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Relationship between clinical anxiety and patient outcomes in patients with chronic obstructive lung disease exacerbation in the emergency department

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Abstract

Purpose: Anxiety is a comorbidity that is not routinely addressed in patients with chronic obstructive lung disease (COPD) exacerbation in the emergency department (ED). Anxiety in patients with COPD exacerbation can be related with negative outcomes. The Generalized Anxiety Disorder 7 (GAD-7) score is an easy-to-use tool to determine anxiety. This study aimed to investigate the relationship between GAD-7 score and patient outcomes in patients with COPD exacerbation in the ED.
Methods: A prospective, cross-sectional study was conducted in a tertiary academic ED between July 2019 and January 2021. Patients admitted to the ED with COPD exacerbation were included. A GAD-7 score of ≥ 10 was defined as clinically significant anxiety. Negative outcomes were defined as a composite outcome that included recurrent ED visits, intensive care unit admission, and mortality. The relationship between clinically significant anxiety and negative outcomes within 30 days was determined.
Results: A total of 92 patients were assessed for eligibility and 80 were included in the study. Thirty-seven patients (46.3%) experienced negative outcomes. Although no significant difference was detected in median GAD-7 scores between patients with positive and negative outcomes, negative outcomes were significantly higher in patients who had a GAD-7 score of ≥ 10 ($n = 25$, $p = 0.03$). A sensitivity of 43.2%, specificity of 79.1%, positive likelihood ratio of 2.1 and negative likelihood ratio of 0.7 were determined for GAD-7 score in predicting negative outcome.
Conclusion: In patients with COPD exacerbation in the ED, a GAD-7 score of ≥ 10 was associated with 30-day negative outcomes.

Keywords
Generalized anxiety disorder · Chronic obstructive pulmonary disease · COPD exacerbation · Emergency department · GAD-7

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Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and limited airflow, usually caused by exposure to harmful particles or gases [1]. COPD is one of the three leading causes of death around the world and the condition often progresses with exacerbations. Exacerbation of COPD, a major reason these patients are admitted to emergency departments (EDs), is generally defined as an acute worsening of respiratory symptoms that results in the need for additional treatment [1–3].

There are many physiological variables that must be evaluated in patients admitted to the ED with COPD exacerbation. Management of such patients usu-

ally focuses on improving dyspnea with respiratory therapies and bronchodilators, treatment of concurrent infections, and measures for other comorbidities [4]. Previous studies have shown that anxiety, like other comorbidities, may play a role in the development of a COPD exacerbation and can have a negative impact on patients' prognoses [5–8]. The prevalence of clinical anxiety ranges from 10–55% among hospitalized patients and 13–46% in outpatients [9]. It has also been reported that COPD patients are 85% more likely to develop anxiety disorders compared to healthy individuals [6].

In the stable period of COPD, it is recommended that many tools be used to measure anxiety levels in patients. Instruments such as the Hospital Anxiety and Depression Scale (HADS), the Beck Anxiety Inventory (BAI), the Anxiety inventory for respiratory disease (AIR) score, and the Generalized Anxiety Disorder-7 (GAD-7) scale have been used to screen COPD patients for anxiety [10–12]. The GAD-7 scale is a validated tool that could be practical for assessing anxiety in COPD patients in the ED [13, 14]. Considering that patients with COPD exacerbation arrive in EDs in relatively poor clinical condition, it is thought that anxiety might be an underrecognized comorbidity in this population. There is no study in which anxiety concurrent with COPD exacerbation was evaluated in an ED setting with an easy-to-use scale such as the GAD-7. The primary aim of the current study was to estimate anxiety levels of patients using GAD-7 scale and to investigate the effects of anxiety on specific outcomes, including ED revisits, admission to the intensive care unit (ICU), and mortality.

Methods

Study design and setting

This prospective, cross-sectional study was conducted with patients presenting with acute exacerbation of COPD in the ED of a university hospital between July 2019 and January 2021.

Institutional review board approval was obtained prior to study initiation and eligible patients gave informed consent to be included in the study.

