

Chronic Obstructive Pulmonary Disease and Anxiety and Depression Disorders: Prospective Cohort Study in Primary Care

Josep MC¹, Pere G²,
Ramon MJ³, Ferran B⁴,
Josep P⁵, Marta O⁶ and
Miquel A²

Abstract

Introduction: Anxiety and depression are underdiagnosed in Chronic Obstructive Pulmonary Disease (COPD) patients. Few studies have tried to identify their association with hospitalization (severe exacerbation). The objective of this study was to determine whether the anxiety/depression was associated with severe exacerbation.

Method: A prospective cohort study based on a sample of 512 patients diagnosed with COPD originating from Primary Care in a rural area in Lleida (Spain) and monitored between 01/11/2012 and 31/10/2014. For each patient, variables of interest were recorded; they were administered the HADS test (Hospital Anxiety and Depression Scale) to determine the possible presence of anxiety/depression, and its association with severe exacerbation was analysed using a logistic regression model.

Results: Initially, the prevalence of anxiety/depression was 15.6%. The incidence of global hospitalization in the first year was 8.2%, and 11.3% in the second. In patients with anxiety/depression, it increased to 17.5% in the first year and 18.8% in the second. In the multivariate regression model, the diagnosis of anxiety/depression almost doubled the risk of hospitalization (ORa=1.94) (p<0.041).

Conclusion: Anxiety and depression are associated with an increased risk of hospitalization. Intervention studies are needed to evaluate the effects of anxiety/depression in the hospitalization.

Keywords: Anxiety; Depression; Chronic obstructive pulmonary disease (COPD)


Received: October 10, 2016; Accepted: October 18, 2016; Published: October 28, 2016

Introduction

It was estimated that the prevalence of chronic obstructive pulmonary disease (COPD) will increase in forthcoming years and by 2020, will have become the third cause of mortality in the world [1]. It is a progressive disease which gradually declines the pulmonary capacity having a negative influence on the quality of life of patients [2]. The prevalence of anxiety and depression in these patients is greater than among the general population [3,4], nevertheless, various studies suggest that there is significant under-diagnosis [5]. Recently, the importance of psychiatric comorbidity (anxiety/depression) in COPD has been objectified and it has been suggested that it has a long-term negative effect on morbidity and mortality in these patients [4,6]. Divo et al. [7] reported that anxiety and depressive symptoms are associated

- 1 Health Department, Biomedical Research Institute (IRB) of Lleida, Public Health Agency of Catalonia, Catalan Institute of Health (ICS), ABS Mollerussa, Spain
- 2 Health Department, Public Health Agency of Catalonia, Biomedical Research Institute (IRB) of Lleida, University of Lleida, Lleida, Catalonia, Spain
- 3 Cardiovascular Department, Epidemiology Unit, Primary Care Research Institute (IDIAP) Jordi Gol, Universitat Autònoma of Barcelona, University Hospital Vall d'Hebron, Lleida, Catalonia, Spain
- 4 Biomedical Research Institute (IRB) of Lleida, Respiratory Diseases Group, Biomedical Research Centre/Respiratory Diseases Network (CIBERES), University Hospital Arnau de Vilanova, Lleida, Catalonia, Spain
- 5 Psychiatry Department, Biomedical Research Institute (IRB) of Lleida, University Hospital Santa Maria, University of Lleida, Lleida, Catalonia, Spain
- 6 Primary Care Research Institute (IDIAP) Jordi Gol, Universitat Autònoma of Barcelona, Catalan Institute of Health (ICS), Lleida, Catalonia, Spain

Corresponding author: Josep MC

 jmontser@alumni.unav.es

Health Department, Biomedical Research Institute (IRB) of Lleida, Public Health Agency of Catalonia, Catalan Institute of Health (ICS), ABS Mollerussa, Avda Rovira Roure, 25006-Lleida, Catalonia, Spain

Tel: +34 676 91 66 70

Citation: Josep MC, Pere G, Ramon MJ, et al. Chronic Obstructive Pulmonary Disease and Anxiety and Depression Disorders: Prospective Cohort Study in Primary Care. *Insights Chest Dis.* 2016, 1:3.

with death. Vanfleteren et al. [8], identify a specific relationship with a different outcome (more myocardial infarction) and more symptoms (Dyspnea and use of rescue inhalers).

