Original Article

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Left Ventricular and Right Ventricular Functional Changes in Cases of COPD and its Corelation with Severity- A Cross-sectional Study

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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a global health problem, mainly in developing countries. It affects pulmonary blood vessels, right ventricle, and also left ventricle leading to pulmonary hypertension, Cor pulmonale and right and left ventricular dysfunction.

Aim: To assess the cardiac, right and left ventricular changes in subjects with increasing COPD severity staged according to Global initiative for chronic Obstructive Lung Disease (GOLD) guidelines and to compare Arterial Blood Gases (ABG), St George Respiratory Questionnaire (SGRQ) percentages and BODE (Body-mass index, airflow Obstruction, Dyspnea, and Exercise) scores to cardiac changes in COPD.

Materials and Methods: The present study was a cross-sectional study conducted at tertiary care hospital in Southern Karnataka, India. The sample size was 60. A structured questionnaire was administered which included demographic, clinical variables followed by a detailed clinical examination, spirometry, Electrocardiograph (ECG), ABG, chest radiograph, echocardiography and a 6-Minute Walk Test (6MWT). Data collected was analysed using Statistical Package for the Social Sciences (SPSS) and Epi INFO software for mean, Standard Deviation (SD) and multivariate analysis.

Results: All the patients diagnosed with COPD (using GOLD criteria) were included in study and assessed for right and left ventricular changes. Out of 60 patients, 58 were males and 02 were females, with mean age being 64.71±28.28 years. Among the study population, 45 (75%) patients had one or the other cardiac condition. Cardiac changes included left ventricular diastolic dysfunction (58.3%), right ventricular dilatation (33.3%), right ventricular hypertrophy, right atrial dilation, tricuspid regurgitation and pulmonary hypertension and left heart changes included left ventricular hypertrophy.

Conclusion: The study highlights the need for early and active cardiac screening of all COPD patients. This will help in early treatment and good prognosis, and will further contribute in reducing the morbidity and mortality.

Keywords: Global initiative for chronic obstructive lung disease guidelines, Right and left ventricular changes, St George respiratory questionnaire percentages

INTRODUCTION

The COPD, defined by GOLD as a preventable and treatable disease with significant extrapulmonary effects, is a common clinical entity in clinical practice [1]. COPD is one of the leading causes of death and disability worldwide. According to World Bank data, it has moved from its status in 2000 as the 4th and 12th most frequent cause of mortality and morbidity, respectively, to the 3rd and 5th leading cause of mortality and morbidity, respectively [2,3].

COPD is associated with significant extrapulmonary (systemic) effects among which cardiac manifestations are the most common. Cardiovascular disease accounts for approximately 50% of all hospitalisation and nearly one third of all deaths, if predicted FEV1 (Forced Expiratory Volume in 1st second) is less than 50% [4]. In more advanced disease cardiovascular disease account for 20-25% of all deaths in COPD [5]. COPD affects pulmonary blood vessels, right ventricle, as well as left ventricle leading to development of pulmonary hypertension, Cor pulmonale, right ventricular dysfunction and left ventricular dysfunction too. Echocardiography provides a rapid, non invasive portable and correct method to evaluate the right ventricle function, right ventricular filling pressure, tricuspid regurgitation, left ventricular function and valvular function [6]. Some studies have confirmed that echocardiography derives estimates of pulmonary arterial pressure co-relate closely with pressures measured by right heart catheter (r>0.7) [7,8].

In human beings, the respiratory and circulatory systems are so intimately related those changes in one eventually may cause changes in the other. The various respiratory diseases may secondarily cause changes in the heart, which may be detected by ECG [9]. In clinical practice, cases having respiratory problems especially COPD should also be assessed for ECG changes. The BODE Index [10] is a tool used by healthcare professionals to help predict COPD morbidity and mortality. Presumably, a higher BODE score correlates with an increased risk of death. Cardiovascular disease accounts for approximately 50% of all hospitalisation and nearly one third of all deaths. Hence, this study aimed to assess the cardiac, right and left ventricular changes in subjects with increasing COPD severity staged according to GOLD guidelines and to compare ABG, SGRQ percentages and BODE scores to cardiac changes in COPD.

