Evaluation of Bode Index in   prognosis and   follow up of COPD patients

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Abstract:

Background: Chronic obstructive pulmonary disease (COPD) is characterized by an incompletely reversible limitation in airflow. The BODE index was devised to better reflect the multisystem effects of chronic obstructive pulmonary disease (COPD), allowing for better prognostic estimation than that provided by forced expiratory volume in 1 s (FEV$_1$) alone. The grading system, based on four parameters—that is, body mass index, airflow obstruction, Modified Medical Research Council (MMRC) dyspnea score and the 6 min walk distance—was verified by population studies. **Materials and Methods:** The diagnosed and undiagnosed COPD patients who visited study center for any respiratory complain and further met the inclusion criteria selected as subjects during specified schedule. A total of 100 COPD patients were randomly chosen from the outpatient department and were evaluated via   FEV1% ,Six Minute walk test ,Body mass index and MMRC dyspnea score and the BODE score was calculated. **Results:** We found that there is an association of increasing age with higher BODE categorization.(p=0.034). MMRC grade of the patients is significantly associated with the BODE index (p<0.001). In the MMRC Grade 4, majority of the patients were in BODE 3 index.45% patients were underweight, 41% were normal weight, 12% were overweight and 2% patients were obese. As the BODE index increases, FEV1 progressively decline. (p<0.001).There was highly significant correlation between BODE index and six minute walk distance (p=0.001). The baseline BODE index of the patients is associated with follow-up BODE index(p<0.001).The improvement in distance travelled was observed in the patients of BODE 2 and BODE 3 index with regular follow up and regular treatment. **Conclusion:** We believe that the BODE index is useful because it includes one domain that quantifies the degree of pulmonary impairment (FEV1), one that captures the patient's perception of symptoms (the MMRC dyspnea scale), and two independent domains (the distance walked in six minutes and the body-mass index) that express the systemic consequences of COPD. BODE score in follow up is a powerful tool in assessing the effect of treatment and progression of the disease.

Keywords: BODE index, COPD, Dyspnea, follow up BODE index

Abbreviations:BODE= body mass index, airflow obstruction, dyspnea, and exercise capacity , COPD= Chronic Obstructive Pulmonary Disease ,MMRC= Modified Medical Research Council

Introduction:

COPD is a major global health problem that increasingly constitutes a burden for the society and has large effects on health-care expenditure. COPD has recently been described as a disease 'characterized by airflow limitation that is not fully reversible' [1]. The airflow limitation in most cases is both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. This progressive and relentless loss of lung function is the result of emphysema due to destruction of lung parenchyma and narrowing of small airways caused by chronic inflammation [2]. In India ,The prevalence of COPD is 5 percent in males and 2.7 percent in females in adults of 30 years age and above[3].

To screen COPD patients in the population in order to prevent a pejorative prognosis, If the objective is research on COPD risk factors, it is necessary to have specific and sensible adapted tools (i.e.

questionnaires and/or biological or environmental measures).

Role of spirometry in Classification of COPD Severity

• Mild COPD(FEV1 80% predicted), Moderate COPD(FEV1 50%−79% Predicted);Severe COPD (FEV1 30% to 49% predicted); Very Severe COPD (FEV1 <30% predicted Or <50% predicted with room air PaO2 <60 mm hg)

∗*Postbronchodilator FEV1/FVC 0.70. Adapted from the 2006 GOLD COPD guidelines, www.goldcopd.com; Celli BR, MacNee W: ATS/ERS Task Force. Standards for the diagnosis and treatment of patients with COPD: A summary of the ATS/ERS position paper.* EurRespir J *23:934; 2004.*

BODE index-

     The BODE index is a multidimensional grading system developed to predict the risk of death from any cause and from respiratory causes in people with COPD [4].

