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Echocardiographic Evaluation of Patients with Chronic Obstructive Pulmonary Disease and Its Relation with the Severity of the Disease.

Amardip Rajput*, Virendra C Patil, Swati C Aundhakar, Chinmay Kulkarni, and Jayesh S. Shetye.

Department of Medicine, Krishna Institute of Medical Sciences Deemed University (KIMSDU), Dhebewadi Road, Karad, Pin: 415110, Dist: Satara, Maharashtra, India.

ABSTRACT

Chronic obstructive pulmonary disease (COPD) is common conditions affecting rural as well as urban population. Pulmonary hypertension, biventricular systolic and diastolic dysfunction are the major and under diagnosed complications of COPD which have a great impact on outcome of the disease. To assess the cardiac changes secondary to chronic obstructive pulmonary disease by echocardiography and to find out the correlation between echocardiography findings and the severity of chronic obstructive pulmonary disease. This was a prospective, observational, case control study conducted over period of 18 months. A total of 50 patients from case and control group each were selected for the study. Total 26 (52%) were males and 24 (48%) were females in case group and in control group 23 (46%) were males and 27 (54%) were females. As per global initiative for chronic obstructive lung disease criteria (GOLD) mild, moderate, severe, and very severe COPD was noted in 8(16%), 30 (60%) and 12 (24%) patients respectively. Pulmonary hypertension (mild) was noted in 22 (44%) and 33 (66%) patients had moderate to severe pulmonary hypertension in case group. Diastolic dysfunction was present in 46 (92%) patients and systolic dysfunction was present in 7 (14%) patients from case group. Pulmonary hypertension and diastolic dysfunction were frequent while systolic dysfunction was less frequent echocardiographic findings in patient with COPD. Echocardiography helps in early detection, pulmonary hypertension, systolic and diastolic dysfunction secondary to COPD cases provide opportunity for early intervention.

Keywords: chronic obstructive pulmonary disease, pulmonary artery hypertension, echocardiography, systolic dysfunction, diastolic dysfunction.

Corresponding author

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of health care burden worldwide and leading cause of death that is increasing in prevalence. It is the fourth leading cause of death, and by 2020, is expected to rise to the 3rd position as a cause of death. [1] Pulmonary hypertension is a serious complication of COPD and is associated with poor prognosis. Pulmonary hypertension associated with COPD is usually mild to moderate, and in <5% patients it is severe. Pulmonary artery pressure is known to increase to a great extent during, acute exacerbations which, eventually leads to right heart failure. Thus, early detection and treatment of pulmonary hypertension becomes important to prevent right heart failure.[2] This study was undertaken to assess the cardiac changes secondary to COPD by Transthoracic 2- Dimensional echocardiography.

MATERIAL AND METHODS

This was a prospective, observational, case - control study conducted over period of 18 months (November 2013 to April 2015). The study was approved by protocol and ethical committee Krishna institute of medical sciences (KIMS) deemed university Karad. Total 50 patients (Case group) of COPD confirmed by clinical history, radiology of chest, and pulmonary function test were selected from KIMS Karad. Age and gender matched control (obviously normal) subjects were selected for comparison. Patients with history of chronic lung disease other than COPD, hypertension, any primary cardiac disease, any systemic disease that can cause pulmonary hypertension and patients with poor echo window, were excluded from the study. All selected stable patients with COPD were subjected to routine investigations, including complete blood count, lipid profile, blood sugar, blood urea, serum creatinine, electrocardiography, and other relevant investigation as needed. All the patients were investigated by spirometry / Pulmonary function test (PFT) and classified according to global initiative for chronic obstructive lung disease (GOLD) guidelines (post-bronchodilator FEV1 /forced vital capacity (FVC) ratio < 70% predicted), mild (FEV 1 ≥ 80% of predicted), moderate (50% ≤ FEV 1 < 80% predicted), severe (30% ≤ FEV 1 < 50% predicted), and very severe (FEV 1 < 30% predicted), respectively.[3] All patients were subjected to resting two-dimension transthoracic echocardiography and Doppler study. The machine used was Seimens X-300. The 2-Dimensional echocardiography, Doppler and M-Mode studies were done. Echocardiography was reviewed to assess the 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 (*CW*). 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 + right atrial pressure (RAP), where trans-tricuspid gradient is 4*v2* (*v* = peak velocity of tricuspid regurgitation, m/s). RAP was empirically estimated as 5, 10, or 15 mmHg based on the variation in the size of inferior vena cava with inspiration. 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. [4,5] Right ventricle dimension were measured by M-Mode echo and right ventricular dilation 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%). Fractional shortening (FS) it is a percentage change in LV dimension with each LV contraction (28%-44%). 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).[6-7]

Statistical analysis for mean standard deviation, pearson correlation and chi-square test was done using *MS excel sheet* and 'p' value < 0.05 was considered statistically significant.