Participant selection

All adult patients admitted to the ED with COPD exacerbation were consecutively included in the study. The patients who had a Glasgow Coma Scale (GCS) score < 15, and those who had been diagnosed with anxiety, depression, psychosis, or neurosis by a psychiatrist within the preceding month, or had been using of neuropsychiatric medication were excluded from the study. COPD exacerbation was defined as "worsening of respiratory symptoms resulting in the need for additional treatment" based on the guidelines developed by the Global Initiative for Chronic Obstructive Lung Disease [1].

Study protocol

Patients admitted to the ED with dyspnea were evaluated by treating physicians. Patients diagnosed with COPD exacerbation were identified at this stage, and treatment for such symptoms was started immediately. Patients received standardized treatment according to current guidelines, including respiratory support, inhaled bronchodilators, and systemic corticosteroids. After the first bronchodilator treatment was completed, the patients were informed regarding the study and informed consent was obtained from those who agreed to participate.

Patients' demographic, clinical, and laboratory characteristics were recorded on a standardized data collection form. The principal investigator evaluated each patient using the GAD-7 anxiety score once their first bronchodilator treatment was completed.

The GAD-7 scale consists of seven questions, each of which has four possible answers. On the GAD-7, a score of 10 or greater—which is defined as clinically significant anxiety [13]—is a suggested cut-off point for identifying individuals who should be evaluated by a mental health professional. After determining the GAD-7 score and initial clinical management, patients were followed up in the ED, hospitalized or discharged from the ED according to current guidelines. The study investigators did not intervene in or contribute to the patients' diagnoses, treatments, or decisions regarding hospitalization.

Outcome measures

The primary outcome of the study was the composite endpoint of recurrent ED visits, intensive care unit (ICU) admissions, and mortality within 30 days. The patients were telephoned 30 days after being discharged from the ED. Patients who experienced one or more of these outcomes were included in the negative outcome group; those who did not experience any of these outcomes were included in the positive outcome group.

Statistical analysis

The data gathered were analyzed using SPSS Statistics for Windows v. 15.0 (IBM, Armonk, NY, USA). The Kolmogorov–Smirnov test was used to test for the normal distribution of continuous variables. Normally distributed continuous variables were tested using the student's t-test and expressed as means and standard deviations. Continuous variables that did not fit the normal distribution were tested using the Mann–Whitney U test and expressed as medians and interquartile ranges (IQRs). The χ^2 and Fisher's exact test were used to analyze categorical variables, and data were expressed as numbers and percentages. Spearman's rank correlation coefficient was used for the correlation analysis. The vassarstats.net website was used for the sensitivity and specificity calculations, and the data were presented with 95% confidence intervals (CIs). A P value < 0.05 was considered statistically significant.