MATERIALS AND METHODS

The present study was a cross-sectional study, done at tertiary care centre, at Southern Karnataka, India. Duration of the study was from January 2014 to December 2016. Institutional Ethical Committee (IEC) clearance was obtained (JSS/2011-12).

Inclusion criteria: Patients who consented, aged above 40 years, diagnosed as COPD according to GOLD criteria of spirometry, smoked at least 10 pack years/exposed to biomass fuel, absence of other chronic pulmonary diseases such as congenital bronchiectasis/Interstitial Lung Disease/active tuberculosis or its

sequelae, absence of co-morbidities such as liver or renal failure or cardiac diseases not related to COPD.

Exclusion criteria: Not willing to give informed consent, associated with other chronic pulmonary diseases such as congenital bronchiectasis/ILD/tuberculosis and associated with other major co morbidities such as liver or renal failure or cardiac diseases not related to COPD.

Sample size was calculated to be 60, using formula $n=4pq/l^2$, where 'n' is the sample size calculated, p is 32% proportion of right ventricular changes in COPD patients [11], q=100-p, l is 0.37 relative proportion at 95% of confidence interval.

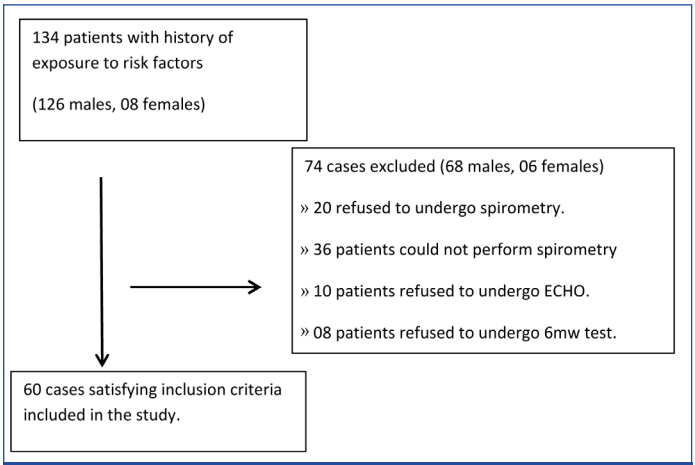
All the patients were explained about the study details and procedures. After informed consent, a detailed structured questionnaire was administered which included demographic, clinical variables followed by a detailed clinical examination, spirometry, ECG, ABG, chest radiograph, echocardiography and a 6MWT. The various changes in the right and left ventricles were evaluated and compared with different severity of COPD staged according to the GOLD criteria.

STATISTICAL ANALYSIS

EPIINFO, MICROSOFT EXCEL and SPSS software were used for data analysis in this study. A descriptive analysis was conducted and the association of various demographic and clinical variables with cardiac, right heart and left heart changes were analysed, using univariate analysis and independent association confirmed with multivariate analysis. Receiver Operating Characteristic (ROC) analysis was performed to find the threshold with highest sensitivity and specificity and that threshold was used for classification in univariate and multivariate analysis. The level of significance was fixed at p-value of <0.05.

RESULTS

As shown in [Table/Fig-1], during the study period, a total of 134 patients with significant history of exposure to risk factors (>10 pack years or 10 years of biomass exposure) were screened; 74 patients were excluded for one of the following reasons: refused to perform Pulmonary Function Test (PFT) or 6MWT, unable to perform PFT and/or refused to undergo blood investigations, echocardiography or other essential tests for the study. Finally, 60 patients were included in the study.



[Table/Fig-1]: Selection of participants in the study.

Mean age of 64.71 years, mean pack years of 43.72, Body Mass Index (BMI) of 20.83 [Table/Fig-2]. Mean FEV1/FVC (Forced Vital Capacity) ratio was 54.86 and FEV1% predicted was 47.51 [Table/Fig-3] among study sample. There were 58 males and 2 females. Among the study population, 45 (75%) patients had one or the other cardiac condition as diagnosed using ECG or 2D echocardiography [Table/Fig-4]. Among those 45 patients, 23 patient's right heart changes, 37 patients had left heart changes and 15 patients had changes in both right and left heart. Cardiac changes included right heart changes or left heart changes. Right heart changes included Cor pulmonale and right ventricular hypertrophy criteria in ECG and right ventricular dilation, right atrial dilation, tricuspid regurgitation and pulmonary hypertension [Table/Fig-5]. Left heart changes included left ventricular hypertrophy criteria of ECG and echocardiography findings include left ventricular hypertrophy, left ventricular systolic dysfunction and left ventricular diastolic dysfunction [Table/Fig-5].

