Section: Pulmonology

Original Research Article

COMPARISON OF MULTIDIMENSIONAL INDICES OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AS A PREDICTOR FOR FUTURE EXACERBATIONS

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ABSTRACT

Background: COPD is an important public health problem. Multidimensional indices of COPD could be used for predicting exacerbations, prognosis or death in patients. BODE index was initially used for assessing COPD patients. This index is found to be superior to FEV1 alone for predicting outcomes. **Aim**: To compare two multidimensional indices (BODE and DOSE) of COPD severity as predictors of future exacerbations. **Materials and Methods:** We conducted an observational prospective study in patients attending department of Pulmonology at Al Azhar Medical College Thodupuzha who satisfy the inclusion and exclusion criteria.109 patients were assessed, proforma filled and his/her six minute walk distance was noted along with spirometry indices. Blood sample was taken to analyse CBC and AEC. Follow up proforma was filled by personal interview method at 3 months and 6 months. BODE and DOSE indices are calculated after the investigations at baseline,3 and 6 months. **Result:** In our study, BODE and DOSE Indices had significant (p value-<0.001) association with exacerbation in 3 month and at 6 month. BODE, DOSE indices were compared for predicting exacerbations at 3 and 6 months. Receiver-operator curve for the both indices at baseline significantly predicts future occurrence of exacerbations. Among which BODE index is found to be superior to DOSE. **Conclusion:** The study highlights that BODE index is better than DOSE in predicting future exacerbations at 3 months and 6 months.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one of the most common causes of death worldwide.[1,2] It constitutes a serious public health problem. It is one of common cause of morbidity in the world. The COPD burden is increasing in coming years because of exposure to risk factors among population.[3] It also leads to increasing economic and social burden.[4,5] The prevalence of COPD and its mortality vary across countries.[6,7] The prevalence of COPD was 11.8% and 8.5% for men and women respectively according to BOLD.[8] Based on various large scale epidemiological studies, global prevalence of COPD was 10.3%.[9,10] Around three million deaths are attributed due to COPD annually.[11] Prevalence of COPD is generally higher in smokers than non-smokers, in people with age >40 years. (9,12,13). The disease prevalence from the eight studies ranged from 2.4% in a cross- sectional study done by Johnson et al in Southern India, to 16.1% by Koul et al conducted in Northern India.[14,15] Total COPD cases in India were 55.3 million in 2016. In Kerala COPD cases was found to be 6.19% among the general population. A gender wise variation in prevalence was found in a number of systematic reviews which showed COPD in males and females was between 2% to 22% and 1.2 to 19% respectively.[16]

Multidimensional indices of COPD were used to assess prognosis in COPD patients. BODE index is superior to FEV1 for predicting outcomes. Later on, many indices were introduced, out of which two indices are similar to the BODE, those are ADO and DOSE index, both are used for clinical care.[17]

A diagnosis of COPD is considered in patients who had any exposure to risk factors which is associated with breathlessness, along with chronic cough or sputum, and/or spirometry showing post-bronchodilator FEV1/FVC < 0.7.[18]

According to GOLD 2023 guidelines, patients with a not fully reversible airflow limitation (FEV1/FVC<0.7 post bronchodilation) measured by spirometry confirm diagnosis of COPD. Patients with

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FEV1≥ 80% of the predicted is categorized as GOLD 1 (Mild), 50%≤FEV1≤80% of the predicted as GOLD 2 (Moderate), 30%≤FEV1≤50% of the predicted as GOLD 3 (Severe), FEV1<30 % of the predicted GOLD 4(Very severe). Furthermore, the groups are divided into A,B and E depending on GOLD grade, mMRC dyspnoea scale and CAT score along with exacerbations history.[19] An exacerbation of COPD (ECOPD) is defined as an event characterized by increased dyspnea and/or cough and sputum that worsen in <14 days which may be accompanied by tachypnea, and/or tachycardia and is often associated with increased local and systemic inflammation caused by infection, pollution or other insult to airway.[20] Currently, exacerbations are classified after event has occurred as: Mild, Moderate and Severe. Acute respiratory failure may be associated with severe exacerbations.[19]

Aims and Objectives

1. To compare two multidimensional indices (BODE and DOSE) of COPD severity as predictors of future exacerbations.

MATERIALS AND METHODS

This was a hospital based observational prospective study. The study was conducted in the Department of Pulmonology at Al Azhar Medical College, Thodupuzha. The study period was between 1st June 2023 to 31th August 2024. It was an OPD and IPD based study. All consecutive registered old and new patients of COPD diagnosed as per GOLD guidelines in the OPD and indoor wards who met our inclusion and exclusion criteria was taken up as study group.