Results

A total of 92 patients with a COPD exacerbation were assessed for eligibility; 80 were included in the study after the exclusion criteria were implemented (◘ Fig. 1). At the end of the 30-day follow-up period, 43 (53.8%) patients were in the positive outcome group and 37 (46.3%) were in the negative outcome group in terms of mortality, ICU admission, and return visits to the ED. Of the 37 patients in the negative outcome group, 33 had revisited the ED, 7 had been admitted to the ICU, and 3 had died within 30 days of initial ED admission.
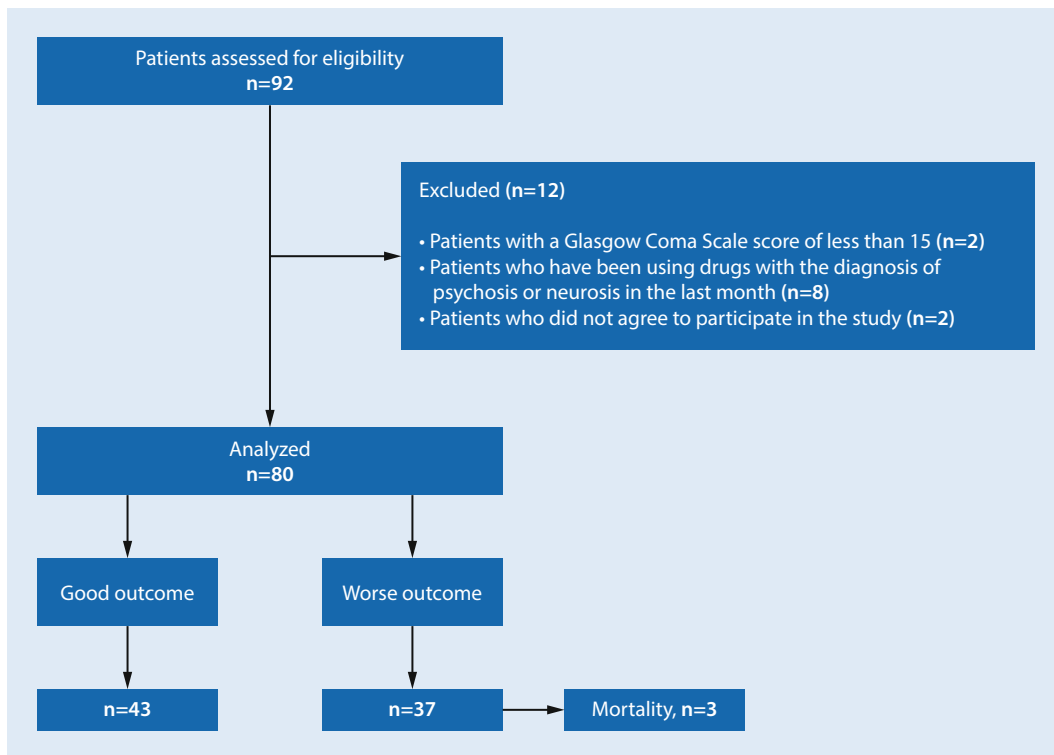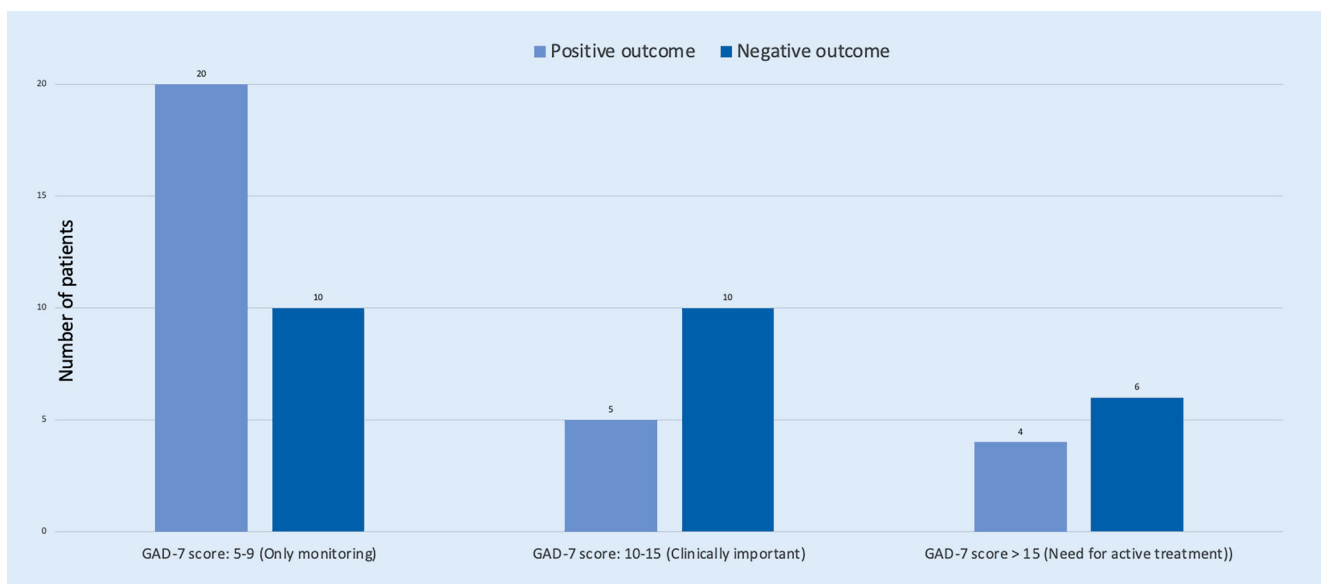
Fig. 1 ◄ Patient flow chart

Fig. 2 ▲ Distribution of patients according to their Generalized Anxiety Disorder 7 (GAD-7) scores

There were no significant differences in demographic and clinical characteristics between the negative and positive outcome groups (◘ Table 1). Also, initial laboratory test results, including arterial blood gas, complete blood count, C-reactive protein levels, were similar between the groups (◘ Table 2).

