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ECHOCARDIOGRAPHIC FINDINGS AND ITS CORRELATION WITH THE SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN A TERTIARY CARE HOSPITAL AT NORTH KERALA: A CROSS-SECTIONAL STUDY

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Abstract:
Chronic obstructive pulmonary disease (COPD) and cardiovascular diseases (CVD) are more frequently associated and their coexistence worsen the prognosis of the condition. The irreversible airflow obstruction in COPD, leads to persistent hypoxia and cardiovascular damage. Our objective was to assess the cardiac changes secondary to COPD by echocardiography and to correlate the echo findings with pulmonary function parameters across the severity of COPD. A total of 120 patients were selected and the severity was graded by Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines using spirometry. All patients were subjected to echocardiographic evaluation. On echocardiographic evaluation, 60.83% patients had abnormal findings. Majority of cases had pulmonary hypertension (PH). Severe grade of PH was present in severe (33.33%) and very severe (66.67%) stages of COPD. There was a significant association ($p < 0.05$) between the severity of COPD and frequency of PH, cor pulmonale and tricuspid regurgitation (TR). The frequency of left ventricular systolic dysfunction (LVSD) and left ventricular diastolic dysfunction (LVDD) were 12.5% and 55.83% respectively. There was a significant($p<0.05$) negative correlation between echo parameters (cor pulmonale, TR degree) and spirometry parameters. To conclude, the prevalence of cardiac dysfunction showed a liner relationship with the severity of COPD, especially cor pulmonale and TR, with a statistical significance ($p<0.05$). Echocardiography detects cardiovascular abnormality in COPD patients at the subclinical stage and helps in the improvement of health care.

Keywords: Chronic obstructive pulmonary disease, cardiovascular disease, spirometry, echocardiography

Introduction:

Chronic obstructive pulmonary disease (COPD) is a major non communicable disease, common in middle aged and elderly chronic smokers. In 2016, COPD accounted for 32% of global DALY (Disability Adjusted Life -Years) in India and ranked third in global mortality rate (1,2). COPD includes chronic bronchitis (inflammation of small airways) and emphysema (destruction of lung

parenchyma) which produces progressive and irreversible obstruction of airways (3). COPD has a complex pathogenesis with the involvement of various molecular mechanisms and it is a multi-system disease (3). Cardiovascular disease is the most common extrapulmonary manifestation of COPD (3). COPD increases the prevalence of CVD and one out of six COPD patients, have coronary heart disease (4). Half of the mortality cause in COPD is attributed to CVD and not due to respiratory failure. COPD is associated with increased carotid intimal medial thickness, which is implicated for the increased mortality (5). Also, the co-existence of COPD and CVD increases hospitalization, morbidity burden and the rate of premature death (5). COPD and CVD involve many common risk factors and the most common one implicated is cigarette smoking. Persistent low grade systemic inflammation, endothelial dysfunction, hypoxia, increased platelet reactivity and arterial stiffness are implicated in the interplay between COPD and CVD (6**).** Dynamic hyperinflation of lungs due to expiratory flow limitation leads to formation of physiological dead space, ventilation-perfusion mismatch and abnormality in gas exchange (7). The long term processes of "inflammageing " affects the pulmonary vessels resulting in vascular wall remodelling and development of pulmonary hypertension, cor pulmonale and ventricular dysfunction (8).

Echocardiography is a non-invasive technique to image the heart using ultra sound waves. It detects any structural or functional abnormality at a stage when clinical symptoms are not manifested (9). Doppler echocardiogram has an additional advantage of assessing the direction and velocity of blood flow (9). Echocardiography plays a vital role in early detection of COPD induced cardiac changes and to halt its progress (9). The cardiac functions of COPD patients are explored by many studies, (10) but the correlation between cardiac function and the grade of severity of COPD, according to GOLD criteria is explored less in Kerala population. So, this study was undertaken to correlate the right and left ventricular functions with spirometry parameters, according to the grade of the disease.

Materials and methods:

This is a prospective cross-sectional study conducted at Malabar Medical College Hospital & Research Centre, Kozhikode, Kerala, after obtaining institutional ethical clearance. Totally,120 patients who attended cardiology out- patient department with chronic obstructive pulmonary disease (COPD) related cardiac issues and clinically stable were recruited. The sample size was calculated using the formula for cross sectional studies utilizing the frequency of COPD patients visiting cardiology OP for a check-up. The duration of the study was one year from January' 2024 to January' 2025.A written informed consent was obtained from each patient and the study was conducted according to the ethical principles framed by the declaration of Helsinki. The presence of COPD was confirmed by clinical history, pulmonary function test and physician diagnosis. Patients with any other chronic lung disease, any systemic disease that can cause pulmonary hypertension, any primary cardiac disease, patients with poor echo window, and patients who were unfit to undergo spirometry procedure were excluded from the study.

