

Relationship between Severity of Chronic Obstructive Pulmonary Disease and Left Ventricular Diastolic Dysfunction

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Background: Chronic obstructive pulmonary disease (COPD) is an inflammatory systemic disorder that affects the respiratory tract airways and breathing. Left ventricular diastolic dysfunction (LVDD), which is the inability of the ventricle to fill to a normal end-diastolic volume, may be observed in patients with severe COPD. This study aimed to evaluate LVDD in patients with COPD.

Materials and Methods: This cross-sectional study included 58 patients under 65 years of age with COPD as the case group. Moreover, 58 patients with normal spirometry and without pulmonary or cardiac disease were included as the control group. They referred to the cardiologist for echocardiography. Patients were tested for C-reactive protein (CRP) and N-terminal pro-B-type natriuretic peptides (NT-pro BNP). Data were analyzed with SPSS for descriptive reports of the relationship between variables.

Results: The results showed that LVDD was significantly higher in COPD patients (60%) than in the control group (12.2%). Also, there was no significant relationship between LVDD and BMI in COPD patients. Evaluation of CRP and PRO-BNP showed that the distribution of patients in different diastolic function classes is similar. It was observed that with increasing COPD severity, LVDD severity increased (p-value =0.101). There is a direct relationship between total lung capacity (TLC) and LVDD (P-value <0.0001). In COPD patients, there was a significant relationship between diastolic function and SPAP (P-value <0.0019).

Conclusion: In general, it should be noted that the prevalence of LVDD in patients with COPD is significantly higher than in other people.

Keywords: Chronic obstructive pulmonary disease; Cardiovascular complications; Left ventricular diastolic dysfunction; Total lung capacity

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an inflammatory systemic disorder that causes limitation of breathing and daily activities of the patient (1). The disease causes symptoms such as closure of the respiratory tract, weakness in breathing, chronic cough, and increased

sputum in patients (2, 3). The severe condition of the disease leads to hospitalization and severe weakness in the patient. It is a serious condition that significantly impacts a patient's health and quality of life (4). The prevalence and severity of the disease are so high that it is thought to be the fourth cause of death in the United States (5). COPD is

the third leading cause of death in the world by 2020, which is projected by the World Health Organization (WHO) (5). Environmental factors and individual lifestyle choices, such as smoking and living in areas with high air pollution, influence the severity of COPD (6-8). However, cardiovascular complications (CVD) and lung cancer have been identified as the primary causes of death among individuals with COPD (9-11).

The importance of cardiovascular disease interactions in the aggravation and deterioration of COPD patients is so high that 50% of hospital admissions and 20% of the total deaths associated with the disease are related to those with cardiovascular complications (12). In other words, people with COPD are at risk of death due to CVD (13). The importance of right ventricular function is recognized as one of the determining factors in the clinical prognosis of COPD, while the potential role of the left ventricle has been less studied (5). Right ventricular overload can increase lung vessel tension, which can also affect the characteristics of left ventricular filling (14). According to the results of the previous studies, left ventricular diastolic dysfunction (LVDD), characterized by the ventricle's inability to fill to a normal end-diastolic volume, may also occur in patients with severe COPD (15). LVDD can be related to reasons such as hypoxia, lung hyperinflation, right ventricular dysfunction, and other factors (16).

However, what we are certain about is the effect of cardiovascular disease on people with COPD. This study aimed to evaluate LVDD in patients with COPD.

MATERIALS AND METHODS

Sample collection

In this cross-sectional study, which was performed at the Messiah Daneshvari Hospital after obtaining patient consent and approval of the Ethics Committee with number IR.SBMU.NRITLD.REC.1396.346, the research team examined the prevalence of LVDD in COPD patients compared to the control group. In the next step, the severity of COPD and LVDD were also evaluated.

Meanwhile, factors affecting the development of LVDD in COPD patients were also studied.

A total of 58 patients whose COPD were diagnosed according to the ATS guideline. Their severity was determined based on the spirometry according to the GOLD criteria. They were included in the study as the case group. On the other hand, 58 patients who did not have a specific complaint regarding pulmonary and cardiac diseases with normal spirometry were considered the control group. All patients with a history of HLP, CHF, HTN, diabetes, myocardial infection, and heart valve disorder, and patients with COPD exacerbation, or those over 65 years of age (due to senile LVDD), were excluded. After confirming COPD, the patients underwent Body Box for the evaluation of pulmonary volume (total lung capacity: TLC, and residual volume: RV). Then, they were referred to the cardiologist for echocardiography and electrocardiography to evaluate LVDD. During this step, patients were tested for CRP and NT-pro BNP tests. It should be noted that all patients were evaluated by the same cardiologist and pulmonologist with the same echocardiography and spirometry devices.

