Physical Activity, Health Status and Risk of Hospitalization in Patients with Severe Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a leading cause of death and 70% of the cost of COPD is due to hospitalizations. Self-reported daily physical activity and health status have been reported as predictors of a hospitalization in COPD but are not routinely assessed. **Objectives:** We tested the hypothesis that self-reported daily physical activity and health status assessed by a simple question were predictors of a hospitalization in a well-characterized cohort of patients with severe emphysema. **Methods:** Investigators gathered daily physical activity and health status data assessed by a simple question in 597 patients with severe emphysema and tested the association of those patient-reported outcomes to the occurrence of a hospitalization in the following year. Multiple logistic regression analyses were used to determine predictors of hospitalization during the first 12 months after randomization. **Results:** The two variables tested in the hypothesis were significant predictors of a hospitalization after adjusting for all univariable significant predictors: >2 h of physical activity per week had a protective effect [odds ratio (OR) 0.60; 95% confidence interval (95% CI) 0.41–0.88] and self-reported health status as fair or poor had a deleterious effect (OR 1.57; 95% CI 1.10–2.23). In addition, two other variables became significant in the multivariate model: total lung capacity (every 10% increase) had a protective effect (OR 0.88; 95% CI 0.78–0.99)

and self-reported anxiety had a deleterious effect (OR 1.75; 95% CI 1.13–2.70). **_Conclusion:_** Self-reported daily physical activity and health status are independently associated with COPD hospitalizations. Our findings, assessed by simple questions, suggest the value of patient-reported outcomes in developing risk assessment tools that are easy to use.

Introduction

Chronic obstructive pulmonary disease (COPD) is a frequent cause of hospitalization [1] and is the fourth leading cause of death in the United States [2]. Hospitalizations not only have a negative impact on the well-being, lung function, and survival rates for patients with COPD, but they also account for 70% of the treatment costs for this disease [3–6]. The development of new instruments to identify risk factors for hospitalization is important because these instruments can help health care providers create and apply appropriate and timely interventions to prevent a hospital admission. The ideal instrument would focus on significant predictive factors to identify patients at high risk for hospitalization by means of a short list of questions since a simple instrument would be more likely to translate into everyday use in clinical practice.

Measures that have started to be more prevalent in the COPD literature are daily physical activity and health status. Self-reported physical activity was reported in a large cohort of patients with COPD to be an independent predictor of hospitalization and mortality [7]. In addition, daily physical activity is associated with a lower decline in lung function in COPD patients [8]. Health status has been associated with an increased risk of hospitalization in COPD patients [9–12]. Importantly, physical activity and health status are potentially modifiable risk factors.

Our study was designed to determine whether those factors were associated with increased rates of hospitalization in a large, prospective cohort of well-characterized patients with severe COPD [13], the National Emphysema Treatment Trial (NETT).

Methods

Database
The data for our analysis were derived from NETT, a randomized controlled trial that involved patients from 17 clinics in various regions of the United States [13]. The design and methods of the trial have been published elsewhere [13–15]. Between January 1998 and July 2002, the NETT investigators enrolled patients who had emphysema, severe airflow limitation, and a forced expiratory volume in 1 s (FEV_1) of 45% of predicted or lower.

The patients completed 6–10 weeks of pulmonary rehabilitation and provided baseline sociodemographic, clinical, and quality-of-life data before they were randomized to receive continued medical treatment or lung volume reduction surgery. The primary outcome measures were mortality and maximum exercise capacity 2 years after randomization.

Our analysis focused on the 610 patients who were randomized to the medical arm, and our primary outcome was hospitalization during the 12-month period after randomization. The information on hospitalizations was based on self-report from patients who completed scripted questionnaires at 1 and 2 months after randomization and every 2 months thereafter in face-to-face encounters or via the telephone.

The multisite trial was approved by the institutional review board at each site, and all patients involved in the trial provided written informed consent. Our analysis was considered exempt from the need for additional consent.

Collection and Processing of Data
For the evaluation of physical activity, patients were asked how many days during the previous week they performed lower-extremity endurance exercises, such as walking or cycling, and for how many minutes each day. The value of daily physical activity used in the analysis was the average of interviews at 1 and 2 months after randomization. That averaged value was used as a proxy for randomization time information. The rationale for using an average of 2 months was twofold: first, the questions used are not psychometrically tested (with test-retest reliability) as there is no validated COPD activity questionnaire, and second the reliability analysis of the activity questions at month 1 versus month 2 showed a moderate intraclass correlation coefficient of 0.64 – cutoff value recommended for a reliable item is 0.7. For the above reasons, the authors believed that the average provided a much more robust indicator of physical activity.

