Echocardiographic Evaluation of Patients with Chronic Obstructive Pulmonary Disease and Its Correlation with Disease Severity

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Abstract
The heart and the respiratory system are closely related anatomically and functionally. Dysfunction of one of these systems can influence the function of the other. Cardiovascular comorbidities are the most common comorbidity found in COPD patients. Objectives of the study are to assess the cardiovascular changes secondary to COPD by echocardiography & to find out the correlation between echocardiographic findings and severity of COPD.

Methodology: It was a Hospital based cross-sectional study. Study samples were COPD patients attending the Department of Respiratory medicine during the study period. Patients were selected according to the inclusion and exclusion criteria. Detailed history, general and systemic examination was done. All routine investigations were done as needed. Patients were investigated by spirometry and diagnosed and classified according to GOLD guidelines. Severity of COPD was classified according to GOLD criteria into groups A, B, C or D. All patients were subjected to resting two-dimensional transthoracic echocardiography in Department of Cardiology.

Statistical Procedure: Descriptive statistical tools like frequency, percentage, mean and standard deviation were used. Inferential statistical tools like t test, chi square test and Spearman’s correlation coefficient were used.

Results: Total 144 patients were included. 120 males and 24 females. Out of these 144 patients, 65 patients had no pulmonary hypertension. 53 had mild PH, 12 had moderate PH and 14 had severe PH. Among the other echo findings, left ventricular diastolic dysfunction (47 patients) was the most common. 7 patients had left ventricular systolic dysfunction and 3 patients had left ventricular hypertrophy.

Conclusion: COPD is associated with numerous cardiovascular co morbidities in the North Malabar area of Kerala. Echo is a portable, non-invasive method and accurate method that can act as a valuable tool in the evaluation of COPD patients.

Keywords: Echo Cardiography, COPD, Right Ventricular Function.

Introduction
COPD is associated with numerous systemic co morbidities. The heart and the respiratory system are closely related anatomically and functionally. Dysfunction of one of these systems can influence the function of the other. Cardiovascular co morbidities are hence the most common comorbidity found in COPD patients.
The presence of common risk factors like smoking, age, sex and inactivity can in part explain the close association between COPD and cardiovascular diseases\(^2\). Smoking can induce local inflammatory changes throughout the tracheobronchial tree including the large airways proximally, small airways peripherally, lung parenchyma and pulmonary vasculature. It can also stimulate the haematopoetic system causing the release of polymorphonuclear leukocytes. It also contributes to systemic oxidative stress and dysfunction of the endothelium of peripheral vessels. These systemic effects of smoking also account for the presence of cardiovascular disease in COPD patients\(^3\).

COPD can affect the pulmonary blood vessels, right ventricle and left ventricle. COPD is the most common pulmonary disease resulting in right ventricular dysfunction\(^4\).

Pulmonary hypertension, associated with COPD, is a significant risk factor for hospitalization\(^5\). Echocardiography is portable, non-invasive and accurate method for evaluating the cardiac status. The right ventricular function, right ventricular filling pressure, left ventricular functioning, valvular function and tricuspid regurgitation can be assessed through echocardiography\(^6\). The pulmonary artery pressures obtained through echocardiography is comparable to the values obtained through right heart catheterization\(^7,8\). It aids in rapid and early detection of cardiac dysfunction and thus help in early initiation of treatment. Early recognition of RV dysfunction and initiation of treatment can prolong the survival of COPD patients as most of the increased mortality associated with COPD is due to cardiac involvement\(^9\). Echo can thus serve as a useful aid to reduce mortality and morbidity associated with COPD.

Left ventricular performance is also affected in patients with severe COPD. This may occur due to the effect of hypoxemia and acidosis on LV relaxation, bulging of the interventricular septum or due to concurrent coronary artery disease. Since it also affects the LV stroke volume, LV filling and cardiac output; cor pulmonale can be considered as a generalized cardiomyopathy\(^10\).

Studying the cardiovascular co morbidities in COPD is important because of the implications it may have on the management of these patients\(^11,12\). It may also aid in the risk prediction of cardiovascular diseases in patients with COPD. The present study was done To assess the cardiovascular changes secondary to COPD by echocardiography & To find out the correlation between echocardiographic findings and severity of COPD.

