International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

Investigating the Association between Hypertension and Chronic Obstructive Pulmonary Disease: A Systematic Review

Thamer alhumodi alenazi [1], SARA Ebrahim Ahmed Hasan Ali Alabood [2], Mona salman alfaifi [3], Wajd hamad Al moqati [4], Randa Majed Ashy [5], Rana Khalid Almuqati [6], Shaima Saad Musallam Aljohani [7], Waleed Yousef Q Alanazi [8], Fayez Abdulaziz Alwadani [9], Basim Mazin Janbi [10]

1- Internal medicine and infectious diseases consultant, KFSH, Tabuk, Saudi Arabia

2- Bachelor of medicine and Surgery, Mansoura university, Egypt. Manama, Bahrain.

3- Medical student, College of medicine, Najran University, Najran City, Saudi Arabia

4- Intern, Medical student, Najran university, Saudi Arabia

5- Medical intern, Medicine & surgery, KAUH, Jeddah, Saudi Arabia

6- Medical intern, Medicine and surgery, Imam Abdulrahman bin faisal university, Al Khobar, Kingdom of Saudi Arabia.

7- Intern, Medicine and Surgery, University of Hail, Yanbu, Kingdom of Saudi Arabia

8- Medical intern, Northern border university, Arar, Saudi Arabia

9- Medical intern, Medicine and surgery, Umm Alqura university, Makkah, Saudi Arabia

10- Medical intern, Medicine and surgery, Umm Alqura university, Makkah, Saudi Arabia

Abstract

Objective: To systematically review existing literature to investigate the potential association between hypertension (HTN) and chronic obstructive pulmonary disease (COPD).
Methods: A thorough search across four databases identified 80 relevant publications. After removing duplicates using Rayyan QCRI and screening for relevance, 93 full-text articles were reviewed, with eight studies ultimately meeting the criteria for inclusion.
Results: We included eight studies with a total of 10979 patients diagnosed with COPD, and most of them 7029 (64%) were males. The prevalence of HTN among COPD patients ranged from 17.8% to 60.7% with a total prevalence of 4471 (40.7%). HTN is commonly observed in COPD patients, particularly in those over 40, smokers, and individuals with a history of HTN. Both systolic and diastolic blood pressure values were elevated in COPD patients, with non-smokers also showing increased rates of HTN. Inflammatory markers, such as the Systemic Immune-Inflammation Index, were significantly associated with the coexistence of these conditions, suggesting that inflammation plays a key role.
Conclusion: This review highlights a strong association between HTN and COPD, with systemic inflammation likely playing a key role in the coexistence of these conditions. The findings emphasize the importance of integrated management approaches that address both respiratory and cardiovascular health in COPD patients. While the evidence points to a significant overlap between the two conditions, further longitudinal studies are needed

to clarify the causal relationship and identify the most effective interventions for managing this comorbidity.
Keywords: Hypertension*;* Chronic Obstructive Pulmonary Disease*;* Pathophysiology*; Systematic review.*

Introduction

The global prevalence of chronic diseases has risen alarmingly over the past few decades, with HTN and COPD representing two significant public health challenges. HTN, characterized by persistently elevated blood pressure, affects approximately 1.38 billion adults worldwide, according to the World Health Organization [1]. COPD, a progressive lung disease primarily caused by prolonged exposure to harmful particulates or gases, affects hundreds of millions of individuals globally, with rising incidence rates. While these two conditions are commonly viewed as distinct entities, emerging evidence suggests a complex interplay between them, necessitating a comprehensive examination of their association [1].

HTN is defined as blood pressure readings equal to or greater than 130/80 mmHg, with potential risks including stroke, heart attack, and chronic kidney disease. Various factors, including genetics, lifestyle choices, diet, and underlying health conditions, contribute to the development of HTN [2]. Chronic Obstructive Pulmonary Disease, on the other hand, encompasses two primary conditions: chronic bronchitis and emphysema. Its hallmark symptoms include chronic cough, sputum production, and dyspnea. The pathophysiology of COPD involves airway inflammation and narrowing, along with alveolar destruction, typically provoked by cigarette smoking or environmental pollutants. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), COPD is the third leading cause of death worldwide, highlighting its significant health impact [3].

