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ECHOCARDIOGRAPHIC EVALUATION OF RIGHT VENTRICLE IN DIFFERENT STAGES OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AND ITS CORRELATION WITH SEVERITY OF THE DISEASE

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory disease of the lung characterized by chronic bronchitis, airway thickening and emphysema. COPD has significant cardiac complications also. Development of secondary pulmonary arterial hypertension (PAH) in COPD is associated with an increased risk of acute severe exacerbation. Pulmonary hypertension progressively leads to right ventricular hypertrophy and dilatation with subsequent RV failure. **Aims and objectives**: The purpose of our study was to evaluate the right ventricular functions in different stages of COPD by echocardiography and to find out it's correlation with the severity of the disease. **Materials and Methods**: We performed an observational and cross-sectional study on 60 COPD patients in R G Kar Medical College, Kolkata. We classified the patients into mild, moderate, severe and very severe COPD according to the GOLD criteria[1], based on their spirometric parameters. Then we have subjected them to 2D echocardiography to evaluate their right ventricular function. For that we focussed on the parameters like RV basal and longitudinal diameters, RV wall thickness, TAPSE (Tricuspid Annular Plane Systolic Excursion), FAC (Fractional Area Change), RIMP (Right ventricular index of myocardial performance) and SPAP (Systolic Pulmonary Arterial Pressure). **Results**: RV wall thickness was progressively increased from mild to very severe COPD with a significant p value of 0.002. In our study SPAP has been increased significantly from mild to very severe COPD (p=0.001). The mean values of SPAP are 14.05(±3.48) mmHg in mild, 16.80 (±4.52) mmHg

in moderate, 21.55(±6.07) mmHg in severe and 29.075(±7.8) mmHg in very severe COPD. Other findings suggestive of RV systolic function also showed progressively decreased values alone with the severity of the disease. **Conclusion**: Though the elevation of pulmonary arterial pressure in COPD is moderate, but its early detection is helpful to prevent right heart failure. Echocardiography can be used as a screening method for early detection of pulmonary hypertension in COPD before undertaking other invasive and complicated procedures.

KEYWORDS: Chronic obstructive pulmonary disease (COPD), Right ventricle (RV), Echocardiography, Systolic Pulmonary Arterial Pressure (SPAP).

INTRODUCTION

COPD is a preventable and treatable disease with some significant extra pulmonary effects that may contribute to the severity in the individual patient. Increased airway resistance, increased residual volume, increased residual volume/total lung capacity ratio (RV/TLC), decreased inspiratory capacity, mal-distribution of ventilation, and ventilation- perfusion mismatching are the typical features of COPD.[2] Unlike asthma, this airflow limitation caused by COPD is not fully reversible. Following the marked increase in tobacco consumption in developing countries like India COPD is gaining importance; if current trends continue, it will become the 3rd most important cause of death world-wide by 2020.[3]

COPD is associated with significant extra-pulmonary effects. Significant structural changes occur in the pulmonary circulation in patients with COPD. The presence of hypoxemia and chronic ventilatory insufficiency is associated with intimal thickening and medial hypertrophy in the smaller branches of the pulmonary arteries.[4] These lead to increased pulmonary arterial pressure. In these patients, due to the slow progression of pulmonary arterial pressure, the right ventricle adapts first by hypertrophy and then by progressive dilatation. The next step in the evolution of PAH is RV dysfunction with subsequent right heart failure. In one study, the 5-year survival rate was 37% in COPD patients with PH versus 63% in patients without PH.[5] So, a timely prediction about the cardiac involvement is of immense importance. The purpose of our study was to evaluate the RV functions in different stages of COPD patients by echocardiography, which is non-invasive and relatively less expensive**,** as per guidelines of American Society of Echocardiography.[6]

MATERIALS AND METHODS

- Study design: The study was an observational and cross-sectional study.
- Study area: The present study was conducted in the Department of Physiology, Department of Pulmonary Medicine OPD and Department of Cardiology, R G Kar Medical College and Hospital, Kolkata.
- Study population: >40 years aged sixty COPD patients of both sexes including smokers, ex-smokers andnon-smokers attending Pulmonary Medicine OPD were taken for the study.
- Sample design: All the patients attending the pulmonary medicine OPD with clinical features of COPD were selected for the study by purposive sampling method.