     Celli et al developed a multidimensional staging system that includes respiratory and systemic expressions of disease known as the 'BODE' index.[4] This index uses four dimensions to classify the severity of COPD and to predict survival: body mass index (BMI) (as a measure of cachexia and muscle wasting); exercise tolerance; severity of dyspnea; and airway obstruction (forced expiratory volume in one second [FEV1]). Population based validation studies have demonstrated that the BODE index may be a better predictor of mortality than lung function alone.[4] Recent studies have also indicated that the BODE index may predict hospitalization rates [5], and that pulmonary rehabilitation programmes may prevent its deterioration. There is, however, limited data regarding changes in the BODE score over time [6].

     The BODE index was calculated according to the algorithm previously published by Celli et al,[4]and the scale was constructed from 0 to 10, with 10 indicating the most severe disease with the highest mortality risk.

VARIABLE	0	1	2	3
FEV1% PREDICTED	>65	50-64	36-49	<35
DISTANCE WALKED IN 6 MIN IN METERES	>350	250-349	150-249	<149
MMRC DYSPNOEA SCALE	O-1	2	3	4
BMI	≤21	≥21		

∗*The BODE index is calculated as the sum of points*
Adapted from: Celli BR, Cote CG, Marin JM, et al: The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive
pulmonary disease. N Engl J Med *350:1005–1012; 2004.*

Bode score could predict the mortality in next 2 years to some extent, as follows:

BODE SCORE	MORTALITY (2 YEAR)
>7	30 %
5 TO 6	15%
<5	<10%

Aims &Objectives
1.To predict prognosis of COPD patients on first visit, on basis of BODE index.
2.To assess accuracy of prediction on basis of BODE index on follow up visit.

Materials and Methods:
RESEARCH DESIGN: This is a longitudinal study design.
STUDY SET UP: The study is conducted in the Department of RespiratoryMedicine andDepartment of General Medicine at Sri Aurobindo Medical College and Post Graduate Institute, Indore (M. P.).
STUDY DURATION: The duration of study was two year; May-2013 to May-2015.
SAMPLING: Simple random sampling technique was used for selection of desired samples according to inclusion-exclusion criterion**.**
Inclusion Criteria: Informed and willing patients,respiratory problem cases attending OPD.Any smoker,undiagnosed COPD patient

attending respiratory OPD,any smoker elderly male admitted in casuality with predominant respiratory complaints.

Exclusion Criteria:

Unwilling patients,Non-cooperative patients,Seriously ill patients,Known case of carcinoma,active pulmonary Tuberculosis ,recent myocardial infarction.Patient unable to perform proper PFT,6MWT.Patient already on Non invasive ventilation device or oxygen therapy at home for past 6 months.

Methodology:

The diagnosed and undiagnosed COPD patients who visited study center for any respiratory complaint and further met the inclusion criteria selected as subjects during specified schedule. A total of 100 COPD patients were randomly chosen from the outpatient department.

The patients were explained clearly about the study and their willingness to participate in the study was recorded in a consent form, duly signed by them. A total of 100 such subjects were available for the study. History recording and data collected and the analysis was performed. Body mass index (BMI), pulmonary function test, dyspnea score according to MMRC score and six minute walk test were carried out in assistance of certified technician.

Results:

Table 1:Distribution of Patients According to Initial BODE Index

BODE Index	Number	Percentage
0	5	5.00%
1-3	35	35.00%
4-6	36	36.00%
7-10	24	24.00%
Grand Total	**100**	**100.00%**

We have divided 0 to 3 BODE index in to BODE 1category ,4 to 6 in to BODE 2 category and 7 to 10 in to BODE 3 category.

There were 40% patients were in BODE 1 category,36% were in BODE 2 category while 24% were in BODE 3 category.

Table 2:Age distribution of patients according to the BODE Scoring(N=100)

Age in years	BODE 1	BODE 2	BODE 3	Total	p value
20-44	7 (50.0)	5 (35.7)	2 (14.3)	14 (100)	
45-64	16 (36.4)	11 (25.0)	17 (38.6)	44 (100)	0.034
65-85	17 (40.5)	20 (47.6)	5 (11.9)	42 (100)	

$Chi^2(4) = 10.5901$

The above table shows the distribution of Age according to BODE index.

