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Original Research Article

CORRELATION BETWEEN BODE INDEX AND CRP LEVELS AS A SYSTEMIC INFLAMMATION MARKER IN COPD PATIENTS

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Abstract

Introduction: COPD is characterised by an incomplete or partially reversible airflow limitation. FEV1 is often used to grade the severity of COPD. Systemic inflammation is now known to exist in COPD, leading to various consequences that the BODE index is a multi-dimensional tool taking into account BMI (B), severity of obstruction (O), dyspnoea grading (D), and exercise tolerance (E) as measured by 6MWT is used to assess the severity of COPD. Hence, this study was undertaken to evaluate the correlation of the BODE Index with the development of Pulmonary hypertension, the number of Exacerbations and Systemic inflammation in COPD. **Material and methods:** This prospective study was conducted in Respiratory Medicine OPD patients. 60 patients diagnosed with COPD (clinically, radiological, spirometry) were taken into the study, and comorbidities were excluded. The BODE index was calculated using four parameters, and ECHO was done to assess PH. C-reactive protein was evaluated for systemic inflammation. **Results:** Out of 60 patients enrolled in the study, BODE index severity was Mild in 17 (28.3%), Moderate in 25 (41.6%) and Severe in 18 (30%). The incidence of PH is 48.3%, which showed a significant correlation with the BODE index's severity. Approximately 56% of patients had more than three exacerbations per year, which correlated with the severity of the BODE index. CRP was positive in 35% of patients, significantly correlating with BODE index severity. **Conclusion:** Our study shows that the BODE index used as a multi-dimensional tool in assessing COPD significantly correlated with the development of PH, number of exacerbations, and CRP.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) has emerged as a significant contributor to morbidity and mortality in the adult population, currently ranking as the fourth leading cause of death globally.[1] This escalating health challenge is marked by a rising mortality rate,[2,3] and stands out as the leading cause of death with a growing prevalence worldwide. It is anticipated that by 2020, COPD will become the third leading cause of death among adults, as projected by a World Health Organization study.[4] The burden of this disease places a substantial strain on global healthcare resources, with treatment and assessment costs intricately tied to both pulmonary and extrapulmonary components of the condition.[3]
"Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease with some

significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterised by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases".[4] COPD was traditionally perceived as primarily involving pulmonary inflammation and structural remodelling. Nevertheless, recent insights have highlighted COPD as a complex disorder encompassing pulmonary issues, systemic inflammation, and extrapulmonary manifestations.
The systemic dimensions of COPD encompass oxidative stress, changes in circulating levels of inflammatory mediators, and variations in acute phase proteins. While local airways and lung parenchyma inflammation have long been recognised as integral to the COPD disease process,

it is increasingly evident that the inflammatory response extends throughout the body.[5] The severity of COPD is commonly assessed using a single physiological variable: forced expiratory volume in one second (FEV1).[6] However, this approach often fails to capture the systemic manifestations present in COPD patients. The BODE index was developed as a multi-dimensional grading system to evaluate COPD's respiratory and systemic aspects and predict patient outcomes to address this limitation. The BODE index takes into account four key factors: body-mass index (B), degree of airflow obstruction (O), dyspnea (D), and exercise capacity (E), determined through the six-minute walk test. These variables are utilised to construct the BODE index, a comprehensive 10-point scale with higher scores indicating a greater mortality risk.[6]

The study aimed to analyse the correlation between the BODE Index and the development of pulmonary hypertension, the frequency of exacerbations, and systemic inflammation in individuals with COPD.

MATERIALS AND METHODS

This prospective cross-sectional study involved 60 clinically confirmed COPD patients who attended our outpatient clinic. They were enrolled after providing written and oral consent, adhering to the inclusion and exclusion criteria outlined in the GOLD guidelines, and with approval from the Institutional Ethical Committee.

Each patient's detailed history was documented, including smoking habits, personal and family medical backgrounds, and a comprehensive account of their dyspnea. Dyspnea severity was assessed using the MMRC dyspnea scale. Patient records were examined to determine the frequency of outpatient visits due to exacerbations within one year. The six-minute walk test, conducted according to standard guidelines, involved patients walking as far as possible on level ground within six minutes, including any rest intervals.

Height and weight measurements were taken during the spirometry procedure, which was carried out using the 'KOKO legend' desktop spirometer (model no. 314000), meeting the American Thoracic Society's performance criteria. Spirometry was conducted 20 minutes after administering Salbutamol (2.5mg) nebulisation for reversibility assessment. The following parameters were recorded: FVC, FEV1, FEV1/FVC, FEF25-75%, and PEFR.

