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Evaluation of BODE index as a predictor of Pulmonary Hypertension in COPD patients

Lokendra Dave[1], Vivek Rajoriya[2], T.N.Dubey[3], R.S Meena[4], Swapnil Garde[5], V.K.Sharma[3]

[1]Professor, Dept. of TB-Chest, Gandhi Medical College, Bhopal, India.
[2]Junior Resident, Dept. of Medicine, Gandhi Medical College, Bhopal, India.
[3]Professor, Dept. of Medicine, Gandhi Medical College, Bhopal, India.
[4]Assistant Professor, Dept of Cardiology, Gandhi Medical College, Bhopal, India.
[5]Senior Resident, Dept of Medicine, Gandhi Medical College, Bhopal, India.

ABSTRACT

Background: The severity of COPD is usually assessed on the basis of 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. The present study was undertaken to determine the predictive value of BODE index (Body-mass index (B), the degree of airflow obstruction (O) ,dyspnea (D), and exercise capacity (E) for development of pulmonary hypertension and as a predictor of severity in COPD patients. The original BODE index is a simple multidimensional grading system which is superior to FEV1 alone for prediction of mortality and hospitalization rates among COPD patients. **Methods**: This study was done from January 2013 to December 2014.Total one hundred male patients who attended the chest medicine department, with the symptoms suggestive of COPD were included in this study and the study was done to evaluate the BODE index and correlated with echo-cardigraphic findings suggestive of pulmonary hypertension as a predictor of severity in patients with COPD. **Result**: Among patients with COPD, there were (21%) patients who had mild COPD with a BODE score between 0 – 2, Moderate COPD (BODE score of 3 – 5) were (23%), Severe COPD (BODE score more than or equal to 6) groups had (56%) patients. The study results showed that as the BODE index scores severity increases the incidence of pulmonary hypertension increases as identified by echocardiography RVSP (Right ventricular systolic pressure) findings. The average RVSP was 59.6 in severe COPD patients (BODE index more than 6) 47.2 in moderate severe COPD (BODE index 3-5), while it was less than 36 in mild groups. These values were found to be significant on comparison to other groups. **Conclusion**: BODE index may offer superior and alternative reliable method to predict severity in patients with COPD in terms of pulmonary hypertension and for following up after medications. 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 referral center. Thus, BODE index can be used for judicious referral of patients with COPD thereby preventing the wastage of the limited resources available.

***Keywords*:** BODE index, COPD, Pulmonary Hypertension.

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, 2] The severity of COPD is usually assessed on the basis of 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 has been designed to predict outcome in these patients.[3]

Name & Address of Corresponding Author
Dr. Lokendra Dave.
Proffesor, Dept of TB-Chest,
Gandhi Medical College,
Bhopal, MP, India
E mail: drlokendradave@yahoo.com

BODE index has been proposed to serve this purpose in patients with chronic obstructive pulmonary disease (COPD).[4] The four factors that predicted the severity 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 worse prognosis. COPD is associated with significant extra-pulmonary (systemic) effects among which cardiac manifestations are most common. Cardiovascular disease accounts for approximately 50% of all hospitalization and nearly one third of all deaths, if forced expiratory volume in one second (FEV_1) < 50% of predicted. One of the manifestation is development of pulmonary hypertension. The development of pulmonary hypertension in COPD adversely affects survival and exercise capacity and is associated with an increased risk of severe acute exacerbations. In hemodynamic terms pulmonary artery pressure (PAP) depends upon cardiac output (CO), pulmonary vascular resistance (PVR), and

pulmonary artery wedge pressure (PAWP). Resting PH in COPD results predominantly from an elevated PVR whereas PH during exercise results predominantly from an increase in CO in the face of a relatively "fixed" PVR, that is, there is reduced recruit ability and distensibility of pulmonary vessels.[5] Hyperinflation increases PVR as well as PAWP and PAP particularly during exercise. Traditionally, elevated PVR in COPD has been considered to be the consequence of hypoxic pulmonary vasoconstriction and vascular remodeling, destruction of the pulmonary vascular bed by emphysema, polycythemia, and hyperinflation.

To identify pulmonary hypertension echocardiography is an important noninvasive tool to screen patients. The definition of PH is based on measurement of the mean PAP greater than 25 mmHg. Current guidelines recommend ECHO to estimate PAP.[6] ECHO can provide an estimate of the pulmonary artery systolic pressure (PASP). The most accurate echocardiographic method for estimating (PASP) uses the simplified Bernoulli equation to obtain a systolic trans-valvular pressure gradient.

$DP_{RV\text{-}RA} = 4(V_{TR})^2$

Where V_{TR} is the velocity of the tricuspid regurgitate jet. This figure is added to an estimate of right atrial pressure (RAP) to produce an estimate of RVSP.