It is important to diagnose anxiety and depression in patients with COPD to be able to treat them correctly, improve their health [9] and their quality of life [5]. It has been pointed out that untreated anxiety/depression in patients with COPD could have negative repercussions on therapeutic compliance, thereby increasing the risk of exacerbation and of hospitalization [9,10]. This would be one of the reasons why previous studies have shown contradictory results on the impact of anxiety and depression on the hospitalization rates. The discrepancies among the studies are based on various reasons: Studies carried out in different countries with non-comparable health services; also differences in the kind of patient; and the methodology used to determine the anxiety/depression. There are different instruments for measuring anxiety and depression. One of them, particularly indicated for detecting anxiety-depression in patients with chronic diseases is the Hospital Anxiety and Depression Scale (HADS), which allows levels of anxiety and depression in these patients to be measured with an acceptable level of sensitivity and specificity [11].

The relationship between anxiety/depression with the exacerbation of COPD is not well defined and more research is needed to explain the pathways to exacerbation.

The objective of this study was to determine the prevalence of anxiety and depression at the beginning of the study in a cohort of patients diagnosed with COPD selected in Primary Care appointments, and to determine a possible association between anxiety and/or depression (diagnosed using HADS) and hospitalization for the exacerbation of the COPD.

Methods

A prospective cohort study was carried out to follow patients diagnosed with COPD originating from the Primary Care Centre of Mollerussa, Lleida (Spain) with a population of 37,462 inhabitants (2015). The Lleida's Catalan Institute of Health Research Support Unit provided the list of patients who, in their computerized medical history were shown, in June 2012, as was diagnosed with COPD based on the GOLD definition [12] (ratio between post-bronchodilator FEV1/FVC<0.70). To estimate the prevalence of anxiety/depression with an accuracy (ϵ) of 0.04, and an α error of 0.05 and an expected prevalence of 0.5 we selected a random sample of 512 patients with COPD. They were interviewed at the beginning of the study to collect information about the variables of interest (age, sex, smoking habit, family situation, level of studies, severity (GOLD), body mass index (BMI), previous admissions for exacerbation of the COPD, exacerbations treated on an outpatient basis during the last year, degree of dyspnoea, BODEx prognostic index, Charlson comorbidity index and quality of life measurement (EuroQol). Also, they were administered the HADS test [13] to determine whether the patient had anxiety and/or depression or not. The HADS test is considered to be an acceptable method to discriminate between healthy patients and those suffering from anxiety and depression [5].

The HADS is a questionnaire consisting of 14 items (7 to assess anxiety and 7 for depression) with scores ranging from 0 to 3 (possible values from 0 to 21 for each of the subscales). The test looks at the situation of the patient's last week and is designed to be administered to subjects with organic diseases. In addition to the quantitative valuation, it can be categorised and for the study, it was decided to use a value of 10 as a cut-off point between the presence or absence of anxiety and depression. Patients who had a positive HAD test were sent to their respective primary care physicians to assess starting a psycho-pharmacological treatment.

Once the initial information was collected in the 512 participants, including the HADS test, the patients were monitored over two years and the existence of severe exacerbation was determined (Hospitalization for exacerbation of the COPD). The sources of information were the register of hospital admissions in both reference hospitals (Hospital Universitario Arnau de Vilanova and Hospital Universitario de Santa María).

The study was approved by the ethical committee of the Institute of Research in Primary Health Care (IDIAP) of Barcelona (code P14/022).

All the participants gave their written informed consent.

Statistical Analysis

A descriptive analysis was made using absolute and relative frequencies for categorical data and using means and standard deviations for continuous variables. For each patient, the exposure was considered in the case of a positive HADS depression and/or HADS anxiety test. Then the patient had not exposed if neither diagnostic of anxiety nor depression. The main outcome was defined as at least one admission in the two hospitals of reference in the study area for exacerbation of the COPD (CIE-10: J44.1) over the next two years. The admissions were estimated also for each year. A bivariate analysis was performed of all the variables and the different outcomes. The differences in categorical data were tested using Fisher's exact test and, for numerical variables, a non-parametric Mann-Whitney test was used. The effect of HADS depression and/or anxiety was assessed using logistic regression, and the crude effect and the adjusted effect for all outcomes were assessed. In all the analyses, p-values of lower than 0.05 were considered significant, and SPSS software was used.

