Echocardiographic Changes in Patients with Chronic Obstructive Pulmonary Disease in a Study of Indian Population

Atanu Pal[1], Arabinda Das[2], JibeswarThakuria[3]

[1]Assistant Professor, Department of Rheumatology and Nephrology, Institute of Post Graduate Medical Education & Research, 242, AJC Bose Road, Kolkata, West Bengal, [2]Assistant Professor, Department of Statistics, Acharya Prafulla Chandra College, New Barrackpore, Kolkata, West Bengal, [3]Professor, Department of Medicine, Fakhruddin Ali Ahmed Medical College, Barpeta-Hospital-Jania Rd, JotiGaon, Assam

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a significant risk factor of cardiovascular morbidity and mortality including tricuspid regurgitation (TR), right ventricular hypertrophy (RVH), left ventricular dysfunction (LVD) and right atrial enlargement (RAE) among others. Echocardiography is a rapid, non-invasive, and accurate method to evaluate cardiac functions and used to diagnose cardiac changes in COPD patients. This study aimed to assess the prevalence of echocardiographic changes in COPD patients and its association with disease severity, duration of disease and smoking.

Methods: Two hundred thirty four patients of COPD fulfilling the inclusion criteria coming to Respiratory Clinic and Medicine OPD of Assam Medical College and Hospital were recruited. They were evaluated by echocardiography. Adjusted odd ratios (ORs) (adjusted to age, gender and BMI) with 95% CIs of echocardiographic changes were computed for different stages of GOLD standard using multiple logistic regression with GOLD stage I as reference. Test for trend was done using chi-square test and statistical significance was taken p-value<0.01.

Results: Most common echocardiographic finding was TR, which was present in 63.25% of cases, followed by RVH (56.84%), LVD (33.33%) and RAE (30.33%). Echocardiographic findings of TR, RVH and RAE increase with GOLD stage progression of COPD (p-value<0.01). Disease duration was correlated with echocardiographic findings of TR, RVH and RAE. A significant trend of change in LVDD was seen for smoking status with severity of GOLD. The similar echocardiographic findings were RAE, RVH and LVD.

Conclusions: Our study finds that echocardiographic examinations of TR, RVH, LVD and RAE are essential for early diagnosis of cardiac screening for COPD patients. The incidence of TR is more common as severity of COPD increases followed by RVH. There is a significant correlation between severity of COPD with echocardiographic findings of TR, RVH and RAE.

Keywords: *COPD, echocardiography, echoabnormalities, odd ratios*

Background

Cardiovascular disease is most frequent co-morbidity and a cause of death among patients with chronic obstructive pulmonary disease (COPD). One of the most important risk factor for the development of COPD is smoking although it alone does not fully explain the frequency. COPD is projected to be the third leading cause of death by 2020 by World Health Organization (WHO).[1,2] In India, a crude estimate of about 30 million people suffering from COPD, and the

Corresponding author:
Arabinda Das,
Department of Statistics, Acharya Prafulla Chandra College, Kolkata – 700 131, West Bengal, India;
E-mail: arabinda@apccollege.ac.in

death rate is among the highest in the world.[3,4] COPD causes considerable effect on the cardiac function, including those of the right ventricles, left ventricles as well as the pulmonary blood vessels.[5] These lead to the development of cardiovascular disease like right ventricular (RV) dysfunction, pulmonary hypertension (PH), coronary artery disease (CAD), and arrhythmias. [6] Arrhythmia, myocardial infarction, or congestive heart failure are significantly higher in occurrence and cause of morbidity among patients with COPD.[7]

Echocardiography is a rapid, non-invasive portable method to detect the arrhythmia, pulmonary hypertension, the right ventricular and left ventricular dysfunction. The detection can serve as a guide to initiation of early treatment and to prolong the survival and improvement of the quality of life of the COPD patients. The present study was addressed to investigate various echocardiographic changes among the COPD patients in the north-eastern part of India and its association with the severity of the disease.

