



BODE Index: A Predictor of COPD Exacerbation

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Abstract

Introduction: The severity of COPD (chronic obstructive pulmonary disease) is often graded using parameter like Forced Expiratory Volume (FEV1). The BODE (body mass index, degree of airflow obstruction, dyspnea grading and exercise testing) index is a multi-dimensional tool taking into account body mass index, severity of obstruction, dyspnea grading and 6MWT (six minute walk test) to assess severity of COPD.

Objective: To study BODE index as a predictor of risk of exacerbation for improving COPD outcome.

Materials and Methods: We conducted a prospective study over a period of 2 years, on 60 stable COPD patients by evaluating the body-mass index, spirometry, Modified Medical Research Council (mMRC) dyspnea scale and 6MWT and categorizing into mild, moderate and severe COPD cases on the basis of spirometry and into 4 quartiles on the basis of BODE index value (scores 0-2, 3-4, 5-6 and 7-10). We investigated the prognostic value of BODE quartiles for both the number and severity of exacerbations requiring ambulatory treatment, emergency room visit or hospitalization.

Results: In our study, spirometry showed mild obstruction in 16.7%, moderate obstruction in 26.7%, severe obstruction in 38.3% and very severe obstruction in 18.3% of patients. According to BODE score 52% of patients were quartile 1, 21% quartile 2, 15% quartile 3 and 12% were quartile 4. There was a significant relation between BODE index and COPD severity ($p < 0.001$). In our study, 8.3% patients had no exacerbation; maximum number of exacerbation were 7 observed in 8.3 % patients and 21.7% of patients had 3 exacerbations in 2 years and 16.7% patients had 1 exacerbation in 2 years. It was observed that higher the BODE index; greater is the severity of COPD and more are the number of exacerbations.

Conclusion: BODE index should be calculated in every COPD patients for better prediction of risk of exacerbation, hospitalization and for judicious referral of patients with COPD, thereby preventing the wastage of the limited resources available.

Keywords: BMI, 6MWT, Spirometry.

Background

Chronic obstructive pulmonary disease (COPD) is defined as a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airway and the lung to noxious

particle or gases. Exacerbations and co-morbidities contribute to the overall severity in individual patients⁽¹⁾. Globally, COPD has emerged as the major cause of morbidity and mortality expected to become the 3rd most leading cause of death and the 5th leading cause of loss of 'Disability Adjusted Life Years' (DALYs) as per

projection of the Global Burden of Disease Study (GBDS)⁽²⁾. An exacerbation of COPD is an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day to day variations and leads to a change in medication⁽¹⁾. COPD exacerbations cause hospital admissions, morbidity and mortality, directly leading to the deterioration of health-related quality of life. It's generally believed that exacerbations are important targets for treatments and prevention of disease progression of COPD⁽¹⁾. BODE index : body mass index (B), degree of airflow obstruction (O), dyspnea (D), and exercise capacity (E), measured by six minute walk test; is a validated, simple, multidimensional 10 point grading system predicting the risk of death from any cause and from respiratory causes among patients with COPD⁽⁵⁾. Hence, this study was undertaken to assess the BODE index as a predictor of exacerbations of chronic obstructive pulmonary disease and for improving COPD outcome by predicting patients having higher risk of developing exacerbation. Quartile 1 is defined by a score of 0 to 2, quartile 2 by a score of 3 to 4, quartile 3 by a score of 5 to 6, and quartile 4 by a score of 7 to 10⁽³⁾.

BODE index is useful because it includes one domain that quantifies the degree of pulmonary impairment (FEV1), one that explains the patient (the MMRC dyspnea scale), and two independent domains (the distance walked in six min and the body mass index- BMI) that express the systemic consequences of COPD.

Methods

This was a prospective study involving 60 stable COPD patients conducted at a Tertiary care center over a period of 2 years, started after institutional ethical committee approval.

