ECHOCARDIOGRAPHIC STUDY OF RIGHT VENTRICLE CHANGES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS OF DIFFERENT SEVERITY

Abhishek Sharma¹, Yogesh Tripathi², Berendra Yadav³, Rinku Garg⁴

¹Assistant Professor, Department of Physiology, S.N. Medical College, Agra.

²Professor, Department of Physiology, School of Medical Sciences and Research, Sharda University, Greater Noida. Former Professor of Physiology, Santosh Medical College, Santosh University, Ghaziabad.

³Assistant Professor, Department of Physiology, Mahamaya Rajkiya Allopathic Medical College, Ambedkar Nagar.

⁴Professor & Head, Department of Physiology, Santosh Medical College, Santosh University, Ghaziabad.

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Corresponding author: Abhishek Sharma

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Abstract

Chronic obstructive pulmonary disease (COPD) characterized by interminable air flow limitation that is not fully reversible COPD includes chronic bronchitis, emphysema, and chronic asthmatic bronchitis. Chronic obstructive pulmonary disease as a complex disease with various systemic manifestations and one of the co-morbidity linked with COPD is cardiovascular disease. Hypoxic vasoconstriction and alterations in pulmonary microvasculature, which are both observed in COPD patients, leads to an increase in pulmonary vascular resistance. As a result, this increase in right ventricular (RV) after load causes right ventricular remodeling, including chamber dilatation and wall hypertrophy and ultimately to functional deterioration. The aim of this study to evaluate the right ventricular changes that develop secondary to COPD using GOLD guidelines and echocardiographic findings. This cross-sectional study involved 134 patients who presented to the pulmonary disease outpatient clinic with COPD. We assessed the right ventricular changes in COPD patients of different severity using echocardiography. COPD patients shown change in the right ventricular dimensions as the severity of COPD increases and right ventricular function as well. It is also observed that frequency of pulmonary hypertension also increased as the severity of COPD increases. The study shows high prevalence of cardiac co-morbidities such as RV dysfunction and pulmonary hypertension in COPD patients. The severity of complications increases with severity of COPD and makes a linear relation.

Keywords: Echocardiography, ECG, COPD

Introduction:

Chronic obstructive pulmonary disease (COPD) characterized by interminable air flow limitation that is not fully reversible, which is usually escalating and is associated with an abnormal inflammatory response of the lung and air passages to inhaled noxious particles or gases including cigarette smoke, biomass fuels and occupational agents. COPD includes chronic bronchitis, emphysema, and chronic asthmatic bronchitis¹. COPD is major health hazard in cases over 40 years of age and continues. It is a major cause of chronic morbidity and mortality worldwide. By 2030, COPD may project to rank seventh as a worldwide burden of disease. The progressive increase in the prevalence of smoking may raise

morbidity and mortality in Asian and African countries over the next two decades. Due to its prolonged development, prevention of COPD takes several decades^{2, 3}. In 2030, the third major etiology for death worldwide will be COPD⁴.

There is plenty of evidence indicating chronic obstructive pulmonary disease as a complex disease with various systemic manifestations. The co-morbidities linked with COPD are cardiovascular diseases, metabolic syndrome, osteoporosis, depression, lung malignancy, skeletal muscle dysfunction, Normocytic anemia, obstructive sleep apnea. Hypoxic vasoconstriction and alterations in pulmonary microvasculature, which are both observed in COPD patients, leads to an increase in pulmonary vascular resistance [2]. As a result, this

increase in right ventricular (RV) after load causes right ventricular remodeling, including chamber dilatation and wall hypertrophy and ultimately to functional deterioration^{5,6}.

Echocardiography (ECHO) is a quick, non-invasive and a relatively accurate means of evaluation right ventricle morphology and function. In this study, we used echocardiography to observe COPD related changes in right ventricular morphology and function of COPD patients of different stages.