Checking RV Dimensions

The RV size in the Apical four-chamber view was evaluated by focusing on the diastolic end point. Thus, the RV size was measured in 30% of the base area. The highest normal value of RV is 4.2cm. The importance of measuring RV is comparable to LV.

RV function review

For this purpose, the Tricuspid Annular Plane Systolic Excursion (TAPSE) method was used. The systolic flow of the free-wall RV in the longitudinal axis at the Apical four-chamber position was measured by M-mode.

Pulmonary artery pressure (PAP) assessment

Pulmonary artery pressure is estimated by estimating Tricuspid Regurgitation (TR). The maximum normal value for the pulmonary artery is 35 mmHg. This is while the reference values for this factor are as follows: severe: PAP > 60 mmHg, moderate: 45 < PAP < 60 mmHg, and mild: 35 < PAP < 45 mmHg.

Evaluation of left ventricular diastolic function

We measured early and late diastolic peak velocities of mitral inflow (E and A), pulmonary vein flow using pulsed-wave Doppler, and mitral annular velocities (Ea and Aa) at four sites via tissue Doppler imaging. When E/A is less than 1.3, diastolic dysfunction of the left ventricle is present. This condition is categorized into mild (impaired relaxation), moderate (pseudonormalization), and severe (restriction) types.

Data analysis

The data from the patients was analyzed by SPSS software. Descriptive reports were generated that included frequency tables and charts for qualitative variables, as well as central indices and measures of dispersion for quantitative variables. A correlation coefficient was used to evaluate the relationships between variables. In all tests, a p-value of less than 0.05 was considered statistically significant.

RESULTS

Of the 58 subjects in this study, LVDD was significantly higher in COPD patients (60%) than the control group (12.2%). However, in some other people, 28 of them had

mild impairment in LVDD, and only 7 with moderate and severe symptoms were reported. There was no significant difference between the mean age (18-64 years old) (p-value=0.706, Table 1), body mass index (BMI) (p-value=0.452, Table 2), and left ventricular diastolic dysfunction (LVDD) in the studied patients. The results of COPD in LVDD using Fisher's exact test (Figure 1) showed that with increasing severity of COPD, the number of people with high LVDD severity increases. Additionally, Spearman's correlation test indicated a correlation between COPD and LVDD (p-value=0.0001).

It is noticeable that with the increase in the severity of SPAP, the number of people with high LVDD severity increases. Spearman correlation test indicated a correlation between two SPAP and LVDD (p-value = 0.0019, Figure 2). The difference in mean TLC in different diastolic functional classes using ANOVA showed that there was a significant difference between mean TLC in normal and mild groups (p-value=0.019, Figure 3). Thus, there is a direct relationship between the mean value of the TLC and LVDD. As the TLC value increases, the LVDD also increases on a proportional scale.

Table 1. The distribution of age in left ventricle diastolic dysfunction (LVDD)

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	p-value
					Lower Bound	Upper Bound			
Normal	23	59.13	8.131	1.696	55.61	62.65	31	65	0.706
Mild dysfunctional	28	59.54	7.084	1.339	56.79	62.28	34	70	
Moderate dysfunctional	7	61.71	2.690	1.017	59.23	64.20	58	65	
Total	58	59.64	7.120	0.935	57.77	61.51	31	70	

Table 2. The distribution of body mass index (BMI) in left ventricular diastolic dysfunction (LVDD)

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum	p-value
					Lower Bound	Upper Bound			
Normal	22	25.681	5.0854	1.0842	23.427	27.936	18.50	35.10	0.452
Mild dysfunctional	28	23.825	4.7890	0.9050	21.968	25.682	16.50	34.20	
Moderate dysfunctional	7	24.214	7.0383	2.6602	17.704	30.723	17.60	37.00	
Total	57	24.589	5.1809	0.6862	23.214	25.964	16.50	37.00	

The results of CRP in LVDD using Fisher's exact test showed that the distribution of patients in different diastolic functional classes was similar and there was no significant difference (p-value=0.250). Investigation of the relationship and distribution of PRO-BNP in LVDD using Fisher's exact test indicated that the distribution of patients in different functional groups was similar and there was no significant difference (p-value=0.101).

