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Impact of Cardiovascular Comorbidities on COPD Prognosis and Treatment Response: A Systematic Review

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Abstract:

Background:

Chronic obstructive pulmonary disease is commonly associated with co-existing cardiac disease, including ischemic heart disease, heart failure, hypertension and arrhythmias. Comorbidities are associated with the same risk factors as COPD; aging, systemic inflammation and smoking. There is now growing evidence that cardiac comorbidities impact the clinical course of COPD, leading to altered mortality, numbers of exacerbations and response to therapy. This systematic review aims to evaluate the impact of cardiovascular comorbidities on COPD prognosis and therapeutic outcomes.

Methods:

A systematic literature search was conducted in PubMed for studies published between January 2012 and February 2026. Studies that examined the relationship between cardiovascular comorbidities and COPD outcomes—such as mortality, hospitalization, exacerbations, and treatment response were included. We considered observational studies, randomized trials, and meta-analyses that reported clinical outcomes in adult populations with COPD. Cardiovascular prevalence, the disease's prognostic impact, and its influence on therapeutic efficacy were the main topics of data extraction and qualitative synthesis.

Results:

In the literature search we identified 1,299 records, of which 1,150 remained after duplicate removal. Following title and abstract screening, 180 articles were selected for full-text review, and 22 studies met the inclusion criteria for qualitative synthesis. The included studies comprised prospective and retrospective cohort studies, case-control analyses, systematic reviews, and meta-analyses published between 2012 and 2026. Across the included studies, cardiovascular comorbidities were consistently associated with poorer outcomes in patients with chronic obstructive pulmonary disease (COPD). The presence of cardiovascular disease was linked to increased all-cause mortality, higher rates of cardiovascular events, including myocardial infarction, stroke, pulmonary embolism, and atrial fibrillation, as well as greater hospitalization rates and healthcare utilization. COPD exacerbations were associated with a significantly increased risk of both acute and long-term cardiovascular complications. Furthermore, cardiovascular comorbidities were associated with greater disease severity, worse functional outcomes, and accelerated disease progression. These findings were consistent across diverse study populations and healthcare settings, highlighting the substantial prognostic impact of cardiovascular disease in COPD.

Conclusions:

Cardiovascular comorbidities significantly impact treatment response and healthcare utilization, and they significantly worsen the prognosis of patients with COPD. Clinical outcomes may be enhanced by integrated cardiopulmonary management techniques and early detection of cardiovascular disease in COPD patients. Future studies addressing the overlap between COPD and cardiovascular disease should concentrate on multidisciplinary approaches and targeted therapeutic strategies.

Key words: chronic obstructive pulmonary disease, cardiovascular comorbidities, cardiovascular disease, treatment outcome, prognosis

1. Introduction:

Chronic obstructive pulmonary disease (COPD) is a long-lasting lung condition that stems from harm to the lungs. This damage leads to swelling and irritation—known as inflammation—within the airways, which restricts the flow of air in and out of the lungs. This

