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Cross-sectional study of pulmonary hypertension among patients with chronic obstructive pulmonary disease

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Abstract

The prevalence graph of chronic obstructive pulmonary disease (COPD) in India is escalating significantly. Pulmonary hypertension (PH) is one of the most important complications of COPD, leading to worsened clinical progression. Various studies have predicted the correlation of PH with the degree of airflow obstruction in COPD, but the association between PH and the ABCD stage of COPD, as per the recent Global Initiative for Chronic Lung Disease (GOLD) criteria, is still ambiguous and underexplored. Thus, we aim to correlate the association of PH with the updated staging of COPD.

This prospective study followed 100 COPD patients diagnosed based on spirometry and clinical symptoms over a 1-year period. The severity and staging of COPD were determined according to GOLD classification criteria. Screening two-dimensional echocardiography was performed to assess PH. The association between PH and COPD staging was analyzed.

Among the 100 subjects with COPD, the mean age was 60.6±7.8 years, and 70% were male. Based on disease staging, 23 patients (23%) were classified as stage A, 25 (25%) as stage B, 13 (13%) as stage C, and 39 (39%) as stage D. PH was present in 72 patients: 25 (25%) had mild PH, 26 (26%) had moderate PH, and 21 (21%) had severe PH. A significant association was observed between the stages of COPD and the severity of PH.

PH is a major complication in COPD, leading to poor prognosis. Therefore, incorporating early cardiac screening in all COPD patients may assist in assessing prognosis, morbidity, and mortality.

Key words: pulmonary hypertension, chronic obstructive pulmonary disease, ABCD staging.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic and progressive inflammatory lung disease that causes persistent airflow limitation [1]. According to WHO data, COPD is expected to become third leading cause of mortality by 2030 [2]. The Global initiative of COPD has evolved significiantly over the past 20 years. In the most recent GOLD consensus statement, spirometry determined airflow limitation (FEV1) was separated from clinical parameters, instead used the combination of modified Medical Research Council dyspnea (mMRC), COPD Assessment Test (CAT Score), exacerbations and hospitalization history was adopted [3-5].

COPD is associated with several extra-pulmonary system manifestations, the most common being cardiac involvement. Pulmonary hypertension (PH), develops in COPD, primarily due to hypoxic vasoconstriction of small arteries leading to structural changes including intimal hyperplasia and later smooth muscle hypertrophy/hyperplasia.

Echocardiography provides a rapid, noninvasive, portable and accurate method to evaluate cardiac changes. Several studies have confirmed that echocardiographic estimates of pulmonary arterial pressure closely correlates with the values obtained via right heart catheterization [6-9].

Pulmonary hypertension (PH) is a major complication in patients with COPD and is linked to worsened clinical progression. This study aims to examine the correlation between the severity of PH and the GOLD staging of COPD.

Materials and Methods

This was a cross sectional study involving 100 COPD patients who attended Outdoor and Indoor department of Institute Of Respiratory Diseases, SMS Medical College, Jaipur over a one year period. Patients with a history of cardiac diseases, liver diseases, stroke patients, other respiratory lung diseases such as asthma, tuberculosis, obstructive sleep apnea (OSA), seriously ill individuals,or any condition likely to elevate pulmonary arterial pressure were excluded.Patients in whom spirometry was contraindicated were also excluded.

Spirometry with reversibility testing was conducted. Only patients meeting the GOLD criteria for COPD ($FEV_1/FVC < 0.70$ and/or $FEV_1 < 0.80$) were included. ABCD staging was done per GOLD guidelines, based on mMRC scores, CAT scores, and history of exacerbations andhospitalizations.

All patients underwent resting two-dimensional transthoracic Doppler echocardiography performed by expert cardiologists. Guidelines of echocardiography assessment of right heart according to American Society of echocardiography were followed to screen Pulmonary arterial

hypertension with severity [10]. Measurements included pericardial and valvular anatomy and function, chamber size, and systolic pulmonary arterial pressure (sPAP). Tricuspid regurgitant flow was assessed using color Doppler, and jet velocity was measured using continuous-wave Doppler.

