

Risk Factors of Death in Chronic Obstructive Pulmonary Disease (COPD) Patients at Dr. Soetomo General Academic Hospital, Surabaya, in 2019

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ABSTRACT

Introduction: The distribution of death and risk factors in chronic obstructive pulmonary disease (COPD) patients varies according to disease severity. This study aimed to determine the risk factors of mortality in COPD patients.

Methods: This was a retrospective descriptive study with a total sampling method using inclusion and exclusion criteria. Data collection was performed on patients' medical records throughout 2019. The inclusion criteria for this study sample were patients diagnosed with COPD who died in 2019, aged over 25 years old (adults), both male and female. The exclusion criteria were COPD patients with incomplete medical record data.

Results: The total number of samples obtained and included in this study was 31 COPD patients (n=31). The characteristics of the patients showed a predominance of males over females, with a ratio of 9:1. Seventeen samples (58.0%) out of 31 were patients aged >66 years old. Comorbidities accounted for 96.8% of the study population. The most prevalent comorbidity was infection (77.41%), with pneumonia accounting for 38.7% of all deaths. Eighteen patients (58.1%) reported having two or more comorbidities, whilst 28 patients (90.3%) scored 0-7 on the Modified Sequential Organ Failure Assessment (mSOFA) when admitted to the hospital.

Conclusion: This study found that the group of patients with the mSOFA score of 0-7 with the characteristics of being aged >60 years old, males, and having pneumonia infection had the highest mortality rate among other COPD patients who died.

Highlights:

1. The highest distribution of chronic obstructive pulmonary disease (COPD) patients' age and gender was over 60 years old and males.
2. The highest distribution of COPD patients' comorbidity was infection, with pneumonia being the most common infection.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a treatable disease characterized by airflow limitation. The airflow limitation is usually progressive and causes tissue damage. Chronic obstructive pulmonary disease is related to structural changes in the lungs caused by chronic inflammation due to prolonged exposure to harmful particles or gases, most often cigarette smoke, environmental and occupational exposures, or alpha-1 antitrypsin deficiency (AATD). Chronic inflammation may cause structural changes such as narrowing the airways and reducing lung recoil. Cases of COPD may range from being asymptomatic to causing respiratory failure. Common symptoms of COPD may include cough, dyspnea, and sputum production.¹ Chronic obstructive pulmonary disease is an inflammatory disease that affects the pulmonary vasculature, lung parenchyma, and airways, where protease-antiprotease imbalances and oxidative stress are theorized to play a role in the process. Emphysema is a structural alteration associated with COPD, characterized by the destruction of the lungs' gas-exchanging surfaces, known as alveoli, causing obstructive physiology. It results from an inflammatory reaction to an irritant such as smoking. Throughout inflammation, the recruitment of neutrophils and macrophages results in the release of many inflammatory mediators. On the other hand, oxidants and excessive proteases also play a role in destroying air sacs. In the end, airways collapse during expiration due to the lack of elastic recoil caused by the protease-mediated degradation of elastin.²

The prevalence of COPD in the world was around 299 million people in 2015, which has increased by 44% since 1990.³ Among those cases, around 3.2 million people worldwide died from COPD.¹ According to World Health Statistics, COPD was the third cause of death in the world in 2019.⁴ The Global Burden of Disease report estimated that COPD is among the top 10 killers in low- and middle-income nations.⁵ The World Health Organization (WHO) also stated that in 2016, chronic respiratory diseases, one of which is COPD, accounted for 6% of the total deaths from noncommunicable diseases in Indonesia.⁶ The incidence of this disease increases with age and is higher in males than females, with a male predominance after the age of 40 years old.⁷ This was further proven by studies conducted in hospitals and primary care clinics in Latin America and the Caribbean, where the prevalence of COPD was higher in males, especially patients who were smokers and ex-smokers.⁸

The distribution of causes of death in COPD patients varies according to the severity of the disease. Even though mortality was lower in females, comorbidity was an independent predictor of mortality with a similar effect in both sexes. In cases of COPD, the most common causes of death were lung cancer, cardiovascular disease, and respiratory disease, such as pneumonia, compared to other comorbidities.⁹⁻¹¹ A study by Divo, *et al.* (2022) indicated that tuberculosis was the most significant mortality risk for young COPD patients at the Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity

(BODE) study centers locations.¹² However, lung cancer was more common in elderly COPD patients before they passed away. Diagnosing and treating this disorder immediately is essential in reducing the significant morbidity and death associated with it. The assessment and management of COPD patients are covered in detail in this exercise, emphasizing the importance of interprofessional teamwork.² The previous explanation indicates that COPD remains prevalent with a significant mortality rate. Therefore, this study was conducted to determine mortality risk factors in COPD patients at Dr. Soetomo General Academic Hospital, Surabaya.

