

# Prevalence and Associated Factors of Paroxysmal Atrial Fibrillation and Atrial Arrhythmias During Hospitalizations for Exacerbation of COPD

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**Purpose:** This study aimed to investigate the proportion and risk factors of paroxysmal atrial fibrillation (AF) and atrial arrhythmias (AA) in patients hospitalized for acute exacerbation of chronic obstructive pulmonary disease (AECOPD) in Vietnam.

**Patients and Methods:** A prospective observational study was conducted at two major hospitals in Hanoi, Vietnam, from January 2022 to January 2023. A total of 197 AECOPD patients were recruited. ECG and 24-hour Holter ECG were used to diagnose paroxysmal AF and AA.

**Results:** The prevalence of paroxysmal AF and AA were 15.2% and 72.6%, respectively. Factors associated with a higher likelihood of paroxysmal AF included aging 75 years old and above (aOR = 3.15; 95% CI: 1.28 to 8.48), Premature atrial complex (PAC) with 500 or more (aOR = 3.81; 95% CI: 1.48 to 10.97) and severity of COPD as group C and D (aOR = 3.41; 95% CI: 1.28 to 10.50). For AA, aging 75 years old and above (aOR = 2.25; 95% CI: 1.28 to 5.20), smoking (aOR = 2.10; 95% CI: 1.07 to 4.23) and P wave dispersion (PWD) with 40 milliseconds or more (aOR = 3.04; 95% CI: 1.54 to 6.19) were associated with a higher likelihood of AA.

**Conclusion:** Overall, our findings highlight the associated factors with the paroxysmal AF and AA among AECOPD patients. This underscores the importance of a multifaceted approach to risk assessment and management in this vulnerable population, focusing not only on respiratory symptoms but also on comprehensive cardiovascular evaluation and intervention.

**Keywords:** chronic obstructive pulmonary disease, atrial fibrillation, atrial arrhythmias, P wave dispersion, associated factor

## Introduction

Chronic Obstructive Pulmonary Disease (COPD) ranks as the fourth most common cause of death worldwide and is a significant contributor to ongoing health issues, especially in developing nations. Cardiovascular diseases, such as hypertension (50–67%), coronary artery disease, arrhythmia, and heart failure (11–34%) are among the most common comorbidities in patients with COPD because of similar risk factors such as advanced age or smoking.<sup>1–3</sup> Co-morbidity of arrhythmias in patients with COPD significantly increases the risk of in-hospital mortality up to 2.7-fold.<sup>2</sup> Besides, patients hospitalized for acute exacerbations of COPD (AECOPD) with concomitant arrhythmias were also at increased risk of death within 3 months of admission with RR of 1.35.<sup>4</sup> Atrial fibrillation (AF) and flutter in COPD patients also increase the risk of in-hospital mortality, respiratory failure, mechanical ventilation, infection, and stroke.<sup>5</sup>

Many risk factors for atrial arrhythmias, especially AF was reported, older age, male gender, diabetes mellitus (DM), valvular heart disease, hypertension, myocardial infarction, congestive heart failure, COPD, increased P-wave dispersion (PWD).<sup>6,7</sup> In COPD patients, there are other factors that can cause and trigger those arrhythmias, including smoking, oxidative stress, tissue hypoxia, effects of beta agonists, systemic glucocorticoid use, and the chronic inflammatory status.<sup>8</sup> Most of the studies have focused on AF while reports about other atrial arrhythmias, especially in COPD patients are lacking.

In Vietnam, the COPD prevalence is ranging from 4.2% to 6.9% and is commonly undiagnosed. Due to poor medication adherence, many patients have been hospitalized for AECOPD, that occupy approximately 25% of beds in the respiratory wards of the hospitals.<sup>9</sup> In addition, the prevalence of atrial arrhythmias (AA), especially paroxysmal atrial fibrillation (paroxysmal AF) in admitted AECOPD has not been evaluated. Thus, this study aimed to investigate the proportion and risk factors of AA and paroxysmal AF in AECOPD patients in Vietnam.

## Materials and Methods

### Study Setting

This prospective observational, multi-center-based study was performed at the 2 big hospitals in Hanoi, Vietnam from January 2022 to January 2023.