Results

At the beginning of the study, the prevalence of anxiety/depression was 15.6% (7.2% of isolated anxiety and 12.5% of isolated depression). Most of these patients (53.7%) unknown to be affected by anxiety and/or depression. The average age was 69.5 years (SD=12.2) and 26.8% were women. The average Body Mass Index (BMI) was 29.5. The average ratio between Forced Expiratory Volume in the First Second (FEV1) and Forced Vital Capacity (FVC) was 65.2. Smokers and ex-smokers represented 66.8% of the sample. Half (50.8%) the patients were suffering from grade 2 (moderate) COPD and 22.1% were severe or very severe. 42.8% of the patients had slight dyspnoea (**Table 1**).

A total of 79 patients (15.4%) required hospitalization in the two year of study. During the first year of follow-up, the global incidence of hospitalization was 8.2% and in the second year it was 11.3%. In patients with anxiety/depression, the incidence of hospitalization in the first year came to 17.5% and in the second year to 18.8% (**Table 2**). The incidence of hospitalization during the two years of the study was greater in patients with anxiety and depression (13.4% vs. 26.3%) (**Table 2**).

The patients admitted had similar characteristics in each of the two years of the study. They had lower FEV1 (55.6 ± 15.5) and FEV1/FVC (63.9 ± 7.7). Patients who were admitted during the two years of study were the older ones mean age 73.8 ($p=0.001$); they had a greater prevalence of anxiety and depression (HADS) 26.6% ($p=0.006$); worse FEV1 ($p=0.001$); greater prevalence of ischaemic heart disease ($p=0.001$); more intense dyspnoea ($p=0.001$); greater scores on the Charlson index ($p=0.001$); lower subjective perception of their quality of life measured using the EuroQol 5D ($p=0.001$) and greater severity of the disease ($p=0.001$). The other variables are shown in **Table 3**. Diabetes and anaemia were the only variables that were associated with

Table 1: Baseline characteristics (variables) of COPD patients at the beginning of study.

Depression and/or Anxiety (HAD _s)	Total (n=512) n (%)
Age (years)-mean (SD)	69.5 (12.2)
Gender (female)	137 (26.8%)
Body Mass Index-mean (SD)	29.5 (8.5)
Anxiety HAD _s	37 (7.2)
Depression HAD _s	64 (12.5)
Anxiety and/or Depression HAD _s	80 (15.6)
FEV1-mean (SD)	65.2 (18.4)
FEV1/FVC-mean (SD)	65.2 (7.7)
Smoking Habit	
Non-smoker	170 (33.2%)
Ex-smoker	243 (47.5%)
Current smoker	99 (19.3%)
Ischemic Heart Disease (Yes)	65 (12.7%)
Stroke (Yes)	17 (3.3%)
Chronic Kidney Disease (Yes)	40 (7.8%)
Diabetes (Yes)	132 (25.8%)
Anaemia (Yes)	12 (2.3%)
History of COPD (years)-mean (SD)	3.7 (3.5)
Dyspnoea	
0	219 (42.8%)
1	180 (35.2%)
2	71 (13.9%)
3	39 (7.6%)
4	3 (0.6%)
Charlson Index-mean (SD)	4.7 (1.9)
EuroQoL (5 q)-mean (SD)	6.5 (1.4)
EuroQoL (EVA)-mean (SD)	6.9 (1.4)
Gold	
G 1	139 (27.1%)
G 2	260 (50.8%)
G 3-4	113 (22.1%)

Table 2: Incidence of severe exacerbations (hospitalizations) during the two years of follow up.

