



Anxiety and depression in Portuguese patients with chronic obstructive pulmonary disease: a multicentre cross-sectional study

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ABSTRACT

Objectives: To assess symptoms of anxiety and depression among Portuguese patients with chronic obstructive pulmonary disease (COPD) and associated predictive factors.

Study design: A multicentre, cross-sectional study.

Setting: Three primary care centres and one district hospital in the central region of Portugal.

Participants: 302 Portuguese outpatients with COPD.

Methods: Symptoms of anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS). Scores ≥ 8 were considered clinically significant.

Results: This sample of patients had a mean age of 67 ± 12 years and 41% were female. COPD was graded as mild in 106 (35.1%), moderate in 106 (35.1%) and severe-to-very-severe 90 patients (29.8%). Clinically significant anxiety was found in 53.3% of patients and symptoms of depression in 45.4%. Symptoms of anxiety were associated with limitation of activities (OR 1.39, 95% CI 1.04-1.84), age (0.97, 95% CI 0.94-0.99) and female gender (OR 0.37; 95% CI 0.20-0.66). Symptoms of depression were associated with functional mobility (OR 1.91, 95% CI 1.38-2.66) and limitation of activities (OR 1.12, 95% CI 1.04-1.21).

Conclusions: A high proportion of Portuguese patients with COPD experience symptoms of anxiety and depression. National pulmonary rehabilitation programmes might need to include collaborative self-management interventions to address patients' emotional needs.

Keywords: Chronic Obstructive Pulmonary Disease; Anxiety; Depression.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) affects 210 million people worldwide. It is projected to be the seventh leading cause of years lived with disability by 2030.¹⁻² In Portugal, the prevalence of COPD is 14.2% in the population above 45 years of age. It is estimated that 800,000 citizens live with COPD.³ COPD is characterised by persistent limitation of airflow that is usually progressive. Exacerbations and comorbidities can cause a highly incapacitating disease.⁴

Anxiety and depression are common symptoms in patients with COPD. This may have a detrimental effect on quality of life and well-being as these symptoms can affect emotional, social and physical functioning.⁵ There is a complex interaction between anxiety and breathlessness that often exists as a vicious cycle of worsening symptoms.⁶

In studies conducted in the United Kingdom, Denmark, Canada and New Zealand, 50% to 74% of patients with COPD presented symptoms of anxiety and 28% to 80% symptoms of depression.⁷⁻¹⁰ In recent systematic



reviews, lower prevalences have been reported, with 10-55%¹¹ of patients showing symptoms of anxiety and 7-46%¹² depression. In Portugal, the prevalence of symptoms of anxiety and depression in patients with COPD is unknown. One retrospective study, of the impact of comorbidities in outcomes of respiratory rehabilitation, reported that 21.1% (n=24) of patients with COPD had anxiety or depression.¹³

The current study aimed to assess symptoms of anxiety and depression among Portuguese patients with COPD and to identify associated factors.

METHODS

Study design

A multicentre, cross-sectional study of Portuguese outpatients with COPD was conducted in the central region of Portugal between December 2010 and December 2012. The study received Institutional Ethics Committee approval. The reporting of this study conforms to the STROBE statement.¹⁴

Participants

The sample was recruited from three primary care centres and one district hospital. The clinicians of these institutions identified patients for the study. They ensured that patients met the criteria for eligibility. Inclusion criteria included a diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria,⁴ age ≥ 18 years old, the ability to understand the purpose of the study and to give voluntarily consent to participate. Exclusion criteria were the presence of severe psychiatric conditions or the inability to understand and co-operate.

Eligible patients were contacted by telephone. The researchers explained the purpose of the study and asked about their willingness to participate. If they agreed to participate, an appointment was scheduled at the patient's primary care clinic or hospital. Before data collection, more detailed information about the

study was provided to the patient and written informed consent was obtained.

Data collection procedures

Socio-demographic data (age, gender, educational level, marital status and occupation) and clinical data (body mass index [BMI], comorbidities, medication) were recorded first. Lung function and functional mobility were then assessed. Lastly, limitation of activities resulting from breathlessness and symptoms of anxiety and depression were assessed.

