Anxiety and depression among patients with chronic obstructive pulmonary disease

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Abstract

Objective: to establish some variables associated with anxiety and depression with clinical importance in patients with COPD from the outpatient clinic in Santa Marta, Colombia.

Design: a cross-sectional analytical study.

Background: chronic obstructive pulmonary disease (COPD) is a chronic disease that affects approximately one in ten people in the general Colombian population. COPD is often associated with anxiety and depression. However, information on the variables associated with anxiety and depression in patients with COPD is limited.

Participants: adult COPD patients were included. The patients were classified according to the GOLD initiative and the combined assessment.

Interventions: none.

Measurements: clinically important anxiety and depression were assessed with the 10-item versions of the Zung scales.

Results: 409 patients between 40 and 102 years of age participated, mean of 73.0 years (SD=10.2 years), 58.7% male, 88.8% married (or in free union), 73.6% residents in low stratum (I, II or III), 92.7% exposed to cigarettes or wood smoke (biomass), 44.5% in GOLD 3 or 4, 22.2% classified in the combined evaluation C or D, 19.1% presented clinically significant anxiety and 27.9% clinically significant depression. Clinically important anxiety showed a significant association with the combined assessment C or D (OR=2.08, 95%CI 1.19-3.63) and female sex (OR=1.80, 95%CI 1.10-2.99) and depression with clinical importance showed a significant relationship with female sex (OR=2.35, 95%CI 1.50-3.70) and the combined C or D evaluation (OR=2.04, 95%CI 1.22-3.42).

Conclusions: The prevalence of clinically important anxiety and depression is high in COPD patients. Anxiety and depression are associated with female gender and the severity of COPD. Anxiety and depression must be evaluated in all patients with COPD evaluated in an outpatient clinic, particularly in women and in patients classified C or D in the combined evaluation. (Acta Med Colomb 2021; 46. DOI: https://doi.org/10.36104/amc.2021.1644).

Key words: *anxiety, depression, chronic obstructive pulmonary disease, outpatients, cross-sectional studies*.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic medical problem with periods of partial remission and exacerbations, characterized by reduced airflow and an increased inflammatory response. These changes in respiratory physiology are expressed in the clinical context as dyspnea, cough and expectoration (1). Chronic obstructive pulmonary disease affects approximately one out of every 10 people in the Colombian population (2).

The prevalence of anxiety and depression tends to be high in patients with chronic diseases like COPD (3-8). One meta-analysis found that patients with COPD were three times as likely to have depression than the general population (9).

Furthermore, cross-sectional studies show that the prevalence of anxiety in patients with COPD ranges from 15.2% to 19.1% (10, 11). In the Santa Marta setting, a cross-sectional study found that 5.8% of patients with COPD reported a history of depression; however, the presence of anxiety was not reported (12).

Studies suggest that the relationship between anxiety, depression and COPD is bidirectional: the presence of each increases the possibility of meeting the criteria for the other (3, 13). Chronic obstructive pulmonary disease significantly decreases people's quality of life (14, 15), and

when anxiety and/or depression are present, the patients' quality of life deteriorates even further (4, 5, 14, 16). In addition, these patients have a significantly greater risk of hospitalization due to COPD exacerbations (17, 18), longer hospital stays, death after hospital discharge (13, 18), and suicide (19, 20).

With regard to variables associated with anxiety and depression in patients with COPD, decreased quality of life has been found to be directly related to clinical severity, mediated by the presence of anxiety and depression in this group of patients (5, 14, 16, 21). This relationship continues to be significant even after controlling for smoking (15), which is necessary since the components of tobacco smoke can modify the prevalence of anxiety and depression in patients without COPD (22, 23).

However, at a global and national level, the study of variables associated with anxiety and depression in patients with COPD has focused particularly on the association with decreased quality of life, without considering other possibly confounding variables (5, 14-16, 21).

Specifying and adjusting the variables associated with anxiety and depression expands knowledge in this area. A better understanding of the relationship between anxiety, depression and COPD can help in implementing early case detection (6), reduce the burden of comorbidities and improve the quality of life (5, 14, 15).

