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ORIGINAL RESEARCH

Post-traumatic Stress Symptoms and Exacerbations in COPD Patients

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Abstract

Background: Post-Traumatic Stress Disorder (PTSD) is a common psychological consequence of exposure to traumatic stressful life events. During COPD exacerbations dyspnea can be considered a near-death experience that may induce post-traumatic stress symptoms. The aim of this study was to evaluate the relationship between COPD exacerbations and PTSD- related symptoms. Method: Thirty-three in-patients with COPD exacerbations were screened for the following: PTSS (Screen for Posttraumatic Stress Symptoms), anxiety (Beck Anxiety Inventory) and depression (Beck Depression Inventory). Patients had a median age of 72 years and 72.7% were female. Results: Mean FEV1 and FVC were 0.8 \pm 0.3 (37.7 \pm 14.9% of predicted) and 1.7 \pm 0.6 (60 \pm 18.8% of predicted), respectively with a mean exacerbation of 2.9 episodes over the past year. Post-traumatic stress symptoms related to PTSD were found in 11 (33.3%) patients (SPTSS mean score 4.13 ± 2.54); moderate to severe depression in 16 (48.5%) (BDI mean score 21.2 ± 12.1) and moderate to severe anxiety in 23 (69.7%) (BAI mean score 23.5 ± 12.4). In a linear regression model, exacerbations significantly predicted post-traumatic stress symptoms scores: SPTSS scores increased 0.9 points with each exacerbation (p = 0.001). Significant correlations were detected between PTSD-related symptoms and anxiety (rs = 0.57; p = 0.001) and PTSD symptoms and depression (rs = 0.62; p =0.0001). In a multivariable analysis model, two or more exacerbation episodes led to a near twofold increase in the prevalence ratio of post-traumatic stress symptoms related to PTSD(PR1.71; p = 0.015) specially those requiring hospitalization (PR 1.13; p = 0.030) Conclusion: PTSD symptoms increase as the patient's exacerbations increase. Two or more exacerbation episodes lead to a near twofold increase in the prevalence ratio of post-traumatic symptomatology. Overall, these findings suggest that psychological domains should be addressed along with respiratory function and exacerbations in **COPD** patients.

Introduction

An important feature of the clinical course of COPD is exacerbation, an acute worsening of symptoms that result in a poorer quality of life and an increased risk of death. The frequency and severity of exacerbations increases the disease progression resulting in an accelerated worsening of pulmonary function (1).

As a cardinal symptom in COPD patients, especially during an acute exacerbation episode, dyspnea is often described as suffocation and as such can be considered a near-death experience. Considering that some patients are prone to frequent exacerbations that may have considerable impact on daily living and well-being, psychiatric conditions are important aspects to be evaluated in these patients.

Keywords: COPD, exacerbations, psychological aspects, post-traumatic stress disorder, airflow limitation

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COPD patients with co-morbid depression have lower quality of life and have greater objective impairment to functional performance when compared with non-depressed patients with the same disease (2). The prevalence of anxiety may be as high as 15.8% in patients who have COPD, which is more than three times the prevalence in the general population (3). Panic attacks also seem to be more frequent in patients who have COPD than in the general population. In one small study, 37% of outpatients who had COPD reported symptoms of a panic attack in the preceding 3 weeks (4). In their study of 110 COPD patients, Laurin et al. (5) found that patients with psychiatric disorders had more exacerbations (40%) and a 56% greater risk of having an exacerbation than patients without a psychiatric disorder. They were also nearly twice as likely to have outpatient exacerbations compared with patients without psychiatric disorders.

Post-Traumatic Stress Disorder (PTSD) is a result of exposure to traumatic events involving death or the threat of death or severe damage to one's physical integrity, in which such symptoms last more than one month (6). Twelve-month prevalence of PTSD is 3.5% (7), whereas estimated lifetime prevalence of PTSD in the general population is 6.8% (8). It has been suggested that COPD may be an etiological factor in PTSD (9) and a recent study showed there is an association of trauma exposure and PTSD with airflow limitation (10). Given that COPD is characterized by progressive airflow obstruction and exacerbations of symptoms, especially dyspneia, appear to result in poorer quality of life and survival, we aimed to evaluate the influence of exacerbations episodes over PTSD-related symptoms.