Measures

Lung function

Spirometry, using a portable spirometer (MicroLab 3500, CareFusion, Kent, UK), was performed according to the American Thoracic Society/European Respiratory Society Task Force standards for lung function testing.¹⁵ The classification of the severity COPD was made in accordance with the GOLD criteria.⁴

Functional mobility

The Timed Up and Go (TUG) test was used as a test of functional mobility. This test is often used in patients with COPD.¹⁶⁻¹⁷ It requires the patient to rise from a standard chair, walk 3 meters, turn around, walk back to the chair, and sit down, after the command "go".¹⁸ Patients were instructed to walk quickly, but as safely as possible. Two TUG tests were performed and the best performance was considered.

Limitation of activities resulting from breathlessness

The Modified British Medical Research Council questionnaire (mMRC) was used to assess symptoms in patients with COPD, as recommended by GOLD.⁴ Patients reported their limitation of activities resulting from breathlessness by selecting the statement that best described their limitation.¹⁹ The questionnaire comprises five grades (statements) on a scale from 0 to 4, with higher grades indicating greater perceived respiratory limitation.

Symptoms of anxiety and depression

The Portuguese version of the Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression.²⁰ This scale has been widely used in patients with COPD and has been reported in-

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TABLE I. Socio-demographic and clinical characteristics of the participants (n=302)

| Characteristics | |
|-----------------------------------|-------------|
| Age (years) M±SD | 67 ± 12 |
| Female n(%) | 124 (41.1) |
| Educational level n(%) | |
| No education completed | 32 (10.6) |
| Primary school | 156 (51.6) |
| Secondary school | 83 (27.5) |
| High school/University | 31 (10.3) |
| Marital status, n(%) | |
| Married/Living as a couple | 210 (69.5) |
| Widowed | 52 (17.2) |
| Single | 18 (6) |
| Separated/divorced | 22 (7.3) |
| Current occupation n(%) | |
| Retired | 220 (72.8) |
| Employed | 58 (19.2) |
| Unemployed | 24 (8) |
| BMI (kg/m ²) M±SD | 27.8 ± 5.6 |
| mMRC Md[IQR] | 2 [1, 3] |
| FEV ₁ % predicted M±SD | 62.4 ± 22.6 |
| GOLD Classification n(%) | |
| Mild | 106 (35.1) |
| Moderate | 106 (35.1) |
| Severe-to-very-severe | 90 (29.8) |

Abbreviations: BMI=body mass index; FEV₁=forced expiratory volume in 1 second; GOLD=Global Initiative for Chronic Obstructive Lung Disease; IQR=interquartile range; M=mean; Md=median; mMRC=Modified British Medical Research Council questionnaire.

ternationally as a valid and reliable instrument.²¹ The HADS contains 14 items. Seven items measure symptoms of anxiety (HADS-A) and 7 symptoms of depression (HADS-D).²² The presence of clinically significant symptoms of anxiety or depression was defined by a HADS-A/HADS-D score of ≥ 8 .²¹ The severity of symptoms of anxiety or depression was categorised as mild (score 8-10), moderate (score 11-14) or severe (score 15-21).²⁰ Coefficients of Cronbach's alpha found in the present study (0.78 for anxiety and 0.74 for depression) were similar to those reported by Pais-Ribeiro et al (0.76

