Article/Review

Chronic obstructive pulmonary disease and congestive heart failure: iarc-icpms. Three clinical applications of the human gene: a narrative literature review of comorbidity, pathophysiology, diagnosis, and management

Abdigaffor G.Gadayev *[1], **Rustam I.Turakulov** [1], **Bakhtiyor A.Nurullayev** [1]

[1] Department of family medicine №2, Tashkent state medical university, Tashkent, 100109, Uzbekistan
abgadaev@yahoo.com (A.G.), rustamturakulov571@gmail.com (R.T.), bahtiyor.nurullayev93@gmail.com (B.N.)
* Correspondence: Abdigaffor G.Gadayev (A.G.)

Abstract: Chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF) are among the leading causes of morbidity and mortality in the world. The high comorbidity burden presents important clinical challenges in exacerbating the issues of diagnosis and treatment due to overlapping symptom profiles, shared risk factors, and interconnected pathophysiological processes. This narrative review summarizes recent evidence on the epidemiology, pathophysiology, diagnostic challenges and therapeutic strategies for these patients. Peer-reviewed studies were identified by conducting a systematic search of PubMed, MEDLINE, and EMBASE from 2016 to 2024. Existing data suggests that COPD occurs in 20–30% of patients with CHF, and a comparable proportion of moderate-to-severe COPD has left ventricular dysfunction. Coginitive impairment is an independent predictor of adverse clinical outcomes, including higher rates of hospitalization and mortality. Systemic inflammation, oxidative stress, skeletal muscle dysfunction and neurohormonal activation are shared pathways linking these different diseases. Differential diagnosis is limited because of clinical symptom overlap; however, each mentioned biomarker has complementary diagnostic utility in general: natriuretic peptides will identify pulmonary hypertension due to left heart failure, echocardiography can assess underlying structural heart disease and pulmonary function testing helps characterize the underlying pathology. Management should be a personalized and multi-faceted approach focusing on drug safety related to beta-blockers and bronchodilators along with non-pharmacologic strategies such as pulmonary rehabilitation and cardiac rehabilitation. This review underscores the need for joint clinical assessment and supports more prospective studies of this high-risk group.

Keyword: COPD, congestive heart failure, cardiopulmonary comorbidity, dyspnea, diagnosis, pharmacotherapy, rehabilitation.

Quoting: Abdigaffor G.Gadayev, Rustam I.Turakulov, Bakhtiyor A.Nurullayev. Chronic obstructive pulmonary disease and congestive heart failure: iarc-icpms. Three clinical applications of the human gene: a narrative literature review of comorbidity, pathophysiology, diagnosis, and management. **2026**, 5, 1, 3. https://doi.org/10.56121/MSU-2026-1-00003

Received: 05.01.2026
Corrected: 16.01.2026
Accepted: 20.02.2026
Published: 27.02.2026

Introduction

Chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF) are among the most common, serious and prevalent chronic diseases facing adult populations worldwide. Based on the GOLD Total Care strategy, COPD is defined generally as a chronic inflammatory lung disease characterized by persistent respiratory symptoms and progressive airflow limitation that is predominantly irreversible. Pathologically, it is characterized by the obstruction of airflow due to an abnormality in either or both airways and/or alveoli that leads airway collapse during expiration and is usually the result of chronic and prolonged exposure to irritants such as environmental pollutants (often leaded to contaminated pulmonary damage) with tobacco smoke being one of the most common causes [13]. Conversely, congestive heart failure (CHF) is a complex clinical syndrome caused by either structural or functional issues of the myocardial muscles that result in the inability of ventricles to fill with and/or eject blood adequately. Such ventricular dysfunction triggers a number of symptoms

such as exertional and resting dyspnea, fatigue, and fluid retention that manifests itself as peripheral edema and pulmonary congestion [26].

COPD and CHF have a number of overlapping epidemiologic risk factors including older age, chronic tobacco smoking, chronic systemic inflammation, and lack of exercise. The presence of these overlapping risks goes a long way in explaining why there is an increased tendency for the two diseases to co-occur. Epidemiological data suggest that close to 20–30% of patients with clinically established COPD also have confirmed CHF, and vice versa: left ventricular dysfunction is identifiable in a similar fraction of patients with moderate-to-severe COPD [17,18]. However, due to the large clinical manifestations overlap (eg, dyspnea and exercise intolerance) between both conditions as well as the intrinsic difficulty in establishing a diagnosis when patients have multiple comorbidities (which complicates the assessment and management), each condition frequently goes unrecognized and undiagnosed in the presence of another.

The clinical implications of carrying this dual pathological burden are especially significant and complex. Patients with concomitant COPD and CHF also suffer from a greater burden of exacerbations, more severe functional impairment, substantial reductions in health-related quality of life and higher all-cause mortality compared with those with single disease [17,34]. The issue is that, from a therapeutic point of view, the first-line pharmacological agents for the condition considered to be secondary can theoretically or actually adversely impact the treatment of the condition that was perceived as primary in order to eschew complications related with systemic diseases (that is unlikely though) — hence there has been a historical hesitance among practicing clinicians to provide optimal dual therapy for both illnesses. This dilemma leads to ineffective disease management with worse prognosis an

Epidemiology and Prevalence

At present, chronic obstructive pulmonary disease (COPD) is estimated to affect nearly 480 million people worldwide, and is thought to be a major global health problem as it moves towards being the third leading cause of death worldwide by 2030 [21,36]. Similarly to atrial fibrillation, congestive heart failure (CHF) affects a large number of people as well, with greater than 64 million people worldwide affected. CHF incidence progressively increases with older age from approximately 1% in those aged between 55 and 64 years up to more than10% in those aged75 years and over, indicating a substantial cause of age-related increase (figure[numbers]–[numbers]) [26].

