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Associations between depression and anxiety index and frequency of acute exacerbation in chronic obstructive pulmonary disease

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Abstract

Background: Comorbidities of chronic obstructive pulmonary disease (COPD) influence clinical characteristics and prognosis.

Objectives: This study compared the clinical characteristics and exacerbation rate of COPD according to the presence of depression or anxiety.

Design: This study used data from The Korea COPD Subgroup Study (KOCOSS) cohort, a nationwide prospective cohort from 54 medical centers, between April 2012 and 2019.

Methods: Depression and anxiety were diagnosed with the Beck Depression Inventory and Beck Anxiety Inventory. Negative binomial regression analysis was performed to analyze the frequency of exacerbations in depressed patients and anxiety. Differences in lung function trajectory according to presence of depression/anxiety were analyzed using a linear mixed model.

Results: In all, 2147 patients were enrolled. Depressed patients or anxiety had lower lung function, higher modified Medical Research Council (mMRC) grade, St. George Respiratory Questionnaire (SGRQ) score, and COPD assessment test score, and higher rates of exacerbation in the past year than those without depression/anxiety. Depressed patients had a higher frequency of moderate to severe exacerbations [Incidence Rate Ratio (IRR): 1.57, CI: 1.17–2.11, $p = 0.002$] and those with anxiety had higher frequencies of moderate to severe (IRR: 1.52, CI: 1.03–2.27, $p = 0.038$) and severe exacerbations (IRR: 2.13, CI: 1.09–4.15, $p = 0.025$) during 1-year follow-up compared to those without these comorbidities. The differences in the change in annual forced expiratory volume in 1 seconds (FEV_1) over 3 years according to the presence of depression or anxiety were not statistically significant.

Conclusion: Depressed and anxious patients showed increased respiratory symptoms and exacerbation rate as well as reduced health-related quality of life, whereas there were no significant differences in changes in lung function between groups with and without depression/anxiety.

Keywords: anxiety, chronic obstructive pulmonary disease, depression, exacerbations, FEV_1 change, psychologic morbidities

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Background

Chronic obstructive pulmonary disease (COPD) is a disease with persistent respiratory symptoms and chronic airflow limitation, which is caused by a combination of small airway disease and parenchymal destruction due to exposure to toxic gases

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or particles.[1,2] COPD constituted 55% of all chronic respiratory diseases in 2017 with a relative increase of 5.9% since 1990. It is estimated that over 300 million people worldwide are affected by COPD in 2019.[3,4] COPD has several clinical impacts, including increased rates of mortality and various comorbidities.[5,6] In addition, it is associated with a high socioeconomic burden, with the global economic burden of COPD in 2010 estimated to reach 49.9 billion dollars.[7,8]

The most important factors affecting the natural course of COPD are the frequency of exacerbations and the presence of comorbidities that impact disease progression and in turn worsen the prognosis of these patients.[5,9,10] Psychological morbidities, such as depression and anxiety, are prevalent in COPD. Depression and anxiety have reported prevalence rates of approximately 25% and 40% in COPD, and prevalence may be associated with younger age, female sex, current smoking, poor lung function, and reduced health-related quality of life (QOL) in COPD patients.[11–17] The prevalence of depression is also high in patients who have recently experienced exacerbations, and the presence of depression can influence patient mortality.[16] Depression and anxiety are associated with poor lung function and reduced health-related QOL in COPD patients.[18] Furthermore, previous studies in the United Kingdom and China have shown that depression and anxiety significantly increased the frequency of acute exacerbations in COPD patients.[19–21]

The aim of this study is to explore the differences in demographic and clinical characteristics, lung function trajectory, and exacerbation frequency among patients with COPD based on the presence or absence of depression or anxiety, in a nationwide multicenter Korean COPD cohort.

Methods

Study population and data collection

The Korea COPD Subgroup Study (KOCOSS) is a nationwide prospective cohort study from 54 medical centers in South Korea that began in April 2012.[22,23] The inclusion criteria for the KOCOSS study were patient age $\geq$ 40 years with fixed airway obstruction according to pulmonary function tests, defined as post-bronchodilator forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) $<$ 70% of the normal predicted value. The clinical data of patients were collected using a case report form by a doctor or trained nurse. We used the data extracted from the KOCOSS database between April 2012 and 2019.

Clinical parameters

Baseline characteristics of patients obtained at the initial visit included age, sex, smoking history, and body mass index (BMI). The Beck Depression Inventory (BDI)-II and the Beck Anxiety Inventory (BAI) psychological tests were used to diagnosis depression and anxiety, respectively. Pulmonary function test parameters, for example, FEV_1, FVC, FEV_1/FVC, diffusing capacity of the lungs for carbon monoxide (DLCO), and residual volume/total lung capacity, were measured at baseline and annually for 3 years. Symptom scores, including the Modified Medical Research Council (mMRC) grade, St. George Respiratory Questionnaire (SGRQ) score, and COPD assessment test (CAT) score, were collected. Exercise tolerance was evaluated using the 6-Minute Walking Test (6MWT). Type 2 inflammation markers, including serum immunoglobulin E, fractional exhaled nitric oxide (FeNO), and blood eosinophil levels, were also measured. Furthermore, the presence of emphysema in chest computed tomography (CT) was assessed. Presence of comorbidities including heart failure, diabetes mellitus, hypertension, cancer, and chronic kidney disease were also collected. Medication regimes for COPD were classified as long-acting beta-agonist or long-acting muscarinic antagonist, long-acting beta-agonist plus long-acting muscarinic antagonist, inhaled corticosteroid plus long-acting beta-agonist, and triple therapy. Exacerbation was defined as acute deterioration of symptoms requiring further treatment.[1] Moderate exacerbation was defined as exacerbation that required antibiotics or systemic corticosteroid on an outpatient basis, whereas severe exacerbation was defined as that requiring an emergency room visit or hospital admission.

