Correlation of the Spirometric and Arterial Blood Gas Variables with Pulmonary Artery Systolic Pressure in Predicting Pulmonary Hypertension in Chronic Obstructive Pulmonary Disease Patients

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Abstract

Pulmonary Hypertension is the major cardio vascular complication of chronic obstructive pulmonary disease and long-standing, frequently undetected pulmonary hypertension leads to the development of right ventricular hypertrophy, dilatation and failure with poor prognosis. Echocardiography is the most useful noninvasive method for detecting pulmonary hypertension but there are few data on the utility of echocardiography for measurement of pulmonary artery systolic pressure in chronic obstructive pulmonary disease patients and correlation with pulmonary function tests and arterial blood gas analysis. A study was conducted to estimate pulmonary artery systolic pressure by echocardiography in chronic obstructive pulmonary disease patients, Correlation of the Spirometric and arterial blood gas variables with the pulmonary artery pressure in prediction of pulmonary hypertension. In the present study mild pulmonary hypertension was found in 16 patients (69.56%), moderate pulmonary hypertension in 6 patients (26.08%), and severe pulmonary hypertension in 1 patient (4.34%). Partial Pressure of Oxygen (PO_2), Forced Expiratory Volume in one second (FEV_1) and Forced Vital Capacity (FVC) were the independent variables significantly correlated with pulmonary artery systolic pressure.

Keywords: Pulmonary Hypertension; Chronic Obstructive Pulmonary Disease; Arterial Blood Gas; Spirometry.

Introduction

Pulmonary Hypertension (PH) is the major cardio vascular complication of chronic obstructive pulmo-nary disease (COPD) , associated with development of Cor pulmonale and poor prognosis [1]. The natural history of chronic obstructive pulmonary disease is characterizes by progressive decrease in expiratory airflow and increase in end expired pulmonary volume. Although deterioration of gas exchange occur, the extent of arterial hypoxemia or hypercapnia is a quite variable and often poorly correlated with the severity of air flow obstruction.

As the disease progress dyspnea becomes manifest at progressively lower level of exertion and pulmo-nary hypertension develops, insidiously [2]. The cause of pulmonary hypertension in chronic obstructive pulmonary disease is hypoxic pulmonary vasoconstriction leading to permanent medial hypertrophy [3]. However recent, pathological studies point, rather to extensive remodeling of the pulmonary arterial walls with prominent intimal changes [4]. As ventila-tory insufficiency progresses respiratory acidosis contribute another stimulus to pulmonary vasocon-striction [5].

The long-standing and frequently undetected pul-monary hypertension leads to the development of right ventricular hypertrophy, dilatation and failure [6].

For the diagnosis of pulmonary hypertension right side cardiac catheterization is the gold standard but it is expensive and has associated risks, which approx-imately limit its routine use, so non-invasive estimation of pulmonary artery pressure by Doppler Echocardi-ography are being used [7,8].

Studies have confirmed the close correlation of echocardiographically estimated pulmonary

arterial pressure with invasive measurements in patient with chronic obstructive pulmonary disease but there are few data on the utility of echocardiography measure-ment in assessing COPD and correlation with pulmo-nary function tests and arterial blood gas (ABG) analysis [9].

The Pulmonary function test and arterial blood gas analysis are routinely obtained in evaluating patients with COPD. Hence A study was conducted to estimate pulmonary artery systolic pressure (PASP) by Doppler Echocardiography in chronic obstructive pulmonary disease patients and Correlated Spirometric, arterial blood gas variables with the pulmonary artery pressure in predicting pulmonary hypertension.

Methods

After institutional ethical committee approval, a prospective case control study was conducted at tertiary care teaching hospital. Cases were COPD patients with pulmonary Hypertension. Controls were COPD patients without pulmonary Hypertension. Age, Sex and risk factors matched controls were selected from OPD. All stable COPD patients with pulmonary Hypertension attending chest OPD and willing to participate in the study were included in study. The study period was 6 months. COPD patients defined according to Global initiative for chronic obstructive lung disease (GOLD) 2003 criteria [10] are chronic symptoms of cough, sputum production and dyspnea; History of exposure to risk factors; spirometric value of **Forced Expiratory Volume in one second(** FEV1) / Forced Vital Capacity (FVC) <70%.