Inclusion Criteria

1. All Confirmed cases of COPD as per GOLD guidelines.

Exclusion Criteria

1. Who don't give consent for the study
2. Refused to follow up
3. Unable to perform test
4. History of tuberculosis, HIV, any other respiratory diseases, recent history of angina or myocardial infarction, cerebrovascular accident, uncontrolled hypertension, heart failure or any psychiatric illness.

Sampling Technique

Every consecutive patient who fulfilled our inclusion and exclusion criteria and attended Department of Pulmonology, Al Azhar Medical College, Thodupuzha was included in the study. All steps were taken to minimize the loss to follow up. Communication was carried out with the patient on a weekly basis by the principal investigator regarding their health status and a rapport was maintained with them. The patients were reminded of the monthly review visit to the hospital. Thus, the follow up assessment on third and sixth month was guaranteed.

Data Collection Technique and Tools

After getting permission from IRC, Ethics committee and permission from Department of Pulmonology, Al Azhar Medical College, Thodupuzha, an observational prospective study was conducted among subjects who fulfilled the inclusion criteria. Informed written consent was taken from the patients for their inclusion in study & willingness to undergo diagnostic evaluation. Study subject was taken by personal interview method. Study subjects were evaluated using pre-structured questionnaire which was adapted from the standard questionnaire used in clinical practice (GOLD and ATS) and were used as open-source material. Patient was asked for name, age, occupation, hospital admission, change in treatment, smoking history, TB, HIV symptoms, exacerbations in last 1 year, history of DM, HTN, LHF, CAD, CVA and his/her 6 min walk distance was noted along with spirometry indices and a sample for CBC with AEC.Follow up proforma was filled by personal interview method at 3 months and 6 months account to annexure no.4.

Collection of blood: A small amount of venous blood was withdrawn for CBC and other investigations. Patient was asked for 3 hospital visits.

DATA ENTRY AND STATISTICAL ANALYSIS

After collecting data, it was coded and entered into "Microsoft Excel". Then it was analyzed and evaluated statistically by using SPSS-27 version. Quantitative data were expressed as mean ± standard deviation. Qualitative data expressed as percentage. Chi square test or Fisher's exact test used to compare difference between categorical data. ROC Curve was prepared to assess the prediction capacity of exacerbation between the two indices. "p" value < 0.05 considered as statistically significant.

CONSENT AND ETHICAL CONSIDERATON

The study was carried out after obtaining approval from the Institutional Human Ethics Committee. An informed, written consent was obtained from all the patients. Patients who had given written consent was enrolled in study. The consent was not obtained by false representation or enticement benefits. All patients had given freedom of opting out of study at any point of time during study.

Confidentiality of data: Confidentiality was ensured and maintained throughout the study. Study result was only be used for scientific purposes and publications. All information about patient's illness and results of the tests was kept confidential and retained in the institute as required under rules. Results may be presented at conferences and published without any disclosure of patient identity directly or indirectly.

RESULTS

This study was conducted among 109 diagnosed cases of COPD as per GOLD guidelines (2023). All patients who attended department of Pulmonology at Al Azhar Medical College Thodupuzha who satisfy the inclusion criteria and exclusion criteria are included in the study. It was an OPD and IPD based

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study conducted between 1st June 2023 to 31th August 2024.

PATIENTS CHARACTERISTICS AT FIRST VISIT (BASELINE)

Total patients (n=109) were divided into 5 age groups .All patients were of 40 or more than 40 years of age .As seen in table most (41.28%) of the patients belong to age group of 61-70. Mean age of COPD subjects was 66.17±8.446 years. Minimum age was 44 and maximum age of the patient taken was 84. Out of total 109 patients,83.49% were male. Majority of patients (37.61%) had grade 2 mMRC dyspnoea at baseline. The 6 MWD covered by maximum patients were in the range of <200 m at baseline (22.94%).Most of the patients had their FEV1 in the range of 50-79% (54.13%)at baseline.Most of the patients taken in this study belong to gold grade 2(54.13%). 37.61% of patients taken in this study were in GOLD group B. Co-morbidities were present in 53.21% of patients. Patients were divided into non-smokers, smokers with different pack years and biomass fuel exposure. Most of the patients were smoker among which maximum (31.19%) patients had pack year (PY) in the range 20-39. Half (51.38%) of the patients had BMI in the range of 18.5-22.9.85.32% of the patients had AEC <300.36.70 % of the patients had BODE index in the range of 0-2 at baseline.34.86% of patients at baseline had DOSE index in the range of 0-1.