Exclusion criteria

1. Patients with h/o chronic lung disease other than COPD.
2. Post bronchodilator reversibility of FEV1>12%.
3. Hypertension, dyslipidemia and diabetes mellitus.
4. Any primary cardiac disease.
5. Any systemic disease that can cause pulmonary hypertension.
6. Patients with any infectious disease.
7. Patients with respiratory failure.
8. Patients with congestive heart failure.

Study technique: It was an observational and cross-sectional study. First of all, the selected cases wereperformed with pulmonary function test at the Department of Physiology, R G Kar Medical Collegeand classified into mild, moderate, severe and very severe COPD according to GOLD criteria.[1] Then the right ventricular function were assessed by resting Two Dimensional Transthorasic Doppler Echocardiography at the Department of Cardiology, R G Kar Medical College, by expert cardiologists. Finally the echocardiographic findings were reviewed to assess the correlation with the severity of COPD.

Investigation

A. Spirometry: It is the measure of airflow during inspiration and expiration. Spirometry was done with the help of computerized electronic spirometer (model: RMS Helios 702) and results of best of three manoeuvres were taken.American Thoracic Society (ATS) recommendations for performingspirometry were followed.[7]

- Effort: maximal, smooth, and cough free.
- Position: sitting.
- Exhalation time: 6 seconds.
- End of test: 2 second volume plateau.
- Reproducibility: FVC within 5% in 3 acceptable tests.

Spirometric measurement[7]: following spirometric parameters were taken.
FVC (Forced vital capacity), FEV1 (Forced expiratory volume in one second), FEV1/FVC ratio (the percentage of the FVC expired in one second.), FEF25-75% (Forced expiratory flow over the middle one half of the FVC), PEFR(Peak expiratory flow rate).

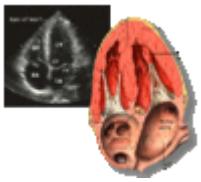
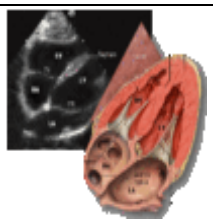
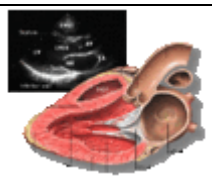
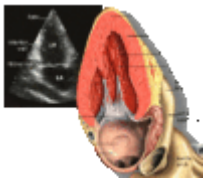
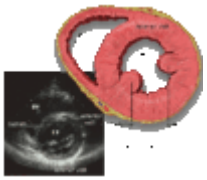
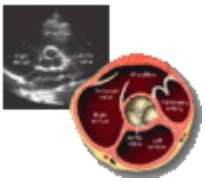
Spirometry was repeated 10 minutes after the administration of bronchodilators (two puffs of Salbutamol, 100 µg each). Post bronchodilator reversibility of FEV1>12% was excluded.

According to GOLD guideline (1) COPD patients were divided into four stages.

GOLD stages	Severity	Symptoms	Spirometry
0.	At risk	Chronic cough, sputum production	Normal
i.	Mild	With or without chronic cough or sputum production	FEV1/FVC<0.7 and FEV1≥80% predicted
ii.	Moderate	With or without chronic cough or sputum production	FEV1/FVC<0.7 and 50%≤ FEV1≤80% predicted
iii.	Severe	With or without chronic cough or sputum production	FEV1/FVC<0.7 and 30%≤FEV1≤50% predicted
iv.	Very severe	With or without chronic cough or sputum production	FEV1/FVC<0.7 andFEV1≤30%predicted

B. Echocardiography: Selected COPD patients are then subjected to resting two dimensional transthoracic doppler echocardiography for assessment of right ventricular size and function.

According to the guidelines of the "**American Society of Echocardiography**" 2012[6] for the assessment of right heart in adults, following imaging windows and views were used.