Exclusion Criteria

1. Patients with history of atopy or significant reversibility of airflow obstruction (FEV1 > 15% post bronchodilator study)

2. Patients with history of heart disease, acute exacerbation of COPD and cor pulmonale

3. Patients with poor thoracic window on Echocardiography

4. Patients with difficulty in detecting tricuspid regurgitation on Echocardiography

Echocardiography was performed in the department of cardiology.

The pulmonary artery systolic pressure was measured by continuous Doppler wave method. It was measured by tricuspid regurgitation (TR) Jet velocity method { Bernoulli's equation} [11].

The Spirometry was performed by all patients in Spirometry room.

The udwadia standard was used. Three acceptable tracing were used and the best of these was taken for the interpretation.

The following parameters were recorded.
1. Forced Vital Capacity (FVC):
2. Forced Expiratory Volume in one second (FEV_1):
3. FEV_1 / FVC:
4. Peak Expiratory Flow Rate (PEFR):

The Arterial blood sample was taken from Radial artery after performing Allen's test. The sample was analyzed on Blood gas analyzer machine. Values of puissance hydrogen (PH), Partial Pressure of Carbon dioxide (PCO_2) and Partial Pressure of Oxygen (PO_2) were obtained from ABG machine. Data was entered in Microsoft excel. Statistical analysis was done by using mean method and results were expressed in terms of percentages. Correlation coefficients of all variable with pulmonary artery systolic pressure were calculated. Stepwise multiple linear regression analysis of these variables was done to know predictors of pulmonary Hypertension in COPD.

Grading of Pulmonary Hypertension

	PASP	GRADE
1)	Up to 30 mm Hg	No PH
2)	30-40 mm Hg	Mild PH
3)	40-70 mm Hg	Moderate PH
4)	> 70 mm Hg	Severe PH

Results

Total patients of COPD with pulmonary Hypertension were 23 while COPD without Pulmonary Hypertension were 16. Total numbers of males in the study were 32 out of which 20 were with pulmonary hypertension and 12 were without pulmonary hypertension. Total numbers of females in the study were 7 out of which 3 were with pulmonary hypertension and 4 were without pulmonary hypertension. All patients were smoker. 28 patients were Beedi Smoker and 11 patients were cigarette smoker.

Mean duration of cough was 13.23 years (±9.09 SD) in cases and 7.88 years (±4.97 SD) in controls.

Mean duration of dyspnea on exertion was12.57 years (±7.36 SD) in cases and 8.75 years (±4.62 SD) in controls.

Statistically no significant differences were detected for age, body mass index (BMI), duration of dyspnea on exertion between the two groups; however there were significant differences between the two groups for duration of cough and packed cell volume (PCV). P value < 0.05is significant. There were statistically significant differences for FVC, FVC%, FEV_1, FEV_1%, FEV_1/FVC, PEFR and PEFR%. P value was significant for FEV_1 and FEV_1% between two groups. p value < 0.05 significant. (Table 1).

Mean values of variables of arterial blood gas analysis were given in Table 2.

Mean Value of puissance hydrogen (PH) was 7.396 (±0.025 SD) for controls and 7.364 (±0.029 SD) for cases. Mean Value of Partial Pressure of Carbon dioxide (PCO_2) was 38.91 (±3.15 SD) for controls and 41.93 (±8.07 SD) for cases. Mean Value of Partial Pressure of Oxygen (PO_2) was 83.90 (±6.25 SD) for controls and 65.22 (±7.96 SD) for cases. Statistically significant low values of PO_2 and PH were found in cases as compared to controls. No significant difference was found for PCO_2 between the two groups.

Mild pulmonary hypertension was found in 16 patients, moderate in 6 and severe in 1 patient. (Table 3).

Correlation coefficients with pulmonary artery systolic pressure were computed for all variables, which included the entire variables detected to differ between the two groups with and without pulmonary hypertension. The result indicated that PO2 had the highest correlation with pulmonary artery systolic pressure r=848 (Table 4).