FOLLOW UP AT 3 MONTHS AND 6 MONTHS

Table 1: mMRC Grading of Dyspnoea in Patients at 3 month and 6 months

mMRC grading of dyspnoea	At 3 month		At 6 month	
	Number	Percentage	Number	Percentage
1	28	25.69	14	12.84
2	41	37.61	48	44.04
3	36	33.03	35	32.11
4	4	3.67	12	11.01

As shown in the table1, most of the patients had grade 2 mMRC at 3 months (37.61%) and at 6 months (44.04%).

Table 2: Exacerbations in Patients at 3 month and 6 months

Exacerbations	At 3 month		At 6 month	
	Number	Percentage	Number	Percentage
Absent	75	68.81	53	48.62
Present	34	31.19	56	51.38

As shown from the above table 2 ,31.19% have exacerbations at 3months and 51.38% at 6 months.

Table 3: 6MWD Distance Covered by Patients at 3 month and 6 months

6MWD Distance covered	At 3 month		At 6 month	
	Number	Percentage	Number	Percentage
<200 m	32	29.36	30	27.52
201 - 300 m	23	21.10	28	25.69
301 - 400 m	21	19.27	18	16.51
401 - 500 m	15	13.76	15	13.76
501 - 600 m	12	11.01	11	10.09
>600 m	6	5.50	7	6.42

As shown in the above table 3, the 6MWD covered by maximum patients was in the range of <200 meter at 3 months (29.36%) and at 6 months (27.52%).

Table 4: Pulmonary Function Parameter FEV1(%) in Patients at 3 month and 6 months

FEV1 (%)	At 3 month		At 6 month	
	Number	Percentage	Number	Percentage
≥ 80	10	9.17	12	11.01
50 – 79	61	55.96	56	51.38
30 – 49	33	30.28	35	32.11
< 30	5	4.59	6	5.50

As seen from the above table 4, most of the patients had their FEV1 in the range of 50-79 (55.96%) at 3 months and (51.38%) at 6months.

Table 5: Absolute Eosinophil Count in study subjects at 3 month and 6 months

AEC	At 3 month		At 6 month	
	Number	Percentage	Number	Percentage
<300	93	85.32	93	85.32
≥300	16	14.68	16	14.68

As shown in table 5, patients with absolute eosinophil count less than 300 and greater than 300 remains same at 3 month and 6 month.

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COMPARISON OF INDICES

BASELINE INDICES AND EXACERBATIONS AT 3 MONTHS

Table 6: Baseline BODE index and exacerbation at 3 months

Baseline BODE	Exacerbation		p-value
	Present	Absent	
0 - 2	0	40	<0.001*
3- 4	2	22	
5 - 6	19	11	
7 - 10	13	2	

Represent Significant

As seen in table 6, BODE Index had significant (p value-<0.001) association with exacerbation in 3 month.

Table 7: Baseline DOSE index and exacerbation at 3 month

Baseline DOSE	Exacerbation		p value
	Present	Absent	
0 - 1	0	30	<0.001*
2 - 3	9	26	
4 - 5	18	11	
6 - 7	7	0	

Represent Significant

As seen in table 7, DOSE Index had significant (p value-<0.001) association with exacerbation in 3 month.

Table 8: Comparison of AUC for BODE and DOSE Indices at 3 Months

Baseline	AUC (95% CI)	p Value
BODE Index	0.920(0.870-0.970)	<0.001*
DOSE Index	0.876(0.813-0.940)	<0.001*

As shown in figure 1, Receiver-operator curve for the BODE and DOSE indices at baseline significantly predicts future occurrence of exacerbation during 3 month follow up. Among which BODE index is a better predictor than DOSE as shown in the curve as area under the curve is maximum for BODE index.

BASELINE INDICES AND EXACERBATIONS AT 6 MONTHS

Table 9: Baseline BODE index and exacerbation at 6 month

Baseline BODE	Exacerbation		p value
	Present	Absent	
0 – 2	0	40	<0.001*
3 – 4	11	13	
5-6	30	0	
7 – 10	15	0	

Represent Significant

As seen in table 9, there is significant association between baseline BODE Index and exacerbation at 6 month. Patients with higher BODE Index had exacerbation at 6 month compared to patient with low BODE Index.

