



A Study On The Bode Index As A Predictor Of Severity And Systemic Involvement In Patients With Copd

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases. In 2004, Celli et al. created a mortality prediction index, known as the BODE index (Body mass index, Airway Obstruction, Dyspnea and Exercise capacity) which is a multistage scoring system that provides useful prognostic information in patients with COPD [4]. BODE scores greater than 7, 5-6, and less than 5 are associated with a 2-year mortality of 30%, 15%, and 10%, respectively. It has been shown that the BODE index is better than the FEV1 at predicting the risk of death among COPD patients.

Aim Of The Study: This study is conducted to determine whether a higher BODE index in Chronic Obstructive Pulmonary Disease correlates with more years of cigarette smoking and also to determine whether a higher BODE index is associated with more days of hospitalization.

Methods: This observational prospective cohort study was conducted at Government Dharmapuri Medical College And Hospital, Dharmapuri, Tamil Nadu, India in the year July 2021- to February 2022 over 8 months on 120 patients. Cases: 90; controls: 30 Spirometry was performed with a piece of equipment that met the American thoracic society performance criteria, in each of the cases on enrollment into the study and 20 minutes following the administration of salbutamol nebulization. To adjust for the height, sex, age, and sex published prediction equations for forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were used. FEV1 and FVC were calculated. The procedure was repeated on 2 occasions and the average value was taken. The BODE index was calculated for each patient using the body mass index, the threshold value of FEV1, the distance walked in 6 min, and the score on the modified Medical Research Council (MMRC) dyspnea scale. The patients received points ranging from 0 (lowest value) to 3 (maximal value). For body mass index the values were 0 (>21) or 1 (<21). The scores for FEV1 were 0 (more than or equal to 65%), 1 (50 – 64%), 2 (36 – 49%), and 3 (less than or equal to 35%). The 6 minute walk test scores were 0 (> 350 ms), 1 (250 – 350 ms), 2 (150 – 249 ms) and 3 (< 150 ms). The MMRC dyspnea class 0 and I were given 0 points, class II – 1 point, class III – 2 points, and class IV – 3 points. The points for each variable were added so that the BODE index ranged from 0 to 10 points in each patient. The BODE score of 0 – 2 was taken as mild COPD. Scores between 3 – 5 were considered a moderate disease and those more than or equal to 6 was considered severe COPD. A standard 12 lead ECG was taken for each of the individual patients. QRS axis was determined by plotting the QRS potentials on a graph with lead I as X-axis and aVF as Y-axis. – 30 to + 90 was considered

as the normal axis, -30° to -90° as the left axis, $+90^{\circ}$ to $+180^{\circ}$ as the right axis, and -90° to $+180^{\circ}$ was considered as the northwest axis.

Results: The average age of participants in the study was 55.71 years. Among the COPD patients, the BODE index was found to increase with age with the mild group having a mean age of 53.47 years, the moderate group 55.00 years, and the severe group with 59.93 years as the mean age. The difference was statistically significant with a P-value of 0.005. The proportion of smokers was higher in the higher BODE index group compared to the lower index group. There was no significant difference between the control group and the lower score group. Thus smoking status had a positive risk correlation with a higher BODE index ($P = 0.000$). On multiple comparisons, the significance between mild and moderate groups was not found to be significant. All other comparisons showed significant differences. The average duration of stay in the moderate study group was 3.17 days while it was 16 days in the group with severe COPD according to the BODE score. Both these values were found to be significant in multiple comparisons to other groups. The values in the other 2 groups were significantly higher (moderate – 12.176 gm/dL and severe 14.869 gm/dL). This was found to be statistically significant at a P-value of 0.05. The QRS axis was found to vary among the different groups studied. The control group had 26 patients with a normal axis and 4 with the left axis. The mild COPD group had 27 patients with normal axis and 5 patients with right axis deviation. Out of 29 patients in the moderately severe COPD group, 20 had normal axis and 9 had right axis deviation. In patients with the highest BODE score, 1 patient had a normal axis, 34 had a right axis deviation, 9 with a left axis deviation, and 3 had northwest axis. This study showed that there was no incidence of pulmonary hypertension in the controls and the group with mild COPD according to BODE scores. In the moderate COPD group, 19 patients did not have pulmonary hypertension while 8 showed mild and 2 patients had severe PHT. However in the severe COPD group, all patients had PHT with 13 patients having mild PHT, 19 having moderate and 7 patients having severe PHT. The marker of systemic inflammation the C reactive protein was found to be highest in the group with the highest BODE scores 105.93 (std. deviation 53.48). it was not significantly different between the control(2.60) and the mild COPD (7.13) groups and in the moderate group, the titer was 33.72. The difference was statistically significant with a P-value of 0.05.