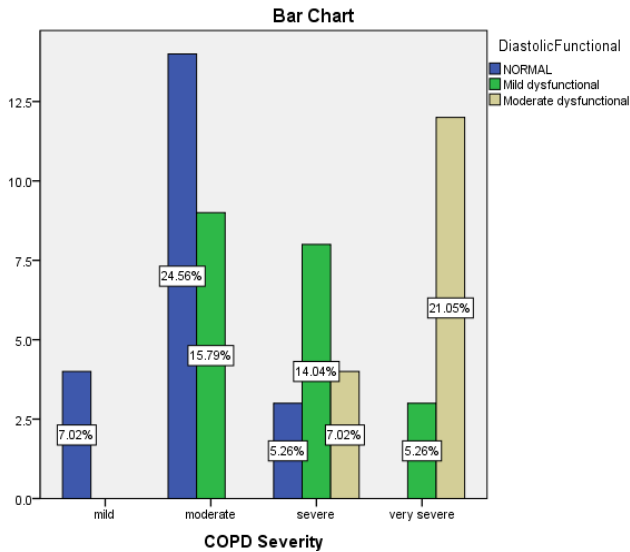


Figure 1. Investigating the relationship and distribution of COPD in Left Ventricle Diastolic Dysfunction (LVDD)

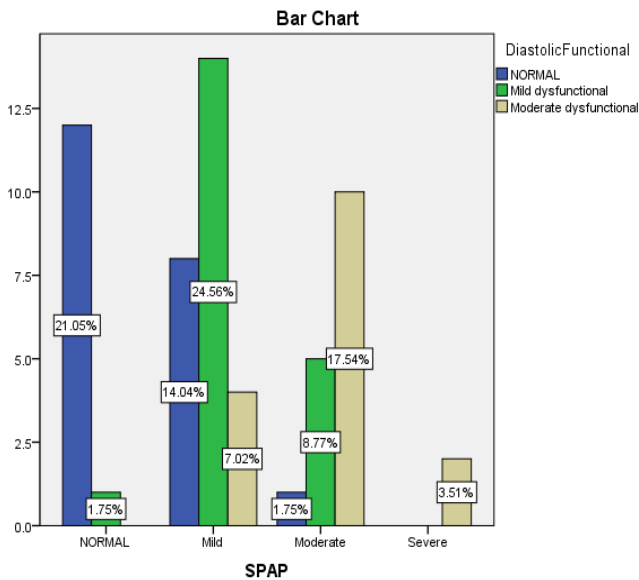


Figure 2. Investigating the relationship and distribution of SPAP in Left Ventricle Diastolic Dysfunction (LVDD)

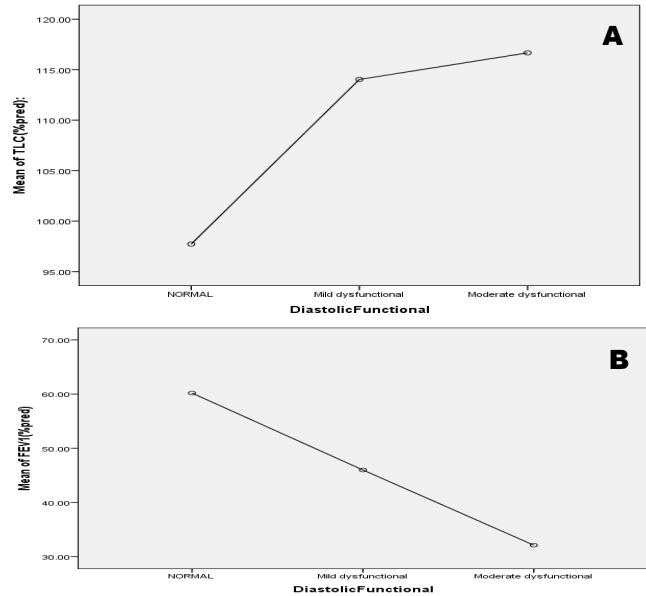


Figure 3. TLC, mean difference in different diastolic functional classes (A). Comparison of mean FEV1 in three groups of LVDD using ANOVA test (B)

