Original Research Article

Association between left ventricular function and severity of chronic obstructive pulmonary disease

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Abstract

Chronic obstructive pulmonary disease (COPD) is a complex disease with various systemic manifestations and one of the co-morbidity linked with COPD is cardiovascular disease. Left ventricular dysfunction is a well-known complication of COPD. 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. Several studies have shown that cardiovascular events are more common in patients with COPD. We used echocardiography to evaluate the changes in left ventricular size and function. The aim of this study to evaluate the Left ventricular changes associated with the severity of COPD using GOLD guidelines and echocardiographic findings. This study was a cross-sectional study and consists of 134 patients with known history of chronic pulmonary obstructive disease (COPD). Echocardiographic assessment of left ventricular systolic function (ejection fraction) revealed that significant difference in COPD patients of different categories and there was significant difference regarding left ventricular diastolic dysfunction (E/A ratio and isovolumic relaxation time, IVRT). Left ventricular functions are affected in COPD patients especially with progression of the disease.

Key Word: left ventricular functions, Echocardiography, COPD.

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INTRODUCTION

The anatomical and functional relationship between the heart and lungs is so close that dysfunction of one of these systems can affect the other[1]. 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. Several studies have shown that cardiovascular events are more common in patients with chronic obstructive pulmonary disease (COPD) compared to smokers without the disease[2-5]. Classification of the severity of COPD according to the Global Initiative for Obstructive Lung Disease (GOLD) classification is based on the degree of air-flow obstruction (percent of predicted FEV1)[6]. The association between cardiovascular diseases (CVD) and COPD is much more complex, and may involve other factors: biological (hypoxemia, endothelial dysfunction, increased platelet activation, arterial stiffness)[7-10], mechanical and/or functional (deterioration in the forced expiratory volume in the first second, emphysema, hyperinflation)[11-12], neurohumoral (excess sympathetic nerve activity)[13]

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and genetic (polymorphisms of the metalloproteinases, telomere shortening)[14-15]. Right ventricular dysfunction is a well-known complication of COPD. Research reports mentioning that there may left ventricular systolic and diastolic dysfunction is associated with right ventricular dysfunction or as a separate complication[16-18]. Echocardiography is simple, non-invasive and reliable technique to assess the left ventricular dimensions and function[19-21]. In this study we used echocardiography to evaluate the changes in left ventricular size and function.

Materials and Methods

The proposed research study was a cross-sectional study and consists of One hundred thirty-four patients (88 male, 46 female: mean age 63 ± 7 years) with known history of chronic pulmonary obstructive disease (COPD). The proposed research study was carried out at Mahamaya Rajkiya Allopathic medical college, Uttar Pradesh and Santosh Medical College, Ghaziabad. This study was commenced after obtaining the ethical clearance from Institutional Human Ethics Committee (IHEC). Patients with known case of Chronic Obstructive Pulmonary disease (COPD) confirmed by medical history and pulmonary function tests were selected using systemic random sampling and informed consent was obtained from the patients before subjecting to research methods. Patients with coronary heart disease (CAD), chronic lung disease other than COPD, chronic kidney disease, valvular cardiac disease, and any systemic or cardiac diseases that may cause pulmonary hypertension, malignant tumors, head and neck abnormalities, patients with exacerbations in the last four weeks, patients with a weak echo window and patients who could not perform spirometry were excluded from the study. All patients have undergone respiratory (spirometry) tests for assessment of pulmonary function. The forced vital capacity (FVC) and forced expiratory volume during first one second (FEV1) were measured and FEV1/FVC ratio was calculated from measured values. The patients were divided into four groups in line with the guidelines of Global Initiative for Chronic Obstructive Lung Disease (GOLD) as mild (FEV1 ≥ 80% expected value), intermediate (50% ≤ FEV1<80% expected value), severe (30% ≤ FEV1<30% expected value) and very severe (30% ≤FEV1<50% expected value), provided that the expected post-bronchodilator FEV1/FVC ratio was less than 70%[6]**.** A two-dimensional trans-thoracic Doppler echocardiography was performed on all patients while in the left lateral lying position using a *eSaote SpA Mylab50 X vision* echocardiographic machine with the cardiologist making all measurements who was blind to the respiratory functional test findings of the patients. All measurements were performed during at least three consecutive cardiac cycles and normal respiration and at the end of experiment. Left ventricular end-diastolic and end-systolic volumes were measured using the two-dimensional images from both the apical four and two-chamber views. Left ventricular mass was calculated from linear measurements obtained from parasternal views. The left ventricular systolic function was evaluated by measuring the ejection fraction (EF%) according to Teichholz formula. The left ventricular diastolic function was evaluated by measuring the early (E wave) and late (A wave) diastolic mitral inflow velocities, their ratio, the E wave deceleration time (DT) and the isovolumic relaxation time (IVRT).