Various transthoracic echocardiographic views					
 **Apical four chamber view**	 **Subcostal view**	 **Left parasternal long axis view**	 **Apical two chamber view**	 **Left ventricle short axis view**	 **Aortic valve short axis view**

Following echocardiographic parameters of right ventricle were measured

- ❖ RV basal diameter.
- ❖ RV mid level diameter.
- ❖ RV longitudinal diameter.
- ❖ RV wall thickness
- ❖ TAPSE: Tricuspid Annular Plane Systolic Excursion.
- ❖ FAC: Fractional Area Change
- ❖ RIMP: Right ventricular index of myocardial performance
- ❖ SPAP: Systolic pulmonary arterial pressure.
- ❖ IVCT: Isovolumic contraction time.
- ❖ IVRT: Isovolumic relaxation time
- ❖ ET: Ejection time.

- Right heart dimensions: "Diameter >42mm at the base and >35mm at the mid level indicates RV dilatation. Similarly, longitudinal diameter>86 mm indicates RV enlargement."
- Right heart wall thickness: The normal cut-off value is 5 mm from either PLAX or subcostal windows.
- TAPSE (Tricuspid annular plane systolic excursion): It acts as an indicator of RV global systolic function. It provides the systolic movement of base of the right ventriclular free wall which is one of the most visibly obvious movements on normal echocardiography. TAPSE <16mm indicates RV systolic dysfunction.
- RIMP (Right ventricular index of myocardial performance): RIMP or Tei index, is a global estimate of both systolic and diastolic function of right ventricle. RIMP is defined as the ratio of isovolumic time divided by ejection time or (IVCT+IVRT)/ET. The upper reference limit for the right sided RIMP is 0.40 using the pulsed Doppler method and o.55 using the tissue Doppler method.

- FAC (Fractional Area Change): Two-dimensional FAC is a measure of RV systolic function. It is defined as (end diastolic area-end systolic area)/end diastolic area × 100.It is expressed as percentage. Two dimensional FAC<35% indicates RV systolic dysfunction.
- Right Atrial pressure (RA pressure): RA pressure is estimated by the IVC diameter and the presence of inspiratory collapse with a sniff. As the RA pressure increases, this is transmitted to the IVC, resulting in reduced collapse with inspiration and IVC dilatation. IVC diameter <2.1cm that collapses >50% with a sniff suggests a normal RA pressure of 3 mm Hg (range,0-5 mm Hg),whereas an IVC diameter>2.1cm that collapses <50% with a sniff suggests a high RA pressure of 15 mm Hg (range, 10-20mmHg).In indeterminate cases an intermediate value of 8 mmHg (range, 5-10mmHg) may be used.
- Systolic Pulmonary Arterial Pressure (SPAP): Based on the modified Bernoulli equation, RVSP is estimated as: RVSP= 4v2 + RAP, where v represents the peak velocity in meters/s of tricuspid regurgitation and RAP is the right atrium estimated pressure mentioned above. Pulmonary hypertension (PH) was defined in this study as sPAP ≥ 30 mmHg. 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).[8]

