Left ventricular diastolic dysfunction in patients with chronic obstructive pulmonary disease (COPD), and its association with disease severity

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Abstract: Introduction: Chronic obstructive pulmonary disease (COPD) exacerbation is a frequent cause of hospital admissions. In one-third of patients, exacerbations have no known cause. We studied whether the presence of diastolic dysfunction (DD) in this subgroup of patients is associated with longer duration of hospitalization and more frequent exacerbations. Methods: 89 patients with COPD exacerbation, 67 with Diastolic dysfunction, and 22 with normal diastolic function hospitalized for acute COPD exacerbation between April 2017 and May 2018 were included in the study. Diastolic dysfunction was defined by the presence of relaxation, filling, or distensibility abnormalities of the left ventricle on transthoracic echocardiogram. Results: patients with severe stages of COPD had advanced stage of LV Diastolic dysfunction contributing to their symptomatology. Conclusion: Patients with COPD should undergo ECHO routinely to assess LV Diastolic Dysfunction which will help to improve the management of COPD.

Keywords: COPD, Diastolic dysfunction, COPD Exacerbation, Pulmonary Artery Pressure

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I. Introduction

Chronic obstructive pulmonary disease (COPD) exacerbation is a frequent cause of hospital admissions, characterized by acute deterioration in baseline dyspnea, cough, or sputum beyond normal daily variations.[1–4]. The most common causes of COPD exacerbation are infection of the tracheobronchial tree and air pollution; however, in one-third of cases, the cause remains unknown.[3,4].

Diastolic dysfunction (DD) is a functional abnormality of diastolic relaxation, filling, or distensibility of the left ventricle (LV) regardless of LV systolic function.5-6 It is frequently diagnosed in older adults, obese individuals, and those with ischemic heart disease, diabetes, and hypertension.[5-6]. Unfortunately, symptoms of COPD and diastolic heart failure are often similar and difficult to differentiate, and few studies have investigated the relationship between DD and COPD exacerbations among COPD patients.7 In this study, we wanted to see if coexistent LVDD is contributing to the longer hospital stay of COPD patients.

II. Methods

This study was conducted in a tertiary care center in Government Tiruvannamalai Medical College Hospital, Tiruvannamalai, India from June 2017 to May 2018. Patients hospitalised with a diagnosis of COPD exacerbation were included in the study. They were classified into various stages according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines[2]. Patients with valvular heart disease, ischemic heart disease, cardiomyopathy, reduced LV systolic function, hypertension, diabetes mellitus and rheumatic heart disease were excluded.

III. Procedure

The COPD diagnosed cases, as per GOLD guidelines, were counseled for the study, and those who gave written informed consent were included in the study. Baseline and demographic characteristics were collected for all the patients. The patients were subjected to pulmonary function tests and echocardiogram (ECHO) to stage the severity of COPD and for cardiac evaluation. Pulmonary function test was carried out using RMS Helios 702 spirometer, and forced expiratory volume in the 1 s (FEV1), forced vital capacity (FVC), and FEV1/FVC ratios were recorded to stage COPD.[2] Standard two-dimensional (2D) ECHO was carried out with ESOATE MY
LAB 40 Cardiac Ultrasound System to measure systolic and diastolic LV dimensions and for the calculation of LV fractional shortening. The measurements of interventricular septum thickness were also taken.

III. 1. Diastolic dysfunction

Diastolic flow from the left atrium and left ventricle across the mitral valve has two components: E wave, early diastolic filling and A wave, atrial contraction. In late diastole, E wave velocity is influenced by both the rate of early diastolic relaxation and the left atrial pressure. An alteration in the pattern of E wave velocity reflects the degree of LV diastolic dysfunction and prognosis. The peak velocity of blood flow across the mitral valve during early diastolic filling corresponds to the E wave. Similarly, atrial contraction corresponds to the A wave. From these findings, the early to late (E/A) ratio was calculated. Under normal conditions, E is greater than A and the E/A ratio is approximately 1.5 m/s. In early diastolic dysfunction, relaxation is impaired and with vigorous atrial contraction, the E/A ratio decreases to less than 0.75 m/s. As the disease progresses, LV compliance is reduced, which increases left atrial pressure and in turn, increases early LV filling despite impaired relaxation. This paradoxical normalization of the E/A ratio is called pseudonormalization. In patients with severe diastolic dysfunction, LV filling occurs primarily in early diastole, creating an E/A ratio greater than 2.0 m/s. LV ejection fraction more than 50% was taken as normal LV Systolic function.

III. 2. Grading of diastolic dysfunction (or diastolic filling pattern)

Grade 1 (mild dysfunction): Mitral E velocity is decreased and A velocity is increased, producing an E/A ratio of less than 0.75 m/s. Grade 2 (moderate dysfunction): As diastolic function worsens, the mitral inflow pattern goes through a phase resembling a normal diastolic filling pattern, that is, an E/A ratio of 1-1.5 m/s and normal deceleration time (DT) (160-240 ms). Grade 3 and grade 4 (severe irreversible dysfunction): Restrictive filling with severe diastolic dysfunction is characterized by increased E velocity and decreased A velocity with an E/A ratio higher than 2 m/s.

IV. Statistical analysis

All analyses within the groups were carried out using SPSS computer software (SPSS version 13.0 SPSS). Data were analyzed by chi-square (X2) test and logistic regression analysis.

