarkably more explanatory power (contribution to $R^2 = 0.875$; Table 6).

DISCUSSION

According to the data from the 2017 Atlas survey, 45.6% of patients with axSpA experience risk of mental disorders. Further, our study identifies several disease-specific factors associated with the risk of mental disorders. Among all factors, the most relevant is disease activity. Higher disease activity is associated with higher risk of mental disorders. In addition, other factors associated with risk of mental disorders are worse functional limitation in daily life, not belonging to a patient association, and a higher degree of cervical stiffness. Moreover, 28% of patients self-reported having a clinical diagnosis of anxiety and 21% of depression. Although the prevalence of anxiety and depression varied depending on the definition used, the prevalence of these diseases in our study lies within the published ranges: 11–64% for depression[8] and 16–20% for anxiety[14,15,16].

These findings are consistent with other evidence suggesting a relationship between disease activity and negative psychological factors associated with axSpA. This relationship has been proven to have a bidirectional character. On the one hand, it shows how negative psychological factors (depression, anxiety, passive coping style, insomnia, and negative affective states) explain the significant variability of disease activity when self-reported by patients, beyond what is explained by the clinical and demographic variables[17,18,19,20]. On the other hand, it is evident how

Table 6. Stepwise forward multivariate analyses of sociodemographic and disease status variables in relation to GHQ-12 (n = 474).

Step	Predictors	β-Weights	CI (95%)	Standard β-Weights	p	R^2 (%), p+*	ΔR^2 (%), p+**
1	BASDAI (0–10)	1.912	1.551, 2.274	0.562	< 0.001	0.875	0.875
2	Patient association membership	2.028	1.012, 3.044	0.161	< 0.001	0.883	0.008
3	Functional limitations (0–54)	0.112	0.053, 0.171	0.170	< 0.001	0.888	0.005
4	Cervical stiffness (1–4)	0.610	0.054, 1.166	0.080	0.032	0.889	0.001

Only values that were statistically significant in the bivariate analysis (or marginally significant: $p < 0.09$) were included in the analysis. All β-weights, 95% CI, and p values for individual variables were estimates derived in the context of the full model (i.e., with all 3 conceptual blocks entered into the equation). * Overall R^2 (%) after adding each conceptual block and accompanying p value for the test of the overall R^2. ** Incremental R^2 change due to the addition of the conceptual block and accompanying p value for the test of the incremental R^2 change. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; GHQ-12: 12-item General Health Questionnaire.

disease activity and functional limitation can explain some variability in patient mental health status (anxiety, depression, and insomnia)[7,16,21,22].

The high prevalence of risk of mental disorders found in our study is discouraging. Nevertheless, one must take into account that the identified factors associated with risk of mental disorders, especially the most influential (disease activity), are not fixed and can be modified with a more appropriate and intensive treatment strategy. Indeed, these results should encourage physicians to develop strategies for improving this situation during the coming years.

In the field of chronic disease, of great importance is an adequate assessment of the information given by patients in addition to their quality of life, because a patient's perspective can guide resource allocation, the design of interventions, and pharmacological treatment[23,24,25]. The results of our study add to the evidence supporting the relationship between disease status (disease activity, spinal stiffness), psychosocial factors (functional limitation in daily activities), and the mental health status of patients with axSpA. However, it is important to understand the mechanism underlying this type of relationship before considering how to use this knowledge in clinical practice. These findings also raise the question of whether a psychological intervention, perhaps directed at certain subgroups of patients, may be useful in the treatment of axSpA. In this context, there is some evidence as to the influence of certain psychological interventions on these pathologies, although they are more commonly observed in patients who have rheumatoid arthritis than those with axSpA[26,27,28,29].

This study has several limitations. First, the use of previously nonvalidated scales or indices for assessing certain factors, such as functional limitations in daily life and stiffness, should be thoroughly considered. The reason for using such scales or composite indices originated during the preliminary phase of the survey development, when patients expressed their concern about not being able to report all aspects of their disease if other scales or indices were to be used. In any case, a good Cronbach's alpha coefficient was obtained for the index used in our study, which testifies to the reliability of these instruments. Second, the bidirectional features of these relationships are another limitation of this study, because it is not possible to establish causality using this cross-sectional approach. In fact, it is difficult to assess whether the risk of mental disorders stems from the problems related to the disease, the underlying inflammatory processes, or other factors associated with this chronic pathology (spinal stiffness or functional limitations in daily life). Conclusions can only be drawn based on the relationship between variables. To establish a causality, it would be necessary to carry out longitudinal studies to evaluate over time the evolution of physical variables and their relationship to mental health or vice versa. Third, a possible overlap between GHQ-12 and the diagnosis of depression and anxiety cannot be completely excluded. However, the diagnosis of depression and anxiety in these respondents was made by a psychologist/psychiatrist based on clinical criteria, while GHQ-12 is a self-reported measure of the risk of mental disorders. The GHQ-12 values show the current risk of mental disorders during the survey period while the diagnoses of depression and anxiety referred to points in the past. Finally, the possible effect of biological therapy on depressive symptoms and mental health–associated quality of life could have influenced the results of our study.

The results of our study underscore the high prevalence of mental disorders in patients with axSpA and its clear association with disease status. About 1 of every 2 patients with axSpA reports risk of mental disorders. Further, this risk of mental disorders seems to be explained to a great extent by the degree of disease activity and to a lesser extent to such factors as the degree of functional limitation in daily life, cervical stiffness, and patient association membership. These findings highlight the benefit of rheumatologists promoting psychiatric evaluations of patients with high disease activity and risk of mental disorders. It is posited that this will contribute to a more integral treatment strategy.

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