Materials and Methods

The proposed research study was a cross-sectional study and consists of One hundred thirty-four patients (88 male, 46 female: mean age 63 ± 7 years) with known history of chronic pulmonary obstructive disease (COPD). The proposed research study was carried out at Mahamaya Rajkiya Allopathic medical college, Ambedkar Nagar and Santosh medical College, Ghaziabad. This study was commenced after obtaining the ethical clearance from Institutional Human Ethics Committee (IHEC). Patients with known case of Chronic Obstructive Pulmonary disease (COPD) confirmed by medical history and pulmonary function tests were selected using systemic random sampling and informed consent was obtained from the patients before subjecting to research methods.

Patients with coronary heart disease (CAD), chronic lung disease other than COPD, chronic kidney disease, valvular cardiac disease, and any systemic or cardiac diseases that may cause pulmonary hypertension, malignant tumors, head and neck abnormalities, patients with exacerbations in the last four weeks, patients with a weak echo window and patients who could not perform spirometry were excluded from the study.

All patients underwent respiratory (spirometry) tests for assessment of pulmonary function. The forced vital capacity (FVC) and forced expiratory volume during first one second (FEV1) were measured and FEV1/FVC ratio was calculated from measured values. The patients were divided into four groups in line with the guidelines of Global Initiative for Chronic Obstructive Lung Disease (GOLD) as mild ($FEV1 \geq 80\%$ expected value), intermediate ($50\% \leq FEV1 < 80\%$

expected value), severe ($30\% \leq FEV1 < 30\%$ expected value) and very severe ($30\% \leq FEV1 < 50\%$ expected value), provided that the expected post-bronchodilator FEV1/FVC ratio was less than 70% ⁷.

A two-dimensional trans thoracic Doppler echocardiography was performed on all patients while in the left lateral lying position using a *eSaote SpA Mylab50 X vision* echocardiography machine with the cardiologist making all measurements who was blind to the respiratory functional test findings of the patients. All measurements were performed during at least three consecutive cardiac cycles and normal respiration and at the end of experiment.

Right ventricular (RV) dimensions like end-diastolic basal, mid and longitudinal diameters were measured from the apical four-chamber view. For the calculation of the values of the dimension of the Right Ventricle Outflow Tract (RVOT), two dimensional echocardiograms of the para-sternal short axis view at the aortic root level was used. End-diastolic and end systolic diameters were measured using the M-mode records of RVOT⁸.

Pulmonary Artery Systolic Pressure (SPAP) was determined through a continuous wave Doppler evaluation of tricuspid insufficiency^{9,10}. Tricuspid Annular Plane Systolic Excursion (TAPSE) was recorded from a four-apical chamber view obtained by an M-mode probe placed on the free wall angle of the tricuspid valve. The distance between the tricuspid ring and RV apex was measured at the end of the diastole and systole of the same cardiac cycle, and TAPSE was calculated as the difference between the end diastolic and end-systolic measurements (in mm)¹¹. For the calculation of the values of the dimension of the Right Ventricle Outflow Tract (RVOT) and RVOT Fractional Shortening (RVOT-FS), two dimensional echocardiograms of the para-sternal short axis view at the aortic root level were used.

Statistical Analysis:

Results were expressed as mean $\pm$ SD. The data were analyzed by one-way analysis of variance (ANOVA) followed by Bonferroni or Tukey's multiple comparison tests, respectively. Statistical significance was considered at $P < 0.05$.

Results:

Table 1: Classification of patients (Gender wise) according to severity of COPD.
(COPD severity stages were based on GOLD classification)

COPD severity	Male		Female		Total	
	n	%	n	%	n	%
Mild	6	5%	1	1%	7	6%
Moderate	24	18%	15	11%	39	29%
Severe	38	28%	16	12%	54	40%
Very Severe	20	15%	14	10%	34	25%
Total	88	66%	46	34%	134	100%

Table 2: showing the baseline and clinical characteristics of study population having mild, moderate, severe and very severe stages of COPD. Results were expressed in Mean $\pm$ SD. SBP-Systolic blood pressure; DBP-Diastolic blood pressure; PP-Pulse pressure; MABP-Mean arterial blood pressure.

