Echocardiographic Right Heart Study in Patients with Chronic Obstructive Pulmonary Disease

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Abstract: Chronic obstructive pulmonary disease (COPD) has considerable effects on cardiac functions, including those of the right ventricle, left ventricle, and pulmonary blood vessels. Most of the increased mortality associated with COPD is due to cardiac involvement. Echocardiography provides a rapid, noninvasive, portable, and accurate method to evaluate the cardiac changes. Aims: We aimed to prospectively study the patients with diagnosed COPD with echocardiogram for evaluating the right heart. Materials & Methods: Our study was an observational, cross sectional study was done on 50 patients with COPD who were admitted at Department of Cardiology, CMCH and underwent echocardiographic evaluation from November 2017 –October 2018. All echocardiographic parameters focused on right heart and its function were assessed. Results: Out of total 50 COPD patients studied, majority of them were male (46 patients, 92%). The mean age group of the studied patients was 58.4 ±7.7 years. Pulmonary hypertension defined as sPAP>30 mmHg was evident in all of the patients; with 30 patients (60%), 14 (28 %) and 6(12 %) patients having severe, moderate and mild pulmonary hypertension respectively. RV dysfunction was evident with reduced average TAPSE values (1.59± 0.38 cm) and elevated RIMP values (0.58±0.16). Conclusion: Majority of COPD patients had evidence of pulmonary hypertension. Echocardiogram can be a helpful tool to assess early changes on the right heart size and function in patients with COPD and also monitor these patients for rapid progression of the illness.

Key words: COPD- Chronic obstructive pulmonary disease, PH- Pulmonary Hypertension, RV dysfunction, CMCH- Chittagong Medical College Hospital.

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Introduction:
Chronic obstructive pulmonary disease (COPD), defined by GOLD as a preventable and treatable disease with some significant extra-pulmonary effects, is a very common clinical entity in clinical practice1. COPD is currently the 4th leading cause of death in the world and a burning problem among the Bangladeshi population. Globally, COPD has emerged as the major cause of morbidity and mortality and is expected to become the 3rd most leading cause of death2. Cardiac manifestations are the most common extra pulmonary effects in COPD patients3. COPD affects pulmonary blood vessels, right ventricle, as well as left ventricle leading to development of pulmonary hypertension, cor-pulmonale, right ventricular dysfunction, and left ventricular dysfunction4. Right ventricle (RV) dysfunction is common in patients with COPD particularly in those with low oxygen saturation. Pulmonary hypertension (PH) affects the right ventricle function leading to cor-pulmonale and once developed these patients have poor prognosis. So, the early recognition of RV dysfunction and pulmonary hypertension may help in treatment and prolonging the survival of the patients with cor-pulmonale. Echocardiography provides a rapid, noninvasive method to evaluate the right ventricle chamber size and function5. This study was done to identify the prevalence and degree of pulmonary hypertension by echocardiography in COPD patients. COPD affects pulmonary blood vessels, right ventricle, as well as left ventricle leading to development of pulmonary hypertension, cor-pulmonale, right ventricular dysfunction, and left ventricular dysfunction too. Echocardiography provides a rapid, noninvasive
portable and accurate method to evaluate the right ventricle function, right ventricular filling pressure, tricuspid regurgitation, left ventricular function and valvular function. Many studies have confirmed that echocardiographically derived estimates of pulmonary arterial pressure co-relate closely with pressures measured by right heart catheter (r > 0.7).  

Hence the present study was undertaken with the following aims to assess the cardiac changes secondary to COPD by echocardiography.

Materials and Methods:

The study was an observational cross sectional study. The study population consisted of patients with a diagnosis of Chronic obstructive pulmonary diseases (COPD), who were admitted to Department of Cardiology of -(CMCH) between November 2017 and October 2018 and who subsequently, underwent Echocardiography. The inclusion and exclusion criteria were as follows:

Inclusion criteria:

1. All COPD patients attending the echocardiography room during the study period.

Exclusion criteria:

1. Patients who cannot lie for long enough to complete the study
2. H/O of diagnosed chronic lung disease other than COPD like-
   a) Interstitial lung disease,
   b) Old pulmonary TB with sequelae.
3. Any systemic disease that can cause pulmonary hypertension,

Fifty (50) patients of COPD confirmed by history, clinical examination, radiology of chest, and pulmonary function test were selected from Department of Cardiology of CMCH, Chattogram.