14 patients were of age group 20-44 years , 44 patients were of 45 to 64 years age group & 42 patients were of 65 to 85 years of age group.

In age group 20 - 44 years 50.0% patients were of BODE category 1 while 35.7% patients were of BODE category 2 & only 14.3% patients belong to BODE category 3 .

In age group 45 – 64 years 36.4 % patients were of BODE category 1 while 25.0% patients were of BODE category 2 & 38.6% patients were of BODE category 3.

Similarly In age group 65 -85 years 40.5 % patients belong to BODE category 1 , 47.6% patients were of BODE category 2 & 11.9% patients were of BODE category 3.

The p value was found to be 0.034, which is statistically significant. Thus, we can say that there is an association of increasing age with higher BODE categorization.

Table 3:Distribution of MMRC grading in relation to BODE Index*(N=100)*

MMRC	BODE 1	BODE 2	BODE 3	Total	p value
Grade 0	5 (100.0)	0 (0.0)	0 (0.0)	5 (100)	
Grade 1	23 (85.2)	4 (14.8)	0 (0.0)	27 (100)	
Grade 2	10 (33.3)	18 (60.0)	2 (6.7)	30 (100)	<0.001
Grade 3	2 (6.7)	13 (43.3)	15 (50.0)	30 (100)	
Grade 4	0 (0.0)	1 (12.5)	7 (87.5)	8 (100)	

$Chi^2(8) =75.1160$

The above table shows the distribution of patients according to their MMRC grade in relation to various BODE index.

There were a total of 5 patients in MMRC Grade 0, 27 patients in MMRC Grade 1, 30 patients in MMRC Grade 2, 30 patients in MMRC Grade 3 and 8 patients in MMRC Grade 4.In grade 0 MMRC 100% patients were of BODE index 1 , 0.0% patients were of BODE index 2 &0.0% were of BODE index 3.In grade 1 MMRC 85.2% patients were of BODE index 1 , 14.8% were of BODE index 2 & 0.0% were of BODE index 3.

In grade 2 MMRC 33.3% patients were of BODE 1 , 60.0% were of BODE 2 & 6.7% were of BODE 3.In grade 3 MMRC 6.7% patients were of BODE 1 , 43.3% were of BODE 2 & 50% were of BODE 3 .In grade 4 MMRC 0.0% patients were of BODE 1, 12.5% were of BODE 2 & 87.5% were of BODE 3.The p value obtained is < 0.001, which is statistically highly significant. Thus, we can conclude that MMRC grade of the patients is significantly associated with the BODE index. In the MMRC Grade 4, majority of the patients are in BODE 3 index.

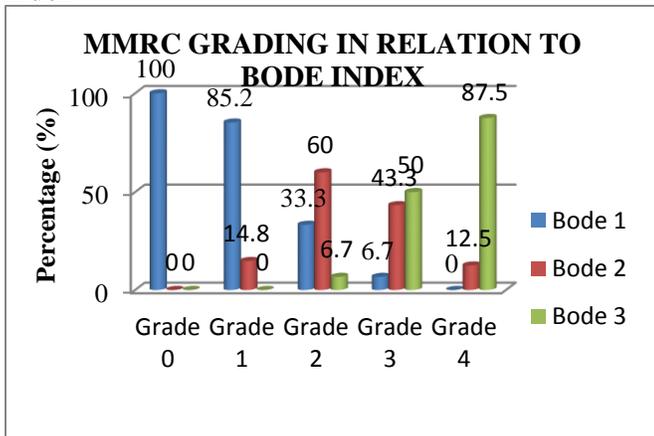**Figure 1: MMRC grading in relation to BODE Index**

Table 4:Distribution of Patients According to BMI (N=100)

BMI	≤21	≥21
No. of Patients	72	28

We have 72 % patients whose BMI was ≤ 21 and 28 % patients who have BMI ≥21.

