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Assessment of Left Ventricular Function in COPD

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Abstract: ***The anatomical and functional relationship between the heart and lungs is so close that dysfunction of one of these systems can affect the other. There are neurological, humoral and mechanical interactions between both organs, and various mechanisms that lead to structural or functional ventricular alterations can coexist in patients with respiratory disease. Chronic obstructive pulmonary disease (COPD) is a disease state "characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema; the airflow obstruction is progressive and partially reversible". Patients with COPD can have sustained (patients with chronic respiratory failure), or intermittent hypoxia (during exercise, exacerbations, or during sleep). Hypoxia can cause abnormalities in ventricular relaxation and contraction due to changes in the myocyte cell metabolism. It can also affect the pathogenesis of atherosclerosis by various mechanisms, including increased vascular and systemic inflammation, elevated C-reactive protein and increased oxidative stress. Furthermore, it can induce hemodynamic stress by increasing the heart rate and activating the sympathetic nervous system. Finally, hypoxia is involved in pulmonary vascular remodelling that increases pulmonary vascular resistance, which may negatively affect LV diastolic filling by the phenomenon of ventricular interdependence. However, LV ejection fraction by two-dimensional echocardiography can be normal despite LV dysfunction. Because of paradox of the previous published literatures and the symptom similarity between LV function and COPD, there was need to conduct the study to find out the assessment of LV function in the COPD patients.***

Keywords: COPD, Left Ventricular Dysfunction, 2D-ECHO, Pulmonary Artery Hypertension, Left Ventricular Failure

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years and die prematurely from it or its complications. COPD is the fourth leading cause of death in the world, and further increases in its prevalence and mortality can be predicted in the coming decades. COPD is now widely prevalent in both developed and developing countries causing major health burden to the society.

According to "WHO" report, COPD at present is the fourth commonest cause of death worldwide. It is proposed to be the third major cause of mortality and fifth major cause of chronic disability by the year 2030.In India every year half a million people die of COPD. Cigarette smoking is the key risk factor, other risk factors being exposure to indoor and outdoor pollution, occupational hazards, infection and genetic factors.

The cardiovascular sequelae of chronic obstructive pulmonary disease (COPD) have been recognized for decades. The spectrum of cardiovascular disease includes right ventricular (RV) dysfunction, pulmonary hypertension (PH), coronary artery disease (CAD), and arrhythmias. Pulmonary vascular disease associated with COPD increases morbidity and worsens survival. Patients with COPD also carry an increased risk of mortality due to arrhythmia, myocardial infarction, or congestive heart failure compared with those who do not.

In patients with chronic obstructive pulmonary disease (COPD), and in particular in those with severe emphysema, pulmonary hypertension and right ventricular (RV) enlargement, the left ventricle is compressed. However, for the majority of these patients, the left ventricular (LV) ejection fraction is within normal limits. The majority of COPD patients with such findings shows a leftward ventricular septum deviation, most marked at end systole and early diastole, associated with a distortion of LV geometry and reduction of early diastolic filling.

Aim

The aim of the present study was to assess left ventricular function in COPD patients without any apparent cardiac disease.

Objective

1) To find out clinical presentations of COPD in the study population
2) To use spirometry for confirmation and assessment of degree of COPD.
3) To find out the role of clinical cardiological evaluation and ECG in assessment of associate LV disease among COPD patients
4) To find out the diagnostic yield of echocardiography in assessment of LV dysfunction in COPD patient

Methods: A Prospective observational study was conducted to assessment of left ventricular function in COPD patients from December 2020 to May 2022

Ethical Clearance: A protocol of the intended study was submitted to the Institutional Ethical Committee and Review Board, J.L.N. Hospital & Research Centre, Bhilai and ethical clearance was obtained. (Ethical approval no JLNHRC/IEC/2020/43)

Permission and Consent: Necessary permissions were obtained from concerned authorities of hospital before conducting the study. Informed consent was obtained from the participants after explaining the procedure and purpose clearly.

Patient Selection Criteria:

i) Inclusion Criteria:

- The study includes all patients of all confirmed uncomplicated COPD disease.

ii) Exclusion Criteria:

- Patients with acute exacerbation of COPD.
- Patients with apparent cardiac disease like hypertension, ischemic heart disease, valvular heart disease, congenital heart disease.
- Patients with ECG findings suggestive of left heart disease or arrhythmia.
- Patients with CXR suggestive of left ventricular hypertrophy.
- Patient with poor echo-window (severe hyper inflated lungs).
- Patients refused to give informed written consent.

Sample Size Calculation

Cochran formula for minimum Sample Size=N = $Z^2 * P * (1-P)/e^2$

Where Z=1.96, z value for 5% confidence level

P= proportion in the target population having given characteristic.

