ORIGINAL ARTICLE

Prevalence and Affecting Factors of Arrhythmias in Stable Chronic Obstructive Pulmonary Disease at a Tertiary Hospital in Indonesia

Achmad Gozali[1], Muhammad Bimo Adi Wicaksono[1]*, Faisal Yunus[1], Ratnawati Ratnawati[1], Muhammad Abbas Basalamah[1], Bagus Radityo Amien[2]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia/Persahabatan National Respiratory Referral Hospital, Jakarta, Indonesia.
[2]Department of Respiratory Medicine, Juntendo University, Tokyo, Japan.

ARTICLE INFO

Article history:
Received 12 January 2025
Received in revised form
25 March 2025
Accepted 23 April 2025
Available online 30 May 2025

Keywords:
Arrythmia,
Cardiovascular diseases,
Chronic respiratory diseases,
Chronic obstructive pulmonary disease (COPD).

Cite this as:
Gozali A, Wicaksono MBA, Yunus F, *et al.* Prevalence and Affecting Factors of Arrhythmias in Stable Chronic Obstructive Pulmonary Disease at a Tertiary Hospital in Indonesia. *J Respi* 2025; 11: 131-139.

ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) represents an increasing global health burden. Among its significant comorbidities, cardiovascular complications, particularly arrhythmias, are of significant concern. Chronic obstructive pulmonary disease and arrhythmias share common risk factors, including advanced age and smoking. This study investigated the prevalence and contributing factors of arrhythmias in stable COPD patients.
Methods: This cross-sectional study was conducted among stable COPD patients attending the Asthma-COPD Clinic at Persahabatan National Respiratory Referral Hospital, Jakarta, Indonesia, from January to April 2018. The inclusion criteria encompassed a clinical diagnosis of COPD and voluntary participation with written informed consent. Each participant underwent laboratory evaluation, electrocardiography (ECG), blood pressure measurement, and a structured interview. Patients were excluded if they had experienced acute COPD exacerbations during the assessment, had a history of other chronic lung diseases, suffered a recent myocardial infarction, had structural heart disease, were diagnosed with fibrillation, or declined to participate.
Results: The prevalence of arrhythmias in stable COPD patients was 24.1%. The types included sinus bradycardia (2.41%), premature atrial contractions/PACs (3.61%), premature ventricular contractions/PVCs (8.43%), and sinus tachycardia (9.64%). Most arrhythmic patients were males, with an average age of 68 years old. These patients also had a history of heart disease, exhibited severe COPD symptoms, and demonstrated significant airflow obstruction (average pCO_2 of 36 mmHg).
Conclusion: Decreased chloride levels were associated with an increased incidence of arrhythmias. However, no significant associations were observed with airflow limitation, sex, age, bronchodilator use, or arterial blood gas parameters.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) presents a significant public health challenge, yet it is both preventable and treatable. The burden of COPD continues to rise worldwide. It has become one of the top three leading causes of death globally, with 90% of these fatalities occurring in low- and middle-income countries.[1] Comorbid chronic diseases are frequently observed in COPD patients, among which cardiac arrhythmias are common and bidirectional, and a systematic review found that COPD is associated with an increased risk of sudden cardiac deaths (SCDs).[2] There are notable similarities in the risk factors associated with both COPD and arrhythmias, including advanced age and smoking. Additionally, arrhythmias can be triggered by several comorbidities, such as coronary heart disease, hypertensive heart disease (HHD), right and/or left heart failure, hypokalemia, hypomagnesemia, and the use of digoxin, as well as

*Corresponding author: bimo.adimuhammad@gmail.com

Jurnal Respirasi (Journal of Respirology), p-ISSN: 2407-0831; e-ISSN: 2621-8372.
Accredited No. 79/E/KPT/2023; Available at https://e-journal.unair.ac.id/JR. DOI: 10.20473/jr.v11-I.2.2025.131-139
This work is licensed under a Creative Commons Attribution-Share Alike 4.0 International License.

macrolide antibiotics. The arrhythmias induced by bronchodilator medications have garnered significant attention, and important warnings have been issued regarding the administration of these drugs, as they can pose life-threatening risks.[3]

Atrial fibrillation (AF) is the most prevalent form of cardiac arrhythmia, with its occurrence increasing with age, affecting 2-5% of individuals over 60 years old and exceeding 17% in those aged 80-89 years old.[4] A study conducted by Konecny, *et al*. (2014) demonstrated that COPD and its severity are associated with a higher likelihood of AF/atrial flutter (23% vs. 11%, p<0.001), nonsustained ventricular tachycardia/NSVT (13% vs. 5.9%, p<0.001), and sustained ventricular tachycardia/VT (1.6% vs. 0.9%, p<0.001) compared to individuals without COPD.[5] No studies have been conducted in Indonesia on the prevalence of arrhythmias in COPD patients. Therefore, this study aimed to investigate the prevalence of arrhythmias in stable COPD patients and the factors that influence them.