and 0.81, respectively).²⁰

Statistical analysis

Descriptive statistics were used to describe the socio-demographic variables, clinical characteristics, and the HADS-A/HADS-D scores. As most of the previous studies of symptoms of anxiety and depression in COPD used "point prevalence", the frequency of symptoms of anxiety and depression (HADS-A/HADS-D ≥ 8) was computed based on this estimation. This facilitated the discussion of results. Frequencies were presented together with the 95% confidence intervals. The severity of symptoms of anxiety and depression was categorised as 'mild' (HADS-A/HADS-D ≥ 8 and ≤ 10), 'moderate' (HADS-A/HADS-D ≥ 11 and ≤ 14) or 'severe' (HADS-A/HADS-D ≥ 15 and ≤ 21).²⁰ To explore associations between variables related to the presence of clinically significant symptoms of anxiety and depression, variables of patients with and without symptoms of anxiety and depression (HADS-A/HADS-D ≥ 8 compared to HADS-A/HADS-D < 8) were compared using independent t-tests for normally distributed data, Mann-Whitney U-tests for non-normally distributed data and ordinal data, and Chi-square tests for categorical data. In the case of chi-square tests, when a statistically significant difference was found for a categorical variable with more than two categories, chi-square multiple comparison tests with Bonferroni correction were performed to explore which categories differed from each other. The variables that were statistically different ($p < 0.05$) between the two groups were used to further explore their relationship with the severity of anxiety and depression and to perform two multivariate logistic regressions (Enter method). The dependent variable in each multivariate logistic regression was the presence of clinically significant symptoms of anxiety symptoms or depression (0 = absent, 1 = present). Multiple logistic regression analysis was used for predictive purposes and to adjust for possible confounders.²³ The level of significance considered was 0.05. Statistical analyses were performed using IBM SPSS Statistics version 20.0 (IBM Corporation, Armonk, NY, USA).

RESULTS

Characteristics of participants

The total number of patients initially screened at the



participating institutions was not possible to obtain due to the recruitment strategy. A total of 340 patients with COPD were approached by the research team for inclusion in the study, however 32 refused to participate due to personal reasons and 6 failed to attend the arranged meeting. The final sample comprised 302 patients with COPD (mean age 67 ± 12 years old; 41.1% female). The majority of participants had completed primary school ($n=156$; 51.6%) and were retired ($n=220$; 72.8%). The mean BMI was $27.8 \pm 5.6 \text{ kg/m}^2$ and the median mMRC grade was 2 ('I walk slower than people of the same age on the level because of the breathlessness', or 'I have to stop for breath when walking on my own pace on the level'). According to the GOLD criteria, 106 (35.1%) patients had mild, 106 (35.1%) moderate and 90 (29.8%) had severe-to-very-severe COPD. Table I shows the socio-demographic and clinical characteristics of the study participants.

Symptoms of anxiety and depression

The mean anxiety score was 8.1 ± 4.4 and the mean depression score was 7.3 ± 4 . A total of 161 (53.3%; 95% CI 48-58.9) patients had clinically significant symptoms of anxiety. Symptoms of anxiety were experienced mainly as 'mild' ($n=74$; 46%, 95% CI 38.5-53.4) or 'moderate' ($n=59$; 36.6%, 95% CI 29.2-44.7) with few 'severe' cases ($n=28$; 17.4%, 95% CI 11.8-23.6). Clinically significant symptoms of depression were present in 45.4% (95% CI 40.1-50.7, $n=137$) of patients. These symptoms were experienced as 'mild' in the majority of the sample ($n=74$; 54%, 95% CI 46-62.8), but also 'moderate' ($n=48$; 35%, 95% CI 27-43.1) and a few 'severe' cases were found ($n=15$; 11%, 95% CI 5.8-16.1). A total of 99 (32.8%, 95% CI 27.5-38.1) patients had both symptoms of anxiety and depression.

Associations between anxiety and depression and socio-demographic characteristics

Symptoms of anxiety and depression were more frequent in female patients ($p < 0.001$ and $p = 0.044$) (table II). Symptoms of anxiety were also more frequent in younger patients ($p = 0.008$) and unemployed patients ($p = 0.002$). Symptoms of depression were more frequent in those with lower educational levels (no education completed, primary school and secondary school; $p < 0.001$) (table II). Regarding the association of gender

and severity of anxiety, it was found that the frequency of females with moderate and severe anxiety (66.1% and 67.9%, respectively) was significantly higher than females with mild anxiety (33.8%, $p < 0.001$). No other statistically significant differences were found.