All selected patients were subjected to routine investigations, including complete blood count, lipid profile, blood sugar, blood urea, serum creatinine, ECG, chest X-ray, Spirometry and Urine R/E.

All patients were subjected to resting two-dimension transthoracic & Doppler echocardiography in the Echo. Room and associated by expert cardiologists. The machine used was VIVID 6 model of GE health care system with a multifrequency probe with a range of 2–4.3 MHz. Both 2D and M-Mode studies were done. Echocardiography was reviewed to assess the pericardium, valvular anatomy and function, left and right side chamber size and cardiac function. Tricuspid regurgitant flow was identified by color flow Doppler technique and the maximum jet velocity was measured by continuous wave Doppler without the use of intravenous contrast.

Right ventricular systolic pressure was estimated based on the modified Bernoulli equation and was considered to be equal to the sPAP in the absence of right ventricular outflow obstruction: sPAP (mmHg) = right ventricular systolic pressure = trans-tricuspid pressure gradient (TTPG) + right atrial pressure (RAP), where trans-tricuspid gradient is 4v2 (v = peak velocity of tricuspid regurgitation, m/s)7,9.  

RV systolic function, as assessed by at least one or a combination of the following: DTI-derived tricuspid lateral annular systolic velocity wave (S'), tricuspid annular plane systolic excursion (TAPSE), and RV index of myocardial performance (RIMP). RV systolic pressure was calculated using the tricuspid regurgitation jet and an estimation of RA pressure based on inferior vena cava (IVC) size and collapsibility. Hence, pulmonary artery systolic pressure (PASP) was calculated by using continuous wave Doppler and applying the equation below:

PASP = 4X(peak TR velocity)2 + RAP

RAP was empirically estimated as 15 mmHg before 1997. Since 1997, RAP was estimated to be 5, 10, or 15 mmHg based on the variation in the size of inferior vena cava with inspiration as follows: complete collapse, RAP = 5 mmHg; partial collapse, RAP = 10 mmHg; and no collapse, RAP = 15 mmHg10.

IVC diameter < 2.1 cm that collapses >50% with a sniff suggests normal RA pressure of 3 mm Hg (range, 0–5 mm Hg), whereas IVC diameter > 2.1 cm that collapses< 50% with a sniff suggests high RA pressure of 15 mm Hg (range, 10–20 mm Hg). In scenarios in which IVC diameter and collapse do not fit this paradigm, an intermediate value of 8 mm Hg (range, 5–10 mm Hg) was used11. TAPSE measures predominately the longitudinal systolic function and values <17mm is highly suggestive of RV systolic dysfunction. Right atrium pressure can be estimated with the IVC diameter and its changes with respiration.

Pulmonary hypertension (PH) was defined in this study as sPAP ≥ 36 mmHg12. This value was chosen according to the definition of pulmonary hypertension. PH was classified into mild, moderate, and severe category as sPAP 30–50, 50–70, >70 mmHg, respectively (using Chemla formula, mean pulmonary arterial pressure (MPAP) =0.61 PASP + 2 mmHg and putting value of 25–35, 35–45, and >45 mmHg of MPAP for mild, moderate, and severe pulmonary hypertension, respectively)13.

Right ventricle dimension was measured by M-Mode echo and right ventricular dilation or cor pulmonale was said to be present when it exceeded the normal range of 0.9–2.6 cm. Right ventricle contractility was also noted and right ventricular systolic dysfunction was said to be present when it was hypokinetic.

Left ventricular function was also assessed by using the following parameters: EF (ejection fraction) = measure of how much end-diastolic value is ejected from LV with each contraction (56%–78%).

FS (fractional shortening) = it is a percentage change in LV dimension with each LV contraction (28%–44%).

LV mass = left ventricular mass (88–224 g).

E/A = diastolic filling of left ventricles usually classified
Initially on the basis of the peak mitral flow velocity of the early rapid filling wave (E), peak velocity of the late filling wave caused by atrial contraction (A). In normal subjects LV elastic recoil is vigorous because of normal myocardial relaxation, therefore more filling is completed during early diastolic, so left ventricular diastolic dysfunction (LVDD) is said to be present when E/A is <1.3 (age group 45–49 years), <1.2 (age group 50–59 years), <1.0 (age group 60–69 years), and <0.8 (age group ≥70 years)\(^4\).

