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Original Research Article

A STUDY OF BODE INDEX ON SEVERITY AND SYSTEMIC INVOLVEMENT IN PATIENTS WITH COPD

Golla Vahini[1], Yerraguntla Shashidhar[2], Raja Mounika[3]

[1]*Assistant Professor, Department of General Medicine, AIIMS Bibinagar, Telangana, India.*
[2&3] *Assistant professor, Department of General Medicine, Nizam's Institute of Medical Sciences, Hyderabad, India.*

A B S T R A C T

Background: In our study we analyzed the BODE index as a predictor of hospitalization and severity of systemic involvement.
Materials and Methods: To evaluate the BODE index as a predictor of hospitalizationand severity of systemic involvement in patients with Chronic Obstructive Pulmonary Disease, a cross sectional study design was chosen. A total of 120 patients who attended our outpatient clinic at the Osmania General Hospital, HYDERABAD were enrolled into the study. Of these, 90 patients with symptoms suggestive of COPD were selected as cases and 30 patients who came for Master health checkup were selected as controls.
Results: BODE index can be used as a reliable index to assessthe severity of chronic obstructive pulmonary disease. BODE index predicts hospitalization due to causesrelated to COPD. Cardiac effects of the disease increases with the severity of disease as assessed by BODE index. BODE index directly correlates with nutritional derangement in patients with COPD as evidenced by the changes in BMI and serum albumin and CRP levels. Intensity of systemic inflammation increases with increase inthe severity of disease. BODE index is directly correlated with the duration and intensity of smoking. Polycythemia is associated with more severe disease.
Conclusion: Thus the BODE index can be used for judicious referral of patients with COPD thereby preventing the wastage of the limited resources available.
Keywords: COPD, BODE Index, Polycythemia, CRP Levels, BMI.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a majorcause 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. It is projected to rank fifth in 2020 in burden of disease caused worldwide, according to a study published by the World Bank/World Health Organization.[1] The disease causes a heavy burden on the global health care resources. The costs involved in the treatment and evaluation is directly proportional to the pulmonary and the extra pulmonary components of the disease.[2]

Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease with some significant extra pulmonary 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'[3]

The pathogenesis and clinical manifestations of COPD are not restricted to pulmonary inflammation and structural remodeling.

The process of allocating scarce medical resources to the most needed patients can be extremely difficult in diseases which 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 health-care budget constraint. BODE index has been proposed to serve this purpose in patients with chronic obstructive pulmonary disease (COPD).[4]

In our study we analyzed the BODE index as a predictor of hospitalization and severity of systemic involvement.

Aims and Objectives

1. To determine whether higher BODE index is associated with more days of hospitalisation and associated with severe disease.
2. To determine the correlation between BODE index and the level of systemic inflammation in patients with COPD.
3. To determine whether higher BODE index is associated with more severe cardiac involvement.
4. To determine whether higher BODE index correlates with poor nutritional status.
5. To determine whether higher BODE index in chronic obstructive pulmonary disease correlates with more years of cigarette smoking and associated with severe disease.

MATERIAL AND METHODS

Setting
Institute of internal medicine Osmania Medical college and Osmania General hospital, HYDERABAD–500095

INSTITUTIONAL ETHICS COMMITTEE APPROVAL Obtained

Study Design
To evaluate the BODE index as a predictor of hospitalization and severity of systemic involvement in patients with Chronic Obstructive Pulmonary Disease, a cross sectional study design was chosen.

Period of Study
july2019 to December 2021

Sample Size
Cases: 90; controls: 30

Inclusion Criteria
1. Patients with symptoms suggestive of COPD as cases
2. Patients who came for master health checkup as controls

Exclusion Criteria
Spirometry proved bronchial asthma defined as an increase in the FEV1of more than 15 percent above the base-line value or of 200 ml after the administration of a bronchodilator
1. Recent myocardial infarction <4 months
2. Unstableangina
3. Congestive heart failure (NYHA class IIIor IV)
4. Inability to perform spirometry or 6-minute walk test
5. Unrelated life threatening major illness
6. Liverdisease
7. Patients with acute exacerbation

Study Protocol
A total of 120 patients who attended our outpatient clinic at the Osmania General Hospital, HYDERABAD were enrolled into the study. Of these, 90 patients with symptoms suggestive of COPD were selected as cases and 30 patients who came for Master health checkup were selected as controls.