Through the process of answering questions related to chronic kidney disease clinical management and opioid prescribing, we identified two important chronic diseases that are regularly seen in conjunction: chronic kidney disease and substance use disorders like those due to benzodiazepines or opioids (and both) for that matter. Rutten et al recently published a landmark population-based study Upon evaluation by PFT, 20.9% of a cohort of unselected patients with concomitant stable CHF were found to have COPD based on spirometry alone (4), and the majority of cases had been undiagnosed, highlighting the frequent under-diagnosis of COPD in this population. Likewise, in a large cohort study of more than 1,000 patients with established COPD, Hawkins et al. found left ventricular systolic dysfunction in almost 17% of them [17]. Moreover, a large number of these patients had heart failure with preserved ejection fraction, which emphasizes coincident pulmonary and cardiac dysfunction in this cohort.

The coexistence of COPD and CHF has a worse outcome than either entity alone. A systematic review and meta-analysis demonstrated that patients with CHF and COPD had a hazard ratio as high as 2.0 for mortality compared to those without COPD, indicating comorbidity as an independent predictor of mortality in this population [7]. On the other hand, patients with coexisting cardiac dysfunction and COPD are more likely to experience acute exacerbations, longer hospital stay periods, and higher rates of 30-day readmission than COPD patients with preserved cardiac function [24].

Socioeconomic disparities also add complexity to this epidemiological facade. In addition, low socioeconomic status is associated with both COPD and CHF, in which populations have reduced access to appropriate care services and are more likely to be exposed to indoor/outdoor environmental and occupational pollutants. The global burden of both diseases is also disproportionately borne by low-income and middle-income countries, which often do not have sufficient diagnostic capacity or therapeutic resources to deal with these chronic conditions [1].

Pathophysiology

Assigned Work and Learn COPD is clinically defined as an important, gradually advancing and largely irreversible limitation of airflow that predominately stems from two main pathological mechanisms: chronic bronchitis and emphysema. Chronic bronchitis is characterized by long-term inflammation in the bronchial airways paired with excessive mucus excretion which leads to narrowing and obstruction of the airways. In contrast, emphysema is pathologically defined as the destruction and permanent distention of alveolar walls, causing substantial loss of elastic recoil necessary for proper lung function. The pathogenesis at the molecular level involves activated inflammatory cells, such as neutrophils, macrophages, and CD8+ T lymphocytes. These immune cells can release multiple proteolytic enzymes including matrix metalloproteinases (MMPs) and neutrophil elastase that degrade target extracellular matrix proteins and sustain tissue destruction and remodeling [5].

Most importantly, COPD should not be regarded just as a pulmonary disease but rather recognized as a systemic syndrome with several extrapulmonary manifestations. Cachexia, weight loss + muscular wasting, skeletal muscle dysfunction = reduced physical capacity = Dyspnea Anemia Osteoporosis (bone metabolism/disease) Cardiovascular disease All systemic effects that are part of the clinical spectrum in COPD. Chronic systemic inflammation, as suggested by increased circulating biomarkers, including C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-), and fibrinogen is apparent in many of these systemic manifestations. The state of continuous inflammation in COPD leads to various extrapulmonary complications, which play a significant role and contribute to the excessive cardiovascular risk present as COS phenotype [2].

Congestive heart failure (CHF) is the end point of different cardiomyopathies which lead to impaired myocardial function and reduced cardiac output. Heart failure with reduced ejection fraction (HFrEF) is primarily due to the loss and/or dysfunction of cardiomyocytes resulting in compensatory but ultimately maladaptive neurohormonal activation. This neurohormonal response is largely a consequence of RAAS activity and increased sympathetic tone which in turn contributes to progressive ventricular remodeling manifesting as pathological dilatation, hypertrophy and extensive fibrolosis of the myocardium [20]. In contrast to HFrEF, HFpEF is characterised by diastolic dysfunction with increased ventricular stiffness and impaired myocardial relaxation [23]. These derangements often associate with systemic hypertension and other metabolic co-morbidities including diabetes mellitus to further complicate the clinical phenotype of HFpEF.

Regardless of the specific phenotype of heart failure, the eventual clinical sequelae includes diminished cardiac output, increased venous pressures, and consequent fluid retention. Fluid overload presents with pulmonary and peripheral edema, chronic pulmonary congestion leading to reactive narrowing of the airways and reduction in pulmonary diffusing capacity. Such pulmonary changes may mask or worsen the physiological deficits seen in COPD, resulting in clinical overlap and diagnostic confusion [4].

The complex interplay of multiple systemic and localized interactions between the two diseases underlies their bidirectional and synergistic nature via different pathobiological mechanisms based on a multitude of studies. Systemic inflammation is a key shared pathway: in COPD, for example, rats PF inhaled pro-inflammatory cytokines released due to chronic pulmonary injury, most notably IL-6, TNF-alpha and CRP release direct cardiotoxic effects linked with endothelial dysfunction and aortic growth. In contrast, the chronic immune-inflammatory activation that defines CHF can amplify airway inflammation and inhibit mucociliary defenses, thus diminishing pulmonary function [31].