RESULTS

A total of 50 subjects from case and control group were enrolled in this study. The mean age for case group was (56 ± 3.90), and control group was (56.16 ± 4.48). In case group 26 (52%) were males and 24 (48%)

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were females. In control group 23 (46%) were males and 27 (54%) were females. Total 26 (52%) male patients were farmers and 24 (48%) female subjects were housewives from case group. In control group 23(46%) male subjects were farmers and 27 (54%) female subjects were housewives. [Table 1]

Table 1: Gender distribution of patients

Gender	Case	Percent	Control	Percent	Total
Male	26	52	23	46	49
Female	24	48	27	54	51
Total	n=50		n=50		n=100

The mean and standard deviation of case and control group is shown in table 2. The *electrocardiogram* (ECG) abnormalities observed were poor 'r' wave progression 17 (34%) patients, p-pulmonale 16 (32%) patients, and right bundle branch block 17 (34%) patients.

Table 2: The mean and standard deviation of clinical, PFT and Echocardiographic parameters in cases and control

Parameters	Control	Case	Mean difference	95% CI of difference
SBP	117.92 ± 8.93	128.24 ± 9.63	10.32	6.63 – 14.0
DBP	78.28 ± 4.55	79.68 ± 7.67	1.40	-3.90 – 1.10
BMI	25.99 ± 5.36	20.58 ± 4.42	5.41	3.46 – 7.36
HB	11.69 ± 1.80	12.47 ± 1.61	0.78	0.09 – 1.45
FEV1	86.24 ± 12.64	36.80 ± 9.93	49.44	44.93 – 53.95
FVC	97.32 ± 9.32	63.80 ± 14.66	33.52	28.64 – 38.39
FEV1/FVC	88.53 ± 9.13	57.99 ± 10.23	30.53	26.68 – 34.37
PEFR	1.88 ± 0.40	2.72 ± 2.0	0.85	0.27 – 1.42
RV	15.22 ± 3.74	29.09 ± 5.07	13.87	12.10 – 15.64
EF	57.97 ± 5.76	60.35 ± 10.61	2.37	-5.79 – 1.04
E	0.73 ± 0.06	0.50 ± 0.15	0.23	0.18 – 0.27
A	0.73 ± 0.05	0.71 ± 0.14	0.02	-0.02 – 0.06
E/A	1.0 ± 0.05	0.73 ± 0.14	0.27	0.24 – 0.31
RVSP	11.39 ± 0.45	29.11 ± 17.32	17.72	12.86 – 22.59
Ea(m)	0.08 ± 0.01	0.07 ± 0.01	0.009	0.003 - 0.01
Aa(m)	0.09 ± 0.02	0.094 ± 0.02	0.007	0.001 – 0.015
Sa(m)	0.093 ± 0.02	0.07 ± 0.02	0.02	0.014 – 0.027
Ea(l)	0.14 ± 0.02	0.07 ± 0.03	0.065	0.056 – 0.074
Aa(l)	0.12 ± 0.02	0.11 ± 0.02	0.015	0.006 – 0.023
Sa(l)	0.10 ± 0.02	0.08 ± 0.02	0.027	0.019 – 0.035
Ea/Aa(m)	0.93 ± 0.26	0.75 ± 0.27	0.17	0.065 – 0.28
E/Ea (m)	9.72 ± 1.55	7.64 ± 2.90	2.08	1.16 – 3.0
Ea/Aa(l)	1.17 ± 0.26	0.68 ± 0.32	0.49	0.37 – 0.60
E/Ea (l)	5.46 ± 0.79	7.97 ± 3.01	2.52	– 3.39