The patients with the following diagnostic criteria (according to the GOLD guidelines) were defined ashaving COPD
1. The presence of cough and sputum production for at least 3 months in each of the two consecutive years
2. Exertional dyspnoea
3. Physical examination showing
a. Signs of air flow limitation like prolonged expiration and expiratory wheeze which is not fully reversible;
b. Signs of hyperinflation
4. Spirometry showing postbronchodilator FEV1/FV C ratio <0.70

The present analysis was restricted to male patients only, who met the acceptability and reliability criteria of the American ThoracicSociety to improve the diagnostic accuracy as sex may be a confounding factor in many of the parameters assessed.

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

$$BMI = Weight\ in\ Kgs / (Height\ in\ Ms)^2$$

Spirometry was performed with an 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 nebulisation. 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.

A detailed history of the dyspnea experienced by the patientwas taken. MMRC dyspnea scale was used to score the patients dyspnea. Six-minute walk test was performed twice with a gap of 30 minutes rest in between andthe average was taken. Patients were asked to walk on a level ground for maximum possible distance within a duration of 6 minutes. Periods of rest taken, was also included in the 6minutes test period.

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(>350ms),1(250–350ms),2(150–249ms) and 3 (<150ms). The MMRC dyspnea class 0 and I were

given 0points, class II–1point, class III –2 points and class IV–3 points. The points for each variable were added, so that the BODE index ranged from 0 to10 points in each patient. The BODE score of 0–2 was taken as mild COPD. Scores between 3–5 was considered as moderate disease and those more than or equal to 6 was considered as severe COPD.

MMRC dyspnea scale

Grade 0 – no dyspnea / only on severe exertion Grade 1 – dyspnea on hurrying / walking up a hill

Grade 2 – walks slower than normal at level/ pause while walking on level ground

Grade 3 – stops for breath after walking 100 yards/few mins on level ground

Grade4–too breath less to leave the house/dyspnea on dressing

BODE INDEX

BODE score	0	1	2	3
FEV1	>/=65%	50—64%	36—49%	</=35%
6 min Walk test	>350 ms	250—349ms	150—249 ms	<149 ms
Dyspne A scale	0—1	2	3	4
BMI	> 21 kg/m^2	<21kg/m^2		

Mild COPD0–2

Moderate COPD3–5 Severe COPD>/=6

Statistical Analysis

Statistical analysis was carried out in all the 120 subjects (including 90 COPD patients and 30 controls) after categorizing the variable. Baseline data was collected from patients without and with mild, moderate and severe COPD. Ages, body mass index, days of hospitalization, mean hemoglobin concentration, QRS, ejection fraction, pulmonary hypertension, serum albumin concentration, and CRP of all subjects were the parameters analyzed.

The significance of difference in means between groups was done by one-way ANOVA TEST and the significance of difference in proportions by the Chi square test. Multiple comparisons were done by fishers 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 2007and SPSS (statistical package for social sciences) version 22.0 software was used for data entry and analysis.

RESULTS

In the present study, the mean age of the cases was 57.74 years with a standard deviation of 5.43 years. Among the COPD patients, mean age was 57.09 years in cases with Mild group, 57.57 years in cases from moderate group and 57.86years in cases from severe group. The difference was found to be statistically not significant. [Table 1]

In the present study, 25.3%, 25.3% and 30.4% of the Male cases belonged to mild, control, severe and moderate group of COPD according to BODE score. 34.1%, 19.6% and 9.7% of female cases belonged to moderate, mild and severe group of COPD according to BODE score. The difference was found to be statistically significant. [Table 2]

In the present study, among the smokers, more smokers had higher BODE index group i.e. 34.2% in severe group and 27.6% in moderate group. Among the non-smokers, more non-smokers had lower BODE index i.e. 38.6% in mild group. The difference between the groups was found to be statistically significant. [Table 3]

In the present study, the mean BMI and Standard deviation of the study group was 23.62 and 3.25 respectively. Mean BMI for the mild group, moderate group and severe group were 25.42, 22.94 and 20.81 respectively and the difference was found to be statistically significant. In multiple comparisons LSD, significant difference was seen with moderate and other groups and severe and other groups. [Table 4]

In the present study, Mean days of hospitalization for the cases were 2.53days. The mean days of hospitalization were 0.38 days for mild group, 2.21 days for moderate group and 7.68 days for severe group and the difference was found to be statistically significant. In multiple comparisons LSD, significant difference was seen with moderate and other groups and severe and other groups. [Table 5]

