Psychological Correlates of Self-reported Disease Activity in Ankylosing Spondylitis

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ABSTRACT. ***Objective.*** To investigate the role of psychological variables in self-reported disease activity in patients with ankylosing spondylitis (AS), while controlling for demographic and medical variables.

Methods. Patients with AS (n = 294) meeting modified New York criteria completed psychological measures evaluating depression, resilience, active and passive coping, internality, and helplessness. Demographic, clinical, and radiologic data were also collected. Univariate and multivariate analyses were completed to determine the strength of the correlation of psychological variables with disease activity, as measured by the Bath AS Disease Activity Index (BASDAI).

Results. In the multivariate regression analysis, the psychological variables contributed significantly to the variance in BASDAI scores, adding an additional 33% to the overall R-square beyond that accounted for by demographic and medical variables (combined R-square 18%). Specifically, arthritis helplessness and depression accounted for the most significant portion of the variance in BASDAI scores in the final model.

Conclusion. Arthritis helplessness and depression accounted for significant variability in self-reported disease activity beyond clinical and demographic variables in patients with AS. These findings have important clinical implications in the treatment and monitoring of disease activity in AS, and suggest potential avenues of intervention. (First Release Feb 15 2010; J Rheumatol 2010;37:829–34; doi:10.3899/jrheum.090476)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS DISEASE ACTIVITY PSYCHOSOCIAL FACTORS

Ankylosing spondylitis (AS) is a chronic inflammatory arthritis that characteristically affects the axial skeleton and sacroiliac joints. Pain, stiffness due to inflammation, and decreased physical function are the hallmarks of this disorder, and can have a profound impact on patients' quality of life, in terms of physical, mental, and social well-being[1]. Patient-reported disease activity, identified by standardized assessment tools, is increasingly used to guide therapeutic management[2,3].

Data from inflammatory arthritides such as rheumatoid arthritis (RA) show that psychological factors influence symptom-reporting. Depression, helplessness, and poor coping strategies contributed significantly to heightened perceptions of pain in patients with RA[4,5]. In addition, pain and depressive symptoms, compared to radiographic damage or disease activity, were found to be major determinants of patient perception of disease burden in 1 large RA cohort[6]. Other research has shown that arthritis severity ratings predicted only 13% of the variance in pain, while psychological factors contributed an additional 41% of the variance in another group of patients with RA[7]. In contrast, evidence for the contribution of demographic and medical variables to pain in chronic arthritic conditions has been less consistent[8-12]. These findings demonstrate the importance of examining the joint contribution of medical and psychological factors to self-reported outcomes in arthritis.

Although the independent relationship between psychological variables and self-reported disease activity has been studied extensively in RA, similar studies in AS are lacking. The only study on this subject reported that anxiety, depression, and internality were significantly associated with disease activity and functional impairment in a sample of 110 patients with AS[13]. However, that study did not incorporate

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a final model that examined the role of psychological factors in disease activity, controlling for demographic and clinical variables.

Our primary objective was to investigate the psychological correlates of disease activity in a large AS cohort. We hypothesized that psychological factors would predict a significant portion of the variance in patient perception of disease activity, beyond what could be predicted on the basis of important demographic and medical variables alone.

MATERIALS AND METHODS

Patients. Study participants were recruited from the Prospective Study of Outcomes in Ankylosing Spondylitis (PSOAS), a longitudinal study of patients with AS enrolled at 4 US study sites: Cedars-Sinai Medical Center, Los Angeles, CA; the National Institutes of Health, Bethesda, MD; the University of Texas Medical School at Houston, TX; and the University of California, San Francisco. Patients enrolled in previous clinical studies at these sites were invited to participate, as well as patients in academic rheumatology clinics at these sites. Others were recruited through Internet advertisements. Patients' written consent was obtained according to the institutional review board specifications. All patients over the age of 18 years who met the modified New York criteria for definitive AS were enrolled[14]. The modified New York criteria consist of radiographic criteria (sacroiliitis = grade 2 bilaterally or grade 3 unilaterally) and clinical criteria (low back pain more than 3 months that improves with exercise but not with rest; limitation of movement in the lumbar spine or chest wall). For the definitive diagnosis of AS, 1 radiographic criterion and at least 1 clinical criterion have to be fulfilled. Age younger than 18 years and unwillingness to participate in genetic studies of AS were the only exclusion criteria.