### Study Participants and Sampling Methods

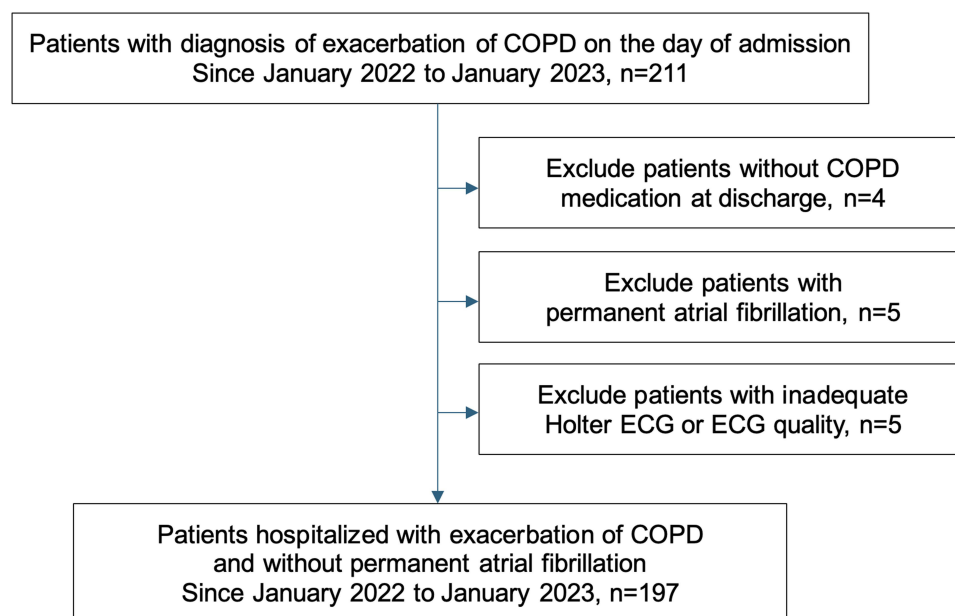
A convenient sample of 197 patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) without permanent atrial fibrillation (AF) was recruited. All patients who met the inclusion criteria were enrolled in the study. Patient selection is illustrated in a flowchart (Figure 1).

### Inclusion Criteria

Patients who were diagnosed with AECOPD were included in the present study. The diagnostic criteria of AECOPD were the presence of dyspnea and/or cough and sputum that worsen over  $\leq 14$  days, which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insult to the airways.<sup>10</sup>

### Exclusion Criteria

Patients who met one of the following criteria were excluded from the study: patient’s preference not to participate in research studies, patients with a history of permanent AF.



**Figure 1** Flow chart identifies the number of patients and study design.  
**Abbreviation:** COPD, chronic obstructive pulmonary disease.

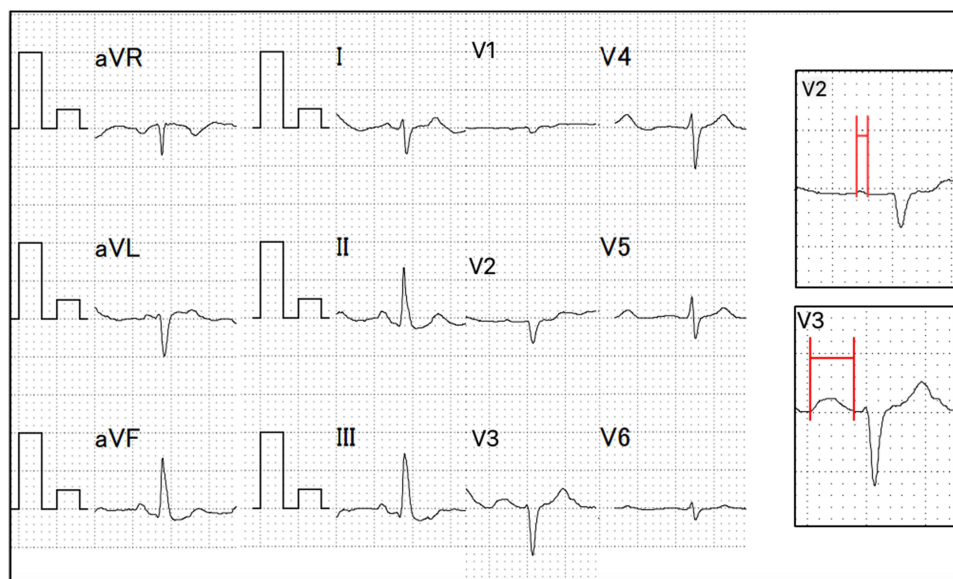
## Study Questionnaire

The approximate 30 minutes long questionnaire consisted of four sections: demographic characteristics, health status, medications, laboratory tests.

The first section collected information on participants' socio-demographic characteristics including their age, sex, address, date of admission. The second section was the information about participants' health status included their history of smoking or drinking, symptoms of COPD or arrhythmias, recent spirometry results, history of prior exacerbations of COPD, medical history hypertension, heart failure, coronary artery disease, heart failure, chronic kidney disease, diabetes, stroke, and other chronic diseases. Treatment method was the third section which included current medication or medication used within one month before hospitalization, ventilation and the treatment of COPD and any other comorbidities. And the final section was the laboratory tests, including 12-lead electrocardiography, 24h Holter ECG, transthoracic echocardiography, arterial blood gas test and other blood tests performed during hospitalization. Patients who lost spirometry results would be asked to perform the test at the clinic when they come back for an examination.