Oxidative stress is the other major convergent mechanism connecting these two diseases. COPD and CHF also induce excess oxidative stress leading to generation of reactive oxygen species (ROS) by activated leukocytes and due to mitochondrial dysfunction that deplete bioavailable nitric oxide, injure vascular endothelium, and impair vasodilatory function. This imbalance of oxidants and antioxidants in the body leads to vascular dysfunction and tissue damage in both diseases [27,33]. Additionally, skeletal muscle dysfunction is a key systemic feature of both COPD and CHF with similar molecular pathways (mitochondrial dysfunction, activation of the ubiquitin-proteasome system w/increased atrophy signaling, and resistance to anabolic hormones) believed to play a role. Together these processes underlie the severe exercise limitation and disabling breathlessness in patients with either or both diseases [14].

Pulmonary hypertension (PH) represents an important mechanistic connection between COPD and CHF. Chronic hypoxia in COPD leads to both hypoxic pulmonary vasoconstriction and vascular remodelling, eventually leading to chronic pulmonary hypertension. It causes a marked increase in pressure in the pulmonary arteries which leads to overload of the right ventricle, and ultimately over time can result in cor pulmonale and right-sided heart failure. Regarding CHF, the increased left-sided filling pressures leads to post-capillary pulmonary hypertension, adding an additional hemodynamic burden to a failing right ventricle further contributing to the initial left ventricular dysfunction which adds on the total cardia impairment [35].(Fig.1)

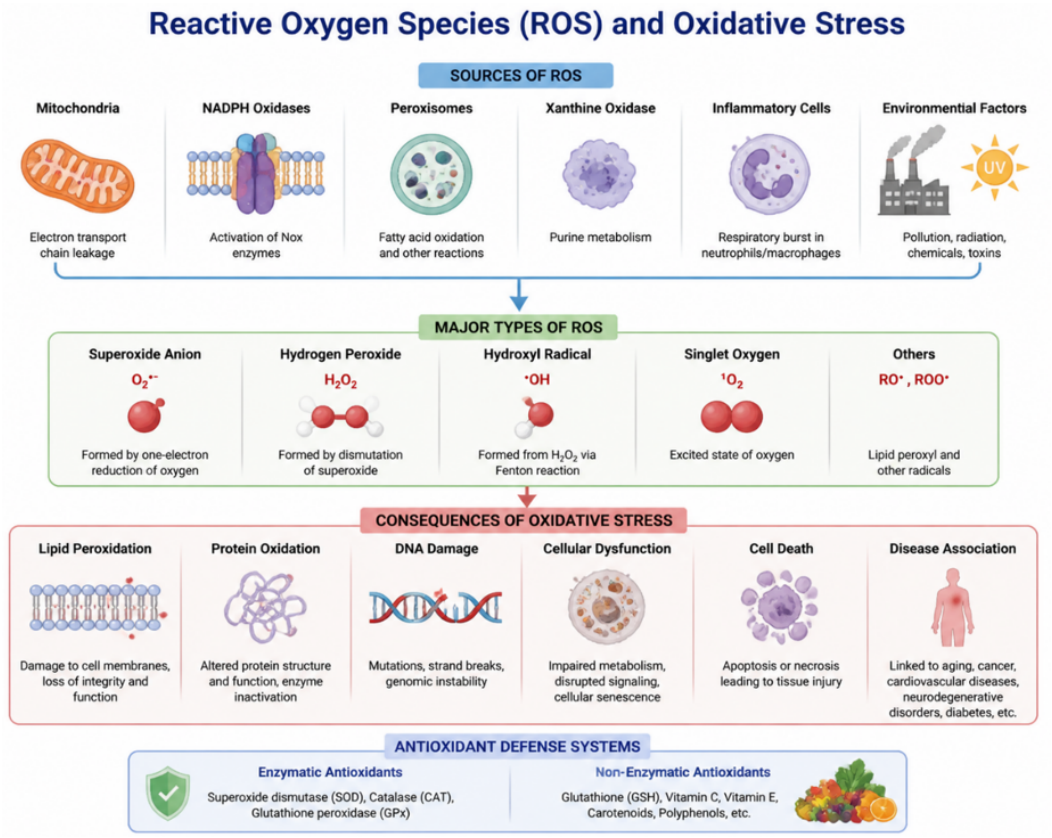

Figure 1. Mechanisms and Systemic Impact of COPD and CHF Overlap

Diagnostic Challenges and Approaches

Dyspnea—the uncomfortable and distressing sensation of breathlessness which frequently occurs in both chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF)—is the hallmark symptom common to both diseases, however being notoriously non-specific is rarely useful for diagnostic purposes as it correlates poorly with underlying pathophysiological mechanisms between patients. Aside from dyspnea, both these conditions share many other clinical features including chronic cough persistently diminished exercise capacity and peripheral edema especially typical in the case of CHF or for those developing cor pulmonale due to pulmonary hypertension. The clinical overlap between COPD and CHF is substantial, contributing to extreme diagnostic ambiguity and confusion [9], especially in the elderly population where age-related physiological changes as well as other comorbidities result in a less distinct clinical picture, thereby greatly complicating accurate disease differentiation [10].