Recent studies have highlighted a significant association between HTN and COPD. The prevalence of HTN among patients with COPD is notably high, ranging from 40% to 80%, which is considerably greater than that observed in the general population. To explain this connection, several mechanisms have been proposed [4].

One of the primary mechanisms is the existence of shared risk factors. Both HTN and COPD are influenced by various common contributors, including smoking, a sedentary lifestyle, obesity, and advancing age. A study published in the journal *Respiratory Medicine* indicated that individuals with COPD typically engage in lower levels of physical activity. This reduced activity can exacerbate weight gain and obesity, which in turn can lead to the development of HTN [5].

Another significant factor is the role of inflammatory pathways. Chronic inflammation is a characteristic feature of both HTN and COPD. The pathogenesis of COPD is associated with systemic inflammation, which negatively impacts cardiovascular health. In patients with COPD, increased levels of inflammatory markers such as C-reactive protein (CRP) have been noted, correlating with greater arterial stiffness and HTN. This suggests that inflammation may serve as a key link between these two conditions [6].

Additionally, the consequences of chronic hypoxemia play a crucial role. Many COPD patients experience chronic low oxygen levels, which can activate the sympathetic nervous system, leading to vasoconstriction and promoting HTN. Prolonged exposure to low oxygen levels may also induce structural changes in the pulmonary vasculature, further exacerbating HTN [7].

Finally, the medications used to treat these conditions may contribute to their association as well. For example, systemic corticosteroids, which are frequently prescribed for COPD management, can result in fluid retention and elevated blood pressure. This necessitates careful monitoring of cardiovascular health in patients undergoing treatment for both conditions to mitigate potential risks [8].

The coexistence of HTN and COPD presents considerable clinical challenges. Patients affected by both conditions often endure exacerbated symptoms and increased morbidity. Effectively managing HTN in these individuals necessitates a customized approach that takes into account potential drug interactions and the risk of worsening respiratory symptoms [9].

One critical aspect of care is risk assessment. Conducting comprehensive evaluations that incorporate pulmonary function tests alongside blood pressure measurements is essential for identifying patients at risk. Recognizing coexisting conditions enables healthcare providers to adopt a holistic strategy, focusing on preventive measures and tailored interventions to enhance patient outcomes [7].

Pharmacological management in COPD patients requires careful consideration of antihypertensive medications. For instance, while beta-blockers are commonly prescribed to manage HTN, they can induce bronchoconstriction; therefore, cardioselective beta-blockers may be preferable in these cases. Additionally, incorporating long-acting bronchodilators into the treatment regimen can help alleviate respiratory symptoms while simultaneously supporting cardiovascular health [9].

Encouraging lifestyle modifications is also an important component of managing patients with both HTN and COPD. Advocating for changes such as smoking cessation, weight management, and regular physical activity can yield significant benefits for these individuals. These lifestyle interventions not only enhance lung function and overall quality of life but also play a crucial role in effectively managing HTN [10].
COPD and HTN are two prevalent non-communicable diseases that significantly contribute to global morbidity and mortality. The significance of this study lies in its potential to enhance our understanding of the interplay between these two conditions. Both diseases are characterized by systemic inflammation and share common risk factors, such as smoking, obesity, and physical inactivity. Understanding the association could lead to improved patient management and treatment strategies, ultimately resulting in better health outcomes and reduced healthcare costs. Given the increasing burden of both diseases, it is crucial to investigate their relationship to inform clinical practice, public health strategies, and future research agendas. Despite the known individual impacts of HTN and COPD on health outcomes, the extent and nature of their association remain inadequately explored and understood. Existing literature presents conflicting evidence about the prevalence of HTN in patients with COPD and its effect on disease progression and management. This lack of clarity poses challenges for clinicians in diagnosing and treating patients who may present with comorbid conditions.

The overarching aim of this systematic review is to investigate the association between HTN and chronic obstructive pulmonary disease comprehensively. By systematically compiling and critically evaluating existing evidence, the study seeks to establish a clearer understanding of the interplay between these two conditions.

Methods

This study followed the protocols established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [11] to conduct a systematic review exploring the relationship between HTN and COPD. A thorough electronic literature search was performed across multiple databases, including PubMed, Web of Science, SCOPUS, and Science Direct, to identify relevant studies published in English that investigate the prevalence and risk factors associated with HTN and COPD. The search incorporated keywords related to both conditions and their interconnections. Two independent reviewers evaluated the search results, selected eligible studies, extracted relevant data, and assessed the quality of the included research using recognized evaluation tools.

