STUDY OF BODE INDEX AND ITS COMPONENTS WITH PO2 AND PCO2 IN PATIENTS WITH COPD.

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Abstract

Chronic obstructive pulmonary disease is a disorder characterized by persistent airflow obstruction which is not fully reversible. The Body Mass Index, Airflow Obstruction, Dyspnea, Exercise Capacity - BODE Index was shown to be better than FEV1 at predicting risk of death among COPD patients. Increase in dead space and abnormalities in ventilation and perfusion impair oxygen uptake and carbon dioxide elimination in patients with COPD. This study aims to find an association between the BODE index, its components and PO2 and PCO2. Diagnosed cases of COPD were included in the study. All patients included were informed about the study protocol and a valid informed consent was taken. They underwent history taking, thorough clinical examination, Pulmonary Function tests, 6MWT and arterial blood gas analysis. Relation between BODE index and PO2 and PCO2 was more significant than relationship between FEV1 and PO2 and PCO2. Diagnosed cases of COPD were included in the study. All patients included were informed about the study protocol and a valid informed consent was taken. They underwent history taking, thorough clinical examination, Pulmonary Function tests, 6MWT and arterial blood gas analysis. Relation between BODE index and PO2 and PCO2 was more significant than relationship between FEV1 and PO2 and PCO2. Similarly, there was a positive correlation between 6MWD and PO2 and inverse correlation between 6MWD and PCO2. For dyspnea, there was a strong positive correlation with PO2 but only weak inverse correlation with PCO2. BMI had no significant correlation either with PO2 or PCO2. Multidimensional BODE index correlated best with oxygen uptake and carbon-dioxide elimination as compared to any of its components.

Introduction: -

Chronic obstructive pulmonary disease is a disorder characterized by persistent airflow obstruction which is not fully reversible and associated with abnormal inflammatory response to noxious particles and gases1. The Spirometry derived parameter of FEV1 is simple and valid measurement of the degree of airflow obstruction and is often used as a surrogate for disease severity. COPD is a complex multidimensional disease and using degree of airflow obstruction alone to predict outcome has limitations. FEV1 is known to correlate poorly with patient’s symptoms2.

The Body mass index, Airflowobstruction, Dyspnea, Exercise capacity - BODE INDEX - was shown to be better than FEV1 at predicting risk of death among patients with COPD3. This multistage scoring system provides useful

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The effects of COPD on lung gas exchange are complex. The abnormalities in lung gas exchange for O\textsubscript{2} and CO\textsubscript{2} (i.e., increased dead-space volume and alveolar-arterial O\textsubscript{2} gradient) require greater than normal levels of ventilation to maintain Eucapnia and Euoxia. Therefore, measurement of arterial blood gases is essential in patients with COPD to confirm degree of hypoxemia and hypercapnea. In patients with chronic airways obstruction, life expectancy is strongly dependent on the severity of blood gas abnormalities\textsuperscript{4}. When significant hypoxemia and hypercapnea are present, a majority of patients will die in a few years. Most commonly, PO\textsubscript{2} is the measurement used to assess the effect of respiratory disease on oxygenation of arterial blood. The adequacy of CO\textsubscript{2} elimination is measured by the partial pressure of CO\textsubscript{2} in arterial blood, i.e., PCO\textsubscript{2}. There is broad relationship between Spirometry and blood gases in patients with COPD where PaCO\textsubscript{2} rises when FEV1 falls below 1.5L\textsuperscript{5}. This study aims to find out correlation of BODE index with PO\textsubscript{2} and PCO\textsubscript{2} in patients with COPD.

Materials and Methods: -
Adult patients diagnosed with COPD as per the GOLD guidelines were included in this study. The patients included in the study did not have any other Respiratory or known systemic co-morbidities. All the patients underwent detailed history taking and clinical examination. All patients underwent Spirometry, 6 MWT and ABG analysis.

Patient’s body mass index was calculated using formula:
Weight (kg)/height (meter)\textsuperscript{2}.

Grade of dyspnea was classified as per Modified Medical Research Council Questionnaire.

The Six minute walk test was performed as per guidelines of ATS\textsuperscript{7}. The BODE score was calculated as per Table1\textsuperscript{3}.

Results: -
The study included 50 COPD patients out of which 43(86\%) were males and 7(14\%) females. Mean age of the study group was 56.78 years. All patients were above 30 year and maximum (64 \%) were in 50-70 years age group (Table 2).