In the present study, the Mean FEV1 of the cases was 55.38% with a standard deviation of 10.33%. The mean FEV1 for the mild group was 62.32% and similar to control group with 64.30%. The mean FEV1 for the moderate group was 52.86% and was less i.e. 39.93% for the severe group. The difference was found to be statistically significant. In multiple comparisons LSD, significant difference was seen with moderate and other groups and severe and other groups. [Table 6]

In the present study, the mean and standard deviation of the CRP in mg/dl was 32.48 and 36.45. The mean CRP of mild group was 8.14 mg/dl and of control group is 3.53 mg/dl. The mean CRP levels of moderate and severe group were highi.e.34.69 mg/dl and 90.84 gm/dl respectively and the difference was found to be statistically significant. In multiple comparisons LSD, significant difference was seen with moderate and other groups and severe and other groups. [Table 7]

In the present study, among the case with Mild BODE index, 97.1% had normal and 2.9% had mild PAH. Among the case with Moderate BODE index, 71.4% had normal, 25% had mild and 3.6% had moderate PAH. Among the case with Severe BODE index, 46.4% had mild, 17.9% had moderate and 35.7% had severe PAH and the difference was found to be statistically significant. [Table 8]

Table 1: Systolic Blood Pressure (mm of Hg)

Group	Number	Mean Age (years)	Standard deviation	Oneway ANOVA F–test
Control	30	58.53	5.975	
Mildcases	34	57.09	5.600	
Moderate cases	28	57.57	4.864	F=0.383 p=0.727
Severe cases	28	57.86	5.345	
Total	120	57.74	5.435	

Table 2: Distribution of cases by BODE Index and Gender

Group	Male		Female		Total	Pearso n Chi-square
	Number	Percent age	Number	Percentage		
Control	15	19%	15	36.6%	30 (25%)	
Mild cases	20	25.3%	14	34.1%	34 (28.3%)	
Moderat ecases	20	25.3%	8	19.6%	28 (23.3%)	X^2 =9.396 p = 0.024
Severe cases	24	30.4%	4	9.7%	28 (23.3%)	
Total	79	100%	41	100%	120 (100%)	

Table 3: Distribution of cases by BODE Index and Smoking status

Group	Smoker		NonSmoker		Total	Pearson Chi-square
	Number	Percentage	Number	Percentage		
Control	12	15.8%	18	40.9%	30 (25%)	$X^2=$21.787
Mild cases	17	22.4%	17	38.6%	34 (28.3%)	p=0.000
Moderate cases	21	27.6%	7	15.9%	28 (23.3%)	
Severe cases	26	34.2%	2	4.5%	28 (23.3%)	
Total	76	100%	44	100%	120 (100%)	

Table 4: Distribution of cases by BODE Index and BMI

Group	Number	Mean BMI (kg/m^2)	Standard deviation	One-way ANOVA F- test	Multiple comparison (LSD)
Control	30	24.83	3.28		1 vs 2,3,4;p= 0.398
Mild cases	34	25.42	2.88	F = 17.221 p = 0.000	2 vs 1,3,4;p= 0.398
Moderate cases	28	22.94	2.76		3 vs 1,2,4;p= 0.010
Severe cases	28	20.81	1.67		4vs 1,2,3;p= 0.000
Total	120	23.62	3.25		

Table 5: Distribution of cases by BODE Index and days of hospitalization

Group	Number	Mean Days of hospitalizati on	Standard deviation	One-way ANOVA F- test	Multiple comparison (LSD)
Control	30	0.47	0.50		1 vs 2,3,4;p= 0.835
Mild cases	34	0.38	0.49	F = 138.61 p = 0.000	2 vs 1,3,4;p= 0.835
Moderate cases	28	2.21	0.99		3 vs 1,2,4;p= 0.000
Severe cases	28	7.68	3.10		4 vs 1,2,3;p= 0.000
Total	120	2.53	3.34		

Table 6: Distribution of cases by BODE Index and FEVI

Group	Number	Mean FEV1 (%)	Standard deviation	One-way ANOVA F-test	Multiple comparison (LSD)
Control	30	64.30	3.60		1 vs 2,3,4;p= 0.048
Mild cases	34	62.32	3.62	F = 232.23 p = 0.000	2 vs 1,3,4;p= 0.048
Moderate cases	28	52.86	3.24		3 vs 1,2,4;p= 0.000
Severe cases	28	39.93	5.16		4 vs 1,2,3;p= 0.000
Total	120	55.38	10.33		