A resting electrocardiogram (ECG) (Nihon Kohden, Japan) was recorded on the day of hospitalization. Other resting ECGs could be obtained during hospitalization if there was any new-onset arrhythmia was suspected. The surface ECG was recorded after the patients had rested in spine position for at least 15 minutes in a comfortable room with suitable temperature and light. The ECG records were converted and stored in digital Portable Document Format (PDF). The 24h Holter ECG was recorded within the first 3 days of hospitalization using 24h Holter device (DigiTrak XT, Philips Medical System, USA) and was then analyzed automatically using application Zymed Algorithm for Holter analysis (DigiTrak XT, Philips Medical System, USA) (Philips Medical System, USA). All the ECG and 24h Holter ECG results were then re-evaluated and discussed by 2 physicians who had qualified in ECG and Holter ECG analysis to get conclusion.

In this study, PWD was calculated by the difference between Pmax and Pmin, which were identified by the P waves with longest and shortest durations in all leads of the standard surface ECG during sinus rhythm (Figure 2). Every participant in the study has at least one relevant ECG for analysis. The P-wave durations were measured on digital records of surface ECGs using magnification and measurement tools provided by PDF reader applications (Foxit Reader, Foxit Software Inc., China) on high-resolution computer screens. The start and the end of the P wave are marked with the cursor. The P-wave onset was defined as the point of the first detectable upward or downward slope from the isoelectric



**Figure 2** Example of P wave dispersion measurement. Twelve-lead surface ECG from a 63-year-old woman with paroxysmal atrial fibrillation. Maximum and minimum P-wave duration were found to be 151 ms in lead V3 and 62 ms in lead V2, respectively. P-wave dispersion was 89 ms.

line for positive or negative waveforms, respectively. The end of the P-wave was when it returned to the isoelectric line. ECGs with  $\leq 9$  measurable leads were excluded from the analysis.

### Data Collection Activities

The informed consent form was directly sent to the patients who were admitted because of acute exacerbation of COPD. If they agree to participate in the study, ECG Holter will be recorded during their first 3 days of hospitalization. If there were any new symptoms of arrhythmias later during the hospitalization, another ECG or Holter ECG would be obtained. Study questionnaires were completed by physician based on the answers of participants and case report form.

### Study Outcomes

The primary study outcomes were paroxysmal AF and atrial arrhythmias (AA) and status. The arrhythmias were collected from ECG and 24h Holter ECG and classified as follows: Atrial tachycardia (AT) is considered when there is a sequence of three or more supraventricular beats at a rate greater than 100 beats per minute (bpm).<sup>11</sup> Multifocal atrial tachycardia (MAT) is considered when there is an AT with at least 3 different P wave morphology and variable PP, PR, and RR interval.<sup>12</sup> Premature atrial complex (PAC) was considered to be significant if there are more than 500 PACs per day.<sup>13</sup> Atrial arrhythmias (AA) were considered if there were more than 500 PACs per day or if there was any AT, MAT or paroxysmal AF or a combination of those. The diagnosis of paroxysmal AF was made if AF was present in the ECG and/or 24h Holter ECG in patients without permanent AF. (Figures 3 and 4).

### Data Analysis

Continuous variables are expressed as mean (standard deviations). Categorical data are presented as frequencies and percentages. To examine differences in the characteristics of the study population according to arrhythmias, paroxysmal AF (Yes vs None) and AA status (Yes vs None), the *t*-test or Mann–Whitney *U*-test was used for continuous variables and Chi-square tests or Fisher’s exact tests for categorical variables.

To examine factors potentially associated with paroxysmal AF and AA status, we carried out a series of unadjusted and adjusted logistic models. Factors associated with paroxysmal AF or AA included demographic characteristics, health status, medications, and laboratory test. Factors that yielded a cut point of  $p < 0.2$  in univariate analysis were included in