Most of patients were with severe (50\%) and very severe (22\%) stage of COPD.
46\% patients had BMI greater than 21 kg/m\textsuperscript{2} and 54\% of the patients were with BMI less than or equal to 21kg/m\textsuperscript{2}.

Most of the patients had Grade I (48\%) or Grade II (44\%) dyspnea.
Most patients 35 (70\%) were with FEV1 less than 50 (Percentage predicted). Mean FEV1 for patient group was 43.94 ±19.83.

Mean six minute walk test distance of the study group was 329.52±96.18. One patient was unable to complete the test due to dyspnea and distance covered was less than 149 m.

BODE Index was categorized into four quartiles\textsuperscript{3}.
Mean BODE Index of the study group was 3.76±1.93.

Mean PO\textsubscript{2} was 71.976±12.71mmHg. Applying Pearson’s correlation test, there was inverse correlation between BODE index and PO2 and it was statistically significant (r = -0.782, P < 0.001). (Table 3, Figure 1)
The mean PCO\textsubscript{2} of patients was 39.67±7.25 mmHg. On applying Pearson’s correlation test, there was a positive correlation between BODE index and PCO2 and was statistically most significant (r=0.570, P < 0.001). (Table 4, Figure 2)

The mean FEV1 of patients was 43.94±19.83(% Predicted). Applying Pearson’s correlation test, there was positive correlation between FEV1 and PO2 and was statistically most significant (r = 0.695, P < 0.001) (Table 5).

Applying Pearson’s correlation test, there was inverse correlation between FEV1 and PCO2 and statistically most significant(r = -0.476, P < 0.001) (Table 6).

The mean 6MWT distance covered was 329.52 ±96.18 m.Applying Pearson’s correlation test, there was positive correlation between 6MWD(distance walked in 6 minutes) and PO2 and it was statistically significant (r = 0.611, P < 0.001) (Table 7).
Applying Pearson’s correlation test, there was inverse correlation between 6MWT (distance walked in six minutes) and PCO2 and it was statistically significant \((r = -0.351, P < 0.05)\) (Table 8).

The correlation between grades of dyspnea and PO2 and PCO2 was also studied. It was found that there was inverse correlation between grades of dyspnea and PO2 \((r = 0.62, p<0.0001)\), and direct but weak correlation between Grade of dyspnea and PCO2 \((r=0.25p=0.07)\) (Table 9).

Finally, the correlation between body mass index and PO2 and PCO2 was also studied. There was no significant correlation either with PO2 \((p=0.288)\) or PCO2 \((p=0.998)\) (Table 9).

**Discussion:**

The diagnosis of COPD, classification of its severity, and progression of the disease can be monitored with Spirometry- a simple, non-invasive, and inexpensive test. The FEV1/FVC ratio, reflecting the rate of emptying of the lung, is used to define the presence of an obstructive ventilatory defect, commonly defined as a ratio less than 0.70. Once airflow obstruction is established, the severity of the disease is classified by the reduction of FEV1 compared with a healthy reference population.

After COPD becomes clinically apparent, the median survival is about 10 years. The prognosis of COPD varies widely. This is because the disease has widely varying rates of progression and because death is often due to susceptibility to inter-current illness and other smoking related Illnesses such as lung cancer rather than progressive respiratory failure.

Several factors have been identified that predict poor survival in COPD. These include low FEV1, active smoking status, hypoxemia, poor nutrition, the presence of Cor pulmonale, resting tachycardia, low exercise capacity, severe Dyspnea, poor health-related quality of life, Anemia, frequent exacerbations, co-morbid illnesses, and low carbon monoxide diffusing capacity.

A multidimensional prognostic index that takes into account several indicators of COPD prognosis is the BODE index, which includes body mass index, obstructive ventilator defect severity, dyspnea severity, and exercise capacity. A BODE score greater than 7 is associated with a 30 percent 2-year mortality; whereas a score of 5 to 6 is associated with 15 percent 2-year mortality. If the BODE score is less than 5, the 2-year mortality is less than 10 percent.

Measuring PaO2 and PaCO2 is the most important factor to determine the severity of COPD and draw an appropriate therapeutic approach. Patients in stable conditions can be expected on average to have an increased alveolar-arterial gradient for oxygen and a decrease in PaO2 due to the disease itself, and therefore to have lower PaO2 than comparable persons with healthy lungs. The worse the obstruction, the lower the oxygen and carbon dioxide exchange. In these patients, life expectancy is strongly dependent on the severity of blood gas abnormalities. When significant hypoxemia and hypercapnia are present, majority of patients will die in a few years. The natural history of such patients in the later stages of disease, as PaCO2 begins to rise, is that FEV1 declines steadily and PaO2 declines slowly at first, then rather rapidly shortly before the patient dies.

