



# Association of anxiety sensitivity-physical concerns and FVC with dyspnea severity in sarcoidosis



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## ABSTRACT

**Objective:** The purpose of the study was to evaluate the relationship of an objective functional lung parameter (FVC) and a subjective psychological factor (physical symptom concerns) with dyspnea in sarcoidosis. Dyspnea constitutes one of the most common and burdensome symptoms in sarcoidosis, yet little is known about its mechanisms and, in particular, psychological.

**Method:** A total of 107 hospitalized sarcoidosis patients (Female = 50,  $M_{age} = 45.3$  years) volunteered to take part in the correlational research study. Participants underwent spirometry and completed the MRC Dyspnea Scale and the Anxiety Sensitivity Index-3 (ASI) questionnaire. Linear hierarchical regression analysis was used to determine the relationship between the studied predictors and dyspnea severity.

**Results:** The best fitting model predicted 18% of variance in dyspnea severity. Physical symptom concerns subscale of ASI ( $\beta = 0.24$ ) and FVC ( $\beta = -0.23$ ) were significantly related to dyspnea MRC severity, but only physical concerns remained significantly related to dyspnea when both predictors were in the model.

**Conclusions:** The current results suggest that both psychological and physiological factors should be taken into account when explaining subjective dyspnea severity in sarcoidosis. More specifically, these findings call for including cognitive vulnerability factors related to anxiety (physical symptom concerns) into the diagnostic procedures and management of dyspnea in sarcoidosis.

## 1. Introduction

Sarcoidosis is an inflammatory disease with a variable clinical course. Although every organ can be involved, including the skin, lymph nodes and eyes, the lungs are affected most frequently in ca. 90% of individuals [1]. The entire respiratory tract can be involved and patients often have a mix of airway obstruction and restrictive symptoms because of interstitium involvement. Pulmonary sarcoidosis manifests as symptoms related directly to the chest, such as dyspnea, coughing, chest pain and wheezing. Dyspnea is one of the most common presentations in early to moderately advanced sarcoidosis [2]. Dyspnea was found to be related to decreased lung functioning testing: forced vital capacity (FVC), forced expiratory volume in 1 s

(FEV<sub>1</sub>), total lung capacity (TLC) and diffusing capacity of the lungs for carbon monoxide (DLCO) [3,4]. Studies have shown that FVC is associated with sarcoidosis severity [4] [5] and a recent study found that dyspnea is predicted by FVC measured during exercise [6]. Interestingly, some studies have shown no relationship between dyspnea severity ratings and lung functions, despite the fact that patients had significant dyspnea and other chest symptoms [2,7]. This suggests that pulmonary function testing cannot serve as a surrogate for dyspnea and health status in sarcoidosis. These findings should not be surprising since dyspnea is a subjective symptom and has not corresponded with spirometric measurements in many previous studies of pulmonary diseases including patients with chronic obstructive pulmonary disease [8].

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There are a number of premises which suggest that dyspnea corresponds with psychological functioning, e.g. neuroimaging studies have demonstrated dyspnea stimuli to be correlated with the activation of cortico-limbic areas involved with interoception and nociception [9]. Some authors have suggested, on the basis of research on early respiratory related evoked potentials (RREP), that dyspneic patients exhibit a general deficit in the neuropsychological processing of perceptual information, which plays a role in blunted perception of dyspnea [10,11]. Research into psychological variables contributing to the perception of dyspnea in pulmonary diseases has long been neglected, although these factors considerably influence this interoceptive process [12]. Studies have shown that in asthma and chronic obstructive pulmonary disease (COPD) the psychological factors seem to be more important than the medical factors in predicting dyspnea severity [13,14]. Importantly for the current study, a review of the psychological factors influencing dyspnea [12] did not include data on sarcoidosis. Although dyspnea is a common symptom in sarcoidosis, very little has been established regarding the potential impact of psychological, subjective variables on breathlessness severity in this disorder. Several of the studies examined the association of health-related quality of life (HRQL) or anxiety with dyspnea in sarcoidosis [5] [15,16,17]. De Boer et al. found that symptoms of dyspnea were associated with worse HRQL and that the scores of HRQL predicted dyspnea in sarcoidosis [15].

Therefore, the multicenter study presented here aimed to fill this gap by evaluating and comparing the relationship of an objective functional lung parameter (FVC) and a subjective psychological factor chosen on a theoretically-driven basis as described in the next section with dyspnea severity.

### 1.1. Psychological correlates and predictors of dyspnea

Studies have shown that dyspnea is linked to depression and anxiety [17] as well as higher fatigue and lower quality of life in sarcoidosis [18]. Furthermore, decreased scores on spirometric tests including FVC and more self-reported dyspnea were associated with reduced health status [5,17] [19]. Yeager et al. investigated the association of psychosocial factors with respiratory health in 736 sarcoid individuals and found that 46% of them reported significant symptoms of depression, which was associated with decreased FVC and greater dyspnea [19]. Some premises suggest that dyspnea may be perceived more inaccurately due to negative emotions, in particular anxiety [12,20].