Parameter	Mild	Moderate	Severe	Very Severe
Age(Years)	62.29 $\pm$ 8.21	62.95 $\pm$ 5.87	62.01 $\pm$ 7.22	64.94 $\pm$ 6.98
Duration of COPD (Years)	2.86 $\pm$ 0.69	7.05 $\pm$ 1.50	11.06 $\pm$ 3.47	14.53 $\pm$ 3.78
Height (Cms)	165.00 $\pm$ 7.09	164.29 $\pm$ 6.94	162.75 $\pm$ 6.19	162.11 $\pm$ 8.4
SBP (mm Hg)	127.14 $\pm$ 5.84	133.49 $\pm$ 8.64	135.46 $\pm$ 3.47	137.34 $\pm$ 5.39
DBP (mm Hg)	83.43 $\pm$ 5.63	85.33 $\pm$ 6.31	89.18 $\pm$ 5.42	87.16 $\pm$ 4.71
PP (mm Hg)	43.71 $\pm$ 8.38	48.16 $\pm$ 7.66	46.28 $\pm$ 6.22	50.18 $\pm$ 7.21
MABP (mm Hg)	98.00 $\pm$ 4.11	101.38 $\pm$ 6.20	104.6 $\pm$ 3.87	103.89 $\pm$ 3.6
Heart Rate (per min)	78.29 $\pm$ 4.92	85.75 $\pm$ 4.92	82.32 $\pm$ 5.97	84.46 $\pm$ 5.03
Rate Pressure Product(RPP)	9937.43 $\pm$ 538	11442.07 $\pm$ 919	11153.08 $\pm$ 884	11598.12 $\pm$ 801

Table 3: showing the Lung function parameters of study population having mild, moderate, severe and very severe stages of COPD. Results were expressed in Mean $\pm$ SD. FVC-Forced vital capacity; FEV1-Forced expiratory volume during first second.

Variable	Mild	Moderate	Severe	Very Severe	P-value
FVC (liters)	3.4 $\pm$ 0.6	3.11 $\pm$ 0.49	2.95 $\pm$ 0.48	2.29 $\pm$ 0.42	<0.0001
FEV1(liters)	2.3 $\pm$ 0.37	1.91 $\pm$ 0.36	0.96 $\pm$ 0.15	0.6 $\pm$ 0.12	<0.0001
FEV1 (% of predicted value)	81 $\pm$ 6	69 $\pm$ 8	35 $\pm$ 3	23 $\pm$ 3	--
FEV1/FVC	0.68 $\pm$ 0.01	0.61 $\pm$ 0.07	0.33 $\pm$ 0.04	0.26 $\pm$ 0.03	<0.0001

Table 4: showing the Right ventricular echo-cardiac measurements of study population having mild, moderate, severe and very severe stages of COPD. Results were expressed in Mean $\pm$ SD. RVBD-Right ventricular basal diameter; RVMD-Right ventricular mid diameter; RVLD- Right ventricular longitudinal diameter; RVOT above PV - Right ventricular outflow tract above pulmonary valve; RVOT above AV - Right ventricular outflow tract above aortic valve; TAPSE-tricuspid annular plane systolic excursion; SPAP-Systolic pulmonary arterial pressure; RVEF-Right ventricular ejection fraction