Already diagnosed and newly diagnosed cases of COPD who meet the GOLD criteria of spirometry diagnosis with a post bronchodilator forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) ratio <70% were included in the study. Asymptomatic patients visiting the

health check-up were also included. Exclusion criteria were patients with diagnosis of bronchial asthma, bronchiectasis, or other chronic lung disorder requiring treatments, interventions or diagnosis. Any other severe systemic co morbidities like congenital or ischemic heart diseases, neoplasm, chronic kidney disease, stroke etc. except hypertension and diabetes mellitus were excluded. The decision where to treat the patient with COPD exacerbation - emergency department, ward or ICU, was left to the discretion of the attending physician. Detailed history including age, smoking status was taken as per the Proforma. Detailed general and physical examination was done. BMI, mMRC, FEV1% and 6MWT were calculated when the patient was stable, i.e. not in exacerbation. BMI was calculated as per the body weight in kg and square of height in meters. Patients were asked to do spirometry to calculate post bronchodilator forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) ratio (desired value was FEV1/FVC <70%) and post bronchodilator FEV1% to grade COPD as mild, moderate, severe and very severe. mMRC scoring system was used on each patient to grade the degree of breathlessness experienced by the patient. Patient's exercise capacity was measured with the help of 6MWT. Patients are asked to walk with their normal pace till they get tired or till 6 minutes, whichever is early, oxygen saturation is measured with the help of pulse oximetry at the start and end of walking. Distance walked in meters is calculated. Patients were asked to contact us either on telephone or personally whenever they had an episode of exacerbations. Study involved clinician-diagnosed COPD exacerbation defined as an acute event characterized by a worsening of respiratory symptoms (dyspnea, sputum purulence, or sputum volume) that is beyond normal day to day variations and leads to a change in medication⁽⁴⁾. BODE index was calculated as mentioned above and patients were divided into 4 quartiles. Patients were followed for a period of two years and each

exacerbation was subdivided on the basis of modality of treatment, whether it required stepping up in medications or requiring emergency visits or hospitalization in wards or ICU admission. Detailed record of exacerbation was maintained, and correlated with BODE index. The data was analyzed systematically.

Statistical Analysis: Qualitative data was represented in form of frequency and percentage. Among Qualitative data, Nominal data included smoking habit, degree of COPD, Quartile of BODE Index, etc. Ordinal data included scores like mMRC & BODE Index. Association between qualitative variables was assessed by Chi-Square test, with Continuity Correction for all 2 X 2 tables and by Fisher's Exact test for all 2 X 2 tables where Chi-Square test was not valid due to small counts. In presence of small counts, in tables with more than two rows and/or columns, adjacent row and/or Column data was pooled and Chi-Square Test reapplied. Continuity Correction was applied for all 2 X 2 tables after pooling of data. Fisher's Exact test was applied for all 2 X 2 tables where p-value of Chi-Square test was not valid due to small counts, in-spite of pooling of data (E.g. Association between number of Exacerbation in past 2 years & Quartile of BODE Index). Quantitative data was represented using Mean \pm SD and Median & IQR (Interquartile range). Correlation between BODE index and various variables was done by using Spearman Rank-Order Correlation. Correlation between number of Exacerbation in past 2 years and

various variables was done by using Pearson Product Moment Correlation. To assess the predictors of number of Exacerbation, number of Emergency, number of Hospitalization, number of ICU admission-all in past 2 years (each separately as a dependent variable), Linear Regression was applied between the dependent variable & a set of Independent (Predictor) variables like FEV1 %, mMRC, 6MWT (cm), BMI etc.

Results

In our study, patients belonged to the age group 35 to 70 years with a mean age of 56.07 ± 7.6 years. Among the 60 patients, 47 (78.3 %) patients were smokers in comparison to 13 (21.7 %) patients who were nonsmoker. The mean and median number of pack years was 20.65 ± 11.55 . BMI of all 60 patients was calculated, minimum BMI was 15.43 kg/m^2 and the highest being 34.77 kg/m^2 with a mean of 22.29 ± 4.63 and 50 % of patients had BMI >21 and $\leq 21\%$. In our study, percentage of mMRC grade 0, 1, 2, 3, 4 are 10 %, 56.7%, 13.3%, 18.3%, 1.7% respectively (figure 1). Maximum patients belonged to grade 1. Mean mMRC is 1.45 ± 0.96 . Spirometry showed mild obstruction in 16.7%, moderate obstruction in 26.7%, severe obstruction in 38.3% and very severe obstruction in 18.3% of patients. Among the 60 patients in our study, 8.3% patients had experienced no exacerbation in the last 2 years, 16.7 % patients had 1 exacerbation in last 2 years and 8.3% patients experienced 7 exacerbations in 2 years (figure 2).

