Disease and Psychological Status in Ankylosing Spondylitis

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Objectives. **Psychological factors may be important in the assessment and management of ankylosing spondylitis (AS). Our primary objective was to describe associations between disease and psychological status in AS, using AS-specific assessment tools and questionnaires. Our secondary objectives were to identify patient subgroups based on such associations and to determine the stability of the measures over time.**

Methods. **One hundred and ten patients were assessed at 6-monthly intervals up to 4 times using tools to measure disease (BASDAI, BASFI, BASMI), psychological (HADS, HLC-C) and generic health (SF-36) status. Data were stored and analysed in SPSS and Stata.**

Results. **Eighty-nine participants completed all 4 assessments. Throughout the study, BASDAI, BASFI and BASMI scores correlated significantly with anxiety, depression, internality and health status, but not with levels of belief in chance or powerful others. Clinically anxious or depressed subgroups had significantly worse BASDAI and BASFI, but not BASMI, scores. BASMI scores were least closely linked to psychological status. Mean scores for disease, psychological and health status were clinically stable over the 18 month period.**

Conclusions. **Disease status scores in AS correlated significantly with anxiety, depression, internality and health status. Interpretation of AS disease scores should take account of psychological status and the choice of measures used. These findings have important potential applications in AS management and monitoring, including the identification of patients for biologic therapies.**

KEY WORDS: Ankylosing spondylitis, Psychological status, Disease assessment, Clinical monitoring.

Ankylosing spondylitis (AS) is a chronic inflammatory disease that characteristically affects the sacroiliac joints and spine. Key features include enthesitis, fibrosis, bony ankylosis [1] and genetic susceptibility determined predominantly by the HLA B27 allele [2]. Clinical management focuses upon symptom relief and maintenance of posture and function, although recent trials of anti-TNFα □therapy [3, 4, 5, 6] have demonstrated strong potential for significantly improving the efficacy of medical treatment.

The major impact of AS on overall health and activity raises the possibility that psychological factors may influence disease status and outcome. If true, this would have important implications for both assessment and management of AS. The potential relevance of this to clinical practice is suggested by studies in other chronic diseases, including back pain [7, 8, 9], as well as by previous studies in AS. For example, Barlow *et al.* found that about one third of AS patients reported symptoms of depression [10] and that features of depression, high internal locus of control and low reliance on powerful others were common amongst AS patients attending a UK self help group [11]. Gunther *et al*. [12] characterised coping behaviour of AS males as "playing down" stressful situations, and found that use of such coping strategies was independent of disease duration, whilst Hidding *et al*. [13] found that self-reported health status was more strongly related to personality traits, particularly neuroticism, than to levels of disability. Such findings highlight the need to determine the relationships between disease and psychological status in AS in order to inform clinical assessment and management, as well as to inform selection and monitoring of AS patients for biologic therapy.

The primary objective of the study reported here was to describe associations between disease and psychological status in a large group of AS patients. The secondary objectives were to identify patient subgroups based on such associations and to determine the stability

of disease and psychological scores in this group over 18 months. This is the first study to utilise a longitudinal approach to address this issue, thereby enabling the consistency of the measures and associations over time to be determined.

Patients and methods

Study participants

Patients with AS, diagnosed according to the Modified New York criteria [14], who were regularly attending the AS Review Group at Wrightington Hospital, Lancashire, UK were invited to participate. Patients with recent serious illness or pregnancy were excluded from the study. From April 2002, appointments for routine review were sent out according to established practice and included an invitation to participate in the study. Consent to participate was sought until 110 patients were recruited. Patients' written consent was obtained according to the Declaration of Helsinki. Ethical approval was obtained both from the Wrightington, Wigan and Leigh Local Research Ethics Committee and the University of Central Lancashire Ethics Committee.

Study design

Baseline assessment of clinical and psychological measurements was completed at recruitment. Patients were then sequentially reassessed at 6-monthly intervals until 3 further assessments had been completed. Other demographic data, such as current work status including retirement on medical grounds and marital status, were also collected at baseline via a self-completion questionnaire. Co-existent disease (including iritis, psoriasis, inflammatory bowel disease), date of birth, age of onset and age of diagnosis were retrieved from the patients' records. If age of disease onset was not available from the records, this

was obtained via patient self-report at baseline. Disease duration was obtained by subtracting age of onset from the age at recruitment into the study.