Table 10: Baseline DOSE index and exacerbation at 6 month

Baseline DOSE	Exacerbation		p value
	Present	Absent	
0 – 1	1	37	<0.001*
2-3	20	15	
4- 5	28	1	
6 - 7	7	0	

Represent Significant

As seen in table 10, there is significant association between baseline DOSE Index and exacerbation at 6 months. Patients with higher DOSE Index had exacerbation at 6 months compared to patient with low DOSE Index.

Table 11: Comparison of AUC for BODE and DOSE INDEX at 6 month

Baseline	AUC (95% CI)	p-Value
BODE Index	0.976(0.955-0.997)	<0.001*
DOSE Index	0.926(0.879-0.974)	<0.001*

Represent Significant

As shown in figure 2, Receiver-operator curve for the BODE and DOSE indices at baseline significantly predicts future occurrence of exacerbation during 6 month follow up. Among which BODE index is a better predictor than DOSE as shown in the curve as area under the curve is maximum for BODE index.

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Comparison of BODE and DOSE INDICES at 3 Months

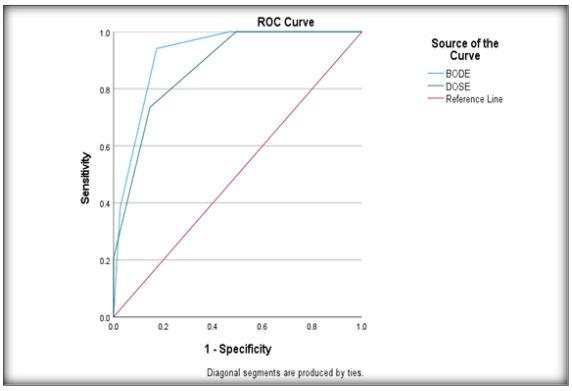

Figure 1: Comparison of AUC for BODE and DOSE Indices at 3 Months

Comparison of BODE and DOSE at 6 Month

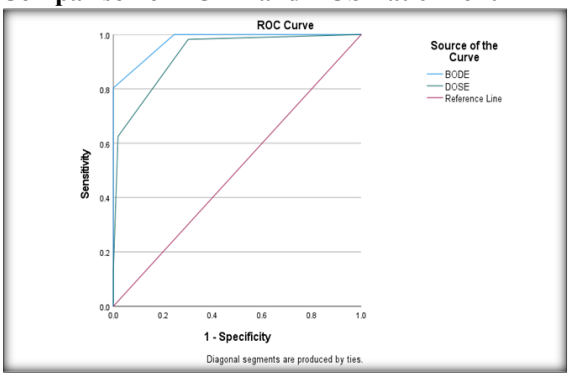

Figure 2: Comparison of AUC for BODE and DOSE INDEX at 6 month

DISCUSSION

Age distribution: In this study, most (41.28%) of the patients belongs to age group of 61-70. Mean age of COPD subjects was 66.17±8.446 years. It means that COPD is most prevalent in older age group due to smoking, exposure to environmental air pollutants, occupational dusts and chemicals over a period of time.

Gender: In this study, most of the subjects were male, 83.49% of total 109 patients. It can be explained by fact that incidence of smoking is more in men as compared to women and men are more exposed to outdoor pollution and chemicals which are also the main risk factors for COPD.

mMRC grading: In the present study, 37.61% of the patients at baseline had grade 2 mMRC dyspnoea. This may be explained as more patient present to clinic when they can't walk at their own pace due to dyspnoea.

Exacerbations: In the present study,31.19% of the patients had exacerbations at 3 months and 51.38% at 6 months. This showed that the number of patients who had exacerbations increased from 3 months to 6 months. This may be due to fact that as time passes ahead there are more chances of environmental tobacco smoke, seasonal variation, persistent increased exposure to pollutants which are the risk factors for exacerbations.

6-minute walk distance: In the present study, the mean 6MWD at baseline was <200 meter, at 3 months and at 6 months. This can be explained due to the fact that 6MWD is a measure of exercise capacity which is decreased in COPD patients.

FEV1%: In the present study, most of the patients had their FEV1 in the range of 50-79 (55.96%) at 3 months and (51.38%) at 6 months. This may be explained due to the fact that patients present to hospital when they have symptoms like dyspnoea due to poor lung function.

GOLD Grade: In this study, maximum patients were in GOLD grade 2, 54.13%. This may be explained as GOLD grade increases, severity of disease also increases.

GOLD Group: In this study, most of the patients belong to GOLD group B and E,37% and 36% respectively.