	No		Anxiety and/or Depression HADS		All		p
	N	n (%)	N	n (%)	N	n (%)	
Admissions 1 st year	432	28 (6.5%)	80	14 (17.5%)	512	42 (8.2%)	0.003
Admissions 2 nd year	432	43 (10%)	80	15 (18.8%)	512	58 (11.3%)	0.033
Admissions 1-2 years	432	58 (13.4%)	80	21 (26.3%)	512	79 (15.4%)	0.006

hospital admission in the second year of the study but not during the first year (**Table 3**).

In the multivariate regression model, the diagnosis of anxiety/depression (HADS) increased the risk of hospitalization to almost double (ORa=1.94) over the two years of the study ($p<0.041$). During the first year, the ORa rose to 2.65; $p<0.010$ and for the second year the ORa was somewhat lower 1.88 ($p=0.07$) (**Table 4**).

Discussion

The study has enabled us to estimate that anxiety/depression doubles the risk of hospitalization in patients with COPD in a health centre.

The prevalence of anxiety/depression at the beginning of the study was 15.6% similar to other studies [14,15]. The prevalence of depression determined in our research was 12.5%. The studies estimate a highly variable prevalence of depression in patients with COPD which varies between 6% and 50% [6,8,16,17]. Van Manen et al. determined that the prevalence of depression was greater in patients with more severe COPD and was double than for the general population [17]. Ng et al. determined that the prevalence of depression in hospitalised patients with COPD rose to 44% [16]. The prevalence of anxiety in the patients in the study was 7.2%, similar to most of the studies which vary between 10% and 15.8% and which triples the prevalence of anxiety among the general population [18].

The incidence of hospitalization during the two years of the study was greater in patients with anxiety and depression (13.4% vs. 26.3%), and in the multivariate regression model, the diagnosis of anxiety/depression (HADS) increased the risk of hospitalization by almost double (ORa=1.94) over the two years of the study ($p<0.041$). The risk of hospitalization associated to anxiety/depression (HADS) was greater during the first year of follow-up (ORa=2.65) than the second year (ORa=1.88) and suggests the loss of predictive value of the test or the greater importance of other factors over time. Other studies have also found a higher rate of hospitalization in COPD patients with anxiety/depression [15,19]. In the study by Ng et al. [19], multivariate analyses showed that depression was significantly associated with mortality (hazard ratio, 1.93; 95% confidence interval, 1.04-3.58).

Some potential pathways could explain the relationship between anxiety, depression and COPD exacerbations. Dysregulation induced by chronic psychological stress may weaken immune functions and potentially increase vulnerability to respiratory infections and COPD exacerbations. Therefore, the fact that psychiatric disorders, and depression in particular, can induce

Table 3: Characteristics in function of the outcome during the two years of follow up.

