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Prevalence of Comorbidities and Their Association with Disease Severity in Patients with Stable Chronic Obstructive Pulmonary Disease

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Abstract

Background: Comorbidities are highly prevalent and significantly impact disease progression, hospitalization rates, and mortality in chronic obstructive pulmonary disease (COPD) patients.

Methods: This cross-sectional study included 209 COPD outpatients aged 40 years or older, treated at Nguyen Tri Phuong Hospital's Respiratory Clinic from February to August 2023. COPD severity is assessed using: (1) symptoms (mMRC, CAT score); (2) exacerbation frequency; and (3) GOLD classification. Comorbidities were determined based on (1) medical records and (2) the answers to the question: "What diseases or health issues have you been diagnosed with by a physician?".

Results: Results revealed a mean of 2.12 comorbidities (SD: 1.33) per patient. The number of comorbidities increased linearly with the CAT score, and patients with ≥2 comorbidities were 2.26 times more likely to exhibit dyspnea (mMRC ≥2) compared to those with <2 comorbidities. Four factors: hypertension, diabetes mellitus, GERD, and history of pulmonary tuberculosis related to more symptoms presentation according to mMRC and/or CAT scores. Additionally, diabetes and GERD significantly associated with the "frequent exacerbators" condition (ORs: 2.55 and 3.13, respectively).

Conclusions: Comorbidities may contribute to the adverse influence on COPD severity. Recognizing these relationships enables clinicians to adopt a comprehensive, patient-centered approach to COPD management.

Keywords: Chronic obstructive pulmonary disease, COPD, comorbidities

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1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death globally, accounting for approximately 212.3 million prevalent cases and 3.3 million deaths in 2019 from 204 countries and territories globally [1]. It remains a significant healthcare burden in low- and middle-income countries like Vietnam, requiring substantial resources for effective control. Comorbidities are common among COPD patients, with 30–60% having at least one comorbid condition and over 40% presenting with two to three [2]. This may be attributed to shared risk factors, such as smoking, or the consequences of systemic inflammation, where airway and lung parenchymal inflammation precedes and predominates, ultimately leading to COPD [3]. The presence of comorbidities significantly impacts outcomes in COPD patients, including increased mortality, hospitalization rates, reduced quality of life, and decreased response to pulmonary

rehabilitation [4]. Nearly two-thirds of COPD patients die from causes unrelated to COPD itself, such as cardiovascular disease and cancer [4]. Additionally, comorbidities pose significant challenges in selecting appropriate medications to avoid drug interactions or adverse effects. The treatment of one condition can potentially worsen the state of other comorbidities, particularly since nearly one-third of COPD patients require 5–10 medications daily [5].

This study aimed to examine the prevalence of comorbidities and their association on COPD severity in Vietnamese patients, specifically those treated as outpatients at Nguyen Tri Phuong Hospital. Findings provide insights for comprehensive, patient-centered COPD management.

2. METHODS

This cross-sectional study, conducted in 2023 at Nguyen Tri Phuong Hospital, involved COPD outpatients. Inclusion criteria included patients aged ≥40 years diagnosed with stable COPD (no acute exacerbations in the preceding 4 weeks) with spirometry results available within one year.

Severity assessments included mMRC and CAT scores, exacerbation frequency, GOLD classification, and ABE group categorization. The subjects were interviewed face-to-face by researcher. Comorbidities and number of exacerbations were determined based on (1) medical records (ICD-10 diagnosis code, medication prescriptions, hospital discharge certificate, tests results from prior clinical evaluations,…) and (2) the answers to the question: "What diseases or health issues have you been diagnosed with by a physician?", "In the past 12 months, have you been admitted to a hospital or visited a healthcare provider due to worsening shortness of breath or other COPD-related symptoms?". Although there were no patients had comorbid active pulmonary tuberculosis and COPD in the study sample, given the historical significance of pulmonary tuberculosis in Vietnam, we still investigated the history of tuberculosis and its relations on COPD severity alongside the current comorbidities. Data were coded, managed in Excel, and analyzed using R software.

3. RESULTS

During the study period, we included 209 patients with stable COPD who had undergone spirometry within the past 12 months.