The median GAD-7 score of all patients was 7 (IQR 4–11). The positive outcome group had a median score of 6 (IQR 2–8), while the negative outcome group had a median score of 7 (IQR 4–13). There was a weak correlation between number of ED revisits each patient had and GAD-7 score (r = 0.230, P = 0.040).

Patients who had a GAD-7 score >10 were defined as having clinically significant anxiety and were analyzed separately. A total of 25 patients were included in this subgroup: 9 patients (20.9%) were in the positive and 16 (43.2%) patients were in negative outcome group. The GAD-7 scores of patients with negative outcomes were significantly higher than those of patients with positive outcomes (P = 0.032).

The performance of GAD-7 scores in predicting negative outcomes was evaluated. For a threshold GAD-7 score of 10, a sensitivity of 43.2%, specificity of

Table 1 Baseline characteristics of the study population

	Positive outcome $n = 43$	Negative outcome $n = 37$	P value
Age [a]	67 ± 11	70 ± 9	0.175
Male sex, n (%)	36 (83.7%)	34 (91.9%)	0.326
Diabetes mellitus, n (%)	13 (30.2%)	12 (32.4%)	0.832
Hypertension, n (%)	18 (41.9%)	18 (48.6%)	0.543
Chronic renal disease, n (%)	6 (14.0%)	2 (5.4%)	0.275
History of stroke, n (%)	2 (%4.7)	1 (2.7%)	1.000
Congestive heart failure, n (%)	10 (23.3%)	10 (27.0%)	0.368
Active smoking, n (%)	12 (27.9%)	8 (21.6%)	0.517
Vital signs			
Temperature (°C) [a]	36.7 ± 0.7	36.7 ± 0.7	0.659
Pulse (beat/min) [a]	101 ± 20	99 ± 19	0.739
Systolic blood pressure (mm Hg) [a]	142 ± 25	146 ± 26	0.557
Respiratory rate (breath/min) [a]	31 ± 9	31 ± 6	0.417
Exacerbation characteristics			
Dyspnea, n (%)	37 (86.0%)	32 (86.5%)	0.955
Increase in sputum, n (%)	20 (46.5%)	15 (40.5%)	0.591
Cough, n (%)	26 (60.5%)	18 (48.6%)	0.289
Rales, n (%)	17 (39.5%)	8 (21.6%)	0.085
Ronchus, n (%)	36 (83.7%)	30 (81.1%)	0.757
Silent chest, n (%)	6 (14.0%)	5 (13.5%)	0.955

[a] *Mean ± SD* Mean ± standard deviation

Table 2 Laboratory evaluation of chronic obstructive lung disease (COPD) exacerbation regarding outcome

	Positive outcome $n = 43$	Negative outcome $n = 37$	P value
pH	7.40 ± 0.05	7.40 ± 0.06	0.674
pO_2 (mm Hg)	52 ± 23	54 ± 24	0.817
pCO_2 (mm Hg)	42 ± 9	40 ± 11	0.370
HCO_3 (mmol/L)	26 ± 4	25 ± 4	0.380
Lactate (mg/dL)	16.7 ± 7.0	19.4 ± 13.5	0.279
O_2 saturation (%)	90 ± 12	89 ± 9	0.708
Hemoglobin (g/dl)	12.9 ± 2.2	13.0 ± 2.4	0.899
Leukocyte count (cells × 10^3/µL) [a]	9.7 (7.6–12.7)	12.0 (9.1–15.7)	0.365
C-reactive protein (mg/dL) [a]	34 (9–104)	16 (7–77)	0.189

[a] *Median (IQR)* Median (interquartile range)

79.1%, positive likelihood ratio of 2.1, and negative likelihood ratio of 0.7 were determined. The distribution of the patients according to their GAD-7 scores is presented in ◘ Fig. 2.