METHODS

Study Design

This cross-sectional observational study was conducted at Persahabatan National Respiratory Referral Hospital, Jakarta, Indonesia, from January to April 2018.

Study Population and Inclusion Criteria

Participants were selected based on the diagnosis of COPD. The diagnosis of COPD was confirmed using spirometry according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) <0.7 post-bronchodilator) and/or verified International Classification of Diseases, 10th Revision (ICD-10) coding (J44.x) in medical records. Inclusion criteria included patients aged ≥40 years old with stable COPD.

Exclusion Criteria

Exclusion criteria included patients experiencing acute exacerbations of COPD at the time of evaluation, those with a history of other chronic pulmonary diseases (such as interstitial lung disease or pulmonary fibrosis), individuals who had a recent myocardial infarction (within the past three months), patients with known structural heart disease, those with AF, and patients who declined to participate.

Chronic Obstructive Pulmonary Disease Grouping and Obesity Criteria

According to spirometry results, patients were categorized based on the GOLD classification into GOLD 1-4. Obesity was defined using the World Health Organization (WHO) classification, with body mass index (BMI) ≥30 kg/m² considered obese.

Data Collection and Study Variables

Demographic data, comorbidities, and clinical characteristics were recorded. The variables included:

1. Electrocardiogram (ECG) assessment: A standard 12-lead ECG was supine. The ECG recordings were analyzed by cardiologists.
2. Arrhythmia classification: Arrhythmia was classified based on ECG findings into different types, including:
   a. Premature atrial contractions (PACs) were defined as early P waves with abnormal morphology and a non-compensatory pause.
   b. Premature ventricular contractions (PVCs) were characterized by vast QRS complexes that occurred prematurely without a preceding P wave.
   c. The detected abnormalities were also recorded, including AF, atrial flutter, and ventricular tachycardia.

Statistical Analysis

Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) version 24. Continuous variables were reported as mean±standard deviation (SD) and analyzed with Student's t-test or Mann-Whitney U test, depending on normality. Categorical variables were presented as frequencies and percentages and analyzed using the chi-square test or Fisher's exact test as appropriate. A p-value <0.05 was deemed statistically significant.

Ethics Statement

This study was reviewed and approved by the Ethics Committee of Health Research at the Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia (No.971/UN2.F1/ETIK/2017) and the Ethics Committee of Health Research at Persahabatan National Respiratory Referral, Jakarta, Indonesia (No.04/KEPK-RSUPP/01/2018). Written informed consent was obtained from all participants. This study adheres to the principles outlined in the Helsinki Declaration.

RESULTS

A total of 93 patients met the inclusion and exclusion criteria. However, ten patients were excluded due to their failure to return for laboratory testing, with most cases attributed to disease exacerbations that required hospitalization. Consequently, the final study population comprised 83 patients who met the eligibility criteria.

Characteristics of Participants

The mean age of the study participants was 66.58 years old, with the youngest being 56 years old and the oldest 82 years old. The mean body weight was 54.89 kg, and the median height was 162 cm. According to BMI classification, most participants were within the normal range (33.7%) or underweight (30.1%), while 19% were pre-obese and 13.3% obese. The mean COPD Assessment Test (CAT) score was 14.02 points, and the median modified Medical Research Council (mMRC) score was 2 points. The median annual exacerbation frequency was one episode per year, although some participants experienced up to seven exacerbations annually.

According to the 2017 GOLD classification, 50.6% of participants exhibited GOLD 3 airflow limitation. Arrhythmias were identified in 20 patients (24.1%), with the following distribution: sinus tachycardia in 8 patients (9.64%), PVCs in 7 patients (8.43%), PACs in 3 patients (3.61%), and sinus bradycardia in 2 patients (2.41%). Other notable electrocardiographic findings included abnormal T waves (27.7%), left atrial enlargement (25.3%), and left-axis deviation (19.3%). The detailed characteristics of the study population are presented in Table 1.