reduced airflow is referred to as obstruction. Common symptoms include difficulty breathing, a persistent cough that produces mucus, and a characteristic tight, whistling sound in the lungs, known as wheezing. COPD is most often caused by long-term exposure to irritating smoke, fumes, dust or chemicals. The most common cause is cigarette smoke[2]. According to WHO chronic obstructive pulmonary disease is the fourth leading cause of death worldwide, causing 3.5 million deaths in 2021, approximately 5% of all global deaths[3]. In addition to the impairments of the respiratory system, it is now also accepted that COPD is a systemic disease with a number of associated and at times life threatening comorbid causes[6], Cardiovascular disease being one of the most common and important of these comorbid factors[1,4]. Comorbidities are highly prevalent in chronic obstructive pulmonary disease (COPD), affecting more than 80% of patients[5]. Cardiovascular disease represents one of the most clinically significant comorbidities, with growing evidence demonstrating that COPD is associated with a markedly increased risk of myocardial infarction, heart failure, atrial fibrillation, and stroke. The coexistence of COPD and cardiovascular disease cannot be explained solely by shared risk factors such as aging and cigarette smoking. Increasing evidence supports the concept of a „cardiopulmonary continuum”, in which systemic inflammation, oxidative stress, endothelial dysfunction, and chronic hypoxia contribute to both pulmonary and cardiovascular pathology. These mechanisms promote atherosclerosis, vascular remodeling and myocardial dysfunction, thereby linking pulmonary disease progression with cardiovascular complications[7]. The clinical presentation and management of COPD are greatly affected by the presence of cardiovascular comorbidities[8]. In spite of this, observational studies have revealed that individuals with concomitant cardiovascular disease experience more hospitalization, exacerbations, and death than those without COPD. In some cohorts studies, cardiovascular events account for a substantial proportion of deaths among patients with moderate COPD, exceeding deaths attributed directly to respiratory failure[9]. Furthermore, cardiovascular comorbidities may alter treatment response and complicate the management of COPD. Pharmacological therapies used in COPD including bronchodilators and corticosteroids, may interact with cardiovascular medications or influence cardiac function. Conversely, cardiovascular therapies such as β -blockers, historically avoided in COPD patients, are now increasingly recognised as potentially beneficial in selected populations. These complex interactions highlight the need for integrated cardiopulmonary management strategies. Despite the growing recognition of the COPD-cardiovascular disease overlap, the overall impact of cardiovascular comorbidities on COPD prognosis and therapeutic outcomes remains incompletely understood. Previous research has tended to show heterogeneous findings regarding the magnitude of risk associated with specific cardiovascular conditions such as heart failure or ischemic heart disease, reflecting differences in study design, populations and diagnostic criteria. Therefore, a comprehensive synthesis of available evidence is necessary[10].

Research Question:

How do cardiovascular comorbidities influence prognosis, clinical outcomes and treatment response in patients with chronic obstructive pulmonary disease?

