

## RELATIONSHIP OF EMOTIONAL DISTRESS AND PHYSICAL CONCERNS WITH FATIGUE SEVERITY IN SARCOIDOSIS

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**ABSTRACT.** *Background:* Fatigue is one of the most common and disabling symptoms of sarcoidosis. The cause of fatigue remains unclear and is usually multifactorial. The majority of previous studies evaluated clinical parameters with only few of them including assessment of psychological factors as contributing to the severity of the symptoms. *Objective:* The aim of this study was to evaluate the relationship of emotional distress, physical concerns, and dyspnea in explaining fatigue in patients with sarcoidosis. *Methods:* Fifty-seven patients with sarcoidosis were enrolled to the study and filled out measures of fatigue (FAS), dyspnea (MRC), anxiety sensitivity (ASI-3), and anxiety and depression (HADS). *Results:* Linear regression revealed that distress and physical concerns subscale of ASI are significant predictors of fatigue explaining jointly 53.5% of fatigue variance. *Conclusions:* The results of the study emphasize the importance of including emotional distress and physical concerns into the diagnostic procedures and management of fatigue in sarcoidosis. (*Sarcoidosis Vasc Diffuse Lung Dis* 2018; 35: 160-164)

**KEY WORDS:** anxiety, anxiety sensitivity, dyspnea, fatigue, physical concerns, sarcoidosis

### INTRODUCTION

Sarcoidosis is an idiopathic inflammatory disease that affects multiple organs and is associated with a variety of general and specific symptoms depending on the organs involved (1). One of the most common, disabling, and perplexing symptoms reported by patients with sarcoidosis is fatigue. It occurs in up to 85% of patients with active sarcoidosis (2), but it is also present in nearly 50% of patients in remission (3). Fatigue is negatively related to the

patients' quality of life (QOL) (4-6), and its severity was found to predict QOL deterioration (7).

The cause of fatigue in sarcoidosis remains unclear and is usually multifactorial. Importantly, most previous studies assessed clinical parameters with an only minority of them focusing on psychological factors as a likely underlying mechanism. These studies showed various associations between fatigue and medical comorbidities (8), as well as clinical (acute phase response, 6-minute walk distance, dyspnea), and psychological parameters (stress, depression) (2). Fatigue was associated with dyspnea, as measured with the Medical Research Council (MRC), and to the 6-minute walking distance (6MWD) (9, 10). With respect to psychological factors, fatigue was shown to be related to depression (6, 11) and high scores on perceived stress, even after depressive symptoms were statistically controlled (12).

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Numerous studies have shown heightened degrees of anxiety and depression in patients with sarcoidosis (11, 13). In a recent study, Holas et al. (14) found that anxiety was correlated with symptoms severity (including asthenia). Furthermore, they found sarcoid patients had significantly more concerns about their physical symptoms than the reference groups of the healthy individuals. The importance of fear of anxiety symptoms in sarcoid patients was also demonstrated in the recent study which showed that physical symptom concerns were significantly related to dyspnea MRC severity in sarcoid individuals (15). As fatigue is a non-specific symptom subjectively assessed by a patient with self-report questionnaires, it seems plausible that anxiety and increased physical concerns might contribute to the perceived symptom's unpleasantness or severity in sarcoid patients.

Therefore, on the basis of findings described above, the present study aimed to examine the role of dyspnea, depression, anxiety and physical concerns in explaining of fatigue severity in sarcoid patients.

## METHOD

### *Sample*

Data from 57 (43.9% women) patients with sarcoidosis who volunteered to participate in this study were collected. Diagnosis of sarcoidosis was made according to the established guidelines (16). Exclusion criteria involved neoplastic diseases, uncontrolled heart failure, chronic obstructive pulmonary diseases and current psychiatric treatment. None of the patients declined participation in the study, and no participants were excluded. Mean age of patients was  $45.47 \pm 10.94$  years. The distribution of the patients' level of education was as follows: primary - 5.3%, secondary - 40.3%, vocational education - 17.5%, higher - 35.1%.