	Admissions 1 st year (n=42)					Admissions 2 nd year (n=58)					Admissions 1-2 years (n=79)				
	N	No n (%)	N	Yes n (%)	p	N	No n (%)	N	Yes n (%)	p	N	No n (%)	N	Yes n (%)	p
Age (years)-mean (SD)	470	69.2 (12.3)	42	73.6 (9.7)	0.025	454	69.1 (12.3)	58	73.4 (10.4)	0.015	433	68.8 (12.4)	79	73.8 (10)	0.001
Gender (female)	470	128 (27.2%)	42	9 (21.4%)	0.472	454	127 (28%)	58	10 (17.2%)	0.085	433	123 (28.4%)	79	14 (17.7%)	0.053
Body Mass Index-mean (SD)	470	29.5 (8.7)	42	29.9 (6.2)	0.524	454	29.6 (8.8)	58	29.2 (5.8)	0.991	433	29.6 (9)	79	29.2 (5.5)	0.759
Anxiety HADS	470	29 (6.2%)	42	8 (19%)	0.007	454	30 (6.6%)	58	7 (12.1%)	0.171	433	26 (6%)	79	11 (13.9%)	0.018
Depression HADS	470	51 (10.9%)	42	13 (31%)	0.001	454	50 (11%)	58	14 (24.1%)	0.010	433	45 (10.4%)	79	19 (24.1%)	0.002
Anxiety and/or Depression HADS	470	66 (14%)	42	14 (33.3%)	0.003	454	65 (14.3%)	58	15 (25.9%)	0.033	433	59 (13.6%)	79	21 (26.6%)	0.006
FEV1-mean (SD)	470	66.2 (18.4)	42	54.7 (15.5)	0.001	454	66.6 (18.2)	58	54.4 (16.2)	0.001	433	67 (18.3)	79	55.6 (15.9)	0.001
FEV1/FVC-mean (SD)	470	65.2 (7.7)	42	64.4 (7.7)	0.685	454	65.3 (7.7)	58	63.9 (7.6)	0.225	433	65.4 (7.7)	79	63.9 (7.7)	0.150
Smoking Habit	470	-	42	-	0.070	454	-	58	-	0.006	433	-	79	-	0.001
Non-smoker	-	160 (34%)	-	10 (23.8%)	-	-	160 (35.2%)	-	10 (17.2%)	-	-	155 (35.8%)	-	15 (19%)	-
Ex-smoker	-	216 (46%)	-	27 (64.3%)	-	-	205 (45.2%)	-	38 (65.5%)	-	-	190 (43.9%)	-	53 (67.1%)	-
Current smoker	-	94 (20%)	-	5 (11.9%)	-	-	89 (19.6%)	-	10 (17.2%)	-	-	88 (20.3%)	-	11 (13.9%)	-
Ischemic Heart Disease (Yes)	470	24 (5.1%)	42	11 (26.2%)	0.001	454	24 (5.3%)	58	11 (19%)	0.001	433	20 (4.6%)	79	15 (19%)	0.001
Stroke (Yes)	470	14 (3%)	42	3 (7.1%)	0.156	454	13 (2.9%)	58	4 (6.9%)	0.115	433	13 (3%)	79	4 (5.1%)	0.314
Chronic Kidney Disease (Yes)	470	34 (7.2%)	42	6 (14.3%)	0.126	454	34 (7.5%)	58	6 (10.3%)	0.436	433	31 (7.2%)	79	9 (11.4%)	0.251
Diabetes (Yes)	470	119 (25.3%)	42	13 (31%)	0.462	454	108 (23.8%)	58	24 (41.4%)	0.006	433	104 (24%)	79	28 (35.4%)	0.037
Anaemia (Yes)	470	11 (2.3%)	42	1 (2.4%)	1.000	454	7 (1.5%)	58	5 (8.6%)	0.007	433	7 (1.6%)	79	5 (6.3%)	0.025
History of COPD (years)-mean (SD)	470	3.7 (3.5)	42	4 (3.7)	0.570	454	3.7 (3.6)	58	4 (3.1)	0.271	433	3.7 (3.5)	79	3.9 (3.4)	0.510
Dyspnoea	470	-	42	-	0.001	454	-	58	-	0.001	433	-	79	-	0.001
0	-	213 (45.3%)	-	6 (14.3%)	-	-	208 (45.8%)	-	11 (19%)	-	-	204 (47.1%)	-	15 (19%)	-
1	-	166 (35.3%)	-	14 (33.3%)	-	-	161 (35.5%)	-	19 (32.8%)	-	-	152 (35.1%)	-	28 (35.4%)	-
2	-	64 (13.6%)	-	7 (16.7%)	-	-	58 (12.8%)	-	13 (22.4%)	-	-	55 (12.7%)	-	16 (20.3%)	-
3	-	24 (5.1%)	-	15 (35.7%)	-	-	26 (5.7%)	-	13 (22.4%)	-	-	21 (4.8%)	-	18 (22.8%)	-
4	-	3 (0.6%)	-	0 (0%)	-	-	1 (0.2%)	-	2 (3.4%)	-	-	1 (0.2%)	-	2 (2.5%)	-
Charlson Index-mean (SD)	470	4.6 (1.9)	42	5.5 (1.6)	0.001	454	4.6 (1.8)	58	5.7 (2)	0.001	433	4.5 (1.9)	79	5.6 (1.8)	0.001
EuroQoL (5 q)-mean (SD)	470	6.4 (1.3)	42	7.8 (1.6)	0.001	454	6.4 (1.3)	58	7.4 (1.4)	0.001	433	6.3 (1.3)	79	7.4 (1.5)	0.001
EuroQoL (EVA)-mean (SD)	469	7 (1.3)	42	5.7 (1.7)	0.001	453	7 (1.3)	58	5.8 (1.4)	0.001	432	7 (1.3)	79	5.9 (1.5)	0.001
Gold	470	-	42	-	0.005	454	-	58	-	0.001	433	-	79	-	0.001
G 1	-	134 (28.5%)	-	5 (11.9%)	-	-	136 (30%)	-	3 (5.2%)	-	-	132 (30.5%)	-	7 (8.9%)	-
G 2	-	238 (50.6%)	-	22 (52.4%)	-	-	227 (50%)	-	33 (56.9%)	-	-	216 (49.9%)	-	44 (55.7%)	-
G 3-4	-	98 (20.9%)	-	15 (35.7%)	-	-	91 (20%)	-	22 (37.9%)	-	-	85 (19.6%)	-	28 (35.4%)	-

