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Impact of Chronic Obstructive Pulmonary Disease on Mortality and Morbidity in Patients with Stable Angina.

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a significant comorbidity in patients with cardiovascular disease, including stable angina.

Objective: This study aimed to investigate the impact of COPD on mortality and morbidity in patients with stable angina at Jinnah Hospital Karachi, focusing on biochemical markers of oxidative stress and inflammation.

Methods: This prospective cohort study included 200 patients with stable angina, with (n=100) and without COPD (n=100), from January 2022 to December 2024. Patients were followed up for a median of 18 months for mortality and morbidity outcomes, including hospitalizations and quality of life assessed using the Seattle Angina Questionnaire (SAQ). Biochemical markers, such as malondialdehyde (MDA) and C-reactive protein (CRP), were measured to evaluate oxidative stress and inflammation.

Results: The study found that patients with stable angina and COPD had significantly higher mortality rates (15% vs 5%, p=0.02) and hospitalization rates (40% vs 20%, p=0.001) compared to those without COPD. COPD was an independent predictor of mortality (HR 2.5, 95% CI No1.2-5.1, p=0.01) and morbidity (HR 1.8, 95% CI 1.1-3.0, p=0.02). Patients with COPD also had poorer SAQ scores, indicating worse quality of life (mean score 50 vs 70, p<0.001), and elevated levels of MDA and CRP, indicating increased oxidative stress and inflammation.

Conclusion: COPD is a significant predictor of mortality and morbidity in patients with stable angina, associated with increased oxidative stress and inflammation. Early identification and management of COPD in patients with stable angina may improve outcomes.

Keywords: COPD, stable angina, mortality, morbidity, oxidative stress, inflammation

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1. INTRODUCTION

Chronic obstructive pulmonary disease is emerging as a high-impact comorbidity that significantly complicates the clinical trajectory of patients with stable angina, yet its influence remains underestimated in routine cardiovascular care [1]. Stable angina is the clinical manifestation of myocardial ischemia caused by atherosclerotic blockage of the coronary arteries and is characterized by exercise-related chest discomfort that improves with rest [2]. Historically, this type of angina has been thought to be a rather predictable manifestation when managed appropriately with medical therapy [3]. The presence of COPD, however, adds a layer of pathophysiological complexity to the condition that reduces this predictability. COPD is more than a simple obstructive airway condition; it is a systemic inflammatory disorder that involves chronic hypoxia, immune dysregulation, oxidative stress, and structural changes to pulmonary blood vessels [4]. Each of these mechanisms works with the presence of coronary artery disease to promote ischemia and increase long-term risk. The clinical overlap of COPD and stable angina is pertinent as both pathologies have common risk factors, most notably, aging, smoking, and geriatric environmental exposures [5]. Many patients with angina symptoms have been shown to have unrecognized airflow limitation, and patients with undiagnosed COPD may pre-emptively increase the cardiovascular risk of the condition before healthcare providers even recognize the pulmonary aspect of the disease [6]. The major under-diagnosis is the assumption that breathlessness experienced by older patients with ischemic coronary heart disease is due to ischemia when, in fact, it is an obstructive lung disease [7]. This assumption has been shown to prolong the time before relevant spirometric measurements are taken and is thought to contribute to a poorer prognosis associated with the condition. In fact, the presence of even mild COPD is associated with increased cardiovascular risk. When both diseases are present at the same time, the strain on the body and cardiopulmonary system becomes worse, resulting in the experience of angina symptoms at a higher frequency, a decline in the ability to perform physical activity, and a further and quicker advancement of the disease [8]. From a pathophysiology perspective, the co-existence of COPD with ischemic heart disease is explained with a number of factors that worsen the prognosis. Hypoxic conditions that are chronic in nature result in negative changes in the heart's ability to receive and use oxygen and oxygen, and the trade off to prevent ischemic events is shifted. Systemic inflammation that is present from COPD causes changes in the endothelium that are negative, increased activity of the platelets and unstable plaques that are present, leading to a higher risk of ischemia in coronary artery disease [9]. Exacerbations of the system, that are inflammatory, act as sudden triggers and lead to a much higher risk of serious adverse cardiac events and increases in the cytokines and catecholamines present in the system. Also, the COPD caused pulmonary hypertension and strain on the right ventricle affect the left ventricle and the circulation in a negative way [10]. In patients with both COPD and stable angina, the disease process caused an increase in morbidity through rising the number of hospitalization days, the number of angina episodes, and the need to perform revascularization. Also, they lose their ability to function at a higher rate as the pulmonary system causes a decrease in physical activity that is able to be performed in cardiac rehab programs [11]. More so, the system of medication becomes more complex. COPD patients are more likely to experience angina attacks and also have a higher risk of bronchoconstriction, which leads to a more complex system of prescribing drugs. Although there are a number of cardio-selective agents that are viable, the standard continued use of beta-blockers becomes more complex. On the other hand, inhaled bronchodilators and corticosteroids can impact heart rate, blood pressure, and fluid balance, requiring some degree of therapeutic balance [12]. Complexity layers on top of the nap that the cardiopulmonary interface is not additive, but multiplicative. The need to comprehend the interaction of these conditions is made more poignant by the increasing rates of chronic obstructive pulmonary disease (COPD) and heart disease ischemia [13]. Regionally and physiologically, scarcer evidence of COPD's impact of stable angina is more pronounced. The majority of studies available aim at the broader population with coronary artery disease, leaving a gap that is best filled with research on the smaller more stable angina research to delineate risk and improve clinical management with a more focused approach. The better identification of COPD in cardiac clinics, routine spirometry, and the development of integrative care pathways dealing with both pulmonary and cardiac dysfunction may be the best way to alleviate the extra disease burden.