Consistent with experience drawn from numerous studies using prospective screening strategies, alarmingly high rates of unrecognised and undiagnosed disease have been demonstrated in cohorts suspected to be suffering cardiorespiratory pathology. Specifically, Rutten et al. found that 83% of COPD diagnoses discovered within a cohort already diagnosed with CHF were newly-missed, suggesting that clinicians seldom obtain spirometry in patients whom they have made an established diagnosis of heart failure [28]. Alternatively, the reverse scenario; avoidance of CHF screening

in known COPD patients is equally common and leaves a large number of co-existent disease undiagnosed and untreated.

The diagnosis of COPD is still confirmed with spirometry, which remains the cornerstone diagnostic test where a post-bronchodilator FEV1/FVC ratio less than 0.70 defines irreversible airflow obstruction as per (GOLD) [12]. However, an assessment of spirometric results during concurrent CHF is far more nuanced and complicated: pulmonary congestion due to left heart failure can lower lung volumes as well as produce a restrictive or mixed spirometric pattern which may be able to thus hide obstructive airway disease. In addition, successful diuresis and adequate CHF treatment also can cause improvement in spirometric parameters independent of changes in lung stiffness or compliance [4], making it difficult to clinically map the dysfunctional physiologic pathways between pathologic cardiac versus pulmonary processes. Within this diagnostic complexity, ancillary tests of pulmonary physiology such as impulse oscillometry and body plethysmography may offer useful additional data to aid in distinguishing obstructive from restrictive ventilatory defects.

BNP and NT-proBNP (N-terminal pro-peptide of brain natriuretic peptide): BNP is a cardiopeptidoy tetradecapeptides secreted from the myocardium in response to overload-induced ventricular wall stress and stretching, which has become one of the paramount biomarkers for both diagnosis and prognosis . . . . . Among such patients with dyspnea, BNP plasma concentration greater than 400 pg/mL or NT-proBNP greater than 1800 pg/mL strongly indicates cardiac decompensation and heart failure exacerbation while values below other well-established exclusion cutoffs (BNP <100pg/ml;NT-proBNP<300pmol/L) effectively rule out CHF as the primary cause of symptoms [22]. Still, it must be remembered that BNP and NT-proBNP can also rise in COPD patients with ACC or relapse according to our data without clinical left ventricular heart failure. Such elevation is presumed to be caused by right ventricular strain as a result of pulmonary hypertension and hypoxia-induced myocardial stress, meaning that biomarker interpretation should always be part of the larger clinical picture and followed with serial/noninvasive imaging.

Transthoracic Echocardiogram (TTE) is the cornerstone and most commonly used imaging technique for detailed assessment of cardiac structure and function in patients with suspected CHF. This noninvasive method eases quantitative assessment of left ventricular ejection fraction (LVEF), volumes, diastolic filling patterns and relationship to most suspect anatomy establishing valvular morphology and function in addition with pulmonary artery pressures regarding size/contractile function within the right ventricle. By contrast, echocardiographic SBH can be demanding in patients with COPD as lung hyperinflation results in poor acoustic windows and a suboptimal image acquisition; technical advancements such as harmonic imaging (especially useful for people over the age of 65 years) and microbubble-based contrast-enhanced echocardiography have enhanced global image quality substantially allowing diagnostic accuracy to even approach what one would expect from technically difficult sets [9].

Chest radiography, although often the first line imaging obtained in patients with unexplained dyspnea has low sensitivity and specificity for distinguishing between COPD versus CHF. In contrast, chest computed tomography (CT) offers the best anatomic characterization of parenchymal lung disease with the ability to simultaneously assess cardiac size and pericardial effusions as well as pulmonary vasculature caliber. High-resolution CT (HRCT), and in particular is the modality of choice for achieving a definitive diagnosis of emphysema/identifying bronchiectasis with exquisite detail of lung architecture / pathology [13].

CPET is the most comprehensive and, perhaps, physiologically informative assessment of exercise intolerance as it assesses ventilatory (breath by breath), cardiovascular and metabolic responses to progressively increasing workloads. In patients with the complex comorbidity of COPD and CHF, it can give insight regarding whether ventilatory limitation (suggestive of predominant pulmonary contribution) or circulatory limitation (indicative of dominant cardiac impairment) is primarily responsible for decreased exercise capacity. Moreover, CPET detects exercise-induced oxygen desaturation and hemodynamic instability with implications for prognosis and management. Role of CPET as a clinical toolDespite having obvious benefits in terms of its clinical utility, the adoption and use of this test in routine practice has been slow primarily due to limited availability with respect to specific equipment alongside greater technical skill required for accurate assessment [16].

Management Strategies

Beta-blockers are central to evidence-based CHF treatment, with reductions in mortality rate; hospitalization and sudden death from HFrEF demonstrated in several landmark studies. This technology was historically a clinical concern for the use in patients with concomitant COPD, attributed to beta-2 adrenergic receptor blockade potentially inducing bronchoconstriction. An increasing amount of evidence indicates that cardioselective beta-blockers—especially bisoprolol, metoprolol succinate and carvedilolin [18] as well tolerated in COPD patients with CHF at conventional doses, and most (Cardiovalscularbenefit outweigh the bronchospastic risk) indicatesthatofmostpatients.

RAAS-modifying agents (ACE inhibitors, angiotensin receptor blockers [ARBs], combined angiotensin-neprilysin inhibition using sacubitril/valsartan) are standard of care in HFrEF and do not carry class-specific concerns for COPD. Importantly, cough related to the use of ACE inhibitors may be confused with COPD exacerbation in co-morbid patients and vigilance for this side effect is clearly justified. Mineralocorticoid receptor antagonists (MRAs), spironolactone and eslperenone, are examples of drugs that ameliorate Mortality Morbidity from acute/ chronic HFrEF but may be employed without clear contraindications in COPD.