**Methodology**

Study was started after obtaining clearance from the institutional ethical & research committee. This was a hospital based cross-sectional study. Study period was for one year( 1\(^{st}\) March 2016 to 28\(^{th}\) February 2017). Study sample were COPD patients attending Department of Respiratory medicine, Pariyaram medical college during the study period.

**Sample Size** was calculated Using level of significance 5%, allowable error of 5% and p of 10%\(^8\); minimum sample size was calculated as 144 patients.

All Patients diagnosed with COPD through spirometry with post bronchodilator FEV1/FVC < 0.70.\(^1\) were included in the study.

**Exclusion Criteria** were 1) Patients below 40 years of age, 2) Patients with history of chronic lung disease other than COPD, 3)Patients with hypertension, 4)Patients with any primary cardiac disease (congenital heart diseases, valvular heart diseases, coronary artery disease), 5)Patients with any systemic disease that can cause pulmonary hypertension, 6)Patients with poor ECHO window, 7)patients with history of Recent respiratory tract infection in the preceding six weeks, 8)Patients unable to perform spirometry, 9)Patients who were unwilling.

**Study Design**

Patients were selected according to the inclusion and exclusion criteria. Written informed consent was taken from the patients. Detailed history,
general and systemic examination was done. All routine investigations, including complete blood count, lipid profile, blood sugar, urea, creatinine, electrocardiography and so on were done as needed. Patients were investigated by spirometry and diagnosed according to GOLD guidelines (postbronchodilator FEV$_1$/FVC ratio <70% of predicted), into mild (FEV$_1$ ≥ 80% of predicted), moderate (50% ≤ FEV$_1$ < 80%), severe (30% ≤ FEV$_1$ < 50%). Severity of COPD were classified according to GOLD criteria into groups A, B, C or D.

All patients were subjected to resting two-dimensional transthoracic echocardiography in Department of Cardiology, Pariyaram Medical College Hospital. Echocardiography was reviewed to assess the pericardium, valvular anatomy and function, left and right side chamber size and cardiac function. Patients with pulmonary hypertension (sPAP> 30 mmHg) were classified into mild (sPAP = 30-50 mmHg), moderate (sPAP = 50-70 mmHg), severe (sPAP> 70mmHg). Patients requiring active cardiac intervention were referred to the Department of Cardiology.

Statistical Procedure: Descriptive statistical tools like frequency, percentage, mean and standard deviation were used. Inferential statistical tools like t test, chi square test and Spearman’s correlation coefficient were used. A p value of <0.05 was considered significant.

Results

Total 144 patients were included in this study. The following observations were made from study. The most common age group was 55-65 years. The mean age of the study population was 61 years. Study group showed 120 males and 24 females.

Based on the severity of airflow obstruction, these 144 patients were classified into mild, moderate, severe and very severe airflow obstruction. There were 21 (15%) patients with mild, 34 (24%) patients with moderate, 51 (35%) patients with severe and 38 (26%) patients with very severe airflow obstruction.

Based on the number of exacerbations and hospitalizations each year and baseline mMRC breathlessness, these 144 patients were grouped into group A, B, C and D. 39 (27%) patients belonged to group A, 31 (21%) to group B, 7 (5%) to group C and 67 (47%) to group D.

Out of these 144 patients, 65 patients had no pulmonary hypertension. 53 had mild PH, 12 had moderate PH and 14 had severe PH. Among the other echo findings, left ventricular diastolic dysfunction (47 patients) was the most common. 7 patients had left ventricular systolic dysfunction and 3 patients had left ventricular hypertrophy.

Pulmonary hypertension and Severity of airflow obstruction

All patients with mild airflow obstruction and most of the patients with moderate airflow obstruction had no PH. Most of the patients with severe and very severe airflow obstruction had PH.

Pulmonary hypertension and groups: Most of the patients belonging to groups A and C had no PH. Majority of the group B and group D patients had PH.

ECG changes and Echocardiographic findings: Even though the ECG was normal a significant proportion of patients with a normal ECG also had PH on echocardiography.

