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Care of Patients with Pulmonary Disorders

# Subgroup analysis of symptoms and their effect on functioning, exercise capacity, and physical activity in patients with severe chronic obstructive pulmonary disease

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ABSTRACT

*Background:* Little is known about symptom clusters and their effect on outcomes in people with chronic obstructive pulmonary disease (COPD).
*Purposes:* To determine whether subgroups of patients with COPD could be identified by symptom ratings, whether they differed on selected demographic and clinical characteristics, and whether they differed on functioning, exercise capacity, and physical activity.
*Method:* Subjects with severe COPD ($n = 596$) were drawn from the National Emphysema Treatment Trial dataset. Data were drawn from questionnaires and clinical measures.
*Results:* Two subgroup clusters emerged from four symptoms. Mean age and the proportion of participants with higher education, higher income levels, and using oxygen at rest were significantly different between subgroups. Participants with high levels of symptoms had lower functioning and decreased exercise capacity. Symptom cluster subgroups were significantly associated with social functioning.
*Conclusion:* These findings suggest that screening for high levels of symptoms may be important in patients with severe COPD.



## Introduction

The social burden of chronic obstructive pulmonary disease (COPD) is substantial, and it is projected to be the seventh leading cause of disability-adjusted life years lost worldwide by 2030.[1] COPD is characterized by gradual deterioration in lung function with multiple distressing symptoms that influence functional status and quality of life.[2,3] It has been suggested that COPD symptoms have a greater effect on functional limitation than disease severity.[4] Now symptoms have been included to determine COPD severity in the Global Initiative for Chronic Obstructive Lung Disease.[5]

Previous research focused on single symptoms. However, people with COPD rarely experience a single symptom in isolation. They are more likely to experience multiple symptoms that potentially interact with each other, referred to as a symptom cluster. A symptom cluster is defined as a group of symptoms that are related to each other and occur together.[6,7] During the past decade, symptom clusters have been examined in people with different chronic diseases including cancer, chronic hepatitis, end stage renal disease, heart failure, and human immunodeficiency virus disease.[8] However, little is known about symptom clusters and their effect on outcomes in people with COPD.

### *Symptom clusters*

Researchers have used two approaches to examine symptom clusters: (1) grouping symptoms using a factor analysis or cluster analysis and (2) grouping subjects based on differences in the severity of symptoms (i.e. one group with high scores from all symptoms vs. one group with low scores from all symptoms) using a cluster analysis. The second approach was applied to populations with cancer,[9–14] heart disease,[15–18] and multiple sclerosis.[19,20] In these studies, researchers identified distinct subgroups, based on 3–23 symptoms. Grouping subjects based on differences in ratings of symptoms may be more useful clinically because it would allow health care providers to identify subgroups of patients who may be at risk of poorer outcomes. This approach would also enable health care providers to develop symptom management strategies that can be tailored to a specific patient subgroup. Patients in a high-risk group who experience high levels of symptoms may need different types or doses of interventions for symptom relief than patients in a

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moderate-risk group.[12] However, an examination of the characteristics of patients who reported high levels of symptoms was inconclusive. The demographic and clinical characteristics did not clearly distinguish those who reported low levels of symptoms from those who reported high levels of symptoms.[9,11–13] To date, no study has examined subgroups of patients with COPD based on their experience with common symptoms or the relationship between symptom clusters, demographic and clinical characteristics.

Symptom clusters in other diseases have been associated with functioning, quality of life, and health status.[10–12,21] Subgroups with high scores on multiple symptoms had worse functioning, quality of life, and health status.[10–12,21] In the oncological literature, self-reported functioning was examined as an outcome of symptom clusters.[9,13] The use of objectively measured exercise capacity as an outcome of symptom clusters would strengthen the science.

In the past literature, single symptoms such as dyspnea or anxiety can influence functioning, exercise capacity, and physical activity in people with COPD.[4,19,22] But symptoms interact with each other and a cluster of symptoms may be more sensitive to a change in health status than a single symptom. If true in the clinical setting it would be important to assess symptoms as a cluster rather than assessing single symptoms one at a time.