Statistical Analysis: Results were expressed as mean ± SD. The data were analyzed by one-way analysis of variance (ANOVA) followed by Bonferroni or Tukey's multiple comparison tests, respectively. Statistical significance was considered at P<0.05.

RESULTS

Table 1: Classification of patients (Gender wise) according to severity of COPD (*COPD severity stages were based on GOLD classification)*

COPD severity	Male		Female		Total	
	N	%	*N*	%	*n*	%
Mild	6	5%	1	1%	7	6%
Moderate	24	18%	15	11%	39	29%
Severe	38	28%	16	12%	54	40%
Very Severe	20	15%	14	10%	34	25%
Total	**88**	**66%**	**46**	**34%**	**134**	**100%**

Table 2: showing the baseline and clinical characteristics of study population having mild, moderate, severe and very severe stages of COPD. Values expressed as Mean + SD. SBP-Systolic blood pressure; DBP-Diastolic blood pressure; PP-Pulse pressure; MABP-Mean arterial blood pressure

Parameter	COPD severity			
	Mild(n=7)	Moderate(n=39)	Severe(n=54)	Very Severe(n=34)
Age(Years)	62.29±8.21	62.95±5.87	62.01±7.22	64.94±6.98
Duration of COPD (Years)	2.86±0.69	7.05±1.50	11.06±3.47	14.53±3.78
Height (Cms)	165.00±7.09	164.29±6.94	162.75±6.19	162.11±8.4
SBP *(mm Hg)*	127.14±5.84	133.49±8.64	135.46±3.47	137.34±5.39
DBP *(mm Hg)*	83.43±5.63	85.33±6.31	89.18±5.42	87.16±4.71
PP (*mm Hg*)	43.71±8.38	48.16±7.66	46.28±6.22	50.18±7.21
MABP *(mm Hg)*	98.00±4.11	101.38±6.20	104.6±3.87	103.89±3.6
Heart Rate *(per min)*	78.29±4.92	85.75±4.92	82.32±5.97	84.46±5.03
Rate Pressure Product(RPP)	9937.43±538	11442.07±919	11153.08±884	11598.12±801

Table 3: showing the Lung function parameters of study population having mild, moderate, severe and very severe stages of COPD. *Values expressed as Mean + SD. FVC-Forced vital capacity; FEV1-Forced expiratory volume during first second.*

Variable	COPD severity				P-value
	Mild (n=7)	Moderate (n=39)	Severe (n=54)	Very Severe (n=34)	
FVC (liters)	3.4±0.6	3.11±0.49	2.95±0.48	2.29±0.42	<0.0001
FEV1(liters)	2.3±0.37	1.91±0.36	0.96±0.15	0.6±0.12	<0.0001
FEV1 (% of predicted value)	81±6	69±8	35±3	23±3	- -
FEV1/FVC	0.68±0.01	0.61±0.07	0.33±0.04	0.26±0.03	<0.0001

As shown Table 3, COPD patients of different stages shown bronchial obstruction and decreased spirometric volumes like forced vital capacity(P<0.0001), forced expiratory volume(P<0.0001) and FEV1/FVC(p<0.0001

Table 4: showing the Left ventricular echo-cardiac dimensions of study population having mild, moderate, severe and very severe stages of COPD