The general objective of this study was to determine some clinically significant variables associated with anxiety and depression in patients with COPD receiving outpatient pulmonology care in Santa Marta, Colombia.

Materials and methods
Design and ethical considerations
A cross-sectional, observational, analytical study was designed taking into account the ethical aspects of human research included in the Colombian Ministry of Health's Resolution 8430 of 1993. The project was approved by the Research Ethics Committee at Universidad del Magdalena, Santa Marta, Colombia. All participants did so voluntarily after signing a consent form. The participants received no incentives for study participation (24).

Participants
Adults consulting at three institutions in Santa Marta between August and December 2019 were requested to participate. Adults over the age of 40 with a diagnosis of COPD and who signed an informed consent were included. Pregnant women and patients with cognitive impairment which would inhibit the completion of the anxiety and depression scales were excluded.

Sampling
Consecuutive nonprobabilistic sampling of evaluated patients was conducted. Based on the historical records of the participating institutions, a sample of at least 267

people was expected. This number was estimated based on an expected prevalence of anxiety or depression of 25%, a margin of error of 5 and a confidence level of 95% (25). An odds ratio (OR) of 3.0 was expected and, for this, at least 87 patients with anxiety or depression and 87 patients without clinically significant anxiety or depression were needed, with a confidence level of 95% and a power of 80% (26). Likewise, this sample size would allow for adjustments in the associations with the inclusion of up to six variables as a unit, under the assumption that at least 67 cases of clinically significant anxiety and depression would be available, aiming for at least 10 cases for each possible confounding variable (27).

Instruments
Sociodemographic data (age, sex, marital status, socio-economic level and home city), clinical findings like the combined assessment and GOLD classification and Zung scale scores for anxiety and depression were recorded.

GOLD classification
The GOLD classification for COPD takes the patient's degree of airflow limitation measured by forced expiratory volume in one second (FEV1) and classifies the degree of restriction as 1, 2, 3 and 4, going from lower to greater restriction (28). In the current study, the patients were categorized in two groups: low restriction (GOLD 1 and 2) and high restriction (GOLD 3 and 4).

Combined assessment
This is a more recent classification of the clinical stage of COPD involving a combined assessment of the patient's symptoms, number of exacerbations and symptom severity, as well as quality of life measured by the COPD Assessment Test (CAT). It includes stages A, B, C and D. Class A is the least severe stage and D is the most severe (27). In the current study, the stages were classified in two groups, a lower severity group (A and B) and a higher severity group (C and D).

Zung Anxiety Scale
The patients completed the brief Zung Anxiety Scale which consists of 10 items exploring anxiety symptoms in the last month. It provides multiple-choice answers with four options: never, sometimes, often or always. These possibilities are scored from zero to three; thus, the possible total scores lie between zero and 30. Scores greater than 10 were classified as clinically significant anxiety symptoms. This scale has had an acceptable performance on some psychometric indicators in Colombian samples (29). In the current study, Cronbach's alpha was 0.82.

Zung Depression Scale
The brief Zung Depression Scale consists of 10 items which explore depression symptoms during the last two

weeks. It offers multiple-choice answers with four response options: never, sometimes, often or always. These responses are scored from zero to three, with total scores between zero and thirty. Scores above 10 are classified as clinically significant symptoms of depression. This scale had a good psychometric performance in a prior Colombian study. In the current sample, Cronbach's alpha was 0.78.

Procedure
First, the research objectives were explained to the patients. The patients who signed an informed consent completed the Zung Anxiety and Depression scales, which are not part of the usual assessment and follow up in the outpatient care of COPD patients. Patients were included by order of arrival up to the proposed end date.

Statistical analysis
The descriptive component included data distribution observations. Frequencies and percentages were estimated for qualitative variables, and mean (M) and standard deviation (SD) and median (Me) and interquartile range (IQR) for quantitative variables. The possibility of missing values was not considered since data were collected prospectively.