3.1. Demographic Characteristics

The mean age of participants was 65 years (SD: 8.25).

Most patients were aged 60–69 (51.7%) and ≥70 (31.1%), collectively accounting for 82.8%.

The mean BMI was 21.5 (SD: 3.55), with males comprising 85.6% of the study.

3.2. Comorbidities in stable COPD patients

The mean number of comorbidities in the study was 2.12 (SD: 1.33), ranging from 0 to 6.

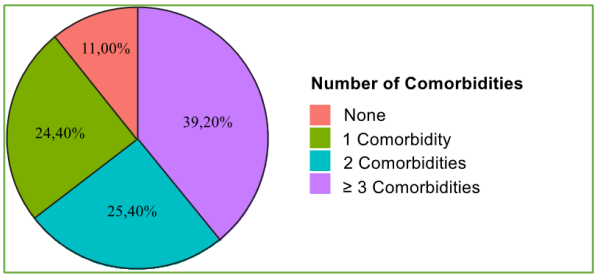

Figure 1. Number of comorbidities

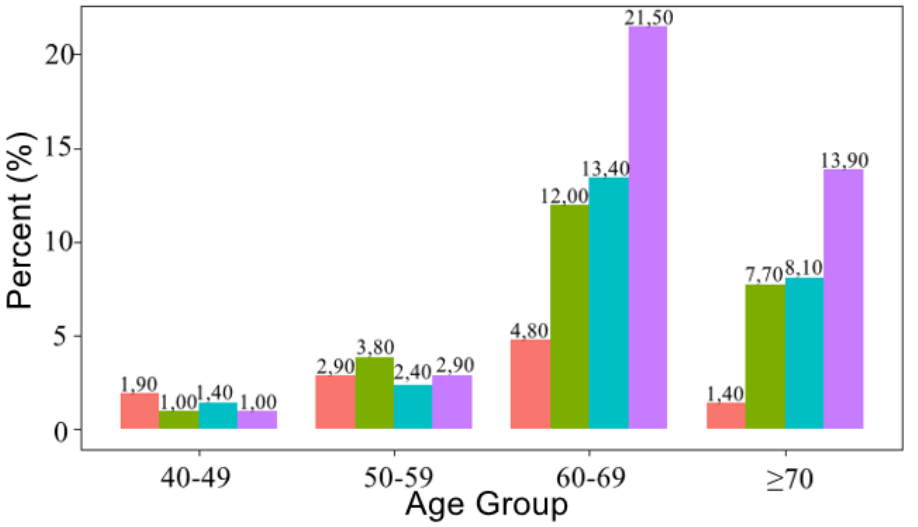

Figure 2. Comorbidities by age group

Only 23 out of 209 COPD patients (11.00%) in this study had no comorbidities, while nearly 40% had ≥3 comorbidities **(Figure 1)**.

When analyzing comorbidities by age group, a clear trend was observed: the older the patients, the more comorbidities they tended to have. In the age groups of 60–69 and ≥70 years, the proportion of patients with ≥3 comorbidities was highest, at 21.50% and 13.90%, respectively **(Figure 2)**.

3.3. Characteristics of Chronic Obstructive Pulmonary Disease

Table 1. Characteristics of Exacerbations, Symptoms, and Airway Obstruction

Characteristics		n (%)	Characteristics		n (%)
Exacerbations	None	151 (72.20%)	**GOLD**	1	17 (8.10%)
	1 episode	25 (12.00%)		2	93 (44.50%)
	2 episodes	10 (4.80%)		3	81 (38.80%)
	≥ 3 episodes	23 (11.00%)		4	18 (8.60%)
CAT	< 10	51 (2.40%)		A	44 (21.10%)
	≥ 10	158 (75.60%)	**ABE**	B	107 (51.20%)
mMRC	0-1	94 (45.00%)	**classification**	E	58 (27.70%)
	≥ 2	115 (55.00%)			

Nearly three-fourths of patients (72.20%) experienced no exacerbations in the past 12 months.

The proportion of patients with ≥1 exacerbation was 27.80%.

