

## ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

# Characteristics of chronic obstructive pulmonary disease patients with depressive disorder

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The aim of this study is to establish the most important characteristics of COPD patients who have depressive disorder.

**Methods** Eighty-nine COPD patients and 65 demographically-matched referents without COPD were included. All the patients underwent lung function examination, and gas exchange, nutritional status, dyspnoea level by the modified Medical Research Council (mMRC) scale and exercise tolerance were also assessed, as well as depressive disorder by Hospital Anxiety and Depression Scale (HADS) and Geriatrics Depression Scale (GDS) and quality of life by St. George's Respiratory Questionnaire (SGRQ).**Results** Depressive disorder has been found in 30.3% of COPD patients evaluated by HADS and 25.3% of COPD patients evaluated by GDS. When COPD subjects were stratified by forced expiratory volume in 1 second (FEV<sub>1</sub>) categorization, all subgroups were more likely to have depressive disorder, according to HADS and GDS, relative to referents with the odds ratio highest (3: 95% confidence interval 1.6–4.9) among those with the FEV<sub>1</sub> < 30%. COPD patients with depressive disorder (HADS) compared to non-depressed patients had (differences in mean values) higher intensity of smoking [6.9 (0.5–10.1)], lower body mass index [-4.9 (-7.2–5.4)], lower value of FEV<sub>1</sub>% [-8.3 (-16.3–1.2)], higher value of total lung capacity (%) [17.8 (2.3–28.4)], higher mMRC score (1.07 (-1–3.0)), and higher SGRQ – giving a total score of 32.9 (24.1–40.3).**Conclusion** Evaluation of depressive disorder should be considered in every patient with COPD, especially in patients with greater degree of airflow limitation and lung hyperinflation, dyspnoea level and malnourished.**Keywords:** COPD; depressive disorder; quality of life**INTRODUCTION**

Chronic obstructive pulmonary disease (COPD) is a severe treatment-resistant pulmonary disease with varying impact on the patient's general physical condition, functioning, and quality of life. It is already known that dyspnoea and poor exercise tolerance are frequently observed in patients with COPD [1]. Aside from dyspnoea, mechanisms responsible for depressive disorder in COPD patients are still not completely known and are probably multifactorial [2]. Influence of aging, smoking and hypoxemia on brain function, most likely contribute to the development of depression. The depressive symptoms in COPD are predominantly irritation, tearfulness, thoughtfulness, anxiety, and too much worry. Therefore, it is difficult to recognize depressive disorders in patients with COPD, because symptoms and signs of depression are incorporated in primary pulmonary disease.

Different questionnaires are used to estimate depressive disorder in COPD. However,

these questionnaires are rather screening than diagnostic tools. In older patients these questionnaires can be less precise, because they contain items exploring somatic state in which patients can answer positive because of aging process, and not for depression existence, which can lead to overestimated prevalence of depression in COPD.

The aim of this study was to analyze characteristics of COPD patients who have depressive disorder and to establish potential influence of depression to quality of life in COPD patients.

**METHODS**

This study included 89 patients with COPD who were treated at Pulmonary Clinic at the Clinical Centre of Kragujevac, Serbia, from 2013 to 2015. We aimed to recruit 65 control subjects without COPD, who were matched to COPD subjects by age and sex. The protocol was approved by the institutional ethics committee and informed consent was signed by every



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patient before inclusion into this study. The patients were evaluated in the stable phase of the disease (respiratory symptoms and therapy not changed at least four weeks before the examination).