Here EBF, P=0.86

e= Precision at 10% = (1.96^2*0.86*0.14)/(0.10)2 =47

Calculated sample size is **47**.

Study Tools

- Chest X-Ray (PA View)
- Lung function test – Spirometer
- Resting 12 lead ECG
- Transthoracic echocardiography

Statistical Analysis

The data collected were entered into excel spread sheet and it was analyzed using the Statistical Package for Social Sciences (SPSS) version 24. Descriptive and inferential statistics was done. Continuous variables were presented as mean ± SD, and categorical variables were presented as absolute numbers and percentage. Data was checked for normality before statistical analysis and found the normal data set. Independent t test was used to find out the mean difference of ECHO findings. Statistical significance was considered at $p<0.05$ (confidence interval of 95% was taken).

2. Results

Table 1: Distribution of Age & Gender among study participants

Age (Years)	Male	Percent	Female	Percent	Total	Percent
30-55	21	42.0	5	10.0	26	52.0
56-60	11	22.0	5	10.0	16	32.0
61-65	7	14.0	1	2.0	8	16.0
Total	39	78.0	11	22.0	50	100.0
Mean Age	53.8 ±4.52		50.7±3.85		52.8±4.2	

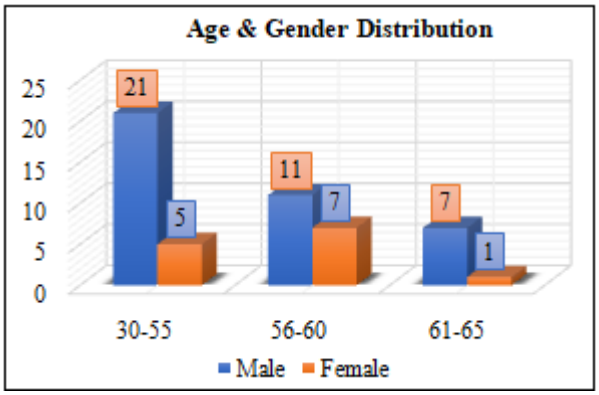

Figure 1: Distribution of Age & Gender among study participants

Table 2: Habits type and distribution among the study participants

	COPD (N=50)		Percent
Smoking History	Yes	45	90.00
	No	5	10.00
Alcohol History	Yes	24	48.00
	No	26	52.00
BMI	<23	39	78.00
	>23	11	22.00
Mean BMI	20.53±4.05		

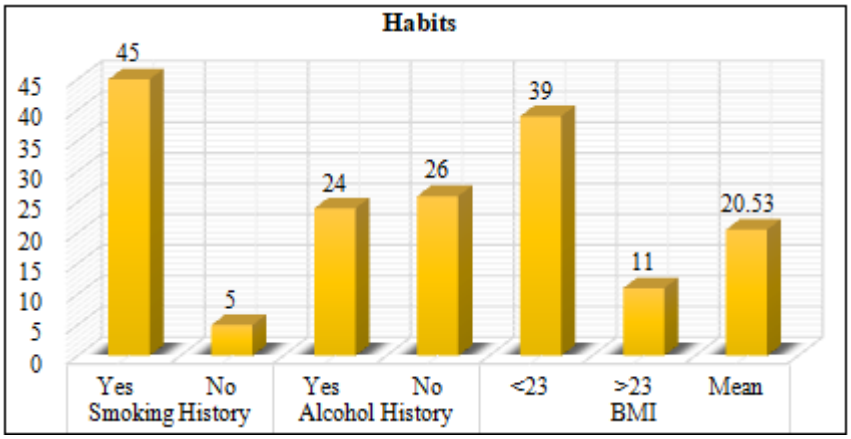

Figure 2: Habits type and distribution among the study participants

Table 3: Smoking history of the study participants

Smoking History	Male	Percent	Female	Percent	Total	Percent
Never	2	4.0	3	6.0	5	10.0
Current Smoker	27	54.0	6	12.0	33	66.0
Past Smoker	10	20.0	2	4.0	12	24.0
Total	39	78.0	11	22.0	50	100.0

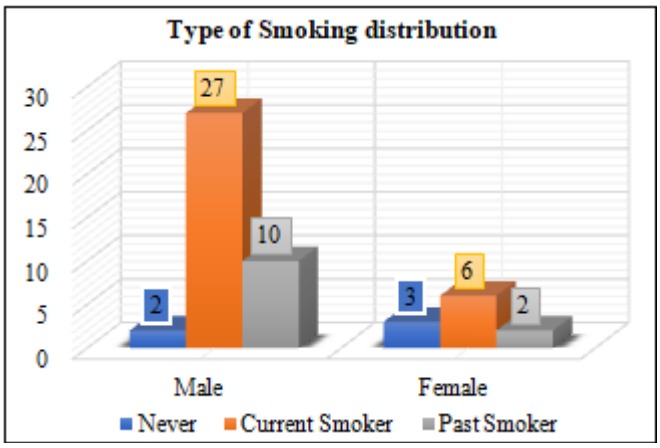

Figure 3: Smoking history of the study participants

Table 4: Symptoms of study participants across gender

Symptoms	Male	Percent	Female	Percent	Total	Percent
Cough	39	78.0	8	16.0	47	94.0
Sputum	21	42.0	5	10.0	26	52.0
Dyspnoea	32	64.0	10	20.0	42	84.0
Chest tightness	7	14.0	4	8.0	11	22.0
Wheeze	30	60.0	7	14.0	37	74.0

