ORIGINAL ARTICLE

The Risk of Atrial Fibrillation in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Muhammad Aneel Razzaq[1*], Muhammad Atif[2], Ubaid Ullah[3], Mohsin Mehmood[4], Muhammad Irfan[5], Kashif Sardar[2]

ABSTRACT

Objective: To evaluate the role of acute exacerbation of COPD in the risk of atrial fibrillation.

Study Design: Cross sectional study design.

Place and Duration of Study: The study was conducted at Bakhtawar Amin Hospital Multan and Recep Tayyip Erdogan Hospital Muzaffargarh, Pakistan from March 2022 to March 2023.

Methods: The patients with acute, hypercapnic chronic obstructive pulmonary disease(COPD) exacerbation were included in the study. A total of 200 patients were analyzed. Baseline data including demographic and clinical details, blood tests, ABG, systolic and diastolic blood pressure, ECG, pulmonary function test, and transthoracic echocardiography were recorded.

Results: Of 200 patients, 40(20%) had an episode of paroxysmal atrial fibrillation (AF). Atrial fibrillation was more prevalent in cases with lower FEV1 (*P*<.05). In addition, it was also more common in cases with higher PaCO2 (*P*<.05). Atrial Fibrillation was significantly higher in cases with larger LA diameters (34.1 ± 2.3 mm vs 46.1 ± 2.3 mm, *P*<.05), area (22.8 ± 4.1 cm2 vs 34.1 ± 5.1 cm2, *P*<.05) and higher PASP (36.1 mmHg ± 2.2 vs 46.4 mmHg ± 3.7, *P*<.05). RA area was larger in patients with AF and COPD compared to those without AF (25.6 ± 5.1cm2 vs 30.2 ± 6.4 cm2, *P*<0.05). These findings suggest COPD patients are at increased risk of AF and require measures to reduce the risk. These data will be helpful for further investigation and development of strategies to prevent AF morbidities in COPD patients.

Conclusion: In patients with acute exacerbations of chronic obstructive pulmonary disease, blood gas fluctuations, hemodynamic alterations, and abnormal pulmonary functions can lead to an increased risk of atrial fibrillation.

Keywords: *Atrial Fibrillation, Chronic Obstructive Pulmonary Disease, Risk Factor.*

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[1]*Department of Pulmonology*
Recep Tayyip Erdogan Hospital, Muzaffargarh, Pakistan
[2]*Department of Pulmonology*
Bakhtawar Amin Hospital, Multan, Pakistan
[3]*Department of Pulmonology*
Social Security Institute, Multan, Pakistan
[4]*Department of Pulmonology*
District Headquarter Hospital, Muzaffargarh, Pakistan
[5]*Department of Pulmonology*
Tehsil Head Quarters, Jampur, Pakistan

Correspondence:
Dr. Muhammad Aneel Razzaq
Consultant, Pulmonology
Recep Tayyip Erdoğan Hospital, Muzaffargarh, Pakistan
E-mail: drsaad1231@gmail.com

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Introduction

Atrial fibrillation (AF) is a common cause of morbidity and mortality. It is more prevalent in the elderly population.[1] Its underlying electrophysiological mechanism is controversial and can be caused by reentrant or non-reentrant activity. Disorders like systemic hypertension, myocardial ischemia, diastolic dysfunction, valvar disease, and persistent tachycardia cause excessive pressure on the left atrium which in response displays various adaptive processes,[2] AF majorly develops due to the random colliding of multiple wavelets of re-entrant arrhythmia. AF mostly originates from the left atrium (LA), and evidence suggests that the extension of

atrial tissues in pulmonary veins is mostly associated with the initiation of arrhythmia.[3]