Patients were excluded if they had any of the conditions where suboptimal lung function results are likely (chest or abdominal pain of any cause, dementia or confusion, etc.) [3], who could not perform the six-minute walking test (6-MWT), if they had a myocardial infarction four months before the beginning of the study, if they had unstable angina pectoris or congestive heart insufficiency (New York Heart Association Functional Classification, classes III and IV). Evaluation of lung function was performed by spirometry (Master Screen Pneumo, Jaeger, Würzburg, Germany) and body plethysmography (Master Screen Body, Jaeger). Measurements followed the criteria of the European Respiratory Society and the American Thoracic Society for spirometric standardization and procedures [3]. Forced expiratory volume in 1 second ( $FEV_1$ ) was expressed as a percentage of predicted values from the European Community for Steel and Coal [4]. The patients were divided according to lung function into three groups: Group I with  $FEV_1 \geq 50\%$ , Group II with  $30\% \leq FEV_1 < 50\%$ , and Group III with  $FEV_1 < 30\%$  of predicted values. Evaluation of gas exchange was done by arterial gas analyzer (GEM Premier 3000, Instrumentation Laboratory Company, Bedford, MA, USA). Dyspnoea level was determined by the Modified Medical Research Council (mMRC) scale. Exercise tolerance was determined by the 6-MWT. Nutritional status was estimated by the body mass index (BMI). For evaluation of depressive disorder we used Hospital Anxiety and Depression Scale (HADS) and Geriatrics Depression Score (GDS) [5, 6]. HADS contains seven questions for depression and anxiety, where borderline disorder exists if the score is 8–10, and depressive disorder if probable if the score is  $\geq 11$ . The GDS score 10–19 is graded as mild and 20–30 as serious. For evaluation of quality of life we used St. George’s Respiratory Questionnaire (SGRQ).

In this study we used descriptive statistics – arithmetic means, standard deviations (SD), percentages. For comparison of arithmetic’s means in two independent groups of patients we used the independent t-test, and ANOVA, as appropriate. To compare differences of measured variables in the same patients at the beginning and the end of the study, a paired T-test was used. The correlation between two numeric features was tested by Pearson’s coefficient of correlation. We used multivariate logistic regression to determine the adjusted odds ratio (OR).

**RESULTS**

A total of 89 COPD patients and 65 control subjects without COPD, who were analyzed between 2013 and 2015, satisfied the eligibility criteria for inclusion into the study. By design, patients with and without COPD were similar in age, sex, BMI (Table 1). Among the 89 patients, 27 (30.3%) were found to be depressed according to the HADS score, and 23 (25.8%) by GDS (Table 1). Compared with referents,

**Table 1.** Characteristics of COPD patients and referents

Variables	COPD patients (n = 89)	Referents (n = 65)	p
Age, (yr) mean $\pm$ SD	62.6 $\pm$ 9.1	64.5 $\pm$ 8.4	0.46
Male sex, n (%)	62 (69.6)	46 (70.7)	0.68
Never smoked, n (%)	9 (10.1)	38 (58.4)	
Ex-smokers, n (%)	38 (42.7)	11 (17)	
Current smokers, n (%)	42 (47.2)	16 (24.6)	
BMI mean $\pm$ SD, kg/m <sup>2</sup>	27.6 $\pm$ 7.8	26.4 $\pm$ 6.9	0.59
Depressive symptoms (HADS), n (%)	27 (30.3)	8 (12.3)	< 0.001
Depressive symptoms (GDS), n (%)	23 (25.8)	6 (9.2)	< 0.001

HADS – Hospital Anxiety and Depression Scale; GDS – Geriatrics Depression Scale

**Table 2.** Airflow limitation and depression scores in COPD patients

Depression score	$FEV_1 \geq 50\%$ (n = 27)	$30\% \leq FEV_1 < 50\%$ (n = 35)	$FEV_1 < 30\%$ (n = 27)	p
GDS (mean $\pm$ SD)	9.16 $\pm$ 6.27	14.0 $\pm$ 8.08	15.33 $\pm$ 4.86	0.048
HADS-D (mean $\pm$ SD)	5.58 $\pm$ 4.05	9.75 $\pm$ 5.01	10.26 $\pm$ 4.63	0.028

$FEV_1$  – forced expiratory volume in 1 second

**Table 3.** Prevalence and odds of depression (HADS) in patients with COPD compared to referents

COPD patients	n	Depressive symptoms (HADS-D $\geq$ 11)	OR (95% CI)
$FEV_1 \geq 50\%$	27	5 (18.5%)	1.8 (1.1–3.4)
$30\% \leq FEV_1 < 50\%$	35	9 (25.7%)	2.1 (1.2–3.8)
$FEV_1 < 30\%$	27	13 (48.1%)	3.0 (1.6–4.9)
Referents	65	8 (12.3%)	1.0 (referent)

**Table 4.** Prevalence and odds of depression (GDS) in patients with COPD compared to referents

COPD patients	n	Depressive symptoms (GDS $\geq$ 10)	OR (95% CI)
$FEV_1 \geq 50\%$	27	4 (14.8%)	1.7 (0.9–3.6)
$30\% \leq FEV_1 < 50\%$	35	8 (22.8%)	1.9 (1.1–4.3)
$FEV_1 < 30\%$	27	11 (40.7%)	2.8 (1.5–6.0)
Referents	65	6 (9.2%)	1.0 (referent)

patients with COPD had a greater prevalence of depressive disorder ( $p < 0.001$  for all).