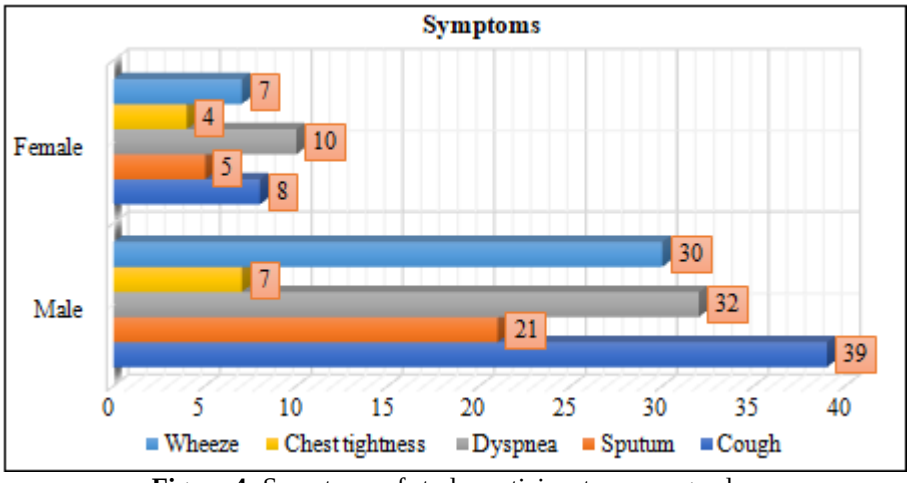

Figure 4: Symptoms of study participants across gender

Table 5: Co-morbidities among the study participants

Co-morbidities	Number	Percent
Diabetes Mellitus	13	26.0
Cor-Pulmonale	7	14.0
Past Tuberculosis	5	10.0
Hypothyroidism	2	4.0
Hypertension	26	52.0
No co-morbidities	17	34.0

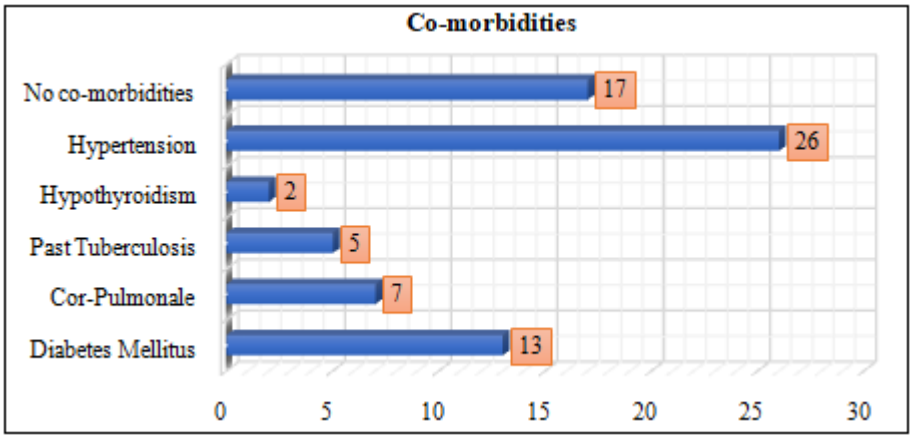

Figure 5: Co-morbidities among the study participants

Table 6: Gold Severity Scale among the COPD patients

GOLD	Stages	Number	Percent
I	FEV1 (>80%)	2	4.0
II	FEV1 (50-80%)	20	40.0
III	FEV1 (30-50%)	17	34.0
IV	FEV1 (<30%)	11	22.0