Risk factors for AF include male gender, aging, smoking history, cardiac disorder, obesity, diabetes mellitus, hypertension, hypoxia, and hyperthyroidism.[4,5] Clinical evidence suggests a frequent link between metabolic abnormalities and cardiac rhythm disorders in critically ill patients. Atrial arrhythmia can sometimes be asymptomatic or can have few symptoms. It is challenging for physicians to identify and treat precipitating causes, manage symptoms, and prevent more severe episodes and complications. The left heart can function normally in chronic hypoxic lung disease, but coexisting coronary disease can cause left ventricular failure due to a combination of hypoxia and respiratory acidosis.[6,7] Chronic airflow limitation can also affect left ventricular function due to hypertrophy of the right ventricle and widely varying intrathoracic pressure. Arrhythmias are frequent in patients with abnormal carbon dioxide tension and hypoxemia. Breathing disorders like chronic obstructive pulmonary disease are associated with an increased risk of cardiac arrhythmias.[8]

Arrhythmias and heterogeneous repolarization are common in patients with COPD. ECG shows that AF is significantly associated with prolonged dispersion of P wave but not with atrial function, atrial blood gas exchange, and pulmonary function.[9] Though studies have been conducted to assess the risk of AF in patients with COPD, but local data are scarce on this topic. Thus, the objective of this study is to evaluate the role of acute exacerbation of COPD in increasing the risk of atrial fibrillation.

Methods

The study was conducted in Bakhtawar Amin Hospital Multan and Recep Tayyip Erdogan Hospital Muzaffargarh, Pakistan from March 2022 to March 2023. The patients aged > 18 years with acute, hypercapnic COPD exacerbation were included in the study. In patients with acute exacerbations oxygen desaturation is ≤4% below that of stable state, C-reactive protein is ≥3 $mg \cdot L^{-1}$ and neutrophils are ≥9000 mm^{-3}. Patients with a history of cardiovascular diseases, AF, neoplasm, and hydro electrolyte disorders were excluded. A total of 200 patients were analyzed. Informed consent of the participants was taken. The Ethical Review Board of the hospital approved the study on 10th March 2021, vide letter no: 20/140.

Baseline data including demographic and clinical details, blood tests, ABG, systolic and diastolic blood pressure, ECG, pulmonary function test, and transthoracic echocardiography were recorded. Transthoracic echocardiography was performed, and ECG was assessed using the modular ECG analysis system.[10] ECGs that indicated any atrial flutter or AF or any arrhythmia were independently recorded to verify AF. The cardiologist made the final diagnosis. Continuous wave Doppler echocardiography was used to determine Pulmonary Artery Systolic Pressure (PASP) and right ventricular systolic pressure (RVSP). Right atrial pressure and pulmonary vascular resistance (PVR) were also recorded. Spirometry was performed for baseline measurement of forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1). Corticosteroids and bronchodilators were not administered before PFT measurement. THE GOLD criteria were used to determine airflow.

SPSS version 23.0 was used for data analysis. Categorical data was represented as frequency and percentage, and continuous data as mean and standard deviation. Wilcoxon or t-test was used to compare continuous variables and Fisher's exact or $\chi 2$ for categorical data. A linear correlation between study variables was measured using the Spearman coefficient. P value < 0.05 was considered statistically significant.

Results

Of 200 patients, 40(20%) had an episode of paroxysmal AF. Of the remaining 160 COPD patients 15 were excluded due to severe complications (diagnosis of cancer, infectious complications, renal failure). Thus, the study included 145 patients with acute exacerbation of COPD (Figure.1). Table-1 shows the baseline data of the participants. AF was more common in older and male patients. BMI, smoking history, diabetes mellitus blood pressure, and sugar did not differ significantly in cases with and without atrial fibrillation.

AF was significantly more prevalent in cases with lower FEV1 (P<.05) (Table-2). In addition, it was also more common in cases with higher PaCO2 (P<.05).