Materials & Methods

The present study was conducted among COPD patients attending Respiratory Clinic and Medicine OPD of Assam Medical College and Hospital who were available during data collection period. Two hundred thirty four adult patients who fulfilled the inclusion criteria were taken for the study. The patients were recruited randomly whenever they obeyed the inclusion and exclusion criteria. The Ethics Committee of the Assam Medical College and Hospital, Assam, approved the study. A written well-informed consent was obtained from all participants and the study was performed according to the Declaration of Helsinki, 1975.

All patients above 40 years of age with or without smoking history, with or without chronic cough and/ or sputum production with FEV1/FVC<0.7 and post bronchodilator FEV_1 < 80% predicted are included in this study.

The patients who were not made as a part of the study were the one with known diagnosis of tuberculosis, bronchial asthma, interstitial lung disease, previous lung surgery, coronary artery disease, diabetic cardiomyopathy, chronic alcoholism, uremia.

After obtaining a detailed clinical history of each case, all patients were subjected to thorough clinical examination and necessary investigations including spirometry. Then fulfilling the inclusion and exclusion criteria for the study all the recruited patients were undergone echocardiography. The presenting symptoms and signs, spirometric value and echocardiographic data were recorded for each patient.

Spirometry was carried out on Transfer Test Model 'C', P K Morgan, Chatham, Kent, UK. All patients withheld the inhaled short acting bronchodilators 6 hours before test, long acting β_2 agonists 12 hours before test, and sustained release the ophyline 24 hours before test. The calibration of the spirometer was done before the beginning of each day's test according to the standard age and sex matched data of the population. The patients were counseled and demonstrated about the procedure of the test. Then the patient was asked to do the procedure repeatedly till the procedure was correct. Spirometric indices were calculated using best out of 3 technically satisfactory performances as per recommendations of American Thoracic Society.[8] The diagnosis of COPD was based on the criteria defined by 'Global Initiative for Chronic Obstructive Lung Disease (GOLD 2008) update'.

Echocardiography was carried out by Aloka SSD- 4000, MNI-1175 model, Tokyo, Japan. The basic procedure was as follows: An echocardiographic examination begins with real-time 2D echocardiography, which produces high-resolution images of cardiac structures and their movements. These images are usually obtained from four standard transducer locations—parasternal, apical, subcostal, and suprasternal—by manually rotating and angulating the transducer. Qualitative and quantitative measurements of cardiac dimensions, area, and volume are derived from 2D images or 2D-derived M-mode recordings. Also, 2D echocardiography provides the framework for doppler examination and color flow imaging. An M-mode recording is derived from 2D tomographic images and graphically represents the motion of cardiac structures. It is used primarily to measure cardiac chamber size and timing of cardiac events and to display subtle abnormalities of cardiac motion. The following parameters in echocardiography were observed: i) Right ventricular hypertrophy/enlargement

(M-Mode), ii) Right atrial enlargement (M-Mode), iii) Tricuspid regurgitation (continuous-wave Doppler echocardiography for an estimate of systolic pulmonary artery pressure), iv) Left ventricular ejection fraction (M-Mode/2D-Mode), v) Left ventricular systolic or diastolic dysfunction [M-mode, 2D, and Doppler (blood flow, tissue, and color)].

Statistical Analysis

Categorical variables were expressed as numbers and percentages and continuous variables were presented with means and standard deviations of the variables. Differences in baseline characteristics were examined with one way ANOVA or chi-square test, when appropriate. Odd ratios (OR) were computed analyzing multivariate logistic regression. Unadjusted and adjusted odd ratios (OR) with 95% confidence interval were calculated for each diagnostic of echocardiogram to evaluate the risk developed in each GOLD stage. Adjusted ORs were calculated with adjusted to age, gender and BMI. ORs with 95% confidence interval were also used to find the association of duration of COPD and smoking status with the different echocardiogram abnormalities. Association between different measures of echocardiogram abnormalities were assessed by chi-square test for trend. A cluster analysis was performed to combine cardiac abnormalities with similar appearance. P-value <0.01 was considered to be statistically significant. All the statistical analysis were performed in R 3.4 statistical software.