Sodium-glucose cotransporter-2 (SGLT-2) inhibitors shown to be strong agents in both heart failure with reduced ejection fraction (HFrEF), and preserved ejection during HFpEF, being dapagliflozin,and empagliflozin. These agents reduce hospitalization for heart failure, cardiovascular mortality, and potentially also exert favorable pulmonary hemodynamic effects along with suppression of inflammation (3;23), although data specifically in COPD-CHF populations remain scarce. However, in symptomatic CHF patients with COPD — especially those who were at risk for CO2 retention — diuretics necessary to achieve decongestion can also lead towards metabolic alkalosis state which could further aggravate hypercapnia. This makes the careful monitoring of acid-base balance very important.

Background Long-acting bronchodilators, long-acting beta 2 agonists (LABAs) and/or long acting muscarinic antagonists (LAMAs), are the mainstay of COPD pharmacotherapy. Although beta-2 agonists are relatively cardio selective regarding their bronchodilating actions at therapeutic doses, they may produce avoidable heart effects due to cardiovascular complications through systemic absorption (e.g., tachycardia, increase of QT interval and hypokaliemia). In COPD patients who have concurrent, pre-existing cardiac disease small increases in cardiovascular events with high-dose or short-acting beta-2 agonists versus placebo were seen in observational studies and meta-analysis suggesting that concomitant use of long acting rather than low dose formulations could be important for assuring safety [29]. Recent evidence, however, indicates that in patients with established CHF both LABAs and LAMAs are safe and effective, thus the benefits of reducing COPD exacerbation should not be avoided [6].

Eosinophilic airway inflammation is present in a subgroup of COPD patients who benefits from inhaled corticosteroids (ICS) by reducing exacerbation frequency but increases the risk for pneumonia. In patients with CHF and COPD, pneumonia leads to increased mortality prohibiting us from lowering the threshold for ICS use as it also precludes our ability to recommend continuing an ICS in the absence of proven benefit without individualised clinical decision making [8].

Phosphodiesterase-4 inhibitors (for example, roflumilast) and xanthines (theophylline family) can be considered in special situations for COPD patients but are associated with cardiovascular adverse effects such as arrhythmias which may become more pronounced in the setting of underlying cardiac dysfunction [33]. Taken together, when using these agents in patients with CHF-COPD comorbidity they should be given carefully and under close monitoring.

Pulmonary rehabilitation (PR), which includes exercise training, education and psychosocial under-pinning is a key component in the management of COPD. PR has also been shown to improve exercise capacity, symptoms and health-related quality of life (HRQoL) in COPD as well as reduce hospitalizations in several randomized controlled trials and meta-analyses [7] . Although CHF has traditionally been regarded as a contraindication to high intensity exercise training, the contemporary evidence favors CR in stable CHF patients and thus likely translate very well into COPDs - although we appreciate that any extrapolation is limited. Integrated cardiopulmonary rehabilitation programs for patients with both conditions, including individualized exercise prescriptions driven by CPET

data, offer a novel and potentially effective strategy; however, randomized evidence supporting the efficacy of this approach in this specific comorbid population remains sparse [25].

The most effective intervention to slow the progression of COPD continues to be smoking cessation, its cardiovascular benefits in patients with CHF should also not be diminished as it significantly reduces sympathetic activation and improves endothelial function while decreasing atherosclerotic risk. Respiratory therapy is performed for COPD patients with resting hypoxemia (PaO2 <55 mmHg) and some CHF patients, who present at night to deteriorate oxygen due to sleep apnea. Non-invasive positive pressure ventilation (NIPPV) has a clear benefit in hypercapnic respiratory failure secondary to acute exacerbations of COPD and is being employed more often for decompensated CHF with cardiogenic pulmonary edema.(Fig.2)