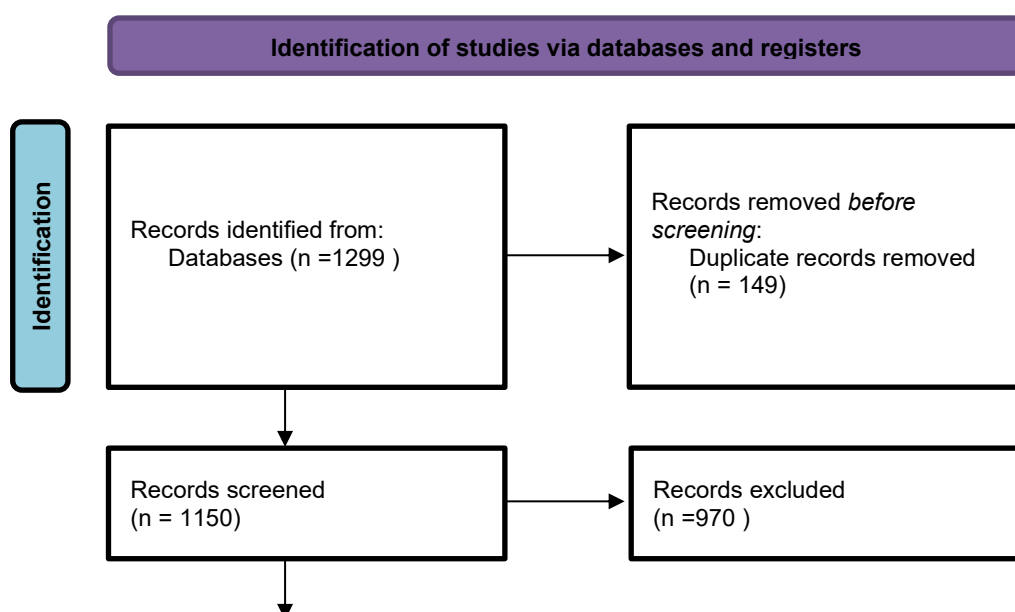
2. Research materials and methods

A systematic literature search was conducted in PubMed for studies that were published between January 2012 and February 2026. Search terms included combinations of key words: „COPD”, „cardiovascular disease”, „cardiovascular comorbidities”, „prognosis”, „treatment outcome”, „heart failure”, „mortality”, „exacerbation” and „hypertension”. Studies were included if they involved adult COPD populations and evaluated the impact of cardiovascular comorbidities on clinical outcomes such as mortality, exacerbations, hospitalization, or treatment response. Observational studies, randomized controlled trials, and systematic reviews were considered. Case reports, conference abstracts, pediatric studies, and non-English publications were excluded. Two reviewers independently screened titles and abstracts, followed by full-text evaluation of potentially relevant studies. Data extracted included study design, population characteristics, cardiovascular comorbidities, and clinical outcomes. Methodological quality assessment focused on study design, population selection, outcome reporting and risk of bias of the included criteria were assessed using established criteria for observational and interventional research designs. The study selection process was conducted according to the PRISMA guidelines. Titles and abstracts were screened, followed up by full text assessment of potentially eligible articles.

3. Results

3.1 Study selection

In the literature search we identified 1299 records. After removal of 149 duplicated records, 1150 studies remained for title and abstract screening. The number of studies that were excluded during this stage was 970. Full texts of 180 potentially relevant studies were sought for retrieval, of which 170 were assessed for eligibility. Following full text evaluation, 148 articles were excluded for not meeting the inclusion criteria. The qualitative synthesis comprised 22 studies in the end. We presented study data in the PRISMA flow chart Fig1.



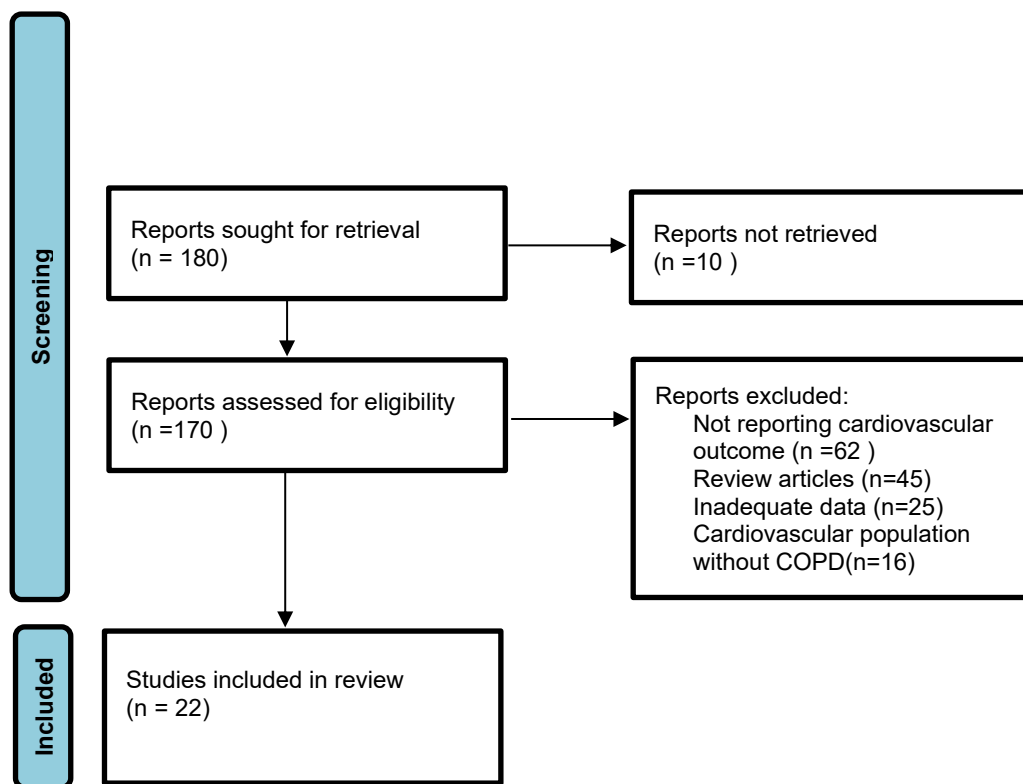


Fig.1 (PRISMA flow diagram). Source based on: [11]Page MJ, et al. BMJ 2021;372:n71. doi: <https://doi.org/10.1136/bmj.n71>

The included studies comprised a mixture of prospective and retrospective cohort studies, as well as case–control analyses and meta-analyses, published between 2012 and 2026. Sample sizes ranged from several hundred to large population-based cohorts involving tens of thousands of participants. The majority of studies evaluated mixed cardiovascular comorbidities, while some focused on specific conditions such as heart failure, atrial fibrillation, myocardial infarction, and thromboembolic disease [Table1.]