The majority of patients exhibited severe symptoms based on both mMRC and CAT scales.

Most patients (83.30%) had moderate-to-severe airway obstruction as per GOLD 2 and 3 classifications. According to GOLD 2023 categorization, over 50% were in Group B, while nearly 30% were in Group E.

3.4. Correlation Between the Number of Comorbidities and COPD Severity (*)

Table 2. Linear Regression Analysis Between Number of Comorbidities and COPD Severity

Comorbidities				
Dependent Variables	**β (Univariate)**	**p-value**	**β (Adjusted)**	**p-value**
Exacerbations	0.086	0.390	0.117	0.246
CAT	**1.382**	**<0.001**	**1.153**	**0.002**
mMRC	**0.142**	**<0.001**	**0.126**	**0.003**
%FEV1	0.004	0.708	-0.006	0.483
%FVC	-0.002	0.833	-0.008	0.400

(*) See in part 2

The number of comorbidities showed a linear relationship with both mMRC and CAT scores, independent of age, sex, BMI, and smoking history.

An additional comorbidity was associated with a 1.153-point increase in the CAT score ($p = 0.002$).

No significant correlation was observed between the number of comorbidities and exacerbation frequency, %FEV1, or %FVC.

Table 3. Logistic Regression Analysis of Comorbidities and COPD Severity

Comorbidities ≥ 2				
	Comparison Unit	**OR (CI95%) (Univariate)**	**OR (CI95%) (Adjusted)***	**p-value**
Frequent exacerbations	**Yes**	0.95 (0.51- 1.79)	0.98 (0.50 - 1.89)	0.943
mMRC	**≥ 2**	**2.49 (1.36 - 4.46)**	**2.26 (1.23 - 4.15)**	**0.008**
CAT	**≥ 10**	**2.14 (1.12 - 4.07)**	1.8 (0.91- 3.55)	0.090
GOLD classification	**GOLD 3-4**	1.00 (0.57 - 1.77)	1.17 (0.64 - 2.14)	0.607

(*) After adjusting for age, sex, BMI, and smoking pack-years

Patients with ≥2 comorbidities is a factor associated with 2.26 times higher odds of more significant breathlessness (mMRC ≥2). Meanwhile, exacerbation frequency, CAT scores, and GOLD classifications were not significantly related to the comorbidity status.

3.5. COPD Severity and Its Relationship with Specific Comorbidities or History.

Apart from several less frequent comorbidities (e.g., heart failure, chronic coronary syndrome, atrial fibrillation, and irritable bowel syndrome), the study identified seven common related conditions. Among these, hypertension (HTN) had the highest prevalence at 55.50%, followed by three comorbidities: dyslipidemia (42.10%), GERD (32.50%), diabetes mellitus (DM) (17.70%) and history of pulmonary tuberculosis (PTB) (24.90%). Osteoarthritis (OA) and osteoporosis (OP) had the lowest prevalence among the seven, at 14.80% and 8.10%, respectively.

Table 4. Univariate Logistic Regression Analysis

Comorbidities	COPD Severity OR (CI95%) (Univariate)			
	Frequent Exacerbations	**mMRC ≥2**	**CAT≥ 10**	**GOLD34**
HTN	1.32 (0.71 - 2.43)	**2.86 (1.62 - 5.03)***	**3.77 (1.92 - 7.40)***	0.86 (0.50 - 1.48)
DM	**2.72 (1.30 - 5.67)***	**2.20 (1.02 - 4.74)***	1.83 (0.72 - 4.68)	1.21 (0.60 - 2.47)
Dyslipidemia	0.79 (0.42 - 1.46)	1.33 (0.76 - 2.32)	1.83 (0.94 - 3.58)	0.81 (0.47 - 1.40)
GERD	**2.87 (1.53 - 5.40)***	**2.40 (1.30 - 4.43)***	**3.29 (1.45 - 7.47)***	1.07 (0.60 - 1.91
OA	0.45 (0.17 - 1.24)	0.54 (0.25 - 1.17)	0.53 (0.23 - 1.19)	0.90 (0.42 - 1.94)
Osteoporosis	1.47 (0.52 - 4.17)	2.07 (0.70 - 6.11)	0.56 (0.20 - 1.60)	1.65 (0.60 - 4.52)
PTB history	1.74 (0.89 - 3.41)	1.43 (0.75 - 2.71)	**2.50 (1.05 - 5.97)***	**1.93 (1.02 - 3.66)***

