Original Research Article

Left ventricular functions in patients with pulmonary arterial hypertension due to chronic obstructive pulmonary disease

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Abstract

Background: Pulmonary hypertension is a frequent complication in the natural history of chronic obstructive pulmonary disease (COPD). Its presence is associated with shorter survival rates and it has been identified as a predictive factor of worse clinical outcomes and frequent use of health resources. **Amis and objectives:** To study the Left Ventricular Functions in Patients with Pulmonary Arterial Hypertension Due to Chronic Obstructive Pulmonary Disease. **Materials and method:** The present study was conducted in the department of Cardiology at Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar for the two year duration. Thirty five consecutive patients of any age with different severity of pulmonary arterial hypertension due to chronic obstructive airway disease (emphysema and chronic bronchitis) constituted the study group (Group-I) and were labelled as "cases". Pulmonary arterial hypertension was diagnosed in them as presence of right ventricular systolic pressure of more than or equal to 40mmHg. Thirty five normal subjects who were matched for age and sex constituted the other group (Group-II or "controls"). The patients in our study were clinically stable and medications such as inhaled steroids, (3-2 agonists and the ophylline were continued. All patients and controls were made to undergo two-dimensional and M-mode echocardiography and Doppler examinations by a cardiologist who was blinded to the group status of the individual subjects. **Results:** The demographic characteristics of the cases and controls were comparable. The control population was largely free of any significant symptoms or abnormal clinical findings. On systemic examination it was observed that TR was the most common finding in cases followed by was Palpable RVI and Wheeze in Chest. While on control group on systemic examination Wheeze in Chest and Hepatomegaly was observed in 5.7% and 2.8% patients only. Echocardiographic assessment results showed that our cases and controls had similar aortic and left atrial dimensions. Left ventricular internal diameters, particularly the systolic diameter, were decreased in patients with pulmonary hypertension than corresponding dimensions in healthy volunteers. Similarly, left ventricular end-diastolic and end-systolic volumes were significantly reduced in cases as compared to the control group. Left ventricular ejection fraction and fractional shortening were both significantly higher in patients with pulmonary hypertension as compared to the controls. Left ventricular posterior wall and interventricular septum were similar in thickness in both the groups. Doppler/echocardiographic assessment of left ventricular diastolic functions revealed that E/A ratio was significantly lower in cases than controls (0.86±0.35 vs 1.34± 0.30, respectively, p=0.000). **Conclusion:** Thus the present study has demonstrated that patients with pulmonary hypertension secondary to chronic obstructive pulmonary disease have reduced left ventricular internal dimension and that this reduction bears a relation with the level of respiratory compromise and with the severity of pulmonary hypertension.

Key Word: Left Ventricular Functions, Pulmonary Arterial Hypertension, COPD.

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Received Date: 03/02/2019 Revised Date: 18/03/2019 Accepted Date: 23/04/2019
DOI: https://doi.org/10.26611/10211038

Access this article online

Quick Response Code:

Website: www.medpulse.in

Accessed Date: 21 June 2019

INTRODUCTION

Pulmonary hypertension is an elevation at rest in the mean PAP above 25mmHg with a pulmonary capillary wedge pressure (PCWP), left atrial pressure or left ventricular end-diastolic pressure of less than 15mmHg and PVR greater than 3 Wood units. In many of the older studies, the cut-off PAP was 20mmHg. In the more recent literature, the cut-off of 25mmHg has been used[1] to bring in a more uniform approach in defining different types of

How to cite this article: Amit Sharma, Pallavi Sharma, Rashmi Sharma. Left ventricular functions in patients with pulmonary arterial hypertension due to chronic obstructive pulmonary disease. *MedPulse International Journal of Medicine.* June 2019; 10(3): 216-221. https://www.medpulse.in/Medicine/