BMI	BMI Class	No.	Percentage
Underweight	< 18.5 kg/m^2	45	45.00%
Normal Wt.	18.5-24.9 kg/m^2	41	41.00%
Overweight	25.0-29.9 kg/m^2	12	12.00%
Obese	>= 30.0 kg/m^2	2	2.00%
Grand Total		**100**	**100.00%**

In our study 45% patients were underweight , 41% were normal weight .12% were overweight and2 % patients were obese.

Table 5:Distribution of Patients According to Initial Gold COPD Grading

COPD Grading	Number	Percentage
Mild COPD	6	6.00%
Moderate COPD	45	45.00%
Severe COPD	32	32.00%
V. Severe COPD	17	17.00%
Grand Total	**100**	**100.00%**

Table No.5 projected that maximum number 45% patients were of moderate COPD based on Gold staging. While 32% were of severe COPD. 17% belong to
very severe COPD and only 6% were of mild COPD category

Table 6:Relationship of Six Minute walk distance and Mean FEV1/FVC with BODE category

	Mean	Mean FEV1/FVC
Bode 1	336.35±98.3	59.34±8.97
Bode 2	218.72±88.36	53.85±9.55
Bode 3	119.17±83.48	46.41±7.38

P Value =0.0001(for SMWD)

Table No.6 shows BODE index and six minute walk test distance correlation at o month.
BODE 1 category patient were having mean six minute walk distance of 336.35 meter(S.D 98.3) . BODE 2 category patients covered mean distance of 218.72 meter(S.D 88.36) while BODE 3 category patient walked mean distance of 119.17 meter (S.D 83.48) .
P value of 0.0001 suggestive of highly significant correlation between BODE index and six minute walk distance thus as the BODE index increases mean distance walked in six minute decreases.

P Value = 0.0001(For FEV1/FVC)

Table No.6 shows correlation between BODE index and FEV1/FVC ratio at o month.
BODE 1 category patients were having FEV1/FVC ratio of 59.34(S.D=8.97) . BODE 2 category patients were having ratio of 53.85(S.D=9.55) while BODE 3 category patients were having FEV1/FVC ratio of 46.41(S.D=7.38).

P value 0.0001 suggestive of significant correlation between BODE index and FEV1/FVC ratio thus as the BODE index increases FEV1/FVC ratio decline.
Unfortunately follow up could be done for only 51 patients after 1 year.

Table 7: Showing the Baseline BODE Index in Relation to Follow-up (1 year) BODE Index(N=100)

Baseline	Follow-up			Total	p value
	BODE 1	BODE 2	BODE 3		
BODE 1	19 (90.5)	2 (9.5)	0 (0.00)	21 (100)	<0.001
BODE 2	7 (38.9)	10 (55.5)	1 (5.6)	18 (100)	
BODE 3	0 (0.0)	5 (41.7)	7 (58.3)	12 (100)	

Chi^2(4) =37.9330

The above table shows the distribution of patients according to baseline BODE Index in relation to Follow-up BODE index. At baseline, there were 21 patients in BODE 1, 18 were in BODE 2 and 12 were in BODE 3 Index. Of these 21 BODE 1 baseline patients, 19 (90.5%) still remained in BODE 1, while 2 (9.5%) shifted to BODE 2 index at follow-up of 1 year.Of the 18 BODE 2 baseline patients, 7 (38.9%) shifted to BODE 2, 10 (55.5%) still remained in BODE 2, while 1 (5.6%) shifted to BODE 3 index at follow-up. Of the 12 BODE 3 baseline patients, 5 (41.7%) shifted to BODE 2 and 7 (58.3%) still remained in the BODE 3 index at follow-up. The p value obtained is <0.001, which is statistically highly significant. Thus, we can conclude that the baseline BODE index of these patients is associated with follow-up BODE index.