Material and Methods

Subjects

A convenience sample of 33 (24 females) COPD patients (forced expiratory volume in 1 second $[FEV_1]/forced$ vital capacity [FVC] < 0.7 and post-bronchodilator $FEV_1 < 70\%$ predicted) presenting with a long history of smoking (>20 pack-years) who were admitted to the medical ward of a hospital, but not to the ICU, to treat an exacerbation were enrolled. The study was previously approved by the Institutional Review Board (IRB), and all subjects gave written, informed consent.

The diagnosis of COPD exacerbation was confirmed if patients had two or more of the following three symptoms (11): worsened dyspnea; worsened sputum volume and/or change in its color; and a new or worsening cough. Exclusion criteria were as follows: current smokers; infiltrate seen on radiograph; infection from any other organ; heart failure; myocardial infarction; pulmonary embolism; asthma; or the need for ventilatory support. None of the patients included in this study have had previous admissions to ICU. The treatment to the in-hospital patients, in the current or previous admissions, included therapy with an inhaled β -agonist and anti-cholinergic agents, IV methylprednisolone, followed by oral prednisone over 2 weeks and IV antibiotics followed by an oral course to complete 10 to 14 days. For those exacerbation episodes treated as outpatients, the medications included antibiotics, optimization of bronchodilatation with short- and long-acting bronchodilators and oral course of steroids.

Clinical variables

We recorded the medical history, number of exacerbations in the previous year, treated as inpatients- or outpatients-based regimen, baseline lung function and medications. Those patients who had a lung function done in the last year were asked to bring the results when it was not recorded in hospital files. The patient's most recent lung function was eligible to be analyzed. Co-morbidities were reviewed in patient's files that allowed to calculate Charlson's co-morbidities index. The most frequent were systemic hypertension [n = 21(63.6%)], diabetes mellitus [n = 8(24.5%)], congestive heart failure [n = 4 (12.1%)], Isquemic Heart Disease [n = 3 (9.1%)], cardiac arrhythmias [n = 2(6.1%)] and others [n = 9 (27.3%)].

Indices of health-related quality of life (HRQoL) were obtained using the St. George's Respiratory Questionnaire (SGRQ) (12). Three component indices were calculated using empirically derived weightings: Symptom, Activity, and Impact scores, from which a total score was computed. Scores vary from 0 (no disability) to 100 (maximum disability).

PTSD symptoms were assessed through the Screen for Posttraumatic Stress Symptoms (SPTSS), which is a brief self-report screening composed of 17 items, presented in the first person, covering the 17 symptoms that compose the diagnostic criteria for PTSD (13).

Anxiety and depression symptoms were assessed through the Beck Anxiety Inventory (BAI) (14) and the Beck Depression Inventory (BDI) (15), respectively. The BAI is a self-report measure consisting of 21 items; each item is rated on a four-point scale ranging from 0 (not at all) to 3 (severely, I could barely stand it). Participants rate items according to how much they were bothered by the particular symptom over the previous week. The BDI is a 21-item self-report depression screening measure; each item is rated on a four-point scale ranging from 0 to 3, with higher scores indicating higher levels of depression. Participants are asked to endorse statements characterizing how they felt over the past 2 weeks.

Statistical analysis

Descriptive analysis was performed using proportions, means and standard deviations. The Shapiro–Wilk test was used to check assumptions regarding data normality. Kendall's Tau coefficient was used to correlate the number of exacerbations with post-traumatic stress symptoms, anxiety and depression and Spearman's correlation coefficient was used to verify the relationship



of anxiety and depression with pulmonary function and with post-traumatic stress symptoms. Likewise this same coefficient was used to analyze the relationship between the quality of life with post-traumatic stress symptoms. A Poisson regression model was used to check the influence of gender, anxiety, depression, pulmonary function, co-morbidities and the number of exacerbations per year on the development of post-traumatic stress. The influence of post-traumatic stress on quality of life was tested using simple linear regression. Statistical analyses were performed using *Stata Software version 8.0*; *p* values <.05 were considered statistically significant.

Results

Of the 33 patients included in the study, there was a predominance of women (72.7%) and median age 72 with a smoking history of 37.8 ± 13.4 pack-years as can be seen in Table 1. All COPD patients included in this study had experienced exacerbation episodes in the previous year, but 25 (75.8%) had two or more episodes and 16(61.5%) required hospitalization. Most of the patients (63.6%) had elementary schooling and only 3 patients (9.09%) had university education. As to employment status, 51.5% of the patients were retired and 6 patients (18.18%) declared they were homemakers i.e., being part of the patient population without a formal job. No military personnel was found in this sample. As to marital status, most of the patients were married or widowed.