* $p < 0.05$

Table 5. Multivariate Logistic Regression Analysis
(Adjusted for Age, Sex, BMI, and Smoking Pack-Years)

	COPD Severity OR (CI95%) (Adjusted)			
	Frequent Exacerbations	**mMRC ≥2**	**CAT≥ 10**	**GOLD34**
HTN	1.38 (0.72 - 2.66)	**2.58(1.42 - 4.69)***	**3.21 (1.58 - 6.55)***	0.96 (0.53 - 1.72)
DM	**2.55 (1.28 - 5.49)***	2.03 (0.91 - 4.52)	1.60 (0.60 - 4.26)	1.37 (0.65 - 2.90)
Dyslipidemia	0.82 (0.43 - 1.59)	1.30 (0.72 - 2.36)	1.71(0.84 - 3.47)	1.02 (0.57 - 1.83)
GERD	**3.13 (1.60 - 6.10)***	**2.12 (1.12 - 4.02)***	**2.86 (1.23 - 6.69)***	1.10 (0.59 - 2.03)
OA	0.44 (0.16 - 1.21)	0.46 (0.20 -1.02)	0.43 (0.18 - 1.00)	1.00 (0.45 - 2.21)
Osteoporosis	1.74 (0.59 - 5.14)	2.03 (0.56 - 6.36)	0.44 (0.14 - 1.36)	1.77 (0.61 - 5.12)
PTB History	1.83 (0.91- 3.67)	1.31 (0.67 - 2.55)	**2.49 (1.60 - 6.18)***	**1.96 (1.01 - 3.79)***

* $p < 0.05$

We identified four conditions–hypertension (HTN), diabetes mellitus (DM), gastroesophageal reflux disease (GERD), and prior tuberculosis–that associated with one or more aspects of COPD severity after adjustments for age, sex, BMI, and smoking pack-years.

Symptom Severity: All four comorbidities were associated with increased symptom severity as measured by mMRC and/or CAT scores. Among them, HTN demonstrated the highest odds ratio (OR: 3.21), indicating more significant symptoms and a greater impact of COPD on patient's daily lives compared to the other comorbid conditions.

Frequent Exacerbations: DM and GERD were specifically linked to frequent exacerbations (>1 exacerbation or ≥1 hospitalization due to exacerbation).

Airway Obstruction Severity: A history of tuberculosis was the only condition that independently related to the severe-to-very-severe airway obstruction (GOLD stages 3–4).

4. DISCUSSION

This study recruited 209 patients with stable COPD. Due to the cross-sectional design, our discussion focuses solely on the association between comorbidities and COPD severity. Causal relationships, however, cannot be established based on this research method.

4.1. Comorbidity Status

Although various tools have been developed to estimate the impact of comorbidities and predict mortality in COPD patients, the number of comorbidities remains a simple yet effective predictor of quality of life, symptom severity, and exacerbations in COPD patients [6]. In this study, the mean number of comorbidities was 2.12 (SD: 1.33), lower than that reported in the national cohort study by Youngmee Kim (2.56; SD: 1.86) and Putcha N. (2.9; SD: 2.1) [6,7].

Putcha N. demonstrated that an increase in the number of comorbidities was associated with a higher likelihood of experiencing ≥1 exacerbation in 12 months (OR: 1.21; 95% CI: 1.17–1.26), an increase in mMRC scores (OR: 1.20; 95% CI: 1.17–1.24), and a reduction in the six-minute walk distance by 34 meters per additional comorbidity [7]. Similarly, Youngmee Kim concluded that the number of comorbidities was an independent risk factor for all-cause mortality in COPD patients [6].