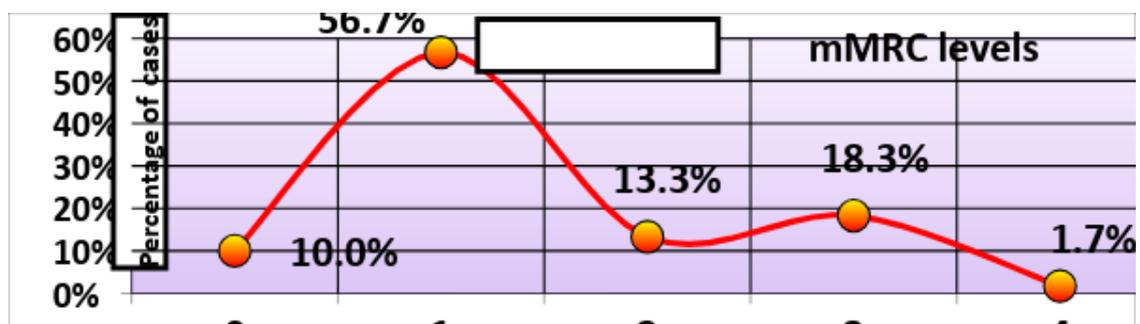


Figure 1: Distribution of mMRC among the study group

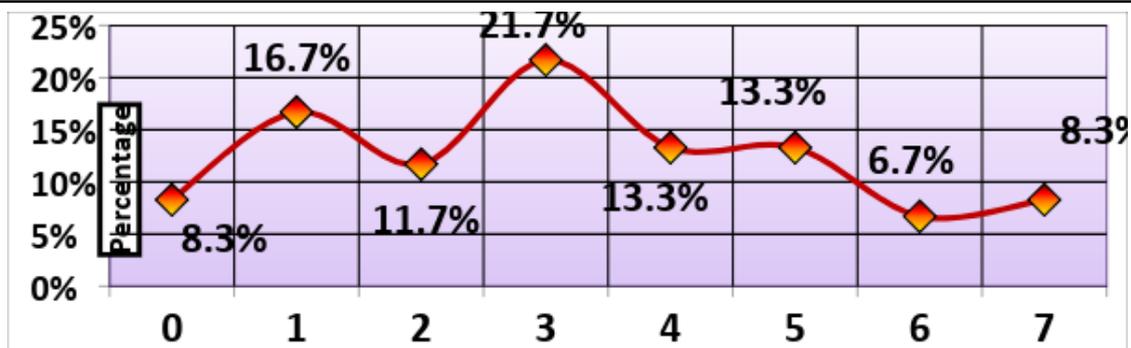


Figure 2: Distribution of number of exacerbation in 2 years

study	M. Grabicki ¹⁴		Nurhan Sarioglu ¹³		Bartolome R. Celli ⁷		Jose M. Marin ⁸		Present study		Association is
	Mean	P value	Mean	P value	Mean	P value	Mean	P value	Mean	P value	
Pack years	33	-	40	-	-	-	56.23	-	20.65	0.739	Not significant
BMI	27.6	-	-	-	27.5	-	-	-	22.29	1.75E-12	Significant
mMRC	-	-	-	-	2.7	0.001 (significant)	1.73	0.002 (significant)	1.45	0.0885	Not Significant

Figure 3: Studies conducted by Celli, Sarioglu and Marin⁶, where the p value are significant for mMRC and BMI