Moderate to severe anxiety scores (BAI total score >16.0) were found in 23 (69.7%) of the patients. The symptoms with the highest mean scores were breathing difficulty (M = 2.49) and suffocating sensation (M = 1.71). Other issues directly associated with anxiety were "feeling nervous" (M = 1.59), indigestion or abdominal discomfort (M = 1.45) and "fear that the worst will happen" (M = 1.24). Moderate to severe depression symptoms (BDI total score > 20.0) were found in 16 (48.5%) of the COPD patients. Symptoms of depression with the highest mean scores were "feeling tired" (M = 2.12), reduced libido (M = 2.07), difficulty to work (M = 1.93), irritability (M = 1.80) and insomnia (M = 1.77).

A predominance of cases of minimum depression (33.3%) could also be observed. Post-traumatic stress symptoms were assessed through the SPTSS, which presents 17 items corresponding to the 17 PTSD symptoms described in DSM-IV. COPD patients reported between 0 and 15 post-traumatic symptoms, with greater prevalence of the following manifestations: difficulty falling or staying asleep, hypervigilance, and exaggerated startled response. In a linear regression model, exacerbations significantly predicted post-traumatic stress symptoms. The PTSD symptom score of the patients with no exacerbations in the previous year was 1.56 points, showing that airflow obstruction was associated to post-traumatic symptomatology (p < 0.001) independently of any exacerbation episode.

Table 1. Characteristics of 33 COPD in-patients with exacerbation

Characteristics	
Age (yr) median(min-max)	72 (43–86)
Female sex (n,%)	24 (72.7)
Smoking history (pack-years) (mean±SD)	37.8 ± 13.4
Pulmonary function (mean±SD)	
FVC(L)	1.7 ± 0.6
FVC (% of predicted)	60.7 ± 18.18
FEV ₁ (L)	0.8 ± 0.3
FEV ₁ (% of predicted)	37.7 ± 14.9
FEV ₁ /FVC	50.2 ± 14.1
Total Exacerbations	
Mean per year (episodes)	2.9
≥ 2 in preceding year, <i>n</i> (%)	25 (75.8)
<2 in preceding year, n (%)	8 (24.2)
Not requiring hospitalization	
Mean per year (episodes)	1.1
≥ 2 in preceding year, n (%)	11 (73.3)
<2 in preceding year, n (%)	4 (26.6)
Mean per year (episodes)	
Requiring hospitalization	
Mean per year (episodes)	1.7
≥ 2 in preceding year, <i>n</i> (%)	16 (61.5)
<2 in preceding year, n (%)	10 (38.5)
Health-related quality of life (SGRQ)	
Symptoms	62.7 ± 16.5
Activities	79.2 ± 16.8
Impact	52.2 ± 21.1
Total	62.1 ± 1.54
Psychological Assessment	
Depression (mean \pm SD)	21.2 ± 12.1
Anxiety(mean \pm SD)	23.5 ± 12.4
PTSS (mean ± SD)	4.13 ± 2.54

FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; PTSS, post-traumatic symptoms score SGRQ, Saint George Respiratory Questionnaire.

On the other hand, each episode of exacerbation added 0.9 points to the PTSD symptoms scores; F(34) = 12.4; p = 0.001. Significant correlations were detected between post-traumatic stress symptoms and anxiety (rs = 0.57; p < 0.001) and post-traumatic stress symptoms and depression (rs = 0.62; p < 0.0001). Figure 1 shows a moderate and significant correlation between post-traumatic stress symptoms and episodes of exacerbation. When we analyzed health related quality of life in the same model of linear regression, it was found that each exacerbation episode added 5.27 points to the total SGRQ score. In a multiple regression analysis model it was found that an increase of one point in the BDI scores increases the total score for quality of life by 1.05 points (p < 0.0001). Using Spearman's coefficient correlation, we found a



Figure 1. Correlation between post-traumatic stress symptoms and exacerbations in COPD patients (p < 0.001).

moderate significant correlation (rs = 0.52; p < 0.001) of the SPTSS total score with the SGRQ activity domain (rs = 0.36; p = 0.031) and impact domain (rs = 0.52; p < 0.001) scores. No significant correlation between the SPTSS score and symptoms domain in the SGRQ was observed (rs = 0.15; p = 0.383).