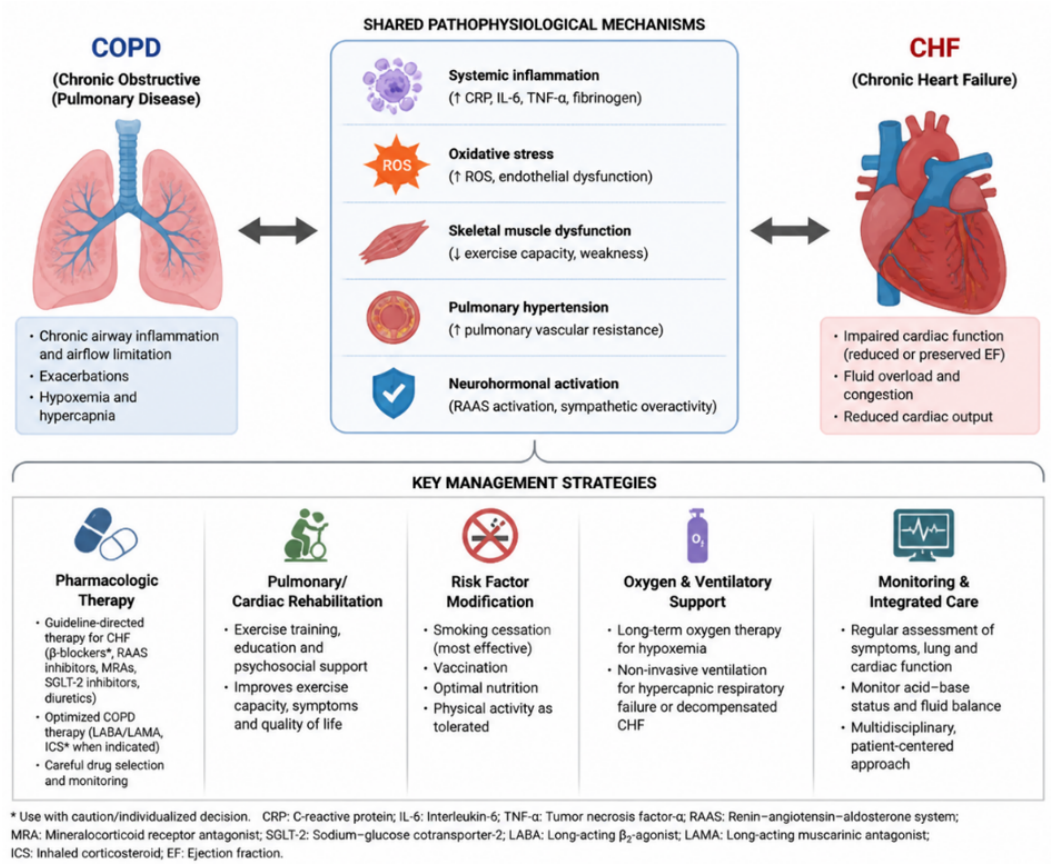

Figure 2. Shared Pathophysiological Mechanisms and Key Management Strategies for Coexisting COPD and CHF

The Role of Multidisciplinary Care

Multidisciplinary team-based care models represent best practice in view of the complexity of COPD-CHF comorbidity management. These models require strong interaction between cardiologists, pulmonologist specialists and specialist nurses (including physiotherapists), pharmacists, GERs. Patterns Integrated care pathways configured jointly to treat both conditions alongside each other—with a shared, coordinated medication reviews and combined supervised rehabilitation programmes—are linked with fewer hospitalisations [19]19].

Patient education regarding monitoring of symptoms, adherence to complex medication regimens including restriction of dietary sodium intake and reversal or prevention of future decompensation is essential. Telehealth and remote monitoring technologies potentially represent attractive avenues to improve continuity of care and early detection of deterioration in high-risk patients although definitive evidence from large trials specific to the COPD-CHF population remains lacking.

Gaps in Evidence and Future Directions

Despite the increasing acknowledgment of COPD-CHF comorbidity as one that is clinically important, such a patient population has been systematically underrepresented or outright excluded in landmark clinical trials pertinent to either condition. This evidence gap results in a situation where clinical practice is mainly based on extrapolation from single-disease trials, resulting uncertainty about efficacy and safety being overestimated (or underestimated) when drugs are used to treat co-morbidity. This is an urgent need for large prospective randomized controlled trials recruiting subjects with confirmed dual diagnosis.

Novel biomarkers such as galectin-3, soluble ST2, growth differentiation factor15 (GDF-15) and microRNA profiles may provide superior diagnostic separation and prognostic stratification alike in patients with overlapping cardiac/ pulmonary disease warranting further examination within prospective cohort-based studies(11,12).

Specifically related to pharmacotherapy, the cardiovascular and pulmonary effects of SGLT-2 inhibitors in COPD-CHF patients merit special study considering their anti-inflammatory diuretic properties and perhaps a bronchodilator effect. Likewise, triple inhaler therapy (LABA/LAMA/ICS) is not rigorously studied in COPD patients with established CHF. Precision medicine strategies, which use genomic, proteomic and phenotypic data to inform specific treatment approaches for individual patients, are an exciting but still comparatively immature new paradigm strategy to manage complex multimorbid patients.

Finally, non-pharmacological innovations involving implantable cardiac monitoring devices, high-flow nasal therapy and novel rehabilitation technologies (e.g., virtual reality programs; neuromuscular electrical stimulation) should be evaluated in this population with patient-centered outcomes—including quality of life, symptom burden and functional capacity—designated as co-primary endpoints along traditional clinical outcomes.

Conclusions

COPD and congestive heart failure (CHF) are prevalent, interacting chronic conditions which when coexisting contribute to a large burden on diagnostic workups and therapeutic choices. The evidence supporting the position that comorbid COPD–CHF has a worse outcome than either condition alone, driven in part by overlapping and bi-directionally reinforcing systemic inflammation mechanisms, oxidative stress, pulmonary hypertension development and key neuro-hormonal dysregulation pathways between them is summarized here.

Careful individualization of therapy, however, is essential in effective clinical management since first-line agents for one condition (ie. beta-blockers, beta-agonists) can be used safely with proper precautions when the other exists as well. The current best practice standard involves the integration of multidisciplinary care, including cardiac and pulmonary rehabilitation, smoking cessation, and education at both home (targeting patients) or in a supervised setting involving inter-physician teams.

The space is stifled by a lack of rigorous trial evidence in dual disease patients. Filling this void through focused clinical trials, translational research examining novel biomarkers and models of integrated care should be a strategy for the cardiovascular and respiratory disease communities. Enhanced awareness, diagnosis and integrated management of COPD-CHF comorbidity could significantly decrease the huge burden these conditions place on patients, health care systems and society.

Authors' contribution

Conceptualization, A.G. and R.T.; methodology, A.G.; software, B.N.; validation, A.G., R.T., and B.N.; formal analysis, A.G.; investigation, R.T.; resources, B.N.; data curation, A.G.; writing—original draft preparation, A.G.; writing—review and editing, R.T. and B.N.; visualization, A.G.; supervision, R.T.; project administration, B.N.; funding acquisition, A.G.. All authors have read and agreed to the published version of the manuscript.