Table.1 Characteristics of included studies

No.	Study	Year	Design	Population	Cardiovascular Focus	Outcomes
1	Müllerova et al.[12]	2013	Systematic review	Multiple	Mixed CVD	Mortality
2	Vogelmeier et al.[13]	2025	Cohort	Large	Mixed CVD	Mortality
3	Noh et al.[14]	2024	Cohort	Nationwide	Mixed CVD	CV events
4	Caram et al.[15]	2016	Cohort	COPD patients	CVD risk	Severity
5	Nikolaou et al.[16]	2021	Cohort/ML	Large	Mixed CVD	Prediction
6	Wallström et al.[17]	2024	Cohort	Large	MI, PE	CV events
7	Spece et al.[18]	2018	Cohort	Moderate	Mixed CVD	COPD Exacerbations
8	Chen et	2015	Meta-	Multiple	Mixed CVD	CV risk

	al.[19]		analysis			
9	Mannino et al.[20]	2013	Cohort	Large	Mixed CVD	Mortality
10	Sá-Sousa et al.[21]	2024	Systematic review	Multiple	Mixed CVD	CV risk
11	Baty et al.[22]	2013	Case-control	Population	Mixed CVD	Burden
12	Divo et al.[23]	2012	Cohort	1664	Mixed CVD	Mortality
13	Ford et al.[24]	2012	Cross-sectional	NHANES	Mixed CVD	CV risk
14	Laforest et al.[25]	2016	Cohort	Large	Mixed CVD	Mortality
15	Miller et al.[26]	2013	Cohort	ECLIPSE	Mixed CVD	Clinical outcomes and Mortality.
16	Durheim et al.[27]	2018	Cohort	Large	Atrial fibrillation	Outcomes
17	Carter et al.[28]	2019	Cohort	Large	HF, IHD, AF	Mortality
18	Cho et al.[29]	2025	Cohort	496 056 patients	Established CVD	Mortality
19	Ingebrigtsen et al.[30]	2020	Cohort	91 692 patients	Mixed CVD	CV risk
20	Vanfleteren et al.[31]	2013	Prospective cohort	Moderate	Multimorbidity	Mortality, disease burden
21	Tang et al.[32]	2021	Cohort	COPD + OSA patients	Mixed CVD	Mortality, CV risk
22	Ding et al.[33]	2026	Cohort	Large	Mixed CVD	Long-term CV events

3.2 Impact of Cardiovascular Comorbidities on Mortality

Cardiovascular comorbidities were consistently associated with increased all-cause mortality in patients with COPD. Foundational cohort analyses demonstrated that the presence of comorbid conditions significantly worsens survival outcomes [23,25]. Similarly, large observational studies confirmed that COPD patients with coexisting cardiovascular disease have higher mortality compared to those without such comorbidities [13,20,28,29]. Additionally, specific comorbidity phenotypes, such as COPD–obstructive sleep apnea overlap syndrome, were associated with significantly increased cardiovascular risk and short-term mortality [32]. Systematic reviews and meta-analyses further reinforced this association [12,19,21].

Systematic reviews and meta-analyses further reinforced this association, demonstrating a significantly elevated risk of cardiovascular-related and all-cause mortality in COPD

populations [12,20,22]. These findings were consistent across different healthcare systems and study designs, highlighting the robustness of the observed relationship.

3.3 Cardiovascular Events and Disease Burden

Several studies reported an increased incidence of cardiovascular events among COPD patients, including myocardial infarction, stroke, pulmonary embolism, and arrhythmias. Large population-based analyses showed that COPD is independently associated with a higher risk of cardiovascular events, even after adjustment for traditional risk factors [14,24,28,30]

In particular, the coexistence of atrial fibrillation was associated with worse clinical outcomes and increased morbidity [28]. Additionally, studies focusing on multimorbidity demonstrated that cardiovascular disease constitutes a substantial proportion of the overall comorbidity burden in COPD patients [22,32].