Stepwise multiple linear regression analysis of these variables with pulmonary artery systolic pressure as the dependent variable sequentially determined that PO_2, FEV_1 and FVC were the independent variables which best predicted the pulmonary artery systolic pressure. PO_2 is the single variable, which was highly significant in predicting pulmonary hypertension. It contributed to 72.2% of total for predication of pulmonary hypertension (multiple r = 0.85). After combining PO2 and FEV_1 it was increased to 75.6% of total variance (r = 0.870). With PO_2, FEV_1 and FVC, these accounted for 79.4% of the total variance (multiple r= 0.891). (Table 5).

Table 1: Mean values of all variables of Spirometry for two groups

Group		FVC	FVC%	FEV_1	FEV_1%	FEV_1/FVC	FEV_1/FVC %	PEFR	PEFR %
Cases	Mean	1.65	58.64	0.82	38.81	50.77	61.44	2.39	37.45
	SD	+ 0.42	+ 12.32	+ 2	+ 11.4	+ 9.73	+ 12.92	+ 0.81	+ 11.8
Controls	Mean	0.04	74.45	1.30	62.53	59.35	70.95	3.62	59.25
	SD	+ 0.57	+ 15.10	+ 0.41	+ 18.73	+ 9.8	+ 12.37	+ 1.56	+ 26.04
	P value	0.017	0.001	0.000	0.000	0.10	0.035	0.003	0.0031

P value < 0.05 significant

Table 2: Mean values of ABG variables

Group		PH	PCO_2	PO_2
Controls	Mean	7.396	38.91	83.90
	SD	+ 0.02	+ 3.15	+ 6.25
Cases	Mean	7.364	41.93	65.22
	SD	+ 0.029	+ 8.07	+ 7.96
	P value	0.001	0.165	0.000

Table 3: Cross Table Showing Relation between Grades of Hypoxemia and Grades of Hypertension

Grade of hypoxemia	Grade of Hypertension				Total
	Normal	Mild	Moderate	Severe	
Mild (60-80 mm Hg)			5		5
Moderate (40-60 mm Hg)	5	16	1	1	23
Severe (<40 mm Hg)					
Normal(>80mmHg)	11				11
Total	16	16	6	1	39

Table 4: Correlation coefficients of all variables (r value)

Variable	Duration of cough	Duration of DOE	PCV	FVC	FVC%	FEV_1
r value	0.432	0.429	0.462	-0.450	-0.536	-0.635
P value	0.007	0.006	0.003	0.004	0.000	0.000

Variable	FEV_1%	FEV/ FVC	FEV/ FVC%	PFER	PFER %	PH	PO_2
r value	0.643	0.370	-0.379	-0.475	-0.387	-0.330	-0848
P value	0.00	0.20	0.022	0.002	0.002	0.040	0.00

Table 5: Multiple linear regression analysis for prediction of Pulmonary Hypertension

Model	R	R square	Adjusted R square	Standard error of estimate
1.	0.850[a]	0.722	0.715	11.855
2.	0.870[b]	0.756	0.742	11.283
3.	0.891[c]	0. 794	0. 776	10.504

a. Predictors (constant), PO_2
b. Predictors (constant), PO_2 FEV_1
c. Predictors (constant), PO_2 FEV_1 FVC

Discussion

Over the past few years, important information has been provided indicating that severity of pulmonary hypertension and the development of Cor pulmonale are major factors influencing mortality in COPD. The fact that pulmonary hypertension develops insidiously, producing few diagnostic clues until Cor pulmonale becomes clinically evident. Early detection of pulmonary hypertension in COPD patients has become important diagnostic challenge.

COPD describe the patients with narrowing of the airways. With narrowing of small airways [12], there is reduced forced expiratory flow (FEF) 25-75 and FEV_1 is still normal. This is found in early stage of COPD. FEV_1 / FVC < 70% is indicative of obstructive disease [13]. The mortality and morbidity associated with COPD are related to the airway obstruction [14].

Frequently recognition of pulmonary hypertension begins with the discovery of right ventricular hypertrophy on the electrocardiogram (ECG) or prominent pulmonary arteries on the chest radiograph. The chest radiograph is inferior to the ECG in detecting pulmonary hypertension [15]. Patients with signs, symptoms, ECG and radiological findings suggestive of pulmonary hypertension should undergo echocardiography with Doppler flow studies. Echocardiography is the most useful noninvasive method for detecting pulmonary hypertension [16].