Co-morbidities: In this study, co-morbidities studied were diabetes mellitus, hypertension, heart failure and CAD and they were evaluated as a whole. In this study, 53.21% of patients had associated co-morbidities. This may be explained as mean age of study population was 66.17±8.446 years and COPD prevalence is higher in old age group which is also better explained amongst the diabetics and hypertensive patients.

Smoking Status: Smoking constitutes a high risk for COPD. In our study 81% of the patients were smokers and 11% of the patients had a history of biomass fuel exposure. Among smokers 31% had pack year in the range of 20-39. Patients who were current smokers or former smokers had higher prevalence of COPD and same is true with exposure with biomass fuel exposure as well as outdoor pollution.

BMI: In the present study, patients were divided according to Asian classification of BMI into different groups.51.3% of patients belong to BMI of 18.5-22.9. This can be better explained with the fact that Caucasians have low BMI as compared to those of western population and as severity of COPD increases, systemic inflammation increases that can lead to low BMI.

Absolute Eosinophil Count: In the present study, 85.3% of study population had AEC <300 at baseline.

BODE index at baseline: Our study pointed out that 36.7% of patients had BODE index within the range of 0-2.

DOSE Index at baseline: In the present study,34.8% of the patients belongs to DOSE index range of 0-1. The distribution has skewed towards low DOSE scores, which constitutes a high proportion of mild-moderate COPD subjects in the cohort.. This can be explained by the fact that as FEV1 decreases, score of DOSE index increases.

Indices and Exacerbation

All 109 patients were followed up at 3 months and 6 months, and FEV1%, 6MWD, eosinophil counts, exacerbations and other parameters was noted at 3

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months and 6 months. After noting all the above required parameters, BODE, DOSE at baseline was co-related with future exacerbations at 3 months and 6 months.

BODE Index

In this study, BODE Index had significant (p value-<0.001) association with exacerbation in 3 month. There is also significant association between baseline BODE and exacerbation at 6 months. Patients with a higher score had exacerbation at 6 months compared to patient with low BODE Index. This indicates that BODE index could be used for predicting the future exacerbations at 3 months and at 6 months.

DOSE Index

In this study, DOSE Index had significant (p value-<0.001) association with exacerbation in 3 month. There is also significant association between baseline DOSE index and exacerbation at 6 month. Patients with higher DOSE Index had exacerbation at 6 months compared to patient with low DOSE Index. This indicates that DOSE index can also be used to predict future exacerbations at 3 months and at 6 months. In a similar study by Jones et al (39) the health status showed correlation with DOSE in all the available data sets. A higher DOSE score (>4) points out that there will be more exacerbation in coming years along with increased probability of hospital admission.

Comparison of Indices

BODE, DOSE indices were compared for predicting exacerbations at 3 and 6 months. Receiver-operator curve for the BODE and DOSE indices at baseline significantly predicts future occurrence of exacerbation during 3 month follow up. Among which BODE index is a better predictor than DOSE as area under the curve is maximum for BODE index. Receiver-operator curve for the BODE and DOSE indices at baseline significantly predicts future occurrence of exacerbation during 6 month follow up. Among which BODE index is a better predictor than DOSE as AUC is maximum for BODE index.

CONCLUSION

The salient findings of this study are enumerated as follows

1. Out of 109 patients taken in study

a) 91 were male.18 subjects belong to female gender with most of the patients belong to 61-70 age group.

b) 41(37.61%) patients had grade 2 mMRC dyspnea and 25 (22.94%) had 6MWD in the range of <200 meter and 59 (54.13%) had FEV1 in the range of 50-79%.

c) 58 (53.21%) of patients had associated co-morbidities and 81% of study population were smokers and 11% had given a history of biomass fuel exposure

d) 59 (54.13%) patients was in GOLD Grade 2.

e) 41(37.61%) patients was in GOLD Group B.

f) 56 (51.3%) had BMI in the range of 18.5-22.9 and 85.3% of the patient have AEC <300 at baseline.

g) 36.7% of patients had BODE index within the range of 0-2.

h) 34.8% of the patients belongs to DOSE index range of 0-1.

2. Patients who had exacerbations increased from 34 at 3 months to 56 at 6 months.
3. Exacerbation was significantly less in GOLD Group A at 3 months and 6 months and exacerbations were more in GOLD group E at 6 months
4. Patients with higher BODE index (5-10) had significantly higher exacerbation at 3 and 6 month.
5. Patient with DOSE index ≥4 had significantly higher rate of exacerbations within 3 months and at 6 months.
6. BODE index is better than DOSE in predicting future exacerbations at 3 months and 6 months.

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