The procedure was repeated three times, and the average values were utilised. Factors such as body mass index, FEV1%, the distance covered in the six-minute walk test, and the modified Medical Research Council (MMRC) dyspnea scale score were considered to calculate the BODE index for each patient. Patients received scores ranging from 0 (lowest) to 3 (highest). Additionally, CRP levels

were determined using a standard kit method. All the data were entered into MS Excel and expressed as a pie chart.

RESULTS

Age-wise distribution of the study population

Most patients were 61 or older (58.33%), with 26.6% in the 51 to 60 age group, 11.6% in the 40 to 50 age group, and none below 40 years old. The majority of the study population was male, with 56 patients (93.3%), when compared to the female population, with only four patients (6.6%). [Figure 1]
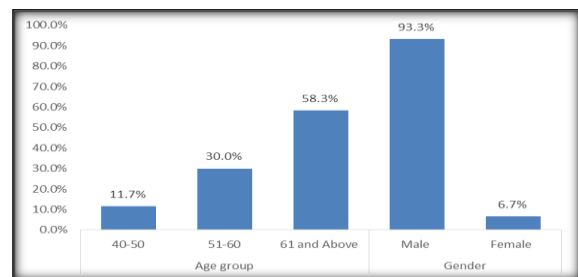

Figure 1: Distribution of age and gender

Out of the 60 COPD patients, 28.3% had Mild COPD (0-2), 41.6% had Moderate COPD (3-5), and 30% had Severe COPD (>6), with the majority falling into the Moderate COPD category. [Figure 2]
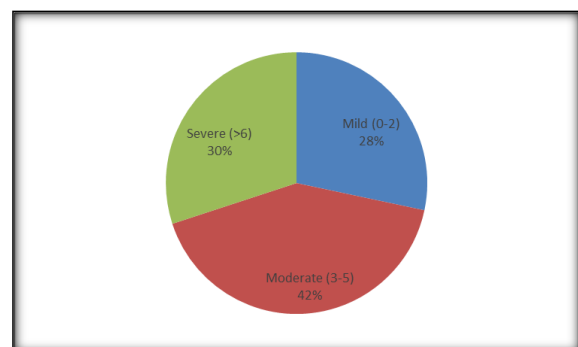

Figure 2: Distribution of COPD

48.33% had elevated pulmonary arterial pressure, with 17.64% in Mild COPD, 40% in Moderate COPD, and 88.8% in Severe COPD. Pulmonary hypertension development was positively correlated with the BODE severity scale (p=0.0001). [Figure 3]
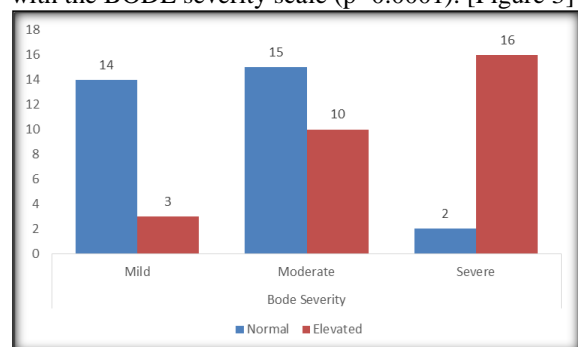

Figure 3: Distribution of BODE severity scale

17.64% of Mild COPD patients developed pulmonary hypertension, with 2 having a mild degree and one having a moderate degree. Among Moderate COPD patients, 40% developed pulmonary hypertension, with 8 having a mild degree and 2 having a moderate degree. In the Severe COPD group, 88.8% developed pulmonary hypertension, with 6 having a mild degree, 6 having a moderate degree, and 4 having a severe degree. No Mild and Moderate COPD group patients developed severe pulmonary hypertension [Figure 4]
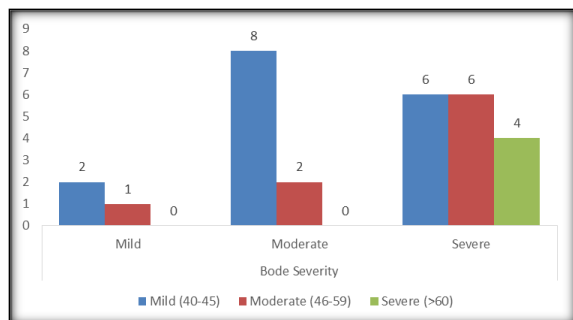