PH, including idiopathic. This figure applies to pressures measured on right heart catheterisation (RHC) in a recumbent position. Corpulmonale is the consequence of PH caused by respiratory disorders and is defined as right ventricular hypertrophy and dilatation or both.[2] Pulmonary hypertension is a frequent complication in the natural history of chronic obstructive pulmonary disease (COPD). Its presence is associated with shorter survival rates and it has been identified as a predictive factor of worse clinical outcomes and frequent use of health resources. At the present time, there is no specific and effective treatment for this condition in COPD. However, recent advances in knowledge of the pathogenesis of pulmonary hypertensive states, along with the development of new and effective strategies in the treatment of pulmonary hypertension, open a new perspective that could be applicable in COPD. Therefore, it is appropriate to revisit this old topic[3,4] in the light of new discoveries in this field. Pulmonary hypertension in COPD progresses over time and its severity correlates with the degree of airflow obstruction and the impairment of pulmonary gas exchange.[5,6] A variety of factors may contribute to the development and maintenance of pulmonary hypertension in COPD. The most significant of which are the remodelling of pulmonary vessels and hypoxic pulmonary vasoconstriction. Understanding of the etiopathogenic mechanisms responsible for pulmonary vascular abnormalities in COPD remain incomplete, however, they have been extensively investigated in recent years.

AMIS AND OBJECTIVES

To study the Left Ventricular Functions in Patients with Pulmonary Arterial Hypertension Dueto Chronic Obstructive Pulmonary Disease

MATERIALS AND METHOD

The present study was conducted in the department of Cardiology at Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar for the two year duration. Thirty five consecutive patients of any age with different severity of pulmonary arterial hypertension due to chronic obstructive airway disease (emphysema and chronic bronchitis) constituted the study group (Group-I) and were labeled as "cases". Pulmonary arterial hypertension was diagnosed in them as presence of right ventricular systolic pressure of more than or equal to 40 mmHg[7].

Thirty five normal subjects who were matched for age and sex constituted the other group (Group-II or "controls").The patients in our study were clinically stable and medications such as inhaled steroids, (3-2 agonists and the ophylline were continued. Complete hemogram including hemoglobin, total leukocyte count, differential leukocyte count, platelet count, and the hematocrit was performed in all the selected patients in both the groups. Liver function tests and Kidney function test was also performed. X-ray chest (PA view) to determine the cardiothoracic ratio, the size of pulmonary arteries and the lung parenchyma was done. Electrocardiograph including all 12leads and Pulmonary function tests to measure Forced Expiratory Volume in first second (FEV1) and Forced Vital Capacity (FVC). The ratio of FEV1 to FVC was noted down. Arterial blood gas analysis to measure the PaO_2, $PaCO_2$, pH and the oxygen saturation was done. All patients and controls were made to undergo two-dimensional and M-mode echocardiography and Doppler examinations h a cardiologist who was blinded to the group status of the individual subjects. After properly explaining the procedure to subject, a phased array transducer was placed in standard transthoracic locations and examination performed using a commercially available echocardiograph (TOSHIBA P0WERV1S1ON UZR 1, Model No: SSA 380A, Tokyo. Japan). All the examinations were performed in partial left lateral decubitus position with careful attention being paid to gain and filter settings to obtain clear images from endocardial and epicardial surfaces. Echocardiography measurements were taken as per the recommendations of American Society of Echocardiography[8]. Diastolic functions of left ventricle were assessed using pulsed Doppler at the tip of mitral valve. The peak velocities (mseci of the early (E-wave) and late (A wave) left ventricular filling and the deceleration time (dt, m sec) of E velocity from its peak to the baseline were recorded with pulsed Doppler sampling at the mitral in flow and a slight veriertilt to the transducer for simultaneously catching the left ventricular outflow signal, the isovolumic relaxation time (IVRT, msec) was measured from the end of left ventricular outflow signal to the beginning of “E” wave. The SPSS (Statistical Package for Social Sciences) for Windows (version 10.0) was used for data analysis. The tests used included the student's t-test, the chi-square test and bivariate (Pearson) correlation analysis. All the data are presented as mean±SD unless indicated otherwise. A P value of <0.05 was taken as the criterion of statistical significance.

