International Journal of Chronic Obstructive Pulmonary Disease

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REVIEW

Prevalence and Risk Factors of Arrhythmias in Patients with Acute Exacerbations of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis

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Background: Cardiac arrhythmias are commonly seen in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD), but their prevalence, risk factors, and prognostic significance are still not fully understood.

Objective: To estimate the prevalence of arrhythmias in patients with AECOPD, identify related clinical factors, and assess their influence on in-hospital mortality.

Methods: A systematic search of PubMed, Embase, Web of Science, CENTRAL, and Cochrane Reviews was conducted to identify observational studies and randomized controlled trials. A random-effects meta-analysis using the DerSimonian–Laird method was performed. Subgroup and sensitivity analyses were conducted to explore heterogeneity, and publication bias was assessed using Egger's and Begg's tests.

Results: Twenty-eight studies were included. The pooled prevalence of arrhythmias in AECOPD patients was 15% (95% CI: 12–18%), with considerable heterogeneity ($I^2 = 99.93\%$). Prevalence was higher in studies from developed countries, particularly those with larger sample sizes and older populations. Advanced age (WMD = 2.79 years) and elevated C-reactive protein levels (WMD = 5.32) were associated with increased arrhythmia risk. Use of long-acting beta-agonists (LABAs) was associated with a reduced risk (OR = 0.42), although the causal mechanism remains uncertain. Arrhythmias were significantly associated with increased in-hospital mortality (RR = 3.33, 95% CI: 3.27–3.38). In a predefined subgroup analysis, atrial fibrillation (AF) was also linked to a higher risk of death (RR = 3.70, 95% CI: 2.40–5.70). Sensitivity analyses confirmed the robustness of these findings, and no significant publication bias was detected.

Conclusion: Arrhythmias are common during AECOPD and are associated with increased short-term mortality, especially in patients with AF. Aging and systemic inflammation appear to be key contributors. While LABA use may have a protective association, this finding requires cautious interpretation. Standardized ECG monitoring and individualized risk stratification are warranted to improve patient outcomes.

Plain Language Summary:

- About 15% of patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) develop abnormal heart rhythms (arrhythmias).
- Older age and higher levels of C-reactive protein (CRP), a marker of inflammation, are linked to an increased risk of arrhythmias.
- Patients who develop arrhythmias during AECOPD have a significantly higher risk of dying during hospitalization. Specifically, those with atrial fibrillation (AF) face nearly four times greater risk of in-hospital death compared to those without AF.
- These findings highlight the need for early identification, continuous heart monitoring, and personalized treatment strategies to reduce complications and improve outcomes for patients with AECOPD.

Keywords: chronic obstructive pulmonary disease, cardiac arrhythmias, hospital mortality, systematic review

Received: 9 June 2025
Accepted: 27 August 2025
Published: 3 September 2025

Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogeneous pulmonary disorder characterised by persistent, often progressive airflow limitation resulting from airway abnormalities (eg, bronchitis and bronchiolitis) and/or alveolar destruction (eg, emphysema). This pathophysiology leads to chronic respiratory symptoms such as dyspnea, cough, sputum production, and/or acute exacerbations. COPD is one of the most prevalent non-infectious lung diseases globally and represents a leading cause of morbidity, mortality, and healthcare burden.[1–3] In China, large-scale epidemiological studies have reported a COPD prevalence of 8.6% in adults over 20 years of age and up to 13.7% in those over 40, with an estimated patient population nearing 100 million.[4]

Acute exacerbation of COPD (AECOPD) refers to an acute episode of worsening respiratory symptoms, typically occurring within 14 days, often accompanied by tachypnea or tachycardia. It is commonly triggered by respiratory infections or environmental pollution that induces local or systemic inflammation.[5–8]AECOPD not only marks a key turning point in disease progression but also contributes significantly to COPD-related mortality, with an in-hospital mortality rate estimated at 1.9% in China.[7]

Repeated exacerbations accelerate the decline in lung function and increase the risk of comorbidities such as cardiovascular diseases, respiratory failure, and death.[9–11]Multinational studies have shown that AECOPD is associated with a significantly increased risk of major adverse cardiovascular events (MACE), including myocardial infarction, stroke, and cardiovascular mortality—even in patients without prior cardiovascular history.[12] The odds of cardiovascular events in COPD patients are approximately 25% higher than in non-COPD populations,[13] and the presence of arrhythmia further elevates the risk of in-hospital mortality by up to 2.7-fold.[14]

Cardiac arrhythmias—particularly atrial fibrillation (AF) and ventricular arrhythmias—are frequently observed in AECOPD patients, with a reported prevalence of 40–60% during hospitalisation.[15–17] Arrhythmias may exacerbate symptoms, contribute to haemodynamic instability, and increase the frequency of subsequent exacerbations. Furthermore, meta-analytic evidence has linked arrhythmias during AECOPD to a significantly increased risk of all-cause mortality.[18]

Despite these findings, the epidemiology, determinants, and prognostic impact of arrhythmias in AECOPD remain incompletely understood. This systematic review and meta-analysis aims to summarize the prevalence of arrhythmias in AECOPD patients, identify clinical risk factors, and evaluate their associations with key clinical outcomes, such as in-hospital mortality and length of stay.