In present study, Echocardiography was used to estimate pulmonary artery pressure in COPD patients. Spirometric and arterial blood gas variable were correlated with pulmonary artery systolic pressure for prediction of pulmonary hypertension. A study was conducted in thirty-nine COPD patients out of which twenty-three patients found pulmonary hypertension (58.97%), 16 patients had mild pulmonary hypertension, 6 patients moderate and 1 patient had severe pulmonary hypertension. There were no statistically significant differences for age, BMI, smoking, duration of dyspnea between the two groups however duration of cough and PCV showed significant differences between the two groups.

Higham M.A. [9] et al. found that there was pulmonary hypertension in 31 (55%) patients out of 56-patients. There were no significant differences between the two groups with regard to age and smoking history.

In our study, there were significant differences between the two groups for FEV_1, FVC, FEV_1/ FVC, PEFR, PH and PO_2. Correlation coefficients with pulmonary artery systolic pressure were calculated for all variables, which were detected to differ between the two groups. These results indicated that PO_2 had the highest correlation with pulmonary artery systolic pressure. Stepwise multiple linear regression analysis of these variables with pulmonary artery pressure as the dependant variable determined that PO_2, FEV_1 and FVC were the independent variable which best

predicted the pulmonary hypertension. These variables accounted for 79.4% of the total variance (multiple r= 0.891).

Higham M.A. [9] et al. found that there were statistically significant correlation of Tran tricuspid pressure gradient with FEV_1 Krogh Constant (KCO) and Carbon Monoxide Diffusing Capacity (DLCO). Stepwise multiple regression analysis showed that age and KCO combined provide a multivariate model for prediction of pulmonary hypertension.

Sarac R et al. [17] studied 80 patients with clinical stable COPD by Doppler echocardiography in the evaluation of pulmonary hypertension in pulmonary artery systolic pressure at rest and during sum maximal exercise using bicycle ergo meter was estimated by tricuspid regurgitation Jet Velocity method. Pulmonary hypertension was found in 56% of the patient out of which 30% of the patient had mild degree latent pulmonary hypertension (41- 47 mm Hg) and 26% of the patient had mild to moderate pulmonary hypertension. Pulmonary artery systolic pressure at rest and during the exercise has best correlation with arterial PaO_2 It has best correlation with index FEF50 / FVC.

Matsuyama W. et al. [18] estimated pulmonary hypertension in COPD patients using transcutaneous Doppler jugular vein flow velocity. The mean pulmonary artery pressure of 64 COPD was examined using cardiac catheterization. The right jugular vein flows velocity was measured using transcutaneous Doppler echo after which the ration of diastolic flow (DF) and systolic flow (SF) velocity was calculated (DF/SF). The DF/SF velocity ration showed significant correlation with mean pulmonary pressure in COPD patient.

The present study demonstrates the utility of Echocardiography to estimate pulmonary artery systolic pressure in COPD patients. Echocardiographically derived right ventricular systolic pressure is normally defined as trans tricuspid pressure gradient plus the right arterial pressure. Initial studies of evaluation of right ventricular systolic pressure by catheterization and Doppler echocardiography suggested that noninvasive method provides an accurate and widely applicable method [19]. These results support the generally accepted point of view that altered gas exchange, as opposed to altered mechanics are the predominant factors related to the development of pulmonary hypertension in COPD. Current guidelines for the diagnosis and management of COPD are not recommended routine investigation of the presence of pulmonary hypertension in COPD [20]. Based on the present data and previous studies it could be made for screening all COPD patients with low lung functions and hypoxemia for pulmonary hypertension. This would contribute to the assessment of prognosis in these patients and helpful in identifying individuals likely to suffer increased morbidity [21].

Conclusion

Out of Twenty three patients of pulmonary hypertension, 16 patients had mild pulmonary hypertension (69.56%), 6 patients moderate pulmonary hypertension (26.08%) and one patient had severe pulmonary hypertension (4.34%). PO_2 FEV_1 and FVC were the independent variables which best correlated with pulmonary artery systolic pressure in predicting pulmonary hypertension.

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