Of total 50 patients in case group 8 (16%) patients had moderate grade COPD (FEV1 50-79%) [M:3, F:5]. Thirty (60%) patients had severe grade COPD (FEV1 30-49%) [M:17, F:13]. Twelve (24%) had very severe grade COPD (FEV1 ≤30%) [M:6, F:6]. [Table 3]

Table 3: Gender distribution according to stages of COPD by GOLD

Stages of COPD	Total	%	Males	%	Females	%
Mild	0	0	0	0	0	0
Moderate	8	16	3	6	5	10
Severe	30	60	17	34	13	26
Very severe	12	24	6	12	6	12
Total	50	100	26	52	24	48

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Total 8 (16%) patients had moderate grade COPD of them 6 had mild pulmonary hypertension (sPAP 30-50), and 2 had moderate to severe pulmonary hypertension (sPAP 50-70, >70). Thirty (60%) patients had severe grade COPD of them 14 patients had mild pulmonary hypertension (sPAP 30-50) and 16 had moderate to severe pulmonary hypertension (sPAP 50-70, >70). Twelve (24%) patients had very severe grade COPD of them 2 had mild pulmonary hypertension (sPAP 30-50) and 10 patients had moderate to severe pulmonary hypertension (sPAP 50-70, >70). Pulmonary hypertension was strongly associated with severity of COPD ['p'= 0.0326]. Total 12 patients had very severe grade COPD out of which 1 patient had systolic dysfunction. Systolic dysfunction was statistically not associated with severity of COPD ['p'=0.283]. [Table 4]

Table 4: Relation of Echocardiographic findings with stages of COPD

Stages of COPD	Mild PH	%	Moderate –severe PH	%	Diastolic dysfunction	%	Systolic dysfunction	%
Mild	0	0	0	0	0	0	0	0
Moderate	6	75	2	25	6	75	0	0
Severe	14	46.66	16	53.33	21	70	6	20
Very severe	2	16.66	10	83.33	6	50	1	8.33
Total	22	44	28	56	33	66	7	14

Total 30 (60%) patients had severe grade COPD out of which 21 patients had diastolic dysfunction. Total twelve (24%) patients had very severe grade COPD out of which 6 had diastolic dysfunction. Diastolic dysfunction was statistically not associated with severity of COPD ['p'=0.650]. Total 30 (60%) patients had severe grade COPD out of which 6 patients had systolic dysfunction. The diastolic dysfunction in case group was significantly more (66%) compared with control group (30%) and ['p'= 0.000314]. [Table 5]

Table 5: Comparison of diastolic function in case and control group

	Diastolic dysfunction	%	Normal diastolic function	%
Case group (n=50)	33	66	17	34
Control group (n=50)	15	30	35	70

Spirometric parameters (FEV1, FVC, FEV1/FVC and PEFR) had significant inverse correlation with the echocardiographic parameters [E/A, RVSP, Ea(m), Aa(m), Sa(m), Ea/Aa(m), E/Ea(l)]. The correlation of echocardiographic parameters with pulmonary function parameters are shown in table 6. [Graph 1]

Table 6: Pearson Correlation of echocardiographic variable with PFT parameters

	FEV1	FVC	FEV1/FVC	PEFR
RV diameter	0.038	0.089	0.030	0.005
EF%	0.063	-0.020	0.107	-0.320
E	0.088	0.015	0.092	-0.176
A	0.142	0.053	0.135	-0.205
E/A	0.075	0.054	0.001	-0.235
TR-vmax	0.105	0.096	0.014	-0.245
TR	0.167	0.138	0.054	-0.277
RVSP	-0.19	0.217	-0.51	-0.197
Ea(m)	-0.019	-1.98	-0.020	-0.288
Aa(M)	0.020	0.030	-0.031	-0.174
Sa(m)	0.027	-0.093	0.08	-0.132
Ea(l)	0.043	-0.089	0.169	-0.199
Aa(l)	0.069	0.007	0.097	0.174
Sa(l)	0.095	-0.027	0.135	-0.141
Ea/Aa(m)	-0.017	-0.017	0.017	-0.102
E/Ea(m)	0.195	0.119	0.116	0.139
Ea/Aa(l)	0.015	-0.059	0.081	-0.111
E/Ea(l)	-0.103	-0.052	-0.096	-0.177

