Original Article

The relation of Echocardiographic findings to pulmonary Function tests in patients with Chronic obstructive Pulmonary Disease

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Summary:

Background: Chronic obstructive pulmonary disease (COPD) is a common disease and it accounts for over 10% of all hospital medical admission. Cigarette smoking is the most important risk factor. Pulmonary arterial hypertension (PHT) is a common complication of COPD and the increase in pulmonary artery pressure is often mild to moderate. The presence of pulmonary arterial pressure and its severity is readily and reliably determined by transthoracic echocardiography in majority of COPD patients.

Patients and Methods: This study included 55 patients with mean age 65.6 ±8.2 years .The mean duration of symptoms was 18 ±10 months. 32 patients (58%) were current smoker, 18 patients (33%) were ex-smoker and 5 patients (9%) were non smoker. The mean intensity of smoking for smoker was 49.5 ± 22.2 pack- years. For all patients, history, clinical examination, ECG, CXR, and routine blood tests were done. For all patients pulmonary function tests were done and patients were classified according to GOLD criteria into 4 stages. Echocardiography was done for all patients; ventricular and atrial dimensions were taken, and using Doppler technique to detect tricuspid and pulmonary regurgitation, estimation of pulmonary artery systolic and/or diastolic pressure using special formulas was undertaken.

Results: Tricuspid regurgitation (TR) jet was found in 70.9% of patients with COPD. Increased pulmonary artery systolic pressure was found in 51% of patients with TR (36% of total patients) and increased pulmonary vascular resistance was found in 48.7% of patients with TR (34.5% of total patients). There were significant associations between echo findings of increasing RV size, TR, increased pulmonary arterial pressure and pulmonary vascular resistance with decrease in FEV1, FEV1/VC and oxygen saturation. There was no significant association with decrease in vital capacity.

Conclusions: There is a high prevalence of pulmonary arterial hypertension with increasing severity of chronic obstructive pulmonary disease.

Key Words: echocardiography, COPD, pulmonary function

Introduction:

Chronic obstructive pulmonary disease (COPD) has bean defined by the Global initiative for COPD as disease state characterized by airflow limitation that is not fully reversible. COPD is a chronic, slowly progressive disorder characterized by airflow obstruction (FEV1<80% predicted and FEV1/VC ratio <70%) which does not change markedly over several months; the impairment of lung function is largely fixed but may be partially reversible by bronchodilator therapy (1). COPD includes emphysema and chronic bronchitis. Emphysema is an anatomically defined condition characterized by destructive enlargement of alveoli. Historically, the term chronic bronchitis was used to define any patient who coughed up sputum on most days of at least 3 consecutive months for 2 or more successive years (provided other causes of cough have been excluded)(2). This condition accounts for over 10% of all hospital admissions. COPD is the fourth leading cause of death and fifth leading cause of disability worldwide; men and women seem to be at equal risk and death attributed to COPD is increasing significantly in both sexes (1,2).

The most important risk factor for COPD is cigarette smoking. The NHANES III survey report showed that 12.5% of current smoker and 9.4% of former smoker had obstructive lung disease. Approximately 20% of regular cigarette smokers develop progressive airflow obstruction at sometime during life; patients with COPD usually have smoking history of at least 20 pack-years. Other known risk factors for COPD include air pollution, occupational exposure to dust, low antioxidant dusts, early childhood infections, airway hyperreactivity, low socioeconomic status, white race, female sex and genetic factors (3).The best diagnostic test for evaluating patients with suspected COPD is lung function measured with spirometry. The GOLD guidelines (4) characterize the severity of COPD according to clinical and spirometric measures. Key spirometric measures should include FEV1 and FVC. Patient with COPD typically presents with obstructive airflow. According to the GOLD criteria, a FEV1/FVC ratio of less than 70% in patient with a post-brochodilator FEV1 of less than 80% of predicted

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value is diagnostic for COPD. Severity is further stratified based on symptoms and FEV1 value (1, 4).

