Relationship between depression with FEV1 percent predicted and BODE index in chronic obstructive pulmonary disease

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Abstract. WHO reported more than 3 million people die from COPD in 2012 and are expected to rank third after cardiovascular and cancer diseases in the future. Recent studies reported the prevalence of depression in COPD patients was higher than in control group. So, it’s important for clinicians to understand the relationship of depression symptoms with clinical aspects of COPD. For determining the association of depression symptoms with lung function and BODE index in patients with stable COPD, a cross-sectional study was in 98 stable COPD outpatients from January to June 2017. Data were analyzed using Independent t-test, Mann-Whitney test, and Spearman’s rank correlation. COPD patients with depression had higher mMRC scores, and lower FEV₁ percent predicted, and then 6-Minutes Walk Test compared to those without depression. There was a moderate strength of correlation (r=-0.43) between depression symptoms and FEV₁ percent predicted, and strong correlation (r=0.614) between depression symptoms and BODE index. It indicates that BODE index is more accurate to describe symptoms of depression in COPD patients.

1. Introduction

According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), Chronic Obstructive Lung Disease (COPD) is a preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation due to non-reversible airway and alveoli abnormalities. The airway and alveolar abnormalities are progressive and usually result from inhalation of harmful particles or gases.[1]

Data from the World Health Organization (WHO) shows more than 3 million people died from COPD in 2012 and this describes 6% of deaths worldwide. At this time, COPD is ranked 4th as the cause of death worldwide and is intended to rank third after cardiovascular disease and cancer in the future.[1,2] Based on data from Riset Kesehatan Dasar 2013 (Basic Health Research), the prevalence of COPD in Indonesia is 3.7%. The prevalence rate of this disease increases with age and is higher in men (4.2%) than women (3.3%).[3] In the United States, data from 2004 to 2011 shows an overall COPD prevalence of 4.18% in adult and working population (40-70 years of age), with a prevalence in
men 3.07% and women 5.4%.[4] Whereas the prevalence of COPD in Asia Pacific countries in 2012 is around at 6.2% with the highest prevalence are in Taiwan (9.5%) and Vietnam (9.4%).[5]

COPD has a negative effect on the quality of life, especially on the rate of the daily physical activity.[6,7,8,9] The persistent dyspnea that causes the restriction in daily physical activity will lead to trigger the emergence of depression symptoms and social isolation.[10,11] It is supported by the results of several studies showed a higher prevalence of depression in COPD patients compared with control groups.[12,13,14] Symptoms of depression in COPD patients can also make a clinical decline of dyspnea and number of exacerbated attacks.[15,16] However, studies about the association between depression symptoms and the clinical components of COPD (degree of airway obstruction, dyspnea symptoms, the capacity for physical activity, BODE index) havenot been in Indonesia.[17] Therefore, researchers want to explore the relationship of depression symptoms with the degree of airway obstruction, dyspnea symptoms, the capacity of physical activity, and BODE index in COPD patients in Haji Adam Malik General Hospital Medan.

2. Methods

It is a non-experimental and cross-sectional study conducted from January to June 2017. Samples were all population of COPD outpatients at Asthma/COPD clinic H. Adam Malik General Hospital Medan. Inclusion criteria were COPD patients diagnosed based on GOLD criteria, the patient's physical and clinical condition was stable, and received information and gave agreement to participate voluntarily (informed consent). Exclusion criteria were a condition of cognitive impairment caused by a variety of disease (dementia), unable to walk/use walking aids, and unwilling to take part in the study.

Personal history, vital sign measurement (blood pressure, pulse and respiratory rate in 1 minute), height and weight measurements were performed directly by the researchers. Symptoms of depression were evaluated using CES-D questionnaire, consisting of 20 questions with a score per question ranging from 0 to 3 (minimum score 0, maximum score 60). Subjects were determined to have depression symptoms if CES-D score ≥ 16. The BODE index is a multidimensional assessment system for determining the severity and predicting mortality risk of COPD patients. There are four parameters assessed: BMI (Body Mass Index), Obstruction (FEV₁ percent predicted), Dyspnea (Modified Medical Research Council (mMRC)), and Exercise Capacity (6 Minutes Walk Test). All subjects completed the mMRC scale to determine the clinical symptoms of dyspnea and activity limitation they experienced. Then the subjects underwent spirometry examination to measure the capacity of lung function (FEV₁ percent predicted, and FVC percent predicted). Next, 6 Minutes Walk Test was performed indoors with a straight path and a hard and flat floor. The track length was 30 meters and marked every 3 meters. Subjects were instructed to walk back and forth on the tracks. Subjects were allowed to decrease walking speed or pause to rest while doing the test (timer keeps running). The test was completed when the 6 minutes time is up, the patient refuses or was unable to continue the test.

Normally distributed data (weight, age, BMI) was compared using Independent t-test, while non-normally distributed data (number of cigarettes per day, duration of smoking, height, mMRC, FEV₁ percent predicted, FVC percent predicted, 6 Minutes Walk Test, BODE Index) was compared using Mann Whitney test. The correlation between CES-D score with FEV₁ percent predicted and BODE index was assessed using Spearman's rank correlation. The p-value < 0.05 was considered significant. Ethical clearance was from the ethics committee of the Faculty of Medicine, University of Sumatera Utara and H. Adam Malik General Hospital (No:74/TGL/KEPK FK USU-RSUP HAM/2017).