We analyzed self-reported physical activity as a continuous variable (number of minutes exercised per week: obtained from how many days per week they reported activity·activity duration, minutes, reported) and as a dichotomous variable (physical activity <2 h a week vs. ≥2 h a week). We used the cutoff of 2 h per week because it was found to be significant in a previous study of a large cohort of patients with severe COPD [7].

Information about depression was obtained prior to randomization from responses to the Beck Depression Inventory, a 21-item instrument with total score that ranges from 0 to 63. A total score of 10 or higher is consistent with mild to moderate depressive symptoms [16, 17] and is associated with the risk of adverse outcomes in several medical conditions [18, 19]. We used this score as a cutoff for the presence or absence of depressive symptoms. However, for purposes of comparison, we also used a score of >15 as a cutoff. Information about anxiety was obtained prior to randomization from the responses of patients to the item in the Quality of Well-Being Scale that queries excessive worry or anxiety in the past 3 days. The response options from the tool were: 'no days, yesterday, 2 days ago and 3 days ago'. For the purpose of the analysis, the responses were grouped as 'no days' or 'at least one day'.

Table 1. Sociodemographic and clinical characteristics of patients at baseline[1]

Characteristics	Patients with no hospital admission during a 12-month period		Patients with at least one hospital admission during a 12-month period		p value
	n	mean ± SD or %	n	mean ± SD or %	
Continuous variables					
Age, years	394	67.14 ± 5.89	203	67.21 ± 5.98	0.90
FEV_1, % predicted	394	27.03 ± 7.34	203	26.16 ± 6.30	0.15
Total lung capacity, % predicted	394	129.43 ± 15.00	203	126.68 ± 14.97	0.04
Body mass index	393	24.78 ± 3.47	203	24.72 ± 3.66	0.84
BODE index (using the SGRQ-derived MMRC)[2]	392	5.94 ± 1.61	202	6.29 ± 1.38	0.01
SGRQ-derived MMRC	394	3.40 ± 1.09	203	3.59 ± 0.97	0.04
Score on SOBQ	394	62.57 ± 18.95	203	64.52 ± 17.76	0.23
Distance (meters) walked in 6 min after NETT pulmonary rehabilitation	394	377.14 ± 99.06	203	355.05 ± 90.77	0.01
Additional meters walked in the 6-min walk test after pulmonary rehabilitation	382	24.65 ± 52.78	199	25.52 ± 52.97	0.85
Maximal workload, W	394	41.29 ± 23.42	203	36.52 ± 19.33	0.01
Self-reported time (minutes) of physical activity per week[3]	382	109.03 ± 61.74	200	94.00 ± 64.93	0.01
Categorical variables	394		203		
Female gender	394	33	203	42	0.03
Married	394	66	203	64	0.55
Use of long-acting β_2-agonist at baseline	394	48	203	55	0.12
Use of inhaled corticosteroid at baseline	394	78	203	72	0.11
Use of oxygen at rest at baseline	394	54	203	55	0.80
Weight loss of 10% of usual weight in previous 3 months	394	1	203	2	0.51
Upper-lobe emphysema on CT scan	393	68	203	62	0.13
History of pulmonary rehabilitation before NETT	394	66	203	63	0.48
Score of ≥10 on the Beck Depression Inventory (pre rehab.)	394	37	203	47	0.02
Self-reported time of ≥2 h of physical activity per week[3]	382	42	200	30	0.003
Self-rated health status as fair or poor	388	42	202	54	0.01
Self-reported anxiety	394	15	203	25	<0.001

CT = Computed tomography; MRC = Medical Research Council; SD = standard deviation; SOBQ = University of California-San Diego Shortness of Breath Questionnaire.

[1] Post Pulmonary Rehabilitation. The outcome of interest was hospital admissions during the 12-month period after randomization in the study. p values are for univariable logistic regression analyses.

[2] See Method section for full explanation of the SGRQ-derived MMRC.

[3] This measure comes from the average between the first and second month after randomization.

In addition to including these self-reported items in our analysis, we included baseline information concerning the sociodemographic and clinical characteristics shown in table 1.

Statistical Analyses

For analysis purpose, we divided the patients into two groups, one with no hospital admissions and the other with at least 1 hospital admission in the first 12 months after randomization. We used descriptive statistics to report the numbers and percentages of patients having each of the sociodemographic, clinical, and other characteristics of interest. To determine the association between each variable and hospitalization, we used univariable logistic regression analyses. If a variable had a p < 0.1 in univariable analyses, we included it in the multiple logistic regression

model to predict the odds of hospitalization. To determine the strength of association between physical activity (self-reported), the 6-min walk test, and the maximum workload test, we used the Pearson correlation coefficient. Analysis was completed using Stata version 9 (StataCorp, College Station, Tex., USA) and considered p < 0.05 to be significant.