3.4 Exacerbations and Cardiovascular Risk

A significant body of evidence highlighted the relationship between COPD exacerbations and acute cardiovascular events. Recent cohort studies demonstrated that exacerbations are associated with a markedly increased risk of myocardial infarction and pulmonary embolism [17,18].

Furthermore, longitudinal analyses showed that exacerbations contribute to long-term cardiovascular risk, suggesting a sustained systemic impact beyond the acute phase [33]. These findings support the hypothesis that exacerbations act as triggers for cardiovascular complications through inflammatory and hemodynamic mechanisms.

3.5 Impact on Hospitalization and Healthcare Utilization

Cardiovascular comorbidities were also associated with increased hospitalization rates and healthcare utilization. Population-based studies demonstrated that COPD patients with cardiovascular disease have a higher likelihood of hospital admissions, particularly for cardiovascular causes [18,31].

Moreover, comorbid conditions were shown to negatively affect recovery following COPD exacerbations, leading to prolonged hospital stays and increased risk of readmission [19].

3.6 Influence on Disease Severity and Clinical Outcomes

Several studies demonstrated that cardiovascular comorbidities are associated with greater disease severity and worse clinical outcomes in COPD. Patients with more advanced COPD stages were found to have a higher burden of cardiovascular risk factors [15].

In addition, systemic inflammation and comorbidity burden were linked to worse functional status and disease progression [27]. Emerging evidence using machine learning approaches further supports the role of cardiovascular phenotypes in predicting outcomes in COPD patients [16]. Specific comorbidity phenotypes, such as COPD-obstructive sleep apnea

overlap syndrome, were associated with significantly increased risk and one-year mortality[32].

Overall, the included studies consistently demonstrate that cardiovascular comorbidities: increase mortality risk, contribute to higher incidence of cardiovascular events, are associated with greater hospitalization rates and worsen clinical outcomes and disease progression. These findings were consistent across a wide range of study designs and populations, underscoring the significant impact of cardiovascular disease on COPD prognosis [12–33].

No.	Study	Key Findings
1	Müllerova et al.	CVD significantly increases mortality in COPD
2	Vogelmeier et al.	COPD patients have higher mortality vs controls
3	Noh et al.	COPD increases risk of cardiovascular events
4	Caram et al.	Greater COPD severity and higher CV risk
5	Nikolaou et al.	ML predicts cardiovascular comorbidities
6	Wallström et al.	Exacerbations increase MI and PE risk
7	Spece et al.	Comorbidities worsen post-exacerbation outcomes
8	Chen et al.	Strong COPD&CVD association confirmed
9	Mannino et al.	CVD increases mortality
10	SÃ¡-Sousa et al.	Elevated cardiovascular risk
11	Baty et al.	High comorbidity burden
12	Divo et al.	Comorbidities predict mortality
13	Ford et al.	Airflow limitation linked to CV risk
14	Laforest et al.	Comorbidities increase mortality
15	Miller et al.	Inflammation + comorbidities worsen outcomes
16	Durheim et al.	AF worsens outcomes in COPD
17	Carter et al.	COPD strongly associated with CVD, increasing mortality risk
18	Cho et al.	COPD worsens outcomes in patients with CVD
19	Ingebrigtsen et al.	Exacerbations linked to CV events
20	Vanfleteren et al.	Multimorbidity highly prevalent patients with COPD
21	Tang et al.	Patients with OS had an increased risk for cardiovascular diseases and 1-year mortality.
22	Ding et al.	Exacerbations increase long-term CV risk

4. Discussion

Principal Findings

This systematic review demonstrates that cardiovascular comorbidities are highly prevalent in patients with chronic obstructive pulmonary disease (COPD) and have a substantial negative impact on prognosis and clinical outcomes. Across the included studies, the presence of cardiovascular disease (CVD) was consistently associated with increased all-cause mortality, higher incidence of cardiovascular events, and greater healthcare utilization [12–33].