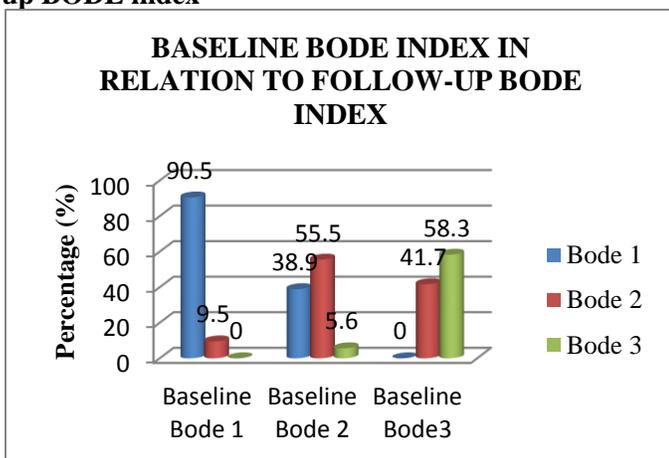**Figure 2: Baseline BODE index in relation to follow up BODE index**

*Table 8:***Mean distance travelled by the patients at baseline and at 12 months follow-up according to their BODE Index***(N=100)*

Distance	Baseline		12 months		t test	DOF	p value
	Mean	SD	Mean	SD			
BODE 1	374.62	88.66	402.29	86.91	-1.7250	20	0.099
BODE 2	219.5	76.31	285.17	89.83	-3.4032	17	0.003
BODE 3	128.75	77.17	187.67	90.72	-3.0167	11	0.012

The above table shows the distribution of patients according to their BODE Index at Baseline and at Follow-up for the parameter distance travelled by these patients in the 6 Min Walk Test.

In BODE 1 the mean distance travelled by the patients was 374.62 meter at baseline, which increased to 402.29 m at 12 months follow-up. The p value was 0.09 which is statistically not significant. Thus, there were not much of improvement in the distance travelled by these patients of the BODE 1 index.

In BODE 2, the mean distance travelled by the patients was 219.5 m at baseline, which increased to 285.17 m at 12 months follow-up. The p value was 0.003, which is statistically highly significant. Thus, there was much improvement in the distance travelled by these patients of the BODE 2 .

In BODE 3, the mean distance travelled by the patients was 128.75 m at baseline, which increased to 187.67 m at 12 months follow-up. The p value was 0.012, which is statistically highly significant. Thus, there was much improvement in the distance travelled by these patients of the BODE 3 index .

Thus, we conclude that improvement in distance travelled was observed in the patients of BODE 2 and BODE 3 index with regular follow up and regular treatment.
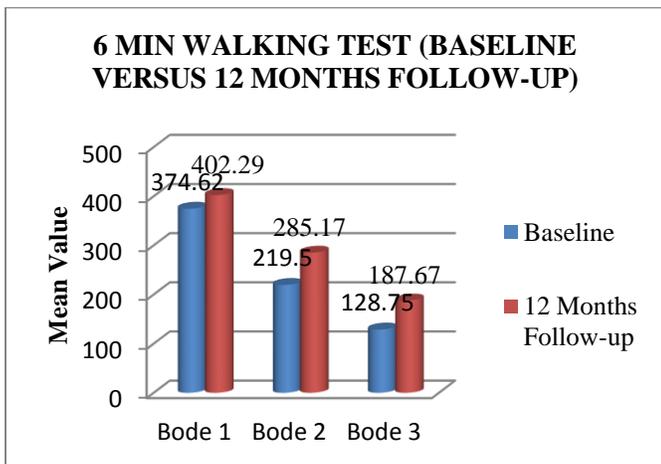
Figure 3:SMWD (Baseline versus 12 months follow up)

Table 9:**Mean FEV1 at baseline and at 12 months follow-up according to various BODE index**(*N=100*)

	Baseline		**12 months**		**t test**	**DOF**	**p value**
FEV 1	**Mean**	**SD**					
BODE 1	59.93	12.69	62.77	7.12			0.276
BODE 2	49.38	13.86	52.66	10.89			0.134
BODE 3	31.52	10.95	31.36	6.76			0.923

The above table shows the distribution of patients according to their BODE Index at Baseline and at Follow-up for the parameter FEV1.