Methods

Literature Search Strategy

We systematically searched the databases of PubMed, Embase, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and Cochrane Reviews from their inception until February 21, 2025. We imposed no language restrictions and considered only peer-reviewed studies. The search strategy included both MeSH/Emtree terms and relevant free-text keywords. Core terms consisted of "COPD", "acute exacerbation", and various synonyms related to cardiac arrhythmias. Detailed search strategies are available in e-Table 1. This systematic review and meta-analysis were prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO, CRD420250649650) and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[19] The PRISMA-S checklist is summarized in e-Table 2.

Study Selection and Eligibility Criteria

Two reviewers (D.N. and Q.W.D.) independently screened and selected studies based on the following inclusion criteria: (i) cohort studies (prospective or retrospective), case-control studies, case-crossover studies, or randomized controlled trials (RCTs); (ii) adult populations diagnosed with chronic obstructive pulmonary disease (COPD), according to clinical or spirometric criteria if reported; (iii) reporting data on arrhythmia prevalence or clinical outcomes during acute exacerbations of COPD (AECOPD); (iv) a total sample size of ≥50 participants; and (v) full-text articles published in peer-reviewed journals. Exclusion criteria included: (i) abstracts, editorials, letters, or preprints without peer review; and (ii) studies lacking extractable data on arrhythmia prevalence, clinical outcomes during AECOPD, or relevant comparator information. Eligible studies were selected through a two-stage process involving title and abstract screening, followed by full-text review. Disagreements between the two reviewers were resolved through discussion and consensus with a third reviewer (C.J.M).

Endpoint Definitions

Arrhythmia Outcomes and Subgroup Classifications

The primary outcome was the in-hospital prevalence of any arrhythmia, defined by clinical or electrocardiographic diagnoses from the original studies. For subgroup analyses, arrhythmias were stratified by: (i) country income level (developed vs developing, according to World Bank classification); (ii) arrhythmia type (atrial fibrillation [AF] vs non-AF); (iii) mean age (<70 vs ≥70 years); (iv) sample size (≥500 vs <500 participants); (v) method of arrhythmia diagnosis (Holter monitoring, standard ECG, or hospital/ICD-based diagnosis); (vi) ICU status (ICU or mixed ICU/non-ICU vs non-ICU populations). These classifications are summarized in e-Table 3.

Risk Factors

The included variables were categorized into three groups: (i) clinical characteristics (eg, age, sex, smoking history); (ii) comorbidities (eg, hypertension, coronary artery disease); (iii) pharmacological treatments (eg, long-acting beta-agonists [LABAs], anticholinergics, inhaled corticosteroids [ICS], systemic glucocorticoids).

Clinical Prognostic Outcomes

The primary prognostic outcome was in-hospital mortality. Prognostic data were extracted according to definitions reported in the original studies.

Risk of Bias Assessment

The risk of bias was assessed using design-appropriate tools. For cohort and case-control studies, the Newcastle–Ottawa Scale (NOS) was used to evaluate selection, comparability, and outcome domains (maximum score = 9); studies scoring ≥7 were considered high quality. The ROBINS-E tool was utilized for dynamic exposure cohort studies based on electronic health records (eg, EXACOS series), addressing seven domains including confounding, selection, exposure classification, and outcome measurement. For prediction model studies (eg, Chen et al, 2023), the PROBAST tool was applied to assess both risk of bias and applicability.[20–22] All assessments were carried out independently by two reviewers (D.N. and Q.W.D)., and any disagreements were resolved through discussion or by consulting a third reviewer.

Statistical Analysis

For prevalence analysis, we applied the Freeman–Tukey double arcsine transformation to stabilize variance, and we calculated pooled prevalence estimates with 95% confidence intervals (CIs) using the DerSimonian–Laird random-effects model. Subgroup analyses were conducted based on country income level (developed vs developing), arrhythmia type (AF vs non-AF), mean age (≥70 vs <70 years), sample size (≥500 vs <500), and detection method (ECG, Holter, or clinical diagnosis) to explore sources of heterogeneity. For risk factor analysis, we assessed dichotomous variables (eg, smoking, hypertension, medication use) using pooled odds ratios (ORs), while we analyzed continuous variables (eg, age, CRP) using weighted mean differences (WMDs), both under a random-effects model. We used the metan or metaprop command for binary variables, and we calculated WMDs using metan. In-hospital mortality data were extracted for prognostic analysis to compute pooled risk ratios (RRs) with 95% confidence intervals (CIs) comparing patients with and without arrhythmias. A predefined subgroup analysis was also performed for atrial fibrillation (AF). We assessed heterogeneity using Cochran's Q and I^2 statistics, with $I^2 > 50\%$ or $P < 0.10$ indicating substantial heterogeneity. We conducted sensitivity analyses (leave-one-out) and subgroup analyses to evaluate the robustness of pooled estimates and explore sources of heterogeneity. We examined publication bias through visual inspection of funnel plots and formal statistical testing using Egger's and Begg's methods, with $P < 0.1$ considered indicative of potential small-study effects. All statistical analyses were conducted using Stata MP version 18.0 (StataCorp LLC, College Station, TX, USA) and R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). We deemed two-tailed $p < 0.05$ statistically significant for all analyses unless otherwise specified.