Conclusion: bode index is directly correlated with the duration and intensity of smoking. Thus this study concludes that the bode index is a reliable method to predict hospitalization and the severity of systemic involvement in patients with COPD.

Keywords: COPD, SMOKING, BODE SCORE , ECG

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world. The prevalence and burden of COPD are projected to increase in the coming decades due to continued exposure to COPD risk factors and the changing age structure of the world's population. [1] It is projected to rank fifth in 2020 in the burden of disease caused worldwide, according to a study published by the World Bank/World Health Organization. The disease causes a heavy burden on the global health care resources. The costs involved in the treatment and evaluation are directly proportional to the pulmonary and the extrapulmonary components of the disease 'Chronic

obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible.[2] The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.[3]

The pathogenesis and clinical manifestations of COPD are not restricted to pulmonary inflammation and structural remodeling. Rather, this disorder is associated with clinically significant systemic alterations in biochemistry and organ function. The systemic aspects of COPD include oxidative stress

and altered circulating levels of inflammatory mediators and acute-phase proteins. As in other chronic inflammatory conditions, weight loss, muscle wasting, hypoproteinemia, and tissue depletion are commonly seen in COPD patients. Selective wasting of fat-free mass coupled with impaired respiratory and peripheral muscle function and a reduced capacity for exercise occur in COPD patients. Indeed, weight loss may directly impact poor prognosis in COPD patients. [4]

The severity of COPD is usually assessed based on a single parameter – forced expiratory volume in one second (FEV₁). However, the patients with COPD have systemic manifestations that are not reflected by the FEV₁. Hence a multidimensional grading system that assessed the respiratory and systemic expressions of COPD was designed to predict outcomes in these patients. The four factors that predicted the severity most were the body-mass index (B), the degree of airflow obstruction (O) and dyspnea (D), and exercise capacity (E), measured by the six-minute-walk test. These variables were used to construct the BODE index, a multidimensional 10-point scale in which higher scores indicate a higher risk of death. [5] The process of allocating scarce medical resources to the most needed patients can be extremely difficult in diseases that affect a large number of patients. Decision-makers need a rational and consistent scoring system that is designed to identify those who are maximally in need of a diagnostic or a therapeutic intervention under a healthcare budget constraint. BODE index has been proposed to serve this purpose in patients with chronic obstructive pulmonary disease (COPD). In our study, we analyzed the BODE index as a predictor of hospitalization and severity of systemic involvement. [6].

Methods

This observational prospective cohort study was conducted at Government Dharmapuri Medical College And Hospital, Dharmapuri, Tamil Nadu, India in the year July 2021- to February 2022 over 8 months on 120 patients. Cases: 90; controls: 30 Spirometry was performed with equipment that met the American thoracic society performance criteria, in each of the cases on enrollment into the study and 20 minutes following the administration of salbutamol nebulization. To adjust for the height, sex, age, and sex published prediction equations for

forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) were used. FEV₁ and FVC were calculated. The procedure was repeated on 2 occasions and the average value was taken. The BODE index was calculated for each patient using the body mass index, the threshold value of FEV₁, the distance walked in 6 min, and the score on the modified Medical Research Council (MMRC) dyspnea scale. The patients received points ranging from 0 (lowest value) to 3 (maximal value). For body mass index the values were 0 (>21) or 1 (<21). The scores for FEV₁ were 0 (more than or equal to 65%), 1 (50 – 64%), 2 (36 – 49%), and 3 (less than or equal to 35%). The 6 minute walk test scores were 0 (> 350 ms), 1 (250 – 350 ms), 2 (150 – 249 ms) and 3 (< 150 ms). The MMRC dyspnea class 0 and I were given 0 points, class II – 1 point, class III – 2 points, and class IV – 3 points. The points for each variable were added so that the BODE index ranged from 0 to 10 points in each patient. The BODE score of 0 – 2 was taken as mild COPD. Scores between 3 – 5 were considered a moderate disease and those more than or equal to 6 was considered severe COPD. A standard 12 lead ECG was taken for each of the individual patients. QRS axis was determined by plotting the QRS potentials on a graph with lead I as X-axis and aVF as the Y axis. – 30 to + 90 was considered as the normal axis, – 30° to – 90° as the left axis, +90° to +180° as the right axis, and – 90° to + 180° was considered as the northwest axis. inclusion criteria: Male patients with symptoms suggestive of COPD as cases, Male patients who came for master health check-ups as controls. exclusion criteria: Spirometry proved bronchial asthma defined as an increase in the FEV₁ of more than 15 percent above the base-line value or of 200 ml after the administration of a bronchodilator, recent myocardial infarction < 4months, unstable angina, congestive heart failure (NYHA class III or IV), inability to perform spirometry or 6-minute walk test, Unrelated life-threatening major illness, liver disease, patients with acute exacerbation

Statistical Analysis. The significance of the difference in means between the two groups was analyzed using the one-way ANOVA F-test and the significance of the difference in proportions by the Chi-square test. Multiple comparisons were done by the fisher's least significant difference (LSD) t-test. Statistical significance was taken when the p-value

was less than 0.05. Statistical analysis was carried out using the standard formula. Microsoft excel 2007 and

SPSS (statistical package for social sciences) version 13 software were used for data entry and analysis.

Results :

Table 1: Age-Wise Distribution In Years

Group	N	Mean (yrs)	Std. deviation	One way ANOVA F-test
Control	30	54.70	5.603	F=4.440 P=0.005 significant
Mild (0-2)	32	53.47	7.362	
Moderate (3-5)	29	55.00	8.627	
Severe (>=6)	29	59.93	7.606	
Total	120	55.71	7.679	

Table :1 shows A total of 120 patients including 90 patients with COPD as cases and 30 healthy individuals as controls were enrolled in the study. All the cases and controls were males. Among patients with COPD, there were 32 (35.56%) patients who had mild COPD with a BODE score between 0 – 2. Moderate (BODE score of 3 – 5) and severe COPD (BODE score more than or equal to 6) groups had 29 patients (32.22%) each. The average age of participants in the study was 55.71 years. Among the COPD patients, the BODE index was found to increase with age with the mild group having a mean age of 53.47 years, the moderate group 55.00 years, and the severe group with 59.93 years as the mean age. The difference was statistically significant with a P-value of 0.005.

Table 2: Smoking Status

Groups	Smoker				Total N	Pearson chi-square test
	Yes		No			
	N	%	N	%		
Control	12	40.0	18	60	30	X ² -19.352 P =0.000 significant
Mild	14	43.7	18	56.3	32	
Moderate	19	65.5	10	34.5	29	
Severe	26	89.7	3	10.3	29	
Total	71	59.2	49	40.8	120	

Table:2 The proportion of smokers was higher in the higher BODE index group compared to the lower index group. There was no significant difference between the control group and the lower score group. Thus smoking status had a positive risk correlation with a higher BODE index (P = 0.000).

