

Assessment of Severity and Systemic Involvement in Chronic Obstructive Pulmonary Disease by Bode Index: A Cross-Sectional Study

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ABSTRACT

Introduction: BODE index is a multidimensional grading system which is based on Body mass index, airway obstruction, Dyspnoea scale, and Exercise capacity, has been in use continuously for the evaluation of chronic obstructive pulmonary disease (COPD). It is now been considered as a better indicator than FEV₁ for predicting mortality and severity of the disease. As stated by Global initiative for Chronic Obstructive Lung Disease (GOLD), the BODE index gives sufficient information in predicting mortality from any cause as well as respiratory causes than FEV₁ based staging system. The aim of this study was to find out whether BODE index is a valuable predictor for analyzing severity and systemic involvement in patients of COPD.

Material and Methods: A total of 123 patients were enrolled into the study. 93 patients with symptoms suggestive of COPD were selected as cases and 30 patients were selected as controls. The lung function parameters were assessed by spirometry and they were categorised into mild, moderate and severe COPD cases. All patients underwent detailed clinical examination, electrocardiography, echocardiography and routine investigations with special reference to Hb%, Albumin and C reactive protein levels.

Results: The findings of this study indicated that there was a notable increase in the BODE index in patients who smoked for a longer duration of time. BODE index is an important predictor of hospitalization. In this study there is a positive association between higher BODE index and longer period of hospitalization. This study findings also describes that the distance walked by patients with higher BODE scores is less when compared to cases with controls. It was also found that FEV₁ levels of BODE score in severe COPD group correlates well.

Conclusion: This study concludes that BODE index is a useful tool in assessing the severity of COPD in terms of hospitalization and mortality.

Keywords: Body Mass Index, Hospitalization, COPD, Bode index, FEV₁

towards risk factors such as smoking and the changing age structure of the world's population.¹

The major manifestation of airflow obstruction in COPD is the reduction in forced expiratory volume in 1 second (FEV₁). The risk of death in patients with COPD is often categorised with the help of use of a single physiological variable, which is the forced expiratory volume in one second (FEV). It is a measure of the amount of the air the lungs hold. The FEV₁ (Forced Expiratory Volume) calculates how easily air flows through the lungs. COPD patients have narrowing or inflammation of the airways and this leads to decrease in the FEV₁. If the FEV₁ is decreased to the FVC, a diagnosis of COPD is made. To make out if the decrease is disproportionate, the FEV₁/FVC ratio is calculated. An FEV₁/FVC ratio of <0.70 is considered to be diagnostic of COPD patient.²

The pathological changes are characterized by excess deposition of extracellular matrix, increased thickness of airway walls, mucus hyper secretions resulting in narrowing of airway diameters. Multiple factors such as inflammatory cytokines, proteinases and oxidative stress molecules are considered to bring structural changes leading to airway obstruction. As in other chronic inflammatory conditions, breathing difficulty (shortness of breath especially during physical activities), mucus (sputum) production, wheezing and other includes symptoms include weight loss, muscle wasting, hypoproteinemia and tissue depletion which are commonly seen in COPD patients.³

Patients with COPD are most likely to develop heart diseases, lung cancer and a variety of conditions. Emphysema and chronic bronchitis are the two commonest conditions which lead to the development of COPD. The main cause of COPD is tobacco smoking. And it often occurs in people exposed to fumes from burning fuel for cooking and heating in poorly ventilated homes. The BODE index, for Body-mass index, airflow obstruction, dyspnoea and exercise,

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease state that is not fully reversible and is described by continual airflow limitation which is progressive and induced by an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. It is a major cause of morbidity and mortality which imposes an economic burden worldwide. The prevalence and burden of COPD is intended to increase in the coming decades due to persistent exposure

is a multidimensional scoring system and capacity index used to test patients who have been diagnosed with chronic obstructive pulmonary disease (COPD) and to predict long-term outcomes for them.⁴

Severity in COPD that incorporates four factors known to be independent predictors of survival in this disease: the body mass index (BMI), the degree of airflow obstruction assessed by the FEV₁, the functional dyspnoea assessed by the modified Medical Research Council (mMRC) questionnaire, and the exercise capacity assessed by the 6 min walking distance (6MWD) test.⁵

New developments in the last few decades have led to the improved knowledge of the systemic nature of COPD, which has given rise to the multidimensional classification system that systematically predicts the degree of mortality in individuals with COPD. Nowadays BODE index is considered better indicator than FEV₁ for predicting mortality and severity of COPD. As per Global initiative for Chronic Obstructive Lung Disease (GOLD), the BODE index gives appropriate knowledge in predicting mortality from any cause as well as respiratory causes than FEV₁-based staging system.⁶