3. Results

The subjects were 98 outpatients who regularly visited Asthma/COPD clinic H. Adam Malik general hospital. The majority of subject’s sex were male; 87 people (88.8%). Mean age was 62.35 years. Subjects who experienced depression were 53 people (54.1%).
Table 1. The basic characteristics of research subjects.

| Characteristics                      | n = 98 |
|--------------------------------------|--------|
| Sex, n (%)                           |        |
| Male                                 | 87 (88.8) |
| Female                               | 11 (11.2) |
| Age, mean (SD), year                 | 62.35 (7.39) |
| Smoking history, n (%)               |        |
| Yes                                  | 87 (88.8) |
| No                                   | 11 (11.2) |
| Cigarettes per day, mean (SD)        | 22.64 (13.12) |
| Weight, mean (SD), kg                | 63.67 (12.20) |
| Height, mean (SD), cm                | 162.53 (7.57) |
| BMI, mean (SD), kg/m²                | 24.14 (4.62) |
| Depression symptoms, n (%)           |        |
| Yes                                  | 53 (54.1) |
| No                                   | 45 (45.9) |
| mMRC score, mean (SD)                | 2.03 (1.19) |
| CES-D score, mean (SD)               | 17.3 (9.54) |
| FEV₁ % predicted, mean (SD)          | 41.91 (19.75) |
| FVC % predicted, mean (SD)           | 44.91 (18.17) |
| 6MWT, mean (SD)                      | 280.17 (69.48) |
| BODE index, mean (SD)                | 4.63 (2.42) |

The mean mMRC score in a group with depression symptoms was significantly higher than in the group without depression symptoms. BODE index comparison showed the same result. The comparative analysis also showed there was a significant difference between mMRC score and BODE index between the two study groups. Spirometry test (FEV₁ percent predicted, and FVC percent predicted) and 6 Minutes Walk Test also showed significant differences between two groups, with lower values in the group with depression symptoms (table 2).

Table 2. Comparison of subject characteristics between groups.

|                        | With Depression Symptoms (n=53) | Without Depression Symptoms (n=45) | p     |
|------------------------|---------------------------------|-----------------------------------|-------|
| BMI, mean (SD), kg/m²  | 23.63 (4.71)                    | 24.75 (4.48)                      | 0.234⁹ |
| mMRC score, mean (SD) | 2.53 (0.95)                     | 1.44 (1.18)                       | <0.001⁸ |
| FEV₁ % Predicted, mean (SD) | 33.76 (12.92)                 | 51.51 (22.10)                     | <0.001⁸ |
| FVC% Predicted, mean (SD) | 37.91 (13.02)                  | 53.15 (19.97)                     | <0.001⁸ |
| 6 Minutes Walk Test, mean (SD), m | 235.02 (42.56)             | 333.35 (56.16)                    | <0.001⁸ |
| BODE index, mean (SD)  | 5.96 (1.97)                     | 3.07 (1.91)                       | <0.001⁸ |

a Mann Whitney  
bIndependent t-test

The CES-D score had a moderate negative correlation with FEV₁ percent predicted (p<0.001) with r=-0.43. A negative correlation score indicates that the FEV₁ percent predicted and CES-D score is inversely proportional (Figure 1).
Figure 1. Correlation of CES-D score with FEV$_1$ percent predicted.

The CES-D score had a strong correlation with BODE index value with $r = 0.614$. A positive correlation value indicates that the CES-D score is directly proportional to the BODE index value (Figure 2).

Figure 2. Correlation of CES-D score with BODE index.

4. Discussion
The prevalence of patients having depression symptoms in this study was 54.1%. The prevalence of depression in COPD patients varied from 7% to 80%. [11,14] Bosley et al. found depression in 20% of their subjects, and White et al. reported 32%. [18,19] Both used HADS instruments to assess symptoms of depression. Meanwhile, according to Asuka et al., the prevalence of depression in COPD was 48.6%, Hanania et al. reported 26% and Van Manen et al. reported 25%. [17,20,21] Those three studies used CES-D instruments for screening depression symptoms, similar to this study. The reason for the higher prevalence of depression symptoms in this study may be due to most subjects were elderly (>60 years), never receiving pulmonary rehabilitation therapy, and the low mean of FEV$_1$ percent predicted (<50%) which according to GOLD classification fall into severe obstruction category. [1] The CES-D and HADS instruments have also been shown to estimate a different prevalence of depression within one COPD outpatients. [22]

We found a moderate strength of negative correlation between CES-D score with FEV$_1$ percent predicted ($r$=-0.43). The $r$ value in this study was higher than that of Asuka et al. ($r$=-0.29). [17] It may be due to the sample in Asuka et al. study was taken from COPD patients who have undergone routine
Pulmonary Rehabilitation procedures which from several studies have proven to improve the status of depression and BODE index.[23,24] The correlation coefficient between CES-D score with BODE index in this study was 0.614. It is stronger than the correlation between CES-D score with FEV\textsubscript{1} percent predicted. It is consistent with the study by Funk et al. and Asuka et al. which reported that BODE index was more accurate in demonstrating the prevalence of depression compared with the GOLD classification which based only on FEV\textsubscript{1} percent predicted.[17,25] It suggests that FEV\textsubscript{1} percent predicted is not the only factor associated with the depression symptoms in COPD patients.

## 5. Conclusion
This study showed significant differences in dyspnea symptoms, lung function, physical capacity and disease severity between groups with and without symptoms of depression. The correlation of CES-D score with BODE index was also stronger than the correlation of CES-D score with FEV\textsubscript{1} percent predicted. It shows that FEV\textsubscript{1} percent predicted is not the only factor associated with depression symptoms in COPD patients.

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