Table 3: Body Mass Index

Group	N	Mean (kg/m ²)	Std. deviation	Oneway ANOVA F test	Multiple comparison (LSD)
Control	30	24.294	2.544	F = 11.431 P = 0.000 Significant	1Vs2,3,4
Mild	32	22.476	2.455		2Vs1,4
Moderate	29	21.711	2.552		3Vs1,4
Severe	29	20.260	3.212		4Vs1,2,3 P = 0.05
Total	120	22.210	3.035		

Table :3 The average BMI of the patients in our study was 22.21 kg/m². The control group had a BMI of 24.294 kg/m² with a standard deviation of 2.544. The BMI was found to be significantly lower in patients with COPD. It was 22.476 kg/m² (standard deviation –2.455) in the mild group, 21.711 (std. deviation – 2.552) in the moderate group, and 20.260 (std. deviation – 3.212) in the severe group. On multiple comparisons, the significance between mild and moderate groups was not found to be significant. All other comparisons showed significant differences.

Table 4: Duration of hospital stay over last 2 years (days)

Group	N	Mean (days)	Std. deviation	Oneway ANOVA F test	Multiple comparison (LSD)
Control	30	0.07	0.365	F = 75.340 P = 0.000 Significant	1Vs3,4
Mild	32	0.13	0.492		2Vs3,4
Moderate	29	3.17	2.929		3Vs1,2,4
Severe	29	16.00	9.177		4Vs1,2,3 P = 0.05
Total	120	4.68	8.041		

Table:4The 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. The control group and the mild COPD group did not have any significant hospital admission during the past 2 years. The average duration of stay in the moderate study group was 3.17 days while it was 16 days in the group with severe COPD according to the BODE score. Both these values were found to be significant in multiple comparisons to other groups.

Table 5: Hemoglobin concentration in gm/ dL

Group	N	Mean (gm/dL)	Std. deviation	Oneway ANOVA F	Multiple comparison (LSD)

				test	
Control	30	11.040	1.305	F = 50.733 P = 0.000 Significant	1Vs3,4
Mild	32	10.713	1.439		2Vs3,4
Moderate	29	12.176	1.566		3Vs1,2,4
Severe	29	14.869	1.460		4Vs1,2,3 P = 0.05
Total	120	12.153	2.168		

Table:5 Comparing the hemoglobin values in various groups of the study it was found that the mean hemoglobin concentration was lower (10.713 gm/dL) in those patients with COPD compared to controls (11.04 gm/dL). However, this correlation was not found to be significant in multiple comparisons trial. The values in the other 2 groups were significantly higher (moderate – 12.176 gm/dL and severe 14.869 gm/dL). This was found to be statistically significant at a P-value of 0.05.

Table 6: QRS axis in ECG and BODE score

Group	ECG axis								Pearson chi-square test
	Normal		RAD		LAD		North West axis		
	N	%	N	%	N	%	N	%	
Control	26	86.7%	0	0 %	4	13.3%	0	0 %	df= 9.0 P = 0.000 significant
Mild	27	84.4%	0	0 %	5	15.6%	0	0 %	
Moderate	20	69.0%	9	31.0%	0	0 %	0	0 %	
Severe	1	3.4 %	25	86.2%	0	0 %	3	10.3%	
Total	74	61.7%	34	28.3%	9	7.5 %	3	2.5 %	

Table:6 The QRS axis was found to vary among the different groups studied. The control group had 26 patients with a normal axis and 4 with the left axis. The mild COPD group had 27 patients with normal axis and 5 patients with right axis deviation. Out of 29 patients in the moderately severe COPD group, 20 had normal axis and 9 had right axis deviation. In patients with the highest BODE score, 1 patient had a normal axis, 34 had a right axis deviation, 9 with a left axis deviation, and 3 had a northwest axis.

Table 7: Ejection fraction Vs BODE score

Group	N	Mean (%)	Std. deviation	Oneway ANOVA F test	Multiple comparison (LSD)

Control	30	73.43	8.597	F = 85.476 P = 0.000 Significant	1Vs2,3,4 2Vs1,3,4 3Vs1,2,4 4Vs1,2,3 P = 0.000
Mild	32	65.06	3.089		
Moderate	29	56.45	6.500		
Severe	29	47.31	7.177		
Total	120	60.78	11.689		

Table:7 The Ejection fraction varied considerably among various groups in the study. For the control group, the mean EF was 73.43% (std. deviation 8.597). The mean ejection fraction for the other groups was the mild COPD group 65.06% (std. deviation 3.089), the moderate COPD group 56.45% (std. deviation 6.500), and the severe group 47.31% (std. deviation 7.177). The difference in mean ejection fractions was significant between the various groups and was statistically significant with a P-value of 0.000.