Pulmonary arterial hypertension (PHT): PHT is a complex problem characterized by non specific signs and symptoms and multiple potential causes. These symptoms are often difficult to dissociate from those caused by a known underlying pulmonary or cardiac disorder. It may be defined as a pulmonary arterial systolic pressure greater than 30 mmHg or a pulmonary artery mean pressure greater than 20 mmHg at rest (5).The etiology of primary PHT is unknown. Secondary PHT may complicate many pulmonary, cardiac and extra-thoracic conditions. Corpulmonale is enlargement of the right ventricle as a consequence of disorders of respiratory system. PHT invariably precedes corpulmonale. Unrelieved PHT, regardless of underlying cause, leads to right ventricular failure. COPD is the most common pulmonary disease resulting in right ventricular dysfunction (6).In persons older than 50 years of age, corpulmonale, the consequence of untreated PHT, is the third most common cardiac disorder (after coronary and hypertensive heart disease. Although the true prevalence of PHT is unknown, an elevation of pulmonary arterial pressure is reported to occur in 5-40% of patient in series of selected individuals with severe COPD undergoing right cardiac catheterization (7, 8).PHT in COPD progresses over time and its severity correlates with the degree of airflow obstruction and impairment of pulmonary gas exchange. 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 (9). Anatomical evidence of right ventricular hypertrophy can be found at autopsy in up to 40% of patient with COPD. However, there are discrepancies between different series because of lack of a unified morphological criteria used to define right ventricular hypertrophy. The increase in pulmonary artery pressure is often mild to moderate; however, 5-10% of patients with advanced COPD may suffer from severe PHT and present with a progressively downhill clinical course because of right heart failure added to ventilatory handicap (10).COPD with severe PHT and no other possible cause shares features with pulmonary vascular disease such as idiopathic PHT. Severe pulmonary hypertension increases right ventricular afterload and eventually leads to clinical syndrome of right ventricular failure with systemic congestion and inability to adapt right ventricular output to peripheral demand at exercise (11).

The cause of PHT in COPD is generally assumed to be hypoxic pulmonary vasoconstriction leading to permanent medial hypertrophy; however, recent pathologic studies point to extrinsic remodeling of all layers of pulmonary artery wall with intimal changes actually being the most prominent. These aspects account for the minimal reversibility with supplemented oxygen (12).There are various methods to evaluate pulmonary artery pressure, such as right-sided cardiac catheterization, echocardiography, electrocardiography and myocardial scintigraghy. However, these methods have some limitations; namely, right sided cardiac catheterization is invasive; echocardiography is sometimes difficult in COPD patients because of over-inflated lungs; the sensitivity and specificity of electrocardiography is low and myocardial scintigraghy is expensive (13).

Ecocardiography in copd:Trans-thoracic echocardiography is an important diagnostic test in any patient with suspected PHT. It is a non-invasive, easily available technique that allows assessment of right ventricular hypertrophy and/or dilatation and ejection flow dynamics and provides an estimate of pulmonary artery pressure; however, this method suffers from technical difficulties in patients with COPD because the over-inflated chest may alter sound wave transmission (14). Two-dimensional echocardiography provides information on morphology and dynamics of cardiac structures and it is also essential for diagnosis of associated left heart disease. Typical signs of corpulmonale are right ventricular and atrial enlargement with a normal or reduced left ventricular cavity and eventually reversal of normal septal curvature. In presence of tricuspid regurgitation, continuous wave doppler echocardiography may provide an estimate of pulmonary artery systolic pressure. However, tricuspid regurgitation is not always present in COPD; the incidence ranges between 24 and 66% of patients, therefore, limiting the possibility to estimate pulmonary artery systolic pressure in a proportion of patients (15). Using exercise echocardiography, it has been possible to identify an abnormal ventricular septal motion with distortion of left ventricle in COPD patients. These findings may help to detect occult right ventricular dysfunction (16).