Results

Two hundred thirty four patients were screened during the course of the study, out of which two hundred thirty four spirometrically confirmed COPD patients were included for the study. The echocardiography of all the patients was done following the method described in the method sub-section and the results were recorded.

The participants were divided into four GOLD stages based on FEV1% predicted and most of the participants belonged to the GOLD Stage III (40%) and least were in the GOLD Stage I (5%). The characteristics of the participants under different categories of GOLD are presented in Table 1. No significant difference in average age of participants under GOLD categories. Among the participants, 63% were male. The average BMI and duration of illness of the participants for different categories of GOLD were not significant. Moreover, gender and biomass exposure were not significantly related to GOLD. Table 2 presents the occurrence of all possible echocardiography changes in the selected COLD population. Table 2 revealed that the TR was the most common findings in echocardiography (63.25%) followed by RVH (56.84%) and LVD (33.33%). RAE (30.33%) was present in 29.91% of patients. Table 3 revealed the adjusted and unadjusted OR of TR, RAE, RVH Echo and LVD under different stages of GOLD.

The studied parameters of echocardiographic changes are now correlated with GOLD stages to establish the relationship between disease severity and echocardiographic changes. Table 3 of adjusted ORs showed that the percentage of patients with TR, RVH and RAE increases with GOLD stage progression of COPD i.e. the increased severity of COPD is positively associated with echocardiographic changes.

In the present study the average duration of the disease was 8.06 years with the longest disease duration of 28 years. Disease duration was correlated with the different echocardiographic abnormalities. The results are shown in the following tables. Table 4 demonstrated that with the increase in disease duration the echocardiographic abnormalities like TR, RVH and RAE also increased. Table 5 showed a significant trend of abnormality in LVD for smoking status with severity of GOLD.

Table 1: Baseline characteristics of the study population stratified by severity of COPD according to the GOLD stage

Characteristics		GOLD Stage				
		I	II	III	IV	p-value
Age (years, SD)		66.33 (5.13)	63.72 (11.64)	64.67 (11.66)	61.33 (10.98)	0.803

Cont... **Table 1: Baseline characteristics of the study population stratified by severity of COPD according to the GOLD stage**

Gender	Male	12	51	54	27	0.144
	Female	4	16	39	31	
Smoking (pack/ years)		27.67 (5.86)	25.72 (17.54)	22.88 (23.17)	15.47 (19.63)	0.492
FEV1 (%pred, SD)		84.67 (6.43)	58.89 (8.55)	43.25 (6.05)	24.07 (3.73)	0.000
Duration of Illness (Years)		7.00 (2.65)	7.28 (3.36)	10.21 (12.68)	7.87 (3.58)	0.684
BMI		21.97 (1.83)	19.72 (4.03)	19.38 (3.43)	19.60 (3.99)	0.729
Biomass Exposure	No	12	51	54	27	0.144
	Yes	4	16	39	31	

Table 2: Echocardiogram changes in COPD patients:

Echocardiogram changes	No. of patients	% of patients
TR	148	63.25
RAE	70	29.91
RVH	133	56.84
LVD	78	33.33

Table 3: Relationship between GOLD Stage and Echocardiographic Changes

Echocardiographic changes		GOLD Stage				Test for trend
		I	II	III	IV	
TR (%)	Unadjusted OR	1	1.15 (0.32,5.28)	1.94 (0.54,6.99)	2.20 (0.50,9.61)	<0.01
	Adjusted OR	1	2.83 (0.62,8.62)	3.38 (0.91,12.55)	4.11 (0.86,19.57)	<0.01
RVH (%)	Unadjusted OR	1	2.13 (0.64,8.39)	4.0 (1.09,14.42)	8.0 (1.61,39.64)	<0.01
	Adjusted OR	1	4.74 (1.33,25.45)	8.13 (1.90,34.88)	20.86 (3.17,137.2)	<0.01
RAE (%)	Unadjusted OR	1	1.11 (0.14,2.23)	1.07 (0.27,4.15)	1.73 (0.40,7.46)	>0.01
	Adjusted OR	1	1.21 (0.15,3.25)	1.45 (0.36,5.86)	2.35 (0.51,10.89)	<0.01
LVD	Unadjusted OR	1	0.83 (0.14,2.33)	1.07 (0.27,4.15)	2.97 (0.69,12.62)	>0.01
	Adjusted OR	1	1.19 (0.21,3.87)	1.44 (0.37,5.68)	4.25 (0.94,19.27)	<0.01