Parameters	Range		Mean±SD
	Min	Max	
Age (years)	42	82	64.71±28.28
Duration of COPD symptoms (years)	1	6	2.75±3.53
Pack years	26	95	43.72±48.79
Weight (kg)	34	90	56.59±8.56
Height (cm)	152	183	165.86±3.53
BMI (Kg/m^2)	13.4	40	20.83±4.44

[Table/Fig-2]: Demographics characteristics.
Min: Minimum; Max: Maximum; SD: Standard deviation; BMI: Body mass index

Spirometry	Range		Mean±SD
	Min	Max	
FEV1/FVC	40.4	68.2	54.86±19.65
FEV1% predicted	21	92	47.51±50.20

[Table/Fig-3]: Spirometric characteristics.
FEV1: Forced expiratory volume in one second; FVC: Forced vital capacity

Variables in COPD Patients	Present n (%)	Absent n (%)
Any Cardiac changes (Right or Left heart changes)	45 (75)	15 (25)
Right heart changes	23 (38.33)	
Left heart changes	37 (61.67)	
Combined Right + Left Heart Changes	15 (25)	

[Table/Fig-4]: Cardiac changes in the COPD patients.

Variables	Present n (%)	Absent n (%)
P wave height >2 mm	18 (30)	42 (70)
Right ventricular hypertrophy	5 (8.33)	55 (91.67)
Right ventricular dilatation	20 (33.33)	40 (66.67)
Right atrial dilatation	15 (25)	45 (75)
Tricuspid regurgitation	11 (18.33)	49 (81.67)
Pulmonary hypertension	10 (16.67)	50 (83.33)
Left ventricular hypertrophy	4 (6.67)	56 (93.33)
Ejection fraction	60 (100)	0
Left ventricular diastolic dysfunction	35 (58.33)	25 (41.67)
RBBB (Right Bundle Branch Block)	2 (3.33)	58 (96.67)
Cor Pulmonale	20 (33.33)	40 (66.67)

[Table/Fig-5]: Heart changes in COPD patients.

On univariate analysis, for any cardiac changes, the following were found significant (Duration >3.5y, Pack year >40, Modified Medical Research Grading >1, 6mw distance <290 m, BODE index >3, St. George Respiratory Questionnaire (SGRQ) activity% >15.01, SGRQ impact% >18.81, SGRQ total% >20.86). But among the above only Pack year >40, SGRQ activity% >15.01, were independently found to be significant in multivariate analysis [Table/Fig-6]. Other parameters which were found to be significant on univariate analysis were not found to be significant as shown in the [Table/Fig-6].

On univariate analysis for right cardiac changes the following were found significant (Duration >2.5y, 6 mw distance <261 m, BODE index >4, paO2 <78 mmol/L, SGRQ activity% >15.31, SGRQ

Variable	Univariate Odds ratio	Adjusted Odds ratio	95% confidence interval		p-value
			Lower limit	Upper limit	
Duration >3.5 years	8.5	10.71	0.41	279.63	0.154
Pack year >40	6	402.33	1.88	8.612E4	0.028*
Modified Medical Research Grading >1	9.14	9.23	0.61	138.36	0.107
6mw distance <290	13.39	7.76	0.49	120.61	0.143
BODE index >3	3.69	5.46	0.39	76.29	0.207
St. George Respiratory Questionnaire (SGRQ) activity% >15.01	4.63	21.49	1.037	445.43	0.047*
SGRQ impact% >18.81	9.75	5.80	0.38	88.12	0.205
SGRQ total% >20.86	6.83	3.21	0.14	73.55	0.464

[Table/Fig-6]: Multivariate analysis-any cardiac changes.
*A p-value <0.05 was considered to be statistically significant; Binomial logistic regression

impact% >18.99, SGRQ total% >26.6). But among the above only duration >2.5y, PaO2 <78 mmol/L, SGRQ impact% >18.99, were independently found to be significant in multivariate analysis [Table/Fig-7].