RESULTS

Table 1: Age, Sex and anthropometric measurements of the study population

		Cases (n=35)	Controls (n=35)	P value
Age (years)	Mean	52.69	52.4	NS
	SD	10.39	10.2	
Sex	Male	14	14	NS
	Female	21	21	
	M:F	2:3	2:3	
Weight (kg)	Mean	54.78	58.54	NS
	SD	9.89	9.29	
Height (cm)	Mean	158.43	159.7	NS
	SD	7.70	6.80	
BMI (kg/m^2)	Mean	21.59	22.86	NS
	SD	2.83	2.73	

NS= not significant, BMI=body mass index

In the present study, a total of 70 adults (35 patients of chronic obstructive pulmonary disease and 35 apparently healthy subjects) were enrolled. The demographic characteristics of the cases and controls were comparable**.**

Table 2: History And General Physical Findings Of The Study Population

Clinical characteristics	Cases (n=35)	Controls (n=35)	P
Breathlessness, n (%)	35 (100%)	09 (25.71%)	0.000
Palpitations, n (%)	08 (22.82%)	09 (25.71%)	0.780
Swelling of feet, n (%)	15 (42.85%)	0	0.000
Cough with expectoration, n(%)	28 (80%)	05 (%)	0.000
Raised mean JVP, n(%)	10 (28.57%)	0	0.000
Clubbing, n (%)	13 (37.14%)	0	0.000
Cyanosis, n (%)	28 (80%)	0	0.000
Flap, n (%)	01 (2.85%)	0	0.314
Pulse (beats/min)	83.54±10.09	83.14±9.10	0.862
Systolic blood Pressure (mmHg)	117.78±10.73	119.78±7.80	0.376
Diastolic blood Pressure (mmHg)	74.29±7.39	74.86±6.12	0.726

JVP=jugular venous pressure

The clinical characteristics of the study population were compared and it was observed that, the control population was largely free of any significant symptoms or abnormal clinical findings. Some subjects in the control group complained of breathlessness and palpitations (9patients each). However, evaluation of these did not reveal any organic basis for these symptoms. Five of the subjects in the control group had cough with expectoration which was attributed to some recent respiratory tract infections. On the other hand, majority of the cases complained of breathlessness and cough with expectoration and other symptoms in varying combinations. Pulse rate and blood pressure were comparative between the two groups. Similarly, majority of subjects in the control population were free of any chest signs or tricuspid regurgitation murmur. Only 2 subjects in the control group had wheeze which was attributed to respiratory tract infections. Majority of cases in the study population had chest signs in the form of wheeze (35) and crepitations, along with tricuspid regurgitation murmur.

Table 3: Systemic examination in the study population**.**

Systemic examination	Cases (n=35)	Controls (n=35)	P value
Pulmoranory rales	17 (48.6%)	0	0.000
Wheeze in Chest	28 (80.0%)	2 (5.7%)	0.000
Palpable RVI	30 (88.7%)	0	0.000
TR	33 (94.3%)	0	0.000
Hepatomegaly	11 (31.4%)	1 (2.8%)	0.002
Ascites	2 (5.7%)	0	0.151

RVI= right ventricular impulse, TR= tricuspid regurgitation

On systemic examination it was observed that TR was the most common finding in cases followed by was Palpable RVI and Wheeze in Chest. While on control group on systemic examination Wheeze in Chest and Hepatomegaly was observed in 5.7% and 2.8% patients only.

Table 4: Echocardiography findings in the study population

	Cases (n=35)	***Controls***(n=35)	p value
Aorta (cm)	2.87±0.53	2.97±0.43	0.370
LA (cm)	3.13±0.67	3.08±0.75	0.800
LVIDd (cm)	3.85±1.04	4.14±0.78	0.187
LVIDs (cm)	2.30±0.76	2.73±0.53	0.008
LVEDV (mL)	75.03±43.89	94.99±25.75	0.024
LVESV (mL)	20.61±20.89	33.36±11.75	0.003
LVSV (mL)	53.90±28.40	63.56±15.92	0.085
LVEF (%)	75.09±8.28	68.71±8.63	0.002
LVFS (%)	47.54±9.06	40.03±5.39	0.000
LVPWd (cm)	1.48±0.49	1.50±0.32	0.820
LVPWs (cm)	1.02±0.36	1.05±0.30	0.708
IVSd (cm)	1.49±0.29	1.43±0.30	0.404
IVSs (cm)	1.08±0.30	1.04±0.22	0.534
IVS motion (paradoxical)	15 (42.8%)	0	
RV flat (cm)	3.05±0.81	2.17±0.36	0.000