All selected patients were subjected to routine laboratory investigations, spirometry and echocardiography. They were classified according to GOLD guidelines as mild (post bronchodilator $FEV_1 \geq 80\%$ of predicted), moderate ($50\% \leq$ post bronchodilator $FEV_1 < 80\%$ predicted), severe ($30\% \leq$ post bronchodilator $FEV_1 < 50\%$ predicted) and very severe (post bronchodilator $FEV_1 < 30\%$ predicted), respectively. Doppler echocardiography was done at cardiology department under expertise guidance. The machine used was Phillips EPIQ CVx GE T8 model with a probe frequency of 3 MHz and 6MHz. Both 2D and M-Mode studies were done.

Doppler echo can approximate pulmonary artery systolic pressure (sPAP) using modified Bernoulli equation, $RVSP=4V^2 + RAP$, (RVSP= Right ventricular systolic pressure, V = peak velocity of tricuspid regurgitation; RAP=Right atrial pressure) (10). This modified Bernoulli equation converts the difference in the velocity of blood flow across the valve into instantaneous pressure gradient. Central venous pressure is identical to right atrial pressure, in the absence of vena cava obstruction and pulmonary artery systolic pressure equals to right ventricular systolic pressure, in the absence of pulmonary stenosis (10). Right atrial pressure was calculated according to the degree of the collapse

of inferior vena cava. During forced inspiration, there is a decrease in intrathoracic pressure which makes the vena cava to collapse and consequently there is a decrease in the venous return and central venous pressure. Right atrial pressure was calculated as follows: no collapse=15 mmHg, partial collapse=10 mmHg, complete collapse=5 mmHg (10).

Pulmonary hypertension is defined as mean pulmonary artery pressure (mPAP) greater than 20 mmHg. In this study, we considered the same value to diagnose pulmonary hypertension. The mean pulmonary artery pressure was calculated according to the Chemla formula, mPAP = 0.61*sPAP + 2; (sPAP -Pulmonary artery systolic pressure) (10). Cor pulmonale is right ventricular enlargement secondary to a lung disorder that causes pulmonary artery hypertension. The pathological section shows hypertrophy and dilatation with the thickening of right ventricle chamber wall. If the thickening exceeds the normal range of 0.9 to 2.6 cm, the diagnosis of cor pulmonale is made (11). Right ventricular function was assessed by measuring tricuspid annular plane systolic excursion (TAPSE) and right ventricular ejection fraction (RVEF) (12). The TAPSE value of less than 16mm and RVEF less than 44% is considered abnormal (12). Tricuspid regurgitation (TR)was detected by colour flow technique and maximum jet velocity was measured using continuous wave doppler (12).

Left ventricular systolic function was assessed by the left ventricular ejection fraction (normal=56%-78%) (13). Ejection fraction is otherwise called as stroke volume, which measures the end-diastolic volume of blood ejected during the contraction of left ventricle during each cardiac cycle (13). Early to late diastolic trans mitral flow velocity (E/A ratio) was the parameter used to assess the left ventricular relaxation impairment, which affects the diastolic filling of left ventricle (14). The normal value of E/A ratio is ascertained based on the age parameter, as, the elastic recoiling capacity of left ventricle declines with age (14). 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), <0.8 (age group ≥ 70 years) (14).

Statistical analysis:

The statistical software used was SPSS (Statistical Package for the Social Sciences) version 22 (IBM SPSS, Inc Chicago, IL, USA). The normality distribution of the data was checked using Kolmogorov-Smirnov test. Qualitative data is presented as frequency and percentage. Quantitative data is represented as mean ± SD (Standard deviation) and range. To compare between the groups of normally distributed variables (parametric data) one-way ANOVA is used. The p value was considered significant if it was less than 0.05. To correlate the variables like spirometry parameters, echo parameters and severity of COPD, we used Spearman's correlation test with r value representing correlation coefficient.

Results:

This study included 120 clinically stable COPD patients, after a drop out of 4 patients who were not fit for undergoing spirometry procedure due to recent suffering from upper respiratory tract infection. The demographic characteristics of patients are outlined in table 1.