Table 8: Pulmonary hypertension and BODE score

Group	pulmonary hypertension										Pearson chi-square test	
	Normal		mild			moderate		severe				
	N	%	N	%	%	N	%	N	%	%		
Control	30	100%	0	0	%	0	0	%	0	0	%	df= 9.0 P = 0.000 significant
Mild	32	100%	0	0	%	0	0	%	0	0	%	
Moderate	19	65.5%	8	27.6%		2	6.9 %		0	0	%	
Severe	0	0 %	5	17.3%		17	58.6%		7	24.1%		
Total	81	67.5%	13	10.8%		19	15.8%		7	5.8 %		

Table:8 This study showed that there was no incidence of pulmonary hypertension in the controls and the group with mild COPD according to BODE scores. In the moderate COPD group, 19 patients did not have pulmonary hypertension while 8 showed mild and 2 patients had severe PHT. However in the severe COPD group, all patients had PHT with 13 patients having mild PHT, 19 having moderate and 7 patients having severe PHT.

Table 9: C reactive protein Vs BODE score

Group	N	Mean	Std. deviation	Oneway ANOVA F test	Multiple comparisons (LSD)
Control	30	2.60	3.410	F = 85.476 P = 0.000 Significant	1Vs3,4 2Vs3,4 3Vs1,2,4 4Vs1,2,3 P = 0.05
Mild	32	7.31	4.993		
Moderate	29	33.72	18.452		

Severe	29	105.93	53.480
Total	120	36.35	49.577

Table:9 The marker of systemic inflammation the C reactive protein was found to be highest in the group with the highest BODE scores 105.93 (std. deviation 53.48). it was not significantly different between the control(2.60) and the mild COPD (7.13) groups and in the moderate group, the titer was 33.72. The difference was statistically significant with a P-value of 0.05

Discussion:

COPD is predicted to be one of the most common killer diseases affecting a large number of individuals by the year 2020. In the recent past, more stress has been given to formulating a simple but effective index for assessing the severity of COPD. Researchers have found that the BODE index would fulfill this necessity. [7]But most of the research has been limited to finding the usefulness of the index in predicting the mortality and hospitalization in patients with COPD. In our study, we tried to evaluate its usefulness in predicting the severity of COPD in terms of hospitalization, systemic involvement, and the level of systemic inflammation. Our research has brought out many results which would have a significant impact on the management of COPD in the future.[8] We included only male patients in our research since COPD is more common among male patients. This was aimed at making the study group as uniform as possible. Such a selection would negate the differences in the BODE index among various patients studied, by removing the gender-related differences in FEV1, BMI, and patient perception of dyspnea. Studies by Corbin RP et.al have proven that grouping COPD patients into three groups with BODE scores of 0 – 2 in the first group, 3 – 5 in the second, and 6 or more in the third group correlates well with severity in terms of hospitalization and mortality. Hence we have accepted the same classification and grouped the above groups as mild, moderate, and severe COPD.[9] A multiple component staging system combining FEV₁, 6-min walking distance, dyspnea scored with the MMRC scale, and PaO₂ was reported to better describe healthcare resource utilization among COPD patients in different geographic areas when compared to international COPD classifications (ATS, British Thoracic Society, and GOLD). The BODE index was also reported to be a much better predictor of the severity of COPD acute