Definition of depression and anxiety

The BDI-II and BAI were used to define depression and anxiety in COPD patients. These self-assessment instruments are widely used worldwide to evaluate depression and anxiety, and there are numerous studies that have investigated their

reliability and validity, including among Korean adults.[24–26] BDI-II score ⩾ 10 was defined as indicating depression, and BAI score ⩾ 8 was defined as indicating anxiety according to the literature.[27,28]

Statistical analysis

Statistical analyses were performed using R software (ver. 3.6.3; R Development Core Team, Vienna, Austria). Data are expressed as the mean ± standard deviation or number and percentage. We compared clinical differences between patients with depression or anxiety and those without depression or anxiety. Clinical differences between two groups were analyzed using the χ^2 test for categorical variables and Student's *t*-test for continuous variables. Negative binomial regression analysis was performed to analyze differences in the frequency of exacerbations between patients with and without depression or anxiety. Age, sex, BMI, smoking history, FEV_1, and past exacerbation history were adjusted in this analysis. The differences in annual FEV_1 change over 3 years between groups were analyzed using a linear mixed model that revised the interaction between time and depression/anxiety. Age, sex, BMI, smoking history, and past exacerbation history were adjusted in this analysis. In all analyses, $p < 0.05$ was taken to indicate statistical significance. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology statement (Supplemental Table 1).

Results

Baseline characteristics

In all, 2147 patients with a mean age of 68.9 ± 7.7 were enrolled. Most patients were male (93.1%); 157 (7.4%) were never smokers and 1974 (92.6%) were ever smokers. Table 1 shows the baseline characteristics of all patients.

Differences between patients with and without depression

Table 2 shows differences in baseline characteristics between patients with and without depression. The incidence of depression in the study population of COPD patients was 27.4%. Depressed patients smoked more (42.5 ± 29.8 pack years *versus* 37.5 ± 25.8 pack years, respectively, $p = 0.008$) and had lower FEV_1/FVC (48.5 ± 13.8 *versus* 50.3 ± 12.2, respectively, $p = 0.014$), lower DLCO (60.5 ± 20.3 *versus* 64.2 ± 20.9, respectively, $p = 0.013$), higher mMRC grade (1.5 ± 1.0 *versus* 1.2 ± 0.8, respectively, $p < 0.001$), higher SGRQ score (41.2 ± 20.1 *versus* 25.7 ± 15.9, respectively, $p < 0.001$), and higher CAT score (18.3 ± 8.4 *versus* 12.1 ± 7.1, respectively, $p < 0.001$) than those without depression. Post-bronchodilator FEV_1 did not significantly differ between the two groups. In addition, depressive COPD patients were more likely to have chronic bronchitis (30.2% *versus* 17.1%, respectively, $p < 0.001$), emphysema (54.1% *versus* 41.4%, respectively, $p = 0.005$), and a higher rate of exacerbation in the past year (24.8% *versus* 16.3%, respectively, $p = 0.001$) than those without depression.

Differences between patients with and without anxiety

Table 3 shows the differences in baseline characteristics between patients according to the presence or absence of anxiety. The rate of anxiety among COPD patients was 19.3%. Anxious COPD patients were younger than those without anxiety (67.3 ± 8.0 *versus* 69.7 ± 7.4, respectively, $p < 0.001$). There were no significant differences in FEV_1 between the two groups, whereas DLCO was lower in the anxiety group (60.1 ± 19.2 *versus* 64.0 ± 20.2, respectively, $p = 0.023$). mMRC grade, SGRQ score, and CAT score were higher in the group with than without anxiety. Patients with anxiety were more likely to have chronic bronchitis (32.8% *versus* 16.6%, respectively, $p < 0.001$) and a history of exacerbation in the past year (28.5% *versus* 14.5%, respectively, $p < 0.001$).

Association between depression/anxiety and frequency of exacerbation

Depressed patients had a higher frequency of moderate to severe exacerbations (IRR = 1.57, CI: 1.17–2.11, $p = 0.002$) during 1 year of follow-up than those without depression (Table 4). Patients with anxiety had higher frequencies of both moderate to severe (IRR = 1.51, CI: 1.02–2.26, $p = 0.040$) and severe exacerbations

Table 1. Clinical characteristics of patients.