Eligibility Criteria

Inclusion criteria comprised peer-reviewed articles published in English that explored the association between HTN and COPD, including observational studies, clinical trials, and meta-analyses. Studies involving adult patients (aged 18 and older) diagnosed with HTN and/or COPD will also be included. Additionally, only studies that report relevant outcomes related to the incidence, prevalence, or risk factors associated with these conditions were considered. On the other hand, exclusion criteria involved studies that focus on populations under 18 years of age, articles not written in English, case reports, reviews, or editorials, and studies that do not specifically assess the relationship between HTN and COPD. Furthermore, research with insufficient data to evaluate the association was also excluded to maintain the rigor of the review process.

Data Extraction

To guarantee accuracy, the search results were validated using Rayyan (QCRI) [12]. The titles and abstracts identified during the search were assessed for their relevance based on the established inclusion and exclusion

criteria. Studies that meet the inclusion criteria were subject to an in-depth review by the research team. Any disagreements among reviewers will be resolved through consensus. Important details about each study, such as titles, authors, publication year, study location, participant demographics, and gender distribution, were documented using a predefined data extraction form.

Data Synthesis Strategy

In order to provide a qualitative evaluation of the research findings and components, summary tables were generated using data extracted from relevant studies. Once the data collection for the systematic review is complete, the optimal approach for utilizing the data from the included studies were determined.

Risk of Bias Assessment

We utilized the ROBINS-I technique to evaluate the risk of bias because it allows for extensive assessment of confounding, which is significant because bias owing to omitted variables is common in studies in this field. The ROBINS-I tool is intended to evaluate non-randomized investigations and can be applied to cohort designs in which participants exposed to various staffing levels are monitored over time. Two reviewers separately assessed the risk of bias for each paper, and disagreements were resolved through group discussion [13].

Results

The specified search strategy yielded 860 publications **(Figure 1).** After removing duplicates (n =464), 396 trials were evaluated based on title and abstract. Of these, 301 failed to satisfy eligibility criteria, leaving just 95 full-text articles for comprehensive review. Two records were identified through citation search and only one was accepted into our review. A total of 8 satisfied the requirements for eligibility with evidence synthesis for analysis.

Sociodemographic and clinical outcomes

We included eight studies with a total of 10979 patients diagnosed with COPD, and most of them 7029 (64%) were males. Five articles were cross-sectional studies [14, 16, 17, 18, 21], two were case-controls [15, 20], and one was a prospective cohort [19]. Three studies were implemented in China [14, 18, 21], two in Indonesia [16, 17], one in Ukraine [15], one in South Korea [19], and one in Iraq [20].

Main outcomes

The prevalence of HTN among COPD patients ranged from 17.8% [18] to 60.7% [16] with a total prevalence of 4471 (40.7%). The main outcomes from these studies indicate a strong association between HTN COPD [14-21], particularly among adults under 60. For individuals with a history of smoking, the correlation between HTN and COPD was even more significant, underscoring the impact of smoking status on this relationship [14]. The prevalence of elevated blood pressure, including systolic and diastolic values, was notably higher among those with isolated COPD, indicating that HTN frequently coexists with COPD, which may worsen cardiovascular outcomes [15].

In several studies, older age and male sex were recurring factors that influenced the prevalence of HTN among COPD patients [16-18]. For example, men over 40 years old, especially those with a smoking history or other risk factors like a history of HTN, showed an increased association with COPD [17, 18]. Additionally, the severity of COPD, reflected by lung function measures, was often linked to higher levels of HTN [16].

Another crucial finding was the observation that non-smokers with COPD also had higher rates of HTN, suggesting that HTN in COPD may not be solely related to smoking [19]. These individuals exhibited a strong positive association with the Systemic Immune-Inflammation Index, suggesting that inflammation may play a crucial role in linking these two conditions [21].