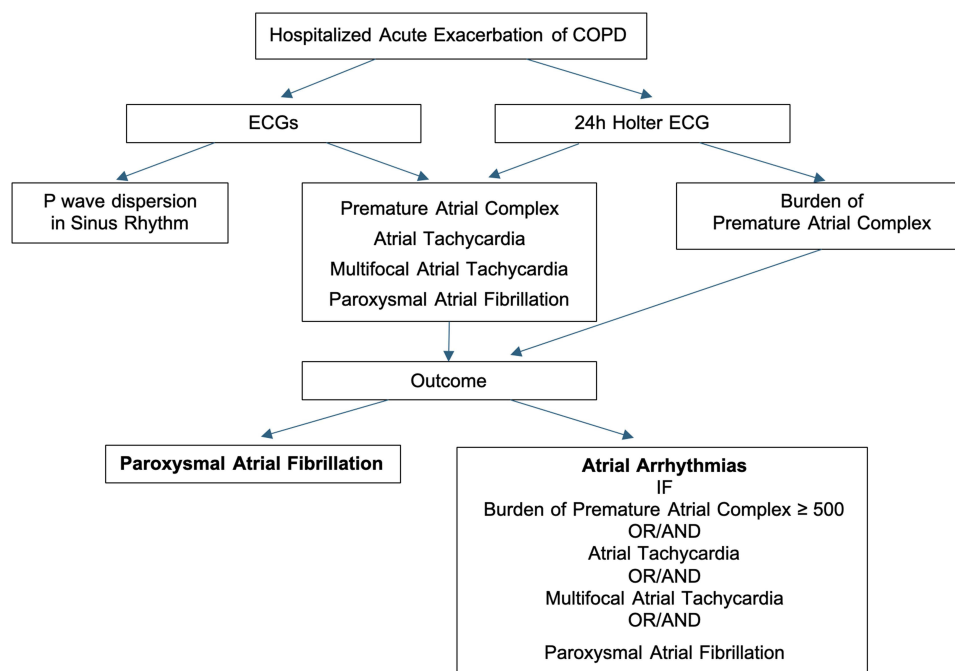
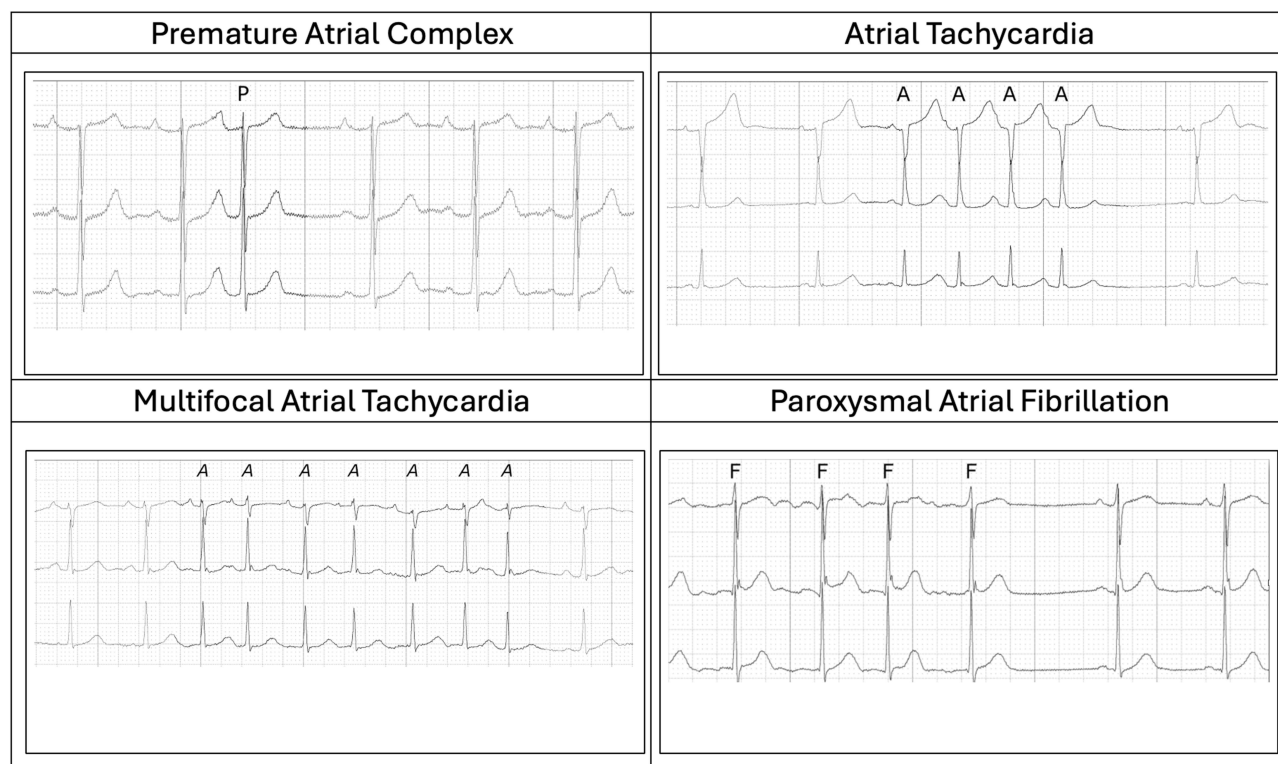


Figure 3 Diagnosis process based on ECG and Holter ECG.