Characteristics	Value
Age	68.9 ± 7.7
Sex (male)	1998 (93.1%)
BMI	23.0 ± 3.4
Smoking Hx	
Never	157 (7.4%)
Ex-smoker	1394 (65.4%)
Current smoker	580 (27.2%)
Smoke pack years	39.3 ± 26.7
mMRC	1.3 ± 0.9
GOLD	
I	209 (9.7%)
II	1112 (51.8%)
III	655 (30.5%)
IV	170 (7.9%)
Blood eosinophil count	225.0 ± 248.1
PostBD FEV_1 (L)	1.7 ± 0.6
PostBD FVC (L)	3.3 ± 0.8
PostBD FEV_1/FVC	50.2 ± 12.7
RV/TLC	0.4 ± 0.1
DLCO	63.8 ± 20.7
Chronic bronchitis	490 (23.0%)
SGRQ score	31.6 ± 18.8
CAT score	14.5 ± 8.1
6MWT	385.1 ± 116.0
Emphysema on CT	494 (44.9%)
FeNO	27.0 ± 17.0
IgE	232.1 ± 347.0
Medications	
LABA or LAMA	529 (24.6%)
LABA/LAMA	385 (17.9%)
ICS/LABA	251 (11.7%)
ICS/LABA/LAMA	468 (21.8%)
Comorbidities	1272 (59.2%)
Heart failure	67 (3.1%)
Diabetes mellitus	366 (3.1%)
Hypertension	854 (39.8%)
Cancer	33 (6.5%)
Chronic kidney disease	5(1%)
Past year exacerbation	414 (20.0%)

Data are presented as *n* (%) or mean ± SD.
BD, bronchodilator; BMI, body mass index; CAT, COPD assessment test; CT, computed tomography; DLCO, diffusing capacity of the lungs for carbon monoxide; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; LABA, long-acting beta2-agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical Research Council; 6MWT, 6-minutes walking test; RV, residual volume; SGRQ, St. George Respiratory Questionnaire; TLC, total lung capacity.

(IRR = 2.12, CI: 1.08–4.15, $p = 0.026$) during 1 year of follow-up than those without anxiety.

Association between depression/anxiety and changes in lung function

The differences in the change in annual FEV_1 over 3 years between groups with and without depression ($p = 0.19$) or anxiety ($p = 0.97$) were not statistically significant (Figure 1).

Discussion

We observed differences in clinical characteristics and exacerbation risk according to the presence or absence of depression or anxiety. Depressed patients were more likely to have higher smoking pack-years, more severe symptoms, chronic bronchitis, exacerbations in the past year, lower health-related QOL, and lower DLCO than those without depression. In addition, patients with anxiety were more likely to be younger, have more severe symptoms, chronic bronchitis, exacerbations in the past year, lower health-related QOL, and lower DLCO than those without anxiety.

Table 2. Clinical characteristics of patients with depression and without depression.

Variables	Depression (+) (n = 334, 27.4%)	Depression (–) (n = 884, 72.6%)	p Value
Age	68.6 ± 7.6	69.3 ± 7.5	0.163
Sex (male)	311 (93.1%)	838 (94.9%)	0.320
BMI	22.8 ± 3.6	23.2 ± 3.5	0.085
Smoking Hx			0.331
Never	22 (6.6%)	57 6.5%)	
Ex-smoker	213 (63.8%)	600 (68.0%)	
Current smoker	99 (29.6%)	225 (25.5%)	
Smoke pack years	42.5 ± 29.8	37.5 ± 25.8	0.008
mMRC	1.5 ± 1.0	1.2 ± 0.8	<0.001
GOLD			0.008
I	27 (8.1%)	115 (3.0%)	
II	171 (51.2%)	454(1.4%)	
III	95 (28.4%)	250 (8.3%)	
IV	41 (12.3%)	65 (7.4%)	
Blood eosinophil count	230.9 ± 229.3	219.6 ± 243.6	0.496
PostBD FEV_1 (L)	1.7 ± 0.6	1.7 ± 0.6	0.113
PostBD FVC (L)	3.4 ± 0.8	3.4 ± 0.8	0.697
PostBD FEV_1/FVC	48.5 ± 13.8	50.3 ± 12.2	0.031
RV/TLC	0.4 ± 0.1	0.4 ± 0.1	0.311
DLCO	60.5 ± 20.3	64.2 ± 20.9	0.013
Chronic bronchitis	101 (30.2%)	151 (17.1%)	<0.001
SGRQ score	41.2 ± 20.1	25.7 ± 15.9	<0.001
CAT score	18.3 ± 8.4	12.1 ± 7.1	<0.001
6MWT	380.7 ± 108.9	389.4 ± 122.8	0.315
Emphysema on CT	99 (54.1%)	181 (41.4%)	0.005
FeNO	28.4 ± 19.7	26.8 ± 16.1	0.535
IgE	207.2 ± 297.8	275.6 ± 418.6	0.018
Medications			0.386
LABA or LAMA	71 (21.3)	179 (20.2%)	
LABA/LAMA	78 (23.4)	232 (26.2%)	

(Continued)

Table 2. (Continued)

Variables	Depression (+) (*n* = 334, 27.4%)	Depression (–) (*n* = 884, 72.6%)	*p* Value
ICS/LABA	40 (12.0%)	101 (11.4%)	
ICS/LABA/LAMA	79 (23.7%)	171 (19.3%)	
Comorbidities	197 (59%)	503(56.9%)	0.610
Heart failure	12 (3.6%)	29 (3.3%)	0.959
Diabetes mellitus	57 (17.1%)	140 (15.8%)	0.671
Hypertension	132 (39.5%)	334 (37.8%)	0.853
Cancer	6 (5.5%)	258 (6.8%)	0.799
Chronic kidney disease	0 (0%)	5 (1.4%)	0.473
Past year exacerbation	79 (24.8%)	137 (16.3%)	0.001

Data are presented as *n* (%) or mean ± SD
BD, bronchodilator; BMI, body mass index; CAT, COPD assessment test; CT, computed tomography; DLCO, diffusing capacity of the lungs for carbon monoxide; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; LABA, long-acting beta2-agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical Research Council; 6MWT, 6-minutes walking test; RV, residual volume; SGRQ, St. George Respiratory Questionnaire; TLC, total lung capacity.