The calculations were done by Microsoft Excel 2007, and Statistical Package for Social Sciences, SPSS version 20; and the data were presented in the form of tables and diagrams. Appropriate statistical tests were carried out to compare the data, and a level of significance of 0.05 was used. Values were expressed as mean ± standard deviation.

**Results:**

Our study included 46 (92%) males and 4 (8%) females, with mean age of 58.4±7.7 years, ranging from 40 to 79 years old. Most patients had moderate to severe obstruction. Demographic characteristics and spirometric results of our cases are shown in Table-I.

**Table-I: Demographic characteristics and spirometric results of the studied cases.**

| Variables               | Mean±SD   | Range     |
|-------------------------|-----------|-----------|
| Age (years)             | 58.4±7.7  | 40.0-79.0 |
| Sex                     |           |           |
| Male                    | 46 (92)   |           |
| Female                  | 4 (8)     |           |
| Occupation              |           |           |
| Manual                  | 42 (84)   |           |
| Official                | 8 (16)    |           |
| Smoker                  |           |           |
| Never                   | 03 (6)    |           |
| Ex-smoker               | 14 (28)   |           |
| Current Smoker          | 34 (68)   |           |
| FEV1/FVC                | 54.6±11.2 | 30.0-70.0 |
| FEV1%                   | 48.6±18.1 | 24.0-86.0 |

Forty seven patients (94%) studied had significant ECG abnormality out of which P' pulmonale was the most common 45 patients (90 %) while atrial arrhythmias in the form of Atrial fibrillation (AF) or Multifocal tachycardia (MAT) (6 patients, 12 %) being the least common finding (Table II).

**Table-II: ECG abnormalities in COPD patients.**

| Characteristics       | Female (n=4) | Overall (n=50) | p value |
|-----------------------|--------------|----------------|---------|
| ECG abnormalities     | 44 (95.6%)   | 47 (94 %)      | >0.05   |
| P’ pulmonale          | 43 (93.4%)   | 45 (90%)       | <0.05   |
| R/S ratio in V1       | R/S ratio in V1 | R/S ratio in V1 | R/S ratio in V1 | R/S ratio in V1 |
| > 1                   | 30 (65.2%)   | 32 (64 %)      | >0.05   |
| < 1                   | 16 (34.7%)   | 18 (36 %)      | >0.05   |
| RBBB                  | 18 (36%)     | 19 (38%)       | <0.05   |
| AF/MAT                | 5 (10.8%)    | 6 (12%)        | >0.05   |

Echocardiography done in the studied patients showed evidence of varying degrees of pulmonary hypertension along with enlargement of right sided chambers of the heart. Tricuspid regurgitation peak gradient a useful marker for indirect evidence of pulmonary hypertension was studied in all the patients. Pulmonary hypertension defined as $sPAP$ (Peak systolic pulmonary pressure) value > 30 mmHg was observed in all of the patients in the study group. The mean TRPG value studied was 63.76 ± 20.57mmHg with the range of 26-100 mmHg and their corresponding peak systolic pulmonary artery pressure (PASP) mean value was 75.26 ±21.18 mmHg. Among patients with evidence of pulmonary hypertension, 30 patients (60%) had severe PAH, 14 patients (28%) had moderate PH and 6 patients (12%) had milder degree of pulmonary hypertension as shown in Table III.

**Table-III: Pulmonary hypertension (PH) Grade (n=50).**

| Pulmonary hypertension | Numbers | Percentage |
|------------------------|---------|------------|
| Mild (>30-50 mmHg)     | 6       | 12 %       |
| Moderate (>50-70)      | 14      | 28 %       |
| Severe (>70 mmHg)      | 30      | 60 %       |

Other parameters of right heart enlargement and function such as RA area, RV base and mid diameter, TAPSE, RIMP, S’ were studied. The mean RV diameters were increased as compared to normal adult values and parameters for RV function like TAPSE and RIMP also showed that majority of patients had significant RV dysfunction in our study (Table IV).