Study design. The study was a cross-sectional evaluation of the baseline patient characteristics in the PSOAS cohort. We are currently collecting the longitudinal data that will be the subject of a future study. Baseline assessments completed at each academic study site included medical history, sociodemographic information, and psychological status, as well as radiographs of the pelvis, lumbar spine, and cervical spine. All radiographs were completed within 1 year of the cross-sectional survey.

Primary outcome. Measurement of disease activity was conducted using the Bath AS Disease Activity Index (BASDAI)[15]. The BASDAI is a self-report 6-item questionnaire in which patients rate the 5 major symptoms of AS, including fatigue, spinal and peripheral joint pain, tender points, and morning stiffness, over the past week using a 10 cm visual analog scale, from none (0 mm) to very severe (100 mm). The final question quantifies the amount of morning stiffness, from 0 to 2+ hours, over the past week. The scores for questions 5 and 6 are averaged first, and the resulting value is averaged with the scores of the other 4 questions, with lower scores indicating less disease activity.

Independent variables. Our database includes variables from the following domains: socioeconomic-demographic, immunologic, genetic, psychological, and clinical.

Sociodemographic information included age (at cross-sectional study baseline), education level (≤ 12, 13–15, 16, and > 16 years), ethnicity (white vs other), current employment, student status, and tobacco use as binary outcome measures.

Medical variables consisted of an inflammatory marker [C-reactive protein (CRP)], number of patient-reported medical comorbidities (0 to ≥ 4), current nonsteroidal antiinflammatory drug (NSAID) use and biologic therapy (yes vs no), disease duration (at time of cross-sectional survey), and radiographic score. Each participant had baseline radiographs of the pelvis (anterior-posterior), lumbar spine (anterior-posterior and lateral), and cervical spine (lateral), which were scored using the Bath AS Radiographic Index Global (BASRI-global) by a single musculoskeletal radiologist. The BASRI-global is a validated method to score radiographic severity in AS, with a range of scores of 1.5 to 16[16].

Six psychological variables were measured: active and passive coping, depression, resilience coping, helplessness, and internality. The Vanderbilt Pain Management Inventory (VPMI) is an 18-item self-report questionnaire that assesses the frequency of utilization of coping strategies in patients with chronic pain when their pain is at a moderate level of intensity or greater. The VPMI has 2 internally reliable and validated subscales: active coping and passive coping[4]. Active coping measures the tendency of patients to control pain (e.g., relaxation, distraction) and to function in spite of pain, while passive coping involves patients' use of such strategies as lying down, taking pain medication, or avoiding activity. In patients with RA, Brown and Nicassio[4] showed that active coping was associated with less pain, disability, and psychological distress, and that passive coping, in contrast, was correlated with greater pain, disability, and psychological distress. The Patient Health Questionnaire (PHQ-9) is a brief 9-item self-report instrument that is a well validated and widely used diagnostic and severity measure for depression. The PHQ-9 score can range from 0 to 27, as each of the 9 items can be scored from 0 (not at all) to 3 (nearly every day), and the scale consists of the actual criteria upon which the diagnosis of DSM-IV depression is made[17-19]. It is recommended for use with medical patients since PHQ-9 items have little overlap with physical symptoms. Scores ≥ 10 have high sensitivity in detecting depressive disorder in either community or medical populations[20]. The Brief Resilient Coping Scale (BRCS) is a 4-item self-report scale that measures patients' ability to feel challenged by, and cope adaptively, with adversity. BRCS scores can range from 0 to 20, higher scores indicating higher resilience[21]. The Arthritis Helplessness Index (AHI) is a 15-item self-report questionnaire designed to measure a patient's perceptions of loss of control in association with their chronic arthritis[22]. We used the 2 subscales of the AHI [internality (7 items) and helplessness (5 items)], which reflect separate structures confirmed through factor analysis and have been found to have greater reliability and validity than the total AHI score[23]. Arthritis internality assesses patients' beliefs that their own behavior can control their arthritis, while arthritis helplessness assesses patients' beliefs that they are helpless in the face of arthritis, reliant on others, and unable to manage their pain.