Assessment tools for clinical status

Measurements of disease status were conducted using the Bath Ankylosing Spondylitis Functional Index (BASFI) [15], the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [16], and the Bath Ankylosing Spondylitis Metrology Index (BASMI) [17]. The BASDAI is scored using a 10 cm visual analogue scale (VAS) for each of five major symptoms over the past week. The individual scores are averaged to form a 0-10 scale, with lower scores indicating less active disease. The BASFI comprises 10 items on ability to perform and cope with activities of daily living, each scored on a 10 cm VAS reflecting status over the past month. The mean of the 10 scales generates the score, with 10 denoting worst possible functional status. The BASDAI and BASFI assessment tools were all self-completed in the clinic without significant assistance from staff. BASMI assessments were performed by 2 senior physiotherapists rigorously-trained in this method and working closely together on this project. The BASMI assesses cervical rotation, tragus to wall distance, lumbar side flexion, lumbar flexion (modified Schober's test) and intermalleolar distance. Measurements for the 5 domains are integrated to provide an overall score between 0 and 10, with lower scores indicating better range of spinal movement.

Assessment tools for psychological and health status

Psychological status was measured using 3 questionnaires, all presented within a booklet. The Hospital Anxiety and Depression Questionnaire (HADS) [18] is a 14 item self-report measure of anxiety and depression. Seven questions assess anxiety and seven questions assess depression. All items are scored on a 4 point scale from 0-3. Each domain is scored

separately with a possible maximum score of 21, and the higher the score, the higher the level of either anxiety or depression respectively. The Health Locus of Control – Form C Questionnaire [19] is a questionnaire relating to beliefs concerning back problems. It provides a measure of the level of perceived control which people have over their health, their beliefs about external control of health by powerful others (for example, health professionals) and their beliefs about the influence of chance, luck or fate over health. The score is calculated according to levels of agreement (1 = strongly disagree; 6 = strongly agree) with 24 statements about belief in chance, belief in powerful others, and internality. The scores obtained from the statements relevant to each of these 3 areas are summed to form domain totals with a possible range of 8-48.

Generic health status was measured using the Short Form (SF)-36 questionnaire [20], which measures 8 multi-item dimensions: physical functioning (10 items), role limitations due to physical problems (4 items), role limitations due to emotional problems (3 items, social functioning (2 items), mental health (5 items), energy/vitality (4 items), pain (2 items), and general health perception (5 items). For each dimension item scores are coded, summed and transformed on a scale from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state).

Statistical analysis

Data were stored and analyzed in SPSS (Release 12), with further analysis performed in Stata (Release 6). Analysis was performed on those completing all four assessments. The stability of each outcome measure over time was investigated using repeated measures ANOVA [21]. The Huynh-Feldt correction for non-sphericity [22] was used to obtain p-values. Relationships between pairs of measures of disease (BASDAI, BASFI, and BASMI), psychological and generic health status, age and disease duration were assessed using

Spearman's rank correlation coefficients. Partial Spearman's rank correlations were also computed to assess the whether any relationships found between disease or psychological status and age (disease duration) remained when controlled for disease duration (age). Based on data collected at enrolment, subgroups were defined by: presence / absence of iritis and presence / absence of psoriasis. Subgroups were also formed at each assessment point based on anxiety and depression scores. Based both on previous work [23] and on current use of the HADS in clinical settings, scores of 11 were used as a threshold to define clinically-anxious and depressed subgroups.. Between-group differences in outcomes on interval scales were analysed using independent-samples t-tests, using its approximate form when group variances appeared different. Characteristics potentially associated with study non-completion were assessed using independent-samples t-tests for characteristics measured on an interval scale and the Fisher's exact test otherwise. Tests resulting in p-values less than 0.05 were classed as statistically significant. The sensitivity of findings to parametric assumptions was assessed when these were in doubt. The sensitivity to exclusion of those not completing all assessments was also investigated.