Variable	Mild	Moderate	Severe	Very severe	P-value
RVBD (mm)	27.31 $\pm$ 2.66	30.37 $\pm$ 2.01	34.35 $\pm$ 2.85	36.43 $\pm$ 2.78	<0.0001
RVMD (mm)	31.92 $\pm$ 2.68	36.66 $\pm$ 2.89	37.16 $\pm$ 3.02	38.28 $\pm$ 4.15	<0.001
RVLD (mm)	64.71 $\pm$ 4.74	62.95 $\pm$ 6.69	67.24 $\pm$ 6.64	69.65 $\pm$ 4.78	<0.001
RVOT above PV (mm)	22.33 $\pm$ 2.62	23.29 $\pm$ 2.44	25.6 $\pm$ 3.69	26.22 $\pm$ 4.49	<0.001
RVOT above AV (mm)	29.44 $\pm$ 2.48	29.6 $\pm$ 2.46	32.35 $\pm$ 3.77	32.88 $\pm$ 4.57	<0.001
Pulmonary artery diameter(mm)	18.73 $\pm$ 2.04	19.166 $\pm$ 1.92	24.04 $\pm$ 4.4	25.28 $\pm$ 4.71	<0.001
TAPSE	18.08 $\pm$ 1.6	18.53 $\pm$ 1.46	16.73 $\pm$ 2.43	16.87 $\pm$ 2.4	<0.001
SPAP(mm Hg)	27.84 $\pm$ 5.42	31.92 $\pm$ 7.06	32.88 $\pm$ 8.09	46.57 $\pm$ 12.39	<0.001
RVEF (%)	60.51 $\pm$ 6.1	51.41 $\pm$ 12.8	47.3 $\pm$ 13.3	44.42 $\pm$ 8.5	<0.05

Table 5: showing the statistical comparison (One-way ANOVA followed by post-hoc tests) between four grades of COPD patients in Right ventricular echo-cardiac dimensions. *RVBD-Right ventricular basal diameter; RVMD-Right ventricular mid diameter; RVLD- Right ventricular longitudinal diameter; RVOT above PV - Right ventricular outflow tract above pulmonary valve; RVOT above AV - Right ventricular outflow tract above aortic valve; TAPSE-tricuspid annular plane systolic excursion; SPAP-Systolic pulmonary arterial pressure; RVEF-Right ventricular ejection fraction.*

Variable	Mild vs. Moderate	Mild vs. Severe	Mild vs. very severe	Moderate vs. severe	Moderate vs. very severe	Severe vs. very severe
RVBD	<0.05	<.0001	<.0001	<.0001	<.0001	<0.001
RVMD	<0.001	<.0001	<.0001	NS	<0.05	NS
RVLD	NS	NS	NS	<0.05	<.0001	NS
RVOT above PV	NS	<0.05	<0.05	<0.05	<0.001	NS
RVOT above AV	NS	NS	<0.05	<0.001	<0.001	NS
Pulmonary artery diameter	NS	<0.001	<0.001	<.0001	<.0001	NS
TAPSE	NS	NS	NS	<0.001	<0.05	NS
SPAP	NS	NS	<.0001	NS	<.0001	<.0001
RVEF	NS	<0.05	<0.05	NS	<0.05	NS

Table 1 shows the distribution of study population which comprises of Seven(7) COPD patients(male=6(4%); female=1(1%)) of mild stage; Thirty nine(39) COPD patients(male=24(18%); female=15(11%)) of moderate stage; Fifty four(54) COPD patients(male=38(28%); female=16(12%)) of severe stage; Thirty four(34) COPD patients(male=20(15%); female=14(10%)) of very severe stage.

The baseline(age, height) and clinical characteristics like duration of COPD, Systolic blood pressure(SBP), Diastolic blood pressure(DBP), Pulse pressure(PP), Mean arterial blood pressure(MABP), Heart rate, Rate pressure product of COPD patients were shown in Table 2. As shown in Table 3, COPD patients of different stages shown bronchial obstruction and decreased spirometric volumes like forced vital capacity($P<0.0001$), forced expiratory volume($P<0.0001$) and FEV1/FVC($p<0.0001$).