Results

Study Selection

After removing duplicates, 1523 potentially relevant articles were identified. Following the screening of titles and abstracts, 71 articles were evaluated for full-text eligibility. Ultimately, 28 studies met the inclusion criteria and were included in the final meta-analysis (Figure 1).[23–50]

Study Characteristics

This meta-analysis included 28 studies involving hospitalized patients with acute exacerbations of COPD (AECOPD). Most studies used retrospective cohort or observational designs, with sample sizes varying from 45 to over 1.2 million. The research was conducted in Asia, Europe, North America, and the Middle East. The mean age of participants ranged from 60 to 81 years, with most being male. Arrhythmias were identified through ECG, Holter monitoring, or diagnosis-based coding. Atrial fibrillation (AF) was the most frequently reported subtype, although some studies included other arrhythmias (eg, PVCs, AA, VT), while others did not specify the type. Approximately one-third of the studies involved ICU or mixed ICU/non-ICU populations. Key study and patient characteristics are summarized in Table 1.

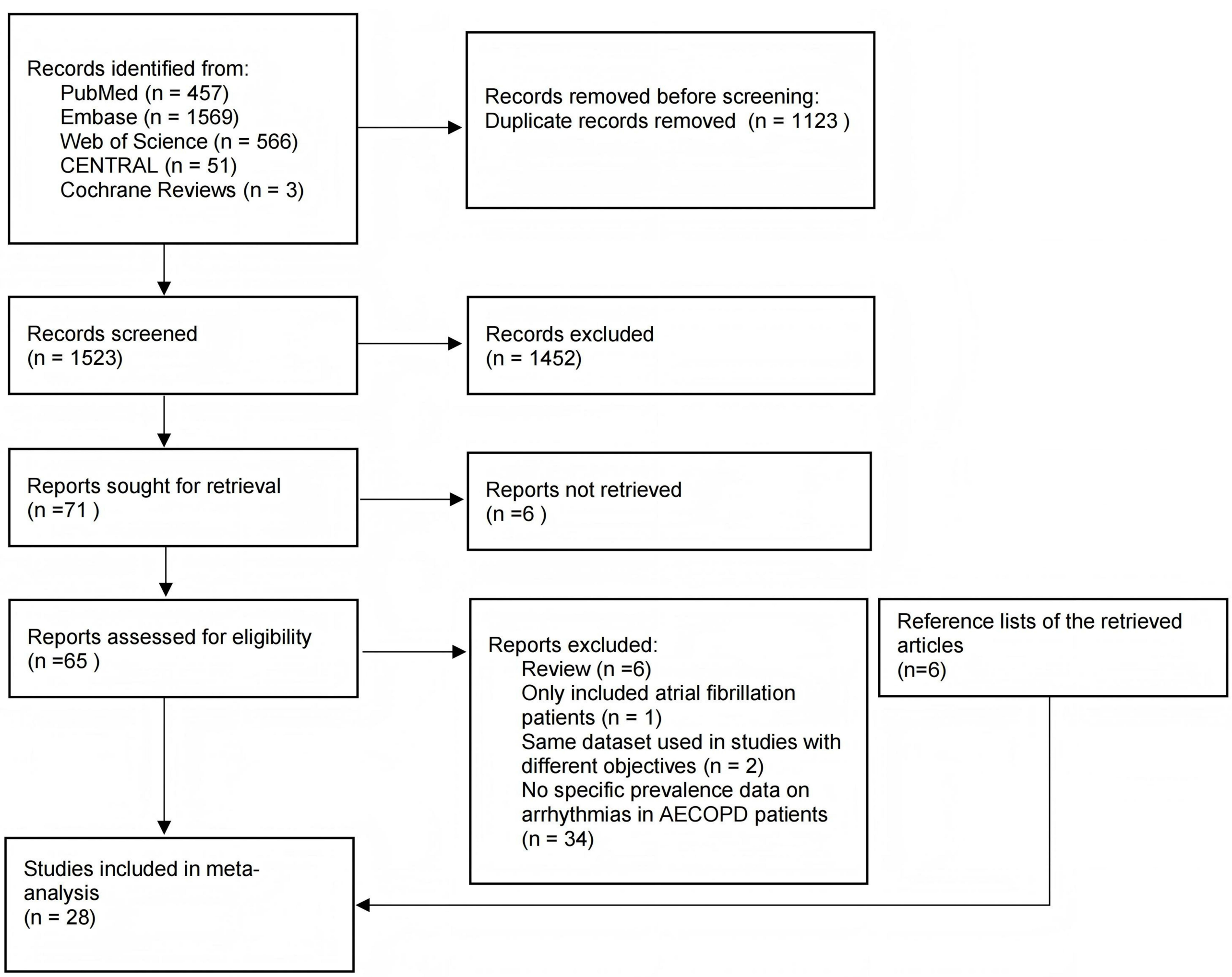

Figure 1 PRISMA 2020 flowchart illustrating the study selection process for the systematic review and meta-analysis. Records were identified through five databases (PubMed, Embase, Web of Science, CENTRAL, and Cochrane Reviews), screened, and assessed for eligibility. A total of 28 studies were included in the final analysis.