Figure 4: Distribution of COPD patients who developed pulmonary hypertension

Severity of BODE index with CRP status

C C-reactive protein (CRP) was positive in 35% of the 60 patients, with 72.2% in Severe COPD, 28% in Moderate, and 6.25% in Mild COPD. CRP positively correlated with the BODE index (p=0.0001). [Figure 5]
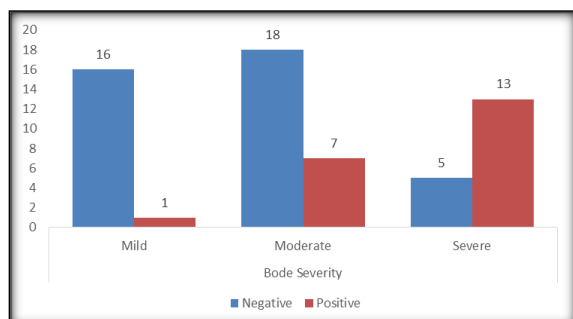

Figure 5: Distribution of Severity of BODE index with CRP status

DISCUSSION

COPD is anticipated to become one of the most prevalent and deadly diseases, affecting a substantial portion of the population by 2020. It stands out as the sole leading cause of death that is on the rise worldwide. COPD, a multifaceted condition, requires classification systems that consider more factors than the degree of airflow obstruction to predict outcomes accurately. FEV1, a common parameter, has a limited correlation with symptoms, quality of life, exacerbation frequency, and exercise tolerance.

In light of these limitations, researchers introduced the BODE index, intended to surpass the FEV1-based severity classification system. This multifaceted scoring system, employed in our study, includes variables that can be easily assessed in various healthcare settings, making the BODE index widely applicable, akin to FEV1. What lends credence to adopting this new classification system is its capacity to offer more valuable prognostic insights than FEV1 alone. Extensive evidence supports that the multi-dimensional staging system of the BODE index is a superior predictor of mortality risk in COPD patients, outperforming the FEV1-based staging system as endorsed by the ATS.

Celli et al,[6] and Agusti AG et al,[7] studies highlighted the predictive utility of the BODE index in forecasting mortality and hospitalisation among COPD patients. In our research, we employed the BODE index to assess the development of pulmonary hypertension, exacerbation frequency over a year, and systemic involvement.

Our findings revealed that most patients fell within the age group over 61 years (58.33%), followed by 29.6% in the 51 to 60-year range, and with only 11.6% aged 41 to 50. Notably, Severe COPD (15 out of 18) and Moderate (13 out of 25) were more common in the over-61 age group, which likely relates to COPD progression with age. This aligns with studies by Celli et al,[6] and Sharma et al,[8] which show an age-related increase in the BODE score.

Our study demonstrated a male predominance (93.3%) among the patient population, with only 6.6% female. We categorised COPD patients into three groups based on the BODE score (0-2, 3-5, and >6), as Celli et al,[6] demonstrated that this classification correlates well with severity in terms of hospitalisation and mortality. Our population primarily comprised Moderate COPD (25 patients), followed by Severe COPD (18 patients) and Mild COPD (17 patients).

Pulmonary hypertension secondary to COPD belongs to group 3 of the WHO classification of PH, and our study showed a total incidence of 48.3% of PH among COPD patients, with a higher proportion in Severe COPD (88.8%) and Moderate COPD (40%). A positive correlation (p=0.0001) was observed between the BODE index and the development of pulmonary hypertension. Severe COPD patients faced a higher risk of pulmonary hypertension and reduced survival. Most patients had Mild to Moderate pulmonary hypertension (40-60 mmHg), consistent with prior studies.

Incorporating C-reactive protein (CRP) as a marker of systemic inflammation, our study detected CRP positivity in 21 patients (35%). CRP elevation was most common in Severe COPD (72.2%), followed by Moderate COPD (28%), with only one patient in Mild COPD having CRP positivity. This aligns with studies by Karadag F,[9] and Cirillo et al,[6] demonstrating a significant (p=0.0001) association between COPD severity and CRP positivity. This suggests an underlying chronic inflammation in severe COPD.

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Innovatively, our study explored the correlation between the number of annual exacerbations and the BODE index. We found that a higher exacerbation rate was associated with severe COPD and airflow obstruction, reinforcing that increased exacerbations contribute to mortality and decreased survival in COPD patients.

Smoking's well-established link to COPD and accelerated lung function decline was supported by our findings, which showed that patients with higher smoking pack years had more severe COPD and systemic inflammation. Quitting smoking was found to slow the decline in lung function. Smoking is a significant risk factor for other diseases, including atherosclerotic vascular disease, cancer, peptic ulcer, and osteoporosis.

CONCLUSION

Our study demonstrates that the BODE index, employed as a multi-dimensional assessment tool for COPD, strongly correlates with the emergence of pulmonary hypertension, frequency of exacerbations, and CRP levels.

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