Statistical analysis. We conducted the data analysis in 4 steps. First, descriptive statistics were computed on our study cohort (Table 1). Second, we completed univariate linear regression analyses to evaluate which independent variables were associated with the BASDAI (Table 2). Then we examined associations between the BASDAI, and demographic, biologic, and psychologic factors using hierarchical regression modeling (Table 3). In order to analyze the contribution of these variables to BASDAI scores, we entered the variables in successive conceptual blocks: demographic variables, biologic variables, and psychological measures. This order of entry tested whether psychological factors would contribute unique variance to AS disease activity independently of demographic and biologic variables. Subsequently, a final model was established using a forward hierarchical variable selection strategy. This approach was chosen to decrease the effect of multicolinearity in our analysis. Initially we entered all variables into the model. Then the number of independent variables was reduced to those that changed the R-square of the entire model by 2% or more. Those variables were entered into the final model (Table 4). Two-sided p values < 0.05 were considered significant. The analyses were performed utilizing the NCSS 2007 statistical program (NCSS, Kaysville, UT, USA).

RESULTS

Sample characteristics. A total of 294 patients were included in the study. Table 1 shows patient demographics and medical and psychological testing scores. The mean age of the sample was 45.1 (± 14.40) years, 68% of the cohort were male, and 82% of the sample were white. The mean disease duration at study baseline was 21.23 (± 13.85) years, and

Table 1. Demographic, medical, and psychological characteristics of study sample.

Characteristic	n = 294
Demographic	
Mean age (SD), yrs	45.1 (14.40)
Mean education level, yrs (1–5) (SD)	3.7 (1.26)
Male, n (%)	197 (68.2)
White, n (%)	241 (82.0)
No. employed (%)	192 (65.5)
No. students (%)	26 (8.9)
No. smokers (%)	32 (11.0)
No. married (%)	153 (55.8)
Medical	
Mean no. medical comorbidities (0–4) (SD)	2.0 (1.34)
Current NSAID use, (%)	136 (46.6)
Current biologic use, (%)	132 (45.2)
Mean C-reactive protein, mg/dl, (SD)	0.9 (1.79)
Mean disease duration, yrs (SD)	21.2 (13.85)
Mean BASRI score (1.5–16) (SD)	6.5 (4.27)
Psychological	
Mean resilience coping (BRCS) score (0–20) (SD)	16.1 (3.33)
Mean arthritis internality score (6–36) (SD)	25.7 (5.94)
Mean arthritis helplessness score (5–25) (SD)	12.4 (4.41)
Mean depression (PHQ-9) score (0–27) (SD)	5.1 (5.01)
Mean active coping score (7–35) (SD)	22.7 (5.22)
Mean passive coping score (11–55) (SD)	25.6 (7.45)

NSAID: nonsteroidal antiinflammatory drug; BASRI: Bath Ankylosing Spondylitis Radiographic Index; BRCS: Brief Resilient Coping Scale; PHQ: Patient Health Questionnaire.

Table 2. Univariate analyses of demographic variables, medical variables, and psychological variables in relation to BASDAI.