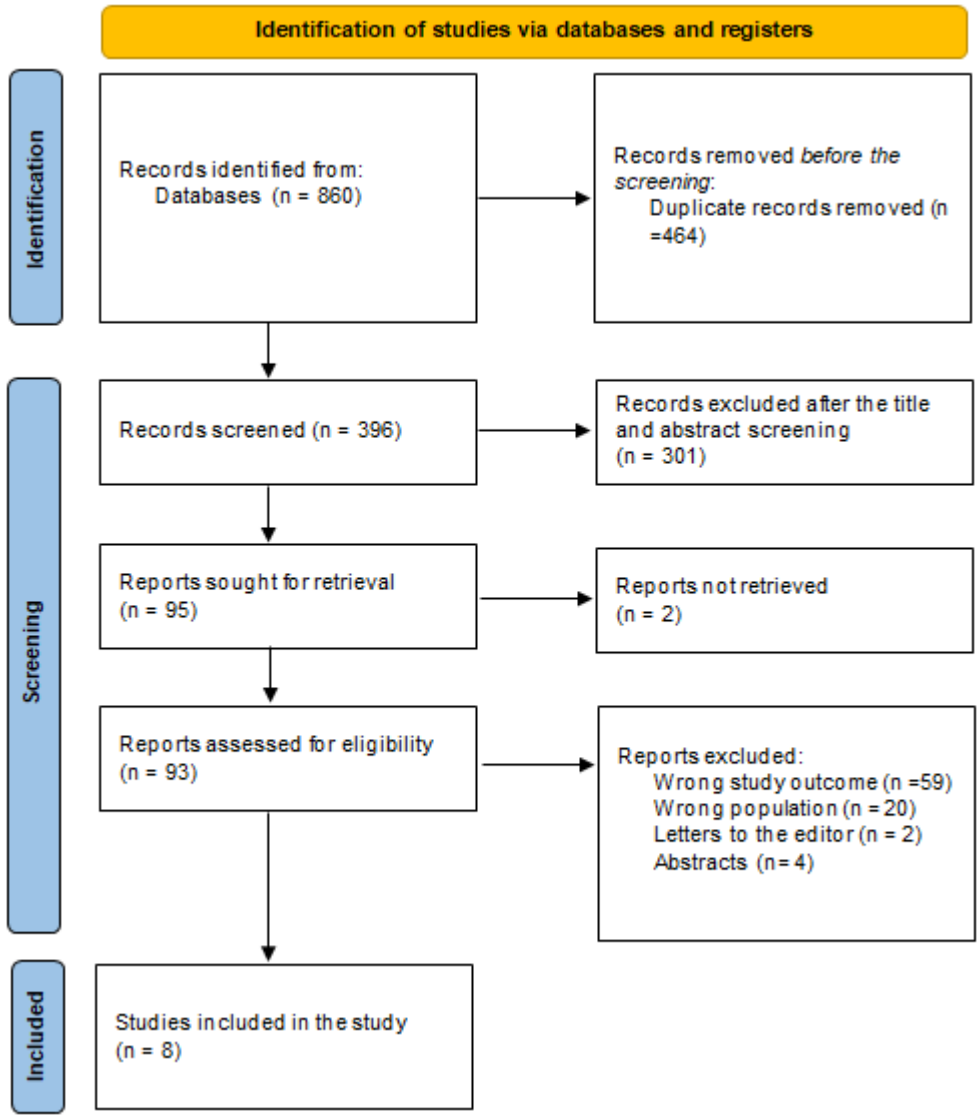

Figure (1): PRISMA flowchart.

Table (1): Outcome measures of the included studies

Study ID	Country	Study design	Sociodemographic	Prevalence of HTN	Main outcomes	ROBINS-II
Liang et al., 2023 [14]	China	Cross-sectional	Participants: 3121 Mean age: 53.7 Males (%): 1185 (34.8)	1965 (58.5%)	Among adults under 60, there was a strong correlation (P<0.01) between HTN and COPD. Among current heavy smokers, there was a significant correlation between HTN and COPD, stratified by smoking status (P=0.04).	Moderate
Тверезовський et al., 2023 [15]	Ukraine	**Case-control**	Participants: 95 Mean age: 61 Males (%): 51 (53.6)	48 (50.5%)	A considerable rise of blood pressure values, both systolic and diastolic, was observed in individuals with isolated COPD as well as in those with COPD and HTN coexisting.	Moderate