Results

Of 610 patients in the medical arm of NETT, 597 (96%) had complete information about hospitalization. The baseline characteristics of patients with and without at

Table 2. Predictors of hospitalization based on multiple logistic regression[1]

Predictor	Odds ratio	p value
Total lung capacity, % predicted (every 10% increase)	0.88 (0.78–0.99)	0.03
Self-reported time of ≥2 h of physical activity per week	0.60 (0.41–0.88)	0.01
Self-rated health status as fair or poor versus good, very good, or excellent (from SF-36 tool)	1.57 (1.10–2.23)	0.01
Self-reported anxiety (from quality of well-being tool)	1.75 (1.13–2.70)	0.01

95% CI are shown in parentheses.
[1] The variables included in the multiple logistic regression model were the ones that were univariable significant at the 0.1 level or less (table 1). The area under the receiver operating characteristic curve for this model was 0.63.

least 1 hospital admission during the first 12 months of the study are shown in table 1.

In univariable analyses, the following characteristics were associated with hospitalization: gender, total lung capacity percent predicted, BODE index (body mass index, airflow obstruction, functional dyspnea, exercise capacity), the MMRC Dyspnea Scale, distance (meters) walked in 6 min after the NETT pulmonary rehabilitation, self-reported time (minutes) of physical activity per week, a score equal or higher than 10 on the Beck Depression Inventory, self-reported time of ≥2 h of physical activity per week, self-rated health status as fair or poor (as opposed to 'good, very good or excellent'), and self-reported anxiety. These variables were included in the multiple logistic regression model.

In the multiple logistic regression model (table 2), only four variables were significant predictors of a hospitalization after adjusting for all univariable significant predictors: two were protective, self-report of ≥2 h of physical activity per week [odds ratio (OR) 0.60; 95% confidence interval (95% CI) 0.41–0.88) and total lung capacity (every 10% increase)– (OR 0.88; 95% CI 0.78–0.99), and two variables increased the risk: self-reported health status as fair or poor (OR 1.57; 95% CI 1.10–2.23) and self-reported anxiety (OR 1.75; 95% CI 1.13–2.70). The area under the receiver operating characteristic curve for the multiple logistic regression model was 0.65.

Although the continuous variable for physical activity displayed a low correlation with exercise capacity defined by the 6-min walk test (R = 0.2) and a low correlation with the maximum workload test on the cycle ergometer (R = 0.2), the correlations were significant (p < 0.05 for each) because of the large sample size. The correlations between the distance walked in 6 min and the maximum workload were stronger (R = 0.6; p < 0.001), but neither of these measures was found to be a predictor of hospitalization.

On the Beck Depression Inventory, a score ≥10 was not associated with hospitalization. Nor was a score of >15 associated with hospitalization but showed a trend toward statistical significance (OR 1.5; 95% CI 0.96–2.84; p = 0.07).

The BODE index, used as a continuous variable, was not associated with hospitalization.

Discussion

In our analysis of data from patients involved in the medical arm of the NETT, we found and confirmed our hypothesis that self-reported daily physical activity, health status and anxiety are predictors of a hospital admission in patients with severe emphysema. Remarkably, each of those important predictors was easily and rapidly assessed by asking simple questions. We definitively confirmed previous data suggesting that the self-report of health status using question 1 of the SF-36 ('Do you rate your health as excellent, very good, good, fair or poor?') and total lung capacity are associated with hospitalization as previously reported [10, 14].

We believe our results on daily physical activity are of great significance for risk assessment of severe COPD and emphasize the need to include the assessment of physical activity in clinical trials and daily practice. Physical activity is a potentially modifiable risk factor to assess that can be impacted by interventions like pulmonary rehabilitation, or by a comprehensive self-management or integrated care programs for COPD. Maintaining long-term physical activity is a desired goal of pulmonary rehabilitation that has not yet been attained. Our findings on physical activity raise interesting questions about the construct. The correlations between self-reported physical activity and results in exercise capacity tests (maximum workload and 6-min walk) were only modest. In the multivariate model, only self-reported physical activity – but none of the measures of exercise capacity – was a predictor of hospitalization. These findings suggest that

exercise capacity and reported physical activity provide different information and that the two measures might actually be different constructs. Furthermore, it is plausible that the level of actual physical activity depends on the patient's mood and/or perception of his or her health.