Patients, materials and methods:

This study was done in Baghdad teaching hospital during the period from September-2005 to October-2006. It included 55 patients with chronic obstructive pulmonary disease. Description of Study population:The mean age of patients was 65.6± 8.2 years. There were 38 male patients (70%) and 17 female patients (30%). The mean age of male patients was 66.7±7 and of female patients was 64.9±8.1. The mean duration of symptoms of patients was 18 months ±10 months. There were 39 patients from Baghdad and 16 patients from other governorates. Thirty-two patients (58%) were current smokers, 18 patients (33%) were ex-smokers and five patients (9%) were non smokers. The mean intensity of smoking for smokers was 49.5 ± 22.2 packs –years.

Methods:For all patients history was taken and included the personal data (age, sex, occupation, residence, and marital status), social data (smoking status) and symptoms of patients. Clinical examination of patients included examination of vital signs, examination for cyanosis, leg edema, JVP, examination of chest for anteroposterior dimension and expansion of chest, breath sounds and added sounds, examination of precordium for left parasternal impulse, intensity of pulmonary component of S2, murmur of tricuspid regurgitation and examination of abdomen for hepatomegaly and ascites. For all patients ECG, CXR, and routine blood tests were done. For all patients pulmonary function tests were done and included measurement of FEV1, VC and FEV1 /VC as a base-line and after bronchodilators and compared with predicted values according to age, sex, and height.

Patients were classified according to results into stages according to GOLD criteria. Pulse oximetry was done for all patients. Echocardiography was done for all patients using trans-thoracic approach by independent operator. It included measurements of left ventricular internal dimension in diastole (LVIDd), left ventricular internal dimension in systole (LVIDs), left ventricular ejection fraction (LVEF), left atrial (LA) and right ventricular (RV) dimensions and use of Doppler technique to detect the presence of tricuspid and pulmonary regurgitations and estimate pulmonary artery systolic and/or diastolic pressure using the following formulas:Pulmonary artery systolic pressure = pressure gradient between RV and RA in systole +10 (10 is a constant used for RA pressure).Pulmonary artery diastolic pressure = pressure gradient between pulmonary artery and RV in diastole + 10.Pulmonary vascular resistance was estimated using the formula:

Pulmonary vascular resistance (Wood units) = (TR peak velocity/TVIRVOT)*10

+ 0.16. TVIROT is time velocity integral of right ventricular outflow tract.

This value was multiplied by 80 to convert to (dyn. sec. cm^{-5}).Patients with echo evidence of left-sided cardiac diseases were excluded from this study.

Results:

There were no significant differences in regard to age, smoking history and pulmonary function variables between the group in which a trans-tricuspid regurgitant jet was detected and the group without trans-tricuspid regurgitation jet.The symptoms and signs of COPD were more likely to be found in patients with TR than in patients without TR and the difference was statistically significant.Tricuspid regurgitation was found in 39 patients (70.9%) and increased pulmonary arterial systolic pressure was found in 20 patients (51%) with tricuspid regurgitation (36% of total COPD patients) and increased pulmonary vascular resistance in 19 patients (48.7%) with TR (34.5% of total COPD patients).We found that there were significant associations between decreasing FEV1 and increasing RV size, presence of TR, increased pulmonary artery systolic pressure more than 30 mmHg and increased pulmonary vascular resistance (table 1). The above echo parameters were also significantly associated with decreasing FEV1/VC (table 2) and decreasing O_2 saturation (table 3) but there was no significant association with decreasing vital capacity (table 4).