Results

Characteristics of the study participants

Eighty-nine (74 men, 15 women) of the 110 participants (80.9%) completed all 4 assessments. Reasons for non-completion were: non-attendance (13), myocardial infarction (2), incomplete fulfilment of AS diagnostic criteria (3), and incomplete data recording (3). Among the 89 study completers, median age was 50 years (inter-quartile range [IQR] 38.5-55.5, range 18-77), median age of reported disease onset was 25 years (IQR 18-33, range 9-58), giving median duration of disease as 18 years (IQR 13-27, range 2-50), and median age of diagnosis was 35 years (IQR 25.3-43, range 12-59). Eight people had co-existent

inflammatory bowel disease, 41 had previous iritis and 14 had clinically mild or moderate psoriasis. Forty-eight participants worked full or part-time, 41 were unable to work or unemployed. Seventy participants were married, 4 divorced and 15 single, of whom 6 were living alone.

Disease, psychological and health status over the study period

Mean (SD) scores for each measure for the 89 study completers are shown in Tables 1a and 1b. Overall, mean scores for disease and psychological parameters over the study period were relatively stable, although there was a statistically significant (p = 0.002) effect of time on mean anxiety score. This effect was due to a lower mean anxiety score at assessment 1, with mean scores at assessments 2, 3 and 4 being very similar to each other, and the significance of this finding is therefore unclear. The mean (SD) scores for each SF-36 domain for the first assessment were: Physical functioning 57.6 (31.2); Role limitation due to physical function 34.4 (26.8); Role limitation due to emotional problems 25.0 (27.7); Social functioning 58.9 (26.2); Mental health 54.5 (18.4); Energy and vitality 36.4 (19.5); Pain 47.2 (26.2); General health perception 45.9 (26.2); and, Change in health 47.9 (15.5). Scores for most SF-36 domains were stable throughout the study (results not shown), although scores of physical functioning declined approximately linearly (p=0.017) to 53.5 (32.1) by the end of the study.

Disease status associations with anxiety and depression

BASDAI, BASFI and BASMI scores correlated quite strongly with anxiety scores at all assessment points, although for BASMI scores the levels of correlation were lower than for BASDAI and BASFI (Table 2). Using HADS scores of 11 or more as a threshold, mean BASDAI and BASFI, but not BASMI, scores were significantly higher in anxious subgroups

(Table 3). Higher levels of depression were quite strongly associated with worse disease status, with correlations lowest for BASMI compared to BASDAI and BASFI scores (Table 2). Using HADS scores of 11 or higher to identify clinically-depressed subgroups, mean BASDAI and BASFI, but not BASMI, scores were significantly higher than in non-depressed subgroups (Table 3).

Disease status associations with internality, belief in chance and belief in powerful others

BASDAI scores consistently showed a negative, albeit relatively weak, correlation with internality and the same generally applied to BASFI and BASMI scores, showing that worse disease activity, function and movement were associated with lower internality (Table 2). At each of the four time points, internality showed similarly significant but relatively weak correlations with anxiety (r_s ranging from -0.27 to -0.41; all $p<0.015$) and with depression (r_s ranging from -0.26 to -0.33; all $p<0.015$). There was no consistent correlation between the strength of belief in chance or powerful others and any of the disease status scores (Table 2), and there was no significant correlation between these parameters and either anxiety or depression scores (results not shown).

Disease status and generic health status

BASDAI, BASFI and BASMI scores correlated significantly with all SF-36 domain scores except change in health throughout the course of the study (results not shown).

Effects of co-existent iritis or psoriasis

There were no significant differences in disease or psychological scores between those with (n = 41) and those without (n = 48) a history of iritis, and anxiety and depression scores correlated significantly and moderately strongly with BASDAI, BASFI and BASMI scores

in both subgroups (results not shown). Likewise, although analysis of the effects of co-existent psoriasis was limited because there were only 14 people in the psoriatic subgroup, all of whom had clinically-mild or moderate psoriasis, no significant differences in either disease or psychological status between subgroups with or without psoriasis were found (results not shown).