The study was approved by the Ethics Committee of the Medical University of Warsaw. All subjects gave informed consent to take part in the study.

### *Measurements*

*Fatigue Assessment Scale (FAS)* (17) was used as a standardized measurement of fatigue. It consists of ten

items which can be rated by patients on a scale from 1 which means "never" to 5 which means "always." The general outcome varies between 5 and 50 points, where higher result reflects a higher level of fatigue.

*Hospital Anxiety and Depression Scale (HADS)* is a scale consisting of two subscales concerning anxiety and depression (18). The scale consists of seven anxiety and seven depression items presented in an alternating order with a four-point response format. An optimal balance between sensitivity and specificity is usually achieved when caseness was defined by a score of 8 or above on both HADS-D and HADS-A. The results of Polish adaptation (19) suggest convincingly that the Polish version of the HADS should be treated as a unidimensional measure of emotionally focused distress.

*Anxiety Sensitivity Index - 3 (ASI-3)* is a measurement of different aspects of fear or concerns related to arousal-related events (20). It consists of three subscales related to physical, cognitive, and social concerns. In this study, we concentrated on the subscale measuring physical (health) concerns related to anxiety. It consists of six items that can be rated on a scale from 0 ("I agree very little") to 4 ("I agree very much"). Scores on this subscale can vary from 0 to 24, where higher results indicate more physical concerns. Polish adaptation has good test-retest reliability and validity (21).

*Medical Research Council Dyspnea Scale (MRC)* is a 5-point single item scale [22] designed to measure perceived breathlessness. A higher score on MRC scale indicates higher level of impairment. Grade one refers to the statement "I only get breathless with strenuous exercise" and grade 5 to "I am too breathless to leave the house."

### *Statistics*

Pearson correlation coefficient and independent samples t-tests were used to assess the strength of relationships between each of the variables and FAS scores. Multiple linear regression model assessed the combined contribution of the predictors in explaining the fatigue. All assumptions of linear regression were satisfied. Statistical analysis was performed using IBM SPSS (version 23).

## RESULTS

### Univariate analysis

In the preliminary analysis, we investigated relationships between each of the predictors and FAS scores. There were no significant differences in average FAS scored between male ( $M = 24.2$ ,  $SD = 6.9$ ) and female ( $M = 22.4$ ,  $SD = 8.5$ ) patients,  $t(55) = 0.87$ ,  $p = 0.39$ . Results for all the continuous predictors are reported in Table 1.

In this preliminary analysis, we included both subscales and the total score of HADS. In line with the results reported by de Kleijn et al. (2), both depression and anxiety were significantly correlated with FAS. At the same time, the relationship between FAS was strongest for the total HADS score, and reliability analysis showed that the HADS total score had slightly better reliability ( $\alpha$  Cronbach = .88), when compared to anxiety ( $\alpha$  Cronbach = .83) and depression ( $\alpha$  Cronbach = .79) subscales. This pattern of results supports conclusions from the meta-analysis of HADS done by Cosco et al. (23) who revealed an inability to consistently differentiate between the constructs of anxiety and depression based on HADS and suggested that "its use needs to be targeted to more general measurement of distress" (p. 180). Therefore, we decided to use a single HADS total score as a measure of general emotional distress in the multivariate regression model.

### Multiple regression

To assess the contribution of each of the predictors in explaining FAS we tested a multiple regression model. Sex and age were not included in this analysis, as they were not significantly related to FAS.

**Table 2.** Multiple linear regression model of fatigue predictors

	Beta	t	Significance	Semipartial correlations
MRC	1.45	1.42	0.16	0.13
HADS-T	0.43	3.96	0.000	0.361
ASI-Ph	0.47	3.09	0.003	0.28

MRC – Medical Research Council Dyspnea Scale, HADS-T – Hospital Anxiety and Depression Scale total score, ASI-Ph – Anxiety Sensitivity Index-Physical concerns subscale

Regression analyses resulted are presented in Table 2. This model ( $F(3.53)=22.46$ ;  $p<0.001$ ) predicts 53.5% of fatigue variance with emotional distress and physical concerns as significant predictors. The effects of dyspnea did not reach statistical significance in this analysis.