la = left atrium; lvidd= left ventricular internal diameter diastolic; lvids = left ventricular internal diameter systolic; lvedv= left ventricular end-diastolic volume; lvesv= left ventricular end-systolic volume; lvsv= left ventricular stroke volume; lvef= left ventricular ejection fraction; lvfs= left ventricular fractional shortening; lvpwd= left ventricular posterior wall diastolic; lvpws= left ventricular posterior wall systolic; ivsd= interventricular septum diastolic, ivsd= interventricular septum systolic; rv= right ventricle

The results of echocardiographic assessment of left ventricular systolic and diastolic functions and Doppler flow studies are illustrated in tables 4 and 5. The results showed that our cases and controls had similar aortic and left atrial dimensions. Left ventricular internal diameters, particularly the systolic diameter, were decreased in patients with pulmonary hypertension than corresponding dimensions in healthy volunteers**.** Similarly, left ventricular end-diastolic and end-systolic volumes were significantly reduced in cases as compared to the control group. Left ventricular ejection fraction and fractional shortening were both significantly higher in patients with pulmonary hypertension as compared to the controls. Left ventricular posterior wall and interventricular septum were similar in thickness in both the groups. However, the interventricular septal motion was paradoxical in 15 (42%) of cases and was normal in controls. Right ventricular dimensions were also significantly higher in the pulmonary hypertension group as compared to the controls (p=0.000)**.**

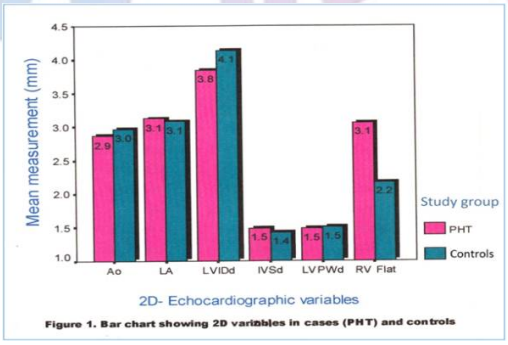

Figure 1. Bar chart showing 2D varibbles in cases (PHT) and controls

Table 5: Mitral Doppler findings in the study population

	***Cases* (n=35)**	***Controls*(n=35)**	**p value**
E velocity (m/s)	*0.53*±0.23	*0.64*±0.16	0.031
A velocity (m/s)	*0.65*±0.20	*0.50*±0.18	0.003
E/A ratio	*0.86*±0.35	*1.34*±0.30	0.000
DT (msec)	*248.97*±23.69	*186.17*±31.77	0.001
IVRT (msec)	*105.91*±48.91	*86.02*±19.04	0.030

DT = declaration time; IVRT = isovolumic relaxation

Doppler/echocardiographic assessment of left ventricular diastolic functions revealed that E/A ratio was significantly lower in cases than controls (0.86±0.35 vs 1.34± 0.30, respectively, p=0.000). In addition the E/A ratio was <1 in majority of cases as compared to the controls. The isovolumic relaxation time was also significantly longer in the cases group as compared to the control group (105.91±48.91 msec versus 86.02il9.04 msec, p=0.030). The deceleration time (DT) was also higher in cases than in controls (248.97±23.67 msec versus 186.17±31.77 msec; p<0.05).