Comparison of Clinical Characteristics

The incidence of arrhythmias in COPD patients, according to the GOLD obstruction criteria, did not reach statistical significance. However, it appeared to be higher in GOLD stage 4 patients (46.2%) compared to those in GOLD stage 1 and 2 (14.3%) and GOLD stage 3 (23.8%). Chronic obstructive pulmonary disease was classified based on exacerbation history into two groups: group A+B (no or one non-hospitalized exacerbation) and group C+D (one hospitalized or multiple exacerbations in the past year). No significant association was found between exacerbations and arrhythmia ($p=0.081$), although arrhythmias were more prevalent in Group C+D (31.8%). Additionally, COPD was categorized by symptom severity (mild: A+C, severe: B+D), with no significant association observed between symptom severity and arrhythmias ($p>0.05$).

This study identified arrhythmias in 20 male participants (25.3%), while no cases were observed among female participants. Only one participant received treatment with a combination of long-acting β-agonists and inhaled corticosteroids (LABA+ICS). The most commonly prescribed medication regimens were long-acting muscarinic antagonists combined with LABA+ICS and short-acting β-agonists (LAMA+LABACS+SABA) at 48.2%, and LAMA combined with LABA and SABA (LAMA+LABA+SABA) at 24.1%. No significant association was found between gender or the use of COPD medications and the occurrence of arrhythmias. Furthermore, a history of heart disease, the Brinkman index, and BMI did not demonstrate a significant correlation with arrhythmias ($p>0.05$). A comparison of clinical characteristics between patients with and without arrhythmias is presented in Table 2.

The Relationship between Age and Laboratory Parameters with the Incidence of Arrhythmia

The mean chloride level was lower in the arrhythmic group than in the non-arrhythmic group, with a mean difference of 3.132. A significant association was observed between chloride levels and the incidence of arrhythmias ($p=0.028$). However, no similar association was found for other electrolytes, including sodium, potassium, magnesium, and calcium. Additionally, no significant correlation was identified between age or C-reactive protein (CRP) levels and the occurrence of arrhythmias ($p>0.05$). Blood gas analysis also revealed no significant relationship between partial pressure of carbon dioxide (pCO_2), partial pressure of oxygen (pO_2), or the combination of hypoxemia and hypercapnia with the incidence of arrhythmias in COPD patients. These findings are summarized in Table 3.

Table 1. Characteristics of participants

Variable	Result (n=83)
Sociodemographic characteristics	
Age [years; n (%)]	66.58±9.1
Gender [n (%)]	
Male	79 (95.2)
Female	4 (4.8)
BMI [kg/m^2; mean±SD; n (%)]	20.78±3.9
Obesity type-2 (kg/m^2)	0 (0)
Obesity type-1 (25-29.9 kg/m^2)	11 (13.3)
Pre-obesity (23-24.9 kg/m^2)	19 (22.9)
Normal (18.5-22.9 kg/m^2)	28 (33.7)
Underweight (18.5 kg/m^2)	25 (30.1)
Clinical characteristics	
CAT score [mean±SD]	14.02±6.5
mMRC score [median (min-max)]	2 (0-4)
Frequency of exacerbation in a year [time; median (min-max)]	1 (0-7)
GOLD classification [n (%)]	
1	6 (7.2)
2	22 (26.5)
3	42 (50.6)
4	13 (15.7)
COPD group [n (%)]	
A	10 (12%)
B	29 (34.9%)
C	7 (8.4 %)
D	37 (44.6%)
Electrocardiographic characteristics	
Arrhythmia	20 (24.1)
Sinus bradycardia	2 (2.41)
Sinus tachycardia	8 (9.64)
PACs	3 (3.61)
PVCs	7 (8.43)
Right axis deviation	5 (6)
Left axis deviation	16 (19.3)
Right atrial enlargement	6 (7.2)
Left atrial enlargement	21 (25.3)
Right ventricular hypertrophy	3 (3.6)
Left ventricular hypertrophy	1 (1.2)
Right bundle branch block	1 (1.2)
Prolonged PR interval	2 (2.4)
Abnormal T wave	23 (27.7)
S_1-S_2-S_3 pattern	2 (2.4)

BMI: body mass index; SD: standard deviation; CAT: chronic obstructive pulmonary disease assessment test; mMRC: modified medical research council; GOLD: global initiative of chronic obstructive lung disease; COPD: chronic obstructive pulmonary disease; PACs: premature atrial contractions; PVCs: premature ventricular contractions

Multivariate Analysis

Based on the previous bivariate analysis, variables with a p<0.25 were included in the multivariate analysis. These variables included a history of heart disease, the COPD group, GOLD classification, chloride and magnesium levels, CRP, and CO_2 levels. As shown in Table 4, only chloride levels were significantly associated with the incidence of arrhythmias (p=0.011).