It is now recognised that COPD is characterized by low-grade chronic systemic inflammation and therefore it is an important component of COPD. The role of inflammatory cytokines has been widely investigated in the natural history of COPD. Besides inflammation, two other processes are involved in the pathogenesis of COPD- an imbalance between proteases and antiproteases and also an imbalance between oxidants and antioxidants (oxidative stress) in the lungs. This disease puts a higher burden on patients and government health-care strategies as the cost of the treatment and evaluation is directly proportional to the pulmonary and the extra pulmonary components of the disease.⁷

The process of providing treatment to the most needed patients from deficient resources can be extremely difficult in diseases which affect a large proportion of patients. Policy makers need a logical and consistent scoring system that should be designed for such patients to meet the required demand of a diagnostic or a therapeutic treatment under a healthcare budget constraint. BODE index has been used to serve this purpose in patients with chronic obstructive pulmonary disease.⁸ So, the aim of study was to find out the usability of BODE index as a predictor of systemic involvement and severity in patients with COPD.

MATERIAL AND METHODS

This was a prospective, observational study. Informed written consent was taken to carry out the study from the institutional ethical committee before enrolment of patients. A total of 130 patients with symptoms suggestive of COPD who attended the Department of Respiratory Medicine out of which 123 patients were chosen as cases and were enrolled into the study. The patients with the following diagnostic criteria (according to the GOLD guidelines) were defined as having patients with COPD:

1. The formation of cough and sputum production for at

least 3 months in each of the two consecutive years.

2. Exertion dyspnoea.
3. Physical examination showing:
 - Signs of airflow limitation like prolonged expiration and expiratory wheeze which is not fully reversible.
 - Signs of hyperinflation.
 - Spirometry showing post bronchodilator FEV₁/FVC ratio < 0.70.

For each enrolled subject, detailed history of smoking, personal and family medical histories were obtained. On the day of enrolment, height and weight were measured two times during the examination. Weight was measured to the nearest 100 grams with bare foot. Height was measured with the help of stadiometer to the nearest mm. Body mass index (BMI) was calculated by the formula.

$$\text{BMI} = \frac{\text{Weight in Kgs}}{\text{Height in m}^2}$$

The inclusion criteria were taken as: All male patients who were smokers aged between 40-70 years suffering from COPD. Diagnosis of COPD consistent with recommendations of GOLD, a stable clinical state / Patient's not on oxygen therapy, acceptable performance of spirometry as recommended by ATS FEV₁/FVC ratio < 70%, chest radiograph PA showing no evidence of acute infection or any other pulmonary. The exclusion criteria for the study was taken as: Females were not included in the study, patients with any other concurrent (or past) pulmonary or systemic disease (bronchial asthma, ILD, active or inactive pulmonary TB), lactating and pregnant females, any active neurological, rheumatologic or peripheral vascular disease, patients with elevated systolic blood pressure >180mmHg and diastolic BP >100mmHg, resting tachycardia > 120 beats/minute, unstable angina, inability to perform spirometry or six min walk test.

GOLD classification

The staging was done as per the GOLD criteria (2010).

Stage I: Mild FEV₁/FVC < 0.70 FEV₁ > 80% Predicted

Stage II: Moderate FEV₁/FVC < 0.70 > 50% FEV₁ < 80% Predicted

Stage III: Severe FEV₁/FVC < 0.70 > 30% FEV₁ < 50% Predicted

Stage IV: Very Severe FEV₁/FVC < 0.70 FEV₁ < 30% predicted or FEV₁ < 50% plus chronic Respiratory failure

FEV₁: Force expiratory volume in one second; FVC: Forced vital capacity

Spirometry was taken with the equipment that met the American Thoracic Society performance criteria. The test was done as per the ATS guidelines after giving salbutamol nebulisation in all cases. Predicted FEV₁ and forced vital capacity (FVC) standardized for ethnicity, height, age and sex were used. FEV₁ and FVC were calculated.

The procedure was repeated on two occasions and the average value was taken. A detailed history of the dyspnoea experienced by the patient was taken. mMRC dyspnoea scale was used to score the patients dyspnoea. Six-minute walk test was performed according to the ATS guidelines of 2002, twice with a gap of 30 minutes rest in between and the

average was taken. Patients were asked to walk on a level ground for maximum possible distance within duration of 6 minutes. Periods of rest taken were also given in the 6 minutes test period.