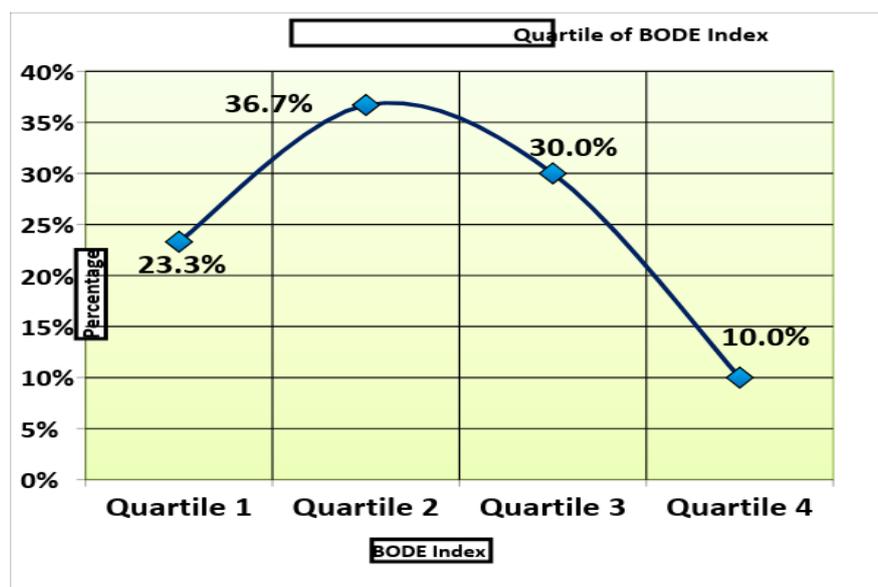


Figure 4: Distribution of Quartile of BODE index among the study group

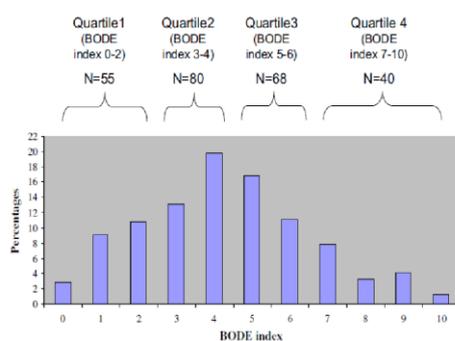


Figure 5: Distribution of BODE index in a study conducted by Fanny W.S. Ko, Wilson Tam and et al⁷