The odds of arrhythmias were 0.839 times lower in participants with a chloride level that was 1 mEq/L lower compared to those with higher chloride levels. The authors were 95% confident that if this study were to be repeated in the population, the odds ratio would fall within the range of 0.734 to 0.960.

According to the previously presented results, the logistic regression equation can be formulated as follows:

$$y=16.828-0.175\ [Cl(mEq/L]$$

With the predictive formula $p = \frac{1}{1+e^{-y}}$, the probability of a participant having an arrhythmia based on their chloride levels can be calculated.

Table 2. Comparison of clinical characteristics between patients with and without arrhythmia

Variable	Arrhythmia (n=20)	No Arrhythmia (n=63)	p-value
GOLD classification			
GOLD 1+2	4 (14.3%)	24 (85.7%)	
GOLD 3	10 (23.8%)	32 (76.2%)	0.085*
GOLD 4	6 (46.5%)	7 (53.8%)	
COPD group			
A+B	6 (15.4%)	33 (84.6%)	0.081*
C+D	14 (31.8%)	30 (68.2%)	
A+C	3 (17.6%)	14 (82.4%)	0.751
B+D	17 (25.8%)	49 (74.2%)	
Gender			
Male	20 (25.3%)	59 (74.7%)	0.568**
Female	0 (0%)	4 (100%)	
History of cardiovascular disease			
Yes	10 (34.5%)	19 (65.5%)	0.105
No	10 (18.5%)	44 (81.5%)	
COPD Medication			
LABACS yes	0 (0%)	1 (100%)	>0.999**
LABACS no	20 (24.4%)	62 (75.6%)	
LAMA+SABA yes	5 (27.8%)	13 (72.2%)	0.758*
LAMA+SABA no	15 (23.1%)	50 (76.9%)	
LABA+SABA yes	0 (0%)	1 (100%)	>0.999**
LABA+SABA no	20 (24.4%)	62 (75.6%)	
LABACS+SABA yes	0 (0%)	1 (100%)	>0.999**
LABACS+SABA no	20 (24.4%)	62 (75.6%)	
LAMA+LABA+SABA yes	6 (30%)	14 (70%)	0.551**
LAMA+SABA+SABA no	14 (22.2%)	49 (77.8%)	
LAMA+LABACS+SABA yes	8 (20%)	32 (80%)	0.400**
LAMA+LABACS+SABA no	12 (27.9%)	31 (72.1%)	

GOLD: global initiative of chronic obstructive lung disease; COPD: chronic obstructive pulmonary disease; LABACS: long-acting beta agonist combination with inhaled glucocorticosteroid; LAMA: long-acting muscarinic antagonist; SABA: short-acting β-agonist; LABA: long-acting β-agonist; *Chi-square test; **Fisher's exact test; §Four participants did not smoke (Brinkman index zero)

Table 3. Comparison of age and laboratory parameters between patients with and without arrhythmia

Variable	Arrhythmia	n	Mean±SD	Mean Difference	95% CI		Med (Min-Max)	p-value
					Min	Max		
Age	Yes	20	68.45±8.8	2.5	-2.19	7.12	68 (50-82)	0.295*
	No	63	65.98±9.2				65 (42-83)	
Natrium	Yes	20	137.25±4.05	-0.988	-2.42	0.44	138 (125-143)	0.358**
	No	63	138.24±2.28				139 (133-144)	
Kalium	Yes	20	3.95±0.55	-0.087	-0.32	0.15	3.95 (2.9-4.9)	0.472*
	No	63	4.04±0.44				4 (2.9-5.2)	
Chloride	Yes	20	100.9±5.76	-3.132	-5.22	-1.04	102 (84-108)	0.028**
	No	63	104.03±3.43				105 (95-112)	
Magnesium	Yes	20	2.11±0.21	0.045	-0.04	0.13	2.15 (1.6-2.4)	0.164**
	No	63	2.06±0.14				2 (1.8-2.5)	
Calcium	Yes	20	8.83±0.45	-0.086	-0.32	0.15	8.8 (8.1-9.6)	0.448**
	No	63	8.92±0.46				8.9 (8.1-10.1)	
CRP	Yes	20	1.95±2.89	1.086	0.20	1.97	0.945 (0.06-11)	0.243**
	No	63	0.86±1.15				0.5 (0-7.15)	
pH	Yes	20	7.44±0.03	0.007	-0.01	0.02	7.44 (7.38-7.50)	0.426*
	No	63	7.43±0.03				34.3 (22.7-42.3)	
pCO_2	Yes	20	36.28±4.9	1.97	-0.39	4.32	35.05 (26.4-46.2)	0.101*
	No	63	34.31±4.5				34.3 (22.7-42.3)	
pO_2	Yes	20	84.76±17.2	1.31	-7.63	10.25	82.15 (65.6-137.9)	0.807**
	No	63	83.45±17.6				82.1 (47.1-171.2)	0.295*
Hypoxemia and hypercapnia§								
Yes	Yes	1						0.241**
	No	0						
No	Yes	19						
	No	63						