## DISCUSSION

The aim of the current study was to examine the extent to which self-reported dyspnea, emotional distress, and fear of physical symptoms can be used to explain fatigue severity in sarcoidosis.

Confirming our initial assumptions concerning the importance of the psychological factors, we found that emotional distress and physical concerns are indeed significantly related to fatigue. This pattern of results supports conclusions of de Kleijn et al. (2), who also found that anxiety and depression are predictors of fatigue scores. Univariate analysis in our study showed a correlation of fatigue with dyspnea, in line with the results of Baughman et al. (9) study. However, interestingly, dyspnea turned out not to be a significant predictor after taking into account distress and concerns levels. In a recent study Atkins et al. (24) didn't find significant predictors of fatigue in

**Table 1.** Descriptive statistics and pearson correlations between predictors and fatigue

	mean (SD)	Age	FAS	MRC	HADS-D	HADS-A	ASI-Ph	HADS-T
Age	5.47 (10.94)	-						
FAS	23.44 (7.64)	-0.02	-					
MRC	1.42 (0.89)	0.44*	0.43*	-				
HADS-D	3.98 (3.34)	0.10	0.58***	0.35**	-			
HADS-A	7.07 (4.00)	0.07	0.61***	0.21	0.66***	-		
ASI-Ph	6.82 (5.71)	0.24 <sup>†</sup>	0.63***	0.44*	0.44*	0.50***	-	
HADS-T	11.05 (6.68)	0.92	0.65***	0.304*	0.89***	0.93***	0.52***	-

FAS – Fatigue Assessment Scale, MRC – Medical Research Council Dyspnea Scale, HADS-D/A/ – Hospital Anxiety and Depression Scale-Depression/Anxiety subscales/Total, ASI-Ph – Anxiety Sensitivity Index-Physical concerns subscale, <sup>†</sup> $p=0,07$ , \* $p=0,05$ , \*\* $p=0,007$ , \*\*\* $p<0,001$

sarcoidosis in regression model which also included MRC dyspnea, anxiety (HADS-A) and depression (HADS-D). Importantly, there are methodological differences when compare with the present study, as we treated HADS as a unidimensional measure. Besides, some aspects of Atkins et al. analysis suggest a questionable validity of statistical conclusions – they were based on regression analysis including 72 subjects and 8 highly intercorrelated predictors.

The feeling of fatigue is a subjective experience (2), and our findings suggest that emotional distress and fear of physical symptoms of anxiety affect its perception. One may speculate that an increased tendency to interpret somatic sensations as threatening and increased vigilance related to anxiety, lead to aggravation of the subjective sense of the severity of fatigue.

The most important limitation of the study is a relatively small sample size. It should be noted, that sarcoidosis patients are difficult to recruit since the rarity of the disease. In our study, we used only one self-report scale to quantify levels of fatigue. Future research may benefit from including more objective and physiologically conceptualized measures of fatigue. It is important to underline, however, that FAS is a well validated and reliable tool often used among sarcoidosis patients (17). The cross-sectional design of the current study makes it impossible to draw definitive conclusions about causal relationships between the evaluated variables. Future work using a prospective design and controlling for baseline differences would allow to establish causal patterns more clearly. Though, it is important to underline, that previous works addressing the topic of fatigue predictors cited above were also based on cross-sectional design. Further research could also benefit from controlling some more potential predictors of fatigue (e.g. pain, and extrapulmonary involvement) which were omitted in the current study.

To summarize, fatigue is broadly identified as a prominent problem in sarcoidosis and its management. The present study contributes to the current literature, by indicating that inclusion of subjective, psychological variables, namely physical concerns, and emotional distress, play a significant role in explaining fatigue levels in sarcoidosis patients. Our results also point towards the importance of the evaluation and, if future studies confirm their causal role, management of emotional distress and physical

concerns as potential interventions targeting fatigue in sarcoidosis.

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