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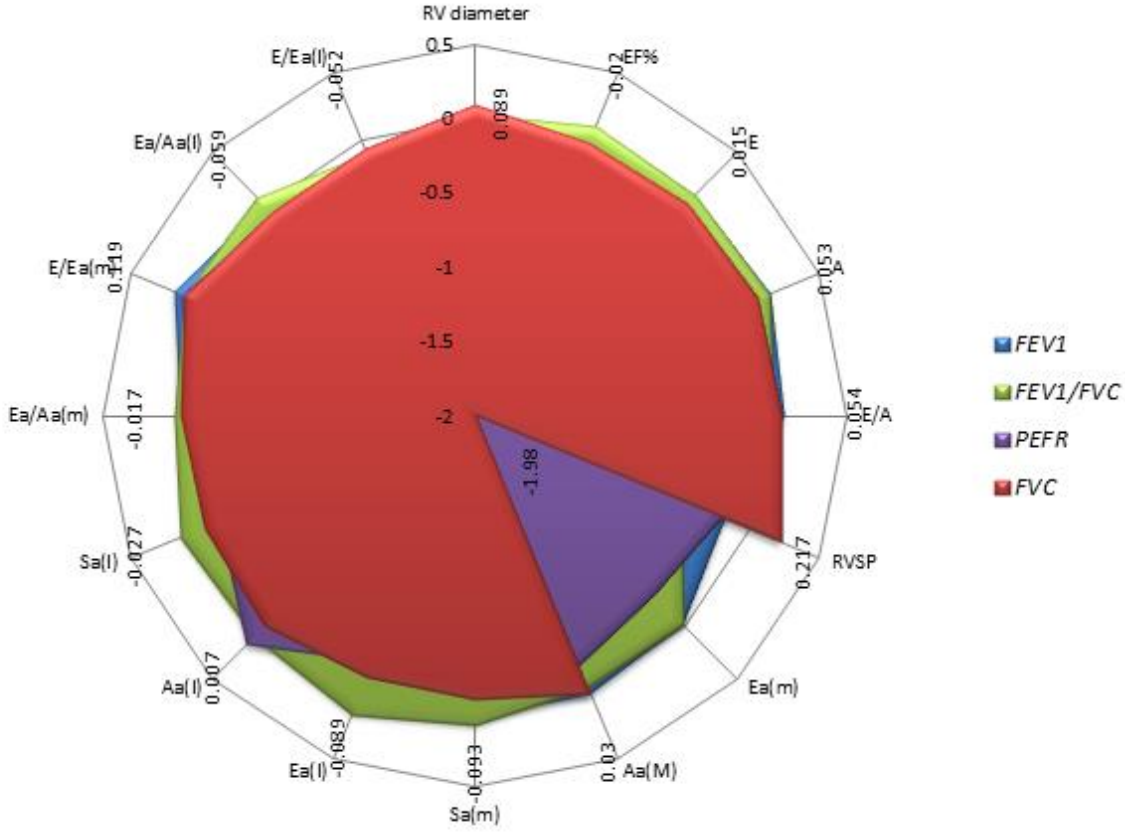
Graph 1: Correlation of Spirometric parameters with echocardiographic parameters