SD: standard deviation; 95% CI: 95% confidence interval; Med: median; Min: minimum; Max: maxium; CRP: C-reactive protein; pCO_2: partial pressure of carbon dioxide; pO_2: partial pressure of oxygen; *Chi-square test; **Fisher's exact test; §Categorized as yes and no

Table 4. Multivariate analysis

Variable	B	SE	p-value	OR	95% CI	
					Min	Max
Chloride	-0.175	0.069	0.011	0.839	0.734	0.960
History of cardiovascular disease	0.868	0.554	0.117	2.382	0.804	7.051
Magnesium	2.562	1.628	0.116	12.966	0.533	315.191
GOLD 4	1.705	0.906	0.060	5.504	0.932	32.483
GOLD 3	0.874	0.738	0.236	2.396	0.564	10.176
CRP	0.216	0.184	0.240	1.242	0.865	1.782
Group C+D	0.510	0.658	0.438	1.665	0.459	6.045
pCO_2	-0.005	0.072	0.949	0.995	0.865	1.146
Constant	16.828	7.034	0.017	-	-	-

B: unstandardized beta; SE: standard error; OR: odds ratio; 95% CI: 95% confidence interval; Min: minimum; Max: maximum; GOLD: global initiative of chronic obstructive lung disease; CRP: C-reactive protein; pCO_2: partial pressure of carbon dioxide

DISCUSSION

The burden of COPD continues to rise globally. Severe airflow limitations associated with advanced stages of COPD lead to ventilation-perfusion mismatches. Consequently, hypoxemia, pulmonary vasoconstriction, vascular remodeling, right ventricular diastolic dysfunction, systemic inflammation, arterial stiffness, hypertension, and other cardiovascular conditions may develop.[6] In addition to affecting respiratory health, COPD is a systemic disease that impacts various organs and is associated with multiple comorbidities. The most common comorbidities in individuals with COPD include osteoporosis, diabetes, cardiovascular disease, lung cancer, metabolic syndrome, and depression.[7]

Based on ECG findings, this study revealed a 24.1% prevalence of arrhythmias in stable COPD patients. These results align with a previous study that reported an arrhythmia prevalence of approximately 21.1% among COPD patients.[8] Previous studies indicated prevalence rates of 15.9% and 12.6%.[9,10] In this study, the arrhythmia diagnosis was confirmed by two ECGs conducted with a minimum 24-hour interval between the first and second tests. Although COPD and arrhythmias are both chronic conditions that may influence one another, the cross-sectional design of this study limits the ability to establish a causal relationship.

The majority of participants in this study were males (95.2%). In Indonesia, the prevalence of COPD in males is three times higher than that in females.[11] According to a systematic review and meta-analysis by Al Wachami, *et al*. (2024), the prevalence of COPD was significantly higher in males than in females.[12] This is in line with this study, in which all 20 participants diagnosed with arrhythmia were males. However, the analysis revealed no significant correlation between gender and the presence of arrhythmia.

This study found that the mean age of COPD patients in the arrhythmic group was higher than that of the non-arrhythmic. Bivariate analysis revealed no significant association between age and the incidence of arrhythmias. Age is a known risk factor for COPD and other comorbidities, and the risk tends to increase with advancing age. This may explain the observation of an older mean age in the arrhythmic group, despite the lack of statistical significance.