DISCUSSION

Pulmonary hypertension is a condition of increased right ventricular afterload. Prolonged increase in the afterload poses a stress on right ventricle, with consequent deleterious effects on right ventricular performance. When the increase in afterload is sufficient, right ventricular end-diastolic pressure rises, as it fails as a pump[9-11]. Since both right and left ventricles share a common interventricular septum and are enclosed within a common pericardial sac, it follows that deterioration of right ventricular functional capacity might affect that of left ventricle as well. In fact, abnormalities of left ventricular functions, especially diastolic functions, have been documented in patients with pulmonary arterial hypertension of various etiologies and of varying severity[12-15]. In the present study, a total of 70 adults (35 patients of chronic obstructive pulmonary disease and 35 apparently healthy subjects) were enrolled. The demographic characteristics of the cases and controls were comparable**.** The clinical characteristics of the study population were compared and it was observed that, the control population was largely free of any significant symptoms or abnormal clinical findings. On systemic examination it was observed that TR was the most common finding in cases followed by was Palpable RVI and Wheeze in Chest. While on control group on systemic examination Wheeze in Chest and Hepatomegaly was observed in 5.7% and 2.8% patients only. The present Doppler-Echocardiographic study was conducted to examine the left ventricular systolic and diastolic functions in patients with pulmonary arterial hypertension due to chronic obstructive pulmonary disease.In the present study, the aortic and left atrial dimensions in patients with pulmonary arterial hypertension were comparable to the average control values (2.87±0.53 cm versus 2.97±0.43 cm, p=0.370 and 3.13±0.67cm versus 3.08±0.75 cm, p=0.800, respectively). The mean diastolic left ventricular internal diameter (LVIDd) and especially left ventricular end-diastolic volume (LVEDV) were reduced in patients with pulmonary hypertension as compared to the control values (3.85±1.04 cm versus 4.14±0.78 cm, p=0.187 and 75.03±43.89 mL versus 94.99±25.75 mL, p=0.024, respectively). These observations are largely in agreement with the published data. Krayenbuehl HP, *et al* (1978) found that the average transverse LVIDd on transthoracic echocardiography in patients with pulmonary hypertension of different etiologies was significantly lower than that of healthy controls[16]. Lazar JM, *et al* (1993) found that LVEDV in patients with pulmonary arterial hypertension was significantly reduced as compared to that of healthy volunteers[17]. In a recent study by Marcus JT, *et al* (2001), LVEDV in patients with primary pulmonary hypertension, as determined by magnetic resonance imaging, was significantly reduced compared to healthy population[18]. The mechanism behind impaired left ventricular diastolic functions in patients with pulmonary hypertension has been attributed to the geometric distortion of the left ventricle[19]. Increased right ventricular pressure and volume overload affects right ventricular systolic function, which in turn results in an upward and leftward displacement of right ventricular pressure-volume curve. The subsequent distortion and hypertrophy of the right ventricle may compress the left ventricle thus altering chamber stiffness. This effect is maximal at end systole and early diastole and leads to impairment of filling of left ventricle in early diastole. During late diastole, the interventricular septum restores its geometry and late ventricular fillings either normal or increased. Some studies have also attributed the left ventricular diastolic dysfunction in patients with pulmonary arterial hypertension to diastolic asynchrony in the apical and lateral walls, left ventricular interstitial edema or alteration in intracellular calcium transportation[20]. The impaired left ventricular diastolic relaxation in patients with pulmonary arterial hypertension is also evidenced by the prolonged deceleration time (DT) of early transmitral flow in these patients. In our study also, DT was found to be significantly prolonged in patients with pulmonary arterial hypertension as compared to normal subjects (248.97±23.69 m/sec versus 186.17±31.77 m/sec; $p<0.05$). We also found the isovolumic relaxation time (IVRT) to be significantly prolonged in patients with pulmonary arterial hypertension than in the normal controls (105.91±48.91 msec versus 86.02 ±19.04 msec; $p<0.05$). These findings are in agreement with some previous observations. Tutor, *et al* (1999) found that both DT and IVRT were prolonged in patients with pulmonary arterial hypertension as compared to normal subjects[21]. Louie, *et al* (1995) in their study, found that left ventricular isovolumic relaxation time was significantly prolonged in patients with pulmonary hypertension than normal subjects[22]. In the study by Moustapha A, *et al* (2001), left ventricular IVRT and the deceleration time of early left ventricular filling were found to be prolonged in patients with pulmonary hypertension[23].

CONCLUSION

Thus the present study has demonstrated that patients with pulmonary hypertension secondary to chronic obstructive pulmonary disease have reduced left ventricular internal dimension and that this reduction bears a relation with the level of respiratory compromise and with the severity of pulmonary hypertension.

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Source of Support: None Declared
Conflict of Interest: None Declared