Funding source

This research received no external funding.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of Tashkent State Medical University. Ethics approval was obtained for all study procedures.

Consent for publication.

Informed consent was obtained from all subjects involved in the study for publication of their data.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgments

The authors would like to express their gratitude to Tashkent State Medical University for providing the necessary resources and support for this study. Special thanks are extended to the Department of Family Medicine №2 for their guidance and assistance. We also thank the study participants for their cooperation and contribution to this research.

Conflict of interest

The authors declare no conflict of interest.

Abbreviations

COPD	Chronic Obstructive Pulmonary Disease
CHF	Congestive Heart Failure
FEV1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
BNP	Brain Natriuretic Peptide
RAAS	Renin-Angiotensin-Aldosterone System
LABA	Long-Acting Beta-Agonist
LAMA	Long-Acting Muscarinic Antagonist
ICS	Inhaled Corticosteroids
SGLT-2	Sodium-Glucose Cotransporter-2

References

[1] Adeloye D., Song P., Zhu Y., et al. (2022). Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. Lancet Respiratory Medicine, 10(5), 447–458. https://doi.org/10.1016/S2213-2600(21)00511-7.

[2] Agusti A., Faner R. (2017). Systemic inflammation and comorbidities in chronic obstructive pulmonary disease. Proceedings of the American Thoracic Society, 14(3), 219–226. https://doi.org/10.1513/AnnalsATS.201606-469AW.

[3] Anker S. D., Butler J., Filippatos G., et al. (2021). Empagliflozin in heart failure with a preserved ejection fraction. New England Journal of Medicine, 385(16), 1451–1461. https://doi.org/10.1056/NEJMoa2107038.

[4] Müllerová H., Agusti A., Erqou S., Mapel D. W. (2020). Cardiovascular comorbidity in COPD: systematic literature review. Chest, 141(5), 1233–1241. https://doi.org/10.1378/chest.11-0890.

[5] Barnes P. J. (2016). Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. Journal of Allergy and Clinical Immunology, 138(1), 16–27. https://doi.org/10.1016/j.jaci.2016.05.011.

[6] Bhatt S. P., Dransfield M. T., Bhatt S. P., et al. (2021). Cardiovascular safety of indacaterol-glycopyrronium versus salmeterol-fluticasone in COPD: FLAME trial. American Journal of Respiratory and Critical Care Medicine, 204(5), 531–542. https://doi.org/10.1164/rccm.202006-2606OC.

[7] Mentz R. J., Kelly J. P., von Lueder T. G., et al. (2016). Noncardiac comorbidities in heart failure with reduced versus preserved ejection fraction. Journal of the American College of Cardiology, 64(21), 2281–2293. https://doi.org/10.1016/j.jacc.2014.08.036.

[8] Vestbo J., Anderson J. A., Brook R. D., et al. (2016). Fluticasone furoate and vilanterol and survival in chronic obstructive pulmonary disease with heightened cardiovascular risk (SUMMIT): a double-blind randomised controlled trial. Lancet, 387(10030), 1817–1826. https://doi.org/10.1016/S0140-6736(16)30069-1.

[9] Schiattarella G. G., Hill J. A. (2018). Inhibition of hypertrophy is a good therapeutic strategy in ventricular pressure overload. Circulation, 131(16), 1435–1447. https://doi.org/10.1161/CIRCULATIONAHA.115.013894.

[10] Chow S. L., Maisel A. S., Anand I., et al. (2017). Role of biomarkers for the prevention, assessment, and management of heart failure: a scientific statement from the American Heart Association. Circulation, 135(22), e1054–e1091. https://doi.org/10.1161/CIR.0000000000000490.

[11] Januzzi J. L., Mann D. L. (2019). Natriuretic peptide measurement in heart failure: the good, the bad, and the future. JACC: Heart Failure, 7(4), 299–301. https://doi.org/10.1016/j.jchf.2019.01.007.

[12] Srivaratharajah K., Coutinho T., deKemp R., et al. (2016). Reduced myocardial flow in heart failure patients with preserved ejection fraction. Circulation: Heart Failure, 9(7), e002562. https://doi.org/10.1161/CIRCHEARTFAILURE.115.002562.

[13] Agustí A., Celli B. R., Criner G. J., et al. (2023). Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. American Journal of Respiratory and Critical Care Medicine, 207(7), 819–837. https://doi.org/10.1164/rccm.202301-0106PP.

[14] Maltais F., Decramer M., Casaburi R., et al. (2014). An official American Thoracic Society/European Respiratory Society statement: update on limb muscle dysfunction in chronic obstructive pulmonary disease. American Journal of Respiratory and Critical Care Medicine, 189(9), e15–e62. https://doi.org/10.1164/rccm.201402-0373ST.

[15] Groenewegen A., Rutten F. H., Mosterd A., Hoes A. W. (2020). Epidemiology of heart failure. European Journal of Heart Failure, 22(8), 1342–1356. https://doi.org/10.1002/ejhf.1858.

[16] Guazzi M., Arena R., Halle M., Piepoli M. F., Myers J., Lavie C. J. (2016). 2016 Focused Update: Clinical Recommendations for Cardiopulmonary Exercise Testing Data Assessment in Specific Patient Populations. Circulation, 133(24), e694–e711. https://doi.org/10.1161/CIR.0000000000000406.