RESULTS AND ANALYSIS

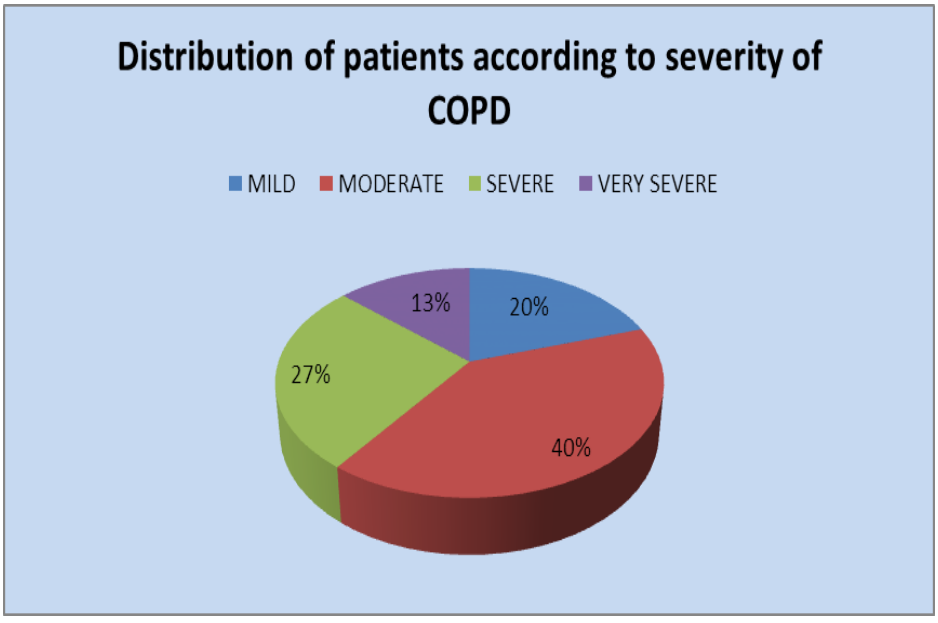


Diagram 1: Distribution of patients according to severity of COPD.

Table 1: Comparison Of Spirometric Parameters With Four Stages Of COPD.

Parameters of PFT	Mild COPD	Moderate COPD	Severe COPD	Very severe COPD	P-value and F – value
FVC (%)	118.34±7.8	90.34±6.52	72.00±8.11	49.37±5.9	F(29,3)=87.086 P=0.001
FEV1 (%)	83.13±6.5	60.40±6.94	44.13±4.17	28.6±4.34	F(29,3)=82.725 P=0.001
FEV1/FVC (%)	69.79±3.86	66.84±6.12	61.28±6.57	57.91±3.7	F(29,3)=5.100 P=0.007
PEFR (%)	49.5±5.34	42.42±9.08	25.63±5.26	18.5±5.57	F(29,3)=23.850 P=0.005
FEF25-75(%)	38±5.6	24.92±3.96	15.63±5.26	8.25±1.5	F(29,3)=44.145 P=0.003

Table 2: Comparison Of Different Right Ventricular Diameters With Four Stages Of COPD.

RVDiameters (mm)	Mild COPD	Moderate COPD	Severe COPD	Very severe COPD	P and F value
Basal diameter	26.265±7.2	30.48±4.28	33.5 ±3.55	37.72±3.74	F(29,3)=5.330 P=0.005
Apex to base diameter	74.5±1.2	76.8±0.53	80.8±0.50	85.7±0.42	F(29,3)=26.086 P=0.000
Mid level diameter	28.32±3.3	31.24±4.45	36.56±2.90	38.09±3.37	F(29,3)=8.866 P=0.003
Wall thickness	6.67±1.02	6.97±0.624	7.87±0.40	7.9±0.55	F(29,9)=10.536 P=0.002

Table 3: Comparison of the parameters indicating Right ventricular functions with four stages of COPD.

Right ventricular parameters	Mild COPD	Moderate COPD	Severe COPD	Very severe COPD	P and F value
TAPSE(mm)	23.82±5.4	20.43±3.46	17.47±2.54	15.61±3.05	F(29,3)=5.313 P=0.005
RIMP	0.149 ±0.31	0.189±0.05	0.222±0.06	0.295±0.036	F(29,3)=0.913 P=0.448
FAC (%)	44.33±6.83	37.5±8.72	27.88±6.90	22.5±4.8	F(29,3)=9.498 P=0.001
SPAP(mmHg)	14.05±3.48	16.81±4.52	21.55±6.07	29.075±7.8	F(29,3)=7.904 P=0.001
IVRT(ms)	28.83±2.05	29.12±4.02	30.88±2.80	33±2.94	F(29,3)=6,983 P=0.002
IVCT(ms)	26.66±1.38	29.33±3.9	30.125±2.1	32.25±2.23	F(29,3)=9.753 P=0.001
ET(ms)	372.33±50.51	329±40.61	305±52.15	251.25±59.9	F(29,3)=5.438 P=0.005

(Abbreviations are given above)