We found that the odds of being hospitalized are about 1.6 times as great in patients who rate their health as fair or poor. The latter seems a very intuitive finding, but it is remarkable that some patients with severe emphysema did perceive their health as 'good' or even 'very good' and suggests about the profound effect that a positive perception of health can have to avoid hospitalization. Previous studies using the same simple first question from the SF-36 questionnaire [10] or other tools [11, 20] have linked self-reported health status with hospitalizations, health system utilization and mortality.

We also found that the odds of being hospitalized are about 1.7 times as great in patients who endorse a single item about anxiety. To our knowledge, this is the first report of an association between hospitalization and anxiety measured with a single question answered by patients with COPD. Our results are consistent with a previous report that found an association between rehospitalization and anxiety that used the Hospital Anxiety and Depression Scale [9] as a tool but contrast with another analysis of NETT data that found no association between hospital admission and anxiety using the State-Trait Anxiety Inventory [21]. It is likely that the specific instrument used to evaluate anxiety may have a significant impact in explaining the findings across studies. The use of behavioral interventions in severe COPD that may reduce anxiety may be a significant research question to test, given our results and the positive results of behavioral interventions in other chronic diseases, such as diabetes [22–24]. It is unknown whether treatment of anxiety symptoms would reduce the risk of hospitalization in patients with severe COPD.

In our study, a score ≥10 on the Beck Depression Inventory was associated with hospitalization in univariable analysis, but neither a score of ≥10 nor a score of >15 was associated with hospitalization in multiple regression analysis. These findings are consistent with the results of a study of depression and COPD-related hospitalizations by Fan et al. [21]. Although depressive symptoms are a potentially modifiable risk factor, Fan et al. [21] found that the use of antidepressants did not reduce the risk of COPD-related hospitalization when their models were adjusted for meaningful covariates. However, they were unable to ascertain the dosage of or compliance with therapy. Studies are needed to test the benefit of a combination of behavioral and pharmacologic interventions for depressive symptoms in these patients.

Our finding on hyperinflation as a protective factor seems to be counterintuitive. We speculate that less hyperinflation may indicate restriction coming from comorbidities like pulmonary hypertension or undetected heart failure that are prevalent in this population of patients with severe emphysema.

The BODE index is an unquestionable predictor of mortality [14, 25, 26], but it was not significant in predicting hospitalization in our analysis. While a previous study found that the BODE index was a significant predictor of the number of hospitalizations [27], the results were somewhat unclear since patients with BODE scores of 5 or 6 (scale 0–10: 0 being the best and 10 being the worst scores) were less likely to require hospitalization than those with BODE scores of 0–2.

In our model, hospitalization is mainly explained by 3 self-reported predictors (physical activity, health status perception and anxiety), suggesting that patients' perceptions are as important or even more important as structural variables in determining a hospitalization.

Our analysis of the self-reported physical activity, anxiety and health status builds on the work of previous studies [7, 9, 10] but extends previous findings to a well-characterized group of patients with severe COPD. It also contributes to the goal of developing effective and parsimonious risk assessment tools.

Several limitations and strengths of our study deserve mention. Because our results are based on the analysis of a sample of patients with severe COPD, the results may have limited generalizability to patients with mild COPD. However, hospitalizations occur with higher frequency in patients with severe disease [28]. Our prediction model explained 65% of the variance of hospitalization, and this allows us to report a strong association but not to create a prediction tool. Our measure of anxiety, coming from a single item from the Quality of Well-Being Questionnaire, is not a standardized measure of anxiety and requires further testing to determine the soundness of the measure.

The strength of our study lies in the fact that the NETT data set had few missing values for the variables and outcome of interest in our analysis. The use of scripted questionnaires during telephone calls or face-to-face encounters to assess hospital admissions every 2 months makes the possibility of recall bias or information bias unlikely. Our results on hospitalizations are consistent with those reported by another group of investigators who used the same dataset but assessed hospitalization from health re-

cords [21], suggesting the robustness of our assessment of the primary outcome (hospitalization).

Our results highlight the importance of assessing daily physical activity and health status to predict a hospital admission. The latter appears to be mainly determined by factors related to patient's perceptions of health, physical activity and emotions, which often tend to be considered as 'soft' parameters.

Our findings also suggest that a simple assessment of those parameters will help clinicians to identify patients with COPD at higher risk. A rapid identification may trigger the initiation of more comprehensive treatments in patients who are at higher risk of hospitalization, such as intensive pulmonary rehabilitation with self-management or integrated care programs for COPD [29–31].

In an era when patient self-reports are often disregarded, it is noteworthy that these simple reports that are easily obtained might offer valuable information for risk assessment and decision making.

Appendix

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