A detailed history related to admissions in the hospital in past two years related to COPD was recorded. BODE index is calculated from four major components: FEV₁, 6 min walk test, MMRC dyspnoea scale and Body Mass Index. The patients received points ranging from 0 (lowest value) to 3 (maximal value). The points for each variable were added, so that the BODE index ranged from 0 to 10 points in each patient as per the table.⁹

BODE Score	0	1	2	3
FEV ₁	>65%	50-64%	36-49%	<35%
6-minute walk test	>350 mtrs.	250-349 mtrs.	150-249 mtrs.	<149 mtrs.
Dyspnoea scale	0-1	2	3	4
BMI	>21 kg/m ²	<21 kg/m ²		

STATISTICAL ANALYSIS

The Statistical software namely SPSS 21.0 was used for the analysis of the data and Microsoft word and Excel have been used to generate inferential tables. Statistical significance was taken when the p value was less than 0.05 with the help

of One-way ANOVA test.

RESULTS

A total of 123 patients including 93 patients with COPD as cases and 30 healthy individuals as controls were enrolled in the study. Among patients with COPD, there were 30 (32.2%) of patients who had mild COPD with a BODE score between 0 - 2. Moderate 31(33.3%) with BODE score of 3 - 5 and severe cases of COPD 32 (34.4%) with BODE score more than or equal to 6.

The average age of participants in the study was 59.62 years (SD deviation-5.423). Among the COPD patients, BODE index was found to increase with age with the mild group having a mean age of 50.13 years (SD- 8.709), moderate group 54.64 years (SD-6.52) and the severe group with 57.35 years as the mean age (SD-9.479). The difference was statistically significant with a p value of 0.005 as shown in Table-1.

The study revealed that the BODE score was significantly associated with the number of pack years of smoking. It was suggestive of the fact that higher duration of smoking was associated with higher BODE index. It was 19.47 pack yrs in mild cases (SD-6.725), 24.341 pack years in moderate (SD-8.901) and 27.979 pack years in severe cases (SD-11.901). The average pack years is 16.46 (SD-7.951). The difference

Group	N	Mean Age (years)	Std. deviation	One-way ANOVA F-Test
Control	30	52.23	5.423	F=12.148 p=0.005 significant
Mild Case	30	50.13	8.709	
Moderate Case	31	54.64	6.52	
Severe Case	32	57.35	9.479	
Total	123	59.62	8.462	

Table-1: Showing age wise distribution of COPD cases and controls

Group	N	Mean Pack (Years)	Std. deviation	One-way ANOVA F-Test
Control	30	21.264	5.041	F= 48.121 p= 0.001
Mild Case	30	19.475	6.725	
Moderate Case	31	24.341	8.901	
Severe Case	32	27.979	11.901	
Total	123	22.342	6.047	

Table-2: Showing association between smoking and COPD cases and controls

Group	N	Mean BMI Kg/m ²	Std. deviation	One-way ANOVA F-Test
Control	30	34.123	4.242	F= 14.131 p= 0.001
Mild Case	30	26.153	3.527	
Moderate Case	31	24.424	3.422	
Severe Case	32	22.476	4.292	
Total	123	32.124		

Table-3: Showing association between Body Mass Index and COPD cases and controls

Group	N	Mean FEV _{1%}	Std. deviation	One-way ANOVA F-Test
Control	30	89.31	7.432	F= -129.47 p= 0.000
Mild Case	30	68.22	4.962	
Moderate Case	31	63.09	6.383	
Severe Case	32	67.59	6.292	
Total	123	71.14		

Table-4: Showing association between (Spirometry) FEV1 and COPD severity among cases and controls

Group	N	Mean 6 min. Walk test (Years)	Std. deviation	One-way ANOVA F-Test
Control	30	548.35	64.232	F= -183.21 p= 0.000
Mild Case	30	439.31	52.341	
Moderate Case	31	345.31	68.310	
Severe Case	32	296.41	54.296	
Total	123			

Table-5: Showing association between 6 minute walk test and COPD severity among cases and controls

Group	N	Mean days	Std. deviation	One-way ANOVA F-Test
Control	30	0	0	F= -78.628 p= 0.000
Mild Case	30	6.401	16.497	
Moderate Case	31	12.462	14.324	
Severe Case	32	19.452	18.979	
Total	123			

Table-6: Showing association between COPD severity and hospital stay among cases and controls

was statistically significant with a p value of 0.000 which has been displayed in Table-2.

The average BMI of the patients in the present study was 32.124 kg/m². The BMI was found to be significantly less in patients with COPD. It was found to be 26.153 kg/m² with SD-3.527 in the mild group, 24.424 kg/m² with SD-3.422 in the moderate group and 22.476 kg/m² with SD-4.292 in the severe group. The difference was statistically significant with a p value of 0.001, as shown in Table-3.

In this study FEV₁ levels of BODE score in severe COPD group correlates well but there is not much of significant difference between mild and moderate groups. The FEV₁ is essential for the diagnosis and quantification of the respiratory impairment resulting from COPD. In addition, the decrease in the FEV₁ score is a good marker of disease progression and mortality. However, the FEV₁ does not adequately reflect all the systemic manifestations of the disease, as concluded from the Table-4.