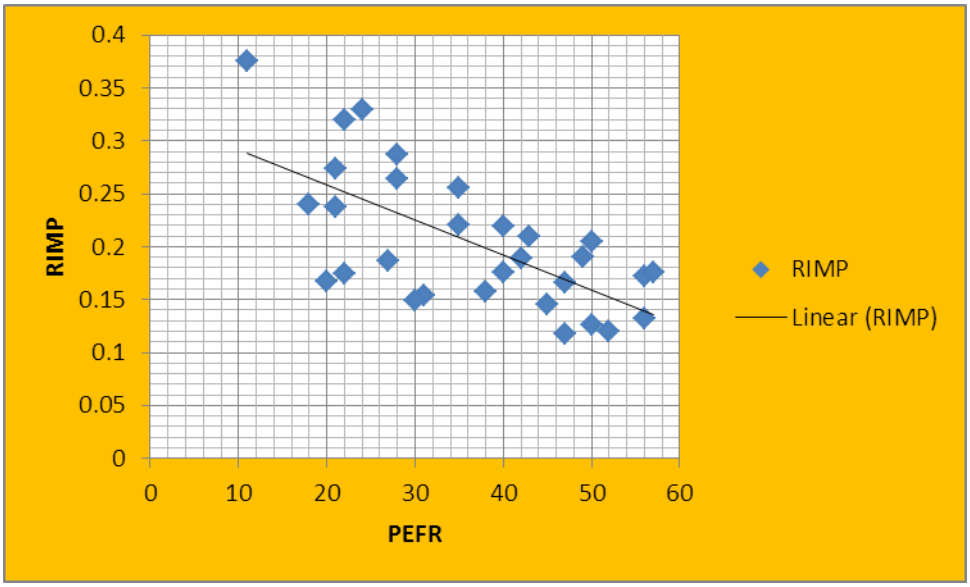


Diagram 2: showing strong negative correlation between PEFR and RIMP (Right ventricular index of myocardial performance) with severity of COPD.

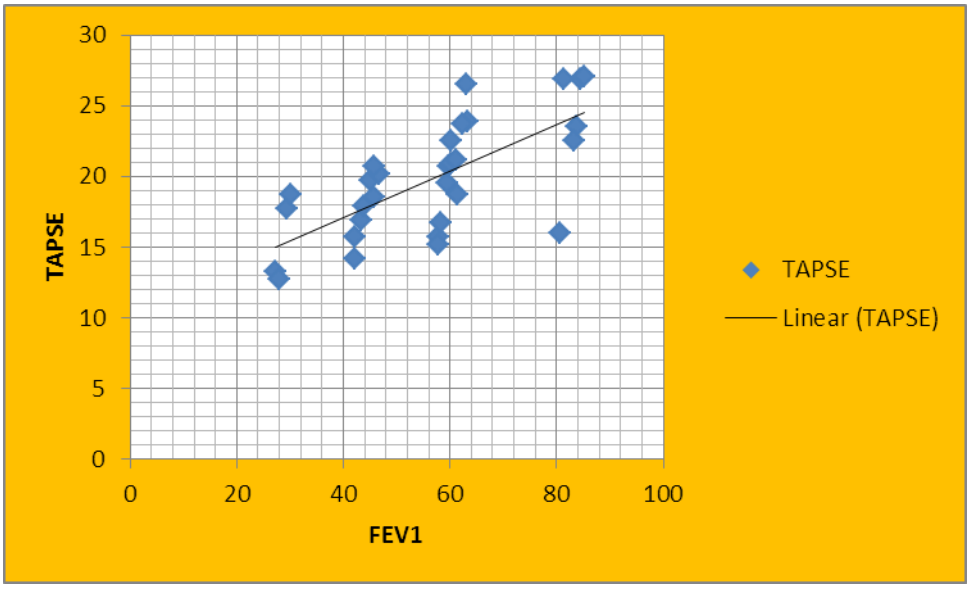


Diagram 3: showing strong positive correlation between FEV1 and TAPSE (Tricuspid annular plane systolic excursion) with severity of COPD

Table 4: Correlation between FEV1 and FAC (Fractional Area Change) in different stages of COPD.

Stages of COPD	FEV1 (%)	FAC (%)	Correlation coefficient (r value)	P value
Mild	83.13	44.33±6.83	0.9750	**0.0093**
Moderate	60.40	37.5±8.72	0.8685	**0.0247**
Severe	44.13	27.88±6.90	0.8868	**0.0332**
Very severe	28.6	22.5±4.8	0.9540	**0.0460**

Table 5: Correlation between FEV1 and SPAP (Systolic pulmonary arterial pressure) in different stages of COPD.