DISCUSSION

Chronic obstructive pulmonary disease (COPD) is a chronic and severe disease and is a growing concern for human societies (17). The disease, with global distribution, causes a variety of symptoms such as chronic cough, respiratory distress, and inflammation of the respiratory tract (18). Different factors are involved in the incidence and severity of COPD, among which cardiovascular events are one of the most important cases in these patients (19). The presence of cardiac disorders can exacerbate COPD (20-22). The present study investigated the relationship between this circumstance and the severity of LVDD with an emphasis on the factors affecting LVDD in patients with COPD.

Based on the results of this study, no significant correlation was found between the age of patients with COPD and LVDD. This may be due to the limitations regarding the age of the patients in the present study (under the age of 65). However, in other similar studies, it has been shown that in elderly patients with COPD, the magnitude and severity of LVDD are higher than in other patients (23). Another point was the lack of a meaningful

relationship between BMI in patients with COPD and the severity of their LVDD.

Several studies have reported the prevalence of cardiovascular disorders in people with COPD. In the meantime, numerous studies have been conducted on right ventricular dysfunction and the severity of COPD, all of which have highlighted the direct relationship between these two factors. However, limited studies have been conducted on the relationship between LVDD and COPD severity. In previous studies, the LVDD prevalence of 50%-90% was reported among people with COPD. Often, these results point to a significant and direct correlation between the severity of COPD and LVDD (24,25). According to the results presented in this study, in most people with COPD (60%), left ventricular diastolic dysfunction has been observed. Due to the lack of direct relationships between the severity of COPD and the occurrence of LVDD, there is an increasing correlation between these two factors. In other words, there is a meaningful relationship between the severity of COPD and the intensity of LVDD.

Pro-BNP is an important indicator in the diagnosis and evaluation of congestive heart failure (26). Since COPD patients are often at risk for cardiovascular disease, this parameter is also helpful in this group of patients (27). On the other hand, given the severity of LVDD in patients with COPD, we see an increase in parameters such as pro-BNP in them (28). However, in this study (due to the optimization of patients and the status of their condition and without COPD exacerbation), there was no significant relationship between the results of the pro-BNP and LVDD study in patients with COPD.

Evaluation of TLC in patients with COPD in this study revealed a direct and significant relationship between TLC severity and left ventricular diastolic dysfunction. As a result of an increase in the mean TLC, LVDD also intensifies.

CONCLUSION

COPD is a common disease around the world that causes many secondary disorders in people. These disorders sometimes have a significant relationship with the severity of COPD, and sometimes they do not have this kind of relationship. Of course, achieving the right results

in this area requires several studies worldwide. All in all, it should be noted that the prevalence of LVDD in patients with COPD is significantly higher than in other individuals.

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Conflict of Interest

Authors declare that they have no conflicts of interest.

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REFERENCES

1. Kubota Y, Asai K, Murai K, Tsukada YT, Hayashi H, Saito Y, et al. COPD advances in left ventricular diastolic dysfunction. *Int J Chron Obstruct Pulmon Dis* 2016;11:649-55.
2. 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. *Am J Respir Crit Care Med* 2007;176(6):532-55.
3. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2013;187(4):347-65.
4. Andrijevic L, Milutinov S, Andrijevic I, Jokic D, Vukoja M. Association Between the Inflammatory Biomarkers and Left Ventricular Systolic Dysfunction in Patients with Exacerbations of Chronic Obstructive Pulmonary Disease. *Balkan Med J* 2017;34(3):226-31.
5. Mahmoud M, Shalan IM, Kawtshy H, Azeem HA. Assessment of left ventricular function in chronic obstructive pulmonary disease Echocardiographics study. *Al-Azhar Assiut Medical Journal* 2015; 13(2):1-7.
6. Vestbo J, Hurd SS, Rodriguez-Roisin R. The 2011 revision of the global strategy for the diagnosis, management and prevention of COPD (GOLD)--why and what? *Clin Respir J* 2012;6(4):208-14.
7. Howard G, Wagenknecht LE, Burke GL, Diez-Roux A, Evans GW, McGovern P, et al. Cigarette smoking and progression of