Variable	Univariate Odds Ratio	Adjusted Odds Ratio	95% Confidence Interval		p-value
			Lower limit	Upper limit	
Duration >2.5y	2.5	348.66	4.42	2.748E4	0.009*
6MW distance <261m	46.8	35.14	0.21	5.881E3	0.173
BODE index>4	7.11	7.62	0.60	95.81	0.116
paO2 <78mmol/L	7.56	37.36	1.75	794.14	0.020*
SGRQ activity% >15.31	4.11	0.07	0.002	2.80	0.158
SGRQ impact% >18.99	11.80	70.56	2.10	2.361E3	0.017*
SGRQ total% >26.6	7.65	0.45	0.001	192.10	0.799

[Table/Fig-7]: Multivariate analysis-any cardiac changes.
*A p-value <0.05 was considered to be statistically significant; Binomial logistic regression

On univariate analysis for left cardiac changes the following were found significant (Pack year >39 years, Modified Medical Research Council (MMRC) >1, 6mw distance <267m, SGRQ impact% >18.81). But among them only Packyear >39 and MMRC >1 were independently found to be significant in multivariate analysis [Table/Fig-8].

Variable	Univariate Odds Ratio	Adjusted Odds Ratio	95% Confidence Interval		p-value
			Lower limit	Upper limit	
Pack year >39	6.17	5.52	1.41	21.54	0.014*
Modified Medical Research Council >1	8.71	6.63	1.17	37.60	0.033*
6MW distance <267m	8	3.48	0.60	19.89	0.161
SGRQ impact% >18.81	4.65	1.97	0.49	7.93	0.339

[Table/Fig-8]: Multivariate analysis left heart changes.
*A p-value <0.05 was considered to be statistically significant; Binomial logistic regression

DISCUSSION

There are many cardiac manifestations seen in COPD, ranging from mild pulmonary hypertension to severe Cor pulmonale requiring long term oxygen therapy and heart failure medications. Conduction defects range from benign arrythmias to right bundle branch block. COPD is also associated with left ventricular dysfunction also. Impairment of right ventricular dysfunction and pulmonary blood vessels are well known to complicate the clinical course of COPD and correlate inversely with survival [12]. Significant changes occur in the pulmonary circulation in patient with COPD [12]. The presence of hypoxaemia and chronic ventilator insufficiency is associated with early evidence of intimal thickening and medial hypertrophy in the smaller branches of pulmonary arteries. Coupled with these pathological changes are pulmonary vasoconstriction arising from presence of alveolar hypoxaemia, destruction of pulmonary vascular bed. All these lead to significant increase in pulmonary vascular resistance, leading to pulmonary hypertension, hypertrophy of right ventricle. In patient with COPD hypoxic vasoconstriction is associated with not only right ventricular hypertrophy but also right ventricular dilatation which eventually leads to clinical syndrome of right heart failure with systemic congestion and inability to adapt right ventricular output to the peripheral demand on exercise [12].

There are contradicting studies of involvement of left heart in patients with COPD. Some suggests left ventricular function remains normal while others suggest left ventricular dysfunction [13,14]. The data highlights left ventricular changes with a range of factors associated with COPD. Abnormal left ventricular performance in persons with COPD may be due hypoxaemia and acidosis, concurrent coronary artery disease, ventricular interdependence. Left ventricular diastolic dysfunction in COPD may be explained by chronic hypoxaemia leading to abnormalities of myocardial relaxation, lung hyperinflation and distension leading to increased stiffness of parietal pleura and thus wall of cardiac fossa leading to added load on ventricle [12].

Spirometry is the diagnostic test for COPD, which suggests airflow obstruction when post broncodilator FEV1/FVC is <0.7 and this airflow obstruction seen in COPD patients is irreversible. In a study conducted by Haltzman D et al., sensitivity of 12 lead electrocardiogram in diagnosing right ventricular hypertrophy was 50% as compared to right ventricular hypertrophy diagnosed by 2D echocardiography [15]. Hence, in the present study echocardiography was considered for the cardiac changes. However, electrocardiogram is helpful in knowing the conduction defects such as arrhythmias, right bundle branch block, which are difficult to be diagnosed by echocardiography.

Various parameters like age, co-morbid illnesses, severity of signs and symptoms have been evaluated and assessed with chest X-ray, ABG analysis, echocardiography, 6MWT, BODE index, while quality of life was assessed using SGRQ percentages.