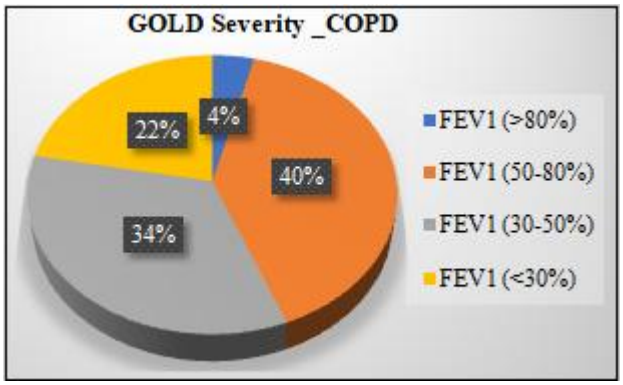

Figure 6: Gold Severity Scale among the COPD patients

Table 7: Pulmonary function Test of the study participants

Pulmonary Function Test	COPD
FVC	1.95 ±0.80
FEV1	1.56 ± 0.73
FEV1%	48.68 ± 4.49
FVC % predicted	63.15 ± 5.54
FEV1/FVC % predicted	66.71 ± 3.64

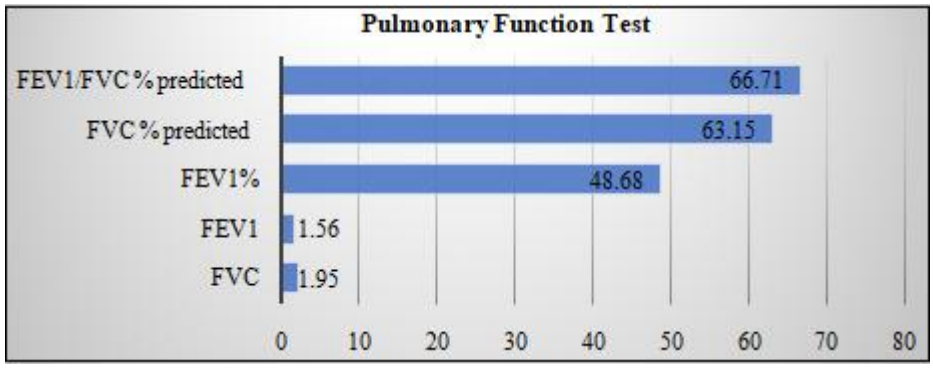

Figure 7: Pulmonary function Test of the study participants

Table 8: The comparison of mean ECHO findings among the patient with COPD with and without Left Ventricle Diastolic Function

Left Ventricle Diastolic Function			
	LVDF (+)	LVDF(-)	p-value
E(cm/s)	60.2±4.01	62.8±4.75	0.22
A(cm/s)	78.33±3.84	81.43±4.55	***0.021***
E/A	0.77±0.03	0.76±0.02	0.884
DT (ms)	322.5±11.2	271.2±9.41	***0.003***
IVRT (ms)	104.2±4.21	77.6±4.75	***0.032***

Independent t test, sig 2 tailed, $p<0.05$,

E-wave, early maximal transmitral flow velocity; A-wave, peak velocity during atrial contraction in late diastole; and ratio between the early peak transmitral flow velocity (E) and late peak atrial systolic velocity (A) [E/A ratio].Also the left ventricular diastolic function was assessed by measuring the isovolumic relaxation time (IVRT).

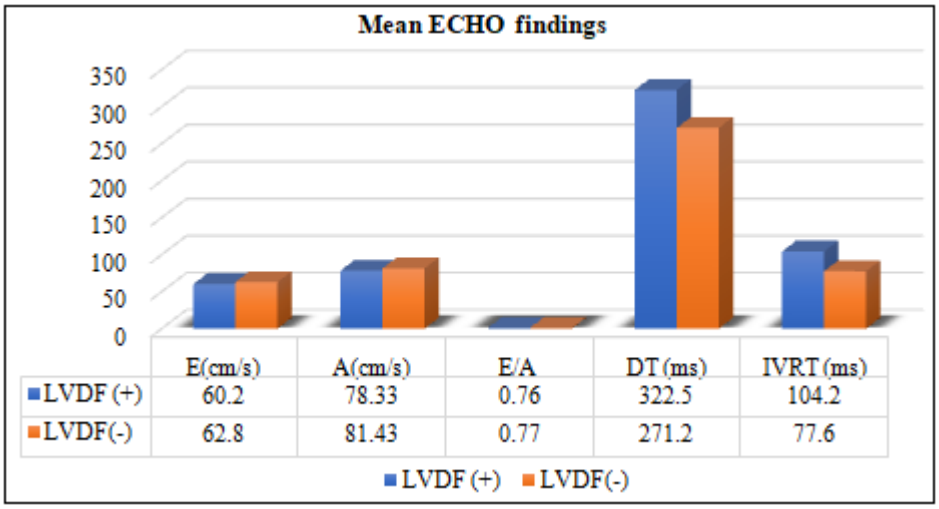

Figure 8: The comparison of mean ECHO findings among the patient with COPD with and without Left Ventricle Diastolic Function