Pulmonary hypertension and number of exacerbations: Patients with PH had more exacerbations than patients without PH.

CorPulmonale and number of exacerbations: Patients with cor pulmonale had more exacerbations (median 2.5) than patients without cor pulmonale.

Pulmonary Hypertension in frequent exacerbators: Most of the frequent exacerbators had PH.
Table 1: Variables

|     |     |     |
|-----|-----|-----|
| SEX |     |     |
| male| 120 | 83% |
| female| 24 | 17% |

GOLD STAGING

| Severity | MILD | MODERATE | SEVERE | VERY SEVERE |
|----------|------|----------|--------|-------------|
| NO       | 100% | 61.8%    | 29.4%  | 12.3%       |
| MILD     | 0    | 38.2%    | 52.9%  | 34.2%       |
| MODERATE | 0    | 0        | 13.7%  | 13.2%       |
| SEVERE   | 0    | 0        | 3.9%   | 31.6%       |

GROUPS

|     | A | B | C | D |
|-----|---|---|---|---|
| NO  | 92.3% | 35.5% | 71.4% | 19.4% |
| MILD| 7.7%  | 48.3% | 28.6% | 49.3% |
| MODERATE | 0 | 6.5% | 0 | 14.9% |
| SEVERE | 0 | 9.7% | 0 | 16.4% |

(p>0.05)

Table 2: Pulmonary Hypertension v/s GOLD staging

| PULMONARY HYPERTENSION | SEVERITY OF AIRFLOW OBSTRUCTION |
|------------------------|--------------------------------|
|                        | MILD | MODERATE | SEVERE | VERY SEVERE |
| NO                     | 100% | 61.8%    | 29.4%  | 12.3%       |
| MILD                   | 0    | 38.2%    | 52.9%  | 34.2%       |
| MODERATE               | 0    | 0        | 13.7%  | 13.2%       |
| SEVERE                 | 0    | 0        | 3.9%   | 31.6%       |

Table 3: Pulmonary Hypertension v/s grouping

| PULMONARY HYPERTENSION | GROUPS |
|------------------------|--------|
|                        | A      | B      | C      | D      |
| NO                     | 92.3%  | 35.5%  | 71.4%  | 19.4%  |
| MILD                   | 7.7%   | 48.3%  | 28.6%  | 49.3%  |
| MODERATE               | 0      | 6.5%   | 0      | 14.9%  |
| SEVERE                 | 0      | 9.7%   | 0      | 16.4%  |

(p>0.05)

Figure 1: Association between exacerbations and pulmonary hypertension

(Kruskal-Wallis Test, p<0.001)
Discussion

The present study conducted at Pariyaram Medical College assessed the echocardiographic findings in patients with COPD. 144 cases of acute exacerbations, who satisfied the inclusion criteria, were studied from 1/3/2016 to 28/2/2017. The most common age group was 55-65 years with 69 patients belonging to that age group. Jatav et al also reported maximum patients a similar age group of 60-69 years\(^{(15)}\). The mean age in a study done by Shresta et al was 66.1 ± 10.9 years\(^{(16)}\). Freixa et al’s study had a mean age group of 67.9 ± 8.6 years\(^{(17)}\). Thus the age group affected was similar with the older age group predominantly involved. Hence COPD is a disease that occurs later in life.

Most of the patients were males (83%). Jatav et al also reported a similar proportion of male patients (86%)\(^{(15)}\). Hasan et al reported a higher proportion of male (88%) patients\(^{(18)}\). The predominance of male patients was due to the higher percentage of smoking among males. Female COPD patients reported exposure to kitchen smoke and other forms of indoor air pollution.

Most of the patients had severe or very severe airflow obstruction on spirometry. A similar scenario can be found in the Jatav et al study\(^{(15)}\). Freixa et al study had most of the patients with moderate to severe airflow obstruction. The mean FEV\(_1\) in their study was 52.4±16.2%\(^{(17)}\). Hasan et al had excluded patients with severe and very severe COPD in their study\(^{(18)}\). The patients with mild airflow obstruction probably aren’t symptomatic enough to seek medical attention. Thus explaining the higher proportion of patients with severe and very severe airflow obstruction.