V. Results

A total of 89 patients were included in the study. Of which 56 (62%) were males and 33 (38%) were females. The average age of males was 73yrs and females was 67 years. Of the total, 58 (65%) persons were smokers. Of the 58 members 20 members had more than 10yrs of smoking and 36 members had more than 5 yrs of smoking.

Of the 89 patients who had COPD, 67 (75%) patients had associated LV Diastolic Dysfunction and 22 (25%) patients had no diastolic dysfunction. 48 (53%) patients had elevated Pulmonary artery pressure and 41 (46%) patients had normal pulmonary artery pressures. Of the elevated 48 patients with increased pulmonary artery pressures, 43 (89%) had LV diastolic dysfunction and 29 (70%) of the normal pulmonary artery pressure group had LV diastolic dysfunction.

Comparison was done between the groups of stages I,II COPD and stages III,IV with Grade IV LV diastolic dysfunction. It showed that the more severe the COPD, the more severe is the LVDD, which has a statistical significance.

Comparison between groups with elevated Pulmonary artery pressure and Normal pulmonary artery pressure with LV Diastolic dysfunction was also done. It shows that LVDD was more prevalent among patients with increased Pulmonary artery pressures and showed a statistical significance.

![Fig 1]
Left ventricular diastolic dysfunction in patients with chronic obstructive pulmonary disease.

Fig 2.

Table 1.

<table>
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Fig 3.

Table 2.

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<th>DD III</th>
<th>DD IV</th>
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<tr>
<td>III</td>
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<td>16</td>
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<td>67</td>
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<td>1</td>
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</table>
Left ventricular diastolic dysfunction in patients with chronic obstructive pulmonary disease..

Fig 4.

COPD STAGE I

- LVDD I
- LVDD II
- LVDD III
- LVDD IV

Fig 5.

COPD STAGE II

- LVDD I
- LVDD II
- LVDD III
- LVDD IV

Fig 6.

COPD STAGE III

- LVDD I
- LVDD II
- LVDD III
- LVDD IV

Fig 7.

COPD STAGE IV

- LVDD I
- LVDD II
- LVDD III
- LVDD IV
Left ventricular diastolic dysfunction in patients with chronic obstructive pulmonary disease...

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This comparison was done between the less severe COPD patients and More severe COPD patients with presence of LVDD; it showed that the more severe the COPD the more severe the LVDD, and also had a statistical significance.[table 5]

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<table>
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VI. Discussion

Cardiovascular disease is a frequent cause of mortality in COPD. Roughly 30% of COPD patients die from a cardiovascular cause [8–13].

The main finding of this study is that LV Diastolic dysfunction contribute to the symptoms of COPD and the more severe the COPD according to the GOLD Classification the more severe is the LVDD. Malerba et al.[12] has observed that the left diastolic dysfunction in COPD to be 65% while in another study, Steinberg et al.[13] observed that diastolic dysfunction to be 78% in COPD patients. Kjaergaard[14] in a cross-sectional study observed that the incidence of diastolic dysfunction increased more sharply with age in women and stated that there was an increased female predominance in diastolic dysfunction. This was not seen in our study.

The mechanisms that might explain the presence of left ventricular diastolic dysfunction in COPD patients are many.

First is chronic hypoxemia leading to intracellular calcium transport disturbances which might result in abnormalities of myocardial relaxation [17,18]. This mechanism usually occurs in severe cases of COPD, grade III and IV as shown in the our study .

Second is the presence of pulmonary hypertension with chronic right ventricular hypertrophy which may develop in COPD patients followed by right ventricle dilatation [19,20]. During early diastole, the ventricular septum displaces toward the left ventricular cavity and the left ventricle becomes distorted from its circular configuration. The severity of left ventricular and septal deformity depends on the transseptal pressure gradient . Thirdly, the presence of emphysema and hyperinflation which has been related to impaired left ventricle filling . This is due to increased intrathoracic pressures which may impair cardiac function by decreasing biventricular preload and increasing left ventricular afterload [24].

In agreement with our results Godoy et al. [23] showed higher prevalence of LVDD among COPD patients which is associated with increased disease severity, but the prevalence was higher 88%, they did not use tissue Doppler which is more accurate in diagnosis of LVDD.

The greater prevalence of LV diastolic dysfunction was observed in stage IV disease (31%) as compared to other stages in the present study. Systemic inflammation may be the biological link between the two, that is, a common tumor necrosis factor-alpha (TNF-α) mediated pathogenesis for these two diseases. Systemic inflammation is now believed to be a contributory factor in the clinical manifestations and natural history of COPD, and is an essential component in diastolic dysfunction.[25]

The study has some limitations. First, the sample size was small. Second, this is a single study center, and hence, the data cannot be generalized for the general population at large. Third, there was no control group in the present study. Further studies are needed to elucidate the specific mechanisms associated with COPD severity and LV diastolic dysfunction.

VII. Conclusion

Hence from this study it can be found that LV diastolic dysfunction do play a role in prolonging the symptoms of COPD esp. severe stages of COPD and it should also be managed in addition to management of COPD.

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It is thus concluded that all patients with COPD should be screened for diastolic dysfunction using echocardiography, which will help in improving the quality of life in these patients and prolong their survival.

Bibliography