Table 9: Left Ventricular dysfunction conditions

LV dimensions, systolic function, interventricular septum thickness	LVDF (+)	LVDF(-)	P-value
LVESD(mm)	26.267 ± 3.433	27.7 ± 2.168	0.09
LVESD(mm)	40 ± 2.66	44.2 ± 1.88	*0.032*
LV FS%	36.27 ± 4.21	38.42 ± 3.01	*0.041*
LV EF%	67.44 ± 3.2	69.41± 4.7	*0.003*
S'(cm/s)	9.64 ± 0.92	10.6±0.84	0.512
IVSd (mm)	10.1 ± 0.6	10.2±0.7	0.787

Independent t test, sig 2 tailed, $p<0.05$

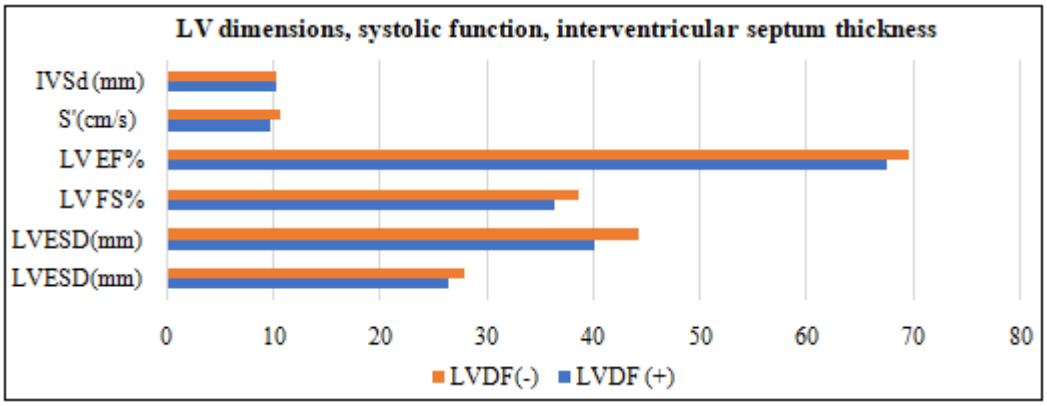

Table 10: Distribution of the Left ventricular dysfunction among COPD study participants

LV Dysfunction	Number	Percent
Left ventricular hypertrophy	7	14.0
Left ventricular systolic dysfunction	27	54.0
Left ventricular diastolic dysfunction	29	58.0
Left ventricular function abnormalities	29	58.0
Type of Left Ventricle Dysfunction	LVDD	15
	LVH+LVDD	6
	LVSD+LVDD	6
	LVH+LVSD+LVDD	2
	LVSD	19

LVDD: Left ventricular diastolic dysfunction, LVH: Left ventricular hypertrophy, LVSD: Left ventricular systolic dysfunction.

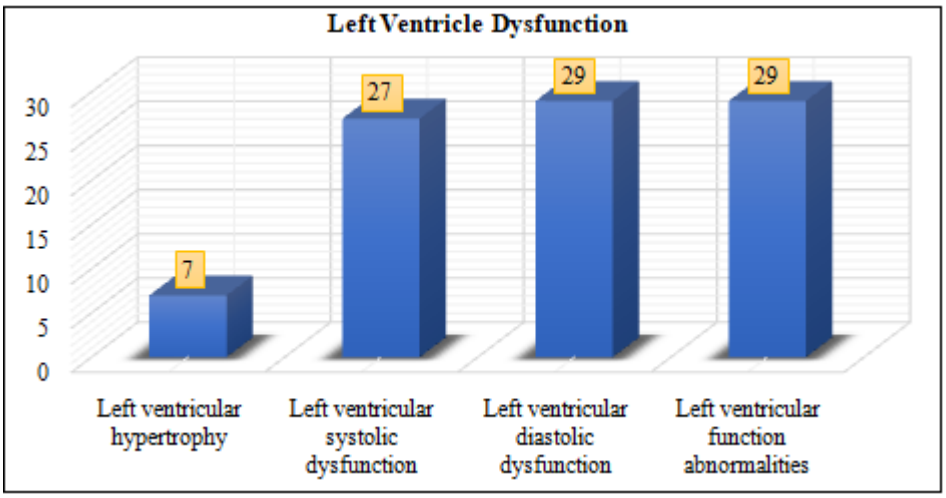

Figure 10: Distribution of the Left ventricular dysfunction among COPD study participants