Effects of age, disease duration and gender

BASMI and BASFI scores were significantly, but relatively weakly, correlated with age, whereas no consistent correlation was observed between age and any of BASDAI, anxiety, depression and internality (results not shown). Furthermore, correlations of disease and of psychological status scores with disease duration at the beginning of the study were all negligible and non-significant (results not shown),. Moreover, the rank correlation coefficients of BASMI and BASFI scores with age remained significant and of similar magnitude on controlling for disease duration (results not shown), indicating that the higher BASMI and BASFI scores in older participants were not simply a reflection of longer disease duration. Analysis of gender effects was constrained by the small number of female (n=15) participants. However, there were no consistently significant differences between males and females in any disease status or psychological scores, whilst anxiety and depression scores consistently and significantly correlated with disease status scores in both sexes (results not shown). Nevertheless, at each time point, the relationships between BASMI and each of anxiety and depression scores appeared consistently stronger in females (r_s ranging from 0.65 to 0.86) than in males (r_s ranging from 0.26 to 0.47).

Although the distributions of anxiety and, particularly, depression scores were highly skewed, none of the between-group comparisons was sensitive to the assumption of normality.

Characteristics of participants who did not complete study

Baseline disease status and psychological scores for the 21 participants (12 men, 9 women) who did not complete 4 assessments were not significantly different on any measure between those who did and those who did not complete the study, although women were significantly more likely than men not to complete all assessments (p=0.017). Additionally, all participants with either bowel involvement or psoriasis, and 41 of 47 (87.2%) with iritis, completed all assessments. Inclusion of these 21 individuals for the analysis of the assessment one results did not materially alter any of the findings described above.

Discussion

Following the recent development of tools for measuring AS disease status [15, 16, 17, 24, 25] it has become feasible to investigate the impact of psychological status on AS. The primary objective of our study was to describe associations between disease and psychological status in AS, using AS-specific assessment tools and questionnaires. Our results have implications for clinical assessment as well as for clinical management in AS.

We found that BASDAI, BASFI and BASMI scores correlated significantly with anxiety, depression and internality scores, but not with levels of belief in chance or powerful others. These findings are consistent with other chronic conditions, such as low back pain [26, 27, 28], and demonstrate clearly that disease status and some (but not all) psychological factors are closely linked in AS. It would be important to understand better the underlying basis of these associations before considering how this knowledge might be utilised in clinical practice, for example, to extend current assessment protocols to incorporate psychological assessments. Our findings also raise the question of whether psychological interventions,

perhaps targeted to particular patient subgroups, may have a useful role in AS treatment and management. However, the fact that we found no significant correlation between disease status and levels of belief in chance or powerful others shows that such associations do not apply broadly to all psychological measures. **Include a little more here on psychological differences between high people with internality scores and those with high belief in chance and powerful others scores – is this consistent with findings on other diseases? Why might this be the case?** More work is needed to identify other psychological characteristics which may be associated with AS disease status and to distinguish them from those which are not.

Our results showed that the 3 disease assessment tools differ markedly in the extent of their linkage with psychological status. Overall, BASMI scores correlated least strongly with psychological status. Similarly, whilst subgroups with clinical anxiety and/or depression had consistently worse BASDAI and BASFI scores, their BASMI scores were not significantly different from non-anxious or non-depressed subgroups. The reasons for these findings may be related to the fact that BASMI scores are derived from an assessment by trained metrologists (in our case, a physiotherapist) whereas BASDAI and BASFI scores are derived from self-completed questionnaires. Our findings are consistent with the possibility that self-report assessment tools may measure different facets of health status than tools which involve measurement by a clinician or metrologist. Whilst the issue of associations between disease scores with anxiety or depression scores has not previously been investigated in AS, the limited extent to which patient-reported measures may capture overall disease status in AS has been raised [24], and the potential for patients' psychological status to influence completion of a self-complete questionnaire has been highlighted [13, 29]. Clearly, BASMI scores would likely be less susceptible to such effects, and may therefore provide a more independent indicator of clinical disease status than BASDAI or BASFI scores.

