The relationship between acidosis and hypercapnia with Cor pulmonale in patients with chronic obstructive pulmonary disease

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Abstract

Introduction: Cor pulmonale or right ventricular (RV) enlargement is cardiovascular complications of the chronic obstructive pulmonary disease (COPD). Hypoxic pulmonary vasoconstriction, hypercapnia, acidosis and pulmonary vascular remodeling are suggested as possible mechanisms of cor pulmonale. In this study, we aimed to evaluate the correlation between acidosis and hypercapnia with corpulmonale in patients with COPD.

Methods: In this cross-sectional analytical study, 100 patients (56 men and 44 women with mean age of 66.53 ± 10.63 years) with moderate to severe COPD exacerbation were included. Complete history taking and physical examination as well as atrial blood gas, pulmonary function test (PFT) and echocardiography were performed. Disease severity was defined according to global initiative for obstructive lung disease (GOLD), Modified Medical Research Council (mMRC) and COPD Assessment Test (CAT) criteria. Patients with cor pulmonale were defined and findings were compared between patients with and without cor pulmonale.

Results: Forty-two patients had cor pulmonale. There was no significant difference in hypercapnia between groups. Cor pulmonale patients, compared to non-cor pulmonale, had significantly lower forced expiratory volume in the first second (FEV1) (P = 0.020), higher tricuspid regurgitation (TR) (P = 0.001) and pulmonary hypertension (P = 0.020). There was significantly negative correlation between RV thickness with FEV1/forced vital capacity (FCV) (r = -0.239, P = 0.010) and RV size with FEV1/FVC (r = -0.312, P = 0.002) and positive correlation with partial pressure of carbon dioxide (PaCO2) (r = 0.312, P = 0.002) and bicarbonate (HCO3) (r = 0.258, P = 0.009).

Conclusion: Cor pulmonale in the course of COPD accompanies with adverse outcome. These patients have worth spirometry and left ventricle echocardiographic findings, but have no difference in arterial blood gas (ABG) findings.

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Introduction

Cor pulmonale describes the enlargement and failure of the right ventricle of the heart as a response to increased vascular resistance or increased pulmonary artery pressure.[1-3] It is a common complication of chronic obstructive pulmonary disease (COPD) with incidence rate of 20-30%.[1-4]

COPD is considered as one of the main causes of morbidity and mortality worldwide and is characterized by progressive airway obstruction leading to reduced lung function and breathlessness.[3,5] Hypoxic pulmonary vasoconstriction, hypercapnia, respiratory acidosis and pulmonary vascular remodeling in COPD can cause an increase in right ventricular (RV) afterload, which in turn, results in RV failure leading to cor pulmonale.[6,7] The severity of cor pulmonale in COPD patients is dependent to hypoxia,

hypercapnia and airway obstruction as it has been reported a prevalence of 40% in patients with forced expiratory volume in the first second (FEV1) < 1 l and 70% in patients with FEV1 < 0.6 l.

With controlling and treatment of the causes and risk factors of cor pulmonale, it is possible to prevent the disease progress and reduce the morbidity and mortality rate.[8] Due to presumed role of acidosis and hypercapnia for cor pulmonale in COPD patients, in this study we aimed to evaluate the correlation between acidosis and hypercapnia with corpulmonale in patients with COPD.

Methods

In this cross-sectional study, 100 patients with COPD exacerbation, global initiative for obstructive lung disease (GOLD) stage II-IV, FEV1 predicted < 60% and chronic hypoxia [partial pressure of oxygen (PaO2) < 60 mmHg)] admitted to Imam Khomeini Hospital, Ardabil, Iran, between February 2016 and February 2017 were included. Patients with previous or current pulmonary thromboemboli, obstructive sleep apnea, interstitial lung disease, left heart disease or left ventricular dysfunction due to ischemic heart disease, cardiomyopathies, congenital heart diseases, valvular heart disease, or other cardiovascular disease, malignancy, metabolic conditions, malnutrition, muscular disease, systemic inflammatory diseases, or renal failure, collagen vascular disease and idiopathic pulmonary hypertension were excluded. The study protocol was reviewed and approved by the Ethics Committee of Ardabil University of Medical Sciences. All patients were provided with written informed consent prior to enrolment.

Study protocol: Detailed clinical history and physical examination were obtained in each patient. Demographic, laboratory, electrocardiogram (ECG), chest X-ray findings were recorded. Atrial blood gas (ABG) was taken to evaluate the respiratory acidosis and hypercapnia. ABG was determined at patients' arrival to the emergency department with a FiO2 of 21%. All patients underwent echocardiography. The severity of COPD was staged according to the GOLD guidelines.[9] The modified Medical Research Council (mMRC)[10] scale and the COPD Assessment Test (CAT) were also recorded. CAT is an eight-item questionnaire designed to quantify the impact of COPD symptoms on the health status of patients, with higher values indicative of worse health status.[11]

The patients were put into two subgroups, COPD with and without cor pulmonale. Cor pulmonale was diagnosed based on an established clinical history of cor pulmonale or the current clinical evidence, chest radiography, ECG, and echocardiography. Findings regarding RV hypertrophy or dilation and RV dysfunction in echocardiography were required for the enrollment.