DISCUSSION

The aim of the present study was to assess the prevalence of echocardiographic everity of the disease. In present study case group 16% patients had moderate COPD (FEV1 50-79abnormalities by conventional echocardiography in COPD patients and its relation with the degree of s%) [M: 3; F: 5]. Thirty (60%) patients had severe COPD (FEV1 30-49%) [M: 17; F: 13]. Twelve (24%) had very severe COPD (FEV1 ≤30%) [M: 6; F: 6]. Similarly in study conducted by Jain B.K. et al 52.5% patients had moderate grade COPD, 32.5% patients had severe COPD, and 12 (15%) patients had very severe COPD.[8] Gupta N K et al quoted severe Pulmonary hypertension was present in severe or very severe COPD and the incidence of PAH is directly proportional to severity of disease.[9] In a study by Higham MA et al 25% patients had mild pulmonary hypertension while 75% patients had moderate to severe pulmonary hypertension.[10] These findings are comparable with our study. In both studies pulmonary hypertension was strongly associated with COPD severity. In our study pulmonary hypertension was strongly associated with COPD severity ['p' =0.0326], which is in accordance with previous studies. De Oliveira et al showed that chronic obstructive pulmonary disease (COPD) patients have a high prevalence of diastolic dysfunction according to disease severity.[11] In present study diastolic dysfunction was significantly present in case group compared to control but statistically not correlated with severity of COPD ('p' =0.650). Lopez-Sanchez M et al reported that the prevalence of LV diastolic dysfunction in patients with severe COPD was high, similarly about two third of COPD patients in present study had biventricular diastolic dysfunction.[12] Rabab A et al showed that left ventricular diastolic function and LV global function are affected in COPD patients especially with progression of the disease. COPD patients with pulmonary hypertension are more liable to LV diastolic and global dysfunction than normal pulmonary pressure COPD patients.[13] In our study systolic dysfunction was statistically not correlated with COPD severity ('p'=0.283). Doppler tissue imaging is evolving as a useful echocardiographic tool for quantitative assessment of left and right ventricular systolic and diastolic function. Beste Ozben et al stated that COPD severity has a negative impact on RV function, and TDI derived variables for RV function may be used in the assessment of subclinical RV dysfunction in patients with severe COPD.[14] These findings are comparable with our findings in which about two third of case population had biventricular diastolic dysfunction diagnosed by TDI. In present study 66% of patient had diastolic dysfunction by various methods including TDI. Similarly Ugurlu A O et al reported that, RV diastolic dysfunction, can be determined by TDI in

more sensitive method in patients with COPD even in the absence of PH.[15] In current study, Pulmonary hypertension was strongly associated with severity of COPD ('p'= 0.0326). Similarly Necla Özer et al reported that with COPD, the development of pulmonary hypertension leads to right ventricular dilation, right ventricular systolic and diastolic dysfunction, and left ventricular diastolic dysfunction, whereas the patients without pulmonary hypertension are spared from right and left ventricular dysfunction.[16] Das M et al in their study found that Fractional area change of RV was positively correlated with FEV1, FEV1/ FVC ratio and PEFR. There was strong negative correlation of Pulmonary Artery Pressure with FEV1/FVC ratio and PEFR.[17] Similarly in our study RV was positively correlated with FEV1 (0.038), FEV1/FVC (0.030), and PEFR (0.005). There was negative correlation between pulmonary artery pressure and FEV1 (-0.19), FEV1/FVC ratio (-0.51) and PEFR (-0.197). We have compared the data of tissue Doppler imaging (TDI) with various studies and found to be fairly correlated. TDI is more sensitive than conventional echocardiography in evaluation of diastolic dysfunction in patients with COPD.[14, 15]

CONCLUSIONS

Prevalence of COPD was equal in males and females. Pulmonary function tests (FEV1, FVC, FEV1/FVC) were significantly deranged in case group as compared with control group. Lung function parameters have significant inverse correlation with the severity of COPD. Right ventricular diameter and RVSP were significantly increased in patients with COPD compared to control group. The elcectrocardiogram evidence of 'p' pulmonale, RBBB, poor 'r' wave progression suggestive of pulmonary hypertension correlated with echocardiographic findings of pulmonary hypertension. Pulmonary hypertension is a common complication of COPD. Significant number of patients with COPD had diastolic dysfunction. Diastolic dysfunction was predominant in patients with severe COPD. Current study highlighted the utility of echocardiogram in early detection of cardiac dysfunction in patients with COPD.

Abbreviations

PFT: pulmonary function test COPD: Chronic obstructive pulmonary disease, GOLD: Global initiative for Chronic obstructive lung disease, FVC: Forced vital capacity: FEV1: forced expiratory volume (1 sec), FEV1%: Forced expiratory volume (1 sec %), sPAP: Systolic pulmonary artery hypertension, E: Early mitral inflow velocity: A: Late mitral inflow velocity, TR: Tricuspid regurgitant velocity, RVSP: Right ventricular systolic pressure, Ea(m): Mitral annular velocity during early diastole, Aa(m): Mitral annular velocity during late diastole, Sa(m): Peak systolic mitral annular velocity Ea(l): Early diastolic velocity of the lateral motion of the mitral annulus, Aa(l): Late diastolic velocity of the lateral motion of the mitral annulus, Sa(l): Peak systolic velocity of the lateral motion of the mitral annulus

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