

## ORIGINAL ARTICLE

# Power of BODE Index in Predicting Future Exacerbations of COPD: A Prospective Observational Study in Indian Population

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## Abstract

**Background:** BODE index is a multidimensional measure of survival in chronic obstructive pulmonary disease (COPD). It is composed of body mass index (B), the degree of airflow obstruction (O), dyspnoea (D), and exercise capacity (E). Studies have shown that BODE index can predict future exacerbations, but similar data in Indian population is unavailable. This study was aimed at evaluating the power of BODE index to predict the frequency of exacerbations of COPD in Indian cohort.

**Methods:** We conducted a prospective observational cohort study that included stable COPD subjects aged above 40 years. We assessed the BODE index at baseline and recorded the number of exacerbations at the end of 12 months. Spearman's Rho and Poisson regression model were used to correlate the BODE index with the frequency of exacerbations.

**Results:** We analysed 78 COPD patients. A significant correlation was seen between BODE index at baseline and number of exacerbations at 12 months (Spearman's Rho 0.738). A unit change in BODE index at baseline would have 1.25 times higher number of exacerbations at 12 months (95% CI: 1.17-1.33).

**Conclusions:** BODE index has significant power to predict the frequency of future exacerbations in Indian COPD patients.

## Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive and distressing condition which is a leading cause of death and disability globally.<sup>1</sup> Major presenting symptoms are chronic cough, difficulty in breathing and sputum production.<sup>2</sup> Chronic inflammation resulting in small airway diseases and parenchymal destruction contributes to the airflow restriction and mucociliary dysfunction.<sup>3</sup>

COPD is characterised by periods of exacerbations, an acute worsening of respiratory symptoms beyond normal daily variations which warrant a change in medication. The goals of COPD assessment include determination of airflow levels, its effect on patient's overall health and the risk for future exacerbations and mortality.<sup>4</sup> Forced Expiratory Volume in one second (FEV<sub>1</sub>) is useful in predicting the severity of COPD and exacerbations.<sup>5</sup> The introduction of BODE index by Celli B R et al. has provided better objectivity to the COPD assessment. BODE index is

a multidimensional grading system for COPD which combines four variables, i.e. body mass index (B), airflow obstruction (O), dyspnoea (D) and exercise tolerance (E).<sup>6</sup> It is a simple but excellent predictor of survival and mortality in COPD. Marin JM et al. reported that BODE index can also be useful in predicting the number and severity of exacerbations.<sup>7</sup> However, to the best of our knowledge there are no Indian studies depicting the utility of BODE index in predicting exacerbations COPD. Hence, we have undertaken this study to assess the power of BODE index in predicting the frequency of future exacerbations in Indian population.

## Materials and Methods

### Patients

We conducted this prospective

observational cohort study on COPD patients reported to the Department of Respiratory Medicine during the period September 2012 to March 2014. We obtained the approval of Institutional Ethics Committee and all the patients signed the informed consent. COPD patients aged 40 years or above who were stable, and smoking history greater than 20 pack years participated in the study. The stable COPD was defined as those who had no exacerbations in last three months. Diagnostic criteria for COPD also included spirometry post-bronchodilator forced expiratory volume in one second (FEV<sub>1</sub>)/forced vital capacity <0.7. The spirometry (KoKo, nSpire Health, Inc., UK) was performed and lung volumes were determined according to the American Thoracic Society (ATS) criteria.<sup>8</sup> The patients were receiving optimal medical therapy as per the GOLD recommendations. The exclusion criteria were: 1) uncontrolled comorbidities that could likely cause death within two years; 2) medical history or clinical signs of asthma, with increase in FEV<sub>1</sub> of greater than 12% and 200 mL after 400 mcg of inhaled salbutamol administration; 3) inability to perform spirometry or six-minute walk tests, or both; 4) unstable angina; or 5) congestive heart failure and 6) myocardial infarction within 4 months.

We documented the demographic details, smoking history, symptoms, and the test values in the data collection sheet. We grouped the COPD patients into Stage I, II III and IV based on FEV<sub>1</sub> as per the GOLD guidelines.

The components of BODE index were measured and the score was calculated as the sum of all which ranged from 1 to 10, in accordance with

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**Table 1: Baseline demographic and clinical characteristics**

Baseline characteristics N=78	Mean (SD)
Age	65.55 (7.21)
FEV1 (%)	42.71 (16.66)
6MWD (m)	256.64 (99.60)
mMRC	1.53 (0.62)
BMI (Kg/m <sup>2</sup> )	20.51 (3.12)
BODE Index	4.37 (2.11)

FEV1, forced expiratory volume in 1 second; 6MWD, 6-minute walk distance; mMRC, modified medical research council; BMI, body mass index.

Celli B R et al.<sup>6</sup>**Follow-up**

Patients included in the cohort were followed up at the end of 12 months from the baseline. At the end of twelve months, we recorded the number of exacerbations the patient experienced. We defined exacerbations as events characterised by persistent worsening of baseline symptoms for at least three days leading to treatment modification with antibiotics and systemic corticosteroids.<sup>9,10</sup> We confirmed the episodes of the exacerbations by reviewing the details of health-care resources utilised as per the medical and the hospital records (non-scheduled visit to the hospital/local physician, intensive care, or hospitalisation).

**Statistical analysis**

Mean, and the standard deviation was used to summarise continuous variables whereas categorical variables were summarised using frequency and percentage. All analysis was done using Statistical Package for the Social Sciences (SPSS) version 18. A P-value of <0.05 was considered statistically significant. Spearman's Rho was done to evaluate the correlation between BODE and number of exacerbations. Poisson regression analysis was done using the frequency of exacerbations as the dependent variable and BODE index as the independent variable.