Table 1 Characteristics of Study Participants

Authors, Year	Country	Study Design	Sample Size (n)	Mean Age(Years)	Male (%)	AECOPD Diagnosis, 0 = GOLD diagnostic criteria; 1 = ICD diagnostic codes	Type of Arrhythmia	Detection Method of Arrhythmia, 0=ECG, 1=Holter, 2=diagnosis	ICU Population (0 = Non-ICU; 1=ICU Only/ Mixed)	Outcomes Reported
Einvik et al 2017[23]	Norwegian	Retrospective cohort study	45	66	51.11	0	PVC	1	0	None
Hu et al 2020[24]	China	Nested case-control study	496	81	83.67	0	N/A	2	0	In-hospital mortality
Lüthi et al 2023[25]	Switzerland	Retrospective observational study	170	74	53.5	0	N/A	2	0	1-year mortality
Nguyen et al 2024[26]	Vietnam	Retrospective observational study	197	74.3	88.8	0	AF	1	0	None
García et al 2020[27]	Spain	Retrospective observational study	602	73.7	86.05	0	AF	2	0	None
Zhang et al 2022[28]	China	Retrospective observational study	392	77.33	77	0	N/A	2	1	In-hospital mortality
Perera et al 2012[29]	USA	Retrospective observational study	1254703	70.6	47.2	1	N/A	2	0	In-hospital mortality
Memon et al 2019[30]	Pakistan	Prospective cohort study	162	67.12	57.4	1	AF	2	1	In-hospital mortality
Pethyabarn et al 2020[31]	Thailand	Retrospective cohort study	220	76.23	90	1	N/A	2	1	None
Thomas et al 2018[32]	USA	Retrospective cohort study	96	62.72	40.62	1	N/A	2	1	None
Zhang et al 2019[33]	China	Retrospective cohort study	890	73	70.2	1	AF	2	0	1-year mortality
Santus et al 2021[34]	Italy	Retrospective observational study	316	71.33	63.8	1	AA	0	0	Length of hospitalization, In-hospital mortality
Wang et al 2016[35]	China	Retrospective observational study	70	61.01	65.71	0	VT	0	0	None
Zidan et al 2020[36]	Egypt	Prospective observational study	100	60.6	87	0	AF	0	1	In-hospital mortality
Calabria et al 2024[37]	Italy	Retrospective cohort study	69620	74	56.8	1	N/A	2	0	None
Nafae et al 2014[38]	Egypt	Retrospective cohort study	200	69.35	51	0	AF	0	1	In-hospital mortality
Chen et al 2023[39]	USA	Retrospective prediction model	1922	71.16	49.06	1	AF	2	1	None

(*Continued*)

https://doi.org/10.2147/COPD.S545658

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Table 1 (Continued).

Authors, Year	Country	Study Design	Sample Size (n)	Mean Age(Years)	Male (%)	AECOPD Diagnosis, 0 = GOLD diagnostic criteria; 1 = ICD diagnostic codes	Type of Arrhythmia	Detection Method of Arrhythmia, 0=ECG, 1=Holter, 2=diagnosis	ICU Population (0 = Non-ICU; 1=ICU Only/ Mixed)	Outcomes Reported
Santos et al 2025[40]	Spain	Retrospective time-dependent cohort study	18901	69.5	78.2	1	AF/Arrest/others	2	0	All-cause mortalitytime periods (1–7, 8–14, 15–30, 31–180, 181–365, and > 365 days)
Almarshoodi et al 2024[41]	UAE	Retrospective cohort study	512	73.3	67	1	AF	2	0	None
TelukuTla et al 2020[42]	India	Prospective cohort study	170	60.61	63.53	1	AF	2	1	In-hospital mortality
García-Sanz et al 2017[43]	Spain	Retrospective cohort study	757	74.71	77.45	0	AF	2	1	1-year mortality5-year mortality
Graul et al 2024[44]	UK	Retrospective time-dependent cohort study	146448	69.8	49.3	0	N/A	2	0	None
Sangwan et al 2017[45]	India	Prospective cohort study	50	62.16	86	1	AF	0	0	None
Goto et al 2018[46]	USA	Self-controlled case series	16424	69.33	43	1	AF	2	0	None
Swart et al 2023[47]	Netherlands	Retrospective time-dependent cohort study	2234	67.6	50	1	N/A	2	0	None
Hawkins et al 2019[48]	Canada	Retrospective time-dependent cohort study	142787	68.1	51.7	1	AF/Arrest/others	2	0	None
Matsunaga et al 2024[49]	Japan	Retrospective time-dependent cohort study	63182	72.5	60.2	1	AF/Arrest/others	2	0	None
Vogelmeier et al 2024[50]	Germany	Retrospective time-dependent cohort study	48982	64.5	60.35	1	N/A	2	0	None

Notes: This table summarises the characteristics of studies included in the meta-analysis, covering demographics, study design, type of arrhythmia, detection method, and clinical outcomes.
Abbreviations: AF, atrial fibrillation; PVC, premature ventricular contraction; ECG, electrocardiogram; ICU, intensive care unit; N/A, not available.

Prevalence of Arrhythmias

In the 28 studies analyzed, the pooled prevalence of arrhythmias among AECOPD patients was 15% (95% CI: 12–18%), showing substantial heterogeneity (I^2 = 99.93%, $p < 0.001$; Figure 2). Given the observed heterogeneity, additional subgroup analyses were performed to explore potential sources of variability in Figure 2.