Table-1: Patients' demographic and clinical data (Mean ± Standard Deviation)

Factors	COPD (n=145)	COPD and Atrial fibrillation (n=40)	*P* value
Male gender*	77 (53.1%)	26 (65%)	0.825
Age	80.4 ± 5.2	79.4 ± 4.6	0.751
BMIS	27.2 ± 3.5	27.7 ± 2.4	0.916
BPD	126.3 ± 18.1	136.2 ± 17.8	0.176
BP	71.4 ± 10.1	81.6 ± 7.4	0.099
Fasting blood glucose	120.5 ± 7.9	118.7 ± 9.9	0.833
Diabetes mellitus	35(24.1%)	8(20%)	0.833
Smokers	109(75.2%)	22(55%)	0.734

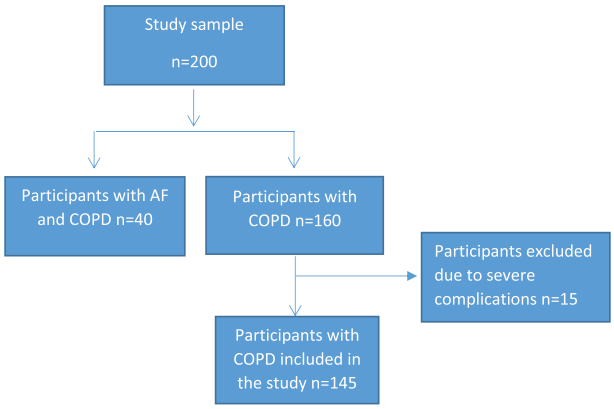

Fig.1: Flow chart showing study participants

An experienced echocardiologist who was unaware of clinical data analyzed ECG results. AF was significantly higher in cases with larger LA diameters (46.1 ± 2.3 mm vs 34.1 ± 2.3 mm, *P*<.05), area (34.1 ± 5.1 cm2 vs 22.8 ± 4.1 cm2, *P*< .05) and higher PASP (46.4 mmHg ± 3.7, vs 36.1 mmHg ± 2.2, *P*<.05).

Acute hypercapnia and increase in LA were directly correlated (*P*<.001, r<.71 and *P*<.001, r<.68 respectively) RA area was larger in patients with AF and COPD compared to those without AF (30.2 ± 6.4 cm2 vs 25.6 ± 5.1cm2, *P*< 0.05). Acute hypercapnia and increase in area of RA were positively correlated (*P*<.001, r<.75).

Discussion

Risk factors for AF include various respiratory

Table-2: Clinical and instrumental factors (Mean±Standard Deviation)

Factors	COPD (n=145)	COPD and Atrial fibrillation (n=40)	*P* value
Forced expiratory volume	77 ± 8.6	58.2 ± 7.8	0.06
PH	7.74 ± 0.02	7.71 ± 0.01	0.3
PaO2	61.3 ± 4.9	59.4 ± 3.02	0.59
PaCO2	51.6 ± 4.1	71.4 ± 5.7	0.06
HCO3	31.7 ± 3.9	36.3 ± 5.8	0.274
Oxygen saturation	92.8 ± 2.5	91.3 ± 3.1	0.37
Ejection fraction	52.6 ± 3.1	42.5 ± 6.7	0.691
Pulmonary artery systolic pressure	36.1 ± 2.2	46.4 ± 3.7	0.06
Tele diastolic left ventricular diameter	46.9 ± 7	55.2 ± 5	0.028
Left ventricular posterior wall thickness	10.1 ± 2	9.4 ± 3	0.71
Interventricular septum thickness	11.7 ± 3	9.4 ± 4	0.793
Left atrial diameter	34.1 ± 2.3	46.1 ± 2.3	0.06
Left atrial area	22.8 ± 4.1	34.1 ± 5.1	0.06
Right atrial area	25.6 ± 5.1	30.2 ± 6.4	0.06
Pulmonary vascular resistance	1.5 ± 0.6	3.2 ± 1.8	0.06