Variable	COPD severity				P-value
	Mild (n=7)	Moderate (n=39)	Severe (n=54)	Very Severe (n=34)	
LVIDd (mm)	49.02±5.95	51.47±3.63	53.72±3.83	56.19±3.44	<0.0001
LVIDs (mm)	34.51±3.85	32.7±3.62	34.07±3.39	34.70±4.17	<0.001
PWT(mm)	8.8±0.97	9.18±0.87	8.97±0.58	10.27±0.74	<0.0001
IVST(mm)	10.61±0.76	10.21±1.65	11.26±2.71	12.82±1.64	NS
LVM(mm)	161.13±15.09	168.32±13.68	166.72±10.21	164.45±14.44	NS
LVEF(%)	63.89±5.96	60.6±7.16	61.13±9.24	56.45±7.72	<0.05
E/A ratio	0.96±0.08	0.93±0.12	0.74±0.16	0.7±0.12	<0.0001
Isovolumic relaxation time(ms)	89.78±3.05	94.03±7.95	108.12±13.11	104.02±12.28	<0.0001
Deceleration time of the E(DT)(ms)	223.16±30.37	228.48±34.03	233.31±34.33	246.97±42.52	NS

LVIDd - Left ventricular internal dimension in diastole; LVIDs - Left ventricular internal dimension in systole; PWT – Posterior wall thickness; IVST – Inter ventricular septal thickness; LVM – Left ventricular mass; LVEF – Left ventricular ejection fraction.

Table 5: showing the statistical comparison (One-way ANOVA followed by post-hoc tests) between four grades of COPD patients in of left ventricular echo-cardiac measurement.

Variable	Mild vs. Moderate	Mild vs. Severe	Mild vs. Very Severe	Moderate vs. Severe	Moderate vs. Very Severe	Severe vs. Very Severe
LVIDd(mm)	NS	<0.05	<.0001	<0.05	<.0001	<0.001
LVIDs (mm)	NS	NS	NS	NS	<0.05	NS
PWT(mm)	NS	NS	<.001	NS	<0.05	<.0001
LVEF(%)	NS	NS	<0.05	NS	<0.05	<0.05
E/A ratio	NS	0.0001	<.0001	<.0001	<.0001	NS
Isovolumic relaxation time(ms)	NS	<0.05	<0.05	<0.05	<0.001	NS

LVIDd - Left ventricular internal dimension in diastole; LVIDs - Left ventricular internal dimension in systole; PWT – Posterior wall thickness; LVEF – Left ventricular ejection fraction. A total of 134 patients were recruited in our study and out of them, the number of patients with mild, moderate, severe, and very severe COPD were 5%, 29%, 40% and 25% respectively [Table 1]. The baseline (age, height) and clinical characteristics like duration of COPD, Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Pulse pressure (PP), Mean arterial blood pressure (MABP), Heart rate, Rate pressure product of COPD patients were shown in Table 2. These baseline and clinical characteristics were represented as descriptive statistics. Left ventricular echo-cardiac measurements of study population having mild, moderate, severe and very severe stages of COPD were shown in Table 4. As shown in Table 4, there was increase in diastolic and systolic left ventricular internal dimension of COPD patients of different stages which is statistically significant ($P<0.0001$). As shown in Table 5, it is observed that there is statistically significant difference in diastolic left ventricular internal dimension between the groups mild vs very severe ($P<0.0001$), moderate vs very severe ($P<0.0001$) and severe vs very severe ($P<0.0001$) where as there is no statistical difference found between mild vs moderate, severe, moderate vs severe. It is observed that there statistically significant difference in systolic left ventricular internal dimension between the groups mild vs moderate ($P<0.05$), severe ($P<0.0001$), very severe ($P<0.05$) where as there is no statistical difference found between moderate vs severe, moderate vs very severe and severe vs very severe. There was increase in posterior wall thickness of COPD patients of different stages which is statistically found to be significant ($P<0.0001$). As shown in Table 6, it is observed that there is statistically significant difference in posterior wall thickness between the groups mild vs very severe ($P<0.0001$), moderate vs very severe ($P<0.0001$), severe vs very severe ($P<0.0001$) where as there is no significant difference found between mild vs moderate, severe, moderate vs severe. As shown in Table 5, there was decrease in left ventricular ejection fraction of COPD patients of different stages which is statistically found to be significant ($P<0.05$). As shown in Table 8, it is observed that there is statistically significant difference in left ventricular ejection fraction between the groups mild vs very severe ($P<0.05$), moderate vs very severe($P<0.05$), severe vs very severe($P<0.05$) where as there is no significant differenced found between mild vs moderate, severe and moderate vs severe. There was decrease in mitral flow E/A ratio of COPD patients of different stages which is statistically found to be significant ($P<0.0001$). As shown in Table 8, it is observed that there is statistically significant difference in mitral flow E/A ratio between the groups mild vs severe ($P=0.0001$), very severe ($P<0.0001$), moderate vs severe ($P<0.0001$), very severe($P<0.0001$), severe vs very severe($P<0.05$) where as there is no significant differenced found between mild vs moderate and moderate vs very severe. There was increase in isovolumic relaxation time of COPD patients of different stages which is statistically found to be significant ($P<0.0001$). It is also observed that there is statistically significant difference in isovolumic relaxation time between the groups moderate vs severe ($P<0.0001$), very severe ($P<0.001$) where as there is no significant differenced found between mild vs moderate, severe, very severe and severe vs very severe. There was no statistical difference found in deceleration time of COPD patients of different stages.