Table 4: Relationship of duration of the COPD with Echocardiographic changes

Echocardiographic changes		Duration (Years)				P-value
		0-5	06-10	11-15	>15	
TR (%)	Unadjusted OR	1	0.58 (0.17,1.95)	3.38 (0.57,19.17)	4.54 (1.46,24.69)	<0.01
	Adjusted OR	1	0.51 (0.15,1.80)	4.46 (0.65,44.29)	6.32 (1.63,58.69)	<0.01
RVH (%)	Unadjusted OR	1	3.95 (1.14,13.71)	4.95 (0.98,24.87)	6.62 (1.45,30.12)	<0.01
	Adjusted OR	1	4.06 (1.14,13.71)	5.43 (1.00,29.45)	6.44 (1.82,41.12)	<0.01
RAE (%)	Unadjusted OR	1	1.69 (0.46,6.19)	1.92 (0.86,15.97)	3.00 (1.23,27.23)	<0.01
	Adjusted OR	1	1.28 (0.46,6.19)	1.37 (0.23,8.12)	2.17 (0.14,32.49)	<0.01
LVD	Unadjusted OR	1	0.47 (0.13,1.71)	1.25 9 (0.28,5.52)	0.5 (0.04,5.70)	>0.01
	Adjusted OR	1	0.42 (0.11,1.58)	1.31 (0.28,6.19)	0.75 (0.06,10.25)	>0.01

Table 5: Relationship of smoking status with Echocardiographic changes

Echocardiographic changes	Smoking status				P-value
	No	1-25	26-50	51-100	
TR	1	1.17 (0.28,4.83)	1.75 (0.44,6.93)	0.19 (0.02,2.24)	>0.01
RAE	1	0.29 (0.07,1.21)	0.17 (0.04,0.67)	0.19 (0.02,2.24)	>0.01
RVH	1	1.03 (0.26,3.99)	1.57 (0.45,5.50)	0.9 (0.10,7.78)	>0.01
LVD	1	1.08 (0.26,4.59)	1.23 (0.28,6.13)	6.5 (0.55,76.18	<0.01