**Figure 4** Classification of Atrial Arrhythmias in this study.

the multivariable models. A backward elimination process was conducted to select the final models, which included only factors with a  $p$  value  $<0.05$ . Data were imported using Epicollect 5 and analyzed using the R program. Statistical significance was set at a  $p$  value level of  $<0.05$ .

## Results

### Study Population Characteristics According to Paroxysmal Atrial Fibrillation and Atrial Arrhythmias

There is a total of 197 patients had participated in our study. The prevalence of paroxysmal AF and AA were 15.2% and 72.6%, respectively (Table 1). Nearly 90% of them were male and the average age of the study population was 74.3 years old (Table 2). Individuals who had paroxysmal AF or AA were more likely to report higher mean age and greater percentage in group 75-year-old and above than those who did not. For medicine history, survey respondents who identify as being paroxysmal AF had a higher prevalence of using LABA. There were no differences in selected medical history among those who had paroxysmal AF or AA compared with those who were not.

Furthermore, individuals who had paroxysmal AF or AA exhibited a significantly higher average of CRP and PWD, in comparison with those who were not diagnosed such concerns. Moreover, individuals who were in paroxysmal AF or AA group demonstrated a significantly higher likelihood of PAC with 500 or more occurrences per day. In addition, patients with paroxysmal AF had a higher percentage of severe COPD in groups compared to those without AF.

### Factors Associated with Paroxysmal Atrial Fibrillation and Atrial Arrhythmias

In the multi-variable model, individuals who aged 75 years old and above exhibited a higher likelihood of having paroxysmal AF compared to those who were younger (Table 3). Additionally, those who had PAC with 500 or more expressed greater concerns about having paroxysmal AF compared to those without such concerns. Furthermore, individuals with the severity of COPD as group C and D were more likely to have paroxysmal AF compared to their counterparts.

**Table 1** The Characteristics and Prevalence of Arrhythmias on ECG and 24h Holter ECG

Characteristics	Value (n=197) - n (%)
Average heart rate on ECG- Mean (SD) (Min-Max)	101 (19) (61–157)
Average heart rate on 24h Holter ECG - Mean (SD) (Min-Max)	96 (12) (65–124)
Atrial arrhythmias	143 (72.59%)
Paroxysmal atrial fibrillation	30 (15.23%)
Paroxysmal atrial fibrillation on ECG	6 (3.05)
Multifocal atrial tachycardia	62 (31.47%)
Atrial tachycardia	78 (39.59%)
Premature atrial complex	191 (96.95%)
Premature atrial complex >100 beat/24 hours	150 (76.14%)
Premature atrial complex >500 beat/ 24 hours	98 (49.75%)
P wave dispersion - Mean (SD)	41 (11)

**Table 2** Study Population Characteristics According to Paroxysmal Atrial Fibrillation (Paroxysmal AF) and Atrial Arrhythmias (AA) Status

Characteristics n (%)	Total (n=197)	Paroxysmal AF		p-value	Atrial Arrhythmias		p-value
		Yes (n=30)	None (n=167)		Yes (n=143)	None (n=54)	
<b>Sex</b>							
Male	175 (88.8)	25 (83.3)	150 (89.8)	0.47	128 (89.5)	47 (87.0)	0.81
Female	22 (11.2)	5 (16.7)	17 (10.2)		15 (10.5)	7 (13.0)	
<b>Age</b>							
Mean (SD)	74.3 (9.40)	79.5 (8.74)	73.4 (9.23)	0.001	75.7 (9.58)	70.9 (7.96)	<0.001
Under 75 years old	98 (49.7)	8 (26.7)	90 (53.9)	0.011	63 (44.1)	35 (64.8)	0.015
75 years old and above	99 (50.3)	22 (73.3)	77 (46.1)		80 (55.9)	19 (35.2)	
<b>COPD treatment</b>							
SAMA	82 (41.6)	15 (50.0)	67 (40.1)	0.42	63 (44.1)	19 (35.2)	0.34
LAMA	149 (75.6)	19 (63.3)	130 (77.8)	0.14	105 (73.4)	44 (81.5)	0.32
SABA	197 (100)	30 (100)	167 (100)	NA	143 (100)	54 (100)	NA
LABA	148 (75.1)	17 (56.7)	131 (78.4)	0.021	106 (74.1)	42 (77.8)	0.73
ICS	183 (92.9)	29 (96.7)	154 (92.2)	0.70 *	134 (93.7)	49 (90.7)	0.54 *
Corticosteroid	126 (64.0)	20 (66.7)	106 (63.5)	0.90	92 (64.3)	34 (63.0)	0.99

(Continued)

Table 2 (Continued).