**Table-IV: Echocardiographic RV parameters.**

| Parameters               | Range    | Mean |
|--------------------------|----------|------|
| RA Area (cm²)            | 8.8-39   | 20.37±6.8 |
| RV diameter (base)/cm    | 3.6-6.8  | 5.04±0.66 |
| RV diameter (mid)/cm     | 3.4-6.8  | 4.68±0.58 |
| RV wall thickness /cm    | 0.5-1.1  | 0.77±0.11 |
| TAPSE /cm               | 0.9-2.3  | 1.59±0.38 |
| TDI s’ /cm/s            | 6.7-19   | 11.5±2.95 |
| RV MPI                  | 0.35-0.98 | 0.58±0.16 |
| TRPG /mmHg              | 26-110   | 63.76±20.57 |
| PASP                    | 36-120   | 75.26±21.18 |

**Table-V: Frequency of cor pulmonale with severity of PH.**

| Severity of PH | Frequency of cor pulmonale |
|----------------|----------------------------|
| Mild (6)       | 16.6% (1)                  |
| Moderate (14)  | 71.4% (10)                 |
| Severe (30)    | 96.6% (29)                 |

Inferior venacava diameter (IVCd) at diastole is a surrogate marker for increased right atrial pressure and is useful for estimation of peak pulmonary artery pressure. The mean IVC diameter was 1.88±0.35 cm as shown in Table VI.

**Table-VI: Echocardiographic LV parameters and IVC size.**

| Parameters | Range   | Mean   |
|------------|---------|--------|
| LVDD /cm   | 2.8-5.7 | 4.01±0.64 |
| LVSD/cm    | 1.5-4.5 | 2.48±0.63 |
| IVS/cm     | 0.6-1.1 | 0.79±0.09 |
| PW/cm      | 0.6-1.2 | 0.82±0.01 |
| EF %       | 50-65   | 60.34±3.89 |
| IVC d/cm   | 1-2.4   | 1.88±0.35 |