Table 3. Clinical characteristics of patients with anxiety and without anxiety.

Variables	Anxiety (+) (*n* = 198, 19.3%)	Anxiety (–) (*n* = 829, 80.7%)	*p* Value
Age	67.6 ± 8.0	69.7 ± 7.4	<0.001
Sex (male)	187 (94.4%)	785 (94.7%)	1.000
BMI	23.2 ± 3.7	23.2 ± 3.5	0.896
Smoking Hx			0.162
Never	9 (4.5%)	53 (6.4%)	
Ex-smoker	126 (63.6%)	562 (68.0%)	
Current smoker	63 (31.8%)	212 (25.6%)	
Smoke pack years	41.7 ± 29.4	38.3 ± 26.5	0.119
mMRC	1.6 ± 1.0	1.1 ± 0.8	<0.001
GOLD			0.319
I	26 (13.1%)	125 (15.1%)	
II	106 (53.5%)	466 (56.3%)	
III	47 (23.7%)	186 (22.5%)	
IV	19 (9.6%)	51 (6.2%)	

(Continued)

Table 3. (Continued)

Variables	Anxiety (+) (*n* = 198, 19.3%)	Anxiety (–) (*n* = 829, 80.7%)	*p* Value
Blood eosinophil count	217.7 ± 204.0	217.7 ± 246.0	0.999
PostBD FEV_1 (L)	1.8 ± 0.7	1.8 ± 0.6	0.674
PostBD FVC (L)	3.5 ± 0.8	3.5 ± 0.8	0.554
PostBD FEV_1/FVC	49.9 ± 13.3	51.2 ± 12.1	0.193
RV/TLC	0.4 ± 0.1	0.4 ± 0.1	0.994
DLCO	60.1 ± 19.2	64.0 ± 20.2	0.023
Chronic bronchitis	65 (32.8%)	138 (16.6%)	<0.001
SGRQ score	41.1 ± 20.7	25.2 ± 16.1	<0.001
CAT score	18.8 ± 8.8	12.0 ± 7.1	<0.001
6MWT	377.9 ± 119.8	106.2 ± 108.8	0.006
Emphysema on CT	59 (52.7%)	205 (46.8%)	0.315
FeNO	24.9 ± 15.7	27.1 ± 16.6	0.442
IgE	243.6 ± 469.3	250.0 ± 359.9	0.884
Medications			0.515
LABA or LAMA	37 (18.7%)	153 (18.5%)	
LABA/LAMA	53 (26.8%)	271 (32.7%)	
ICS/LABA	37 (18.7%)	87 (10.5%)	
ICS/LABA/LAMA	39 (19.7%)	134 (16.2%)	
Comorbidities	119 (60.1%)	487 (58.7%)	0.501
Heart failure	5 (2.5%)	24 (2.9%)	0.922
Diabetes mellitus	33 (16.7%)	145 (17.5%)	0.527
Hypertension	74 (37.4%)	331 (39.9%)	0.778
Cancer	4 (4.9%)	27 (6.6%)	0.781
Chronic kidney disease	0 (0%)	5 (1.2%)	0.599
Past year exacerbation	53 (28.5%)	114 (14.5%)	<0.001

Data are presented as *n* (%) or mean ± SD.
BD, bronchodilator; BMI, body mass index; CAT, COPD assessment Test; CT, computed tomography; DLCO, diffusing capacity of the lungs for carbon monoxide; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; LABA, long-acting beta2-agonist; LAMA, long-acting muscarinic antagonist; mMRC, modified Medical Research Council; 6MWT, 6-minutes walking test; RV, residual volume; SGRQ, St. George Respiratory Questionnaire; TLC, total lung capacity.

Table 4. Frequency of exacerbation in patients with depression compared with without depression.

Variables	Moderate to severe exacerbation			Severe exacerbation		
	IRR	95% CI	*p*-Value	IRR	95% CI	*p* Value
Depression	1.57	1.17–2.11	0.002	1.50	0.92–2.45	0.104
Anxiety	1.51	1.02–2.26	0.040	2.12	1.08–4.15	0.026

Adjusted variables: age, sex, BMI, smoking history, FEV_1, past exacerbation history.
FEV_1, forced expiratory volume in 1 second; IRR, incidence rate ratio.