Predictors	ß Weights	95% CI	p
Age	0.05	–0.07 to 0.17	0.391
Education	–0.17	–0.28 to –0.05	< 0.001
Sex (male)	–0.18	–0.29 to –0.06	< 0.001
Ethnicity (white)	–0.08	–0.20 to 0.03	0.157
Employment (yes)	–0.19	–0.31 to –0.08	< 0.001
Student (yes)	0.01	–0.10 to 0.13	0.820
Smoking (yes)	0.14	0.03 to 0.26	0.015
Married (yes)	–0.01	–0.13 to 0.11	0.825
No. medical comorbidities	0.08	–0.04 to 0.19	0.200
NSAID use	0.21	0.09 to 0.32	< 0.001
Biologic use	–0.08	–0.20 to 0.03	0.160
C-reactive protein	0.11	–0.004 to 0.23	0.060
Disease duration	0.03	–0.08 to 0.15	0.578
Bath AS Radiographic Index	0.005	–0.13 to 0.14	0.965
Resilience coping	–0.11	–0.22 to 0.01	0.068
Arthritis internality	–0.36	–0.47 to –0.26	< 0.001
Arthritis helplessness	0.53	0.43 to 0.62	< 0.001
Depression (PHQ-9)	0.58	0.48 to 0.67	< 0.001
Active coping	–0.06	–0.18 to 0.06	0.552
Passive coping	0.47	0.36 to 0.57	< 0.001

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; NSAID: nonsteroidal antiinflammatory frug; PHQ: Patient Health Questionnaire.

less than half of the sample was taking NSAID and/or biologics, 47% and 45%, respectively. The time between enrollment and radiographic examination was relatively short (63 ± 158 days), and the majority of patients (58%) had undergone radiographic examination on the day of enrollment. Participants reported a high level of resilient coping (mean score 16.09, ± 3.33) and relatively low depression scores (mean score 5.14, ± 5.01). Thus, the preponderance of the sample fell below the depressive disorder cutoff. The mean score for arthritis internality was 25.66 (± 5.94), for helplessness 12.42 (± 4.41), for active coping 22.74 (± 5.52), and for passive coping 25.59 (± 7.45). The latter scores are all within 1 SD of mean scores obtained from samples of patients with RA[4,23] and osteoarthritis[24] on these measures.

Measures. Indices of psychological variables (i.e., VPMI, AHI, PHQ-9) and measures of disease-related activity and function [i.e., BASDAI and the Bath AS Functional Index (BASFI)] demonstrated adequate internal consistency reliability in the sample. Active and passive coping subscales of the VPMI yielded Cronbach's alpha coefficients of 0.77 and 0.83, respectively. Cronbach's alphas for the internality and helplessness subscales of the AHI were 0.66 and 0.70, respectively. These values closely parallel those reported in initial psychometric studies of the scales[4,23]. The PHQ-9 yielded a Cronbach's alpha of 0.87. Finally, Cronbach's alphas for the BASDAI and BASFI were 0.92 and 0.95, respectively.

Univariate analyses. The univariate regression analysis found the following variables to be significantly associated with the higher BASDAI scores: female sex, lower education level, unemployment, tobacco and NSAID use, high passive coping, low internality, high helplessness, and high depression. The other variables examined, including age, ethnicity, marital and student status, current use of biologic therapy, medical comorbidities, inflammatory markers, disease duration, radiographic scores, and active and resilience coping did not correlate significantly with BASDAI scores (Table 2).

Hierarchical modeling with successive conceptual blocks. In order to determine the variance of the BASDAI scores, the independent variables were added into the analysis in the following successive conceptual blocks: sociodemographic variables, medical variables, and psychological variables. The contribution of the demographic variables accounted for an overall R-square of 0.14 ($p < 0.001$). Female sex ($p < 0.001$), unemployment ($p < 0.001$), low education ($p = 0.035$), and smoking ($p = 0.006$) contributed independent variability to BASDAI scores. The addition of the medical variables, including NSAID and/or biologic therapy, BASRI scores, medical comorbidities, CRP, and disease duration, did not result in a significant increase of R-square ($p = 0.814$). The overall R-square of the model for the demographic and clinical variables was 0.18 ($p < 0.001$). Only 1

Table 3. Hierarchical multivariate analysis of demographic, medical, and psychological variables in relation to BASDAI. All ß-weights, confidence intervals, and p values for individual variables are estimates in the context of the full model (i.e., with all 3 conceptual blocks entered into the equation). R-square is overall-r-square (%) after the addition of each conceptual block and accompanying p value for the test of the overall R-square. R-square value in last column is the incremental R-square change due to the addition of the conceptual block and accompanying p value for the test of the incremental R-Square change.