*LVDD – LV internal diastole diameter, LVSD- LV systole diameter, IVS – Inter-ventricular septum, PW – Posterior wall thickness, EF – Ejection fraction.*
Discussion:
The cardiac manifestations of COPD are numerous. Impairment of right ventricular dysfunction and pulmonary blood vessels are well known to complicate the clinical course of COPD and co-relate inversely with survival. Significant structural changes occur in the pulmonary circulation in patients with COPD. The presence of hypoxemia and chronic ventilator insufficiency is associated with early evidence of intimal thickening and medial hypertrophy in the smaller branches of the pulmonary arteries. Coupled with these pathological changes are pulmonary vasoconstriction arising from the presence of alveolar hypoxemia, destruction of pulmonary vascular bed, changes in intrinsic pulmonary vasodilator substances (such as decrease in PGI2s (prostacyclin synthase), decrease in eNOS (endothelial nitric oxide synthase), and increase in ET1 (endothelin1) leads to remodeling, increase in blood viscosity, and alteration in respiratory mechanics. All these lead to a significant increase in pulmonary vascular resistance, the consequence of which is pulmonary hypertension. Although the true prevalence of PH in COPD is unknown, an elevation of pulmonary arterial pressure is reported to occur in 20%–90% of patients when measured by right heart catheterization with some evidence that pulmonary hypertension is associated with some evidence that pulmonary hemodynamic worsens with worsening airflow obstruction\(^\text{15-20}\). Two studies have shown an abnormal increase in mean pulmonary arterial pressure (Ppa) in COPD of 0.4–0.6 mmHg per year. These studies illustrate that PH in COPD progresses slowly and occurs in mild as well as severe forms of disease\(^\text{21,22}\). The level of PH has a prognostic value in COPD patients that has been demonstrated by several studies. In one of these studies, the 5-year survival rates were 50% in patients with mild PH (20 30 mmHg), 30% in those with moderate-to-severe PH (30–50 mmHg), and 0% in the small group of patients with very severe PH (>50 mmHg). Thus a high degree of PH bears a poor prognosis, and this also has been observed in COPD patients receiving long-term oxygen therapy\(^\text{23}\). In our study, all 50 patients had evidence of pulmonary hypertension (sPAP> 30 mmHg) with majority of them (60%) having higher grades of pulmonary hypertension maybe because of the chronicity of the disease and the study was mainly done in admitted patients with COPD. There was significant evidence of right ventricular enlargement as well as decline in RV systolic function through various parameters studied by echocardiography. All COPD patients studied had shown an increase in RV enlargement in form of increased RV diameters (RV base = 5.04±0.66 and RV mid = 4.68 ±0.58 cm). RV systolic function as assessed by TAPSE and RIMP also showed values below normal adult population values which indicate majority of COPD patients studied had evidence of RV dysfunction as well. (TAPSE, mean = 1.59 ±0.38 , RIMP = 0.58±0.16 ). Saxena N et al.\(^\text{24}\) showed tricuspid annular systolic velocity (TAPSE) is a useful measurement in determining right ventricular systolic function regardless of pulmonary artery pressures in a study of 52 patients. Evidence of right ventricular hypertrophy was also seen in most patients with the average RV wall thickness of 0.77±0.11 mm as compared to normal adult value of 3-5 mm. In the current study, no motion wall abnormalities were found in the echo findings of the patients. This disagreed with Freixa et al.\(^\text{25}\) who found that 30% of patients with LVSD presented left ventricle wall motion abnormalities. This difference might be owing to a large number of included-patients. In current study, no statistical significant correlation was found between left ventricular systolic function and dimensions and the severity of COPD. This is similar to Freixa et al.\(^\text{22}\). Frequent reports about the prevalence of LVDD in patients with COPD have been shown in many studies. The prevalence of LVDD in this study was 20%. This was in contrary to Huang and colleagues, who showed a higher frequency of LVDD in patients with COPD (65.6%) and Caram and colleagues who reported high frequency up to 88%. Another study by Lopez Sanchez et al.\(^\text{26}\) focused on severe COPD outpatients and showed a highest prevalence of LVDD (90%)\(^\text{26,27}\). In this study, there was no correlation between LVDD and the severity of COPD. This is similar to the study conducted by Huang et al.\(^\text{28}\). The current study showed that RV dilatation was found in early stages of COPD. This agreed with Hilde et al.\(^\text{29}\). Moreover, there was a positive correlation between severity of COPD and RV size. This is similar to the study conducted by Jatav et al.\(^\text{30}\). In the present study, tricuspid regurgitation was present in ~75% of the patients with variable grades from mild to severe. There was a positive correlation between grades of obstruction and tricuspid regurgitation. Similar findings were observed in study of Maula et al.\(^\text{31}\). True prevalence of PH in COPD is unknown. A reported elevation of pulmonary arterial pressure is between 20 and 90% measured by right heart catheterization, with some evidence that PH increases with increase airflow obstruction\(^\text{32,33,34}\). The current study showed that the presence of PH, that is, moderate pulmonary artery systolic pressure more than 50 mmHg, was 28%. PH appeared more in severe and very severe grades of the disease than in mild/ moderate disease. These results agreed with Jatav et al.\(^\text{30}\) and El Wahsh et al.\(^\text{35}\) who showed that increased pulmonary artery systolic pressure was found in 44 and 55.56% of patients, respectively, and also showed a positive correlation with severity of COPD. Most of the patients (12%) in the current study with PH had mild degree of PH, and this was in agreement with Freixa et al.\(^\text{25}\) who found that the magnitude of PH was mild in most cases and only 3% of patients had severe PH. In the current study, TAPSE was used as easily obtainable measure of RV systolic function, and it was normal in all patients, who is in contrary to Hilde et al.\(^\text{30}\) who included some patients with COPD with very severe degree of obstruction with respiratory failure and TAPSE was lower in them than controls. In this study, there were some limitation such as using two-dimensional Doppler echocardiogram with color flow without using...
tissue Doppler echocardiography, which made the assessment of prevalence of LVDD less accurate. Right heart catheterization was not available for definitive diagnosis of PH and detection of its prevalence.

**Conclusion:**
This study reveals that chronic obstructive pulmonary disease with pulmonary hypertension is highly prevalent in our country. Echocardiographic right heart profile assessment should be an additional tool to detect and prognosticate patients with various degrees of pulmonary hypertension.

**Conflict of Interest:** None.

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