Subgroup Analysis

Subgroup analyses were carried out based on predefined study-level characteristics to investigate potential sources of heterogeneity. As shown in the Supplementary Figures (e-Figures 1–6), studies from developed countries reported a higher prevalence of arrhythmias compared to those from developing countries (18% vs 12%, p = 0.035; e-Figure 1). The prevalence was similar between AF-focused and non-AF studies (16%, p = 0.942; e-Figure 2). Studies with a mean participant age of ≥70 years demonstrated a significantly higher prevalence than those with younger populations (19% vs 11%, p < 0.001; e-Figure 3). Larger studies (≥500 participants) reported a higher prevalence than smaller ones (20% vs 11%, p = 0.003; e-Figure 4). In terms of detection methods, studies using ECG reported a lower

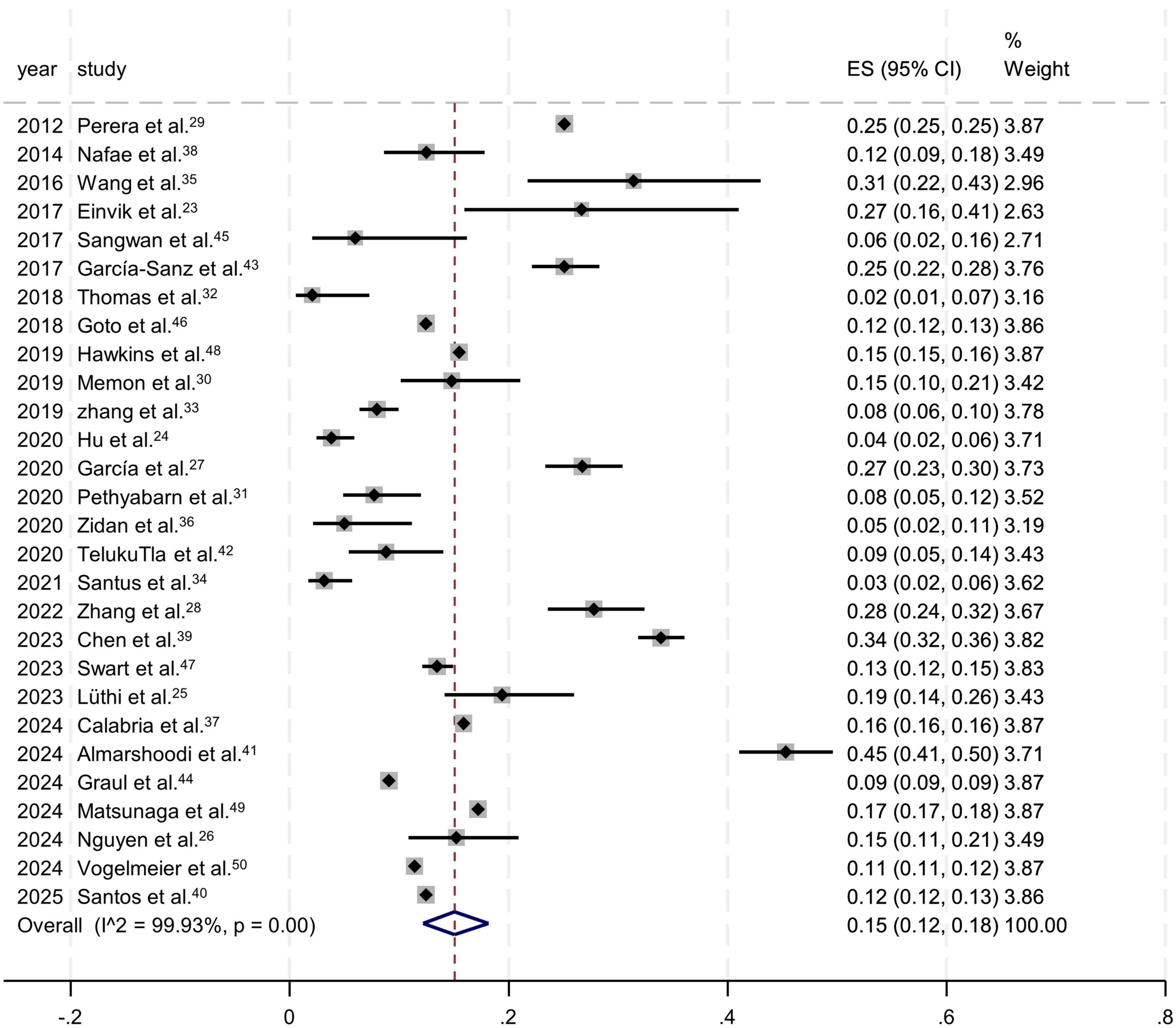

Figure 2 Forest plot showing the pooled prevalence of cardiac arrhythmias in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Estimates were calculated using a random-effects model. The effect size (ES) and 95% confidence intervals (CIs) are presented for each study. The size of each square reflects the weight assigned to that study. Heterogeneity across studies is indicated by the I^2 statistic.

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prevalence (10%) than those using Holter monitoring or diagnosis-based classification (both 17%, p = 0.146; e-Figure 5). No significant difference was noted between non-ICU and ICU or mixed populations (16% vs 15%, p = 0.853; e-Figure 6). High heterogeneity remained across all subgroups.

Risk Factor Analysis

Risk factor analyses were conducted for both dichotomous and continuous variables. A comprehensive summary of the pooled effect estimates is presented in Table 2, which outlines key risk factors associated with arrhythmia in patients with AECOPD. Except for Table 2, all supporting data and visualizations referenced in this section are provided in the Supplementary Material. Baseline clinical characteristics of the included study populations are detailed in e-Table 4, while extracted data for dichotomous and continuous variables are shown in e-Tables 5 and 6, respectively. Among the dichotomous variables, only the use of long-acting β_2-agonists (LABAs) was significantly associated with a reduced risk of arrhythmia (OR = 0.42, 95% CI: 0.24–0.76; I^2 = 0%). No significant associations were found for smoking, female sex, hypertension, cardiovascular disease, inhaled corticosteroids (ICS), systemic corticosteroids, or anticholinergic use. Forest plots for these variables are presented in e-Figures 7–14.