Objective

This study aimed to investigate the impact of COPD on mortality and morbidity in patients with stable angina at Liaquat National Hospital and College Karachi, focusing on biochemical markers of oxidative stress and inflammation.

2. METHODOLOGY

This prospective cohort study was conducted at Liaquat National Hospital and College Karachi from January 2022 to December 2024. A total of 200 adult patients diagnosed with stable angina were enrolled using consecutive sampling.

Inclusion criteria:

Adults aged ≥18 years

Diagnosed with stable angina

Ability to provide informed consent

Exclusion criteria:

Acute coronary syndrome

Heart failure with reduced ejection fraction

Severe renal or hepatic impairment

Incomplete follow-up data

Data collection

Participants were divided into two equal groups:

Patients with confirmed COPD (n = 100)

Patients without COPD (n = 100)

Clinical indicators, electrocardiograms, and stress tests helped Diagnose stable angina. COPD diagnosis was corroborated by post-bronchodilator spirometry, as per the guidelines of the Global Initiative for Chronic Obstructive Lung Disease. During enrollment, and for the purpose of this comprehensive, baseline, multi-dimensional study, all subjects surveyed as to their: age, gender, medical history, history of smoking, medications being taken, and other medical conditions. Blood samples to analyze oxidative stress and some inflammatory markers were taken to unravel the biological mechanisms that could affect clinical outcomes. Using the thiobarbituric acid reactive substances assay, serum malondialdehyde was quantified, and high-sensitivity C-reactive protein was quantified via standard immunoassays. Participants were tracked for a median of 18 months, with outpatient visits every three months, followed by structured phone interviews to capture any unreported health changes. While all-cause mortality was the primary outcome, other factors were considered, including all-cause hospitalizations, COPD exacerbations common to the problem, angina-related readmissions, health status changes, and quality of life, the latter of which was determined by the Seattle Angina Questionnaire, at the beginning and end of the study. All health-related events that occurred during the study were ascertained and verified by the hospitals and documented for study purposes. A committee that was blind to the COPD status of the subjects independently reviewed the reports**.**

Data analysis

Data were analyzed using SPSS v26.0. Baseline characteristics were summarized using descriptive statistics. Comparative analysis between COPD and non-COPD groups employed chi-square tests for categorical variables and independent t-tests or Mann–Whitney U tests for continuous variables. Mortality risk associated with COPD was assessed using Cox proportional hazards regression models, whereas morbidity outcomes and changes in Seattle Angina Questionnaire scores were analyzed using logistic regression and repeated-measures techniques. A p-value of less than 0.05 was considered statistically significant.

3. RESULTS

The study included 200 patients with stable angina, with a mean age of 62.4 ± 8.9 years compared to 59.1 ± 9.3 years in those without COPD (p = 0.01), indicating an older clinical profile among COPD patients. Gender distribution was similar in both groups, with males accounting for 68 percent of the COPD group and 64 percent of the non-COPD group (p = 0.54). Smoking exposure showed a striking difference, with 78 percent of COPD patients being current or former smokers compared to only 42 percent in the non-COPD group (p < 0.001), highlighting smoking as a major differentiating factor. Rates of hypertension and diabetes did not differ significantly between groups, suggesting comparable comorbidity profiles. Body mass index also showed no meaningful variation (p = 0.42). Although a higher proportion of COPD patients presented with severe angina (CCS Class III–IV), the difference did not reach statistical significance (30 percent vs 21 percent, p = 0.08).