For the bivariate analysis, clinically significant anxiety and depression were taken separately as dependent variables, and demographic variables, GOLD stage and the combined assessment were taken as independent variables, all dichotomously. Odds ratios (ORs) with 95% confidence intervals (95%CI) were calculated.

The multivariate analysis was adjusted for variables with probabilities of less than 20% on the bivariate analysis. This strategy is based on Greenland's recommendations, who adjusts for variables with p values less than 20% and which cause a greater than 10% change in the main association (for the current study, clinically significant anxiety or depression) (31). The adjustment was accepted if the Hosmer-Lemeshow test showed probability values greater than 0.05 (32). Odds ratio values were considered significant if they had a 95%CI that did not include the unit. The analysis was run on the IBM-SPSS version 23.0 program (33).

Results
A total of 409 patients participated, with ages ranging from 40 to 102 years, a mean of 73.0 years (SD=10.2 years), and a median of 74.0 years (IQR=65-80 years). More details on the demographic characteristics are provided in Table 1. The anxiety scores ranged from 10 to 34, with a mean of 16.2 (SD=5.2) and a median of 15 (IQR=12-19), and the depression scores ranged from 10 to 32, with a mean of 17.0 (SD=5.3) and a median of 16 (IQR=13-21). The classified clinical variables are found in Table 2.

The associations for clinically significant anxiety and depression are shown in Tables 3 and 4. In the (adjusted) multivariate analysis, clinically significant anxiety maintained a significant association with a combined assessment

Table 1. *Demographic description of the population..*

Variable	Frequency	%
Age (years)		
44-64	91	22.2
65 or more	318	77.8
Sex		
Female	169	41.3
Male	240	58.7
Marital status		
Married (and cohabiting)	254	88.8
Single	46	11.2
Socioeconomic status		
Low (I, II or III)	301	73.6
High (IV, V or VI)	108	26.4
History of smoking		
Yes	355	86.8
No	54	13.2

Table 2. *Clinical characteristics of the population.*

Variable	Frequency	%
GOLD		
1 or 2	182	44.5
3 or 4	227	55.5
Combined assessment		
A or B	318	77.8
C or D	91	22.2
Clinically significant anxiety		
Yes	78	19.1
No	331	80.9
Clinically significant depression		
Yes	114	27.9
No	295	72.1

Table 3. *Raw associations for clinically significant anxiety.*

Variables	OR	CI:95%
Age between 40 and 64 years	1.49	0.85-2.61
Female sex	1.65	1.01-2.71
Married (or cohabitng) marital status	1.14	0.51-2.54
Low socioeconomic status	1.64	0.89-3.03
History of smoking	0.71	0.36-1.39
GOLD 3 or 4	1.16	0.71-1.90
Combined assessment C or D	1.89	1.10-3.27

Table 4. *Raw associations for clinically significant depression.*

Variables	OR	CI: 95%
Age 65 years or over	1.19	0.86-2.59
Female sex	2.10	1.35-3.25
Single marital status	1.29	0.67-2.49
Low socioeconomic status	1.72	1.01-2.92
History of smoking	1.41	0.71-2.79
GOLD 3 or 4	0.97	0.62-1.49
Combined assessment C or D	1.89	1.16-3.10

C or D (OR=2.08; 95%CI 1.19-3.63) and the female sex (OR=1.80; 95%CI 1.10-2.99), Hosmer-Lemeshow test: chi^2=1.41; df=2; p=0.49.

On multivariate analysis, after adjusting, clinically significant depression was associated with the female sex (OR=2.35; 95%CI 1.50-3.70) and combined assessment C or D (OR=2.04; 95%CI 1.22-3.42). Low socioeconomic status was not related to clinically significant depression after adjusting for sex and the combined assessment (OR=1.65; 95%CI 0.95-2.84). Hosmer-Lemeshow test: chi^2=4.59; df=4; p=0.33.

Discussion

In this study, 19.1% of the patients were found to have clinically significant anxiety and 27.9% had clinically significant depression. Clinically significant anxiety and depression were associated with the female sex and greater COPD severity measured by the combined assessment. Clinically significant anxiety and depression were preferred over anxiety disorder or depressive disorder because the scales do not make a formal diagnosis, but rather identify individuals at high risk of having a disorder. Nevertheless, it should be noted that the Zung Depression Scale had a 95% sensitivity and 75% specificity (30).