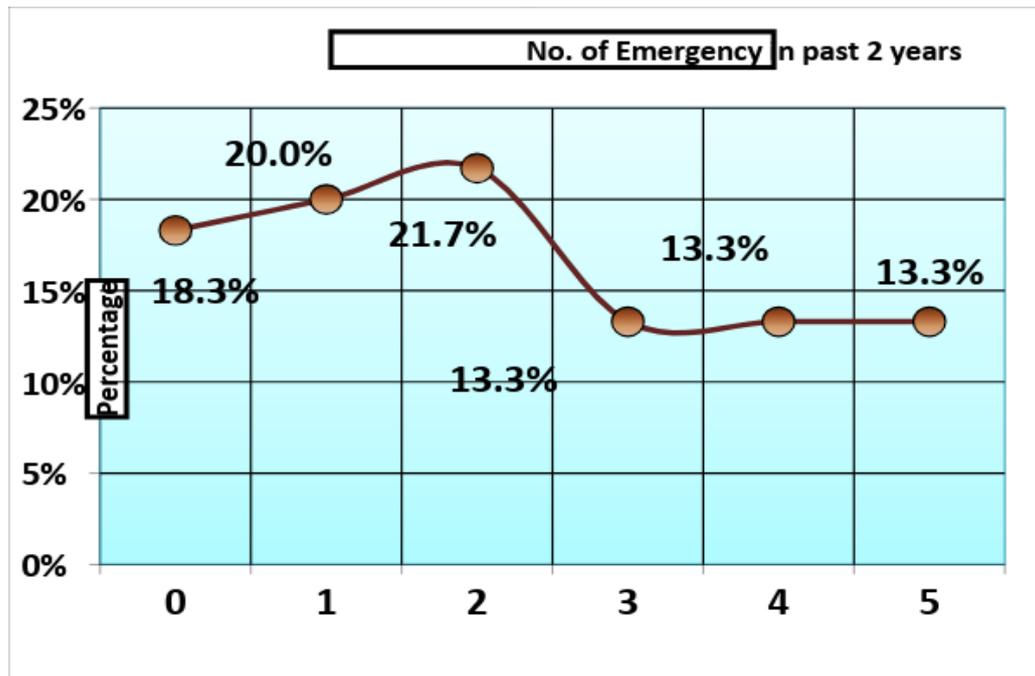


Figure 6: Distribution of No of emergency visits in 2 years

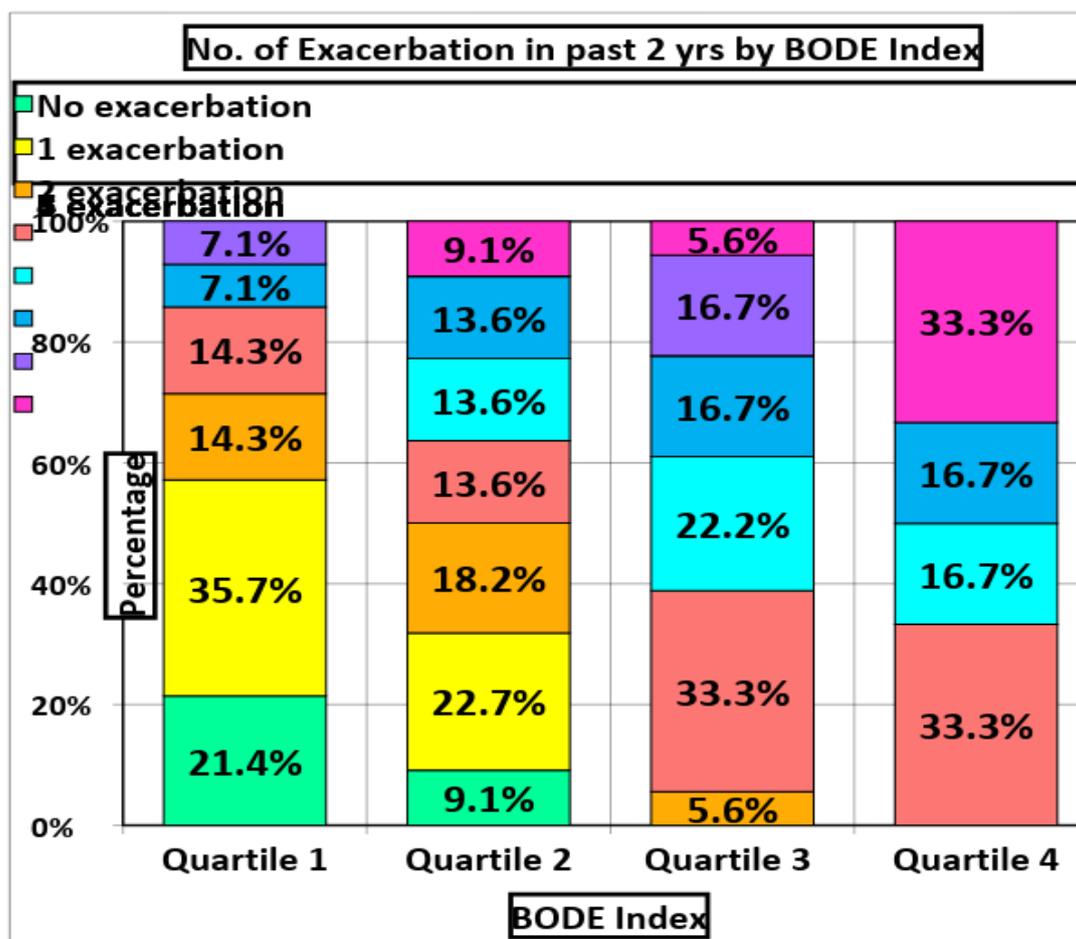


Figure 7: Association among the cases between no. of exacerbations in 2 years and Quartile of Bode index

Discussion

Assessment of COPD is based on patient's symptoms, risk of exacerbations, the severity of spirometric abnormality, and the identification of co-morbidities. Calculating BODE index can be helpful to predict the risk of exacerbations and co-morbidities.

Smoking is a risk factor for developing COPD, but as per the present study it is not helpful in predicting the risk of COPD exacerbation as the p value is not significant. BMI can be helpful for predicting COPD exacerbation as the association is significant. More the BMI less is the chances of infection and exacerbations and vice versa. BODE index is a better predictor than its individual components. In our study mMRC is not a good predictor for COPD exacerbation which is in conflict with the results of studies conducted by Celli et al⁽⁵⁾ and Marin et al⁽⁶⁾, where the p value is significant (figure 3). The reason for conflicts in our study and above mentioned study regarding mMRC being a good predictor of COPD exacerbation could be due to small sample size in our study group. Quartile 1, 2, 3, 4 had 23.3% (14 patients), 36.7 % (22 patients), 30% (18 patients), 10% (6 patients), respectively (figure 4). In our study, maximum patients belonged to quartile 2 (BODE score 3-4), this result is in accordance with the data in the study performed by Celli et al⁽⁵⁾. It was observed from our study that as the severity of COPD increases BODE index also increases. Minimum and maximum BODE score observed in our study was 1 and 9 respectively, present in 13.3% (8 patients) and 1.7% (1 patient) respectively. Mean BODE index in our study was 4.03.