This study also revealed that the distance walked by patients with higher BODE scores is less when compared to other groups and controls. In mild cases (439.31), moderate cases (345.31) and in severe cases (296.41) as shown in Table-5.

The study results showed that a higher BODE score was associated with a higher incidence of hospital stay due to reasons related to COPD, over the past 2 years. It was found that in the mild study group was 6 days (std. deviation – 16.497), 3.17 days in the moderate group 12 days (std. deviation -14.324), while it was 19 days in the group with severe COPD (std. deviation – 18.979). The difference was statistically significant with a p value of 0.000, which has been displayed in Table-6.

DISCUSSION

COPD is predicted to be one among major threatening disease affecting a large number of populations by the year 2020. In the recent past, it was the requirement to formulate a simple but effective index for assessing the severity of COPD. From the previous studies, it was found that BODE index is an effective method to predict systemic involvement in patients with COPD. Only male patients were included in this study, since COPD is more common among male patients. This

was done to make the study group as consistent as possible by removing the gender related differences in FEV₁, BMI and patient perception of dyspnoea which might create the differences in the index when studied in various patients.^{10,11} In our study, we found that maximum number of patients belong to age group 45 to 65 years which is suggestive of physiological decline in lung function (FEV₁) as the age progresses. So as the age increases, severity of COPD also increases and we can predict the severity of COPD based on higher BODE index and cumulative effect of smoking. This finding is in concordance with the studies conducted by kapil et al and Manik et al.^{12,13}

Results from this study are consistent with other studies, in the association of smoking to BODE index. Studies conducted by Kian Chung et al, Celli et al, and Karoli have found that beyond doubt higher the duration of smoking higher will be the BODE index. The study also revealed that there was significant increase in the BODE index in patients with a higher duration of smoking. The difference was not statistically significant among the control group and those in the mild COPD group. This probably means that the disease could still be reversed with the cessation of smoking.^{14,15,16}

COPD is more commonly present in underweight patients. Mean BMI was found to be lower in severe cases of the disease. Depletion in nutritional status is a frequent finding among patients with disease, in particular to those with advanced disease.¹⁷ The results obtained by the study conducted by Pitta et al demonstrated that the reduced distance walked in 6MW test was the best marker of the inactivity during the daily life of patients with COPD which is similar to the results obtained by the present study.¹⁸

It was also found that as BODE index score increases there is decline in FEV₁ ratio which was found to be statistically significant. In this study BODE index is used to assess the severity of COPD and Categorize COPD cases into mild, moderate and severe cases. Studies done by Celli et al and Kian Chung et al has proved that grouping COPD patients into three groups with BODE scores 0 -2 as Mild COPD group, 3-5 as Moderate and 6 or more as the Severe group correlates well with severity in terms of hospitalization and morbidity.^{14,15} Hence, this study has adopted the same

classification. Moderate and severe patients of COPD have higher risk of exacerbations, which leads to hospitalization and ICU admissions; hence there are increased chances for morbidity and mortality. Similar studies conducted by Kian-chung et al clearly indicated that BODE scoring is superior in assessing risk of hospitalization compared to FEV₁ alone. Studies showed that a single measurement of BODE index could predict mortality and readmissions of COPD patients.^{14,19}

Admission to the hospital and heavy use of health-care resources is a common feature of COPD. A clinical implication of the present study is that the BODE scoring system may prove to be helpful in health-care resource allocation and in guiding therapy for individual patients in the future. This multistage scoring system, which included variables that can be evaluated easily in any office setting, should not be difficult or costly to implement routinely. As the BODE index can provide useful prognostic information of survival and hospitalization, the findings of this study are in support of the efficacy of the BODE index as an assessment tool for COPD patients.²⁰

A clinical significance of the present study is that the BODE scoring system may prove to be beneficial in health-care resource allocation and in guiding therapy for individual patients by dividing patients in respect to severity of COPD in the future. This multistage scoring system, which incorporates variables that can be evaluated easily in any office setting, should not be difficult or costly to implement routinely. The findings of the present study are in support of the usefulness of the BODE index as an assessment tool for COPD patients in providing useful prognostic information of survival and hospitalization.²¹

Some limitations in our study should be addressed. First, this study is a cross-sectional study; longitudinal follow-up studies are required for the better correlation among factors studied. Second, the number of patients taken for the study was less. Third, the type of study was a hospital based and results cannot be extrapolated to the general population. Lastly, as female patients were excluded, this study was limited for application to male population only.

CONCLUSION

It is strongly recommended that calculation of BODE index should be performed at least every 3 months in a COPD patient. This index is a good predictor of COPD severity than FEV₁ alone. Besides, its excellent predictive capacity in regard to outcome, the index is simple to calculate and requires no special equipment. This makes it a practical tool of potentially widespread applicability.

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