Regarding continuous variables, patients who developed arrhythmias were generally older (WMD = 2.79 years, 95% CI: 0.05–5.52; I^2 = 34.6%) and had higher C-reactive protein (CRP) levels (WMD = 5.32 mg/L, 95% CI: 1.43–9.22; I^2 = 0%). These associations are illustrated in e-Figures 15 and 16, respectively. Together, these findings suggest that increasing age and systemic inflammation may contribute to arrhythmogenesis in the context of AECOPD.

In-Hospital Mortality Outcomes

Seven studies reported in-hospital mortality among AECOPD patients with and without arrhythmias. Pooled analysis showed a significantly higher risk of death in patients with arrhythmias (RR = 3.33, 95% CI: 3.27–3.38; e-Figure 17). Leave-one-out sensitivity analysis confirmed the robustness of this finding. The study by Perera et al, with a disproportionately large sample size, yielded an extreme RR (143.19), suggesting potential bias and warranting cautious interpretation when pooling heterogeneous arrhythmia types.

To explore subtype-specific effects, a predefined subgroup analysis focused on atrial fibrillation (AF) was conducted using four studies. The pooled RR for in-hospital mortality was 3.70 (95% CI: 2.40–5.70), with no significant heterogeneity (I^2 = 0.0%, p = 0.520) (Figure 3). These findings suggest that AF is independently associated with increased in-hospital mortality in AECOPD patients. Supporting definitions and prognostic data are summarized in e-Tables 7 and 8.

Table 2 Summary of Risk Factors Associated with Arrhythmia in AECOPD Patients

Risk Factor	Type	No. of Studies	Effect Size (95% CI)	I^2 (%)	p-value	Association
Smoking	Categorical	2	OR = 1.05 (0.55–2.02)	0%	0.803	NS
Female Sex	Categorical	4	OR = 1.44 (0.83–2.48)	0%	0.234	NS
Hypertension	Categorical	2	OR = 1.57 (0.96–2.59)	0%	0.338	NS
CVD	Categorical	3	OR = 0.86 (0.03–2.42)	19.70%	0.862	NS
LABA Use	Categorical	4	OR = 0.42 (0.24–0.76)	0%	0.004	↓ Risk *
Anticholinergic Use	Categorical	3	OR = 0.60 (0.31–1.13)	0%	0.12	NS
ICS Use	Categorical	2	OR = 099 (0.32–3.057)	2.70%	0.977	NS
Systemic Corticosteroid Use	Categorical	2	OR = 1.13 (0.53–2.44)	0%	0.748	NS
Age	Continuous	4	WMD = 2.79 (0.05–5.52)	34.60%	0.1002	NS
CRP	Continuous	2	WMD = 5.32 (1.43–9.22)	0%	0.008	↑ Risk *

Notes: ↑ Risk: indicates increased risk of arrhythmia; ↓ Risk: indicates reduced risk of arrhythmia.
Abbreviations: NS, not significant; CVD, cardiovascular disease; LABA, long-acting beta agonists; ICS, inhaled corticosteroids; CRP, C-reactive protein; WMD, weighted mean difference; OR, odds ratio. *Statistically significant (P < 0.05).

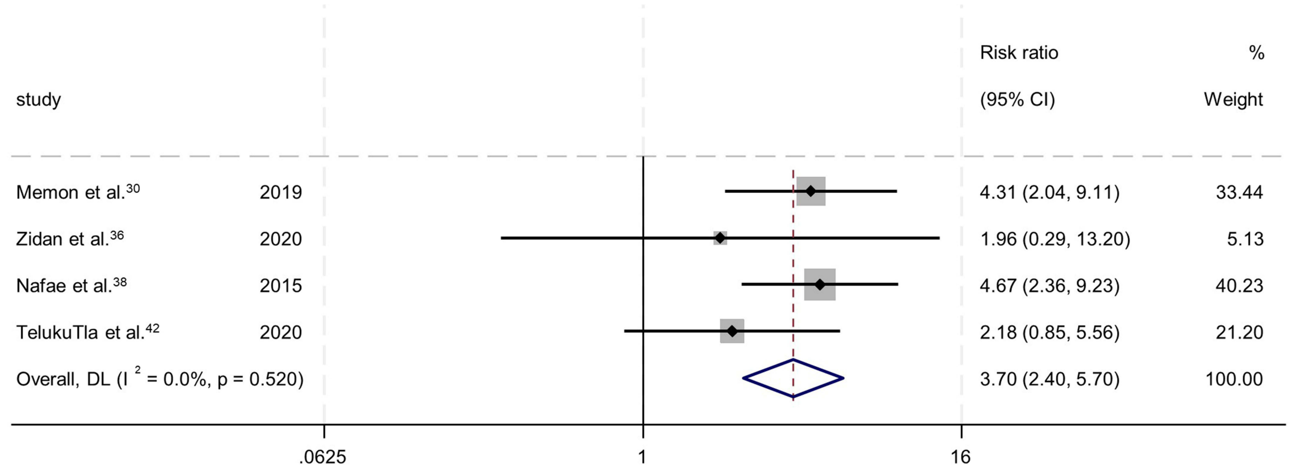

Figure 3 Association between atrial fibrillation (AF) and in-hospital mortality in patients with AECOPD. This forest plot shows the pooled risk ratios (RRs) and 95% CIs for in-hospital mortality in patients with AECOPD with versus without AF. A total of four studies were included. Estimates were calculated using a random-effects model. The pooled RR was 3.70 (95% CI: 2.40–5.70), indicating a significantly increased risk of in-hospital mortality associated with AF. The size of each square reflects the weight of each study, and the diamond represents the pooled estimate. Between-study heterogeneity was low (I^2 = 0.0%, p = 0.520).