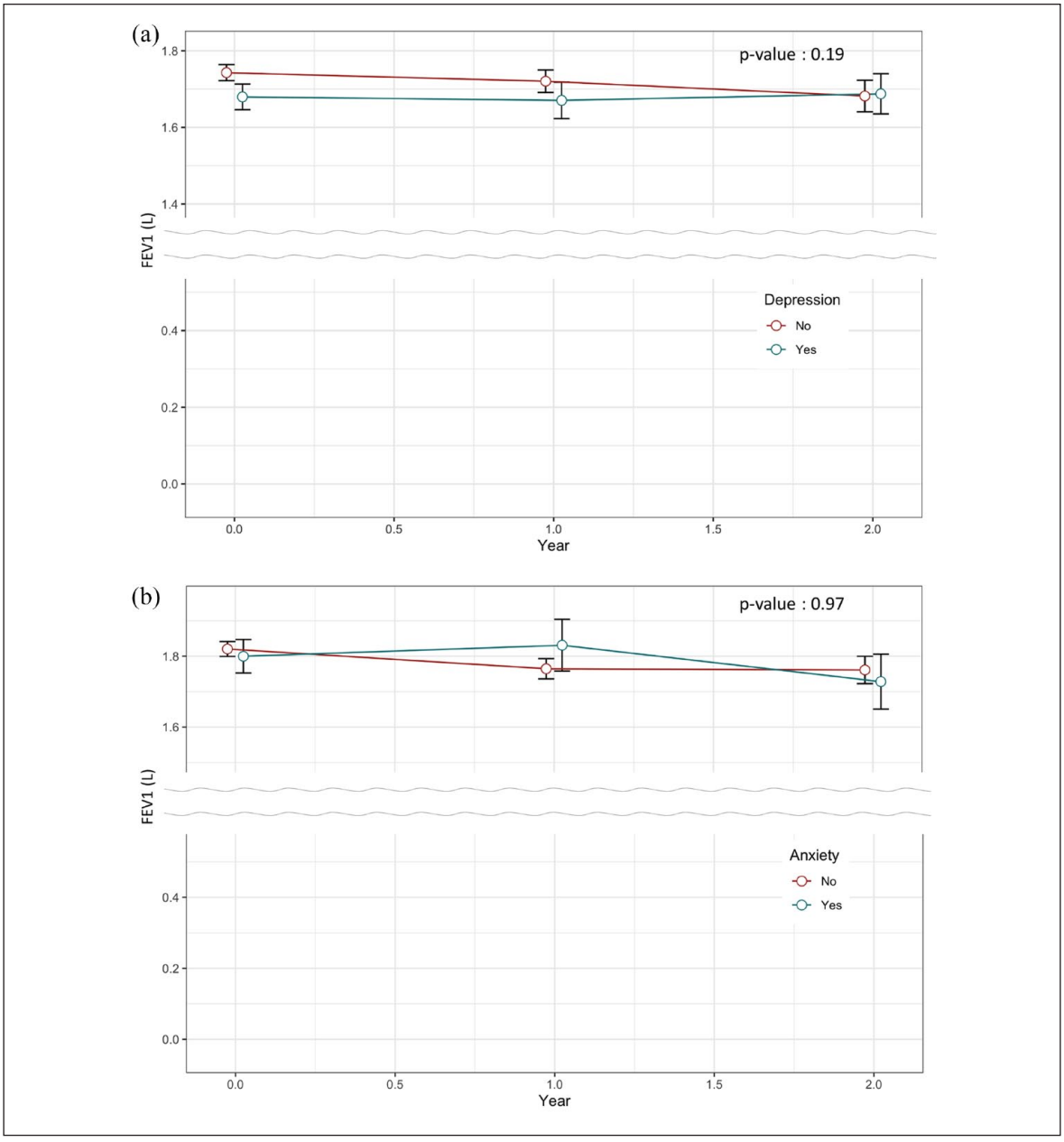

Figure 1. Lung function change in patients with depression and anxiety: (a) Depression, (b) Anxiety.

There were no significant differences in rates of lung function decline according to presence of depression or anxiety. We found that depressed patients were at higher risk for moderate to severe exacerbations, and those with anxiety showed significantly higher risk for moderate to severe and severe exacerbations during 1 year of follow-up than those without these comorbidities.

The impacts of comorbidities in COPD have been studied in detail, as they may substantially affect disease course and prognosis. These comorbidities may arise independently or be causally related to COPD; the two diseases may share risk factors or one disease may affect the severity of the other.[1] Depression and anxiety are among the most frequent comorbidities of COPD and are associated with poor clinical course.[17,21,29,30] Several studies have investigated the relations between depression or anxiety and acute exacerbations of COPD, and our results are consistent with most of those studies. Of 24 studies included in a systematic review from the United Kingdom in 2014, 17 showed that depression and anxiety are significantly associated with higher risk of hospital admission and readmission due to acute exacerbation of COPD.[31] Yohannes *et al.*[19] demonstrated that a high depression score at baseline was associated with a significantly increased risk for moderate to severe exacerbations and severe exacerbations, whereas past moderate-to-severe exacerbation history was the strongest predictor of exacerbations during 3 years of follow-up. Similarly, Huang *et al.*[21] reported that depressed patients with a self-rating depression scale score $\geqslant 53$ and patients with a self-rating anxiety scale score $\geqslant 50$ had higher risk for acute exacerbation.