Relationship between symptoms of anxiety and depression and clinical characteristics

The frequency of symptoms of anxiety and depression was higher in patients with greater limitation of activities resulting from breathlessness (mMRC, $p = 0.043$ and $p < 0.001$) (table III). The frequency of symptoms of depression was also higher in patients with higher medication intake ($p = 0.002$), advanced COPD ($p = 0.036$) and lower functional mobility ($p < 0.001$) (table III). Limitation of activities resulting from breathlessness was higher in patients with moderate or severe anxiety (Median 2, Interquartile range [1,3]; 2[2,3]) and depression (3[2,3]; 3[1.5,3]) than in those with mild anxiety (2[1,2], $p = 0.026$) and depression (2[1,3], $p = 0.016$). No other statistically significant differences were observed regarding the severity of symptoms.

Predictors of anxiety and depression

Two multivariate logistic regressions were performed to identify the predictors of symptoms of anxiety and depression. Symptoms of anxiety were predicted by limitation of activities resulting from breathlessness (OR 1.39, 95% CI 1.04-1.84), age (0.97, 95% CI 0.94-0.99), and female gender (OR 0.37; 95% CI 0.20-0.66). Symptoms of depression were predicted by functional mobility (OR 1.91, 95% CI 1.38-2.66) and limitation of activities (OR 1.12, 95% CI 1.04-1.21). These logistic regression models predicted 13% of the total variance of anxiety and 22.4% of the total variance of symptoms of depression.

DISCUSSION

This study showed that a large proportion of Portuguese patients with COPD present symptoms of anxiety and depression. Limitation of activities resulting from breathlessness, female gender, age and functional mobility were predictors of these distressing symptoms.

More than half of patients had symptoms of anxiety (53.3%) and 45.4% had symptoms of depression. This


TABLE II. Socio-demographic characteristics of patients with and without symptoms of anxiety and depression

| Characteristics | Not anxious (n=141) | Anxious (n=161) | p-value | Not depressed (n=165) | Depressed (n=137) | p-value |
|----------------------------|------------------------|--------------------|---------------------|--------------------------|----------------------|---------------------|
| Age (years) M±SD | 68.9±12.4 | 65.2±11.5 | 0.008* | 65.9±12.5 | 68.3±11.3 | 0.084* |
| Gender n(%) | | | | | | |
| Female | 41 (29.1) | 83 (51.6) | <0.001 [†] | 60 (36.4) | 64 (46.7) | 0.044 [†] |
| Male | 100 (70.9) | 78 (48.4) | | 105 (63.6) | 73 (53.3) | |
| Educational level n(%) | | | | | | |
| No education completed | 12 (8.5) | 20(12.4) | 0.055 [†] | 13 (7.9) | 19 (13.9) | <0.001 [†] |
| Primary school | 66 (46.8) | 90(55.9) | | 73 (44.2) | 83 (60.6) | |
| Secondary school | 41 (29.1) | 42(26.1) | | 55 (33.3) | 28 (20.4) | |
| High school/University | 22 (15.6) | 9(5.6) | | 24 (14.6) | 7 (5.1) | |
| Marital status, n (%) | | | | | | |
| Married/Living as a couple | 104 (73.7) | 106(65.8) | 0.086 [†] | 114(69.1) | 96 (70.1) | 0.099 [†] |
| Widowed | 17 (12.1) | 35(21.8) | | 23 (13.9) | 29 (21.2) | |
| Single | 11 (7.8) | 7(4.3) | | 12 (7.3) | 6 (4.4) | |
| Separated/divorced | 9 (6.4) | 13(8.1) | | 16 (9.7) | 6 (4.4) | |
| Current occupation n(%) | | | | | | |
| Retired | 109 (77.3) | 111 (69) | 0.002 [†] | 115 (69.7) | 105 (76.6) | 0.083 [†] |
| Employed | 29 (20.6) | 29 (18) | | 39 (23.6) | 19 (13.9) | |
| Unemployed | 3 (2.1) | 21 (13) | | 11 (6.7) | 13 (9.5) | |

*, independent t-tests; [†], Chi-square tests.