Studies conducted by Shih, *et al*. (1988) found that inhaled β-agonists increased the risk of arrhythmias in COPD patients.[13] However, this study did not find a significant link between the use of COPD medications, whether individually or in combination with bronchodilators, and the occurrence of arrhythmias. These findings align with previous studies, which concluded that LABA therapy did not result in an increased incidence of arrhythmias among COPD patients and no association between the use of anticholinergics and a heightened risk of arrhythmias.[14,15]

Oxidative stress and inflammation play a central role in the pathogenic mechanisms of COPD. These same factors also contribute to the development of arrhythmias, including AF.[16] Although this study did not find a significant correlation between CRP levels and arrhythmia, a higher median CRP in the arrhythmic group was observed. Specifically, this study identified two patients with elevated CRP levels (>5 mg/L), with a median CRP of 0.945 mg/L (ranging from 0.06 to 11 mg/L). Mittal, *et al*. (2024) found that patients who developed arrhythmia exhibited significantly higher CRP levels.[17] This discrepancy may be attributed to the smaller sample size in this study.

The pathogenesis of arrhythmias in COPD patients is multifactorial, with a reduction in FEV1 identified as a significant risk factor. Zhang, *et al*. (2024) demonstrated that a decrease in FEV1 is an independent predictor of AF in COPD patients.[18] This study further indicated that the incidence of arrhythmias increased with the severity of airflow limitation, with arrhythmia occurrences of 46.2% in GOLD stage 4, 23.8% in GOLD stage 3, and 14.3% in GOLD stages 1 and 2. The non-significant findings in this study align with those of Dabadghao, *et al*. (2016), who also reported no significant relationship between the degree

of airflow obstruction and the incidence of arrhythmias.[19]

Hypercapnia increases the atrial refractory period and delays atrial conduction, potentially triggering arrhythmias.[20] In this study, one participant (1.2%) experienced hypercapnia, 32 participants (38.55%) had hypoxemia, and one participant (1.2%) had both hypoxemia and hypercapnia. However, no significant correlation was found between pCO_2 and pO_2 levels and the occurrence of arrhythmias. These findings differ from the study by Shih, *et al*. (1988), who identified pCO_2 levels as a significant predictor of recurrent ventricular arrhythmias.[13] The discrepancy may arise from variations in the baseline characteristics of the study populations. Shih, *et al*. (1988) reported a mean pCO_2 level of 45 mmHg, whereas the mean pCO_2 in the arrhythmia group of this study was 36.28 mmHg, with only one participant experiencing hypercapnia (pCO_2 of 45.40 mmHg).[13] The lower mean of pCO_2 in this study may have contributed to the absence of an association between pCO_2 levels and the incidence of arrhythmias. Similarly, this study aligns with those of Park, *et al*. (2011), who found no significant link between hypoxemia and arrhythmias in patients with interstitial lung disease.[21]

Chronic obstructive pulmonary disease has been identified as a significant risk factor for atherosclerosis, which can ultimately lead to coronary heart disease. It is also associated with hypercholesterolemia and hypertension. The presence of coronary heart disease and/or heart failure in COPD patients can create conditions that promote arrhythmias.[16] In this study, although no significant association was found between a history of heart disease and the incidence of arrhythmias, a higher frequency of arrhythmias in participants with a history of heart disease was observed. Xu, *et al.* (2024) reported a significant association between a history of myocardial infarction and the occurrence of arrhythmia.[22] The lack of significance in this study may be attributed to the small sample size.

Chronic obstructive pulmonary disease patients can experience various metabolic disorders, which may arise from the disease or the treatments administered. Verma, *et al*. (2023) found that COPD patients showed lower serum sodium and potassium levels, while Can *et al*. (2014) reported a significant association between serum sodium levels and AF.[23,24] This study did not find a significant correlation between sodium, potassium, magnesium, and calcium levels and the incidence of arrhythmias. However, a significant association between lower chloride levels and the occurrence of arrhythmias was observed. These discrepancies may be attributed to variations in the subject populations.

This study is similar to those of Mandai, *et al*. (2017), who identified a significant link between low chloride levels and an increased risk of cardiovascular events in patients with chronic kidney disease.[25] Other additional factors can contribute to the onset and exacerbation of arrhythmias in COPD patients, such as smoking, tissue hypoxia, oxidative stress, systemic glucocorticoid therapy, β-agonist effects, and persistent chronic inflammation.[26] Electrolytes play a crucial role in cardiac signaling and help regulate cellular excitability within the cardiovascular system. Activating chloride channels in the heart influences membrane potential and alters the action potential duration in the sinoatrial node, potentially leading to arrhythmias.[27]

Routine chloride testing is not strictly mandatory for COPD patients who have suspected arrhythmias. However, since chloride imbalances can affect acid-base status, electrolyte homeostasis, and cardiac excitability, assessing chloride levels may prove beneficial. Although current guidelines do not specifically recommend routine chloride monitoring for assessing arrhythmia risk, its evaluation could be considered part of a comprehensive electrolyte assessment for high-risk COPD patients. To further validate the findings of this study, a multivariate analysis was conducted to support the association between low chloride levels and the incidence of arrhythmias. In this study, not all participants could undergo ECGs and laboratory tests on the same day, which might have influenced the results. Therefore, additional research is needed to better understand the relationship between low chloride levels and arrhythmias in stable COPD patients.