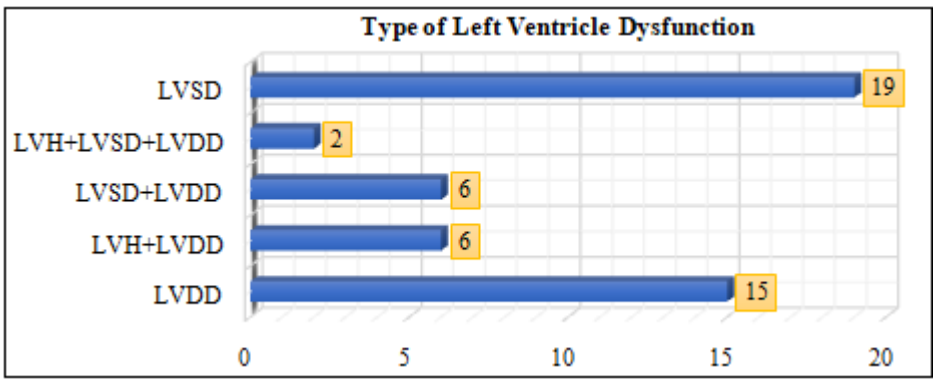

Figure 10A: Distribution of the Left ventricular dysfunction among COPD study participants

Table 11: Association between Gold COPD severity and LVDD

	GOLD COPD Severity Index				
Left ventricular diastolic dysfunction	I	II	III	IV	Total
Grade 1	0	2	1	0	3
Grade 2	0	5	5	3	13
Grade 3	0	1	4	8	13
No dysfunction	2	12	7	0	21
Total	2	20	17	11	50

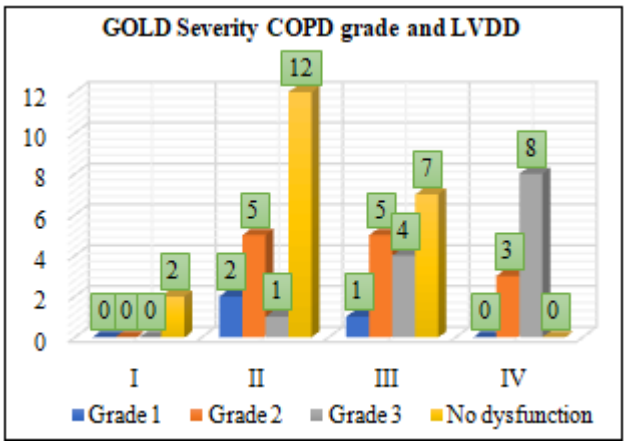

Figure 11: Association between Gold COPD severity and LVDD

Table 12: Left Ventricular Systolic Dysfunction

Left Ventricular Systolic Dysfunction	Ejection Fraction	Number	Percent
	<50%	6	22.2
	>50%	21	77.8

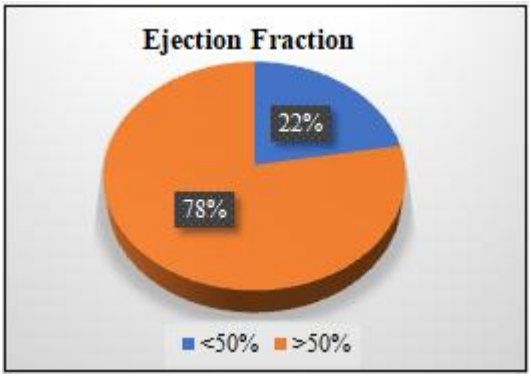

Figure 12: Left Ventricular Systolic Dysfunction

Table 13: Association between Gold COPD severity and LVSD

	GOLD COPD Severity Index				
Ejection Fraction	I	II	III	IV	Total
<50%	0	0	2	4	6
>50%	11	6	3	1	21

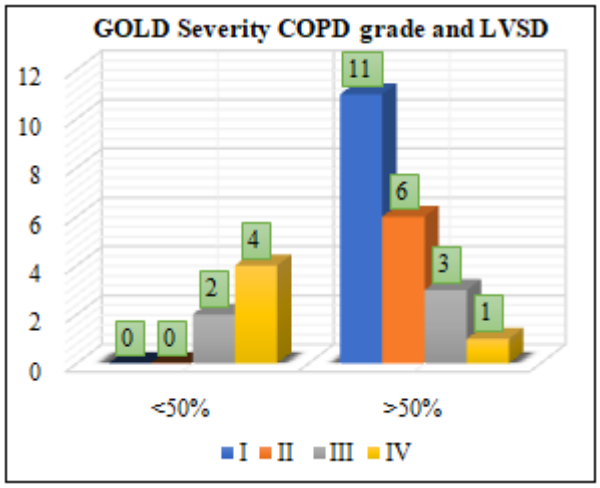

Figure 13: Association between Gold COPD severity and LVSD

3. Discussion

COPD is now more prevalent in both developed and developing countries. It is a major health burden in the world. According to "WHO "report, COPD at present is the fourth commonest cause of death worldwide. It is projected to be the third most common cause of death and fifth most common cause of chronic disability by the year 2030. In India half a million people die of COPD. This is four times the mortality that it causes in USA and Europe.