There are several possible reasons for the increased risk for COPD exacerbation in patients with poor mental health. There may be some risk factors in common between poor mental health and COPD exacerbation, for example, both cigarette smoking and poor socioeconomic status are risk factors for both COPD exacerbation and depression/anxiety.[32–35] In addition, depressive and anxious patients may neglect use of medications, including inhalers, leading to reduced adherence to therapy, which may increase the risk for future exacerbation.[36] It is a vicious circle in that past exacerbations cause poor mental health, leading to reduced physical activity and QOL, which may provoke frequent exacerbation and lead to progressive worsening of the patient's condition.[36] Finally, there is evidence that systemic inflammation may be associated with depression and lung function decline in COPD patients, which may explain the increased risk for exacerbation in depressive patients.[37]

Our data showed no significant differences in lung function according to the presence of depression or anxiety. However, previous studies have shown that depressive patients have greater impairment of lung function.[18,29,38] Consistent with Yohannes *et al.*,[29] we also found no significant differences in lung function decline according to the presence or absence of depression or anxiety. Interestingly, in our study, depressive or anxious patients had decreased DLCO compared to patients in good mental health. Frequent presentation of chronic bronchitis may explain reduced DLCO in depressed patients and anxiety, but further investigations are necessary to address this issue.[39]

Due to their clinical and socioeconomic importance, it is important to manage psychological comorbidities in patients with COPD. Depressive patients with COPD have a significantly increased rate of suicide attempts compared to non-COPD patients.[40–42] However, only 27–33% of depressed COPD patients receive treatment for depression.[31] As there may be veiled psychological comorbidities among COPD patients, efforts should be made to identify depressed/anxious patients and administer appropriate treatment, including psychological and pharmacological interventions as well as pulmonary rehabilitation. Psychological therapy includes relaxation therapy, cognitive behavioral therapy, and self-management strategies.[43] Several studies have reported positive effects of psychological therapy in COPD patients.[44–46] A systemic review showed that mind–body exercise (e.g. yoga, qigong) can improve the symptoms of depression and anxiety in COPD patients, which may be part of the benefits of relaxation therapy.[47] In terms of pharmacotherapy, some studies have reported improvement of symptoms using selective serotonin reuptake inhibitors and tricyclic antidepressants in COPD patients.[48,49] In addition, some studies have shown the importance of pulmonary rehabilitation in depressed and anxious COPD patients.[50,51]

This study had some limitations. First, the patients enrolled in our study were from the KOCOSS cohort and were mostly from tertiary hospitals, and so may not be representative of the general population. Second, as most enrolled patients were male (93.1%) and smokers (92.6%), the population may not accurately reflect depression and anxiety in COPD patients as both are associated with female sex and nicotine dependence.[29,32] Third, as the cutoff value of the BDI score was lower than in some other studies, patients with milder depression may have been included in our cohort[26]; we used a BDI cutoff value of 18 points, and although there was a trend, it was not statistically significant. However, as a BDI score of 10 has been validated in several studies, the cutoff value of 10 points may also be appropriate.[28,52,53]

Conclusion

Depression and anxiety are both associated with more severe symptoms and poorer health-related QOL in patients with COPD. In addition, depression and anxiety can independently predict the frequency of exacerbations of COPD, which is associated with prognosis. Therefore, this study provides evidence that mental health should be taken into account when treating patients with COPD, particularly those with severe symptoms and frequent exacerbations. Clinicians should always strive to evaluate depression and anxiety early, from the diagnosis of COPD to the treatment period, to manage them appropriately.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of each medical center participating in KOCOSS. We also received approval from each center to use their subjects' clinical records for the study while maintaining the confidentiality of the data. Written informed consent was obtained from patients from each cohort. The study protocol of KOCOSS was approved by the Institutional Review Board of KONKUK University Medical Center (IRB No. KHH1010338).

Names of ethics committees

Gacheon University Gil Medical Center, Hallym University Kangnam Sacred Heart Hospital, Gangnam Severance Hospital, Kyung Hee University Hospital at Gangdong, Hallym University Kangdong Sacred Heart Hospital, Kangbuk Samsung Hospital, Kangwon National University Hospital, Konkuk University Hospital, Konkuk University Chungju Hospital, Kyungpook National University Hospital, Gyeongsang National University Hospital, Korea University Guro Hospital, Korea University Anam Hospital, Seoul Eulji Hospital, Dongguk University Gyeongju Hospital, Dongguk University Ilsan Hospital, Keimyung University Dongsan Medical Center, Dong-A University Hospital, Hallym University Dongtan Sacred Heart Hospital, Pusan National University Hospital, Inje University Busan Paik Hospital, The Catholic University of Korea Bucheon St Mary's Hospital, Soonchunhyang University Hospital Bucheon, Seoul National University Bundang Hospital, Bundang CHA Hospital, Seoul Metropolitan Government Seoul National University Bora-mae Medical Center, Samsung Medical Center, Soonchunhyang University Hospital Seoul, The Catholic University of Korea Seoul St Mary's Hospital, The Catholic University of Korea St Paul's Hospital, The Catholic University of Korea St Vincent's Hospital, Severance Hospital, Asan Medical Center, Ajou University Hospital, The Catholic University of Korea Yeouido St Mary's Hospital, The Catholic University of Korea Uijeongbu St Mary's Hospital, Yeungnam University Medical Center, Ulsan University Hospital, Wonkwang University Sanbon Hospital, Wonju Severance Christian Hospital, Ewha Womans University Mokding Hospital, Incheon St Mary's Hospital, Inha University Hospital, Chonnam National University Hospital, Chonbuk National University Hospital, Jeju National University Hospital, Soonchunhyang University Hospital Cheonan, Hallym University Chuncheon Sacred Heart Hospital, Hallym University Sacred Heart Hospital, and Hanyang University Guri Hospital.