Discussion

Patients experiencing COPD exacerbation usually arrive at the ED in poor clinical condition, and therefore concurrent psychiatric comorbidities might be underrecognized. In this study, we found that an easy-to-use screening tool could predict various adverse outcomes and identify patients who might benefit from psychiatric support in the ED setting. Especially in patients with clinically significant anxiety, intervening at this stage could improve patient outcomes.

Many studies have confirmed a relationship between COPD and anxiety. A systematic review of 24 articles revealed that anxiety and depression are common comorbid conditions in patients hospitalized for COPD [15]. According to a prospec-

tive cohort study, COPD was associated with a greater risk of anxiety (odds ratio [OR] 1.85; 95% CI 1.072–3.18) compared to matched controls. In the same study, anxiety was found to be related to poorer health outcomes, including worse submaximal exercise performance and a greater risk of self-reported functional limitations (OR 2.41; 95% CI 1.71–3.41) [6]. COPD patients are also approximately 10 times more likely to experience panic disorder or panic attacks than healthy individuals [16]. However, all these studies were conducted on stable COPD patients. No study that evaluated the anxiety of COPD patients experiencing exacerbated symptoms who were assessed using a valid tool was found in the literature.

Data reported in the literature concerning the diagnosis of anxiety in COPD patients varies, and it is therefore not possible to clearly determine the frequency of the condition in this cohort. The main reason for this is that a wide variety of diagnostic tools are used to diagnose anxiety. In a multicenter study, Baker et al. compared the test performance characteristics of three anxiety screening questionnaires used for COPD patients [12]. Using the Mini-International Neuropsychiatric Interview as the gold standard, they found that the area under the curve values of the three anxiety scores were 0.78 (95% CI 0.69–0.87) for GAD-7, 0.74 (95% CI 0.64–0.84) for HADS-A, and 0.66 (95% CI 0.56–0.76) for AIR, respectively [12]. The area under the curve value of the GAD-7 was significantly higher than the AIR score. In our study, we preferred to use the GAD-7 score because of its stronger diagnostic performance and its ease of application in the ED setting.

Delayed diagnosis of anxiety in COPD patients is associated with many barriers caused by patients, physicians, and the healthcare system [17]. Using standardized diagnostic criteria or screening instruments may facilitate the diagnosis and referral of patients. As Spitzer et al. revealed, higher scores on the GAD-7 scale are an excellent measure of severity, as evidenced by the fact that they are strongly associated with multiple functional impairments and an increased number of disability days [13]. In this study, a GAD-7 score was recorded for all patients who scored over 4 (29 of the patients with positive outcomes and

36 of the patients with negative outcomes). Nine of the 29 patients (31%) with positive outcomes were found to be experiencing clinically significant anxiety (GAD-7 score > 10), compared to 26 of the 36 patients (62%) with negative outcomes. Although anxiety is not directly associated with mortality here, considering that the most common negative outcome in our study was readmission to the ED, it is possible that there may be a link between anxiety and repeated COPD exacerbation.

Many factors can influence readmission to the ED in COPD exacerbation. Gudmundsson et al. investigated the risk of rehospitalization in patients with COPD exacerbation and associated risk factors [18]. They found no significant association between 1-year readmissions and anxiety symptoms, which were evident in 41% of the patients they assessed [18]. However, of 406 consecutive patients hospitalized for acute COPD exacerbation, those with poorer health status (as measured by the St. George's Respiratory Questionnaire) and more severe anxiety symptoms (but not more severe depression symptoms) had a 1.36 times higher risk of readmission at 1 year (adjusted hazard ratio: 1.36; 95% CI 1.12–1.65). Furthermore, the duration of a patient's exacerbation can also be affected by anxiety. A multicenter prospective cohort study of 491 patients with stable COPD revealed that the duration of event-based exacerbation episodes was 1.92 times longer (95% CI 1.04–3.54) in patients with probable anxiety (HADS anxiety score > 10) compared to those with no anxiety (score < 8) [10]. As this study evaluated patients being treated in an ED, it was not possible to determine the long-term effects of anxiety and its relationship to the duration of exacerbation symptoms.