Values of thresholds for numerous factors were taken at their highest sensitivity and specificity using ROC analysis for various outcome measures i.e., any cardiac dysfunction, right ventricular dysfunction and left ventricular dysfunction. In a similar study done by Kaushal M et al., showed 32%, 48%, and 8% changes of right ventricular dilatation, pulmonary hypertension and left ventricular hypertrophy respectively in COPD patients while 14% of them were normal [11]. Dave L et al., showed right ventricular dilatation in 33.5%, Right ventricular hypertrophy in 34.5%, Right atrial dilatation in 29.55%, pulmonary hypertension in 41%, left ventricular hypertrophy in 10.5% and right bundle branch block in 7.5% of COPD patients. The study also revealed that 12% of the COPD patients had no heart changes [16]. Gupta NK et al., conducted a similar study in 2012 demonstrating 17, 5% right ventricular dilatation, 67.5% tricuspid regurgitation, 42.5% of pulmonary hypertension and 47.5% of left ventricular diastolic dysfunction [12].

In the present study right ventricular dilatation was found in 33.3% of COPD patients, which was similar to the study by Kaushal M et al., (32%), and 39.5% in Dave L et al., (39.5%) [11,16], but higher than what Gupta NK et al., found (17.5%). Right atrial dilatation was found in 25% of COPD patients, which was less than the findings of Dave L et al., (29.5%) [12,16].

Other changes like tricuspid regurgitation, pulmonary hypertension, left ventricular hypertrophy and right bundle branch block were recorded as 18.33%, 16.67%, 6.67% and 3.33%, respectively. These findings are much lower than the studies by Kaushal M et al., Gupta NK et al., and Dave L et al., [11,12,16]. Some more studies have been compiled in [Table/Fig-9] [17-21].

Parameters	Present Study (2022)	Jatav VS et al., (2017) [17]	Pothal S et al., [19] (2018)	Prem-ananth P et al., [20] (2019)	Kabir MA et al., (2020) [18]	Kumar H et al., [21] (2021)
Sample Size	N=60	N=100	N=80	N=120	N=70	N=110
RA/RV dilatation	-	43%	30%		41.4%	
RV Dilatation	33.33%	-	-	57%	-	-
RA Dilatation	25%	-	-	17.5%	-	-
RVH	8.33%	42%		80%	44.3%	
Cor pulmonale	33.33%	62%	30%	-	60%	9.1%
PAH	16.67%	44%	32.5%	78.3%	42.9%	45.5%
LVDD	58.33%	46%	17.5%	63.3%	45.7%	39.1%
RVSD	-	14%		-	15.7%	-
LVH	6.67%	11%	12.5%	-	12.9%	11%
Reduced EF/ LVSD	-	-	10%	-	-	13.6%

[Table/Fig-9]: Results of the various studies on cardiac evaluation in COPD [17-21]. RA- Right artrial; RV- Right ventricular; PAH-Pulmonary arterial hypertension; LVDD- Left ventricular diastolic dysfunction; RVSD- Right ventricular systolic dysfunction; LVH- Left ventricular hypertrophy; EF- Ejection fraction; LVSD -Left ventricular systolic dysfunction

Limitation(s)

The gender differences for right and left ventricular functions in COPD patients could not be assessed, as there were only two females.

CONCLUSION(S)

The study evaluated various factors associated with severity of COPD and cardiac dysfunction and observed that GOLD grading of severity of COPD was not associated with right ventricular or left ventricular dysfunction, BODE index of more than 4 was associated with right ventricular dysfunction, MMRC grading of breathlessness more than 1 was associated with left ventricular dysfunction, SGRQ Impact % scores above 18.99% was associated with right ventricular dysfunction and pack years >40 years was associated with left ventricular dysfunction.

Hence apart from right ventricular dilatation which is commonly seen one should also be also be vigilant about other cardiac changes as mentioned above and should actively look for them in 2D echocardiography. Special emphasis should be given to left ventricular diastolic dysfunction left ventricular diastolic dysfunction as it will progress to systolic dysfunction in future.

REFERENCES

[1] Global Initiative for Chronic Obstructive Lung Disease–Global Strategy for Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary disease. http://www.goldcopd.com. [Accessed on 24-04-2017]

[2] Higham MA, Dawson D, Joshi J, Paulos PN, Morell NW. Utility of echocardiography in assessment of pulmonary hypertension secondary to COPD. Euro Resp J. 2001;17:350-55.