All patients underwent spirometry and FEV1, forced vital capacity (FVC) and FEV1/FVC ratio were recorded.

A cardiovascular ultrasound system (Vivid E9, General Electric, Horten, Norway) was used to perform echocardiography, using M mode and two-dimensional ultrasonography. RV thickness and size, right ventricular hypertrophy (RVH), tricuspid regurgitation (TR) were recorded. Continuous wave Doppler was used to detect TR and calculate the systolic pulmonary artery pressure (sPAP). Pulmonary artery hypertension (PAH) was considered if sPAP value was above 30 mmHg and divided into mild (30-50 mmHg), moderate (50-70 mmHg) and severe (< 70 mmHg).[12]

All data were analyzed using SPSS software (version 17, SPSS Inc., Chicago, IL, USA). Results are expressed as mean ± standard deviation (SD) or percentage. To compare the parameters, Student's independent t-test, analysis of variance (ANOVA) and chi-square or Fisher's exact tests were used to compare data between groups of patients. Pearson correlation was used to define possible correlations between echocardiographic and ABG and Pulmonary function test (PFT) findings, as well as between CAT and MMRC

scores. P of less than 0.050 was considered statistically significant.

Results

One-hundred patients including 56 men and 44 women with mean age of 66.53 ± 10.63 were studied. Mean duration of the disease was 12.50 ± 5.44 years. Comorbidities were diabetes mellitus (3 cases), hypertension (51 cases) and smoking (93 cases). Eighty-five patients had hypercapnia and 86 had respiratory acidosis. Cor pulmonale was present in 42 patients based on echocardiography findings.

Mean CAT score was 15.44 ± 10.84 and mean MMRC was 3.00 ± 0.81. According to GOLD criteria, 23 had stage II, 52 had stage III and 25 had stage IV. There was significantly positive correlation between CAT score and MMRC (r = 0.673, P < 0.001). Mean CAT score in GOLD stage II, III and IV were 7.26 ± 1.76, 13.59 ± 1.18 and 26.80 ± 7.69, respectively. With the increase in the GOLD stage, CAT score and health status were worsened (P < 0.001).

Demographic and clinical findings among COPD patients with and without cor pulmonale are shown in table 1. We found no significant difference among these variables between groups. Although cor pulmonale patients had higher CAT score and MMRC and more cases with a higher stage of GOLD, the difference was not significant.

Table 2 demonstrates PFT, ABG and echocardiography findings between COPD patients with and without cor pulmonale. Cor pulmonale patients had significantly lower FEV1, higher TR and pulmonary hypertension. PFT, ABG and echocardiography variables were similar between groups. Hypercapnia prevalence was similar between groups. Also, 36 (42.4%) of patients with hypercapnia and 6 (40.0%) of patients with normocapnia had cor pulmonale (P = 0.900).

We found significant correlations between RV thickness with FEV1/FVC (r = -0.239, P = 0.010) and RV size with FEV1/FVC (r = -0.312, P = 0.002) and between RV size and partial pressure of carbon dioxide ($PaCO_2$) (r = 0.312, P = 0.002) and bicarbonate (HCO_3) (r = 0.258, P = 0.009).

Discussion

In our study, 100 patients with COPD including 56 men with mean age of 66.53 years were studied. We found cor pulmonale in 42 cases. In previous studies, COPD has been more prevalent in men, older age, lower socioeconomic state and smokers.[13]

Table 1. Demographic and clinical findings between chronic obstructive pulmonary disease (COPD) patients with and without cor pulmonale

Variable		With cor pulmonale	Without cor pulmonale	P*
Age (year) (mean ± SD)		65.85 ± 9.97	67.01 ± 11.14	0.590
Sex [n (%)]	Male	28 (66.7)	28 (48.3)	0.100
	Female	14 (33.3)	30 (51.7)	
BMI (kg/m^2) (mean ± SD)		27.98 ± 6.08	27.02 ± 4.71	0.370
Disease duration (year) (mean ± SD)		13.25 ± 5.93	11.96 ± 5.05	0.250
Diabetes mellitus [n (%)]		1 (2.4)	2 (3.4)	0.750
Hypertension [n (%)]		19 (45.2)	32 (55.2)	0.320
Chronic cough [n (%)]		38 (90.5)	57 (98.3)	0.070
Chronic sputum [n (%)]		41 (97.6)	58 (100)	0.420
Edema [n (%)]		31 (37.8)	34 (58.6)	0.110
CAT score (mean ± SD)		17.85 ± 10.73	13.68 ± 10.66	0.057
MMRC score (mean ± SD)		3.00 ± 0.79	2.75 ± 0.82	0.140
GOLD stage [n (%)]	II	6 (14.3)	17 (29.3)	0.056
	III	21 (50.0)	31 (53.4)	
	IV	15 (35.7)	10 (17.2)	