Sensitivity Analysis and Publication Bias

Among the 28 included studies, risk of bias was assessed using study design–appropriate tools: 20 studies (19 cohort and 1 nested case-control) were rated high quality by the Newcastle–Ottawa Scale (e-Table 9); 7 dynamic exposure cohort studies were evaluated with ROBINS-E and found to have low overall risk; and 1 prediction model study assessed with PROBAST was rated high overall risk (e-Table 10).Leave-one-out sensitivity analyses confirmed the robustness of the pooled estimates, with minimal changes observed for both arrhythmia prevalence (e-Figure 18) and in-hospital mortality (e-Figure 20) after sequential exclusion of individual studies. For in-hospital mortality, the pooled risk ratio remained stable (RR: 3.33 [3.27–3.38]), and no single study significantly altered the overall effect size or direction. Although omission of Perera et al resulted in a slightly wider confidence interval (RR: 3.55 [2.43–5.20]), the effect remained statistically significant and consistent with the overall estimate, suggesting high robustness of the findings.For overall arrhythmia prevalence, the funnel plot showed slight asymmetry with clustering of smaller studies to the right. Egger's test yielded a borderline p-value of 0.078, and Begg's test indicated potential bias ($p = 0.009$), suggesting a small-study effect and warranting cautious interpretation (e-Figure 19, e-Table 11). No significant publication bias was detected for other outcomes, including atrial fibrillation prevalence, risk factor associations, and in-hospital mortality, as confirmed by both Egger's and Begg's tests ($p > 0.1$ for all; e-Table 11).

Discussion

This meta-analysis, encompassing 28 studies of hospitalized patients with AECOPD, revealed several clinically relevant findings.

First, the pooled prevalence of arrhythmias during AECOPD reached 15%, which is substantially higher than that reported in the general population (typically 1–3%) or among patients with stable COPD (ranging from 5% to 10%).[44,51,52] National data from China further illustrate this disparity: atrial fibrillation prevalence was estimated at 0.85% in males and 0.63% in females, with rates of only 0.32% in individuals under 65 years, compared to 3.56% in those aged 65 and above.[51] These differences suggest that arrhythmia burden sharply increases during acute exacerbations. Pathophysiologically, this may be attributed to hypoxaemia, systemic inflammation, acid–base imbalance, sympathetic activation, and increased pulmonary vascular pressure—all of which are common during AECOPD episodes and may precipitate electrophysiological instability.[53,54]

Second, subgroup analyses revealed that the prevalence of arrhythmias was notably higher in studies conducted in developed countries, among older patient populations, and in larger cohorts. These findings suggest that demographic characteristics and the intensity of rhythm surveillance influence arrhythmia detection rates. Age remains the most significant risk factor for atrial fibrillation (AF), with incidence rising sharply after 65 due to cumulative effects of oxidative stress, chronic low-grade inflammation, and atrial structural remodeling.[55,56] The association between systemic inflammation and arrhythmia risk, particularly AF, has been well documented. Aviles et al[57] first demonstrated that elevated C-reactive protein (CRP) levels were significantly associated with both prevalent and incident AF. More recently, Yang et al[58] confirmed this association in a large UK Biobank cohort, where higher CRP levels independently predicted new-onset AF. These findings suggest that chronic inflammation may promote atrial remodeling and electrical instability, supporting CRP as a potential biomarker for risk stratification. Furthermore, the relative prevalence of AF is highest in high-income countries, potentially due to more intensive cardiac monitoring and higher detection rates.[59] These results emphasize the need for standardized surveillance protocols, especially in aging and high-risk groups.

Third, arrhythmias were associated with a significantly increased risk of in-hospital mortality (RR = 3.33), underscoring their prognostic significance. Consistent with our findings, Pirera et al[18] reported that the first week after AECOPD onset represents a critical window for cardiovascular events. Large registries further support this association: in the EORP-AF and GLORIA-AF cohorts, COPD comorbidity in patients with atrial fibrillation was linked to significantly increased risks of all-cause mortality and major adverse cardiovascular events, even after adjustment for confounders.[60–62] These findings reinforce the importance of timely rhythm monitoring and cardiovascular risk stratification during AECOPD hospitalization.

In subgroup analysis, atrial fibrillation alone was associated with an even greater mortality risk (RR = 3.70, 95% CI: 2.40–5.70), with no heterogeneity across studies. This suggests that AF confers particularly poor short-term prognosis in AECOPD, likely due to overlapping hemodynamic stress, atrial dysfunction, and comorbid burden. These findings support early identification and targeted management of AF during exacerbations.

In our analysis, LABA use was associated with a significantly lower risk of arrhythmias (OR = 0.42, 95% CI: 0.24–0.76). While this finding appears to contradict earlier concerns regarding β_2-agonists' pro-arrhythmic potential, it aligns with recent evidence supporting their cardiovascular safety in COPD populations. A 24-trial meta-analysis reported that inhaled LABAs significantly reduced fatal cardiovascular events without increasing arrhythmia risk.[63] Another review of 43 RCTs showed that certain LABAs, such as olodaterol and formoterol, were not associated with increased cardiovascular risk and may potentially reduce events such as cardiac ischemia and hypertension.[64] However, it is important to interpret these findings with caution. The observed association may reflect indirect benefits—such as improved oxygenation, reduced lung hyperinflation, and decreased sympathetic drive—rather than a direct anti-arrhythmic mechanism. Current evidence does not support a causal or cardioprotective role for LABAs in arrhythmia prevention, and further prospective studies are warranted. In contrast, no significant associations were observed with corticosteroids or ICS, despite their anti-inflammatory potential. These observations highlight the necessity of a balanced, evidence-based evaluation of pharmacotherapy safety in COPD patients at risk of cardiac complications.