[3] Klinger JR, Hill NS. Right ventricular dysfunction in chronic obstructive pulmonary disease, evaluation and management. Chest. 1991;99:715-23.

[4] Garrad CS, Lourenco RV, Mucociliary clearance. Chapter 2 HugoD Montenegro. Contemporary issues in pulmonary diseases- Chronic Obstructive Pulmonary Disease Vol. 1. Churchill Livingstone. Newyork. 1984:29-48.

[5] Ian TT, Higgins. Epidemiology of Bronchitis and Emphysema. Chapter 36 Pulmonary Diseases and Disorders. Alfred P Fishman vol. 1, McGraw-Hill Inc USA, 1980:470-75.

[6] Vishwanathan R. Definition, incidence and pathogenesis of chronic corpulmonale. Indian Journal of Chest diseases.1965;VII: 155-169.

[7] Wasserburger RH, Kerley JR, Rasmussen HK, Julh JH. The eletrocardiographic pentalogy of pulmonary emphysema – A correlation of roentgenographic findings and pulmonary function studies. Circulation. 1959;(XX):831-41.

[8] Myers GB, Klein HA, Stofer BE. The electrocardiographic diagnosis of right ventricular hypertrophy. American Heart Journal. 1948;35(1):01-40.

[9] Starling MR, Crawford MH, Sorensen SG, O'Rourke RA. A new two dimensional echocardiographic technique for evaluating right ventricular size and performance in patients with obstructive lung disease. Circulation. 1982;66:612-20.

[10] Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004;350(10):1005-12.

[11] Kaushal M, Shah PS, Shah AD, Francis SA, Patel NV, Kothari KK. Chronic obstructive pulmonary disease and cardiac comorbidities: A cross-sectional study. Lung India. 2016;33:404-09.

[12] Gupta NK, Agrawal RK, Srivastav AB, Ved ML. Echocardiographic evaluation of heart in chronic obstructive pulmonary disease patient and its co-relation with the severity of disease. Lung India. 2011;28:105-09.

[13] Murphy ML, Adamson J, Hutcheson F. Left ventricular hypertrophy in patients with chronic bronchitis and emphysema. Ann Intern Med. 1974;81:307-13.

[14] Fluck DC, Chandrasekar RG, Gardner FV. Left ventricular hypertrophy in chronic bronchitis. Br Heart J. 1966;28:92-97.

[15] Holtzman D, Aronow WS, Mellana WM, Sharma M, Mehta N, Lim J, et al. Electrocardiographic abnormalities in patients with severe versus mild or moderate chronic obstructive pulmonary disease followed in an academic outpatient pulmonary clinic: ECG in COPD. Ann Noninvasive Electrocardiol. 2011;16(1):30-32.

[16] Dave L, Dwivedi P, Srivastava N, Yadav BS, Dohre R. A study of cardiovascular manifestations of COPD. Int J Res Health Sci. 2014;2(3):812-17.

[17] Jatav VS, Meena SR, Jelia S, Jain P, Ajmera D, Agarwal V, et al. Echocardiographic findings in chronic obstructive pulmonary disease and correlation of right ventricular dysfunction with disease severity. Int J Adv Med. 2017;4:476-80.

[18] Kabir MA, Haque SD, Baker A, Alam MK, Rahman SA. Study on association between echocardiographic findings in COPD patients with severity of COPD. Mediscope. 2020;7(1):44-50.

[19] Pothal SS, Dani P, Manjhi R, Dutta P, Behera BS, Behera A. Correlation between chronic obstructive pulmonary disease and cardiovascular abnormality: A cross-sectional study. J Clin Diag Res. 2018;12(8):OC17-OC21.

[20] Premananth P, Deiveegan C, Nagarajan N, Gnanasekaran R. COPD severity and right heart status among patients attending a tertiary care hospital in Madurai, Tamilnadu. Indian J Immunol Respir Med. 2019;4(4):239-44.

[21] Kumar H, Verma A, Pandey A, Srivastava U, Pandey M, Chaudhary R, et al. Echocardiographic evaluation of stable J Clin Diag Res (COPD) patients. J Assoc Chest Physicians. 2020;8:88-91.

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