Characteristics n (%)	Total	Paroxysmal AF		p-value	Atrial Arrhythmias		p-value
		Yes	None		Yes	None	
	(n=197)	(n=30)	(n=167)	(n=143)	(n=54)		
<b>Noninvasive ventilation</b>	92 (46.7)	12 (40.0)	80 (47.9)	0.55	70 (49.0)	22 (40.7)	0.38
<b>Invasive ventilation</b>	13 (6.6)	2 (6.7)	11 (6.6)	0.99 *	12 (8.4)	1 (1.9)	0.12 *
<b>Medical history</b>							
Smoking	115 (58.4)	17 (56.7)	98 (58.7)	0.99	88 (61.5)	27 (50.0)	0.19
Hypertension	101 (51.3)	20 (66.7)	81 (48.5)	0.10	76 (53.1)	25 (46.3)	0.49
Heart failure	23 (11.7)	5 (16.7)	18 (10.8)	0.36 *	19 (13.3)	4 (7.4)	0.33 *
Diabetes	41 (20.8)	4 (13.3)	37 (22.2)	0.39	25 (17.5)	16 (29.6)	0.09
Coronary artery disease	24 (12.2)	5 (16.7)	19 (11.4)	0.61	18 (12.6)	6 (11.1)	0.99 *
Chronic kidney disease	23 (11.7)	5 (16.7)	18 (10.8)	0.54	19 (13.3)	4 (7.4)	0.33 *
<b>Laboratory test</b>							
<b>CRP (mg/dl)</b>							
Mean (SD)	6.05 (8.13)	10.60 (10.60)	5.24 (7.34)	0.013	6.84 (8.85)	3.97 (5.31)	0.006
< 5	125 (63.5)	15 (50.0)	110 (65.9)	0.15	87 (60.8)	38 (70.4)	0.28
≥ 5	72 (36.5)	15 (50.0)	57 (34.1)		56 (39.2)	16 (29.6)	
<b>PaO<sub>2</sub> ≤ 60 mmHg</b>	10 (5.1)	3 (10.0)	7 (4.2)	0.18 *	8 (5.6)	2 (3.7)	0.73 *
<b>PaCO<sub>2</sub> ≥ 40 mmHg</b>	73 (37.1)	10 (33.3)	63 (37.7)	0.80	48 (33.6)	25 (46.3)	0.14
<b>Severity of COPD</b>							
Group A + B	73 (37.1)	6 (20.0)	67 (40.1)	0.041 *	53 (37.1)	20 (37.0)	0.99
Group C + D	124 (62.9)	24 (80.0)	100 (59.9)		90 (62.9)	34 (63.0)	
<b>ECG and Holter</b>							
<b>PWD (ms)</b>							
Mean (SD)	41.8 (11.4)	58.4 (11.8)	38.8 (8.44)	<0.001	43.6 (12.1)	37.0 (7.79)	<0.001
< 40	95 (48.2)	9 (30.0)	86 (51.5)	0.049	59 (41.3)	36 (66.7)	0.003
≥ 40	102 (51.8)	21 (70.0)	81 (48.5)		84 (58.7)	18 (33.3)	
<b>PAC</b>	191 (97.0)	27 (90.0)	164 (98.2)	0.047 *	139 (97.2)	52 (96.3)	0.67 *
<b>PAC &gt;100/24h</b>	150 (76.1)	25 (83.3)	125 (74.9)	0.44	130 (90.9)	20 (37.0)	<0.001
<b>PAC &gt;500/24h</b>	98 (49.7)	23 (76.7)	75 (44.9)	0.003	98 (68.5)	0 (0)	<0.001 *

Note: \*Fisher's Exact test.

Abbreviations: SAMA, Short-Acting Muscarinic-Antagonists; LAMA, Long-Acting Muscarinic-Antagonists; SABA: Short-Acting Beta2-Agonists; LABA, Long-Acting Beta2-Agonists; ICS, Inhale Corticosteroid; CRP, C reactive protein; PWD, P wave dispersion; PAC, Premature atrial complex; PaO<sub>2</sub>, Partial Pressure of Oxygen; PaCO<sub>2</sub>, Partial pressure of arterial Carbon Dioxide.

Smoking patients and those aged 75 years old and above were high likely to have AA as compared to their counterparts (Table 4). In addition, patients who had a PWD of 40ms and above linked to a higher likelihood of being diagnosed with AA.