Importantly, the relationship between COPD and cardiovascular disease appears to be bidirectional and synergistic, with COPD contributing to cardiovascular risk and, conversely, cardiovascular conditions worsening respiratory outcomes [14,28,29]. This interaction underscores the need to consider COPD as a systemic disease rather than an isolated pulmonary disorder.

Pathophysiological Mechanism

Several mechanisms may explain the strong association between COPD and cardiovascular comorbidities. Chronic systemic inflammation plays a central role, with elevated inflammatory mediators contributing to atherosclerosis progression, endothelial dysfunction, and plaque instability [26,33]. The ECLIPSE cohort demonstrated that systemic inflammation correlates with both comorbidity burden and worse outcomes in COPD patients [26].

Additionally, hypoxia and oxidative stress in COPD patients may exacerbate cardiovascular dysfunction by increasing sympathetic activation and promoting vascular remodeling. Recurrent exacerbations further amplify these effects, acting as acute triggers for cardiovascular events such as myocardial infarction and pulmonary embolism [17,30,33].

Another important contributor is the presence of overlapping comorbid conditions, such as obstructive sleep apnea, which has been shown to significantly increase cardiovascular risk and short-term mortality in COPD patients [32]. This highlights the complexity of multimorbidity in COPD and the need for integrated clinical assessment.

Clinical Implications

The findings of this review have several important clinical implications. First, they emphasize the necessity of routine cardiovascular risk assessment in patients with COPD, particularly in those with advanced disease or frequent exacerbations. Several studies demonstrated that cardiovascular conditions such as heart failure, atrial fibrillation, and ischemic heart disease are major determinants of mortality in this population [28,29].

Second, the presence of cardiovascular comorbidities may influence treatment response and disease management strategies. Comorbid conditions can complicate pharmacological

therapy, limit treatment options, and increase the risk of adverse events. Furthermore, they contribute to higher rates of hospitalization and poorer recovery following exacerbations [18,19,31].

Finally, the strong association between exacerbations and cardiovascular events suggests that preventing exacerbations may reduce cardiovascular risk, providing an additional rationale for optimal COPD management, including pharmacotherapy and lifestyle interventions.

Comparison with Previous Literature

The findings of this review are consistent with previous large-scale analyses and systematic reviews, which have reported a high prevalence of cardiovascular comorbidities in COPD and their significant impact on outcomes [12,20,22]. However, the present study extends prior knowledge by incorporating more recent data, including studies published up to 2026, which further strengthen the evidence linking exacerbations and long-term cardiovascular risk [33].

Moreover, newer studies included in this review highlight the importance of specific clinical phenotypes, such as COPD patients with pre-existing cardiovascular disease or overlap syndromes, in whom the prognostic impact appears to be particularly pronounced [29,32].

Strengths and Limitations

A key strength of this review is the inclusion of recent, high-quality studies, including large population-based cohorts and meta-analyses, ensuring a comprehensive and up-to-date synthesis of the available evidence. The use of a systematic approach and predefined inclusion criteria enhances the reliability of the findings.

However, several limitations should be acknowledged. First, the included studies exhibited heterogeneity in study design, populations, and definitions of cardiovascular comorbidities, which may limit direct comparability. Second, most studies were observational, which precludes definitive conclusions regarding causality. Third, potential confounding factors, such as smoking status and treatment differences, were not consistently adjusted for across studies. Finally, publication bias cannot be excluded.

Future Directions

Future research should focus on prospective, longitudinal studies to better understand the causal relationships between COPD and cardiovascular disease. Additionally, there is a need for studies evaluating integrated management strategies targeting both pulmonary and cardiovascular components.

The development of risk stratification tools incorporating cardiovascular comorbidities may also improve prognostic assessment and guide personalized treatment approaches. Emerging technologies, including machine learning models, may play a role in identifying high-risk patients and optimizing clinical decision-making [16].

5. Conclusion

Cardiovascular comorbidities are a major determinant of prognosis in patients with COPD, significantly contributing to increased mortality, cardiovascular events, and healthcare burden. The complex interplay between pulmonary and cardiovascular disease highlights the importance of a multidisciplinary, integrated approach to patient management.

Early identification and targeted management of cardiovascular risk factors in COPD patients may improve outcomes and reduce the overall disease burden.

Disclosure:

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