[17] Rutten F. H., Cramer M. J., Lammers J. W., Grobbee D. E., Hoes A. W. (2016). Heart failure and chronic obstructive pulmonary disease: an ignored combination? European Journal of Heart Failure, 8(7), 706–711. https://doi.org/10.1016/j.ejheart.2006.01.010.

[18] Lipworth B., Skinner D., Devereux G., et al. (2016). Underuse of beta-blockers in heart failure complicated by chronic obstructive pulmonary disease. Heart, 102(23), 1909–1914. https://doi.org/10.1136/heartjnl-2016-309458.

[19] Holland A. E., Mahal A., Hill C. J., et al. (2017). Home-based rehabilitation for COPD using minimal resources: A randomised controlled equivalence trial. Thorax, 72(1), 57–65. https://doi.org/10.1136/thoraxjnl-2016-208514.

[20] Tham Y. K., Bernardo B. C., Ooi J. Y. Y., Weeks K. L., McMullen J. R. (2017). Pathophysiology of cardiac hypertrophy and heart failure: signaling pathways and novel therapeutic targets. Archives of Toxicology, 89(9), 1401–1438. https://doi.org/10.1007/s00204-015-1477-x.

[21] GBD 2019 Diseases and Injuries Collaborators. (2020). Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet, 396(10258), 1204–1222. https://doi.org/10.1016/S0140-6736(20)30925-9.

[22] Januzzi J. L., Prescott M. F., Butler J., et al. (2019). Association of change in N-terminal pro-B-type natriuretic peptide following initiation of sacubitril-valsartan treatment with cardiac structure and function in patients with heart failure. JAMA, 322(11), 1085–1095. https://doi.org/10.1001/jama.2019.12821.

[23] McMurray J. J. V., Solomon S. D., Inzucchi S. E., et al. (2019). Dapagliflozin in patients with heart failure and reduced ejection fraction. New England Journal of Medicine, 381(21), 1995–2008. https://doi.org/10.1056/NEJMoa1911303.

[24] Pellicori P., Kallvikbacka-Bennett A., Dierckx R., et al. (2017). Prognostic significance of changes in ejection fraction in patients with chronic heart failure. Heart, 104(9), 744–751. https://doi.org/10.1136/heartjnl-2017-311614.

[25] Piepoli M. F., Conraads V., Corrà U., et al. (2016). Exercise training in heart failure: From theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. European Journal of Heart Failure, 13(4), 347–357. https://doi.org/10.1093/eurjhf/hfr017.

[26] Ponikowski P., Voors A. A., Anker S. D., et al. (2016). 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. European Heart Journal, 37(27), 2129–2200. https://doi.org/10.1093/eurheartj/ehw128.

[27] Kirkham P. A., Barnes P. J. (2016). Oxidative stress in COPD. Chest, 144(1), 266–273. https://doi.org/10.1378/chest.12-2664.

[28] Rutten F. H., Cramer M. J., Lammers J. W., Grobbee D. E., Hoes A. W. (2016). Heart failure and chronic obstructive pulmonary disease: an ignored combination? European Journal of Heart Failure, 8(7), 706–711. https://doi.org/10.1016/j.ejheart.2006.01.010.

[29] Cazzola M., Rogliani P., Matera M. G., et al. (2019). Cardiovascular effects of bronchodilators: between myths and realities. Expert Opinion on Drug Safety, 18(11), 1017–1028. https://doi.org/10.1080/14740338.2019.1670149.

[30] Bhatt S. P., Wells J. M., Kinney G. L., et al. (2017). Beta-blockers are associated with a reduction in COPD exacerbations. Thorax, 71(1), 8–14. https://doi.org/10.1136/thoraxjnl-2015-207251.

[31] Celli B. R., Locantore N., Yates J., et al. (2019). Inflammatory biomarkers improve clinical prediction of mortality in chronic obstructive pulmonary disease. American Journal of Respiratory and Critical Care Medicine, 185(10), 1065–1072. https://doi.org/10.1164/rccm.201110-1792OC.

[32] Spruit M. A., Holland A. E., Singh S. J., Tonia T., Ward D. E., Puhan M. A. (2020). COVID-19: interim guidance on rehabilitation in the hospital and post-hospital phase from a European Respiratory Society and American Thoracic Society-coordinated International Task Force. European Respiratory Journal, 56(6), 2002197. https://doi.org/10.1183/13993003.02197-2020.

[33] Peoples J. N., Saraf A., Ghazal N., Pham T. T., Kwong J. Q. (2019). Mitochondrial dysfunction and oxidative stress in heart disease. Experimental and Molecular Medicine, 51(12), 1–13. https://doi.org/10.1038/s12276-019-0355-7.

[34] Agustí A., Celli B. R., Criner G. J., et al. (2023). Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. American Journal of Respiratory and Critical Care Medicine, 207(7), 819–837. https://doi.org/10.1164/rccm.202301-0106PP.

[35] Bozbay M., Atalay M. K., Karabay C. Y., et al. (2018). Pulmonary hypertension in patients with chronic obstructive pulmonary disease: hemodynamic, echocardiographic, and clinical evaluation. Cardiology Journal, 25(4), 465–473. https://doi.org/10.5603/CJ.a2017.0147.

[36] World Health Organization. (2023). Chronic obstructive pulmonary disease (COPD) fact sheet. Retrieved from https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)