In our study COPD is more prevalent in males and male to female ratio is approx. 4:1(78:22). This is mainly attributed to high prevalence of smoking among males. But according to WHO report the disease affects men and women equally. In a large, multicentre study from India, the prevalence of COPD among general population was 4.1 per cent and the male to female ratio of 1.56:1.

COPD is common in young to middle age, so lower age limit of 30 had been taken in our study. More than half of the study participants were 30-55 years age. Due to the less case fatality of the COPD, the prevalence of the disease is correlated with the age. Hence, in our study the age related decline in FEV1 were compensated/nullified.

Swedish cohort study concluded that smoking was a causative risk factor of COPD with 76.2 percent attributed risk in a given population where as in Denmark study it was 74.6 percent. BTS guidelines reported that most COPD patients have history of at least 20 pack-year of smoking.

Non-smokers commonly have decline the rate FEV1 of about 30mL. Smokers on the other hand have a decline inFEV1. In the present study, 90% had smoking history and Out of 45 smokers in the study, 33 were current smokers and 12 were past smokers.

The development of hypertension is a poor prognostic sign in patients with COPD, affecting both mortality and quality of life. Mild-to-moderate pulmonary hypertension is a common complication of COPD. Such a complication is associated with increased risks of exacerbation and decreased survival. Circumstantial and experimental

evidence suggests that products of cigarette smoke can initiate pulmonary vascular changes in COPD. In the present study, hypertension was present in 52% of the study participants.

In the present study, GOLD severity scale among the COPD patients, about 56% were grade III and grade IV, suggestive of the moderate to severe condition of the COPD, this might also give the insight of development of the left ventricular dysfunction in the study participants.

During diastole, the LV receives blood from the left atrium, which is subsequently ejected into the systemic circulation. In simple terms, the efficiency of LV filling can be measured as the ability to receive a large volume of blood at rapid filling rate but under low pressures. Consequently, various physiological parameters interact in LV diastole, principally relaxation, ventricular distensibility and atrial contraction.

Among the most common causes of diastolic dysfunction are PH, senility and CAD. Various studies in COPD patients describe a high rate of LV diastolic dysfunction (LVDD) compared to age-matched controls, even in those without CVRF. Its prevalence also varies considerably, reaching 90% in COPD patients with severe airflow limitation.

Robotham et al has found that LV dysfunction may be due to Hypoxia and acidosis, Reverse Bernheim phenomena or ventricular interdependence and large changes in intrathoracic pressure. (Due to hyperinflation, there is increase in negative pleural pressure which decreases LV stroke volume and increases afterload).

A recent study Mallick et al43 reported that 7.50% COPD patients had LV systolic dysfunction and 47.5% patients had evidence of LV diastolic dysfunction. Other studies have shown LV systolic dysfunction was present in 4% to 32% COPD patients and LV diastolic dysfunction was even found in COPD patients with normal pulmonary arterial pressure.

Boussuges et al found a high prevalence of left ventricular diastolic dysfunction in COPD patients relative to control subjects (76% vs. 35%). Rutten et al47 and Funk et al48 also reported a prevalence >50%. In the present study, about 29(58%) of the study participants had LV Dysfunction, among them 15 patients had LVDD, 6 had LVH+LVDD, 6 had LVSD+LVDD, 2 had LVH+LVSD+LVDD and 19 had LVSD.

Sarkar et al reported parameters of LV systolic function like EF were depressed in patients of COPD with cor-pulmonale. However, in this study we dint find any such co-relation due to none availability of data set. A definite correlation of LV diastolic dysfunction and the age was found in patients with LV diastolic dysfunction. However, age-related myocardial changes are known to occur in even in normal individuals.

Left ventricular diastolic dysfunction were divided into the grade I, II and grade III. There was association between the GOLD COPD Severity Index and severity grade of the Left ventricular diastolic dysfunction. About 77.8% of the study participants had Ejection fraction >50%. Also, reduced ejection fraction was related to the increase GOLD COPD Severity Index.

In present study, analysis failed to show any significant association between symptom nature and LV diastolic dysfunction due no absence of data set. Another important observation in our study was that LV diastolic dysfunction was significantly more marked in the advanced stage of COPD (GOLD stage IV) than in early stage of the disease (GOLD stage I). Higher percentage of pulmonary hypertension and right ventricular strain by the virtue of inter-ventricular dependence in advanced COPD was the probable responsible factor.

Suchon et al found that ejection fraction, shortening fraction and lateral mitral annular peak systolic velocity in COPD patients, were in the normal value range and did not differ significantly from control group. Similar results were obtained by other investigators. On the other hand, Gupta et al, in their study, found that left ventricular systolic dysfunction (LVSD) was present in 7.5% of COPD patients.