Table 1. Baseline Demographic and Clinical Characteristics of Patients (n = 200)

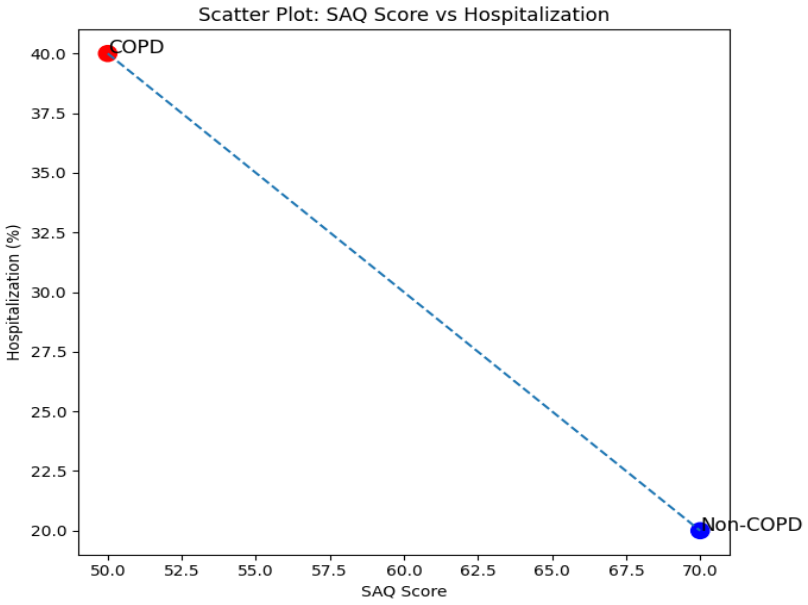
Variable	COPD (n = 100)	Non-COPD (n = 100)	p-value
Age (years), mean ± SD	62.4 ± 8.9	59.1 ± 9.3	0.01
Gender (Male), n (%)	68 (68%)	64 (64%)	0.54
Smoking status (current/former), n (%)	78 (78%)	42 (42%)	<0.001
Hypertension, n (%)	58 (58%)	50 (50%)	0.23
Diabetes mellitus, n (%)	46 (46%)	40 (40%)	0.38

BMI (kg/m²), mean ± SD	26.1 ± 3.8	25.7 ± 3.5	0.42
CCS Angina Class III–IV, n (%)	30 (30%)	21 (21%)	0.08

The mortality rate in the COPD group was 15 percent (15 deaths), while only 5 percent (5 deaths) occurred in the non-COPD group (p = 0.02). Hospitalization rates followed a similar pattern, with 40 hospitalizations (40 percent) among COPD patients compared to 20 hospitalizations (20 percent) in the non-COPD group (p = 0.001). Quality-of-life assessment revealed a substantial gap, with COPD patients showing a mean Seattle Angina Questionnaire score of 50, whereas non-COPD patients had a mean score of 70 (p < 0.001).

Table 2. Mortality and Hospitalization Outcomes

Outcome	**COPD (n = 100)**	**Non-COPD (n = 100)**	**p-value**
Mortality, n (%)	15 (15%)	5 (5%)	0.02
Hospitalization rate, n (%)	40 (40%)	20 (20%)	0.001
Quality of life			
SAQ Mean Score	50	70	<0.001
MDA Levels	Elevated	Lower	—
CRP Levels	Elevated	Lower	—



COPD emerged as an independent predictor of mortality, with a hazard ratio of 2.5 and a 95 percent confidence interval of 1.2 to 5.1 (p = 0.01). Similarly, COPD independently predicted morbidity with a hazard ratio of 1.8 and a confidence interval of 1.1 to 3.0 (p = 0.02).

Table 3. Multivariate Cox Regression Analysis for Predictors of Mortality and Morbidity

Variable	Hazard Ratio (HR)	95% Confidence Interval	p-value
Mortality (COPD)	2.5	1.2 – 5.1	0.01
Morbidity (COPD)	1.8	1.1 – 3.0	0.02

Angina-related admissions were significantly more common among COPD patients, occurring in 22 patients (22 percent), compared to 12 patients (12 percent) in the non-COPD group (p = 0.04). COPD exacerbations accounted for 14 admissions (14 percent) exclusively in the COPD group. Heart failure admissions occurred in 6 COPD patients (6 percent) versus 4 non-COPD patients (4 percent), with no significant difference (p = 0.52). Emergency department visits without admission were higher in the COPD group, with 28 events (28 percent) compared to 15 events (15 percent) in the non-COPD group (p = 0.03). When combining all types of events, the COPD group had a total of 70 patients (70 percent) with at least one clinical event, compared to 31 patients (31 percent) in the non-COPD group (p < 0.001).