**Results**

A total of 540 patients were screened for inclusion and exclusion criteria in our department out of which 131 patients satisfied the inclusion criteria among whom 99 patients consented to participate in this study. Seven patients failed to perform spirometry, and three subjects could not complete six-minute-walk test. A total of 89 patients were

**Table 2: BODE score at baseline and number of exacerbations in 12 months**

		N	%
BODE index at baseline	0-2	18	23 %
	3-4	21	27%
	5-6	25	32 %
	7-10	14	18 %
Number of Exacerbations in 12 months	1	21	27 %
	2	14	18 %
	3 or more	42	55 %

recruited in the study out of which eight were lost to follow-up, and three patients had missing data of number of exacerbations. Finally, only 78 patients had complete data.

The sample consisted of predominantly males (92%). Mean age was 65.55 ± 7.21 years, baseline post-bronchodilator FEV1 42.71 ± 16.66%, 6MWD 256.64 ± 99.60 meters, mMRC dyspnoea score 1.53 ±.62, BMI 20.51 ± 3.12 Kg/m<sup>2</sup>, and BODE index score 4.37 ± 2.11 (Table 1).

Majority of the patients belonged to 5-6 category in BODE index (32 %) and more than half of the patients (55 %) had three or more exacerbations in the last one year (Table 2). A highly significant correlation was seen between BODE index at baseline and number of exacerbations at 12 months (Spearman's Rho 0.738; P-value<0.001). Poisson regression model was employed to evaluate the power of baseline BODE index to predict the number of exacerbations of COPD at the end of 12 months (Table 3). A unit change in BODE index at baseline had 1.25 times higher number of exacerbations at 12 months (95% CI: 1.17-1.33). Similarly, after adjusting for severity, a unit change in BODE index at baseline had 1.24 times higher number of exacerbations at 12 months (95% CI: 1.14-1.34).

**Discussion**

The present study confirms BODE index has significant power to predict the frequency of exacerbations in Indian COPD patients. The natural course of COPD disease has frequent episodes of exacerbations mainly triggered by repeated infections. The frequency of exacerbations is directly proportional to the severity of COPD. FEV1 is commonly used objective measure to assess the severity of COPD. Several tools have been proposed to counter the limitations

**Table 3: Association of BODE index and number of exacerbations in 12 months**

	p-value	Exacerbation at 12 months		
		RR	95% CI	
			Lower	Upper
BODE at baseline	<0.001	1.25	1.17	1.33
BODE at baseline <sup>†</sup>	<0.001	1.24	1.14	1.34

<sup>†</sup>Adjusted for severity

of this unidimensional evaluation of COPD. Introduction of BODE index was an effort to assess the disease in multiple domains which could reflect the disease status more objectively.<sup>6</sup> Due to its high validity, BODE index was found useful in predicting survival and mortality. BODE Index score is also a valuable predictor of the severity and frequency of future exacerbations including hospitalizations, response to interventions and rehabilitative procedures.<sup>11-13</sup>

We assessed the power of BODE index in predicting the risk of exacerbations in our set of COPD patients. In our study, BODE index at baseline predicted the number of exacerbations at 12 months. Similar result was seen in the many studies.<sup>7,14-17</sup>

To best of our knowledge, our study serves to be the first Indian study to ascertain the usefulness of BODE index in predicting the number of exacerbations at the end of 12 months in COPD patients. Other aspects of BODE index has been studied in an Indian setting. An observational study by Sarkar et al. compared the BODE index to health-related quality of life in Indian COPD patients and reported a strong correlation between both variables.<sup>18</sup> In another study by Khan NA, et al., they observed strong correlation of BODE index and various systemic inflammatory biomarker levels.<sup>19</sup>

The usefulness of BODE index in predicting exacerbations in COPD stresses on the importance of initiation of preventive measures at an early stage and close monitoring of the patients having high scores. As COPD exacerbations lead to hospitalisations, morbidity, emotional distress, and financial burden to the patients, BODE index could indirectly caution the physician for prompt interventions, modifications of therapy and patient surveillance with resultant improvement in the quality of care provided.

Our study has many limitations. Our sample size was small. We could not assess the severity of exacerbations as it was based on a retrospective interview during their follow up visits. Data from hospitals where they got admitted during exacerbations were not available for analysis. Hence, we could not eliminate the potential reporting bias. Low educational status of our patients was another hindrance leading to inadequate documentation and reporting. Each exacerbation of COPD topples the disease stability. The treatment with antibiotics and steroid would have affected the BODE index which could not be addressed in our study. Financial constraints and inadequate primary health care facilities also impede proper monitoring process.<sup>20</sup> The number of female COPD cases was decidedly less in the group studied. Moreover, most patients had COPD severity stages II to IV. There was only one patient in stage I. Hence, we could not collate the results of the present study to milder COPD cases. The status of comorbidities, which could negatively affect patient's overall health and the exacerbations could not be assessed.

In conclusion, our study confirms the power of BODE index in predicting the frequency of exacerbations of COPD and its applicability in Indian population as well. BODE index is a

valuable multidimensional tool for COPD assessment and predictor of frequency of exacerbations in our patients with moderate to severe COPD. Taking into consideration all the confounding factors, long-term evaluation could throw more light on strategic changes needed in the management of COPD patients. Further research is needed to assess the usefulness of BODE index in stage 1 as compared to other stages of COPD.

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