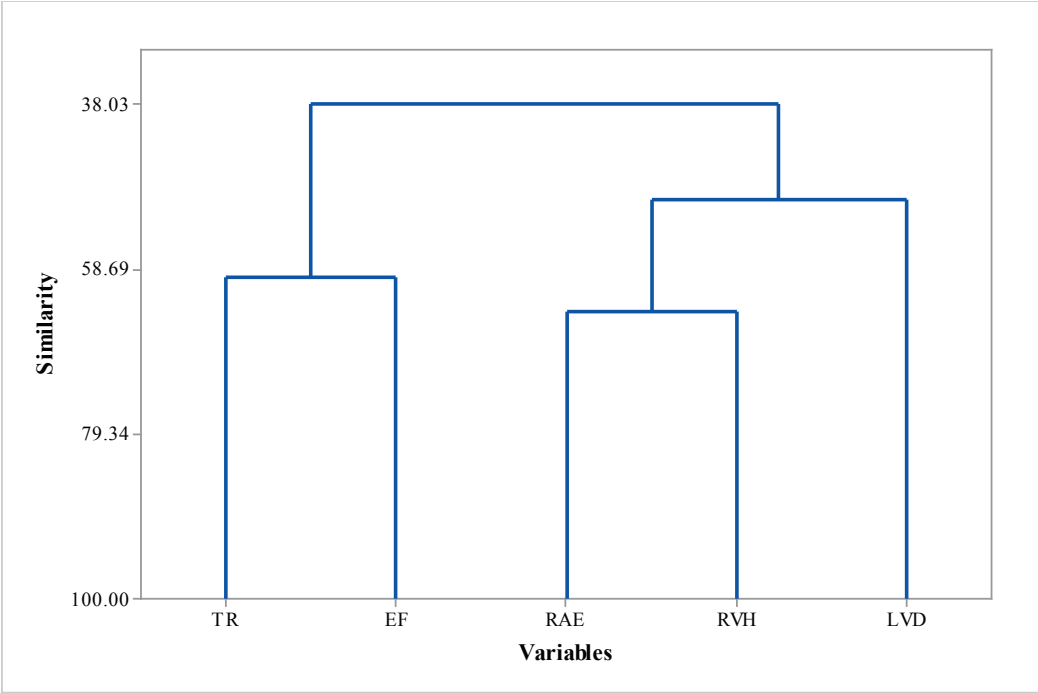

Fig 1: Dendogram showing similarity among different echocardiographic changes

The dendrogram showed the abnormalities which might be combined, by totaling. We have found that a group of patients had common abnormalities in RAE, RVH and LVD whereas TR and EF were common to other group of patients.

Discussion

Typical signs of corpulmonale in 2D echocardiography are right ventricular and atrial enlargement with a normal or reduced left-ventricular cavity and eventually reversal of the normal septal curvature. In the presence of tricuspid regurgitation, continuous-wave Doppler echocardiography may provide an estimate of systolic pulmonary artery pressure (PPA). However, tricuspid regurgitation (TR) is not always present in COPD, the incidence ranges between 24–66% of patients [5,6,7], therefore limiting the possibility to estimate PPA in a number of patients. In our study the TR was present in 63.33% of patients. Higham et al.[9] found measurable TR was observed in 56/73 patients (77%) in their study. The incidence of TR ranges between 24-66% of patients in different studies. [5,6,7]

The current study showed that the percentage of patients with TR increases with the GOLD stages i.e. the decrease in FEV1 or increase in the severity of the COPD. The other studies [9,10] also confirmed that there is an inverse relationship between FEV1 expressed as % predicted.

In the present study LVD was present in 33.33% of patients. The present study also demonstrates the direct relationship between the LVD and the GOLD stages (i.e. inverse relationship with FEV1 expressed as percentage predicted). In a study by Render et al.[11] of patients with moderate to severe COPD, 32% who presented with clinical deterioration had LVD contributing to their poor exercise tolerance.

Funk et al.[12] showed a good relationship between the LVD and decrease in FEV1 expressed in percentage predicted. Suchoń et al.[13] found that LVD is significantly impaired and its magnitude is related with increase in pulmonary artery pressure in COPD patients. In another study diastolic dysfunction appeared in about 70% of advanced COPD patients independent of the presence of ischemia or hypertension. Low FEV1 (less than 35% predicted) was one of the risk factors for developing diastolic dysfunction.[14]

In the present study 41.66% of COPD patients were having RVH and there is direct relationship between

RVH and GOLD stages (i.e. inverse relationship with FEV1 expressed as percentage). The study by Suchoń et al.[12] found RV end-diastolic diameter and RV wall thickness was significantly larger in COPD patients. One study by Vonk-Noordegraaf et al.[15] found that concentric RV hypertrophy is the earliest sign of RV pressure overload in patients with COPD. This structural adaptation of the heart does not alter RV and LV systolic function.

Disease duration at any stage of GOLD in almost all cases determines the severity of echocardiographic change which increases more rapidly with duration when adjusted to age, gender and BMI. Again LVD in echocardiography had an increasing trend with the severity of smoking status.

In our study, OR of TR, RVH and RAE showed a uniformly increasing trend with the severity of GOLD stages i.e. the chances of developing TR, RVH and RAE increases with severity of GOLD stages. Gunen et al.[16] in their study showed that the longer duration of COPD is related to significant morbidity and mortality because of pulmonary hypertension. Similarly study by Vij et al.[17] revealed that incidence of right ventricular hypertrophy, right atrial enlargement and left ventricular diastolic dysfunction all increases with the longer duration of the disease.