TABLE III. Clinical characteristics of patients with and without symptoms of anxiety and depression

| Characteristics | Not anxious (n=141) | Anxious (n=161) | p-value | Not depressed (n=165) | Depressed (n=137) | p-value |
|--------------------------|------------------------|--------------------|--------------------|--------------------------|----------------------|---------------------|
| Comorbidities Md[IQR] | 2[1, 3] | 2[1, 3] | 0.655 [‡] | 2[1, 2] | 2[1, 3] | 0.075 [‡] |
| Medications Md[IQR] | 3[2, 5] | 4 [2, 6] | 0.091 [‡] | 3[2, 5] | 4[2.75, 6] | 0.002 [‡] |
| GOLD Classification n(%) | | | | | | |
| Mild | 51 (36.2) | 55 (34.2) | 0.053 [†] | 68 (41.2) | 38 (27.7) | 0.036 [†] |
| Moderate | 43 (30.5) | 63 (39.1) | | 56 (33.9) | 50 (36.5) | |
| Severe/Very severe | 47 (33.3) | 43 (26.7) | | 41 (24.9) | 49 (35.8) | |
| mMRC Md[IQR] | 2[1, 2] | 2[1, 3] | 0.043 [‡] | 1.5[1, 2] | 2[1, 3] | <0.001 [‡] |
| Functional mobility M±SD | 10.1±5.8 | 10.6±4.2 | 0.451* | 9.2±3.9 | 11.8±5.8 | <0.001* |

*, independent t-tests; [‡], Chi-square tests; [†], Mann-Whitney U-tests. Abbreviations: IQR=interquartile range; M=mean; Md=median; mMRC=Modified British Medical Research Council questionnaire.



is higher than the value reported by Carreiro (21.1%).¹³ The proportions found in the present study fall within the range of estimates found among patients with COPD in other countries.⁷⁻¹² Comparisons need to be interpreted with caution as different instruments were used in other studies.

The presence of symptoms of both anxiety and depression was predicted by limitation of activities resulting from breathlessness. The severity of anxiety and depression was also related to the severity of breathlessness. Respiratory symptoms have been associated with patients' anxiety and depression.⁸ The frequency of symptoms of anxiety was similar in early and advanced COPD. The results strengthen previous findings stating that even at earlier stages of the disease, the uncertain and unpredictable nature of the symptoms and acute exacerbations have an impact on patients' emotional well-being.²⁴

Anxiety was also predicted by female gender and age. Female gender was related to higher emotional distress, consistent with previously published results.²⁵⁻²⁶ This may reflect the gender differences already found in the general population.²⁷ A higher frequency of symptoms of anxiety was found in younger and unemployed patients, which has been found previously.^{25-26,28} These findings are relevant for clinical practice. It can be hypothesised that older patients interpret the occurrence of an illness as an expected late-life stressor.²⁸⁻²⁹ Low educational levels were associated with a higher frequency of depression. This was expected since having a high educational level has been shown to be an important contributor to enhanced personal internal resources.³⁰

Regarding symptoms of depression, the severity of COPD had a different role. More advanced disease was associated with a higher frequency of symptoms of depression. This might be explained by the role of physical functioning on symptoms of depression.³¹⁻³² Patients with advanced COPD experience more physical disability. This was confirmed by the logistic regression analysis, which identified patients' functional mobility as a predictor of clinically significant symptoms of depression.

These findings suggest that many patients with COPD suffer from symptoms of anxiety and depression and thus interventions are needed to promote a healthy adjustment to the disease. Pulmonary rehabilitation

programmes are recommended to improve the physical and psychological condition of patients with COPD.³³⁻³⁴ According to recent international guidelines, these programmes should include exercise training, education and behavioural change through collaborative self-management interventions.³³ In COPD and other chronic diseases, there is evidence that these interventions have a significant positive effect on patients' emotional function.³⁵⁻³⁸ In Portugal, pulmonary rehabilitation programmes are scarce and typically combine exercise training with education.³⁹⁻⁴⁰ Patients' emotional needs are not often directly addressed. It would be logical to complement national programmes with collaborative self-management interventions, since they may increase instrumental and emotional coping abilities to allow patients to manage the demands of the disease. Collaborative self-management interventions place patients and health professionals in partnership to enhance patients' self-efficacy and self-management abilities.³³ It remains to be determined if involving the family caregiver in this partnership brings additional benefits to patients.