Pulmonary arterial hypertension is defined in this study as systolic Pulmonary Arterial Pressure (sPAP) >/=36 mm Hg. PH was classified into mild, moderate and severe category as sPAP 36-50,50-70,>70 mm Hg, respectively (using Chemla formula, mean pulmonary Arterial Pressure(MPAP)=0.61PASP +2 mm Hg and putting values of 25-35,35-45 and >45mm Hg of MPAP for mild, moderate and severe pulmonary hypertension respectively as per the guidelines [6,10,11].

According to Guidelines of echocardiography assessment of right heart from American Society of echocardiography, Right ventricular systolic pressure(RVSP) is estimated based on the modified Bernoulli equation and considered equal to systolic pulmonary arterial pressure (sPAP) in the absence of right ventricular outflow obstruction. sPAP(mmHg)= right ventricular systolic pressure = trans-tricuspid pressure gradient(TTPG) + right atrial pressure(RAP), where TTPG is 4v2(v=peak velocity of tricuspid regurgitation, m/s) [10]. Inferior vena cava (IVC) diameter 2.1 cm that collapses >50% with a sniff suggests a normal RA pressure of 3 mm Hg (range, 0-5 mm Hg), whereas an IVC diameter > 2.1 cm that collapses <50% with a sniff suggests a high RA pressure of 15 mm Hg (range, 10-20 mm Hg). In indeterminate cases in which the IVC diameter and collapse do not fit this paradigm, an intermediate value of 8 mm Hg (range, 5-10 mm Hg) may be used. Indirect 2D echocardiographic signs include right ventricular (RV) hypertrophy, RV dilation ,RA dilation ,Tricuspid annular plane systolic excursion (TAPSE)< 16 mm indicates RV systolic dysfunction, systolic flattening of the interventricular septum and pericardial effusion.

Statistical analysis

The data entry was done in the Microsoft EXCEL spread sheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software ,IBM manufacturer, Chicago, USA,ver 21.0.

The presentation of the categorical variables was done in the form of number and percentage(%).On the other hand, the quantitative data were presented as the means +/- SD and as median with 25^{th} and 75^{th} percentiles (interquartiles range). The following statistical tests were applied for the results:

1. The association of the variables which were qualitative in nature were analyzed Chi-square Test. If any cell had an expected value of less than 5, then Fisher's exact test was used.
2. The association of variables which were quantitative in nature were analyzed using ANOVA.

Results

Among the 100 subjects with COPD, 70.0% were male and 30.0% were female. The mean age of the study population was 60.6 ± 7.8 years, and the mean body mass index (BMI) was 20.88 ± 3.31 kg/m^2. According to the GOLD classification, 23 patients (23%) were in Stage A, 25 (25%) in Stage B, 13 (13%) in Stage C, and 39 (39%) in Stage D (Table 1).

PH was observed in 72 patients, with 25 (25%) having mild PH, 26 (26%) moderate PH, and 21 (21%) severe PH. A significant association was found between the stages of COPD and PH severity (Fisher's exact test, $p = 0.001$). Notably, among patients with Stage A COPD, 19% had no PH and 16% had mild PH, whereas among those with Stage D, 2% had no PH, 3% had mild PH, 14% had moderate PH, and 20% had severe PH (Table 2).

In addition, indirect signs of PH—such as right atrial enlargement, right ventricular enlargement, small left chamber size, and interventricular septal flattening—were significantly more prevalent in Stage D compared to Stages A, B, and C ($p< 0.001$) (Table 3).

Discussion

It is well established that PH severity in COPD increases with airflow obstruction—specifically,a lower FEV1 correlates with more severe PH.Although FEV1 was once central to GOLD staging, it was later deemphasized because FEV1 is an imperfect measure of the individual disease experience and hence, it was separated from the clinical parameters.

In our study, among the four stages of COPD (A, B, C, and D), the prevalence and severity of PH was highest in stage D. Kumar *et al.* studied PH in 109 COPD patients and found a positive correlation between PH and stages of COPD [12].

Interestingly, even though the mMRC and CAT score of patients in stage B is higher than stage C, PH severity was more in stage C. This would be the reason of increased hospitalizations and exacerbation history in stage C patients than B. EC Alexapaulos *et al.*found that patients with GOLD stage IV had five fold-higher expected number of exacerbations and hospitalizations, respectively, and nearly threefold-higher risk of admission to the ICU compared to stage I patients [13]. A Chaouat *et al.* also reported increased PH as a predictor of exacerbation risk and reduced survival [14].