We analyzed the presence of depressive disorder using GDS and HADS in patients with different airflow limitation. The values of both scores differed significantly among the groups (Table 2). In the group with  $FEV_1 < 30\%$  we observed the highest average values for both scores. In this group the mean HADS depression score was 10.2 (SD 4.6) and GDS score was 15.3 (SD 4.8) (Table 2).

In addition, when COPD subjects were stratified by  $FEV_1$  categorization, all subgroups were more likely to have depressive disorder, according to HADS, relative to referents, with the OR highest (3.0, 95% CI 1.6–4.9) among those with the  $FEV_1 < 30\%$  (Table 3). Similar results were obtained in the group with the  $FEV_1 < 30\%$  using GDS (OR 2.8, 95% CI 1.5–6.0) (Table 4). The results are from multivariate logistic regression adjusted for age, sex, body mass index, and smoking status (Table 3 and 4).

We divided the COPD patients into two groups based on HADS depression score. Table 5 shows that depressed

**Table 5.** HADS scores and COPD patient characteristics

Subject characteristics	Nondepressive disorder (HADS ≤ 10) n = 62	Depressive disorder (HADS ≥ 11) (n = 27)	Difference* in means or proportions (95% CI)
Age, yr (mean ± SD)	64.1 ± 8.1	63.2 ± 9.2	-0.8 (-0.5–4.1)
BMI (kg/m <sup>2</sup> ), (mean ± SD)	26.2 ± 4.3	21.3 ± 3.8	-4.9 (-7.2–5.4)†
Cumulative smoking, pack-years (mean ± SD)	30.2 ± 8.4	37.1 ± 9.6	6.9 (0.5–10.1)
FEV <sub>1</sub> , % of predicted value (mean ± SD)	42.5 ± 10.1	34.2 ± 7.4	-8.3 (-16.3–1.2)†
TLC, % of predicted value (mean ± SD)	101.2 ± 15.4	118.1 ± 19.6	17.8 (2.3–28.4)†
PaO <sub>2</sub> (Kpa), (mean ± SD)	8.5 ± 2.2	8.1 ± 1.9	-0.4 (-0.8–1.2)
mMRC, (mean ± SD)	1 ± 1	2.07 ± 0.75	1.07 (-1–3)†
6MWT (m), (mean ± SD)	402 ± 40.1	346.2 ± 59.6	-56 (-124–26)†
SGRQ total and subscore (mean ± SD)			
SGRQ total score	43.3 ± 16.7	76.6 ± 10.5	32.9 (24.1–40.3)†
SGRQ symptom	36.2 ± 9.4	69.4 ± 7.3	33.2 (25.3–38.9)†
SGRQ activity	49.8 ± 11.5	81.7 ± 8.4	32.4 (23.9–39.6)†
SGRQ impact	38.3 ± 18.9	78.9 ± 10.4	40.6 (21.7–47.3)†
Long-term oxygen therapy, n (%)	8 (12.9%)	6 (22.2%)	9.3% (2.1–11.5)†

\*Differences (95% CI) in mean values (for continuous variables) and in proportions (for categorical variables) between patients with and without psychological disorders;

†p-value < 0.05; unpaired two-tailed t-test was used for continuous variables (compare two means);  $\chi^2$ -test was used for categorical variables (compare percentages)

patients with depressive disorder had lower FEV<sub>1</sub>, higher TLC expressed in percentage of predicted values, lower BMI, had more severe dyspnea and a shorter 6-MWT compared to non-depressed patients. Finally, they had worse HRQL (higher SGRQ total score and all subscores) compared to COPD patients without depressive disorder (Table 5).