**Table 3** Factors Associated with Paroxysmal Atrial Fibrillation

Predictors	Uni-variable Model		Multi-Variable Model	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value
<b>Age</b>				
< 75 years old	1.00	0.008	1.00	0.016
75 years old and above	3.21 (1.40 to 8.07)		3.15 (1.28 to 8.48)	
<b>Hypertension</b>				
No	1.00	0.07	1.00	0.053
Yes	2.12 (0.96 to 4.99)		2.50 (1.01 to 6.62)	
<b>Heart failure</b>				
No	1.00	0.36	1.00	0.12
Yes	1.66 (0.51 to 4.60)		2.81 (0.73 to 10.02)	
<b>CRP (mg/dl)</b>				
< 5	1.00	0.10	1.00	0.06
≥ 5	1.93 (0.88 to 4.26)		2.30 (0.95 to 5.66)	
<b>PWD (ms)</b>				
< 40	1.00	0.034	1.00	0.08
≥ 40	2.48 (1.10 to 5.99)		2.32 (0.92 to 6.29)	
<b>PAC &gt;500/24h</b>				
No	1.00	0.002	1.00	0.008
Yes	4.03 (1.72 to 10.63)		3.81 (1.48 to 10.97)	
<b>Severity of COPD</b>				
Group A + B	1.00	0.041	1.00	0.020
Group C+ D	2.68 (1.10 to 7.55)		3.41 (1.28 to 10.50)	

**Abbreviations:** cOR, Crude Odds Ratio; aOR, Adjusted Odds Ratio; CI, Confidence Interval; CRP, C reactive protein; PWD, P wave dispersion; PAC, Premature atrial complex.

**Table 4** Factors Associated with Atrial Arrhythmias

Predictors	Uni-Variable Model		Multi-Variable Model	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value
<b>Age</b>				
< 75 years old	1.00	0.01	1.00	0.008
75 years old and above	2.34 (1.23 to 4.54)		2.55 (1.28 to 5.20)	
<b>Smoking</b>				
No	1.00	0.14	1.00	0.034
Yes	1.6 (0.85 to 3.02)		2.1 (1.07 to 4.23)	

(Continued)



**Table 4** (Continued).

Predictors	Uni-Variable Model		Multi-Variable Model	
	cOR (95% CI)	p-value	aOR (95% CI)	p-value
<b>Noninvasive ventilation</b>				
No	1.00	0.30	1.00	0.15
Yes	1.39 (0.74 to 2.65)		1.65 (0.84 to 3.32)	
<b>PWD (ms)</b>				
< 40	1.00	0.002	1.00	0.002
≥ 40	2.85 (1.49 to 5.58)		3.04 (1.54 to 6.19)	

**Abbreviations:** cOR, Crude Odds Ratio; aOR, Adjusted Odds Ratio; CI, Confidence Interval; PWD, P wave dispersion.

## Discussion

Our study aimed to investigate the prevalence and risk factors for paroxysmal AF and AA in patients hospitalized for AECOPD in Vietnam. The results revealed a significant prevalence of both AF and AA among these patients. Additionally, our study identified several key factors associated with the occurrence of paroxysmal AF and AA in the context of AECOPD. These findings highlight the complexity of the relationship between AECOPD and arrhythmias and suggest that there are many aspects of our results that warrant further discussion and exploration.

In our study, aging at 75 years old or above was associated with both paroxysmal AF and AA. As nearly half of the participated patients were in this age group, this underscored the necessity for early diagnosis of arrhythmias and other diseases in them. Most of the COPD patients are elderly. As age increases, the prevalence of COPD patients also rises.<sup>14</sup> On the other hand, elderly patients tend to have more severe COPD and also have a higher risk of arrhythmia. A 2019 study in the USA, which analyzed data from the National Inpatient Sample (NIS) spanning 2010 to 2014, found that adults hospitalized with COPD had a 3.3 times higher risk of developing arrhythmias, including atrial fibrillation (AF), if they were aged 65 or older compared to those aged 18–44.<sup>15</sup> Furthermore, patients aged 75 years old and above were considered a risk factor in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score – that not only shows the effectiveness of risk stratification in systemic embolism in AF but also in predicting the risk of new-onset atrial fibrillation.<sup>16,17</sup>

The presence of PAC greater than 500 in 24h was associated with a higher likelihood of paroxysmal AF. A systematic review conducted by researchers from UK in 2023 reported similar findings.<sup>18</sup> The authors demonstrated that PAC greater than 500 in 24h was associated with a higher risk of AF, stroke, heart failure and mortality. Recently, a consensus from the European Heart Rhythm Association, Heart Rhythm Society and several major Rhythm Societies set a threshold of 500 PAC or more within 24 hours as clinically significant.<sup>19</sup>

Our findings indicated a significant association between COPD groups C or D and paroxysmal AF. The severity of COPD correlated with the frequency of arrhythmias, with patients experiencing more severe respiratory impairment being at a higher risk of arrhythmias, including ventricular arrhythmias and AA, particularly AF.<sup>20,21</sup> Additionally, a study in Turkey reported that AF was more common in COPD patients with a higher number of disease attacks and/or hospitalization (COPD group C+D).<sup>22</sup> These findings highlight the importance of monitoring cardiac health in COPD patients, especially those with advanced stages of the disease. Early detection and management of arrhythmias in these patients can potentially improve their overall prognosis and quality of life. Furthermore, integrating cardiovascular risk assessment into the routine care of COPD patients may help in reducing the burden of comorbidities and healthcare costs associated with these conditions.