CONCLUSION

The arrhythmias observed included sinus bradycardia, PACs, PVCs, and sinus tachycardia. This study found that COPD patients with a higher prevalence of arrhythmias were predominantly males, with an average age of 68 years old. These patients often had a history of heart disease, experienced more severe COPD symptoms, and demonstrated significant airflow obstruction. No significant relationship was found between the degree of airflow limitation in COPD and the occurrence of arrhythmias. However, a notable correlation was identified between lower chloride levels and the incidence of arrhythmias. These differences may be attributed to the study populations. Further research is needed to explore the association between arrhythmias and the influencing factors.

LIMITATIONS OF THE STUDY

The nature of the study design made it difficult to draw a relationship between risk factors for COPD and its

effects on arrhythmia. Furthermore, heart rhythm was not assessed using a Holter monitor. Additionally, not all participants underwent ECG and laboratory examinations on the same day, which may impact the results of the study.

Acknowledgments
None declared.

Conflict of Interest
The authors declared there is no conflict of interest.

Funding
This study did not receive any funding.

Authors' Contributions
Conceptualization, drafting, data collection, manuscript writing: AG. Supervision, critical insights, and guidance on the direction of the manuscript: FY, RR. Enhanced the manuscript's relevance and clarity: MAB. Data refinement and critical analysis, condensing data presentations, assessing analytical strength of the findings, and recommending necessary corrections: MBAW. Manuscript formatting, administrative coordination, and final proofreading prior to submission: BRA.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2024 Report)*, https://goldcopd.org/2024-gold-report/ (2024).
2. Liu X, Chen Z, Li S, *et al*. Association of Chronic Obstructive Pulmonary Disease With Arrhythmia Risks: A Systematic Review and Meta-Analysis. *Front Cardiovasc Med* 2021; 8: 732349. [PubMed]
3. Papaporfyriou A, Bartziokas K, Gompelmann D, *et al*. Cardiovascular Diseases in COPD: From Diagnosis and Prevalence to Therapy. *Life (Basel, Switzerland)*; 13. Epub ahead of print May 2023. [PubMed]
4. Hazarapetyan LG, Zelveian PH, Grigoryan SV. Features of Atrial Fibrillation Pathogenesis and Prognosis in Chronic Obstructive Pulmonary Patients during the COVID-19 Pandemic. *Rev Cardiovasc Med* 2023; 24: 51. [PubMed]
5. Konecny T, Park JY, Somers KR, *et al*. Relation of Chronic Obstructive Pulmonary Disease to Atrial and Ventricular Arrhythmias. *Am J Cardiol* 2014; 114: 272–277. [PubMed]
6. Dewantoro L, Wiyono W, Yunus F, *et al*. Proportions of Hypertension in Stable COPD Patients at the National Respiratory Center Persahabatan Hospital. *J Respirologi Indones* 2024; 44: 187–195. [Journal]
7. Choudhury G, Rabinovich R, MacNee W. Comorbidities and Systemic Effects of Chronic Obstructive Pulmonary Disease. *Clin Chest Med* 2014; 35: 101–130. [PubMed]
8. Curkendall SM, DeLuise C, Jones JK, *et al*. Cardiovascular Disease in Patients with Chronic Obstructive Pulmonary Disease, Saskatchewan Canada Cardiovascular Disease in COPD Patients. *Ann Epidemiol* 2006; 16: 63–70. [PubMed]
9. Cazzola M, Bettoncelli G, Sessa E, *et al*. Prevalence of Comorbidities in Patients with Chronic Obstructive Pulmonary Disease. *Respiration* 2010; 80: 112–119. [PubMed]
10. Cui H, Miao DM, Wei ZM, *et al*. Prevalence of Cardiovascular Disease in Subjects Hospitalized due to Chronic Obstructive Pulmonary Disease in Beijing from 2000 to 2010. *J Geriatr Cardiol* 2012; 9: 5–10. [PubMed]
11. Aprilen N, Indratama IMB. Profile of Chronic Obstructive Pulmonary Disease (COPD) Patients in Oksibil Regional Public Hospital at 2020. *J Penyakit Dalam Udayana* 2022; 6: 10–14. [Journal]
12. Al Wachami N, Guennouni M, Iderdar Y, *et al*. Estimating the Global Prevalence of Chronic Obstructive Pulmonary Disease (COPD): A Systematic Review and Meta-Analysis. *BMC Public Health* 2024; 24: 297. [PubMed]
13. Shih HT, Webb CR, Conway WA, *et al*. Frequency and Significance of Cardiac Arrhythmias in Chronic Obstructive Lung Disease. *Chest* 1988; 94: 44–48. [PubMed]
14. Jacques MR, Kuhn BT, Albertson TE. Update on the Pharmacological Treatment of Chronic Obstructive Pulmonary Disease. *Expert Opin Pharmacother* 2024; 25: 1903–1922. [PubMed]
15. Andreas S. Effects of LAMA/LABA Alone and in Combination on Cardiac Safety. *International Journal of Chronic Obstructive Pulmonary Disease* 2020; 15: 1931–1933. [PubMed]
16. Goudis CA, Konstantinidis AK, Ntalas IV, *et al*. Electrocardiographic Abnormalities and Cardiac Arrhythmias in Chronic Obstructive Pulmonary Disease. *Int J Cardiol* 2015; 199: 264–273. [PubMed]
17. Mittal S, Bhushan R, Jhajhria N, *et al*. The Significance of Systemic Inflammatory Markers in 'New-Onset Atrial Fibrillation' Following Cardiac Surgeries. *Cureus* 2024; 16: e59869. [PubMed]
18. Zhang J, Wang J, Ma X, *et al*. Rapid FEV1 Decline and the Effects of Both FEV1 and FVC on Cardiovascular Disease: A UK Biobank Cohort Analysis. *BMC Public Health* 2024; 24: 3214. [PubMed]
19. Dabadghao VS, Patil R, Sharma SK, *et al*. A Clinical Study of Cardiac Rhythm Disturbance in Patients with Chronic Obstructive Pulmonary Disease Using 24 Hour Holter Monitoring. *Int J Res Med Sci* 2016; 4: 702–705. [Journal]
20. Mehra R, Chung MK, Olshansky B, *et al*. Sleep-Disordered Breathing and Cardiac Arrhythmias in Adults: Mechanistic Insights and Clinical Implications: A Scientific Statement from the American Heart Association. *Circulation* 2022; 146: e119–e136. [PubMed]