## DISCUSSION

The main finding of this study is that depressive disorder identified in patients with stable COPD was significantly associated with lower FEV<sub>1</sub>, higher TLC expressed in percentage of predicted values, lower BMI, more severe dyspnea, shorter 6-MWT and worse HRQL. Compared with referents, the patients with COPD had greater prevalence of depressive disorder. In the group with FEV<sub>1</sub> < 30% we observed the highest average values for both scores for assessment of depression. When COPD subjects were stratified by FEV<sub>1</sub> categorization, all the subgroups were more likely to have depression relative to referents adjusted for age, sex, body-mass index, and smoking status.

In our study, the incidence of depressive disorder in COPD patients was 30.3% according to HADS. Data from clinical research show that in clinically stable patients with COPD, prevalence of depression which requires medical treatment varies in the 10–57% range [7, 8]. Such large difference between depression frequencies in patients with COPD can be explained by differences in size of examined population, especially the difference between methodology and instruments and borderline scores used for depression evaluation. We showed a higher prevalence of depressive disorder in COPD patients, according to HADS, compared to the control group, although there were no significant differences in age between the groups. The questionnaires for the assessment of depression in older people may be less accurate because they contain somatic compartments

which can exist as part of the aging process, which may overestimate the prevalence of depression. Geriatric Depression Scale is specifically designed to overcome these limitations. Using this score, we have also found a higher frequency of depressive disorder (25.8%) compared to the control group, which could indicate that depression is not a consequence of age but of COPD itself.

Smoking increases the risk and severity of COPD, makes daily activities effortful and stressful, and increases the risk of depression in patients with COPD [9]. Smoking and depression have a bidirectional interaction. Depressed individuals are more likely to smoke, display higher risk to commence smoking, and find smoking cessation more difficult. Conversely, smokers are more likely to be depressed, which could be caused by the activation of nicotinic acetylcholine receptors, or direct inflammatory effects of smoking [10]. When COPD subjects in our study were stratified by FEV<sub>1</sub> categorization, all subgroups of COPD patients were more likely to have depressive disorder relative to referents adjusted for smoking status. In a study conducted by Negi et al. [11], there is no statistically significant relationship between the occurrence of depression and smoking status in COPD patients.

We found the highest frequency and scores for depression evaluation in COPD patients who had severe airflow limitation. Explanation for significant depressive disorder in more advanced stages in COPD can be expressive dyspnoea, decreased physical activity, worse exercise tolerance, frequent exacerbations which can lead to further physical activity decrease, social isolation, fear, and depression [12]. In a study by Tse et al [13], only the exacerbation frequencies in prior year and dyspnea level remained significant independent predictors for depression in COPD patients. This study has shown that the COPD phenotype of frequent exacerbator represents a significant independent predictor for depression in COPD patients.

In patients with advanced COPD, respiratory failure is common and treated with long-term oxygen therapy

(LTOT). The influence of LTOT on depression symptoms in patients with COPD is less known. Balbo et al. [14] found that LTOT can decrease movements and social communications in patients with COPD, which can aggravate depression. In our study, the percentage of patients who have used LTOT was significantly higher in the group with depressive disorder (22.2%).

In the present study, group of COPD patients with depressive disorder had lower average value of BMI compared to non-depressed COPD patients. Malnutrition shows to be connected with muscle mass loss, leads to worse exercise tolerance, and possible social isolation and depressive disorders. Study by Negi et al. [11] showed that the incidence of depressive disorder is associated with lower BMI. On the other hand, Ghoddusi et al. [15] had shown that higher depression score according to HADS is connected with higher BMI in patients with COPD. It is considered that several factors contribute to psychiatric disorders in obese patients, such as social status, degree of obesity and negative perception about own body.

We found that depressed COPD patients had more severe dyspnea compared to non-depressed patients. The cause and relationship between psychological factors and dyspnea is, however, unclear. There are indications that dyspnea may induce psychiatric disorders while other studies indicate that psychological illnesses intensify with the subjective sensation of dyspnea [16].

In our study, depressed COPD patients, according to HADS, tolerated physical effort significantly worse compared to non-depressed ones. Kim et al. [17] found that depression had greater prognostic significance than FEV<sub>1</sub> value on the level of decrease of physical activity in patients with COPD.