PASP » RVSP = $4(V_{TR})^2$ + RAP

The accuracy of this method depends the continuous wave Doppler beam being parallel to the regurgitate jet.[6, 7, 8]

The present study was done with aims and objectives to determine whether higher BODE index correlates with presence of pulmonary hypertension in patients with chronic obstructive pulmonary disease.

MATERIALS AND METHODS

After clearance and permission of institutional ethical committee, a total of 100 COPD patients who attended our outpatient clinic and admitted (January 2013 to December 2014) at Gandhi Medical College & Hamidia Hospital Chest Medicine Department Bhopal were enrolled into the study. The present analysis was restricted to male patients only, to improve the diagnostic accuracy as sex may be a confounding factor in many of the parameters assessed Informed consent from patients was taken.

During selection, patients with chronic lung disease other than COPD, hypertension, any primary cardiac disease, any systemic disease that can cause pulmonary hypertension, and patients who were unable to perform spirometry were excluded from the study.

For each enrolled subject, detailed history of smoking, personal and family medical histories were obtained and patients were subjected to routine investigations, including complete blood count, lipid profile, blood sugar, blood urea, serum creatinine, ECG, chest x-ray, on the day of enrollment, height and weight were measured twice during the examination.

Body mass index (BMI) was calculated by the formula.-BMI = Weight in Kgs / (Height in Ms)^2

Spirometry was performed with an equipment RMS Helios 401 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. The procedure was repeated on 2 occasions and the average value was taken. FEV1 (% predicted) was calculated. A detailed history of the dyspnea experienced by the patient was 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 and the average was taken.

Patients were asked to walk on a level ground for maximum possible distance within duration of 6 minutes. 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 as following.

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 was considered as moderate disease and those more than or equal to 6 was considered as severe COPD.

Transthoracic echocardiographic assessment of pulmonary hypertension was done for all the patients. Echocardiographic evaluations were performed on ultrasound systems Phillips Healthcare HD7-XE Classic model according to the guidelines of the American Society of Echocardiography.

The comprehensive examination included standard 2D echocardiography for anatomic imaging and Doppler echocardiography for assessment of velocities. Doppler measurements were carried out over 3 heart cycles during passive expiration). Images were obtained in left lateral decubitus for parasternal and apical views and supine position for sub-xyphoidal views using 1.5 to 4.0 MHz phased array transducers.

Noninvasive assessment of pulmonary artery systolic pressures (sPAP) was achieved by measurement of right ventricular systolic pressure (RVSP). RVSP was derived from the peak systolic velocity of the tricuspid regurgitation obtained with continuous

wave (CW) Doppler using the modified Bernoulli equation: ΔP=4×Vmax.

Pulmonary hypertension (PH) was defined in this study as sPAP ≥ 45 mmHg.[9, 10]This value was chosen according to the definition of pulmonary hypertension. PH was classified into mild, moderate, and severe category as sPAP 30–50, 50–70,>70 mmHg, respectively (using Chemla formula, mean pulmonary arterial pressure (MPAP) =0.61 PASP + 2 mmHg and putting value of 25–35, 35–45, and>45 mmHg of MPAP for mild, moderate, and severe pulmonary hypertension, respectively). BODE index was calculated and compared with RVSP/sPAP evaluated in these patients.

RESULTS

A total of 100 patients with COPD as cases were enrolled in the study. All the cases were males. Among patients with COPD, there were (21%) patients who had mild COPD with a BODE score between 0 – 2. Moderate COPD (BODE score of 3 – 5) were (23%).While Severe COPD (BODE score more than or equal to 6) groups had (56%) patients.

The study results showed that with higher bode index scores, as the severity increases incidence of pulmonary hypertension increases as identified by echocardiography RVSP findings. The average RVSP was 59.6+/-4.4 in severe COPD patients (BODE index more than 6), 47.2 +/- 5.8 in moderate severe COPD (BODE index 3-5), while it was less than 39.3 +/- 5.1 in mild groups. These values were found to be significant on comparison to other groups [Table 1, Figure 1]. (p<0.001)

DISCUSSION

In the recent past, more stress has been given to formulate a simple but effective index for assessing the severity of COPD. The natural history of COPD usually being one of a progressive downhill course, pH has generally been viewed as a late stage development occurring in patients with severe airways obstruction and a chronic hypoxemic state.

Table 1: Comparison of Body mass index with pulmonary functions.

BODE SCORE	0	1	2	3
FEV 1 (% predicted)	≥ 65%	50 – 64%),	36 – 49%)	≤ 35%).
6 min walk test(meters)	>350 ms	250 – 350 ms	150 – 249 ms	< 150 ms
Score on (MMRC) dyspnea scale	class 0 and I	class II	class III	class IV
Body mass index(kg\m^2)	(>21)	(<21).		