Table 7: Distribution of cases by BODE Index and CRP in mg/dl

Group	Number	Mean CRP (mg/dl)	Standard deviation	One-way ANOVA F- test	Multiple comparison (LSD)
Control	30	3.53	1.87		1 vs 2,3,4;p= 0.135
Mild cases	34	8.14	3.35	F = 3.315 p = 0.022	2 vs 1,3,4;p= 0.135
Moderate cases	28	34.69	10.20		3 vs 1,2,4;p= 0.000
Severe cases	28	90.84	22.84		4 vs 1,2,3;p= 0.000
Total	120	32.48	36.45		

Table 8: Distribution of cases by BODE Index and Pulmonary Arterial Hypertension (PAH)

| Group | Pulmonary Arterial Hypertension (PAH) | | | | Total | Pearson Chi-square |
	Normal	Mild	Moderate	Severe		
Control	30 (100%)	0	0	0	30 (100%)	X^2=96.422
Mild cases	33 (97.1%)	1 (2.9%)	0	0	34 (100%)	p=0.000
Moderate cases	20 (71.4%)	7 (25%)	1 (3.6%)	0	28 (100%)	
Severe cases	0	13 (46.4%)	5 (17.9%)	10 (35.7%)	28 (100%)	
Total	83 (69.2%)	21 (17.5%)	6 (5%)	10 (8.3%)	120 (100%)	

DISCUSSION

COPD is predicted to be one among the most common diseases affecting a large number of individuals by the year 2020. In the recent past, more stress has been given to formulate a simple but effective index for assessing the severity of COPD. Researchers have found that BODE index would fulfill this necessity. 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 predicating 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 in the management of COPD in the future.

We included both male and female patients in our research. 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 Celli et al,[5] and Kian-Chung et al2has proven that grouping COPD patients in to three groups with BODE scores 0–2 as first group, 3–5 as second and 6 or more as 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. Our study individuals were almost equally distributed in the various groups. 30 controls were also selected.

Kian-chungetal,[2] and Celli et al,[5] has shown in their respective studies that BODE score increases with age. But in our study doesn't show a significant increase with compared to controls. This can be supported from other studies that there is no significant progression with age. This difference is mainly due to the fact that duration of smoking was not proportional to age in those groups like inourstudy.

Results from this study go along with most other studies, in the relationship of smoking status to BODE index. Studies by Kian-chungetal,[2] Celli

etal,[5] and Karoli et al,[6] have all proven beyond doubt that higher duration of smoking is associated with higher BODE index. Our study revealed that smokers have higher BODE index compared to non-smokers. This difference between the groups was found to be statistically significant. This clearly shows that smoking is a significant risk factor for severity of COPD. Our study also revealed that the disease could still be reversed with the cessation of smoking.

A multiple component staging system combining FEV1, 6- min walking distance, dyspnea scored with the MMRC scale, and PaO1was reported to better describe health-care resources utilization among COPD patients in different geographic areas when compared to international COPD classifications (ATS, British Thoracic Society, and GOLD).[7] The BODE index was also reported to be a much better predictor of the severity in COPD acute exacerbations than FEV 2. Our findings of the usefulness of the BODE index in predicting hospitalization for COPD are also supported by the findings of a prospective study,[8] of risk factors of hospital readmissions for COPD exacerbation. 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 FEV1or 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 investigators9. Therefore, it may be speculated that the superior value of the BODE index compared to FEV1in 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. 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 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 of 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.

To our knowledge, this is the first study to show that the BODE staging system predicts the severity of systemic involvement in patients with COPD. The parameters that we assessed to this regard were the body mass index, hemoglobin and albumin concentration, ejection fraction and 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 the patients with COPD. Emil et al,[10] had described the depletion of free fat mass and thereby a reduction in BMI in patients with COPD. Our finding is further supported by other study done by Lowie vanfleteren, Bernd lamprecht, Emielwouters published in ERS journal stated that the presence and severity of COPD is associated with lower BMI.

Among the markers of systemic inflammation, we concentrated on C reactive protein since it has been shown to up regulate the production of pro inflammatory 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. 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. Cirillo et al,[11] showed an increasing CRP value with worsening airflow obstruction. Our study has shown that as the severity of COPD increases, CRP levels also shows an increasing trend. Study done by Sin et al,[12] also revealed similar findings.

CONCLUSION

Thus our study concludes that BODE index is reliable method to predict hopitalisation and the severity of systemic involvement in patients with COPD. Since the assessment of 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 are at need for 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.

Conflict of Interest: None
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