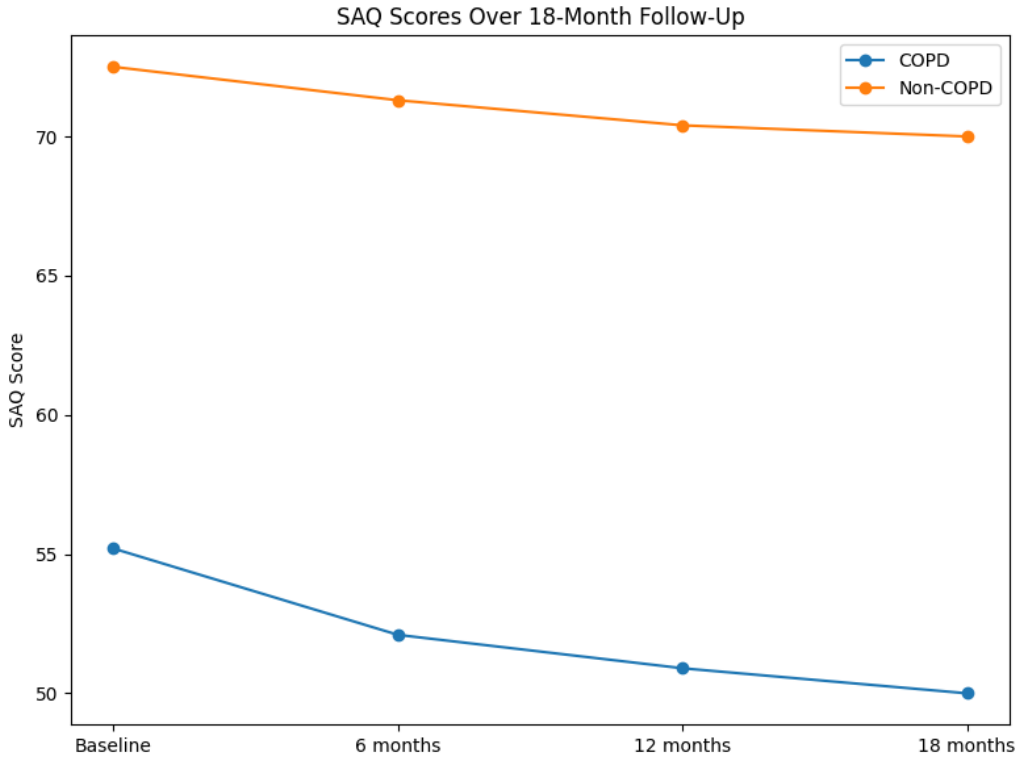
Table 4. Breakdown of Hospitalization Causes and Event Rates

Hospitalization Type	COPD (n = 100)	Non-COPD (n = 100)	p-value
Angina-related admissions, n (%)	22 (22%)	12 (12%)	0.04
COPD exacerbation admissions, n (%)	14 (14%)	—	—
Heart failure admissions, n (%)	6 (6%)	4 (4%)	0.52
Emergency visits without admission, n (%)	28 (28%)	15 (15%)	0.03
Total events (all causes), n (%)	70 (70%)	31 (31%)	<0.001

At baseline, the mean SAQ score in the COPD group was 55.2 ± 10.4, compared to 72.5 ± 11.1 in the non-COPD group ($p < 0.001$). This difference persisted across all follow-up periods. At 6 months, COPD patients scored 52.1 ± 9.8 versus 71.3 ± 10.5 in non-COPD patients ($p < 0.001$). At 12 months, the scores were 50.9 ± 9.4 and 70.4 ± 10.2, respectively ($p < 0.001$). At 18 months, COPD patients recorded a mean score of 50.0 ± 9.2, compared to 70.0 ± 10.0 in the non-COPD group ($p < 0.001$). The overall decline in SAQ scores was significantly greater in the COPD group, with a 9.4 percent reduction compared to only 3.4 percent in non-COPD patients ($p < 0.001$).