disorders like sleep-disordered breathing and impaired lung function.[11] In this study, we evaluated the risk of AF in COPD patients. Results showed that 20% of patients with COPD had AF. A previous study conducted on morbidity and mortality in COPD showed that AF was a commonly occurring comorbidity and REFI index was a predictor of morbidity and mortality.[12] Another study reported that 10.1% of controls and 14.5% of COPD patients had AF.[13] A previous found that 17.8% of COPD patients had AF, this is close to the finding of our study.[5] Acute hypercapnia alters electrophysiology. Structural remodeling affects the electrical association between muscles and regional conduction heterogeneities, which initiates and perpetuates AF. In this context, this study evaluated the association between acute hypercapnia and an increase in LA and RA size. Patients with acute exacerbation of COPD and severely reduced pulmonary function may have frequent hypoxia. As a result of chronic hypoxia sympathetic drive is stimulated which increases the risk of atrial fibrillation.[11] In the contrast, atrial electrophysiology is altered by acute hypercapnia and its reversal. Hypercapnia in COPD patients is majorly caused by impaired ventilation and perfusion that causes an increase in the amount of dead space. Acute hypercapnia causes a decrease in myocardial contractility leading to a rightward shift of oxyhemoglobin dissociation curve and increased oxygen release to tissue. Additionally, hypoxemia and hypercapnia cause pulmonary arteriolar constriction resulting in pulmonary hypertension. Right ventricular hypertension causes dilation of the right atrium thus inducing arrhythmias. COPD can lead to both hypercapnia and hypoxia. This affects adrenergic activity and has a complex impact on intracellular Ca2+ handling, atrial electrophysiology, and the risk of AF.[14] In the current study, AF was more common in patients with hypercapnia and low PaO2 levels. Low pulmonary function may increase pulmonary artery pressure. In COPD pulmonary hypertension can be caused by hypoxic vascular contraction and damaged pulmonary vasculature. A study reported that AF patients had low respiratory function and increased pulmonary artery pressure.[15] In the current study, an increase in PVR and PASP was associated with an increased risk of AF. In this study we did not perform cardiac catheterization, a previous study reported a significant association between catheterization and echocardiographic parameters.[16] A previous study on the association between AF and FEV1 reported that reduced FEV1 was an independent predictor of AF onset,[8] which is similar to the findings of the current study.

Studies have found that comorbid COPD inhibits successful treatment of AF, causes progression of clinical AF, and increases overall mortality.[17] A cohort study found that concurrent COPD in patients with paroxysmal atrial fibrillation was a risk factor for the development of persistent AF.[18] Another study reported that COPD was significantly associated with increased recurrence of AF following catheter ablation.[19] There is evidence of associations between AF morbidity and COPD. Our results are in line with earlier studies and add to the literature by indicating temporal association with acute exacerbation of COPD and increased risk of AF morbidity.

There is a multifactorial explanation of the mechanism underlying this association. A major factor is increased systemic inflammation due to acute exacerbations of COPD. Prior studies show that inflammation has an important role in the prognosis and incidence of AF.[20] Moreover, factor-1α, induced by hypoxia, promotes atrial remolding leading to AF.[21] Lastly, drugs for the management of acute exacerbations (eg β-agonists) modify atrioventricular nodal conduction and impact AF control.[22] These data will be helpful for further investigation and development of strategies to prevent AF morbidities in COPD patients. The limitation of this study is the small sample size larger studies are required for further analysis.

Conclusion

In patients with acute exacerbations of COPD, blood gas fluctuations, hemodynamic alterations, and abnormal pulmonary functions can lead to an increased risk of AF. Such complications increase morbidity in these patients.

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Authors Contribution

MAR: Study designing, data analysis, results, and interpretation
MA: Idea conception, data collection
UU: Study designing, data collection
MM: Idea conception, data analysis, results, and interpretation
MI: Idea conception, data analysis, results, and interpretation
KS: Study designing, manuscript writing, and proofreading