Dewantoro et al., 2024 [16]	Indonesia	**Cross-sectional**	Participants: 84 Males (%): 73 (86.9)	51 (60.7%)	Significant relationships have been found between HTN and age (P=0.0001), severity degree of clinical COPD (P=0.004), and lung functional values (P=0.021).	Moderate
Pertiwi et al., 2022 [17]	Indonesia	Cross-sectional	Participants: 130 Males (%): 62 (47.7)	22 (16.9%)	Male sex, age over 40, a history of HTN combined with COPD, and the amount and pattern of smoking are all associated with the disease.	Low
Huang et al., 2024 [18]	China	**Cross-sectional**	Participants: 3913 Mean age: 66.6 Males (%): 2699 (69)	697 (17.8%)	The most common comorbidity with COPD is HTN, which may have an impact on prognosis.	Low
Choi et al., 2022 [19]	South Korea	Prospective cohort	Participants: 2477 Mean age: 69.2 Males (%): 2268 (92.3)	974 (39.5%)	Patients with COPD who did not smoke had higher rates of HTN.	Moderate
Ghafil et al., 2023 [20]	Iraq	Case-control	Participants: 100 Mean age: 52.6 Males (%): 85 (85)	35 (35%)	Patients with COPD were frequently found to have HTN.	Moderate
Ye et al., 2023 [21]	China	Cross-sectional	Participants: 1054 Mean age: 61.2 Males (%): 606 (50.5%)	679 (59.5%)	Subgroup analysis results indicated that individuals with COPD who had a history of HTN and the Systemic Immune-Inflammation Index exhibited a strong positive connection.	Moderate

Discussion

This review found that the prevalence of HTN among COPD patients ranged from 17.8% [18] to 60.7% [16] with a total prevalence of 4471 (40.7%). The main outcomes from these studies indicate a strong association between HTN COPD [14-21], particularly among adults under 60 years. The prevalence of elevated blood pressure, including systolic and diastolic values, was notably higher among those with isolated COPD, indicating that HTN frequently coexists with COPD, which may worsen cardiovascular outcomes [15]. **Cordeiro dos Santos *et al.*** reported that among COPD patients, HTN and coronary artery disease are the two most common comorbidities [22].

It follows that cardiovascular illness is a common cause of death for persons with mild to moderate COPD. The systematic assessment of cardiovascular disorders in COPD patients is warranted due to the high prevalence and significant effects of cardiovascular comorbidities. It's unclear exactly how COPD and cardiovascular disease are related. The high incidence of cardiovascular comorbidities in COPD may be explained by shared significant etiologic factors (such as smoking), systemic inflammation, lung hyperinflation, decreased oxygenation, and related variables such obesity [23, 24]. Another crucial finding was the observation that non-smokers with COPD also had higher rates of HTN, suggesting that HTN in COPD may not be solely related to smoking [19]. This highlights that even among non-smoking populations, the interaction between COPD and cardiovascular health is significant and requires further exploration.

For individuals with a history of smoking, the correlation between HTN and COPD was even more significant, underscoring the impact of smoking status on this relationship [14]. This implies that people with HTN should be restricted from tobacco use. Smoking negatively impacts endothelial function and stiffens the systemic arteries [25, 26]. This leads to hypertrophy and injury to the vascular wall [25]. Organ damage is caused by the aforementioned pathway, particularly to the lungs [27]. It was recently suggested that vascular inflammation and the reduction of antioxidants could be the cause of endothelial dysfunction and pulmonary lesions in COPD [28]. But although current smokers have lower endothelial function than people who used to smoke, the endothelial damage caused by smoking may be reversible [29].

In several studies in this review, older age and male sex were recurring factors that influenced the prevalence of HTN among COPD patients [16-18]. For example, men over 40 years old, especially those with a smoking history or other risk factors like a history of HTN, showed an increased association with COPD [17, 18]. This association may be attributed to cumulative exposure to smoking and environmental toxins, as well as age-related vascular changes that contribute to both HTN and respiratory impairments. These results underscore the importance of targeted interventions in older male patients with a smoking history or other cardiovascular risk factors, to mitigate the combined burden of COPD and HTN.