We found no effect of co-existent mild / moderate psoriasis or iritis on disease or psychological status, and only 5 patients with psoriasis had significant peripheral joint involvement which is too few to determine whether they were more functionally impaired, as has been suggested by others [30]. Similarly, we found no evidence of an effect of gender or disease duration on either disease or psychological status, although such effects have been suggested in previous studies using retrospective or cross-sectional approaches [31-34]. However, in our study BASMI and BASFI (but not BASDAI) scores were significantly positively related to age, having controlled for disease duration, whereas no relationship was found between these disease status measures and disease duration itself.   This suggests that age rather than disease duration may influence disease status. Alternatively, BASMI and BASFI scores might increase with age alone irrespective of disease, and even though these tools are AS-specific it would therefore be important to determine the range of these scores in otherwise healthy older people in order to explain this.

Our group was recruited from the AS Review Group at Wrightington Hospital. We cannot exclude the possibility that the characteristics of patients who attend such groups may be substantially different from those who do not. However, mean BASDAI, BASFI and BASMI scores in our group were very similar to those in groups described in several previous studies [30, 31, 35, 36, 37], but, as would be expected, were generally lower than in groups participating in clinical trials of anti-TNFα therapy [3, 38, 39]. Nevertheless, the mean BASDAI scores for our group were consistently higher than 4 (Table1), indicating that many of these patients satisfied current criteria for persistently-active disease and would therefore be eligible for treatment with anti-TNFα therapy if this option were available here. Regarding the group's psychological status, normative data for anxiety and depression scores among healthy UK residents show mean (SD) HADS scores of 6.14 (3.76) for anxiety and 3.68 (3.07) for depression [40], and the reported incidence of clinical anxiety in

otherwise healthy people is 7%, rising to 33% among those with health complaints and 36% of people with back pain [23]. Similarly, clinical depression has been reported in 5%, 13% and 29% respectively of these groups. In our group, about 25% were clinically anxious and 15% clinically depressed, suggesting that, within the inherent limitations of comparing different groups in this way, there was no substantive bias in our assessment of psychological status.

We used a longitudinal study design in order to determine whether associations between disease and psychological status were consistent over time. Our results show not only that the associations between these measures were stable over the 18 month study period, but also that the mean scores for the study group as a whole were relatively consistent throughout the study. The analysis of the data presented here does not attempt to address variation in disease status over time at the level of individual patients. We are currently exploring this issue by analysing data from patients identified within the study group who showed demonstrable change in one or more disease measure over this time. A longitudinal approach was also used by others to annually monitor 74 patients attending an AS specialist clinic [30]. Although mean BASDAI scores were not significantly different at the beginning compared with the end of their 5-year study, final mean BASFI score was significantly higher than the initial score. However, this change did not necessarily result from progressive deterioration, since some scores actually improved from one year to the next. In contrast, we monitored patients only for 18 months and would need to considerably extend this time in order to fully compare findings from the two studies and to determine whether the disease and psychological scores remain stable over a longer period.

In summary, we found that BASDAI, BASFI and BASMI scores correlated significantly with anxiety, depression, internality and health status, but not with levels of belief in chance or powerful others, over 18 months. BASMI scores were least closely linked to

psychological status. Interpretation of disease status scores in AS may therefore need to take account of psychological status. These findings have important potential applications in the clinical management and monitoring of AS patients. They also have important implications for patient assessment in the context of selection for and responses to biological therapies. Such assessments depend heavily upon the use of tools such as BASDAI and BASFI, and our findings suggest that the effects of psychological status on these scales should be taken into account when interpreting and utilising the data obtained both in clinical trials and clinical practice.

Acknowledgements

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Tables

TABLE 1a.   Disease score at each assessment (n=89)

	Assessment				
	1	2	3	4	*p
BASDAI	4.89 (2.25)	4.91 (2.40)	5.00 (2.36)	4.85 (2.40)	0.78
BASFI	4.48 (2.61)	4.64 (2.71)	4.74 (2.75)	4.73 (2.81)	0.12
BASMI	3.37 (1.74)	3.49 (1.71)	3.41 (1.66)	3.45 (1.73)	0.43

TABLE 1b.   Psychological status at each assessment (n=89)

	Assessment				
	1	2	3	4	*p
Anxiety	6.76 (4.48)	7.69 (4.51)	7.51 (4.58)	7.57 (4.50)	0.002
Depression	5.35 (4.32)	6.07 (4.93)	5.76 (4.31)	5.84 (4.56)	0.10
Internality	30.13 (6.81)	29.42 (7.18)	28.90 (6.51)	29.43 (6.62)	0.15
Belief in chance	23.49 (6.65)	23.84 (6.48)	24.15 (6.49)	24.85 (6.26)	0.13
Belief in powerful others	26.31 (6.49)	26.07 (6.58)	26.30 (6.11)	26.58 (5.51)	0.79

Tables 1a and 1b show mean (SD) scores for each measure of disease and psychological status at assessments 1, 2, 3 and 4. Differences in disease and psychological scores over time were tested using repeated measures ANOVA. *P-values are shown for each measurement tool.