This study has some limitations. Possible sources of bias were the recruitment strategy using clinicians in the institutions involved and the fact that the sample was recruited from only the central region of Portugal. Future studies containing a larger sample and including patients with COPD from other regions of the country would be more representative of the Portuguese population with COPD. A control group of healthy individuals with similar socio-demographic characteristics should also be included in further research to increase the validity of these findings. The use of HADS to assess symptoms of anxiety and depression may have introduced a bias in the study since some authors have recently emphasised that the assumed bi-dimensionality of the HADS may not be appropriate.⁴¹⁻⁴² However, this instrument was used as a screening tool for symptoms of anxiety and depression and not as an instrument for diagnosis of clinical anxiety or depression. The HADS has shown to be a reliable instrument internationally for measuring emotional distress of patients with COPD. This study focused on the presence of clinically significant symptoms of anxiety and depression (i.e., HADS-A/HADS-D \geq 8). It may be interesting to explore the absolute scores of HADS-A and



HADS-D and derive predictive equations. Another limitation of the present study is related to its cross-sectional nature. The frequency of distressing symptoms and the relationships with associated factors could not be established along the progression of the disease. Longitudinal studies following a cohort of patients with COPD would address this issue and identify other predictors of symptoms of anxiety and depression. For instance, the predictive value of alexithymia could be investigated. Recent research found a strong association between this condition and distressing symptoms in patients with COPD.⁴³

CONCLUSION

A large proportion of Portuguese patients with COPD experience symptoms of anxiety and depression. Limitation of activities resulting from breathlessness, female gender, age, and functional mobility were predictors of these distressing symptoms. To address patients' emotional needs, national pulmonary rehabilitation programmes should include a collaborative self-management component. Future research could explore the effects of involving family caregivers in these interventions on beneficial outcomes for patients.

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DECLARATION OF INTEREST

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RESUMO

ANSIEDADE E DEPRESSÃO EM PACIENTES PORTUGUESES COM DOENÇA PULMONAR OBSTRUTIVA CRÓNICA: UM ESTUDO MULTICÊNTRICO, TRANSVERSAL

Objetivos: Avaliar sintomas de ansiedade e depressão em pacientes Portugueses com doença pulmonar obstrutiva crónica (DPOC) e fatores preditores associados.

Tipo de estudo: Estudo multicêntrico, transversal.

Local: Três centros de saúde e um hospital distrital da região centro de Portugal.

População: 302 pacientes com DPOC.

Métodos: Os sintomas de ansiedade e depressão foram avaliados através da Escala de Ansiedade e Depressão (HADS). Pontuações ≥ 8 foram consideradas clinicamente significativas.

Resultados: Esta amostra de pacientes tinham em média de 67 ± 12 anos de idade e 41,1% era do género feminino. A DPOC era de grau ligeiro em 106 (35,1%) pacientes, moderado em 106 (35,1%) e grave-a-muito-grave em 90 (29,8%). Sintomas de ansiedade clinicamente significativos estavam presentes em 53,3% dos pacientes e sintomas de depressão em 45,4%. Os sintomas de ansiedade estavam associados a limitação nas atividades (OR 1,39, 95% CI 1,04-1,84), idade (0,97, 95% CI 0,94-0,99) e género feminino (OR 0,37; 95% CI 0,20-0,66). Os sintomas de depressão estavam associados à mobilidade funcional (OR 1,91, 95% CI 1,38-2,66) e a limitação nas atividades (OR 1,12, 95% CI 1,04-1,21).

Conclusão: Uma elevada proporção de pacientes com DPOC experienciam sintomas de ansiedade e depressão. Os programas nacionais de reabilitação respiratória deveriam incluir intervenções colaborativas de autogestão que respondam a estas necessidades emocionais.

Palavras-chave: Doença Pulmonar Obstrutiva Crónica; Ansiedade; Depressão.