Limitations

Our study has several limitations. First, it was conducted in a single center with a small sample population, which limits the generalizability of the results. Second, the patients with a GAD-7 score of > 10 were recommended for further psychiatric follow-up. However, we did not evaluate the benefit of the psychiatric evaluation because the short-term negative outcomes were the focus of this study. Future

prospective cohort studies are needed to understand whether negative outcomes improve with such support. Third, the decision of admission to hospital wards was at the discretion of chest physicians. Because of limited hospital resources during the coronavirus disease 2019 (COVID-19) pandemic, the decision for the admission to hospital wards was affected by hospital capacity. Therefore, we did not analyze hospital ward admission as a negative outcome. Finally, although we used the GAD-7 tool to evaluate patients after their first treatment for an exacerbation, the chaotic and fast-paced environment of the ED may have affected the patients' responses.

Conclusion

Patients with COPD exacerbations experience multiple comorbidities and frequent ED visits. Early recognition and treatment of all comorbidities in these patients is essential to reduce the frequency of exacerbation episodes. Anxiety is a comorbidity that is not routinely addressed in the ED setting in this patient group. The GAD-7 anxiety score is a tool that can be implemented in the ED to predict negative outcomes.

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Declarations

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Zusammenfassung

Zusammenhang zwischen klinischer Angst und Ergebnissen bei Patienten mit Exazerbation chronisch obstruktiver Lungenerkrankung in der Notaufnahme

Ziel: Angst ist eine Komorbidität, die in der Notaufnahme nicht routinemäßig bei Patienten mit Exazerbation einer chronisch obstruktiven Lungenerkrankung (COPD) angesprochen wird. Angst bei Patienten mit COPD-Exazerbation kann mit einem negativen Verlauf einhergehen. Der Generalized Anxiety Disorder 7 (GAD-7) Score ist ein einfach zu benutzendes Instrument, um Angst festzustellen. Die vorliegende Studie hatte das Ziel, den Zusammenhang zwischen dem GAD-7-Score und den Ergebnissen bei Patienten mit COPD-Exazerbation in der Notaufnahme zu untersuchen.

Methoden: Eine prospektive Querschnittstudie wurde in einer Notfallaufnahme eines akademischen Lehrkrankenhauses der Tertiärversorgung zwischen Juli 2019 und Januar 2021 durchgeführt. Darin einbezogen wurden Patienten in der Notaufnahme mit COPD-Exazerbation. Ein GAD-7-Score von ≥ 10 wurde als klinisch bedeutsame Angst definiert. Negative Ergebnisse wurden definiert als zusammengesetzter Endpunkt aus Wiedervorstellung in der Notaufnahme, Aufnahme auf die Intensivstation und Mortalität. Es wurde der Zusammenhang zwischen klinisch bedeutsamer Angst und negativen Ergebnissen innerhalb von 30 Tagen ermittelt.

Ergebnisse: Insgesamt wurden 92 Patienten hinsichtlich ihrer Eignung beurteilt, und 80 wurden in die Studie aufgenommen. Negative Ergebnisse gab es bei 37 Patienten (46,3%). Zwar wurde kein signifikanter Unterschied bei den medianen GAD-7-Scores zwischen Patienten mit positiven und negativen Ergebnissen festgestellt, aber die negativen Ergebnisse waren signifikant höher bei Patienten mit einem GAD-7-Score von ≥ 10 ($n = 25$; $p = 0,03$). Für die Vorhersage eines negativen Ergebnisses durch den GAD-7-Score wurden eine Sensitivität von 43,2%, eine Spezifität von 79,1%, eine positive Likelihood-Ratio von 2,1 und eine negative Likelihood-Ratio von 0,7 ermittelt.

Schlussfolgerung: Bei Patients in der Notaufnahme mit COPD-Exazerbation steht ein GAD-7-Score von ≥ 10 mit negativen Ergebnissen innerhalb von 30 Tagen in Zusammenhang.

Schlüsselwörter

Generalisierte Angststörung · Chronisch obstruktive Pulmonalerkrankung · COLD-Exazerbation · Notfallabteilung · GAD-7