In BODE 1, the mean FEV1 at baseline was 59.93%, while it was 62.77% at 12 months follow-up. There was a slightly improvement in FEV1%. The p value obtained was 0.276, which is statistically not significant. Thus, no statistical difference was seen between the baseline FEV1% and 12 months follow-up FEV1% in BODE 1 index.

In BODE 2, the mean FEV1 at baseline was 49.38%, while it was 52.66% at 12 months follow-up. There was a slightly improvement in FEV1%. The p value obtained was 0.134, which is statistically not significant. Thus, no statistical difference was seen between the baseline FEV1% and 12 months follow-up FEV1% in BODE 2 index.

In BODE 3, the mean FEV1 at baseline was 31.52%, while it was 31.36% at 12 months follow-up. There was a slightly improvement in FEV1%. The p value obtained was 0.923 which is statistically not significant. Thus, no statistical difference was seen

between the baseline FEV1% and 12 months follow-up FEV1% in BODE 3 index.

Thus, we conclude that no statistical difference could be seen between the baseline and follow-up mean values of FEV1% in all three BODE index.
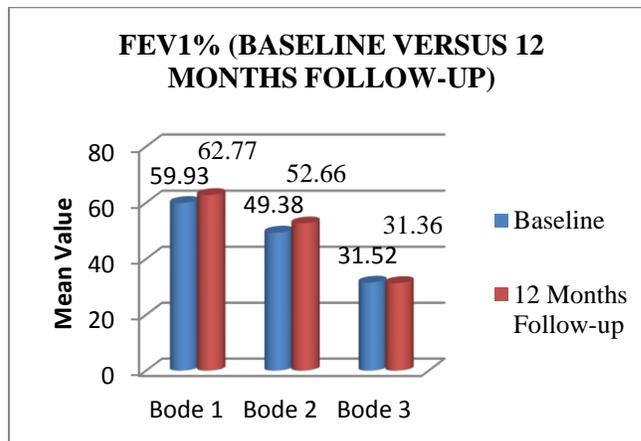

Figure 4:FEV1% (Baseline versus 12 months follow up)

Discussion:

In our study we found that maximum number of patients belong to agegroup 45 to 64 years and maximum were under BODE 3 category, reason behind this is as the age increases there is physiological decline in lung function (FEV1) along with exposure to other risk factor for COPD.

So our study showed as the age increases severity of COPD also increases (p = 0.034) and we can predict severity of COPD based on higher BODE index.

C. Raherisonet al[7] found that the majority of the studies (62%) concerned patients over 40 yrs of age, in particular those aged between 40 and 64 yrs.

Postma ds et al found that the prevalence of COPD increases with age, with a five-fold increased risk for those aged over 65 yrs compared with patients aged less than 40 yrs[8].

In our study majority of patients were male (90%) and only 10% were female.

We found that majority of our patients comes under moderate to severe dyspnea based on MMRC dyspnea score .We observed that in our study higher the MMRC grade, higher the BODE index and more severe is COPD.(P=0.001).So we can predict severity of COPD based on MMRC grading.

R.R.Hegde et al found that a highly significant inverse correlation was found between MMRC scale of dyspnea and FEV1%, i.e. as the scale of dyspnea increases, the FEV1 decreases [9].

The degree of dyspnea was measured with the modified Medical Research Council (mMRC) dyspnea scale, which correlates well with the prognosis of COPD [10].

In our study we have got 45% patients underweight. So COPD is more prevalent in underweight patients.Nutritional depletion is a frequent finding among patients with COPD, in particular those with advanced disease.

Landbo et al [11] found BMI to be an independent predictor of all-cause and respiratory mortality among COPD patients with and FEV1 < 50% predicted in the Copenhagen City study.