Table (1): Shows the relationship between FEV1 (% predicted) and RV dimensions, TR, Pulmonary systolic artery systolic pressure and pulmonary vascular resistance.

parametes	FEV1 (%pred.) >80%	FEV1 (%pred.) 50-79%	FEV1 (%pred.) 30-49%	FEV1 (%pred.) <30%	total
Number	0	22	22	11	55
RV dimensions >26	0	6	14	9	29
TR +ve	0	11	18	10	39
Pulmonary artery systolic pressure >30mmHg (in pt with TR)	3/11 (27%)	3/11 (27%)	9/18 (50%)	8/10 (80%)	20/39 (51%)
Pulmonary vascular resistance > normal (in pt with TR)	2/11 (18%)	2/11 (18%)	10/18 (56%)	7/10 (70%)	19/39 (48.7%)

Normal pulmonary resistance is up to 130 dyn.sec.cm^{-5}

Table (2): Shows relationship between FEV1/VC ratio and RV dimensions, TR,
Pulmonary artery systolic pressure and pulmonary vascular resistance

PARAMETERS	FEV1/VC 50-70%	FEV1/VC 30-50%	FEV1/VC <30%	TOTAL
Number	9	35	11	55
RV dimensions >26	2	18	9	29
TR +ve	2	27	10	39
Pulmonary artery systolic pressure >30mmHg (in pt with TR)	0/2	12/27 (44%)	8/10 (80%)	20/39 (51%)
Pulmonary vascular resistance > normal (in pt with TR)	0/2	12/27 (44%)	7/10 (70%)	19/39 (48.7%)

Normal pulmonary vascular resistance is up to 130 dyn.sec.cm-5

Table (3): Shows relationship between O2 saturation (by pulse oximatry) and RV dimension, TR, pulmonary artery systolic pressure and pulmonary vascular resistance.

PARAMETERS	O2 sat. ≥90%	O2 sat. 85-90%	O2 sat. <85%	TOTAL
Number	20	25	10	55
RV dimentions >26 mm	6	29	8	15
Tricuspid regurgitation +ve	10	20	9	39
Pulmonary artery systolic pr >30 mmHg (in pt with TR)	0/10	13/20 (65%)	7/9 (78%)	20/39 (51%)
Pulmonary vascular resistance>normal (in pt with TR)	0/10	11/20 (55%)	8/9 (89%)	19/39 (48.7%)

*Normal pulmonary resistance is up to 130 dyn.sec.cm-5

Table (4): Shows relationship between VC (% predicted) and RV dimension, TR,
pulmonary artery systolic pressure and pulmonary vascular resistance.

PARAMETERS	VC (%pred.) >80	VC (%pred.) 70-80	VC (%pred.) <70	TOTAL
Number	3	40	12	55
RV dimension >26	3	19	7	29
Tricuspid regurgitation +ve	1	30	8	39
Pulmonary artery systolic pressure >30 mmHg (in pt with TR)	0/1	16/30 (53%)	4/8 (50%)	20/39 (51%)
Pulmonary vascular resistance>normal (in pt with TR)	0/1	15/30 (50%)	4/8 (50%)	19/39 (48.7%)

*Normal pulmonary resistance is up to 130 dyn.sec.cm-5

Discussion:

In this study there were no significant differences in regard to age, smoking history and pulmonary function variables between the groups in which a trans-tricuspid regurgitation jet was measurable compared with that in which there was no signal. Similar findings were found by M.A. Higham et al in their study (6). In this study, TR was found in 39 patients (70.9%) with COPD .M.A. Higham et al found TR in 77% (6) and Burgess et al have found TR in 68% of patients with COPD (25). Our study is compatible with these studies but the slight difference in detection of tricuspid regurgitation jet is because the detection is affected by several factors like the type of equipment used, the experience of operator and the quality of image obtained. The latter is affected by the body habitus of the patient and degree of lung hyperinflation due to COPD (6).In this study, it is shown that the symptoms and signs of COPD were more likely to be found in patients with TR than in patients without TR and the difference was statistically significant.