Consent for publication

Study participants provided their written informed consent to publish the data collected during the investigation period.

Author contributions

Yu Jin Hong: Investigation; Writing – original draft; Writing – review & editing.

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The authors declare that there is no conflict of interest.

Availability of data and materials
The data analyzed in the current study are not publicly available. They may be made available from the corresponding authors upon reasonable request.

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References
1. Global Initiative for Chronic Obstructive Lung Disease. Global initiative for chronic obstructive lung disease (GOLD) guidelines, global strategy for the diagnosis, management and prevention of chronic obstructive lung disease. https://goldcopd.org/2021-gold-reports/ (2021).
2. Adeloye D, Chua S, Lee C, *et al.* Global and regional estimates of COPD prevalence: systematic review and meta-analysis. *J Glob Health* 2015; 5: 020415.
3. GBD Chronic Respiratory Disease Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med* 2020; 8: 585–596.
4. Stolz D, Mkorombindo T, Schumann DM, *et al.* Towards the elimination of chronic obstructive pulmonary disease: a Lancet Commission. *Lancet* 2022; 400: 921–972.
5. Recio Iglesias J, Díez-Manglano J, López García F, *et al.* Management of the COPD patient with comorbidities: an experts recommendation document. *Int J Chron Obstruct Pulmon Dis* 2020; 15: 1015–1037.
6. Sin DD, Anthonisen NR, Soriano JB, *et al.* Mortality in COPD: role of comorbidities. *Eur Respir J* 2006; 28: 1245–1257.
7. Vos T, Flaxman AD, Naghavi M, *et al.* Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2163–2196.
8. Guarascio AJ, Ray SM, Finch CK, *et al.* The clinical and economic burden of chronic obstructive pulmonary disease in the USA. *Clinicoecon Outcomes Res* 2013; 5: 235–245.
9. Mannino DM and Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007; 370: 765–773.
10. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of COPD. https://

goldcopd.org/wp-content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf (2022).

11. Willgoss TG and Yohannes AM. Anxiety disorders in patients with COPD: a systematic review. *Respir Care* 2013; 58: 858–866.
12. Kunik ME, Roundy K, Veazey C, *et al.* Surprisingly high prevalence of anxiety and depression in chronic breathing disorders. *Chest* 2005; 127: 1205–1211.
13. Zhang MW, Ho RC, Cheung MW, *et al.* Prevalence of depressive symptoms in patients with chronic obstructive pulmonary disease: a systematic review, meta-analysis and meta-regression. *Gen Hosp Psychiatry* 2011; 33: 217–223.
14. Volpato E, Toniolo S, Pagnini F, *et al.* The relationship between anxiety, depression and treatment adherence in chronic obstructive pulmonary disease: a systematic review. *Int J Chron Obstruct Pulmon Dis* 2021; 16: 2001–2021.
15. Hanania NA, Müllerova H, Locantore NW, *et al.* Determinants of depression in the ECLIPSE chronic obstructive pulmonary disease cohort. *Am J Respir Crit Care Med* 2011; 183: 604–611.
16. Maurer J, Rebbapragada V, Borson S, *et al.* Anxiety and depression in COPD: current understanding, unanswered questions, and research needs. *Chest* 2008; 134: 43s–56s.
17. Ng TP, Niti M, Tan WC, *et al.* Depressive symptoms and chronic obstructive pulmonary disease: effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. *Arch Intern Med* 2007; 167: 60–67.
18. Iguchi A, Senjyu H, Hayashi Y, *et al.* Relationship between depression in patients with COPD and the percent of predicted FEV(1), BODE index, and health-related quality of life. *Respir Care* 2013; 58: 334–339.
19. Yohannes AM, Mülerová H, Lavoie K, *et al.* The association of depressive symptoms with rates of acute exacerbations in patients with COPD: results from a 3-year longitudinal follow-up of the ECLIPSE cohort. *J Am Med Dir Assoc* 2017; 18: 955–959.e956.
20. Huang K, Huang K, Xu J, *et al.* Anxiety and depression in patients with chronic obstructive pulmonary disease in China: results from the china pulmonary health [CPH] study. *Int J Chron Obstruct Pulmon Dis* 2021; 16: 3387–3396.
21. Huang J, Bian Y, Zhao Y, *et al.* The impact of depression and anxiety on chronic obstructive pulmonary disease acute exacerbations: a prospective cohort study. *J Affect Disord* 2021; 281: 147–152.
22. Choi JY, Kim JW, Kim YH, *et al.* Clinical characteristics of non-smoking chronic obstructive pulmonary disease patients: Findings from the KOCOSS cohort. *COPD* 2022; 19: 174–181.
23. Lee JY, Chon GR, Rhee CK, *et al.* Characteristics of patients with chronic obstructive pulmonary disease at the first visit to a Pulmonary Medical Center in Korea: the KOrea COpd subgroup study team cohort. *J Korean Med Sci* 2016; 31: 553–560.
24. Kühner C, Bürger C, Keller F, *et al.* [Reliability and validity of the Revised Beck Depression Inventory (BDI-II). Results from German samples]. *Nervenarzt* 2007; 78: 651–656.
25. Park K, Jaekal E, Yoon S, *et al.* Diagnostic utility and psychometric properties of the beck depression inventory-II among Korean adults. *Front Psychol* 2019; 10: 2934.
26. Wang YP and Gorenstein C. Psychometric properties of the Beck Depression Inventory-II: a comprehensive review. *Braz J Psychiatry* 2013; 35: 416–431.
27. Hynninen MJ, Pallesen S and Nordhus IH. Factors affecting health status in COPD patients with co-morbid anxiety or depression. *Int J Chron Obstruct Pulmon Dis* 2007; 2: 323–328.
28. Beck AT, Steer RA and Carbin MG. Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. *Clinical Psychol Rev* 1988; 8: 77–100.
29. Yohannes AM, Müllerová H, Hanania NA, *et al.* Long-term course of depression trajectories in patients with COPD: a 3-year follow-up analysis of the evaluation of COPD longitudinally to identify predictive surrogate endpoints cohort. *Chest* 2016; 149: 916–926.
30. Yohannes AM and Alexopoulos GS. Depression and anxiety in patients with COPD. *Eur Respir Rev* 2014; 23: 345–349.
31. Pooler A and Beech R. Examining the relationship between anxiety and depression and exacerbations of COPD which result in hospital admission: a systematic review. *Int J Chron Obstruct Pulmon Dis* 2014; 9: 315–330.
32. Fluharty M, Taylor AE, Grabski M, *et al.* The association of cigarette smoking with depression and anxiety: a systematic review. *Nicotine Tob Res* 2017; 19: 3–13.
33. Viniol C and Vogelmeier CF. Exacerbations of COPD. *Eur Respir Rev* 2018; 27.