TABLE 2. Correlations between disease and psychological scores at each assessment (n = 89)

	Assessment			
	1	2	3	4
	BASDAI			
anxiety	$r_s = 0.58$**	$r_s = 0.63$**	$r_s = 0.67$**	$r_s = 0.61$**
depression	$r_s = 0.64$**	$r_s = 0.65$**	$r_s = 0.66$**	$r_s = 0.67$**
internality	$r_s = -0.35$**	$r_s = -0.33$**	$r_s = -0.26$*	$r_s = -0.24$*
belief in powerful others	$r_s = -0.02$	$r_s = 0.09$	$r_s = 0.18$	$r_s = 0.08$
belief in chance	$r_s = 0.05$	$r_s = 0.07$	$r_s = 0.04$	$r_s = 0.11$
	BASFI			
anxiety	$r_s = 0.60$**	$r_s = 0.55$**	$r_s = 0.57$**	$r_s = 0.67$**
depression	$r_s = 0.61$**	$r_s = 0.71$**	$r_s = 0.62$**	$r_s = 0.68$**
internality	$r_s = -0.25$*	$r_s = -0.25$*	$r_s = -0.18$	$r_s = -0.22$*
belief in powerful others	$r_s = 0.09$	$r_s = 0.19$	$r_s = 0.21$*	$r_s = 0.18$
belief in chance	$r_s = -0.03$	$r_s = 0.04$	$r_s = 0.01$	$r_s = 0.08$
	BASMI			
anxiety	$r_s = 0.43$**	$r_s = 0.33$**	$r_s = 0.46$**	$r_s = 0.38$**
depression	$r_s = 0.43$**	$r_s = 0.53$**	$r_s = 0.46$**	$r_s = 0.43$**
internality	$r_s = -0.25$*	$r_s = -0.23$*	$r_s = -0.23$*	$r_s = -0.13$
belief in powerful others	$r_s = 0.18$	$r_s = 0.21$*	$r_s = 0.23$*	$r_s = 0.26$*
belief in chance	$r_s = -0.12$	$r_s = 0.09$	$r_s = 0.05$	$r_s = 0.06$

Table 2 shows correlations between each psychological and disease measure at assessments 1, 2, 3 and 4. Correlations between variables were assessed using Spearman's rank correlations (r_s). P-values are denoted as: * $p < 0.05$, ** $p < 0.001$.

TABLE 3.   Disease status of anxious or depressed subgroups at first assessment

	BASDAI	BASFI	BASMI
Anxiety score ≥ 11, n = 18	6.30 (1.23)	6.10 (1.71)	3.99 (1.55)
Anxiety score < 11, n = 71	4.52 (2.31)	4.06 (2.65)	3.21 (1.76)
	p < 0.001	p < 0.001	p = 0.074
Depression score ≥ 11, n = 11	6.80 (1.28)	6.80 (1.46)	4.52 (1.55)
Depression score < 11, n = 78	4.61 (2.23)	4.14 (2.58)	3.21 (1.71)
	p < 0.001	p < 0.001	p = 0.022

Table 3 shows mean (SD) values for each measure of disease status in anxious / non-anxious and depressed / non-depressed subgroups, using HADS scores of 11 or above to identify clinical anxiety or depression. Data are shown for assessment 1. Similar findings were obtained for assessments 2, 3 and 4. Between-group differences were tested using independent-samples t-tests.

Key messages:

- There are significant associations between disease and psychological status in AS.

- Among AS disease specific tools there are important differences in strength of linkage with scores for psychological status.

- Interpretation of AS specific disease scores should take account both of psychological status and choice of assessment tool.