Stages of COPD	FEV1 (%)	SPAP (mmhg)	Correlation coefficient (r value)	P value
Mild	83.13	14.05±3.48	-0.7548	0.0828
Moderate	60.40	16.81±4.52	-0.9008	**0.0453**
Severe	44.13	21.55±6.07	-0.9110	**0.0016**
Very severe	28.6	29.075±7.8	-0.9816	**0.0184**

DISCUSSION

COPD has considerable effects on cardiac functions primarily affecting the pulmonary vasculature and then right ventricle along with left ventricle. One of the important causes of increased morbidity and mortality associated with COPD is cor-pulmonale which is defined as right ventricular hypertrophy and dilatation, secondary to pulmonary hypertension caused by lung diseases.[9] Echocardiography provides a rapid, non-invasive method to evaluate cardiac changes. Our aim was to evaluate the right ventricular function in COPD and its correlation with severity of disease.

In our study mean age of the patients was 58.55 (±8.57) years ranging from 42 to 78 years. Out of the sixty patients we taken from pulmonary medicine OPD for study purpose 73% were male and 27% were female, 42 patients were smoker (70%) and the 18 patients were non-smokers (30%). Out of the smokers again18 patients had H/O cigarette smoking < 20 pack years; 19 had H/O smoking 20-30 pack years and 5 patients had H/O smoking for>30 pack years. In our study we got the moderate COPD (40%) patient maximum in number than mild and other groups.

In our study FVC has been significantly (P value=0.001) decreased with the severity of COPD.FVC showed a negative correlation with RV basal diameter in all stages of COPD with a significant p value (p=0.0414) found only in severe COPD (r =-0.8876).It also showed a strong negative correlation with RV wall thickness with p= 0.0617 in moderate COPD(r=-0.7662) and a significant p value(p =0.0392) in very severe COPD(r =-0.9308).FVC did not show anysignificant relation with any other diameters. FVCshowed strong positive correlation with FAC(Fractional area change) in severe(r= 0.6465 and p=0.0431)and very severe COPD(r=0.9332 and p=0.0368),which suggests persistent fall of RV systolic function with reduction of FVC. We also found a strong negative correlation between FVC and

systolic pulmonary arterial pressure(s PAP) only in very severe COPD(r= -0.9857; p=0.0143). Barbera JA et all showed near similar results in their study.[10]

In our study FEV1 has been significantly decreased (p value=0.001) with the severity of COPD. FEV1 has showed strong negative correlation with the RV basal diameter in all the four stages of COPD, most significantly with severe COPD (r=-0.9205, p value=0.00059). Similarly we got a strong negative correlation between FEV1 and RV mid level diameter. Moreover FEV1 in our study also showed very strong negative correlation with RV longitudinal diameter, significant p values were found in moderate (r=-0.7363, p =0.0184), severe (r=-0.9462, p =0.0231) and very severe (r=-0.9744, p=0.0256) COPD. This gradual increase of RV diameters with reduction of FEV1 signifies the chance of development of right ventricular dilatation with increased severity of COPD. Badesch D.B. et al in their study also found almost similar results.[11]

When we compare the right ventricular wall thickness in different stages of COPD, we found a gradual increase in wall thickness with severity of the disease. RV wall thickness is well negatively correlated with FVC (r=-0.9308, p=0.0392 in very severe COPD) and FEV1 (r=-0.8599, p= 0.0063 in severe, r=-0.9655, p=0.0345 in very severe COPD) but less significant correlation with FEV1/FVC. Right ventricular hypertrophy is determined by this gradual increase of wall thickness with severity of COPD. Massin et all showed the similar result in their study.[12]

TAPSE or Tricuspid annular plane systolic excursion acts as an indicator of RV global systolic function. In the present study TAPSE has been decreased gradually from mild to very severe COPD. The decrease of TAPSE with severity of COPD is statistically significant (p=0.005). TAPSE has strong positive correlation with FEV1 in moderate (r=0.8987, p=0.0458), severe (r=0.9246, p=0.0012) and very severe(r=0.9519, p=0.048) COPD. It has good positive correlation with FVC only in very severe COPD(r=0.9459, p=0.0541).But no such significant correlation with FEV1/FVC ratio was found.