The results in this study shows that increased pulmonary artery systolic pressure more than 30 mm Hg was found in 51% of patients with tricuspid regurgitation (36% of total COPD patients) and increased estimated pulmonary vascular resistance was found in 48.7% patients with TR (34.5% of total COPD patients). M.A. Higham et al found that increased pulmonary systolic pressure was found in 57% of patients with tricuspid regurgitation. They did not measure the pulmonary vascular resistance (6). Matsuyama et al (11) have found elevated pulmonary artery systolic pressure in 32.8% of patients with COPD. Weitzenblum et al found pulmonary hypertension in 35% of patients with COPD measured invasively (16). Burgess et al have found elevated pulmonary systolic pressure in 34.4% and elevated pulmonary vascular resistance in 33.7% of COPD patients. The results of these studies seem to be equivalent with our results although they measured the pulmonary artery pressure by slightly different methods. For example M.A.Higham et al measured the pulmonary artery systolic pressure by estimating the trans-tricuspid pressure gradient (TTPG) without the addition of the estimated right atrial pressure. Matsuyama et al on other hand added the estimated right artial pressure from examination of jugular venous pulse to TTPG. In our study we added the constant 10 as right atrial pressure to TTPG. This is the same method used by Abaci et al (17). The pulmonary vascular resistance was not measured by M.A.Higham et al and Matsuyama et al. Tables (1,2,3 and 4) show that the selected echo findings (increased right ventricular dimentions, TR, increased pulmonary artery systolic pressure, increased pulmonary vascular resistance) were more frequently found with decreasing FEV1 (% predicted), decreasing FEV1/VC ratio and decreasing O_2 saturation and the associations were statistically significant. On the other hand there was no significant association with decreasing VC (% predicted). M.A. Higham et al found similar associations between increased pulmonary artery pressure and FEV1, diffusion coefficient for carbon monoxide (KCO), diffusion capacity for carbon monoxide (DLCO) and O_2 saturation but they did not find significant association with FEV1/VC and VC (6). In our study we did not measure KCO and DLCO because these tests are not available in our centre. Burgess et al reported significant association between increased pulmonary artery systolic pressure and increased pulmonary vascular resistance with decreasing FEV1 and FEV1/VC ratio but they did not compare the findings with VC and O_2 saturation (15). In a series of 175 patients with COPD and hypoxia reported by Weitzenblum et al, there was significant

association between elevated pulmonary artery pressure and decreasing FEV1/VC ratio and PaO_2 (16). In our study we did not measure PaO_2 but we measured O_2 saturation as a measure of adequacy of oxygenation. A previous study of 33 patients found that pulmonary artery end diastolic pressure estimated echocardiographically correlated with pulmonary function indices and with KCO but not PaO_2 (18) . A large multicenter study of 370 patients with COPD correlated invasively-derived pulmonary arterial pressure with spirometry, but not gas transfer measurements (19). These points to the accuracy of echocardiographic estimation of pulmonary arterial pressures reported in these studies. However, it should be noted that, even though statistically significant, the correlations of pulmonary arterial pressure with spirometry and gas transfer indices are fairly poor (6). Although a better predictor for PHT than other measurements, the partial pressure of arterial oxygen has also previously been shown to correlate poorly with pulmonary arterial pressure measured invasively (19).Our study shows that PHT is increasingly common with increasing severity of COPD. Indeed, it has previously been suggested that loss of alveolar capillary bed surface area may contribute to the elevation of pulmonary arterial pressure associated with severe emphysema (20). Taken together the present and previous data suggest that factors other than severity of COPD are contributors to the pathogenesis of PHT. These factors may include nocturnal desaturation, frequent exacerbations, changes in hematocrit and ventilatory response to hypoxia. Data is currently limited, but it is also possible that genetic influences are involved, acting synergistically with the effects of chronic hypoxia and predisposing certain COPD patients to PHT (21). Routine investigations of the presence of pulmonary artery hypertension are not currently part of UK (22 or US (23) guidelines for the diagnosis and management of COPD.

Conclusion:

There is high prevalence of pulmonary arterial hypertension correlating with increasing severity of chronic obstructive pulmonary disease.

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