Using an SPTSS cut-off score \geq 3.5 (sensitivity 0.70; specificity 0.84; +LR 4.55 and –LR 0.35) for this sample of exacerbated COPD patients, 16 (48.5%) of the participants showed symptoms compatible with a PTSD diagnosis. Using a more conservative SPTSS cut-off score \geq 5.0 (sensitivity 0.55; specificity 1.0), the estimated prevalence of current PTSD-related symptoms

was 33.3% (n = 11 patients). The univariable analysis showed that moderate to severe anxiety scores led to a twofold increase in the estimated prevalence ratio for PTSD [2.10 (CI95% 1.33–3.25); p = 0.001] and moderate to severe depression led to a near twofold increase [1.91 (CI95% 1.34–2.70); p = 0.0001]. The occurrence of two or more episodes of exacerbation in the previous year led to a near twofold increase in the estimated prevalence ratio for PTSD in both the univariable analysis and the multivariable analysis and was the only variable capable of predicting an increase in the estimated prevalence ratio for PTSD (*Goodnessof-fit test* 21.26 and p = 0.774) (Table 2).

Discussion

The principal finding of this study is that two or more episodes of exacerbation led to a near twofold increase in the estimated prevalence ratio of PTSD-related symptoms, specially those ones requiring hospitalization. We also observed that each exacerbation episode increased 0.9 points in the SPTSS score and there was a moderate and significant correlation between COPD exacerbation episodes and post-traumatic stress symptomatology in this non ICU hospitalized patients. We found that 33.3% of our sample showed SPTSS scores compatible with the clinical diagnosis of PTSD. This is in contrast with earlier findings, which describe a lifetime prevalence of PTSD in 1.6% (10), or a current prevalence of 8% (16) to 20.7% (assessed 3 months after ICU discharge) (17).

Variables	Univariable analysis			Multivariable analysis		
	PR	(CI95%)	p ^a	PR	(CI95%)	pb
Age						
\leq /2 years old	1.0	(0.05 1.00)	0.007			
72 years old	1.2	(0.85 - 1.68)	0.287			
Gender						
Male	1.00					
Female	1.03	(0.70 – 1.50)	0.885			
Anxiety						
Mínimum/Mild	1.0			1.0		
Moderate/Severe	2.10	(1.33 – 3.25)	0.001	1.45	(0.86 - 2.45)	0.167
Depression						
Mínimum/Mild	1.0			1.0		
Moderate/Severe	1.91	(1.34 – 2.70)	0.0001	1.37	(0.89 - 2.10)	0.150
Pulmonary Function						
FUC (L)	0.83	(0.61 - 1.14)	0.269			
FVC (% of predicted)	1.0	(0.01 - 1.14) (0.99 - 1.0)	0.203			
FEV ₁ (I)	0.49	(0.26 - 0.91)	0.026	0.85	(0.43 - 1.71)	0.655
FEV ₁ (% of predicted)	0.99	(0.98 - 1.01)	0.358	0.00	(0.10)	01000
Exacerbation/ previous year						
<2 exacerbation episodes	1.00			1.00		
≥2 exacerbation episodes	2.4	(1.44 - 3.9)	0.0001	1.71	(1.10 - 2.65)	0.015
Requiring hospitalization	1.2	(1.08 - 1.33)	<0.001 ^a	1.13	(1.01 - 1.26)	0.030
Not requiring hospitalization	1.0	(0.89 - 1.11)	0.976		. ,	
Charlson Co-morbidity Index	0.97	(0.90 - 10.5)	0.421			

FVC: Forced Vital Capacity; FEV₁: Forced Expiratory Volume in 1 second. ^aVariables with a p < 0.2; ^bPoisson Regression I < 0.05 PR: Prevalence Ratio CI: Confidence interval.



JOURNAL OF CHRONIC OBSTRUCTIVE

PULMONARY DISEASE

The discrepancies between studies can be at least partially attributed to methodological questions regarding the instruments used to assess PTSD and posttraumatic stress symptoms. The Spitzer et al. study (10) demonstrated that after adjusting for sociodemographic, clinical and lifestyle factors, subjects with PTSD had significantly higher odds ratios for most asthma-related symptoms than PTSD-negative participants (OR 3.2-8.8). These authors used the PTSD module of the Structured Clinical Interview for DSM-IV (SCID). Although structured clinical interviews are the preferred instruments when epidemiological aspects are a major concern, self-reported measures are less time consuming and usually not so dependent upon the interviewers' expertise or training. Therefore, measures such as Posttraumatic Diagnostic Scale (PDS) (18) and The Impact of Event Scale - Revised (IES-R) (19) were used to establish PTSD diagnosis in COPD patients.