In our study FAC has been decreased significantly (p value of 0.001) with severity of disease. Strong positive correlation was observed between FAC and FVC in severe(r=-0.6465, p=0.0431) and very severe(r=0.9332, p=0.0368) COPD patients. FAC showed a very strong positive correlation with FEV1values in the four stages of COPD.

In the present study sPAP has been increased significantly from mild to very severe COPD (p=0.001). The mean values of sPAP are 14.05(±3.48) mmHg in mild, 16.81(±4.52) mmHg in moderate, 21.55(±6.07) mmHg in severe and 29.075(±7.8) mmHg in very severe COPD.s PAP showed strong negative correlation with FVC in moderate (r=-0.6162, p=0.0328) and very severe (r= -0.9857, p=0.0143) COPD. With reduction of FEV1, sPAP has been increased significantly in moderate(r=-0.9008, p=0.0453) severe(r=-0.9110, p=0.0016) and very severe(r=-0.9816, p=0.0184) COPD. Gupta et al. also showed in their study that prevalence of Pulmonary Arterial Hypertension (PAH) has a linear relationship with severity of COPD.[13]

CONCLUSION

Elevated pulmonary arterial pressure is a well known complication of COPD. It has a 'negative impact' on the progression of disease. In our study, right ventricular wall thickness has been increased significantly with the severity of COPD, which is suggestive of development of right ventricular hypertrophy with the progression of disease. But no significant right ventricular dilatation was found. Systolic pulmonary arterial pressure has been increased with severity of COPD. But the value of sPAP was not very high, suggesting moderate elevation of pulmonary arterial pressure in COPD. Echocardiography can be used as a screening method for early detection of pulmonary hypertension in patients with COPD before undertaking other invasive and complicated procedures. However, our study population was small and further studies with larger number of subjects with multicentric design are required for confirmation.

REFERENCES

1. http://www.goldcopd.com/.Global Initiative For Chronic obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of Chronic obstructive pulmonary disease(COPD).
2. Rabe KF, Hurd S, Anzueto A, et al:Global strategy for the diagnosis, management and prevention of Chronic obstructive pulmonary disease. Am. J. Respir. Crit Care Med, 2007; 176(6): 532-55.
3. J A Innes, P T Reid:Respiratory disease in Davidson's Principal and Practice of Medicine. Nicholas A.Boon, Nicki R, Brian R, Churchill Livingstone, 2006; 20th ed: 678-84.

4. Fletcher C, Peto R. The natural history of chronic airflow obstruction. BMJ, 1977; I: 1645–1658.
5. Kjaergaard J, Mortensen J, Nielsen-Kudsk JE, Bendstrup E et al. Prevalence, predictors and survival in pulmonary hypertension related to end-stage chronic obstructive pulmonary disease. J Heart Lung Transplant, 2012; April, 31.
6. Rudskilg, Lai WW, Afilalo J, Hua L, Handschumacher MD, ChandrasekeranK et al. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography Endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr, 2010; 23: 685–713.
7. American Thoracic society-Standardization of spirometry 1995 update.Am J Respir Crit. Care Med, 1995; 152: 1107-36.
8. Rappaport E. Cor pulmonale. In: Murray JJ, Nadel JA, Mason RM, Boushey H, editors. Textbook of respiratory medicine. 4th Edition. Philadelphia: W.B. Saunders 2000; 1631-48.
9. Chaouat A, Minaioa, Pulmonary hypertension in patients with COPD in Pulmonary Hypertension European Respiratory Society Monograph, 57: 2012.
10. Barbera JAA, Peinado VI, Santos S. Pulmonary Hypertension in COPD. Eur Respir J 2003; 21: 892–905.
11. Badesch D.B., Champion H.C., Sanchez M. A., Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol*, 2009; 54: S55-S66.
12. Massin N, Westphal JC, Schrijen F, Polu JM, Sadoul P Valeurpronostique dii bilan hemodynamique des bronchiteux chro-niques. Bull Eur Physiopathol Respir, 1979; 15: 821-37.
13. Gupta NK, Agarwal RK, Srivastav AB, et al. Echocardiographic evaluation of heart in chronic obstructive pulmonary disease patient and its co-relation with the severity of disease. Lung India, 2011; 28(2): 105-9.