*Student's independent t-test, analysis of variance (ANOVA), chi-square or Fisher's exact tests
SD: Standard deviation; BMI: Body mass index; CAT: COPD Assessment Test; mMRC: Modified Medical Research Council; GOLD: Global initiative for obstructive lung disease

Table 2. Pulmonary function test (PFT), arterial blood gas (ABG) and echocardiographic findings between chronic obstructive pulmonary disease (COPD) patients with and without cor pulmonale

Variable		With cor pulmonale	Without cor pulmonale	P*
PFT (mean ± SD)				
O2Sat		76.69 ± 7.65	80.51 ± 6.03	0.540
FEV1		34.30 ± 13.77	40.77 ± 14.76	0.020*
FVC		47.40 ± 16.85	52.68 ± 16.71	0.120
FEV1/FVC		0.61 ± 0.06	0.64 ± 0.05	0.070
ABG (mean ± SD)				
pH		7.28 ± 0.07	7.30 ± 0.06	0.200
PaO2		53.07 ± 5.25	53.94 ± 6.11	0.450
PaCO2		60.32 ± 13.20	56.36 ± 12.31	0.120
HCO3		29.90 ± 5.29	28.04 ± 4.44	0.060
Hypercapnia [n (%)]		36 (85.7)	49 (84.5)	0.860
Echocardiography (mean ± SD)				
RV size		3.60 ± 1.06	3.13 ± 1.41	0.060
TR [n (%)]		28 (66.7)	19 (32.8)	0.001*
Pulmonary hypertension [n (%)]	None	17 (40.5)	38 (65.5)	
	Mild	6 (14.3)	9 (15.5)	0.020*
	Moderate	8 (19.0)	7 (12.1)	
	Severe	11 (26.2)	4 (6.9)	

*Student's independent t-test, analysis of variance (ANOVA), chi-square or Fisher's exact tests
SD: Standard deviation; PFT: Pulmonary function test; O2Sat: Oxygen saturated; FEV1: forced expiratory volume in the first second; FVC: Forced vital capacity; ABG: Arterial blood gas; PaO2: Partial pressure of oxygen; PaCO2: Partial pressure of carbon dioxide; HCO3: Bicarbonate; RV: Right ventricular; TR: Tricuspid regurgitation

In COPD patients, hypoxemia, hypercapnia, inflammation and vascular changes due to airway dilatation and changes in RV pressure lead to RV dysfunction and right heart failure.[14] Cor pulmonale is the main cardiac side effect of COPD[15] and is considered as the main cause of mortality and morbidity in COPD.[16]

We observed cor pulmonale in 42.0% of COPD patients. Similarly, Gupta et al.[17] reported cor pulmonale in 41.2%. The prevalence was 48.1% in the study of Ju et al.[18]

In our study, cor pulmonale patients were mostly men with longer duration of the disease and higher body mass index (BMI). Similarly, in the study of Ju et al,[18] patients with and without cor pulmonale had similar age and sex with higher prevalence in men, lower BMI and lower O2 saturation with no difference between groups.

Cor pulmonale patients in our study had lower FVC and FEV1/FVC, but there was the only significant difference between groups in the lower FEV1. ABG findings were not different between groups. There was no difference between hypercapnic and normocapnic COPD patients in the prevalence of COPD. Ju et al.[18] observed that cor pulmonale patients had lower FEV1 and FEV1/FVC. Unlike our findings, Yang et al.[19] observed that cor pulmonale was significantly higher in hypercapnic as compared to normocapnic patients. Verbitskii et al.[20] reported insignificant hypoxemia in cor pulmonale, which progressed with decompensation of chronic cor pulmonale.

In our study, cor pulmonale patients had significantly higher TR and pulmonary hypertension with a higher incidence of moderate and severe types. Likewise, Ju et al.[18] reported higher sPAP and RV thickness in cor pulmonale patients. Gupta et al.[17] observed that in corpulmonale patients, pulmonary hypertension prevalence is higher and with an increase in the severity of PHTN, the cases with cor pulmonale increases.

We also found significant negative correlations between FEV1/FVC with size and thickness of RV and positive correlation between RV size with PaCO2 and HCO3. We found a significantly positive correlation between CAT score and MMRC in COPD patients. We also observed that with an increase in the GOLD stage, CAT score and health status were worsened.

In our study, cor pulmonale patients had higher CAT score and MMRC and more cases with a higher stage of GOLD, but the difference was not significant. Ju et al.[18] showed that stage IV GOLD was significantly higher in cor pulmonale patients.

Conclusion

In conclusion, Cor pulmonale, in the course of COPD, accompanies with adverse outcome. These patients have worth spirometry and left ventricle echocardiographic findings, but have no difference in ABG findings.

Authors' Contribution

All authors have read and approved the manuscript. SH, SAK and BZ performed the data collection, writing, critical revision and drafting of the manuscript. AH and SK and SSA contributed to the study design and performed the statistical analysis, data analysis, and data interpretation.

Conflict of Interest

Authors have no conflict of interest.

Ethical Approval

This study was approved by Ethics Committee of Ardabil University of Medical Sciences.

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