Fanny et al⁽⁷⁾ conducted a prospective cohort study involving 243(208males) COPD patients hospitalized for acute exacerbations of COPD [AECOPD], in this study distribution of BODE index is as shown in figure 5.

In our study group, 66.7% patients belonged to quartile 2 and 3, in comparison to above study population, in which 61% patients belonged to quartile 2 and 3.

In our study, a patient was followed up for 2 years and observed for number of exacerbations requiring only change of medications or emergency visits, hospitalization and ICU admission. Greater the severity of COPD, more was the BODE index and more was the number of exacerbation, emergency visits (figure 6), need of hospitalization and ICU admission. Maximum number of exacerbation in our study was 7 observed in 8.3 % patients and majority of patients (21.7%) had 3 exacerbations in 2 years. 3.23 ± 2.04 was the mean number of exacerbations in our study (figure 7). It was observed that higher the BODE index; greater the severity of COPD and more the number of exacerbations.

When correlating BODE index with number of exacerbation, emergency visits, hospitalization and ICU admission and PASP with the help of Spearman's rho correlation coefficient, the p value is < 0.05 , i.e. significant. This shows that BODE index is a significant predictor of exacerbation and predicting co-morbidities like pulmonary hypertension. BODE index can be utilized to predict the risk of exacerbation and helps in assessment of COPD.

Minimum number of exacerbation in 2 years duration in this study group was 1 which was seen in 35.7% patients belonging to quartile 1. Maximum number of exacerbation was 7 which were seen in 33.3% patients belonging to quartile 4. This shows that patients with higher BODE index have more number of exacerbation. After applying Pearson Chi Square test, the association between number of exacerbation and different quartile of BODE index is significant (p value is < 0.05). On applying Linear Regression with number of exacerbation in 2 years and individual components of BODE index as an independent variables, it is observed that the association of number of exacerbation with FEV1% and BMI is significant, p value is < 0.05 whereas with mMRC and 6MWT is not significant, p value is > 0.05 . In our study we found that the BMI progressively declined with severity among the patients with

COPD. These results were similar to the study conducted by Shivakumar et al⁽⁸⁾. As per the study conducted by Celli et al⁽⁵⁾, FEV1%, BMI and mMRC are good predictors of COPD exacerbation and BODE index is better than its individual component in predicting risk of exacerbation of COPD, mortality and its systemic involvement. In the BODE index, we included two descriptors of systemic involvement in COPD: the body-mass index and the distance walked in six minutes. BMI and 6MWT can be easily calculated and can independently predict the risk of death^(9, 10). It is likely that they share some common underlying physiological determinants, but the distance walked in six minutes contains a degree of sensitivity not provided by the body-mass index. In the study conducted by Sarioglu et al⁽¹¹⁾, each single BODE component and the BODE index itself were compared with disease duration, number of exacerbations and number of hospitalizations separately. BMI was not found to be correlated with any of these parameters. A significant relationship was found between mMRC, 6MWT and FEV1%. Thus in the above mentioned studies conducted by Shivakumar et al⁽⁸⁾, Celli et al⁽⁵⁾, Sarioglu et al⁽¹¹⁾ there are conflicting results regarding association of individual components of BODE index- BMI, obstruction, mMRC dyspnea grading, exercise tolerance with number of exacerbation and hospitalization but all mentioned BODE index is better predictor than its individual component in predicting severity of disease, exacerbation, mortality and its systemic involvement which is in accordance with our present study. Thus our study conclude that BODE index is a reliable method to predict exacerbation.

Conclusion

BODE index should be calculated in every COPD patients for better prediction of risk of exacerbation, hospitalization and systemic involvement. This can be helpful in better understanding of outcome of COPD for individual

patients. If risk of exacerbation can be predicted then patient can be monitored differently as per the condition of the patient. Detailed history for patients having higher BODE index can also be helpful to monitor the outcome of the disease.

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