In our study, the number of comorbidities was positively correlated with symptom severity and quality of life (CAT scores), with patients having ≥2 comorbidities being 2.26 times more likely to exhibit significant symptoms (mMRC ≥2). However, the number and presence of comorbidities were not associated with exacerbation frequency or airway obstruction severity.

These differences may be attributed to the smaller number of comorbidities considered in our study compared to Putcha N. (11 comorbidities) and Youngmee Kim (19 comorbidities) [6,7]. Furthermore, our study did not include certain impactful conditions such as cancer or cardiovascular diseases other than hypertension, which might have significantly influenced COPD outcomes.[8]

4.2. Hypertension (HTN)

Among the seven comorbidities analyzed, hypertension had the highest prevalence (55.50%). Previous studies have consistently highlighted cardiovascular diseases as a common and critical cause of mortality in COPD patients. Hypertension, along with other cardiovascular conditions, shares a pathophysiological link with COPD via systemic inflammation [4]. Additionally, both conditions share common risk factors such as smoking, aging, and sedentary lifestyle.

In our study, hypertension was found to independently increase symptom severity, as indicated by higher CAT (OR: 3.21) and mMRC (OR: 2.58) scores, even after adjusting for age, sex, BMI, and smoking history.

4.3. Diabetes Mellitus (DM) and Metabolic Disorders

Despite their relatively high prevalence among COPD patients, at 42.10% in our study, dyslipidemia–commonly considered a risk factor for cardiovascular and metabolic diseases–did not exhibit a significant adverse impact on COPD outcomes. This aligns with findings from Kathrin K [8].

COPD patients are at higher risk for developing diabetes mellitus (DM) compared to the general population. This increased risk can be attributed to the systemic inflammation inherent in COPD and the effects of certain COPD treatments, including both systemic and inhaled corticosteroids [8]. In our study, DM was

associated with a 2.55-fold increase in frequent exacerbations and more severe dyspnea, as measured by mMRC scores.

4.4. Gastroesophageal Reflux Disease (GERD)

GERD is a frequently observed comorbidity among COPD patients, affecting nearly one-third of cases in our study, consistent with recent research [9]. The pathophysiological mechanisms include direct microaspiration and indirect bronchospasm mediated by the vagus nerve. Acid reflux can exacerbate respiratory symptoms, often leading to diagnostic confusion, and significantly increases the risk of frequent exacerbations, by as much as 3.10 times compared to COPD patients without GERD.

4.5. History of pulmonary tuberculosis

We noticed no active case in our study sample, but the history of PTB only. In line with the epidemiological burden of tuberculosis in Vietnam, nearly one-quarter of COPD patients in our study had previous tuberculosis. Although TB is curable, a prior TB diagnosis remains a significant risk factor for developing COPD, even after successful treatment. That is why we investigated this factor.

Most patients with a history of TB in our study exhibited mixed ventilator defects, combining obstructive and restrictive patterns. Over 80% of these patients experienced moderate-to-severe obstruction as classified by GOLD. Our findings reaffirm the structural damage caused by TB, which is linked to rapid declines in %FEV1 predicted and a 1.96-fold increased risk of severe-to-very-severe airway obstruction per GOLD criteria, consistent with existing studies [10].

4.6. Osteoarthritis (OA) and Osteoporosis (OP)

COPD is a risk factor for increasing the likelihood of osteoporosis (OP) by 2.8 times [8]. OP and osteoarthritis (OA) often co-occur with weight loss, muscle atrophy, and reduced physical activity, leading to a negative impact on the quality of life of COPD patients. However, our study did not find these two conditions to significantly influence symptoms, exacerbation rates, or airway obstruction severity in COPD. The underdiagnoses or low detection rate of OP may explain this negative result, as the prevalence of OP in our study was only 8.10%, considerably lower than reported in recent literature.

In summary, our study provides additional insights into the dual burden and impact of comorbidities on COPD severity, assessed through exacerbation frequency, symptom severity via mMRC and CAT scores, and airway obstruction. While many previous studies demonstrated a clear association between specific comorbidities and increased mortality in COPD patients, our findings emphasize the need to evaluate the unique burden of comorbidities within a Vietnamese population.