21. Park JH, Jegal Y, Shim TS, *et al.* Hypoxemia and Arrhythmia during Daily Activities and Six-Minute Walk Test in Fibrotic Interstitial Lung Diseases. *J Korean Med Sci* 2011; 26: 372–378. [PubMed]
22. Xu X, Wang Z, Yang J, *et al.* Burden of Cardiac Arrhythmias in Patients with Acute Myocardial Infarction and Their Impact on Hospitalization Outcomes: Insights from China Acute Myocardial Infarction (CAMI) Registry. *BMC Cardiovasc Disord* 2024; 24: 218. [PubMed]
23. Verma P, Jain M, Sharma A, *et al*. Electrolyte Disturbances in Acute Exacerbation of Chronic Obstructive Pulmonary Disease at SMS Medical College, Jaipur. *Glob J Res Anal* 2023; 31–33. [Journal]
24. Can Ç, Gulacti U, Kurtoglu E, *et al*. The Relationship between Serum Sodium Concentration and Atrial Fibrillation among Adult Patients in Emergency Department Settings. *EurAsian J Biosci* 2014; 13: 131–134. [Journal]
25. Mandai S, Kanda E, Iimori S, *et al*. Association of Serum Chloride Level with Mortality and Cardiovascular Events in Chronic Kidney Disease: The CKD-ROUTE Study. *Clin Exp Nephrol* 2017; 21: 104–111. [PubMed]
26. Xu J, Zeng Q, Li S, *et al*. Inflammation Mechanism and Research Progress of COPD. *Front Immunol* 2024; 15: 1404615. [PubMed]
27. Turner D, Kang C, Mesirca P, *et al*. Electrophysiological and Molecular Mechanisms of Sinoatrial Node Mechanosensitivity. *Front Cardiovasc Med* 2021; 8: 662410. [PubMed]