immunodeficiency and increase the risk of post-infarction death, for e.g., de Jonge et al. [20] makes us believe that these disorders can have a prospective impact on COPD. However, the lack of research among patients with COPD using reliable biomarkers for exacerbations, the precise nature of the biological mechanisms linking anxiety and depression to exacerbations remains

unclear. Patients with anxiety and depression often suffer from low self-confidence or self-efficacy, which may lead to worse disease-related coping and poor self-care behaviours; that is, unwillingness to engage in pulmonary rehabilitation, decreased physical activity, failure to quit smoking, poor eating habits, and poor medication adherence [21]. This, in turn, could increase a

Table 4: Effect (crude and adjusted) of the HADS diagnostic (anxiety and/or depression) on admission during the two years of follow up.

	Crude Effect			Adjusted Effect		
	OR	CI 95%	p	OR	CI 95%	p
Admissions 1 st year*	3.06	(1.53-6.12)	0.002	2.65	(1.26-5.56)	0.010
Admissions 2 nd year**	2.09	(1.1-3.97)	0.025	1.88	(0.94-3.76)	0.076
Admissions 1-2 years***	2.30	(1.3-4.06)	0.004	1.94	(1.03-3.65)	0.041

patient's vulnerability to COPD exacerbations or "speed up" the progression of the disease.

The study identified other factors associated with a greater risk of hospitalization which should also be mentioned. Most patients in the study had a GOLD 2 level of COPD and almost half (42.8%) the patients referred to slight dyspnoea. These percentages are higher than in other studies [22], no doubt because the patients come from primary care where patients with less severe are monitored and therefore they are ones with fewer symptoms.

The patients admitted in a hospital had a lower FEV1 and FEV1/FVC. López et al. considered the severity (GOLD) to be a very important factor on deciding whether to start a treatment for depression [23]. At the same time, the associated comorbidity was also more prevalent among COPD patients who are hospitalised, a finding previously described [24,25].

Hospitalised patients have a higher level of dyspnoea (Medical Research Council-MRC). This progressive limitation to the airflow in COPD leads to dyspnoea and difficulty in breathing. This situation is one of chronic stress for the patient that limits the activities of their everyday life and deteriorates their state of health. Therefore, it is not surprising that 50% of patients have anxiety/depression [23].

Patients who were admitted into hospital during the two years of the follow up had a worse prognosis, measured using the Charlson index, a worse perception of quality of life (EuroQol) and greater severity (GOLD). These results have been previously described by other authors, such as Hanania et al. [26], who determined that chronic diseases such as COPD can be accompanied by psychiatric disorders, in particular depression, which complicate and aggravate the prognosis and the quality of life. Other studies have also determined a relationship between a lower quality of life (EuroQol) [27], a higher frequency of hospitalization [28] and a poorer prognosis of the disease [29].

Diabetes and anaemia are the two variables that are associated with hospitalization in the second year of the study, but not the first. This could be explained partly due to the cohort effect, as

over time the effect of inflammatory anaemia in the COPD would increase [30] and the effect of diabetes would increase due to the accumulative effect of treatment with systemic and/or inhaled corticoids. Therefore, the risk of developing "steroid-induced diabetes" varies between different studies, with Odds Ratios that vary between 1.36 and 2.31 [31,32].