However, our study has several limitations. First, comorbidities and the number of exacerbations were determined through face-to-face interviews, which are subject to recall bias. Second, although a statistically significant association between comorbidities and the severity of COPD was observed, our major limitation was that we cannot establish a cause-and-effect association from the cross-sectional data gathered, as mentioned before. Single-center sampling also limits the generalizability of the findings to the broader population. Third, the lack of specific documentation of other cardiovascular conditions, such as heart failure, chronic coronary syndromes, arrhythmias, stroke, sleep apnea, lung cancer, and psychiatric disorders like anxiety and depression, which also warrant

attention. Additionally, addressing multi-comorbidity in COPD should go beyond merely summing up individual conditions, as complex synergistic interactions often exist among comorbidities. Thus, assessing the impact of multi-comorbidity solely through the number of conditions may not fully capture the intricate interrelations between diseases.

5. CONCLUSION

Through this study, we found that the number of CMs increased linearly with the CAT score, and patients with ≥2 CMs were 2.26 times more likely to experience dyspnea (mMRC ≥2) compared to those with <2 CMs. Certain CMs were associated with more intensity of symptoms according to mMRC and/or CAT scores, including hypertension (HTN), diabetes mellitus (DM) and gastroesophageal reflux disease (GERD). The history of pulmonary tuberculosis is also related. Additionally, DM and GERD were significantly associated with frequent COPD exacerbators condition, while a history of pulmonary tuberculosis was the sole factor linked to the severity of airway obstruction as classified by GOLD.

REFERENCES

1. Safiri S, Carson-Chahhoud K, Noori M, et al. Burden of chronic obstructive pulmonary disease and its attributable risk factors in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study 2019. BMJ. Jul 27 2022;378:e069679. doi:10.1136/bmj-2021-069679
2. Milkowska-Dymanowska J, Bialas AJ, Zalewska-Janowska A, Gorski P, Piotrowski WJ. Underrecognized comorbidities of chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2015;10:1331-41. doi:10.2147/COPD.S82420
3. Patel AR, Hurst JR. Extrapulmonary comorbidities in chronic obstructive pulmonary disease: state of the art. Expert Rev Respir Med. Oct 2011;5(5):647-62. doi:10.1586/ers.11.62
4. Divo M, Celli BR. Multimorbidity in Patients with Chronic Obstructive Pulmonary Disease. Clin Chest Med. Sep 2020;41(3):405-419. doi:10.1016/j.ccm.2020.06.002
5. Martinez CH, Mannino DM, Divo MJ. Defining COPD-Related Comorbidities, 2004-2014. Chronic Obstr Pulm Dis. May 6 2014;1(1):51-63. doi:10.15326/jcopdf.1.1.2014.0119
6. Putcha N, Puhan MA, Drummond MB, et al. A simplified score to quantify comorbidity in COPD. PLoS One. 2014;9(12):e114438. doi:10.1371/journal.pone.0114438
7. Kim Y, Kim YJ, Cho WK. Effect of multiple comorbidities on mortality in chronic obstructive pulmonary disease among Korean population: a nationwide cohort study. BMC Pulm Med. Feb 11 2021;21(1):56. doi:10.1186/s12890-021-01424-7
8. Kahnert K, Jorres RA, Behr J, Welte T. The Diagnosis and Treatment of COPD and Its Comorbidities. Dtsch Arztebl Int. Jun 23 2023;120(25):434-444. doi:10.3238/arztebl.m2023.027
9. Lê TKH, Trần ĐS, Nguyễn NV, Trần VT, Trần TKT. Tỉ lệ trào ngược dạ dày thực quản trên bệnh nhân bệnh phổi tắc nghẽn mạn tính và các yếu tố liên quan. Tạp chí Y học Việt Nam. 02/05/2024; 535(1)doi:10.51298/vmj.v535i1.8352
10. Kamenar K, Hossen S, Gupte AN, et al. Previous tuberculosis disease as a risk factor for chronic obstructive pulmonary disease: a cross-sectional analysis of multicountry, population-based studies. Thorax. Nov 2022;77(11):1088-1097. doi:10.1136/thoraxjnl-2020-216500