Table 1: Demographic characteristics of all patients

Variable		**Frequency (n=120)**
Age (years) Mean ± SD (range)		60.52 ± 6.02 (50-73)
BMI (kg/m^2) Mean ± SD (range)		25.83 ± 1.56 (20- 31)
Duration of symptoms (years) Mean ± SD (range)		21.62 ± 15.73 (17-25)
		n (%)
Gender	Male	116(96.67%)
	Female	4 (3.33%)
Smoking status	Current smoker	30(25%)
	Ex smoker	90 (75%)
BMI	Underweight	18(15%)
	Normal	42(35%)
	Overweight	37(30.83%)
	Obese	23(19.17%)
Comorbidities	Absent	32 (26.67%)
	DM	12(10%)
	HT	47(39.17%)
	DM+HT	12(10%)
	CVD	17(14.17%)

DM- Diabetes mellitus; HT- Hypertension; DM +HT- Diabetes mellitus + Hypertension; CVD- cardiovascular disease.

The spirometry parameters like post bronchodilator FEV_1, FVC, FEV_1/FVC and PEFR were significantly reduced with the increase in severity of COPD (Table 2)

Table 2: Spirometry values of patients with different grades of COPD (n=120)

Variable	Mild (n=30) Mean ± SD	Moderate (n=30) Mean ± SD	Severe (n=30) Mean ± SD	Very severe (n=30) Mean ± SD	Test	p value
Post bronchodilator FEV_1	80.21± 1.05	62.34± 4.53	42.3± 3.13	26.86± 1.6	F= 1623	p<0.05
FVC	91.75± 2.43	84.86± 3.52	76.13± 4.21	71.42± 4.42	F= 167	p<0.05
Post bronchodilator FEV_1/FVC	67.18± 1.03	57.15± 3.89	41.32± 2.31	28.16± 1.47	F= 1142	p<0.05
PEFR	161.7 ± 34.3	153.1± 22.4	145.3± 13.3	132.3± 12.4	F= 649	p<0.05
PaO_2 mmHg	86.32± 2.34	81.35± 2.42	76.21± 26	71.27± 47	F= 268	p<0.05

FEV_1- Forced Expiratory Volume in one second; FVC- Forced Vital Capacity; PEFR-Peak Expiratory Flow Rate; PaO_2 mmHg- Partial oxygen saturation in mmHg; F- F test value for one-way ANOVA.

The prevalence of cardiac dysfunctions increases with the severity of COPD. Left ventricular diastolic dysfunction is more common than pulmonary hypertension (table 3).

Table 3: Echocardiographic findings according to severity of COPD

Echo Findings	Mild (n=30)	Moderate (n=30)	Severe (n=30)	Very severe (n=30)	Total numbers	Percentage
Normal study	28	17	02	0	47	39.17%
PH	05	08	24	26	63	52.5%
Cor pulmonale	02	04	06	09	21	17.5%
TR	06	09	26	30	71	59.16%
RVSD	03	-	06	03	12	10%
LVSD	02	05	04	04	15	12.5%
LVDD	21	08	18	20	67	55.83%

PH- Pulmonary hypertension; TR- Tricuspid regurgitation;
RVSD- Right ventricular systolic dysfunction; LVSD- Left ventricular systolic dysfunction;
LVDD- Left ventricular diastolic dysfunction

The frequency of cor pulmonale increases with the severity of pulmonary hypertension (table 4).

Table 4: Frequency of cor pulmonale with severity of PH

Severity of PH	Frequency of cor pulmonale
Mild (38)	05 (13.5%)
Moderate (16)	07 (43.75%)
Severe (09)	09 (100%)

There is a positive correlation with statistical significance between severity of COPD and PH degree, TR degree, cor pulmonale (table 5).

Table 5: Correlation between echo findings and severity of COPD

Variable----severity of COPD	Spearman correlation coefficient (rho)	P value
LVSD	-0.062	0.45
LVDD	-0.051	0.57
RVSD	0.238	0.021
PH degree	0.721	$p<0.05$
TR degree	0.811	$p<0.05$
Cor pulmonale	0.731	$p<0.05$

There is significant negative correlation between spirometry parameters (FEV_1, FVC, FEV_1/FVC) and TR degree, cor pulmonale (table 6).

Table 6: Correlation between echo findings and spirometry parameters in COPD patients.

Parameter	FEV_1		FVC		FEV_1/FVC	
	r	p	r	p	r	p
LVSD	-0.432	0.421	-0.456	0.531	0.479	0.832
LVDD	0.387	0.731	-0.426	0.572	-0.386	0.842
RVSD	-0.463	0.631	-0.475	0.831	-0.468	0.963
Cor pulmonale	-0.265	<0.05	-0.253	<0.05	-0.275	<0.05
EF (%)	0.831	0.426	0.632	0.962	0.482	0.174
PH degree	0.188	0.264	0.163	0.642	0.174	0.863
TR degree	-0.321	<0.05	-0.362	<0.05	-0.374	<0.05

r- correlation coefficient

Discussion:

In this study, we included 120 clinically stable COPD patients. The approximate male to female ratio was 4:1. The age of patient ranges from 50 to 73 years with a mean of 60.52 ± 6.02 years. The mean duration of symptoms was 21.62 ± 15.73 years. The result was in concordance with the study conducted in India by Gupta NK et al (15), who showed male majority among COPD patients and similar mean duration of symptoms. COPD is a disease of late adulthood. The average age of COPD diagnosis is 40 years. Normally young patients won't develop symptoms of COPD unless they have genetic disorder like alpha1-antitrypsin deficiency. The absence of this enzyme accelerates the proteolytic damage in the lungs and the presentation of symptoms is early (16). COPD is a male dominant disease, due to the high prevalence of smoking in this gender. In present study, 75 % were current smokers and 25% were ex-smokers. The main risk factor for development of COPD in female is due to the use of coal for household needs (17).

The mean BMI in our study population was 25.83 ± 1.56, ranging from 20 – 31 kg/m^2. The percentage of patients with low and high BMI were15% and 50%, respectively. COPD patients with low BMI have a higher risk of mortality compared to those with high BMI, which is so called 'obesity paradox' in COPD (18). The presence of co morbidities increases the morbidity in COPD patients. Particularly, the prevalence of cardiovascular diseases (CVD) in COPD patients increases the mortality to a higher rate. In present study, 14.17% patients had associated cardiovascular ailments. This finding was in concordance with the statement about the prevalence of CVD among COPD patients by Nirupama Putcha et al (19). The frequency of other comorbidities was 10% with diabetes, 39.17% with hypertension and 10% with both diabetes and hypertension.

The spirometry parametric values (Predicted FEV_1%, FEV_1/FVC, FVC, PEFR) decline with the increase in severity of COPD. This finding was alike to the observation made by Ramachandran P et al (20). We found, 60.83% of COPD patients with abnormal echocardiography findings and the prevalence of pulmonary hypertension (PH) was found to be more. The frequency of PH in mild, moderate, severe and very severe COPD were 4.17%, 6.67%, 20% and 21.67% respectively (table-3). The prevalence of tricuspid regurgitation (TR) was 59.16% (table-3). PH severity among COPD patients was distributed as follows: 15.83% mild, 44.17% moderate and 5.83% severe (table -4). These observations were similar to the findings made by Nasir et al (21). Also, there was a significant association ($p<0.05$) between the prevalence of cor pulmonale and severity of PH (table-4). The incidence of PH, TR and cor pulmonale were directly proportional to the severity of COPD (table-5). These findings were very similar to the remark made by Gupta NK et al (15). The annual hospital admission rate for heart failure in United States is 10-30%, out of which, 85% patients have COPD. This explains the significance of the coexistence of cor pulmonale and COPD (22).

There was a difference of opinion regarding the presence of left ventricular dysfunction (LVDD) in COPD, as reflected by some studies (23). In our study, out of thirty patients with mild grade COPD, 21 patients had LVDD. Also, we noted 55.83% of LVDD, across different grades of COPD, out of which, 14.17% had PH and 85.83 % didn't had PH in association. This observation authenticates the data published by Hilde JM et al (24), who remarked on the absence of LVDD in a large cohort of COPD patients. In this study, we found a negative correlation between spirometry parameters and TR

degree, cor pulmonale. These findings were similar to the study result, conducted by Gupta et a (15). COPD is the leading cause for cor pulmonale, which is a maladaptive response to PH (25). Cor pulmonale parvus is the mild form of right sided heart failure due to a lung disorder. As the stage progress, it may lead to TR and a substantial fall in pulmonary function values (25). The presence of echocardiographic changes (70% LVDD, 20% TR, 16.6% PH, 10% RVSD) in mild stage of COPD, in our study (table-3), warrants the need of echocardiographic evaluation at the earliest stage of disease onset.

Limitations of the study:

Foremost limitation is clinical outcome of the patient is not correlated with echocardiographic changes. For this we need to follow-up the patient with a prospective study design. The second limitation is electro cardiac changes are not monitored, which helps to add information in the diagnosis of left and right ventricular dysfunctions.

Conclusion:

Prevalence of abnormal echocardiographic (ECHO) changes secondary to COPD is very common at subclinical stage, before the presentation of symptoms. The abnormal ECHO findings were evidenced even in mild stage of COPD severity. There exists a significant positive correlation between the severity of COPD and ECHO parameters (PH, cor pulmonale and TR). There was a significant inverse correlation between spirometry values and ECHO parameters (cor pulmonale and TR). Echocardiography is a non-invasive measure which helps to detect these changes at an early stage, which helps to mitigate the expenditure towards health care and preventing the incidence of heart failure.

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