The results of a recent study showed that higher dyspnea-related fear was associated with higher levels of dyspnea during ergometer exercise [21]. Studies have also shown that in COPD, asthma and hyperventilation, the respiratory rate is increased by psychophysiological arousal resulting from anxiety, which markedly worsens breathlessness by causing bronchoconstriction and lung hyperinflation.

Anxiety Sensitivity (AS) [22], a fear of anxiety-related symptoms based on beliefs about their potential harmful consequences, was shown to be the cognitive vulnerability factor for anxiety symptoms and panic [23,24]. AS was shown to predict more severe subjective dyspnea, even after adjustment for anxiety disorders and pulmonary dysfunction in COPD individuals [8]. Also in sarcoidosis, Holas et al. (2013) found that dyspnea was related to anxiety, the anxiety sensitivity index and its subscale of physical concerns, but not to depression [25]. Moreover, they found that sarcoidosis patients obtained higher scores of the total ASI and had significantly more concerns about physical symptoms than a comparable group of healthy participants. Holas et al. proposed that this elevated anxiety through heightened awareness of bodily sensations and increased physical concerns might contribute to the perceived unpleasantness and severity of dyspnea [25]. Their findings indicate that anxiety sensitivity, and its physical concerns subscale in particular, is a plausible candidate for being a predictor of subjective dyspnea severity in sarcoidosis.

In the present study, we verified if physical symptom concerns along

with FVC are significantly associated with dyspnea severity as measured by the MRC scale in sarcoidosis patients and we evaluated their relative contribution. Because there was no previous research it was difficult to formulate any firm expectations, but we hypothesized that ASI physical concerns would be significantly related to dyspnea severity along with FVC in sarcoidosis patients.

We added age to the regression model which was based on the observation that lung function decreases along with age and that dyspnea is a common symptom in older patients with pulmonary diseases [26]. The increase of dyspnea along with age is associated not only with pulmonary problems but also with increasing non-pulmonary comorbid conditions, such as heart failure, anemia, deconditioning and muscle weakness [26].

## 2. Method

### 2.1. Participants

A total of 107 volunteers were enrolled in this multi-center study. These were consecutive patients with confirmed pulmonary sarcoidosis. The process of enrolling was conducted by chest physicians who were able to assess the accuracy of the diagnosis of sarcoidosis, the stage of the disease and adequate clinical data. The outpatients were from the following centers: Department of Pneumology, Medical University of Gdansk; Department of Pneumology, Medical University of Silesia; Department of Pneumology, Oncology and Tuberculosis, Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz; and the Department of Internal Medicine, Pneumology and Allergology, Medical University of Warsaw. The part of the survey concerning clinical characteristics was filled in by a physician, whereas the psychological tests were filled in by the patient. In each center, the study's common protocol was used and the number of enrolled patients was comparable. Only in one of the centers, 15% of patients declined participation in the study, whereas in three others all patients agreed to take part and none of them was excluded. The diagnosis of sarcoidosis was established according to guidelines from the Statement on Sarcoidosis (1999) [27]. Patients with neoplastic diseases, uncontrolled heart failure, chronic obstructive pulmonary disease or those receiving any types of antidepressants were excluded from the study. The group comprised 50 women and 57 men. The mean age of the subjects was 45.3 years, range: 26–83 years old. The study was approved by the Ethics Committee of the Medical University of Warsaw. All subjects signed informed consent to take part in the study.

### 2.2. Measures

The patient questionnaire included items assessing age, sex, education, social situation, history of the disease, Löfgren syndrome, smoking history and the treatment they were undergoing. Patients were additionally asked to report the presence of the following symptoms: dyspnea, cough, fever, weakness, sweating, weight loss and myalgia. The comorbidities taken into account were as follows: diabetes, hypertension, ischemic heart disease, peptic ulceration, nephrolithiasis or cholelithiasis.

A spirometry and body-plethysmography examination were performed. The stage of the disease was established according to chest X-ray results (guidelines from the Statement on Sarcoidosis, 1999) [28]. All subjects completed self-report tests, including the Medical Research Council (MRC) Dyspnea Scale and Anxiety Sensitivity Index-3.

*Medical Research Council Dyspnea Scale (MRC)* is a short, 5-point scale [29] designed for measurement of perceived breathlessness. A higher score on the MRC scale indicates higher levels of impairment connected with the feeling of breathlessness. 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".

*Anxiety Sensitivity Index-3* [30,31] is an 18-item self-reported

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