Our study revealed that smoking patients were significantly more likely to develop AA compared to non-smoking counterparts. This finding aligns with the results of a 2020 study conducted in Korea, which involved 201,788 participants (106,375 men, mean age 37 years) who had both urinary cotinine measurements and electrocardiograms.<sup>23</sup> Authors reported that self-reported current smoking was associated with a 1.42 times higher risk of AA. Smoking

increases oxidative stress, systemic inflammation, and autonomic dysfunction, contributing to arrhythmogenesis.<sup>24</sup> Nicotine and other harmful substances in tobacco smoke led to reactive oxygen species formation, causing cellular damage and atrial remodeling. Smoking also impairs heart autonomic regulation, increasing sympathetic activity and reducing parasympathetic tone, further elevating AA risk. These findings underscore the importance of smoking cessation programs in managing patients at risk of AA, particularly those with comorbidities like COPD. Healthcare providers should integrate smoking status into arrhythmia risk assessments and offer tailored interventions, including smoking cessation support and regular cardiac monitoring, to improve outcomes for this high-risk group.

In our study, multi-variable model showed that patients with increasing PWD had a significantly higher chance of having AA than those without and exhibited a tendency toward having paroxysmal AF. Increased PWD, which reflects the inhomogeneous propagation of atrial depolarization, has been reported as a predictor for the development of AF in different patient groups such as hypertension, after coronary artery bypass grafting, valvular heart diseases, heart failure, and some other clinical conditions.<sup>25</sup> Furthermore, that index has been found to be greater in COPD patients and was significantly associated with the presence of AF. A review in 2016 demonstrated the cut-off value of 40 ms was proved to have a sensitivity of 83%, a specificity of 85% for the identification of patients with a history of paroxysmal lone AF.<sup>25</sup> Another study found that PWD was greater during acute exacerbation than during the stable phase in 30 patients hospitalized for AECOPD.<sup>26</sup>

The strength of our study lies in being the first multi-center study in Vietnam to reveal the burden and associated factors of atrial arrhythmias, particularly paroxysmal atrial fibrillation, in AECOPD. Given the low prevalence of arrhythmias detected on the ECG alone, it is advisable to conduct a Holter ECG in patients with one or more of the aforementioned risk factors. A discussion with cardiologist would be conducted if there were any significant arrhythmias.

However, the study has some limitations. Although our study included patients from various provinces in northern Vietnam who visited selected hospitals for examination and treatment, we used a convenient sample size, which may limit the generalizability of our findings. Nonetheless, the study was conducted during the COVID-19 pandemic, which imposed significant restrictions. Many patients with symptoms of COPD exacerbation were unable to travel to our facilities and had to remain in local hospitals. Additionally, patients admitted with acute exacerbation of COPD who tested positive for COVID-19 were transferred to specialized COVID-19 centers, resulting in a lower-than-expected number of participants. Furthermore, many patients had lost their previous spirometry results, preventing us from drawing definitive conclusions about the role of pulmonary function in the occurrence of arrhythmias. The relatively small sample size may also have limited our ability to detect the impact of common risk factors for paroxysmal AF, such as heart failure, CAD, or CKD. Lastly, this study focused specifically on patients with AECOPD; a larger study comparing these findings with those in stable COPD or non-COPD patients would help contextualize the results in broader clinical settings. Additionally, follow-up research is necessary to assess the impact of these arrhythmias on patients' symptoms, quality of life, treatment outcomes, and prognosis.

## Conclusion

Overall, our findings highlight the complex interplay of demographic, clinical, and biochemical factors in the development of paroxysmal AF and AA among AECOPD patients. This underscores the importance of a multifaceted approach to risk assessment and management in this vulnerable population, focusing not only on respiratory symptoms but also on comprehensive cardiovascular evaluation and intervention.

## Data Sharing Statement

The data in this research is unavailable to access because research data includes patient data which is sensitive and confidential information.

## Ethical Approval

This study was approved by the Ethical Committee of Hanoi Medical University (No:480/GCN-HĐĐĐNCYSH-ĐHYHN). All human research procedures followed the committee's ethical standards responsible for human

experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2013. Informed consent was obtained from all the participants.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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