Conclusion

In this study most of the echocardiography parameters showed a strictly increasing trend of cardiac disorders with the severity of COPD i.e. the severity of complication increases with severity of COPD. Therefore, echocardiographic evaluation in timely basis has pivotal role in early detection of the hemodynamic and mechanical alterations like LVDD, TR, RAE, RVH etc. The severity of the echocardiographic changes increases with the duration of the disease except LVDD, which is a non-specific finding. A prospective longitudinal study with more number of patients will be more informative in this respect.

Conflict of Interest*:* There is no conflict of interest and financial disclosure of authors with this study.

References

1. Chen JC, Mannino DM. Worldwide epidemiology of chronic obstructive pulmonary disease. Curr Opin Pulm Med. 1999;5:93-99.
2. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet. 1997;349:1436-1442.
3. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, et al. Chronic obstructive pulmonary disease: Current burden and future projections. European Respiratory Journal. 2006;27:397-412.
4. Salvi S, Agrawal A. India needs a national COPD prevention and control programme. J Assoc Physicians India. 2012;60:5-7.
5. Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galie N, Pruszczvk P et al. Guidelines on the diagnosis and management of acute pulmonary embolism: The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). *European Heart Journal*. 2008; 29,8(18):2276–2315.
6. Laaban, JP, Pascal-Sebaoun S, Bloch, E et al. Left ventricular systolic dysfunction in patients with obstructive sleep apnea syndrome. Chest. 2002;1133–1138.
7. Naeije R, Vachiery J-L, Yerly P, Vanderpool R. The transpulmonary pressure gradient for the diagnosis of pulmonary vascular disease. European Respiratory Journal, 2013;41:217-222.
8. Lindberg A, Bjerg A, Rönmark E, Larsson LG, Lundbäck B. Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking report from the obstructive lung disease in Northern Sweden studies. Respir Med. 2006;100(2):264-272
9. Higham MA, Dawson D, Joshi J, Nihoyannopoulos P, Morrell NW. Utility of echocardiography in assessment of pulmonary hypertension secondary to COPD. European Respiratory Journal, 2001;17:350-355
10. *Oswald-Mammosser M, Weitzenblum E, Quoix E, et al. Prognostic factors in COPD patients receiving long-term oxygen therapy: Importance of pulmonary artery pressure.* Chest, 1995;107*:*1193–*1198.*
11. Render ML, Weinstein AS, Blaustein AS. Left ventricular dysfunction in deteriorating patients with chronic obstructive pulmonary disease. Chest, 1995;107(1):162-168.
12. Funk GC, Brever Mk, Burghuber OC, Kink E,

Kirchheiner K, Kohansal R, Schmidt I, Hartl S. Long-term non-invasive ventilation in COPD after acute-on-chronic respiratory failure. Respir Med, 2011;105(3):427-434.

13. Suchoń E, Tracz W, Podolec P, Pieculewicz M, Płazak W, et al. Evaluation of left ventricular function in patients with chronic obstructive pulmonary disease. Pol Arch Med Wewn, 2007;117:26–30
14. Bhattacharyya P, Saha D, Bhattacharjee P, Paul R, Dey R, Ghosh M. Long-term doxycycline and lung function in chronic obstructive pulmonary disease: A pilot observation. Lung India, 2014;31(3):306-307.
15. Vonk-Noordegraaf A, Marcus JT, Holverda S, et al. Early changes of cardiac structure and function in COPD patients with mild hypoxemia. Chest. 2005;127:1898-1903.
16. Gunen H, Hacievlivaail SS, Kosar F, Mutlu LC, Gulbas G, Pehlivan E, Sahin I, Kizkin O. Factors affecting survival of hospitalised patients with COPD. European Respiratory Journal. 2005;26(2):234-241.
17. Vij A, Kapila S, Vij C, Sachdeva GS, Gill BS et al. Study of Electrocardiographic and Echocardiographic Profile of COPD patients. JAPI. 2008;56:290.