exacerbations than FEV. Our findings of the usefulness of the BODE index in predicting hospitalization for COPD are also supported by the findings of a prospective study of risk factors of hospital readmissions for COPD exacerbation.[10] In that study, a strong association between the usual physical activity and reduced risk of COPD readmission was demonstrated. Moreover, the association did not change when adjusted for FEV₁ or nutritional status. These results are in agreement with the increased risk of COPD hospital admission associated with a limited 6-min walking test reported by another group of investigators. Therefore, it may be speculated that the superior value of the BODE index compared to FEV₁ in predicting hospital admissions for COPD that we have observed, is accounted for by the evaluation of physical performance status among the individual components of the BODE scoring system.[11] Admission to the hospital and heavy use of healthcare resources is a common features of COPD. A clinical implication of the present study is that the BODE scoring system may prove to be helpful in healthcare resource allocation and in guiding therapy for individual patients 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. As the BODE index can provide useful prognostic information on survival and hospitalization, the findings of the present study are in support of the utility of the BODE index as an assessment tool for COPD patients.[12] The parameters that we assessed in this regard were the body mass index, hemoglobin and albumin concentration, ECG axis, ejection fraction, pulmonary hypertension in ECHO, and systemic inflammation as assessed by the CRP value. While considering BMI as a criterion for BODE index scoring, significance is only given to whether it is more, or less than 21. In our study, we found that the BMI progressively declines with severity among

patients with COPD. Emil et al⁴ had described the depletion of free fat mass and thereby a reduction in BMI in patients with COPD. Our finding is further supported by various studies that evaluated the systemic effects of COPD.[13] An imbalance in the continuously ongoing process of protein degradation and replacement can be hypothesized as a mechanism contributing to this wasting condition. Polycythemia has frequently been reported in patients with COPD, owing to the increased erythropoietin production induced by chronic hypoxia. However, in our study, we found that in the group with the mild disease according to BODE scores, the mean hemoglobin concentration was lower than the control group. But as severity increases the mean hemoglobin concentration was found to increase.[14] Though the initial decrease was statistically insignificant, it could be attributed to the nutritional deficiencies that occur due to the disease state. More studies are required to prove this. Janoff A et al have shown that most of the cases (80%) of severe COPD are associated with right axis deviation. [15] We could replicate this in our study population. In our study 61.7 % of individuals had a normal axis, 28.3 % had a right axis deviation, 7.5 % LAD and 2.5 % had a northwest axis. However, in the severe COPD group, 86.3 % of individuals had a right axis and 10.3 % Northwest axis which was significantly higher compared to other groups. This could be attributed to the higher level of deterioration in lung function and pulmonary hypertension in these individuals. The echocardiography findings in our study were generally in agreement with other studies conducted. However, studies have detected only a mild reduction in ejection fraction among patients with COPD. In our study, the reduction in ejection fraction was very significant, especially in the group with severe COPD[16]. Pulmonary hypertension in patients with COPD occurs due to a variety of factors including pulmonary vasoconstriction due to alveolar hypoxia, acidemia, and hypercarbia; compression of pulmonary vessels due to increased lung volume; loss of small vessels due to lung destruction, and increased blood viscosity and cardiac output due to polycythemia secondary to hypoxia[17]. In our study, we found a significant reduction in serum albumin concentrations with an increase in severity of COPD as assessed by the BODE score. Among the markers of systemic inflammation, we concentrated on C

reactive protein since it has been shown to upregulate the production of proinflammatory cytokines and tissue factors by monocytes, increase the uptake of LDL by macrophages and directly induce expression of adhesion molecules by the human endothelial cells. [18] Additionally, CRP may deposit directly into the arterial wall during atherogenesis, interacting with other inflammatory mediators to create foam cells, which serve as building blocks to atherosclerotic plaques. Our study has shown that moderate and severe, but not mild COPD is associated with significant levels of low-grade systemic inflammation. [19,20]

Conclusion

Thus our study concludes that the BODE index is a reliable method to predict hospitalization and the severity of systemic involvement in patients with COPD. Since the assessment of the BODE index requires only a spirometer, which is relatively inexpensive and can easily be made available, this index could be of great practical value in primary health care set up to identify individuals who need further evaluation in a higher center. Thus the BODE index can be used for judicious referral of patients with COPD thereby preventing the wastage of the limited resources available.

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