In this study, 19.1% of the participants had clinically significant anxiety and 27.9% had clinically significant depression. These prevalence rates are somewhat higher than those found in previous studies in Spain, which found a prevalence of anxiety between 15.2 and 19.1% and a prevalence of depression between 9.8 and 14%, using a clinical interview (10, 11). Similarly, in Colombia, 5.8% of the patients reported a history of a depressive disorder (12). The difference may be due to the manner of assessing the symptoms. The prevalence of the disorder decreases significantly when assessed through a clinical interview (34). The prevalence of emotional symptoms is greater in patients with chronic illnesses. For example, Matte et al. performed a systematic review and meta-analysis and found that the prevalence of depression in COPD was 27.1% (95%CI 25.9-28.3), and 10.0% (95%CI 9.2-10.8) in the controls; that is, patients with COPD had a three times greater frequency of depression symptoms (OR=3.7; 95%CI 2.4-5.9) (9).

In the current study, clinically significant anxiety and depression were found to occur more frequently in women. This finding is consistent with most studies which show that symptoms of anxiety and depression are found more often in women, whether due to biological predisposition (34) or gender, social and cultural factors that facilitate the expression of symptoms (35, 36).

In this analysis, we found that the GOLD stage was not associated with clinically significant symptoms of anxiety and depression. This finding is consistent with another study which showed a lack of association between pulmonary function and the presence of anxiety or depression

(10). However, Gunawan et al. found that in 98 ambulatory patients with COPD in Indonesia, the predicted percentage of forced expiratory volume in one second (FEV1) was moderately correlated with symptoms of depression measured with the CES-D scale (r=-0.43; p<0.001) (37).

The study found that a history of smoking was independent of the presence of clinically significant anxiety or depression. This fact is similar to what Pascal et al. reported, that a history of smoking or current smoking was not related to a diagnosis of anxiety or depression (15). This finding suggests that smoking is not a strategy for dealing with symptoms of anxiety and depression in COPD patients, as is seen in the general population (22, 23). A technical aspect should also be considered: the ceiling effect; that is, it is hard to find differences when a characteristic is close to 100% in a given sample. Consequently, given the high prevalence of smoking in COPD patients, it may be difficult to determine a clear difference based on this variable. Studies with a much larger sample are required (25). Symptoms of anxiety and depression must be routinely assessed in COPD patients. Unfortunately, these symptoms are not regularly explored because they are considered to be normal, or the patients do not spontaneously report them to avoid the stigma-discrimination associated with mental illness (3). Anxiety and depressive disorders are diagnosed less frequently in this group of patients and, consequently, they do not receive the appropriate medical treatment (6, 14, 18, 37, 38).

This study has the strength of assessing symptoms of anxiety and depression in a large sample of ambulatory patients diagnosed with COPD in Colombia. However, it has the limitation inherent in cross-sectional studies which limit our understanding of the directionality of the association (39). Similarly, the associations for anxiety should be taken with caution since the number of cases required for the predetermined confidence level and power was not reached (26). Nevertheless, it must be recognized that the overall sample size duplicated the minimum sample and sufficiently narrow confidence intervals were found (40). The assessment of clinically significant anxiety and depression was carried out using measurement scales rather than clinical interviews. But the findings must be considered given the sensitivity and specificity shown by the Zung scales in Colombian populations (29). New studies should evaluate the prevalence of anxiety and depression based on clinical interviews, as well as the best pharmacological and psychotherapeutic management for COPD patients with anxiety or depression comorbidities. (29).

In conclusion, the prevalence of clinically significant anxiety and depression is high in COPD patients. Anxiety and depression are associated with the female sex and greater severity of COPD. Anxiety and depression must be assessed in all COPD patients followed as outpatients. Studies are needed to assess the presence of anxiety and depressive disorders through clinical interviews.

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