Although both PDS and IES-R are measures that link responses to a single event (the worst event), the SPTSS does not require the patient to establish a causal link between a single traumatic event and current posttraumatic symptoms. Thus, it seems reasonable to assume that post-traumatic symptomatology resulting from exposure to multiple traumatic events can be reliably assessed with measures such as the SPTSS. As can be seen in Figure 2, a cut-off score \geq 3.5 for this sample of exacerbated COPD patients could be used with an estimated prevalence of PTSD of 48.5%, but we used a cut-off score \geq 5 similar to Carlson's study (13) that found a good internal consistency for the SPTSS, with a Cronbach's alpha of .91 and bivariate item-total correlations ranging between r = .49 and r = .75 (p < .00001). His data were also provided on sensitivity and specificity scores for the SPTSS, considering DSM-IV clinical diagnosis criteria. Little is known about obstructive airflow diseases and risk factors for PTSD, especially in relation to exacerbation episodes.

A multicenter study (17) with 126 COPD exacerbated patients who had survived to an ICU stay determined



Figure 2. Receiver operating characteristics (ROC) analysis of SPTSS to estimate PTSD in COPD patients with exacerbation. The AUC for SPTSS was 0.819 (Cl95% 0.674-0.964); p = 0.002.

the prevalence of anxiety, depression and post-traumatic stress symptoms. Post-traumatic stress symptoms were present in 20.7%. By multivariable analysis, factors independently associated with PTSD-related symptoms in the patients were previous ICU experience (OR, 2.17/point [1.05–4.48]), worse Peritraumatic Dissociative Experiences Questionnaire (PDEQ) score at ICU discharge (OR, 1.08/point [1.01–1.15]), and recollection of bothersome noise in the ICU (OR, 7.52/point [1.35–54.72]). In our sample no influence of gender, co-morbidities, anxiety, depression and pulmonary function was observed in multivariable analysis.

When a patient who has COPD exacerbation is anxious and has dyspnea, he or she may misconstrue the severity of the breathlessness. This leads to a heightened state of physiologic arousal, which leads to additional misperception of the sensations of dyspnea and an exaggerated feeling of breathlessness (3). In this sample of patients admitted with COPD exacerbation, moderate to severe symptoms of anxiety were present in 69.7% of them and had an effect on the estimated prevalence ratio of PTSD in the univariable analysis. Of the 33 patients with COPD exacerbation, 48.5% had moderate to severe depression, which was a predictor for post-traumatic stress symptoms in the univariable but not in the multivariable analysis.

Although it is well known that the more obstruction of airflow the more exacerbations, a recent study showed that a history of exacerbations in the previous year is a better predictor of exacerbations (20) that are an important outcome, not only because they pose a considerable economic burden but more importantly because repeated exacerbations of COPD lead to deteriorating health-related quality of life (21). Considering that exacerbation frequency is strongly correlated with the SGRQ total score and component scores (22) health-related quality of life parameters may be determined by several factors, so psychological aspects may influence the subjective perception and seems to be important issues in this context. Even though the SGRQ was applied during hospitalization in our study, we were able to demonstrate moderate and significant correlations between PTSS and all the SGRQ domains, except for symptoms. One possible explanation for this finding is the fact that the domain symptoms refer not only to dyspnea but also to coughing, wheezing and sputum expectoration.

Our study has some limitations that must be noted. First, we included only patients hospitalized in order to treat exacerbations and all of them had severe to very severe disease. Since no traumatic events were defined for each patient, it is not possible to establish that dyspnea *per se* was the determinant factor for the posttraumatic symptoms, although a correlation between exacerbations and post-traumatic symptomatology was found. We did not use DSM-IV clinical diagnosis criteria and for this reason, we could only estimate the prevalence of PTSD in our sample.

95

In conclusion, the exacerbation episodes are associated to pos-traumatic stress symptoms related to PTSD and patients with two or more exacerbations had a near twofold increase in the estimated prevalence ratio of this psychological disorder. Future studies including all degrees of airflow limitation, which identify the traumatic events and follow up the patient's HRQoL are necessary to better understand the relationship between PTSD, post-traumatic symptoms and COPD exacerbations. Finally, the present findings suggest that, regarding clinical practice, post-traumatic symptoms must be assessed in all COPD patients with exacerbation, especially those who need hospitalization.

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The authors Paulo Jose Zimermann Teixeira and Lucia Porto should be considered as co-first author.

Declaration of Interest Statement

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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