Classification schemes that incorporate more parameters than degree of airflow obstruction are likely to predict outcome more accurately (Rennard 2004). It has been shown that - BODE INDEX to be better than FEV1 at predicting risk of death among patients with COPD (Celli et al 2004).

We have studied the correlation between BODE Index and severity of blood gas abnormalities (PO2 and PCO2) as derangements in these will spell a poorer prognosis. There is strong correlation between BODE Index and PO2 \((r = -0.782, P < 0.001)\) which is in inverse relation. There is also strong correlation between BODE Index and PCO2 \((r = 0.570, P < 0.001)\) which is positive. A study was carried out by Mansour RahimiFard et al to study relationship between FEV1 and PO2, PCO2 in patients with COPD. The study concluded that a reliable equation could be established indicating a correlation between FEV1 and PO2 as well as PCO2 in patient with chronic bronchitis. In this study, they found that FEV1 had positive correlation with PO2 \((r = 0.418, p<0.0001)\) inverse correlation with PaCO2 \((r = -0.533, p<0.0001)\). In a study conducted by B. Delclaux et al, there were significant correlations between blood gases and Spirometric parameters. PaO2 was positively correlated to FEV1 \((r=0.268, p<0.001)\). PaCO2 was negatively correlated to FEV1 \((r=0.358, p<0.001)\). In patients with more severe impairment in blood
gases (PaO₂<60mmHg or PaCO₂ ≥45mmHg) there was no correlation between FEV1 and PaCO₂, and PaO₂ was positively but weakly correlated to FEV1 (r=0.14; p<0.05).

In our study, we found that there was a strong positive correlation between FEV1 and PO₂ (r = 0.695, P < 0.001) and inverse correlation with PCO₂ (r = -0.476, P < 0.001). This suggests that the more the obstruction, the lower the oxygenation and greater the hypercapnia.

Six-minute–walk test predictsthe risk of death in patients with COPD. A study was conducted by V H F Mak et al to study the effect of arterial oxygen desaturation on Six minute walk distance, perceived effort, and perceived breathlessness in patients with airflow limitation. In this study, they found that baseline saturation before the walk correlated significantly with distance walked (0.32, p < 0.01). In our study, we found that there is positive correlation between 6MWT and PO₂ and which is statistically significant (r = 0.611, P < 0.001) and there is negative significant correlation between 6MWT and PCO₂ (r = -0.351, P < 0.05).

Dyspnea represents the most disabling symptom of COPD; the degree of dyspnea provides information regarding the patient's perception of illness and can be measured. Nishimura K et al conducted a study in which they followed a large cohort of patients with COPD, in which they used the threshold values included in the BODE index, they found the score on the MMRC dyspnea scale was a better predictor of the risk of death than was the FEV₁. In this study, patients were grouped on the grades of dyspnea and it was found that there were significant differences in PO₂ and PCO₂ between the groups. In our study, there was strong inverse correlation between dyspnea and PO₂ (r=0.62, p<0.0001), and positive but weak correlation between dyspnea and PCO₂ (r=0.25, p=0.07).

There was no significant correlation of Body Mass Index with either with PO₂ (p=0.288) or PCO₂ (p=0.998).

The study thus suggests that relationship between BODE index and PO₂ and PCO₂ is more significant than relationship between FEV₁ and PO₂ and PCO₂. It has been shown that FEV₁ does not adequately reflect all the systemic manifestations of the disease. For example, the FEV₁ correlates weakly with the degree of dyspnea and the change in FEV₁ does not reflect the rate of decline in patients' health. BODE Index, thus better correlates with arterial blood gas changes.

To conclude, BODE index relates more significantly with the oxygenation status of the patient than its individual components including FEV₁.

Multidimensional BODE Index can be considered as a better index for reflecting arterial blood gas changes and thus severity of COPD than any other single parameter including FEV1. The study supports the view that the BODE index should be widely used in assessing COPD patients.

Scatter Diagram 1- BODE Index and PO₂
Scatter Diagram 2: BODE index with PCO2

Table 1 - BODE Index

| Variable                        | Points on the BODE Index |
|---------------------------------|--------------------------|
| FEV1 (% predicted)              | 0 | 1 | 2 | 3 |
| Distance walked in 6 min (meters) | >350 | 250-349 | 150-249 | < 149 |
| MMRC dyspnea scale              | 0-1 | 2 | 3 | 4 |
| Body-mass index (kg/M²)         | >21 | <21 |

BODE index was calculated as a sum of all the points from each row.