Step	Predictors	ß Weights	95% CI	p	R^2 (%) (p+)	ΔR^2 (%) (p+)
1	Demographics				13.8 (< 0.001)	
	Age	0.15	–0.06 to 0.36	0.157		
	Employment	–0.13	–0.26 to 0.01	0.061		
	Sex	–0.08	–0.20 to 0.04	0.186		
	Marital	0.06	–0.06 to 0.19	0.330		
	Education	–0.03	–0.16 to 0.09	0.597		
	Smoking	0.02	–0.10 to 0.14	0.748		
	Student	–0.03	–0.18 to 0.12	0.737		
	Ethnicity	–0.13	–0.25 to –0.01	0.034		
2	Medical variables				18.1 (< 0.001)	4.3 (0.814)
	NSAID therapy	0.11	–0.01 to 0.23	0.076		
	BASRI	0.01	–0.13 to 0.14	0.901		
	Biologic therapy	–0.02	–0.14 to 0.09	0.726		
	No. medical comorbidities	–0.08	–0.21 to 0.05	0.203		
	CRP	–0.07	–0.19 to 0.05	0.236		
	Disease duration	–0.02	–0.21 to 0.17	0.811		
3	Psychological variables				51.4 (< 0.001)	33.3 (< 0.001)
	Arthritis internality	–0.19	–0.32 to –0.06	0.005		
	Arthritis helplessness	0.16	0.02 to 0.31	0.029		
	BRCS	0.08	–0.04 to 0.19	0.203		
	Depression (PHQ-9)	0.34	0.19 to 0.49	< 0.0001		
	Active coping	0.11	–0.01 to 0.24	0.072		
	Passive coping	0.16	0.02 to 0.29	0.027		

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; PHQ: Patient Health Questionnaire; BASRI: Bath Ankylosing Spondylitis Radiographic Index; CRP: C-reactive protein; BRCS: Brief Resilient Coping Scale; PHQ: Patient Health Questionnaire.

Table 4. Final model of correlates of the BASDAI.

Independent Variable	ß Weight	95% CI	R-square (%)	p
Overall model			39.5	< 0.0001
Arthritis helplessness	0.31	0.20–0.42		< 0.0001
Depression (PHQ)	0.40	0.29–0.51		< 0.0001

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; PHQ: Patient Health Questionnaire.

medical variable, current use of NSAID ($p < 0.001$), was significantly related to BASDAI scores. The other variables, including inflammatory markers, disease duration, and radiographic damage scores, did not reach statistical significance. Finally, the entry of arthritis internality, helplessness, resilient coping, depression, active coping, and passive coping resulted in an R-square of 0.51 ($p < 0.001$). Higher depression, helplessness, passive coping, and lower internality had significant, independent associations with BASDAI scores ($p < 0.001$, 0.030, 0.005, and 0.027, respectively), while the contribution of active coping ($p = 0.072$) and resilience coping ($p = 0.203$) fell short of significance. The psychological variables contributed significantly to the overall variance, adding an additional 33% variance above that accounted for by demographic and medical variables ($p = 0.001$; Table 3).

Final model. The hierarchical forward model found that higher helplessness ($p < 0.001$) and depression (PHQ-9; $p < 0.001$), were significantly associated with higher BASDAI scores (Table 4). These 2 variables explained 39% of variance in BASDAI scores. More specifically, each numerical increase in depression (range of scores 0–27, higher numbers equaling more depression) resulted in an increase of 0.19 in the BASDAI score (scale 0–10 cm), and each numerical increase in the arthritis helplessness score (range of scores 5–25, higher scores indicating more helpless behavior) resulted in an increase of 0.16 in the BASDAI score. All demographic and biologic factors we investigated failed to explain a significant portion of the variance of BASDAI scores in the final model. Inspection of the variance inflation factor did not suggest multicolinearity among predictors in the resulting model.