Most of the patients in our study according to Gold criteria were under moderate to severe COPD. Lisette van den Bemt et al found that, 76% of the patients with COPD were classified as mild to moderate COPD according to airflow obstruction criteria, which is comparable to the findings of Hoogendoorn (82%) [12].

In our study we found that baseline BODE index related FEV1 was, in BODE 1 mean FEV1 was 60.93 while in BODE 3 it was 31.76 . So we concluded that as the baseline BODE index severity increases FEV1 progressively decline .**(P = 0.0001)**

The landmark study of Fletcher and Peto[13]identified a relationship between airflow obstruction and survival in a study of over 850 of 2700 British men the investigators found that in patients with COPD, the risk of death was significantly associated with the initial value of measured FEV1.

On a single visit assessment of BODE index after patient stabilization,we found that higher the BODE index less is the distance covered by patients in 6 minute walk test exercise.(p=0.0001)

The results found by Pitta et al [14] which have demonstrated that the reduced distance walked in the 6MWT was the best marker of the inactivity during the daily life of patients with COPD.

In our study we found that as the BODE index increases there is decline in FEV1/FVC ratio. (**P = 0.0001**)

We have tried follow up of all the patients on 6 months and on 12 months, included in study but due to practical issue could make it possible for only 51 patients. Majority of patients lost follow up due to staying far from hospital, few improved symptomatically n lost follow up and others due to unknown reason.

After the 1 year follow up of 51 patients we found that compare with baseline BODE index, as the BODE index increases severity of COPD increases.

So we have got interpretation that base line BODE index is associated with follow up BODE index (p=0.001) . Base line BODE index predicts the future outcome in COPD patients. The results of our study indicated that the BODE index is a much better predictor of mortality than any of the individual variables alone.

Claudia G. Cote, Bartolome R. Celli et al[15] prospectively validated BODE index in a separate cohort of 625 predominantly male patients with COPD who were evaluated every 6 months for at least 2 years, or until death. They found that each quartile increase in the BODE Index score yielded an increase in the risk for mortality. Those patients with a BODE index in the quartile 4 (BODE Index score of 7 to 10) had a mortality rate of 80% at 52 months.

We observe mean distance by 6 minute walk test after 12 month follow up was improved in baseline BODE 2 (p=0.003) and baseline BODE 3 (0.012) due to their regular follow up and on continuous inhaler therapy. (anticholinergic or LABA or ICS) Baseline BODE 1 patients were not having significant improvement in mean distance after 12 month follow up.(p=0.099)

After 12 months of follow up, predicted FEV1 alone was not a proven criteria to define COPD severity. So neither of the baseline BODE index was significantly associated with predicted FEV1 value. (p=0.276)

Imfeld [16] and colleagues tested the predictive value of the change in BODE they found that the ability of the BODE index was able to predict the risk of death (0.74), better thanthe FEV1 (0.63).

Claudia G. Cote, Bartolome R. Celli In a study assessing the impact of exacerbations on several patient-centered outcomes [15] and BODE, this multidimensional index proved to be a more sensitive tool than FEV1 alone to reflect progression of disease over a 2 year follow up period.

Limitations:

Data are not available for BODE index and Epidemiological factor correlation so need more study to establish relation.

Follow up of all patient was a limiting factorin our study as number of follow up patients decreased.

Our Studypopulation was restricted by various exclusion criteria and by the willingness of patients to participate in this study.

Conclusion:

BODE index is a good predictor of COPD severity than FEVI alone.Six minute walk test is a better way of reflecting daily physiological activity and predictor of disease severity.Follow up of a COPD patient is must to assess disease severity and to control

disease progression.Besides its excellent predictive power with regard to outcome, the BODE index is simple to calculate and requires no special equipment. This makes it a practical tool of potentially widespread applicability.We strongly recommend the calculation of BODE Index atleast every 3 months in a COPD patient.

Acknowledgements:

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