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Original article:

"Study of Bode index as a predictor of severity and systemic involvement in patients with COPD"

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Abstract:

Background and objectives: Chronic obstructive pulmonary disease (COPD) is defined a preventable and treatable disease with some significant extra pulmonary effects. This study emphasizes on the fact that BODE index can be used as a valuable predictor of hospitalization and severity of systemic involvement in patients with COPD.

Materials and Methods: A total of 120 patients were enrolled into the study. 90 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 average age of participants in the study was 56.91yrs.The BODE score was significantly associated with the number of packyears of smoking. It was 5.16 packyears in mild ,6.5 in moderate and 17.1 in severe cases.ECG axis was found to be normal in control and mild groups. While 8 patients in moderate group and 26 patients in severe group had RAD. Ejection fraction was found to decrease with increasing severity of COPD with mild group having61.6%and severe group have 48.96%.

Conclusion: BODE index is reliable method to predict hospitalization 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,. Thus, the BODE index can be used for judicious referral of patients with COPD thereby preventing the wastage of the limited resources available.

Keywords: Bodeindex, COPD, Spirometry

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. 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 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

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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 particals or gases[3].

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, hypo proteinemia and tissue depletion are commonly seen in COPD patients[4]. The severity of COPD is usually assessed that assessed the respiratory and systemic expressions of COPD was designed to predict outcome in these patients[5]. 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.[7,8]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)[6].

Objectives

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

Methodology

Setting :

Department of General Medicine , J.J.M. Medical college and CG hospital, Davangere.

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 for a period of one and half years.

Inclusion criteria :

Patients with symptoms suggestive of COPD as cases

Exclusion criteria :

Spirometry proved bronchial asthma.

- Recent myocardial infarction < 4months
- Unstable angina
- Congestive heart failure (NYHA class III or IV)
- Inability to perform spirometry or 6 minute walk test
- other comorbid illness.
- Patients with acute exacerbation

Study protocol:

A total of 120 patients were enrolled into the study. of these, 90 patients with symptoms suggestive of COPD were selected

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as cases and 30 patients were selected as controls.

The patients with the following diagnostic criteria (according to the GOLD guidelines) were defined as having 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 airflow limitation like prolonged expiration and expiratory wheeze which is not fully reversible;

b. Signs of hyperinflation

4. Spirometry showing post bronchodilator FEV1/FVC ratio < 0.70

For each enrolled subject, detailed history of smoking, personal and family medical histories were obtained. BMI was calculated.

Spirometry was performed with an equipment that met the American thoracic society performance criteria.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 and the average was taken. The BODE index was calculated for each patient using the BMI, the threshold value of FEV1, the distance walked in 6 min, and MMRC score. A standard 12 lead ECG & Echocardiography was performed using 2D echo. Ejection fraction and pulmonary pressure gradient was assessed.

Statistical analysis:

Statistical analysis was carried out in all the 120 subjects after categorizing the variable.

The significance of difference in means between two groups was analyzed using the one way ANOVA F-test and the significance of difference in proportions by the Chi square test. Statistical significance was taken when the p value was less than 0.05.

Results

A total of 120 patients including 90 patients with COPD as cases and 30 healthy individuals as controls were enrolled in the study. Among patients with COPD, there were 31 (34.44%) patients who had Mild COPD (BODE score of 0 – 2). 29 (32.22%) patients had Moderate COPD (BODE score of 3 – 5) and 30 (33.33%) patients had Severe COPD (BODE score more than or equal to 6).

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Table 1: Age wise distribution in years

Group	N	Mean (yrs)	Std. deviation	One way ANOVA F- test
Control	30	51.3	6.513	F=9.137 P=0.005 significant
Mild (0-2)	31	52.3	6.803	
Moderate (3-5)	29	57.82	9.790	
Severe (>/=6)	30	61.63	7.867	
Total	**120**	**56.91**	**9.137**	

Table 2: Smoking status

Groups	Smoker				Total N	Pearson chi square test
	Yes		No			
	N	%	N	%		
Control	14	46.6	16	53.3	30	X^2 -18.892 P =0.000 significant
Mild	16	53.3	15	46.6	30	
Moderate	20	66.6	9	33.3	30	
Severe	25	83.3	5	16.6	30	
Total	**75**	**62.5**	**45**	**37.5**	**120**	

Table 3: Smoking in pack years

Group	N	Mean (pack yrs)	Std. deviation	One way ANOVA F test
Control	30	0.7	0.749	F = 25.81 P = 0.003 Significant
Mild	31	5.16	6.513	
Moderate	29	6.5	3.491	
Severe	30	17.1	9.345	
Total	**120**	**7.36**	**7.915**	

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Table 4: Body Mass index

Group	N	Mean (kg/m^2)	Std. deviation	Oneway ANOVA F test	Multiple comparison
Control	30	23.375	3.692		1Vs2,3,4
Mild	31	22.406	2.692		2Vs1,4
Moderate	29	21.211	3.252	F = 14.229	3Vs1,4
Severe	30	19.37	2.876	P = 0.0304	4Vs1,2,3
Total	**120**	**21.823**	**3.778**	Significant	P = 0.05

Table 5: Duration of hospital stay over last 2 years (days)

Group	N	Mean (days)	Std. deviation	Oneway ANOVA F test	Multiple comparison (LSD)
Control	30	0.133	0.345		
Mild	31	0.2	0.406		1Vs3,4
Moderate	29	4.16	2.614		2Vs3,4
Severe	30	14.16	2.118	F = 56.095	3Vs1,2,4
Total	**120**	**4.66**	**5.987**	P = 0.0260	4Vs1,2,3
				Significant	P = 0.05