- atherosclerosis: The Atherosclerosis Risk in Communities (ARIC) Study. *JAMA* 1998;279(2):119-24.
8. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364(9438):937-52.
 9. Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE; Lung Health Study Research Group. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. *Ann Intern Med* 2005;142(4):233-9.
 10. Sin DD, Wu L, Man SF. The relationship between reduced lung function and cardiovascular mortality: a population-based study and a systematic review of the literature. *Chest* 2005;127(6):1952-9.
 11. Maclay JD, McAllister DA, Macnee W. Cardiovascular risk in chronic obstructive pulmonary disease. *Respirology* 2007;12(5):634-41.
 12. Sin DD, Man SF. Impact of cancers and cardiovascular diseases in chronic obstructive pulmonary disease. *Curr Opin Pulm Med* 2008;14(2):115-21.
 13. Caram LM, 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)* 2013;68(6):772-6.
 14. O'Brien C, Guest PJ, Hill SL, Stockley RA. Physiological and radiological characterisation of patients diagnosed with chronic obstructive pulmonary disease in primary care. *Thorax* 2000;55(8):635-42.
 15. Watz H, Waschki B, Boehme C, Claussen M, Meyer T, Magnussen H. Extrapulmonary effects of chronic obstructive pulmonary disease on physical activity: a cross-sectional study. *Am J Respir Crit Care Med* 2008;177(7):743-51.
 16. Alter P, Jörres RA, Watz H, Welte T, Gläser S, Schulz H, et al. Left ventricular volume and wall stress are linked to lung function impairment in COPD. *Int J Cardiol* 2018;261:172-8.
 17. Mannino DM, Sonia Buist A, Vollmer WM. Chronic obstructive pulmonary disease in the older adult: what defines abnormal lung function? *Thorax* 2007;62(3):237-41.
 18. Portillo K, Abad-Capa J, Ruiz-Manzano J. Chronic obstructive pulmonary disease and left ventricle. *Arch Bronconeumol* 2015;51(5):227-34.
 19. Anderson WJ, Lipworth BJ, Rekhraj S, Struthers AD, George J. Left ventricular hypertrophy in COPD without hypoxemia: the elephant in the room? *Chest* 2013;143(1):91-7.
 20. Garcia-Aymerich J, Gómez FP, Benet M, Ferrero E, Basagaña X, Gayete À, et al. Identification and prospective validation of clinically relevant chronic obstructive pulmonary disease (COPD) subtypes. *Thorax* 2011;66(5):430-7.
 21. Vanfleteren LE, Spruit MA, Groenen M, Gaffron S, van Empel VP, Bruijnzeel PL, et al. Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2013;187(7):728-35.
 22. Burgel PR, Paillasseur JL, Peene B, Dusser D, Roche N, Coolen J, et al. Two distinct chronic obstructive pulmonary disease (COPD) phenotypes are associated with high risk of mortality. *PLoS One* 2012;7(12):e51048.
 23. Huang YS, Feng YC, Zhang J, Bai L, Huang W, Li M, et al. Impact of chronic obstructive pulmonary diseases on left ventricular diastolic function in hospitalized elderly patients. *Clin Interv Aging* 2014;10:81-7.
 24. López-Sánchez M, Muñoz-Esquerre M, Huertas D, Gonzalez-Costello J, Ribas J, Manresa F, et al. High Prevalence of Left Ventricle Diastolic Dysfunction in Severe COPD Associated with A Low Exercise Capacity: A Cross-Sectional Study. *PLoS One* 2013;8(6):e68034.
 25. 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(2):105-9.
 26. Kraen M, Frantz S, Nihlén U, Engström G, Löfdahl CG, Wollmer P, et al. Brain natriuretic peptide levels in middle aged subjects with normal left ventricular function in relation to mild-moderate COPD. *Clin Respir J* 2018;12(3):1061-7.
 27. Gale CP, White JE, Hunter A, Owen J, Allen J, Watson J, et al. Predicting mortality and hospital admission in patients with COPD: significance of NT pro-BNP, clinical and echocardiographic assessment. *J Cardiovasc Med (Hagerstown)* 2011;12(9):613-8.
 28. Ayesta A, Martínez-Sellés H, Bayés de Luna A, Martínez-Sellés M. Prediction of sudden death in elderly patients with heart failure. *J Geriatr Cardiol* 2018;15(2):185-92.