### *Dyspnea, anxiety, depression, and fatigue in people with COPD*

People with COPD experience four symptoms that are highly prevalent and closely related to each other: dyspnea, anxiety, depression, and fatigue. Dyspnea is the most common and disabling symptom.[2,23] As the disease progresses, patients experience a downward cycle of dyspnea, inactivity, and physical deconditioning, often accompanied by anxiety and depression.[24] Research has confirmed that dyspnea is closely related to anxiety and depression in people with COPD.[25,26] Solano et al[27] found that the prevalence of anxiety in people who have recently recovered from an acute exacerbation of COPD ranged between 50% and 57%; the prevalence of depression in people who have recently recovered from an acute exacerbation of COPD ranged between 37 and 71%. Dyspnea and fatigue appear to interact with each other and fatigue is associated with anxious and depressed mood.[4] Fatigue has been identified as one of the important, disease-related problems that adversely affects the lives of people with COPD.[4] After dyspnea, the second most prevalent symptom in a study of people with COPD was lack of energy.[2,23] The prevalence of fatigue was 50–71% in people with COPD.[2,28] This symptom becomes increasingly prevalent as disease progresses.[29]

### *Purposes*

The purposes of this study were to determine whether subgroups of patients with COPD could be identified by their ratings of symptoms (i.e. dyspnea, anxiety, depression, and fatigue), whether they differed on selected demographic and clinical characteristics, and whether they differed on functioning, exercise capacity, and physical activity, using data from the National Emphysema Treatment Trial (NETT).

## Methods

### *Design*

This cross-sectional secondary analysis used data from the National Emphysema Treatment Trial (NETT). The NETT study's aim was to evaluate the safety and effectiveness of lung volume reduction surgery.[30] It was conducted by the Centers for Medicare and Medicaid Services, the National Institutes of Health, and the Agency for Healthcare Research and Quality. The trial's methods have been reported in-depth elsewhere.[31,32] Briefly, 3777 patients were screened for the NETT from 1998 to 2002 (Fig. 1). Patients were included if they had moderate-to-severe emphysema (FEV1 $\leq$ 45% predicted, residual volume $\leq$ 150% predicted), had been non-smokers for at least 6 months, and had completed a pulmonary rehabilitation program before randomization. Exclusion criteria included characteristics that placed patients at risk of perioperative morbidity or mortality, such as, pulmonary hypertension, emphysema unsuitable for lung volume reduction surgery, and medical conditions or other circumstances that precluded a patient from completing the trial. Primary outcomes of the original study were mortality and maximum exercise capacity 2 years after randomization.

### *Sample, settings, and procedures*

All participants at the 17 NETT clinics were randomly assigned to usual medical therapy alone or to usual medical therapy plus lung volume reduction surgery.[32] All participants completed 16–20 sessions of pulmonary rehabilitation before randomization, and six sessions of rehabilitation after randomization. For this analysis, we included participants in the medical therapy group. We used baseline data for all study variables, except physical activity. Baseline data were collected prior to rehabilitation and prior to randomization. Data for physical activity were collected one month after randomization. All participants provided written, informed consent, and the institutional review board at each clinic approved the study. This secondary study protocol was approved by the Institutional Committee on Human Research at the primary investigator's hospital.

### *Instruments*

#### *Demographic data*

Information about age, gender, marital status, smoking history, race, income, medication use, and current oxygen use were obtained by interview. All questionnaires were administered after clinical measures were performed and study eligibility was determined.

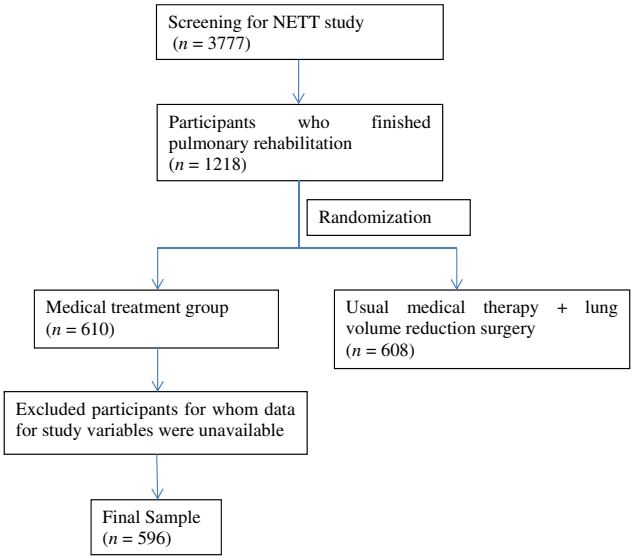


**Fig. 1.** Flow chart for study sample.