DISCUSSION

The present work included 134 COPD patients and categorized on the basis of severity of COPD. Echocardiographic assessment of left ventricular systolic function (ejection fraction) revealed that significant difference in COPD patients of different categories and there was significant difference regarding left ventricular diastolic dysfunction (E/A ratio and isovolumic relaxation time, IVRT). An increase in right ventricular (RV) after load induces a left ventricular (LV) diastolic dysfunction because of biventricular interdependence. An increase in RV after load is common in COPD patients. Transthoracic echocardiography (TTE) can estimate LV diastolic dysfunction using early E and late (A) peak diastolic velocities measure with Doppler transmitral flow, and tissue Doppler imaging of mitral annulus velocities including early (Ea) peak diastolic velocity. (21) Lamia *et al*. studied sixteen COPD patients and 16 control subjects they excluded patients with a LV systolic dysfunction or any other reason of LV diastolic dysfunction. They found that the *E* wave was significantly lower and the A wave was significantly higher in COPD patients compared to control subjects. The E/A ratio was significantly lower in COPD patients, indicating a LV diastolic dysfunction. In the present study, left ventricular systolic function assessment revealed a statistically significant difference in ejection fraction (EF) between mild vs. very severe, moderate vs. very severe, severe vs very severe COPD grades. Left ventricular diastolic dysfunction assessment revealed statistically significant difference in E/A ratio between all the COPD grades excepting mild vs. moderate and severe vs. very severe. Also, isovolumic relaxation time (IVRT) was significantly different between the moderate vs. severe, moderate vs. very severe COPD grades. This left

ventricular dysfunction may be due to chronic hypoxemia leading to abnormalities of myocardial relaxation, lung hyperinflation and distension leading to increased stiffness of the parietal pleura and thus of the wall of cardiac fossa leading to added load on ventricle, and also due to ventricular interdependence.

CONCLUSION

Left ventricular dysfunction is affected in COPD patients especially with progression of the disease. Echocardiographic assessment can be a better non-invasive tool to assess left ventricular dysfunction in COPD patients.