The findings of this review have significant clinical implications for the management of patients with COPD. The high prevalence of HTN in COPD patients suggests that routine cardiovascular screening should be an integral part of COPD management, particularly given the potential for HTN to exacerbate respiratory symptoms and increase the risk of cardiovascular events. Physicians should be vigilant in monitoring blood pressure in COPD patients and consider early interventions to manage HTN, which may improve overall outcomes and quality of life. Additionally, the association between systemic inflammation and both conditions indicates that therapeutic strategies targeting inflammation could be beneficial. Anti-inflammatory treatments that extend beyond the lungs to address systemic inflammation may offer new avenues for improving outcomes in patients with coexisting HTN and COPD.

Strengths and limitations

One of the key strengths of this review is its comprehensive scope, incorporating data from diverse studies across multiple countries and patient populations. This global approach enhances the generalizability of the findings, allowing a broader understanding of the relationship between HTN and COPD across different demographic and clinical contexts. Another strength lies in the focus on systemic inflammation as a potential link between the two conditions. Several studies examined inflammatory markers, such as the Systemic Immune-Inflammation Index, offering valuable insights into the underlying mechanisms that may contribute to the coexistence of HTN and COPD. These findings could inform future research and therapeutic strategies aimed at mitigating the inflammatory processes that drive both conditions. Additionally, the inclusion of both smokers and non-smokers provides a more nuanced view of how HTN and COPD interact, highlighting that the comorbidity is not solely attributable to smoking-related lung damage.

However, there are notable limitations in this review that should be considered. The majority of the studies included were cross-sectional in design, which limits the ability to draw causal inferences between HTN and COPD. While associations between the two conditions were observed, it remains unclear whether one directly contributes to the development or worsening of the other. Another limitation is the heterogeneity across the studies in terms of population characteristics, diagnostic criteria, and definitions of HTN. This variability may affect the consistency and comparability of the results, potentially limiting the strength of the conclusions. Furthermore, some studies did not account for important confounding factors, such as medication use, comorbid conditions, and socioeconomic status, which could have influenced the observed associations. These uncontrolled variables may introduce bias into the findings and affect the reliability of the conclusions.

Conclusion

In conclusion, this review highlights a strong association between HTN and COPD, with systemic inflammation likely playing a key role in the coexistence of these conditions. The findings emphasize the importance of integrated management approaches that address both respiratory and cardiovascular health in COPD patients. While the evidence points to a significant overlap between the two conditions, further longitudinal studies are needed to clarify the causal relationship and identify the most effective interventions for managing this comorbidity. Addressing both HTN and COPD in a holistic manner has the potential to improve clinical outcomes, reduce complications, and enhance the quality of life for affected patients.

References:

1. Liang X, Chou OHI, Cheung BM. The Association Between Systemic Arterial Hypertension and Chronic Obstructive Pulmonary Disease. Results from the U.S. National Health and Nutrition Examination Survey 1999-2018: A Cross-sectional Study. *Chronic Obstr Pulm Dis*. 2023;10(2):190-198.
2. Rapsomaniki E,Timmis A,George J,et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. *Lancet*. 2014;383(9932):1899-1911.
3. Vogelmeier CF,Criner GJ,Martinez FJ,et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 Report. GOLD Executive Summary. *Am J Respir Crit Care Med*. 2017;195(5):557-582.
4. Morgan AD,Zakeri R,Quint JK. Defining the relationship between COPD and CVD: what are the implications for clinical practice? *Ther Adv Respir Dis*. 2018;12:1-16.
5. Buch P,Friberg J,Scharling H,Lange P,Prescott E. Reduced lung function and risk of atrial fibrillation in the Copenhagen City Heart Study. *Eur Respir J*. 2003;21(6):1012-1016.
6. Kim SH,Park JH,Lee JK,Heo EY,Kim DK,Chung HS. Chronic obstructive pulmonary disease is independently associated with hypertension in men: a survey design analysis using nationwide survey data. *Medicine* (Baltimore). 2017;96(19):e6826.
7. Feinstein L,Wilkerson J,Salo PM,et al. Validation of questionnaire-based case definitions for chronic obstructive pulmonary disease. *Epidemiology*. 2020;31(3):459-466.
8. Barr RG,Celli BR,Mannino DM,et al. Comorbidities, patient knowledge, and disease management in a national sample of patients with COPD. *Am J Med*. 2009;122(4):348-355.
9. Mills NL,Miller JJ,Anand A,et al. Increased arterial stiffness in patients with chronic obstructive pulmonary disease: a mechanism for increased cardiovascular risk. *Thorax*. 2008;63(4):306-311.
10. Gan WQ,Man SF,Senthilselvan A,Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a meta-analysis. *Thorax*. 2004;59(7):574-580.
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. International journal of surgery. 2021 Apr 1;88:105906.
12. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systematic reviews. 2016 Dec;5:1-0.
13. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. bmj. 2016 Oct 12;355.
14. Liang X, Chou OH, Cheung BM. The Association Between Systemic Arterial Hypertension and Chronic Obstructive Pulmonary Disease. Results from the US National Health and Nutrition Examination Survey 1999-2018: A Cross-sectional Study. Chronic Obstructive Pulmonary Diseases: Journal of the COPD Foundation. 2023;10(2):190.
15. Тверезовський ВМ. Laboratory and instrumental characteristics of patients with chronic obstructive pulmonary disease and hypertension. Медицина сьогодні і завтра. 2023 Jun 30;92(2):6-16.
16. Dewantoro L, Wiyono WH, Yunus F, Agustin H, Damayanti T, Antariksa B, Fachrucha F, Samoedro E, Elhidsi M. Proportions of Hypertension in Stable COPD Patients at the National Respiratory Center Persahabatan Hospital. Jurnal Respirologi Indonesia. 2024 Jul 31;44(3):187-95.
17. Pertiwi MD, Martini S, Artanti KD, Widati S. the Relationship of Hypertension, Genetic and Degree of Smoking With the Incidence of Copd At Haji Public Hospital Surabaya. The Indonesian Journal of Public Health. 2022;17(2):241-51.
18. Huang K, Zheng Z, Li W, Niu H, Lei J, Dong F, Yang T, Wang C. Sociodemographic correlates with prevalence of comorbidities in patients with chronic obstructive pulmonary disease: a study from a Chinese National Survey. The Lancet Regional Health–Western Pacific. 2024 Jan 1;42.
19. Choi JY, Kim JW, Kim YH, Yoo KH, Jung KS, Lee JH, Um SJ, Lee WY, Park D, Yoon HK. Clinical characteristics of non-smoking chronic obstructive pulmonary disease patients: findings from the

KOCOSS cohort. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2022 Dec 31;19(1):174-81.

20. Ghafil NY, Dananah FM, Hassan ES, Alkaabi YS. Comorbidities in patients with chronic obstructive pulmonary disease: a comprehensive study. Journal of Medicine and Life. 2023 Jul;16(7):1013.
21. Ye C, Yuan L, Wu K, Shen B, Zhu C. Association between systemic immune-inflammation index and chronic obstructive pulmonary disease: a population-based study. BMC pulmonary medicine. 2023 Aug 10;23(1):295.
22. Cordeiro dos Santos N, Miravitlles Fernández M, Camelier A, Durier Cavalcanti de Almeida V, Rodrigues Bandeira Tosta Maciel R, Warken Rosa Camelier F. Prevalence and impact of comorbidities in individuals with chronic obstructive pulmonary disease: a systematic review.
23. Divo M, Celli BR. Multimorbidity in patients with chronic obstructive pulmonary disease. Clin Chest Med. 2020;41:405–19.
24. Putcha N, Puhan MA, Drummond MB, Han MK, Regan EA, Hanania NA, et al. A simplified score to quantify comorbidity in COPD. PLoS One. 2014;9:e114438.
25. Doonan RJ, Hausvater A, Scallan C, Mikhailidis DP, Pilote L, Daskalopoulou SS. The effect of smoking on arterial stiffness. Hypertens Res. 2010;33(5):398-410.
26. Karatzi K, Papamichael C, Karatzis E, et al. Acute smoke-induced endothelial dysfunction is more prolonged in smokers than in non-smokers. Int J Cardiol. 2007;120(3):404-406.
27. Maclay JD, McAllister DA, Rabinovich R, et al. Systemic elastin degradation in chronic obstructive pulmonary disease. Thorax. 2012;67(7):606-612.
28. Polverino F, Celli BR, Owen CA. COPD as an endothelial disorder: endothelial injury linking lesions in the lungs and other organs? (2017 Grover Conference Series). Pulm Circ. 2018;8(1):1-18.
29. Celermajer DS, Sorensen KE, Georgakopoulos D, et al. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. Circulation. 1993;88(5 Pt 1):2149-2155.