Recent advances in the understanding of PH of idiopathic origin, extension of that knowledge as well as increased understanding of the pulmonary vascular pathology in PH associated with COPD as well as the recognition that it is an important determinant of exercise limitation, dyspnoea and survival, have led to renewed interest into the pathogenesis and therapeutics of this facet of COPD. Further, identification of a subset of patients of COPD who have an unusually severe form of PH as well as the observation that pulmonary vascular changes may occur in smokers even without hypoxemia have provided additional impetus into research in PH associated with COPD.

Researchers have found that BODE index would fulfil 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 this study we tried to evaluate its usefulness in predicting the severity of COPD in terms of development of pulmonary hypertension.

Recently 6 minute walk test has been used to evaluate and stratify performance and prognosis in pulmonary hypertension patients.[11, 12]

Mathai and colleagues[13] retrospectively analyzed data from the Pulmonary Hypertension Response to Tadalafil trial , in which PAH subjects were randomized to tadalafil, a phosphor-diesterase type-5 inhibitor, or placebo and found that an improvement in 6MWT of approximately 33 m is associated with improvement in quality-of-life .and hence used 6MWT for assessment.

More recent data do strongly suggest that the baseline 6MW is predictive of outcome in PAH.[14,15,16] Data from the Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL) and the French Registry demonstrate that the baseline 6MW is predictive of outcome.[14,15] In the REVEAL Registry[14] a baseline 6MW ≥440m was associated with longer survival, whereas a 6MW of <165 m was associated with increased mortality at 1 year. In the French Registry,[15] a greater 6MW was significantly and the

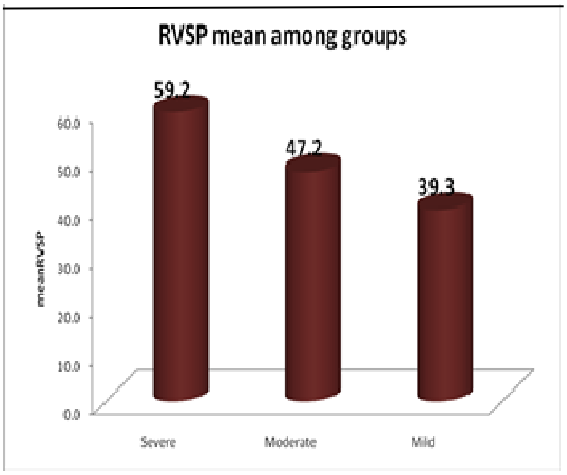

Figure 1: RSVP among groups

positively associated with survival. In addition, multivariable analysis indicated that a greater 6MW, among other factors, was significantly associated with improved survival and was a strong predictor of death in PAH. In addition, in a recent study of follow-up assessments in patients with PAH, the baseline 6MW was an independent predictor of survival.

As BODE index includes 6 minute walk test along with other cardio respiratory and physical indicators(BMI,PFT, dyspnea on MMRC scale,6minute walk test) so it may be considered superior for evaluation and follow up of pulmonary pressures in COPD patients, especially where resources are limited.

While comparing BODE index severity and pulmonary hypertension findings on transthoracic echocardiography (RVSP) it was found that as the BODE score increases incidence of pulmonary hypertension increases. .

Same results were cited in study by C. Siddhuraj, R. Srinivasan,[17] for early diagnosis of pulmonary arterial hypertension using transthoracic Doppler echocardiography in patients with chronic obstructive pulmonary disease where study revealed approximately 58% of patients had more than three exacerbations per year which correlated with severity of BODE index and incidence of PHT was 47% which also showed positive correlation with severity of BODE index.

In this study it is found that BODE score can be used to predict severity in COPD patients in terms of pulmonary hypertension. Though not evaluated in our short term study but the patients can also be followed up after using medications and oxygen therapy whether it can be reversed or not. It can be used where health resources are scarce to predict severity in COPD patient.

A relatively small number of patients were evaluated and this is a hospital based study and may not be representative of the general population. Only male patients were included in this study, 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. Hence, perhaps the results of this study cannot be used in female patients with COPD without further confirmation. Accurate measurements of pulmonary hypertension is done by right heart catheterization and there may be some pit falls in echocardiographic measurements however being noninvasive method it was preferred. Patients who were not able to perform tests (PFT, 6min walk test) could not be evaluated. As a cross-sectional and time bound short study, the present analysis is limited in its ability to elucidate, whether improving the BODE index after treatment, reverses various parameters

CONCLUSION

BODE index may offer as a reliable superior and alternative method to assess the severity of chronic obstructive pulmonary disease as it is correlated with the severity of pulmonary hypertension in COPD patients and may offer help in following up of patients. 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 in need for further evaluation at higher referral center and for better care of these patients.

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