Table 6: Hemoglobin concentration in gm/ dL

Group	N	Mean	Std.	Oneway ANOVA F test	Multiple comparison (LSD)
Control	30	12.476	1.446		
Mild	31	12.3	1.48		1Vs3,4
Moderate	29	12.75	1.375	F = 36.675	2Vs3,4

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Severe	30	13.693	1.822	P = 0.0469	3Vs1,2,4
Total	**120**	**12.799**	**1.61**	Significant	4Vs1,2,3

Table 7: QRS axis in ECG and BODE score

Group	**ECG axis**						**Pearson chi-square test**
	Normal		**RAD**		**LAD**		
	N	**%**	**N**	**%**	**N**	**%**	
Control	26	86.6%	0	0 %	4	13.3%	Df=9.0 P=0.001 significant
Mild	25	80.6%	0	0 %	6	19.3%	
Moderate	20	68.9%	8	27.5%	1	3.4 %	
Severe	2	6.6 %	26	86.6%	2	6.6 %	
Total	**73**	**60.83%**	**34**	**28.33%**	**13**	**10.83%**	

The QRS axis was found to vary among the different groups studied. The control group had 26 patients with normal axis and 4 with left axis. Mild COPD group had 25 patients with normal axis and 6 patients with left axis deviation. Out of 29 patients in moderate COPD group 20 had normal axis, 8 had right axis deviation and 1 had left axis. In patients with the highest BODE score (severe COPD group) 2 patients had normal axis, 26 had right axis deviation and 2 had left axis deviation.

Table 8: Ejection fraction Vs BODE score

Group	**N**	**Mean (%)**	**Std. deviation**	**Oneway ANOVA Ftest**	**Multiple comparison (LSD)**
Control	30	64.6	2.485	F = 49.520 P = 0.0374 Significant	1Vs2,3,4 2Vs1,3,4 3Vs1,2,4 4Vs1,2,3 P = 0.000
Mild	31	61.66	4.495		
Moderate	29	57.66	3.623		
Severe	30	48.96	2.965		
Total	120	58.1	6.772		

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The Ejection fraction varied considerably among various groups in the study. For the control group, mean EF was 64.6% (std. deviation 2.485). The mean ejection fraction for the other groups were mild COPD group 61.66% (std. deviation 4.495), the moderate COPD group 57.66% (std. deviation 3.623) and the severe group 48.96% (std. deviation 2.965). The difference of Mean ejection fractions was significant between the various groups was statistically significant with a P value of 0.0374.

Albumin concentration was found to progressively decrease with increase in BODE score. The mean albumin concentrations were 4.31 gm/dL(std. deviation .382) in the control group, 3.93 gm/dL (std. deviation .213) in the mild group, 3.47 gm/dL (std. deviation 0.240) in the moderate group and3.01 gm/dL (std. deviation 0.299) in the severe COPD group. The difference was not significant between the controls and patients with mild COPD. However the difference of the moderate and severe COPD groups with the other groups was significant (P = 0.0408).

The marker of systemic inflammation the C reactive protein was found to be highest in the group with the highest BODE scores 21.08 (std. deviation3.516). it was not significantly different between the control(3.84) and the mild COPD (7.68) groups and in the moderate group the titer was 16.72. The difference was statistically significant with a P value of 0.01.

Discussion

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. 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. Kian-chung et al[2] and Celli et al[5] has shown in their respective studies that BODE score increases with age. This study also shows a significant increase in the severe and moderately severe group compared to controls.

Results from this study go along with most other studies, in the relationship of smoking to BODE index. Studies by Kian-chung et al[2], Celli etal5, and Karoli et al[17] have all proven beyond doubt that higher duration of smoking is associated with higher BODE index. The study 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. The BODE index was also reported to be a much better predictor of the severity in COPD acute exacerbations than FEV_1[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[18] 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 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[9].

While considering BMI as a criteria 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[4] 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[10,11] that evaluated the systemic effects of COPD

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 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. 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. Burch et al[12] and Caird et al[10] have shown that most of the cases (80%) of severe COPD are associated with right axis deviation. We could replicate this in our study population. In our study 60.83 % of individuals had normal axis, 28.3 % had right axis deviation, 10.87 % LAD However in the severe COPD group 86.6 % individuals had right 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.

Arcasoy et al[14] has demonstrated an incidence of pulmonary hypertension of around 16 % in patients with COPD. Stevens et al[15] showed that the proportion of patients with pulmonary hypertension is higher among patients with severe COPD. Our study revealed a total incidence of 32.5 % of PAH among patients with COPD. The proportion was higher in the severe group with 60 % having moderate PAH and 23.3 % having severe PAH. The 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.

Among the markers of systemic inflammation, we concentrated on C- reactive protein. Cirillo et al[19] showed an increasing CRP value with worsening airflow obstruction. Our study has shown that moderate and severe, but not mild COPD is associated with significant levels of low grade systemic inflammation. Study done by Sin et al[16], also revealed similar findings.

Conclusions

BODE index can be used as a reliable index to assess the severity of chronic obstructive pulmonary disease.

Thus our study concludes that BODE index is reliable method to predict hospitalisation 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 a primary health care setup 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 resources.

This makes it a practical tool of potentially widespread applicability.

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