Right ventricular echo-cardiac measurement of study population having mild, moderate, severe and very severe stages of COPD were shown in Table 4. As shown in Table 4, there was increase in right ventricular basal($P<0.0001$), mid($P<0.001$) and longitudinal($P<0.01$) diameter of COPD patients of different stages which is statistically found to be significant. There was decrease in tricuspid annular plane systolic excursion ($P<0.001$), right ventricular ejection fraction ($P<0.001$), and increase in systolic pulmonary arterial pressure($P<0.05$) of COPD patients of different stages which is statistically found to be

significant. Table 5 shows the multiple group comparison between the groups.

Discussion:

The present study included 88 male (66%) and 46 female (34%) patients. The mean age of the study population was 63 ± 7 years. In the present study patients were classified into four categories based on the severity of COPD, namely mild category 7 (6%), moderate category 39 (29%), severe category 54 (40%) and very severe 34 (25%).

The maximum numbers of COPD patients in the present study were in 6th and 7th decades (70%) with the mean age 63.18 years, which is similar to previous studies(12). Although ECHO is a non-invasive diagnostic test, it may be technically limited in a substantial percentage of patients with COPD. The configuration of the chest wall, air imprisonment and changes in the structure of the heart ventricles complicate ultrasonographic evaluations of the heart in patients with COPD^{13,14}.

There are various cardiac changes seen in the patients suffering from COPD. In this study Echocardiographic changes seen in COPD patients were studied and correlated to severity of the disease. In the present study, the incidence of most of the ECHO findings, increased as the severity of the disease (as measured by FEV1 and graded according to GOLD criteria) increased. Statistical correlation were found with echo findings suggestive of RV dysfunction in COPD patients i.e. Pulmonary arterial hypertension, right ventricular

hypertrophy, and right ventricular systolic dysfunction which were also significant (i.e. $p < 0.05$). This means that the increase in incidence of the above ECHO findings, with increasing disease severity (decreasing FEV1) was statistically significant. Other studies correlating the ECHO findings with severity of the disease have also made similar observations, and also have given different explanations for their observation^{15,16}.

COPD is associated with significant extra-pulmonary effects among which cardiac complications are most common. The cardiac manifestations of COPD are numerous. Impairment of RV function and alteration of pulmonary blood vessels are well known to complicate the clinical course of COPD and correlate inversely with survival. Long term changes with chronic pulmonary vascular remodeling and vasoconstriction impose increase in RV after load and ultimately result in RV dilation and later dysfunction manifesting as cor pulmonale¹⁷. 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 catheterization¹⁸. The level of PH has a prognostic value in COPD patients that has been demonstrated by several studies¹⁹. 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)^{20,21}.

In our study, 69(51%) patients had evidence of pulmonary hypertension (sPAP>30 mmHg) and this maybe because of the chronicity of the disease. 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 systolic function as assessed by TAPSE also showed values below normal adult population values which indicate COPD patients studied had evidence of RV dysfunction as well. Saxena N et al. 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 patients²².

These results indicate that further large scale studies using a more accurate assessment method for PH are warranted, to achieve a more detailed assessment of the RV dysfunction associated with COPD. Echocardiographic evaluation of right heart can be used as an important risk assessment tool for assessing RV function and pulmonary artery pressure and should constitute part of a periodic screening tool for all COPD patients.

Regular cardiac monitoring by echo in these COPD patients can help to identify individuals at risk of increased morbidity and mortality, warranting close monitoring and aggressive treatment to prevent or delay complications. Major limitation of the study was that it was a single centre cross-section study and with a small sample size.

Conclusion:

The study shows high prevalence of cardiac co-morbidities such as RV dysfunction and pulmonary hypertension in COPD patients. The severity of complications increases with severity of COPD and makes a linear relation. Echocardiography provides a rapid, non-invasive, portable, and accurate method to evaluate cardiac functions. Early diagnoses and intervention for cardiac co-morbidities would reduce mortalities in COPD patients.

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