In our study, there was significant difference between the LVDF (+) group and LVDF (-) group related to A (cm/s), DT (ms) and IVRT (ms). The E/A ratio was lower in COPD patients as well. as the Em velocity, indicating a LV diastolic dysfunction. They concluded that LV diastolic dysfunction does exist in COPD patients with increased RV afterload and no pre-existing LV dysfunction.

The most frequently described pattern is slow relaxation, which is characterized by a reduced E wave (due to a decrease in the relaxation velocity of the myocardial fibers) and an increased A (atrial contraction) wave with an E:A ratio.

The morphological description of the heart chambers in COPD using echocardiography raises the issue of suboptimal quality if hyperinflation and diaphragmatic flattening coexist. Despite this, various echocardiographic series have been published in the last 20 years showing alterations in structural and functional parameters over the entire spectrum of disease severity.

The variability in the findings reported depends, in some cases, on the inclusion of “selected” patients (no CVRF except smoking), the presence of associated PH, the setting (specialist clinic/primary care) and the degree of airflow obstruction. There are also studies with other imaging techniques that are less commonly used in routine clinical practice, such as MRI and nuclear medicine techniques.

There are certain limitations to our study. There were less number of patients in stage IV as most of patients were too unstable to be enrolled and had poor echo-window. Also, coronary angiography or myocardial biopsy were necessary but these procedures were not included in our study. Large sample size with multicentric setting should be done for temporal association between the COPD and left ventricle dysfunction.

4. Summary

1) The age range of the study participants was from 30-65 years. More than half of the study participants were 30-55 years age and about 78% of the study participants were male and 22% were females.
2) About 90% of the study participants had smoking history and 48% of the study participants had alcohol history. Most of the study participants had BMI <23 Kg/m2. Mean BMI of the study participants was 20.53 Kg/m2.
3) Out of 45 smokers in the study, 33 were current smokers and 12 were past smokers.
4) Most common symptoms was cough (94%), followed by dyspnoea (84%). About 74% of the participants had wheeze, 52% had sputum and 22% had chest tightness.
5) Related to co-morbidities among the study participants, Hypertension was present in 52% of the study participants, diabetes mellitus was present in 26% of the study participants. About 34% of the participants did not have co morbidities.
6) Gold severity scale among the COPD patients, about 56% were grade III and grade IV.
7) The pulmonary function test, FVC was 1.95 ±0.80, FEV1 was 1.56 ± 0.73, FEV1% was 48.68 ± 4.49, FVC % predicted was 63.15 ± 5.54 and FEV1/FVC % predicted was 66.71 ± 3.64.
8) There was significant difference between the LVDF (+) group and LVDF (-) group related to A (cm/s), DT (ms) and IVRT (ms).
9) LV dimensions, systolic function, interventricular septum thickness were significantly different in case of LVDF (+) group as compared to LVDF (-) group. VESD (mm), LV FS%, LV EF% were lower in the LVDF (+) group.
10) About 58% of the study participants had LV Dysfunction, among them 15 patients had LVDD, 6 had LVH+LVDD, 6 had LVSD+LVDD, 2 had LVH+LVSD+LVDD and 19 had LVSD.
11) There was association between the GOLD COPD Severity Index and severity grade of the Left ventricular diastolic dysfunction.
12) About 77.8% of the study participants had Ejection fraction >50%. Also, reduced ejection fraction was related to the increase GOLD COPD Severity Index.

5. Conclusion

The present study was to assess left ventricular function in COPD patients without any apparent cardiac disease. The age range of the study participants was from 30-65 years, about 78% of the study participants were male. About 90% of the study participants had smoking history and mean BMI of the study participants was 20.53 kg/m2. Most common symptom was cough (94%), followed by dyspnoea (84%). GOLD severity scale among the COPD patients, about 56% were grade III and grade IV. About 58% of the study participants had LV Dysfunction, among them 15 patients had LVDD, 6 had LVH+LVDD, 6 had LVSD+LVDD, 2 had LVH+LVSD+LVDD and 19 had LVSD. There was significant difference between the LVDF (+) group and LVDF (-) group related to A (cm/s), DT (ms) and IVRT (ms). VESD (mm), LV FS%, LV EF% were lower in the LVDF (+) group. There was significant association between the GOLD COPD Severity Index and severity grade of the Left ventricular diastolic dysfunction and ejection fraction.

6. Recommendations

1) All patients with COPD should be followed up with Spirometry and 2 D Echocardiography.
2) Spirometry is the investigation of choice to establish diagnosis and look for the severity of the disease.
3) As part of assessment 2 D ECHO is recommended to assess left ventricular function in COPD patients without any apparent cardiac disease.
4) As our study showed significant association between the GOLD COPD Severity Index and severity grade of the Left ventricular diastolic dysfunction and ejection fraction, all patients should undergo 2D Echocardiography.

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