Table 2 - Age and Sex distribution

| Age group (in years) | Males | Females | Total | Percentage(%) |
|----------------------|-------|---------|-------|---------------|
| 30-40                | 2     | 0       | 2     | 4             |
| 41-50                | 7     | 1       | 8     | 16            |
| 51-60                | 15    | 4       | 19    | 38            |
| 61-70                | 11    | 2       | 13    | 26            |
| 71-80                | 7     | 0       | 7     | 14            |
| 81-90                | 1     | 0       | 1     | 2             |
| Total                | 43(86%) | 7(14%)   | 50    | 100           |

The study included 50 COPD patients out of whom 43 (86%) were males and 7 (14%) females. Mean age was 56.78 years. All patients were above 30 years and 64% were in 50-70 years age group.

Table 3 - Correlation between BODE index and PO2:

| Indices   | N   | Mean   | S.D.    |
|-----------|-----|--------|---------|
| BODE      | 50  | 3.76   | ±1.933  |
| PO2 (mmHg)| 50  | 71.976 | ±12.7147|

(r = -0.782, p < 0.0001)
Table 4- Correlation between BODE index and PCO2:

| Indices | N  | Mean   | S.D.   |
|---------|----|--------|--------|
| BODE    | 50 | 3.76 ±1.933 |
| PCO₂(mmHg) | 50 | 39.670 ±7.2529 |

(r=0.570, p<0.0001)

Table 5- Correlation between FEV1 and PO2:

| Indices | N  | Mean   | S.D.   |
|---------|----|--------|--------|
| FEV1    | 50 | 43.94 ±19.832 |
| PO₂(mmHg) | 50 | 71.976 ±12.7147 |

(r=0.695, p<0.0001)

Table 6- Correlation between FEV1 and PCO2

| Indices | N  | Mean   | S.D.   |
|---------|----|--------|--------|
| FEV1    | 50 | 43.94 ±19.832 |
| PCO₂(mmHg) | 50 | 39.670 ±7.2529 |

(r=-0.476, p<0.0001)

Table 7- Correlation between 6MWT Distance (6MWD) and PO2

| Indices | N  | Mean   | S.D.   |
|---------|----|--------|--------|
| 6MWD(m) | 50 | 329.52 ±96.185 |
| PO₂(mmHg) | 50 | 71.976 ±12.7147 |

(r= 0.611, p<0.0001)

Table 8- Correlation between 6MWT Distance (6MWD) and PCO2

| Indices | N  | Mean   | S.D.   |
|---------|----|--------|--------|
| 6MWD    | 50 | 329.52 ±96.185 |
| PCO₂(mmHg) | 50 | 39.670 ±7.2529 |

(r=-0.351, p=0.01)

Table 9- Consolidated Significance Table

| Parameters                  | Correlation | Significance                  |
|-----------------------------|-------------|-------------------------------|
| BODE index and PO2          | Inverse     | Statistically significant     |
|                             |             | (r = -0.782, p<0.001).       |
| BODE index and PCO2         | Positive    | Statistically significant     |
|                             |             | (r=0.570, p<0.001).          |
| FEV1 and PO2                | Positive    | Statistically significant     |
|                             |             | (r = 0.695, p < 0.001)       |
| FEV1 and PCO2               | Inverse     | Statistically significant     |
|                             |             | (r = -0.476, p < 0.001).     |
| 6MWT distance and PO2       | Positive    | Statistically significant     |
|                             |             | (r = 0.611, p < 0.001)       |
| 6MWT distance and PCO2      | Inverse     | Statistically significant     |
|                             |             | (r = -0.351, p < 0.05).      |
| Grades of dyspnea and PO2   | Inverse     | Statistically significant     |
|                             |             | (r=0.62, p<0.0001).         |
| Grades of dyspnea and PCO₂  | Weak positive | Weak correlation             |
|                             |             | (r=0.25, p=0.07).           |
| Body mass index and PO₂     | Not significant | Statistically not significant |
|                             |             | (p=0.288)                   |
DECLARATION OF INTEREST: None

List of Figures:
Figure 1: Scatter Diagram with BODE Index and PO2
Figure 2: Scatter Diagram with BODE Index and PCO2

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