The results would be generalizable because 77.9% of patients in the sample (From primary care consultations) have a mild or moderate level (GOLD) of the disease; therefore they represent the actual spectrum of the disease at population level. Therefore, the risk of hospitalization that is attributable to anxiety/depression is representative of the general population.

Limitations

Given the complex nature of COPD, the high number of risk factors associated with exacerbations [33] and the probable circular relationship between these variables and psychological stress, for example, when anxiety and depression, and COPD risk factors each contribute to mental and physical health decline, it would be difficult to isolate one particular causal factor. In the logistic regression model, we decided not to enter the variables associated with quality of life and co-morbidity due to their collinearity with anxiety and depression. In other studies, the association between anxiety and depression, and hospitalizations became nonsignificant when adjusting for this covariate [27].

As in other studies [15,19] anxiety and depression were measured with the HADS test, nevertheless there is a shortage of studies that have used a measure of anxiety and depression that has been validated in patients with COPD. A better knowledge of their screening properties would have given us a better idea of the outcome of this study.

Conclusion

The outcome of this study suggests that anxiety and depression may increase the risk of COPD hospitalization. Nevertheless, the relationship between these and other factors is complex, as it is influenced by the multiple manifestations of COPD including clinical presentation, biological and physiological processes, and patient-related outcomes.

Anxiety and depression should routinely be evaluated by clinicians to be able to offer the best therapeutic options for patients, including pulmonary rehabilitation, cognitive-behavioural therapy and pharmacotherapy. This will be an important advance in the direction of the promising Predictive, Personalized, Preventive, and Participatory (P4) medicine model [34].