To our knowledge, this is the first meta-analysis to quantify the burden and prognostic impact of arrhythmias in patients with acute exacerbations of COPD (AECOPD). By synthesizing evidence from various clinical contexts, our findings demonstrate strong generalizability. Importantly, our analysis emphasizes the clinical relevance of early rhythm surveillance and its association with in-hospital mortality.

These findings support integrating dynamic cardiac monitoring—such as Holter ECG or telemetry—into both hospital admission assessments and post-discharge follow-ups for COPD patients, particularly during and after acute exacerbation episodes. The 2023 ACC/AHA/HRS guidelines emphasize that intermittent and continuous ECG monitoring—rather than one-time recordings—provides superior atrial fibrillation (AF) detection, especially in patients with elevated risk profiles such as older adults or those with cardiopulmonary comorbidities.[65] While the benefit of screening on hard outcomes remains to be proven, targeted rhythm surveillance may still support timely diagnosis and intervention. Evidence from large-scale wearable monitoring studies (eg, the Fitbit Heart Study) further supports the value of early detection, demonstrating a 98.2% positive predictive value of wearable-based AF detection and over one-third of notified individuals initiating AF-specific therapies.[66]

These insights highlight the importance of integrating continuous cardiac rhythm surveillance into AECOPD management. A multidisciplinary approach involving pulmonologists, cardiologists, and critical care teams is essential to interpret arrhythmia findings and tailor management to individual cardiopulmonary risk profiles. This strategy may optimize inpatient recovery and enhance long-term disease control.

Limitations

This study has several limitations. First, the analyses were based on aggregated data from published studies, which may introduce ecological bias and limit the ability to adjust for individual-level confounders. Second, there was significant heterogeneity among studies regarding arrhythmia definitions, detection methods, and baseline population characteristics, which could have influenced the pooled estimates. Third, not all included studies reported arrhythmia subtypes, timing of onset, or monitoring modalities, limiting our ability to conduct stratified or time-dependent analyses. Fourth, residual confounding cannot be excluded, as several potential modifiers, such as baseline severity of AECOPD, prior arrhythmia history, and medication adherence, were not consistently reported. Lastly, some variables of interest could not be included in the meta-analysis or meta-regression due to missing data across studies.

Future research should prioritise individual participant data meta-analyses and prospective studies with standardised arrhythmia monitoring and outcome definitions. These approaches will help clarify temporal relationships, identify high-risk phenotypes, and inform personalised prevention strategies for arrhythmias in AECOPD. Moreover, most of the included studies were conducted in Europe, North America, and East Asia, with limited data from South Asia, Central, and South America. This geographic imbalance may limit the generalizability of our findings, and future studies should aim to include more diverse populations from underrepresented regions.

Conclusion

This systematic review and meta-analysis demonstrates that cardiac arrhythmias are common among patients hospitalised for AECOPD, with a pooled prevalence of 15%, and are significantly associated with increased in-hospital mortality. Older age and systemic inflammation—as reflected by elevated C-reactive protein (CRP) levels—were key risk factors. Conversely, LABA use, when appropriately prescribed, was associated with a reduced risk of arrhythmias, though causality remains uncertain. These findings support and extend prior evidence highlighting the cardiovascular burden in AECOPD, and underscore the importance of integrating cardiopulmonary monitoring into routine management. Early identification of high-risk patients through dynamic ECG surveillance and multidisciplinary collaboration may improve short-term prognosis and enhance long-term outcomes. Future research should focus on prospective validation of these findings and further development of personalised risk prediction models.

Data Sharing Statement

All data are extracted from published original articles, and in some instances, through correspondence with the authors. Our dataset is available upon request.

Ethical Approval

Ethical review and informed consent were waived, as the study utilised secondary data from prior studies.

AI Tools Use Disclosure

ChatGPT (OpenAI, version GPT-4) was used to assist in checking the English language and formatting of tables during the preparation of this manuscript. The authors reviewed and approved all AI-assisted outputs to ensure accuracy and scientific integrity.

Author Contributions

All authors made a significant contribution to the work reported, whether 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. Specifically, D.N. and Q.W.D. contributed equally to this work. D.N. was responsible for conceiving the study, acquiring data, conducting statistical analyses, and drafting the manuscript. Q.W.D. was involved in the study design, data interpretation, and manuscript drafting. W.K.H. and C.Z.Y. assisted with literature screening, data extraction, and quality assessment. C.R.L. contributed to data visualization and figure preparation. C.J.M. provided methodological consultation and technical support. C.A.L. served as the lead corresponding author, offering critical revisions, overall supervision, and coordination of the multidisciplinary collaboration.

Funding

This work was supported by the National Natural Science Foundation of China (Grant No. 81903421) and the Guangzhou Science and Technology Project (Grant No. 2021020510515)

Supplementary Material

Supplementary materials are available in the International Journal of Chronic Obstructive Pulmonary Disease.

Disclosure

The content of this manuscript has not been previously presented at any scientific meeting or conference. The authors report no conflicts of interest in this work.

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