DISCUSSION

Our study found that psychological variables, specifically

arthritis helplessness and depression, account for significant variability in self-reported AS disease activity. The contribution of medical variables to disease activity was negligible, as NSAID and/or biologic use, radiographic findings, disease duration, and inflammation measurements did not account for the independent variance seen in BASDAI scores.

Univariate regressions revealed that low education, unemployment, female sex, and tobacco use correlated with higher disease activity. High helplessness, low internality, depression, and passive coping also were related to higher BASDAI scores. When hierarchical multiple regression analysis was conducted to examine whether psychological variables would contribute to self-reported disease activity after controlling for sociodemographic and medical variables, it was seen that higher depression, helplessness, and passive coping scores, as well as lower internality scores, continued to be related to higher disease activity, while resilience and active coping did not reach significance. Depression and helplessness had the strongest relationship with the perceived disease activity of all the variables (demographic, biologic, and psychological) in the final model, accounting for 39% of the variance in BASDAI scores. While PHQ-9 (depression) scores were low in this sample, depression correlated closely with disease activity. Arthritis helplessness showed the same association with the investigated outcome. It is particularly noteworthy as this was robust after controlling for all other sociodemographic, medical, and psychological variables. This finding converges with results of studies of patients with RA and systemic lupus erythematosus that have demonstrated a significant association between indices of disease activity and mood disturbance[4,25]. In addition, the relationship between helplessness and higher disease activity has been confirmed in research in other arthritis populations[22,25,26]. The association between depression and self-reported AS disease activity may reflect a common underlying biological process or the effect of the disease itself. This is an intriguing question for future research that has major ramifications for the clinical management of patients with this condition.

Although it was surprising that the clinical markers, including disease duration, radiographic scores (BASRI scores), and systemic markers of inflammation, were not associated with the BASDAI in this study, it is well known that inflammatory markers often do not parallel disease activity in AS, and the correlation of disease damage with radiographic progression is still unclear[27-30].

Alternatively, self-reports of AS disease activity may not directly reflect underlying biological dysfunction, but rather the perceptions of patients regarding their symptomatology on an everyday basis. This may partly explain the significant relationship between BASDAI scores and psychological variables in this study. Self-reports are critical, however, because they lead to medical help-seeking and influence treatment decision-making. Their economy and brevity enhance their value in clinical situations and reflect a growing trend in the importance of patient-reported outcomes in the field of arthritis care[31-36]. However, our findings also highlight the need for the development of instruments that capture the complexity of disease activity in AS and include more objective measurements.

The primary limitation of our study was its cross-sectional design, which provided only correlational findings. It cannot be determined from our data whether higher depression scores caused a heightened perception of disease activity or vice versa. A longitudinal study, in which patients' depression and disease activity are monitored over time, is needed to determine directionality, as higher helplessness and depression could be driving BASDAI or vice versa.

We found that helplessness and depression accounted for significant variability in perceived AS disease activity in a cross-sectional study sample. This is the first study to highlight the importance of psychological factors in shaping patients' perceptions of disease activity in AS, above and beyond that explained by important demographic and biologic variables. It is noteworthy that only helplessness and depression, not internality or passive, active, or resilience coping, accounted for significant variability in the final model, showing that such associations do not apply across a broad range of psychological measures. Further, and perhaps more importantly, the medical variables including CRP, radiographic severity, disease duration, and therapeutics did not have an association with the patient- reported disease activity in the final model. Therefore, interpretation of disease status, as measured by the BASDAI, might need to occur in the context of evaluating the patient's psychological status. These findings have important clinical implications in the treatment and monitoring of disease in AS. Psychological screening would help to identify patients with AS who might benefit from the addition of psychosocial interventions to complement their medical therapy.

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