It is considered that depressive symptoms are correlated with psychological, physical, and social functioning which determines the quality of life [18]. We have found significant worsening in every area of the quality of life in depressed COPD patients and the highest score was noted in the area connected with physical activities (SGRQ-subscore

activity). Depressive symptoms, controlling for COPD severity as well as sociodemographics and comorbidities, were strongly associated with worse respiratory-specific quality of life and worse overall physical quality of life, as reported by Omachi et al. [18]. In a study by Blakemore et al. [19], depression predicts the quality of life in COPD patients, but this longitudinal analysis did not show the cause and effective relationships between depression and future quality of life.

There is evidence that treating depression in COPD patients improves the quality of life [20]. Although this might include antidepressive pharmacotherapy, interventions such as pulmonary rehabilitation, which often includes psychosocial support, may also improve the mood and reduce depressive symptoms. Because of the strong association between depressive symptoms and the quality of life, further studies regarding effective methods of treating depression in COPD appear clearly warranted.

Several study limitations must be considered. There were significantly more smokers in the group with COPD compared to the control group. The study did not consider the impact of comorbidity in patients with COPD in the development of depressive disorder.

## CONCLUSION

Depressive disorder is very common in COPD patients. It is not easy to diagnose depressive disorder in COPD patients because of the overlapping symptoms between COPD and depression. However, the seven-item HADS depression subscale and GDS appear to be useful screening tools. Although the respiratory disorder is the dominant somatic problem, emotional response on COPD significantly correlates to poor quality of life. Evaluation of depressive disorder should be considered in every patient with COPD, especially in patients with greater degree of airflow limitation and lung hyperinflation, dyspnoea level, and malnourished patients.

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## Карактеристике болесника са хроничном опструктивном болешћу плућа и депресивним поремећајем

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### САЖЕТАК

**Увод/Циљ** Порекло депресивног поремећаја код болесника са хроничном опструктивном болешћу плућа (ХОБП) још увек није потпуно познато и вероватно је узроковано различитим факторима.

Циљ ове студије је да се утврде најважније карактеристике болесника са ХОБП који имају депресивни поремећај.

**Метод** У студију је укључено 89 болесника са ХОБП и 65 особа без ХОБП сличне старосне доби, као контролна група. Код свих са ХОБП урађено је испитивање плућне функције, проценен нутритивни статус, степен диспное помоћу скале *mMRC*, постојање депресивног поремећаја помоћу Болничке скале за процену анксиозности и депресије (БСАД) и Геријатријске скале за процену депресије (ГСД). Квалитет живота је проценен помоћу респираторног упитника болнице „Свети Ђорђе“ (РУСЋ).

**Резултати** Депресивни поремећај је имало 30,3% болесника са ХОБП на основу БСАД и 25,3% болесника на основу ГСД. Када смо болеснике са ХОБП поделили према тежини на

основу вредности форсираног експираторног волумена у првој секунди (ФЕВ<sub>1</sub>), ризик за развој депресивног поремећаја, на основу БСАД и ГСД, био је значајно већи у свим групама са ХОБП у односу на контролну групу. Највећи ризик је био у групи са ФЕВ<sub>1</sub> < 30% (*OR* 3,0; *CI* 95%; 1,6–4,9). Болесници са ХОБП са депресивним поремећајем (БСАД) имали су у односу на остале болеснике са ХОБП (разлика у средњим вредностима) значајно већи интензитет пушења (6,9 (0,5–10,1)), мањи индекс телесне масе (-4,9 (-7,2–5,4)), мањи ФЕВ<sub>1</sub>% (-8,3 (-16,3–1,2)), већи тотални плућни капацитет (%) (17,8 (2,3–28,4)), већи *mMRC* скор (1,07 (-1–3,0)) и укупни скор РУСЋ 32,9 (24,1–40,3).

**Закључак** Процену депресивног поремећаја треба урадити код свих болесника са ХОБП, а посебно код оних са тежом бронхопструкцијом и хиперинфлацијом плућа, већим степеном диспное и неухрањених.

**Кључне речи:** ХОБП; депресивни поремећај; квалитет живота