References

- 1 López-Campos JL, Tan W, Soriano JB (2016) Global burden of COPD. *Respirology* 21: 14-23.
- 2 Celli BR, MacNee W, ATS/ERS Task Force (2004) Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 23: 932-946.
- 3 Dahlén I, Janson C (2002) Anxiety and depression are related to the outcome of emergency treatment in patients with obstructive pulmonary disease. *Chest* 122: 1633-1637.
- 4 Jennings JH, Digiovine B, Obeid D, Frank C (2009) The association between depressive symptoms and acute exacerbations of COPD. *Lung* 187: 128-135.
- 5 Rubio MC, Rodríguez Hermosa JL, Nebreda MJ (2009) Anxiety and COPD. *Arch Bronconeumol* 45: 51-53.
- 6 Almagro P, Calbo E, Ochoa de Echagüen A, Barreiro B, Quintana S, et al. (2002) Mortality after hospitalization for COPD. *Chest* 121: 1441-1448.
- 7 Divo M, Cote C, de Torres JP, Casanova C, Marin JM, et al. (2012) Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 186: 155-161.
- 8 Vanfleteren LEGW, Spruit MA, Groenen M, Gaffron S, van Empel VPM, et al. (2013) Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 187: 728-735.
- 9 Kunik ME, Roundy K, Veazey C, Soucek J, Richardson P, et al. (2005) Surprisingly high prevalence of anxiety and depression in chronic breathing disorders. *Chest* 127: 1205-1211.
- 10 Gudmundsson G, Gislason T, Janson C, Lindberg E, Suppli Ulrik C, et al. (2006) Depression, anxiety and health status after hospitalisation for COPD: a multicentre study in the Nordic countries. *Respir Med* 100: 87-93.
- 11 Wilkinson MJ, Barczak P (1988) Psychiatric screening in general practice: comparison of the general health questionnaire and the hospital anxiety depression scale. *J R Coll Gen Pract* 38: 311-313.
- 12 Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, et al. (2007) Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 176: 532-555.
- 13 Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. *Acta Psychiatr Scand* 67: 361-370.
- 14 González-Gutiérrez MV, Guerrero Velázquez J, Morales García C, Casas Maldonado F, Gómez Jiménez FJ, et al. (2016) Predictive Model for Anxiety and Depression in Spanish Patients with Stable Chronic Obstructive Pulmonary Disease. *Arch Bronconeumol* 52: 151-157.
- 15 Xu W, Collet JP, Shapiro S, Lin Y, Yang T, et al. (2008) Independent effect of depression and anxiety on chronic obstructive pulmonary disease exacerbations and hospitalizations. *Am J Respir Crit Care Med* 178: 913-920.
- 16 Ng TP, Niti M, Tan WC, Cao Z, Ong KC, et al. (2007) Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. *Arch Intern Med* 167: 60-67.
- 17 van Manen JG, Bindels PJ, Dekker FW, IJzermans CJ, van der Zee JS, et al. (2002) Risk of depression in patients with chronic obstructive pulmonary disease and its determinants. *Thorax* 57: 412-416.
- 18 Brenes GA (2003) Anxiety and chronic obstructive pulmonary disease: prevalence, impact, and treatment. *Psychosom Med* 65: 963-970.
- 19 Cao Z, Ong KC, Eng P, Tan WC, Ng TP (2006) Frequent hospital readmissions for acute exacerbation of COPD and their associated factors. *Respirology* 11: 188-195.
- 20 de Jonge P, Rosmalen JGM, Kema IP, Doornbos B, van Melle JP, et al. (2010) Psychophysiological biomarkers explaining the association between depression and prognosis in coronary artery patients: a critical review of the literature. *Neurosci Biobehav Rev* 35: 84-90.
- 21 Burgess A, Kunik ME, Stanley MA (2005) Chronic obstructive pulmonary disease: assessing and treating psychological issues in patients with COPD. *Geriatrics* 60: 18-21.
- 22 Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, et al. (2004) The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med* 350: 1005-1012.
- 23 Lopez F, Pineda MCJ (2007) Ansiedad y depresión en la EPOC. *Rev Clin Esp* 2: 53-57.
- 24 Alcázar B, García-Polo C, Herrejón A, Ruiz LA, de Miguel J, et al. (2012) Factors associated with hospital admission for exacerbation of chronic obstructive pulmonary disease. *Arch Bronconeumol* 48: 70-76.
- 25 Montserrat-Capdevila J, Godoy P, Marsal JR, Barbé F (2015) Predictive Model of Hospital Admission for COPD Exacerbation. *Respir Care* 60: 1288-1294.
- 26 Hanania NA, Müllerova H, Locantore NW, Vestbo J, Watkins ML, et al. (2011) Determinants of depression in the ECLIPSE chronic obstructive pulmonary disease cohort. *Am J Respir Crit Care Med* 183: 604-611.
- 27 Almagro P, Barreiro B, Ochoa de Echagüen A, Quintana S, Rodríguez Carballeira M, et al. (2006) Risk factors for hospital readmission in patients with chronic obstructive pulmonary disease. *Respiration* 73: 311-317.
- 28 Miravittles M, Ferrer M, Pont A, Zalacain R, Alvarez-Sala JL, et al. (2004) Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease: a 2 year follow up study. *Thorax* 59: 387-395.
- 29 Domingo-Salvany A, Lamarca R, Ferrer M, Garcia-Aymerich J, Alonso J, et al. (2002) Health-related quality of life and mortality in male patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 166: 680-685.
- 30 Juárez MC, de Miguel J, Castuera AP, de OC (2013) Anemia en pacientes ingresados por una exacerbación de EPOC. Influencia sobre el pronóstico de la enfermedad. *Rev Patol Respir* 16: 37-41.
- 31 Gulliford MC, Charlton J, Latinovic R (2006) Risk of diabetes associated with prescribed glucocorticoids in a large population. *Diabetes Care* 29: 2728-2729.
- 32 Blackburn D, Hux J, Mamdani M (2002) Quantification of the Risk of Corticosteroid-induced Diabetes Mellitus among the Elderly. *J Gen Intern Med* 17: 717-720.
- 33 Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, et al. (2010) Susceptibility to exacerbation in chronic obstructive pulmonary disease. *N Engl J Med* 363: 1128-1138.
- 34 Bousquet JS, Anto JM, Sterk PJ, Adcock IM, Chung KF, et al. (2011) Systems medicine and integrated care to combat chronic noncommunicable diseases. *Genome Med* 3: 43.