34. Angstman KB, Wi CI, Williams MD, *et al.* Impact of socioeconomic status on depression clinical outcomes at six months in a Midwestern, United States community. *J Affect Disord* 2021; 292: 751–756.
35. Lange P, Marott JL, Vestbo J, *et al.* Socioeconomic status and prognosis of COPD in Denmark. *COPD* 2014; 11: 431–437.
36. Zareifopoulos N, Bellou A, Spiropoulou A, *et al.* Prevalence, contribution to disease burden and management of comorbid depression and anxiety in chronic obstructive pulmonary disease: a narrative review. *COPD* 2019; 16: 406–417.
37. Lu Y, Feng L, Feng L, *et al.* Systemic inflammation, depression and obstructive pulmonary function: a population-based study. *Respir Res* 2013; 14: 53.
38. Schneider C, Jick SS, Bothner U, *et al.* COPD and the risk of depression. *Chest* 2010; 137: 341–347.
39. Choi JY, Yoon HK, Lee SY, *et al.* Comparison of clinical characteristics between chronic bronchitis and non-chronic bronchitis in patients with chronic obstructive pulmonary disease. *BMC Pulm Med* 2022; 22: 69.
40. Goodwin RD. Is COPD associated with suicide behavior? *J Psychiatr Res* 2011; 45: 1269–1271.
41. Hegerl U and Mergl R. Depression and suicidality in COPD: understandable reaction or independent disorders? *Eur Respir J* 2014; 44: 734–743.
42. Webb RT, Kontopantelis E, Doran T, *et al.* Suicide risk in primary care patients with major physical diseases: a case-control study. *Arch Gen Psychiatry* 2012; 69: 256–264.
43. Pumar MI, Gray CR, Walsh JR, *et al.* Anxiety and depression-Important psychological comorbidities of COPD. *J Thorac Dis* 2014; 6: 1615–1631.
44. Devine EC and Pearcy J. Meta-analysis of the effects of psychoeducational care in adults with chronic obstructive pulmonary disease. *Patient Educ Couns* 1996; 29: 167–178.
45. Hynninen MJ, Bjerke N, Pallesen S, *et al.* A randomized controlled trial of cognitive behavioral therapy for anxiety and depression in COPD. *Respir Med* 2010; 104: 986–994.
46. Bourbeau J, Julien M, Maltais F, *et al.* Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med* 2003; 163: 585–591.
47. Li Z, Liu S, Wang L, *et al.* Mind-body exercise for anxiety and depression in COPD patients: a systematic review and meta-analysis. *Int J Environ Res Public Health* 2019; 17: 22.
48. Lacasse Y, Beaudoin L, Rousseau L, *et al.* Randomized trial of paroxetine in end-stage COPD. *Monaldi Arch Chest Dis* 2004; 61: 140–147.
49. Borson S, McDonald GJ, Gayle T, *et al.* Improvement in mood, physical symptoms, and function with nortriptyline for depression in patients with chronic obstructive pulmonary disease. *Psychosomatics* 1992; 33: 190–201.
50. Griffiths TL, Burr ML, Campbell IA, *et al.* Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: a randomised controlled trial. *Lancet* 2000; 355: 362–368.
51. Paz-Díaz H, Montes de Oca M, López JM, *et al.* Pulmonary rehabilitation improves depression, anxiety, dyspnea and health status in patients with COPD. *Am J Phys Med Rehabil* 2007; 86: 30–36.
52. González-Roz A, Gaalema DE, Pericot-Valverde I, *et al.* A systematic review of the diagnostic accuracy of depression questionnaires for cardiac populations: implications for cardiac rehabilitation. *J Cardiopulm Rehabil Prev* 2019; 39: 354–364.
53. Osman A, Barrios FX, Gutierrez PM, *et al.* Psychometric properties of the Beck Depression Inventory-II in nonclinical adolescent samples. *J Clin Psychol* 2008; 64: 83–102.