Due to their persistent symptoms and frequent exacerbations, patient belonging to group D were
more likely to seek medical care. Thus they were the majority of patients who took part in the study. 49% of the patients had ≥2 exacerbations per year. Out of the 144 patients, 65 patients had normal echo findings. Pulmonary hypertension was the most common echo finding. 18 patients showed evidence of RV dysfunction along with PH and hence were diagnosed as having cor pulmonale. Among the left ventricular abnormalities, diastolic dysfunction was the most common abnormality. The other abnormalities noted were LVSD and LVH. Mandal et al also reported that diastolic dysfunction was the most common abnormality affecting the LV in patients with COPD\textsuperscript{19}. Rawy et al found significant association between LVDD and the severity of airflow obstruction\textsuperscript{20}. The National emphysema treatment trial, which evaluated 120 patients with severe emphysema, the mean PAP was 26.3 ± 5.2 mmHg\textsuperscript{21}. Vizza et al, in their study, evaluated 168 patients listed for lung transplantation. They also obtained similar values of PAP with a 95% CI of 24.1 – 25.9 mmHg\textsuperscript{22}. Candidates from lung volume reduction surgery and lung transplantation were investigated by Thabut et al. 36.7%, 9.8% and 3.7% patients had mild, moderate and severe PH in their study\textsuperscript{23}. Patients with moderate to severe airway obstruction without hypoxia usually have preserved right ventricular function\textsuperscript{24}. Vizza et al reported that 59% of the patients who were evaluated for lung transplant had right ventricular dysfunction. This may be due to the increased severity of airflow obstruction in these patients\textsuperscript{22}. Thus the findings in our study are in concordance with the other studies. When pulmonary artery pressure was compared the severity of airflow obstruction was compared with the severity of airflow obstruction, majority of the patients with severe and very severe airflow obstruction had PH. The association, however, was not significant. Jatav et al found significant association between the RV echo findings and the severity of airflow obstruction\textsuperscript{15}. Gupta et al also reported that as the severity of COPD increases the prevalence of cardiac dysfunction increases\textsuperscript{25}. Hasan et al had also come to the conclusion that the echo findings like RVH, TR, PR and PH correlated significantly with the severity of airflow obstruction\textsuperscript{18}. Thus the findings are in concordance with the other studies. When the association between PH and the groups of COPD were analysed, we arrived at the conclusion that patients that fell under groups B and D had a majority of patients with PH. These are the patients with baseline mMRC dyspnea of ≥2. Hence, PH can have a significant influence on the quality of life of patients with COPD. No correlation was found between ECG changes and the findings on echocardiography. Many patients with a normal ECG also were found to have PH on echo. Hasan et al also reported no correlation between ECG findings such as p-pulmonale, RVH, RBBB with the echo findings\textsuperscript{18}. We also analyzed the association between the number of exacerbations and PH. Patients with PH had more exacerbations than patients with normal echo findings. The correlation was significant. The presence or absence of cor pulmonale also showed significant association with the number of exacerbations. Majority of the frequent exacerbators also had PH. Chaouat et al had stated that the presence of PH is associated with an increased risk of exacerbation and decreased survival. Frequent exacerbations can also result in a decline in pulmonary function which can in turn worsen PH\textsuperscript{21}. Hence our results corroborated with the available literature.

**Conclusion**

COPD is associated with numerous cardiovascular co morbidity in the North Malabar area of Kerala. Patients with pulmonary hypertension are more prone to exacerbations. The early diagnosis and initiation of treatment of PH like LTOT could help reduce the morbidity and mortality associated with COPD. Thus, treatment of cardiac co morbidities should also be included as an essential component of treatment of COPD patients along
with bronchodilators and pulmonary rehabilitation. Patients with PH should also be monitored closely and treated intensely to prevent recurrent exacerbations and reduce mortality.

Ethical Consideration
Informed consent was taken from each individual and there were no associated harm to them during the study. There were no major ethical issues involved as no invasive procedures were performed on the patient as a part of the study. All of the above said investigations mentioned were done as a part of routine work up. This study didn’t have financial support from any source and the study didn’t cause any additional financial burden to the patient.

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