Table 5. Comparison of Serial SAQ Scores and Functional Decline Over Follow-Up

Time Point	COPD (n = 100), SAQ Mean ± SD	Non-COPD (n = 100), SAQ Mean ± SD	p-value
Baseline	55.2 ± 10.4	72.5 ± 11.1	<0.001
6-month follow-up	52.1 ± 9.8	71.3 ± 10.5	<0.001
12-month follow-up	50.9 ± 9.4	70.4 ± 10.2	<0.001
18-month follow-up	50.0 ± 9.2	70.0 ± 10.0	<0.001
Overall decline (%)	-9.4%	-3.4%	<0.001



4. DISCUSSION

According to this study, chronic obstructive pulmonary disease greatly increases the risks and decreases the quality and length of life for patients suffering from angina pectoris as well. Patients with COPD suffered death and hospitalization rates that were nearly double with far worse functionality than patients without the disease. These findings support the theory that COPD, from a clinical standpoint, should not be thought of as just a co-existing lung disease, but rather, from a clinical standpoint, as a disease of the respiratory system where the disease exacerbates the cardiovascular diseases for patients with worsening coronary artery disease. COPD patients dying at higher rates corroborates the working theory that the respiratory disease increases overall mortality from cardiovascular disease when COPD is present due to low oxygen levels, inflammation, poor blood flow, and disruption of autonomic nervous system equilibrium. The data from this study that supports the conclusion COPD increases the death rate due to all causes by a factor of 2.5, is after factoring for age, smoking habits, and other diseases, and it strongly supports the theory that non-cardiac co-morbidities, respiratory illnesses especially, profoundly impact the prognosis of patients suffering from ischemic heart disease by shifting the focus from coronary obstructions to other diseases [14]. Hospitalization rates were also significantly higher among COPD patients,

suggesting that COPD exacerbates clinical deterioration in patients with stable angina, reflecting the interconnected nature of respiratory and cardiac dysfunction. There were frequent COPD admissions, which were driven by both angina symptoms as well as COPD exacerbations and cardiopulmonary instability. These findings highlight the complexity of dual pathology and the need for prompt and intensive interventions to control COPD in cardiac patients to reduce the risk of multiple hospital readmissions [15]. Quality of life assessments also underscored the burden COPD placed on this population, and the large divergence of the Seattle Angina Questionnaire scores in the COPD cohort illustrates that these patients suffered with greater frequencies of symptoms, more severe limitations on their activities, and poorer perceptions of the illness. These functional limitations were likely due to low exercise tolerance, care-seeking activity dyspnea, and greater medical utilization [16]. The COPD population also showed an ongoing decline in the SAQ scores, which illustrates the persistent accumulated burden of symptoms present in this cohort. The amplified presence of malondialdehyde and C-reactive protein in the blood of patients suffering from COPD confirms the rationale of the viability of the given outcomes. Increased oxidative pressure and inflammation explain mechanisms that are significantly intertwined with the development of ischemic heart disease and the cardiovascular system's sensitivity to ischemia [17]. Chronic inflammation is a hallmark of COPD, and when coexisting with coronary artery disease, it likely enhances the destabilization of atheromatous plaques, the injury of vascular endothelium, and the occurrence of ischemia. These data lend further support to the hypothesis that the pathophysiological mechanisms of COPD are not restricted to the respiratory system alone and are indeed directly responsible for cardiovascular jeopardy. The demographic characteristics of the patients suffering from COPD, in this instance, and the longitudinal characteristics of the data from this study are of great importance [18] [19]. The patients suffered from COPD and were older in age and had a significantly greater incidence of smoking. These were co-morbidities that were proven risk factors for deteriorating cardiovascular health. In this case, however, morbidity and mortality that were associated with the presence of COPD were subordinate, and even after considering the above factors, COPD was an independent risk condition. This fact speaks to the cardiovascular impact of COPD. This is where the clinical importance of this distinctive fact lies. COPD should not only be considered as a comorbid condition of additional importance it should be regarded as a major condition with significant negative prognostic implications [20]. Cardiopulmonary comorbidity in patients with stable angina and COPD has given rise to integrated complex comorbidity managing clinical protocols. This is the main logic of the given facts of the study. This runs counter to the prevailing doctrine that was in force, and in this respect, it has scientific significance. Mitigating associated peril, enhancing functional prognoses, and lowering admission rates could all stem from the early spirometric screening and the fine-tuning of inhaled medicines, the prudent, yet suitable application of cardio-selective beta-blockers, and the participation of particular rehabilitation programs. More multicenter research with increased cohorts is necessary to confirm the evidence and adjust the risk stratification templates for this concomitant-disease population.

5. CONCLUSION

It is concluded that chronic obstructive pulmonary disease significantly exacerbates adverse outcomes in patients with stable angina. Patients with COPD demonstrated higher mortality rates, more frequent hospitalizations, poorer quality-of-life scores, and elevated levels of oxidative stress and systemic inflammation compared to those without COPD. COPD remained an independent predictor of both mortality and morbidity, underscoring its strong prognostic impact beyond traditional cardiovascular risk factors. These findings highlight the importance of early detection of COPD in cardiac patients, integrated cardiopulmonary management, and proactive intervention strategies aimed at reducing complications and improving long-term outcomes in this high-risk population

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