REFERENCES

1. Portillo K, Abad-Capa J, Ruiz-Manzano J. Chronic obstructive pulmonary disease and left ventricle. Arch Bronconeumol [Internet]. 2015;51(5):227–34. Available from: http://dx.doi.org/10.1016/j.arbr.2015.02.025
2. Sin DD, Man SFP. Chronic obstructive pulmonary disease as a risk factor for cardiovascular morbidity and mortality. Proc Am Thorac Soc. 2005;2(1):8–11.
3. Agustí AGN, Noguera A, Sauleda J, Sala E, Pons J, Busquets X. Systemic effects of chronic obstructive pulmonary disease. Eur Respir J [Internet]. 2003;21(2):347–60. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12608452
4. Rutten FH, Cramer M-JM, Grobbee DE, Sachs APE, Kirkels JH, Lammers J-WJ, *et al*. Unrecognized heart failure in elderly patients with stable chronic obstructive pulmonary disease. Eur Heart J [Internet]. 2005;26(18):1887–94.
5. Brashier BB, Kodgule R. Risk factors and pathophysiology of chronic obstructive pulmonary disease (COPD). J Assoc Physicians India [Internet]. 2012;60 Suppl(February):17–21.
6. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Vol. 176, American Journal of Respiratory and Critical Care Medicine. 2007. p. 532–55.
7. Peinado VI, Barberà JA, Ramírez J, Gómez FP, Roca J, Jover L, *et al*. Endothelial dysfunction in pulmonary arteries of patients with mild COPD. Am J Physiol - Lung Cell Mol Physiol. 1998;
8. Barbera JA, Peinado VI, Santos S. Pulmonary hypertension in chronic obstructive pulmonary disease. Eur Respir J [Internet]. 2003;21(5):892–905.
9. Sabit R, Bolton CE, Edwards PH, Pettit RJ, Evans WD, McEniery CM, *et al*. Arterial stiffness and osteoporosis in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2007;175(12):1259–65.
10. Chaouat A, Bugnet A-S, Kadaoui N, Schott R, Enache I, Ducoloné A, *et al*. Severe pulmonary hypertension and chronic obstructive pulmonary disease. Am J Respir Crit Care Med [Internet]. 2005;172(2):189–94. Available from: http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmedandid=15831842andretmode=refandcmd=prlinks%5Cnpapers2://publication/doi/10.1164/rccm.200401-006OC
11. Elganady AA, Beshey BN, Abdelaziz AAH. Proportional assist ventilation versus pressure support ventilation in the weaning of patients with acute exacerbation of chronic obstructive pulmonary disease. Egypt J Chest Dis Tuberc. 2014;
12. Watz H, Waschki B, Meyer T, Kretschmar G, Kirsten A, Claussen M, *et al*. Decreasing cardiac chamber sizes and associated heart dysfunction in COPD: Role of hyperinflation. Chest. 2010;138(1):32–8.
13. Andreas S, Anker SD, Scanlon PD, Somers VK. Neurohumoral activation as a link to systemic manifestations of chronic lung disease. Chest. 2005;
14. Zilz C, Blaas SH, Pfeifer M, Jörres RA, Budweiser S. Mental health, serum biomarkers and survival in severe COPD: A pilot study. Multidiscip Respir Med. 2016;
15. Oudijk EJD, Nijhuis EHJ, Zwank MD, Van De Graaf EA, Mager HJ, Coffer PJ, *et al*. Systemic inflammation in COPD visualised by gene profiling in peripheral blood neutrophils. Thorax. 2005;
16. Mishra US, Gantayat CK. Left Ventricular Dysfunction in Copd With or Without Cor Pulmonale. J Evid Based Med Healthc. 2018;5(2):194–7.
17. Pelà G, Li Calzi M, Pinelli S, Andreoli R, Sverzellati N, Bertorelli G, *et al*. Left ventricular structure and remodeling in patients with COPD. Int J Chron Obstruct Pulmon Dis [Internet]. 2016 May [cited 2018 Feb 2];11(1):1015–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27257378
18. Caram LMDO, Ferrari R, Naves CR, Tanni SE, Coelho LS, Zanati SG, *et al*. Association between left ventricular diastolic dysfunction and severity of chronic obstructive pulmonary disease. Clinics (Sao Paulo) [Internet]. 2013;68(6):772–6. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3674261andtool=pmcentrezandrendertype=abstract
19. Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, Sawada SG. American Society of Echocardiography Recommendations for Performance, Interpretation, and Application of Stress Echocardiography. Journal of the American Society of Echocardiography. 2007.
20. Echocardiographic evaluation of heart___the severity of disease.pdf.
21. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, *et al*. Recommendations for Cardiac Chamber Quantification. J Am Soc Echocardiogr. 2015;28(1):1-39.e14.

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