Significant association was seen in 2D ECHO readings:RAP(mmHg), TTPD(m/sec), sPAP(mmHg), MPAP(mmHg), TR velocity(m/sec), TAPSE(mm) with stages of COPD (p value <.05).Stage D had the highest mean RAP values(-9.95 +/- 3.99),highest mean sPAP value (70.05 +/- 22.65),highest mean MPAP value (44.73 +/- 13.81) highest TR velocity value(3.81 +/- 0.7) lowest mean TAPSE value(15.95 +/- 1.93)(p value<.0001). Stage D had significant high proportion of other indirect 2D Echo PH findings such as RV enlargement (76.92%), small left chamber size (30.77%),interventricular septum flattening (30.77%) (p value<.0001). N.K Gupta *et al.* reported a similar trend of increasing cardiac dysfunction with COPD severity [9].

Pulmonary hypertension and corpulmonale being major complications of COPD associated with a significant high risk of mortality and morbidity, this study gives an insight , how important is the early diagnosis of COPD complication helps for improving the quality of life of patients and adequate timely intervention can be done.

Conclusions

Our study concludes that COPD staging, based on GOLD criteria, is significantly associated with PH severity. However, further studies with large sample sizes are needed to verify this. We emphasize that early cardiac screening in all COPD patients can aid in assessing prognosis, morbidity, and mortality.

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Table 1. Distribution of stage of COPD of study subjects.

Stage of COPD	Frequency	Percentage (%)
A	23	23.00
B	25	25.00
C	13	13.00
D	39	39.00
Total	100	100.00

Table 2. Association of stage of COPD with pulmonary artery hypertension.

Stage of COPD	Nil (n=28) n (%)	Mild (n=25) n (%)	Moderate (n=26) n (%)	Severe (n=21) n (%)	Total n (%)	p
A	19 (67.86)	4 (16)	0 (0)	0 (0)	23 (23)	<0.0001*
B	6 (21.43)	16 (64)	3 (11.54)	0 (0)	25 (25)	
C	1 (3.57)	2 (8)	9 (34.62)	1 (4.76)	13 (13)	
D	2 (7.14)	3 (12)	14 (53.85)	20 (95.24)	39 (39)	
Total	28 (100)	25 (100)	26 (100)	21 (100)	100 (100)	

*Fisher's exact test

Table 3. Association of 2D echo findings with the stages of COPD.

2D ECHO readings	A (n=23)	B (n=25)	C (n=13)	D (n=39)	Total	p
RA enlargement, n (%)	0 (0)	0 (0)	2 (15.38)	30 (76.92)	32 (32)	<0.0001*
RV enlargement, n (%)	0 (0)	0 (0)	2 (15.38)	30 (76.92)	32 (32)	<0.0001*
Small size left chamber, n (%)	0 (0)	0 (0)	0 (0)	12 (30.77)	12 (12)	<0.0001*
IV septum flattening, n (%)	0 (0)	0 (0)	0 (0)	12 (30.77)	12 (12)	<0.0001*
Pericardial effusion, n (%)	0 (0)	0 (0)	0 (0)	1 (2.56)	1 (1)	1*
RAP(mmHg), mean ± SD	5±0	5.4±1.38	6.54±2.4	9.95±3.99	7.23±3.5	<0.0001‡
TTPG(m/sec), mean ± SD	17.04±9.28	34.24±9.44	45.85±9.96	60.1±19.72	41.88±22.2	<0.0001‡
sPAP(mmHg), mean ± SD	21.91±9.43	39.84±9.62	52.38±10.15	70.05±22.65	49.13±24.88	<0.0001‡
MPAP(mmHg), mean ± SD	15.37±5.75	26.3±5.87	33.95±6.19	44.73±13.81	31.97±15.18	<0.0001‡
TR velocity(m/sec), mean ± SD	2±0.52	2.9±0.42	3.21±0.48	3.81±0.7	3.09±0.9	<0.0001‡
TAPSE(mm), mean ± SD	19.48±0.9	18.88±0.88	17.85±1.34	15.95±1.93	17.74±2.08	<0.0001‡

*Fisher's exact test, ‡ANOVA. RAP, right atrial pressure; TTPG, tricuspid trans pulmonary pressure gradient; sPAP, systolic pulmonary arterial pressure; MPAP, mean pulmonary arterial pressure; TR velocity, tricuspid regurgitation velocity; TAPSE, tricuspid annular plane systolic excursion.