Methods

This was a retrospective descriptive study. The sample of this study was retrieved from medical records of all COPD patients who died at Dr. Soetomo General Academic Hospital, Surabaya, in 2019. The inclusion criteria were patients diagnosed with COPD who died in 2019 with more than 25 years of age (adult), male or female, and with complete data to meet the study variables (gender, age, comorbidities, Modified Sequential Organ Failure Assessment/mSOFA score). The exclusion criteria in this study were incomplete COPD patients' medical record data. The sampling technique in this study was the total sampling method. The data is presented in tabular form, according to the data obtained in the medical record. This study was performed in the Department of Pulmonology and Respiratory Medicine, Dr. Soetomo General Academic Hospital, Surabaya, from February to July 2022. This study was approved by the Research Ethic Commission, Dr. Soetomo General Academic Hospital, Surabaya (No. 0853/LOE/301.4.2/IV/2022).

Results

This study used 31 samples that met the inclusion and exclusion criteria. Data presentation included sample characteristics based on the dependent variable (COPD patients who died at Dr. Soetomo General Academic Hospital, Surabaya) and independent variables (gender, age, comorbidities, mSOFA score).

Table 1. Sample characteristics based on age and gender

Age Group (years old)	n	%
36-45	1	3.2
46-55	2	6.5
56-65	11	35.5
>66	17	54.8
TOTAL	31	100
Gender	n	%
Female	3	9.7
Male	28	90.3
TOTAL	31	100

Source: Research data, processed

Table 1 shows that out of 31 samples, the most predominant age group was above 66 years old, with 17 patients (54.8%). On the other hand, there was only one patient aged 36-45 years old. The sex of the sample of

COPD patients who died at Dr. Soetomo General Academic Hospital, Surabaya, in 2019 was primarily males, with a total of 28 samples (90.3%).

Table 2. Sample characteristics based on comorbidity

Comorbidity	n	%
No	1	3.2
Yes	30	96.8
TOTAL	31	100
None	1	3.2
1 comorbidity	12	38.7
>1 comorbidity	18	58.1
TOTAL	31	100
Cardiovascular disease		
No	20	64.5
Yes	10	32.3
>1 cardiovascular disease	1	3.2
DCM	1	3.2
Cor pulmonale+CAD	1	3.2
Cor pulmonale	5	16.1
AF	2	6.5
Hypertension	2	6.5
Lung cancer		
No	27	87.1
Yes	4	12.9
T2DM		
No	29	93.5
Yes	2	6.5
Anaemia		
No	30	96.8
Yes	1	3.2
Infection		
No	7	22.6
Yes	20	64.5
>1 infectious disease	4	12.9
Acute gastroenteritis	1	3.2
Pneumonia + TB	4	12.9
Pneumonia	12	38.7
LRTI	3	9.7
TB	4	12.9
Others		
No	22	71
Yes	9	29
AKI	5	16.1
DIH	2	6.5
Encephalopathy	1	3.2
Pneumothorax	1	3.2

Source: Research data, processed
DCM: dilated cardiomyopathy; CAD: coronary artery disease; AF: atrial fibrillation; T2DM: type 2 diabetes mellitus; TB: tuberculosis; LRTI: lower respiratory tract infection; AKI: acute kidney injury; DIH: drug-induced hepatitis

Table 2 shows that almost all COPD patients at Dr. Soetomo General Academic Hospital, Surabaya, who died had comorbid factors, with 30 patients (96.8%) affected, of whom 18 patients (58.1%) had more than one comorbidity. By contrast, there was only one patient who had no comorbidity. Of all the comorbidities, the most common was infections, with 20 patients suffering from one infection, whilst four others suffered from >1 infection (77.4%). In addition, 12 other patients (38.7%) died with pneumonia as a comorbidity. Following infections were other comorbidities such as cardiovascular diseases (32.3%), acute kidney injury (16.1%), and lung cancer (12.9%).

Table 3. Sample characteristics based on Modified Sequential Organ Failure Assessment score

mSOFA Score (Initial entry)	Total Patients	F (%)
0-7	28	90.3
8-11	3	9.7
TOTAL	31	100

Source: Research data, processed

mSOFA: Modified Sequential Organ Failure Assessment

Table 3 shows that out of 31 samples, most patients had an mSOFA score (initial entry) of 0-7, with 28 patients in total (90.3%).

Discussion

Chronic obstructive pulmonary disease is one of the leading causes of death, contributing to 6% of the total deaths from noncommunicable diseases in Indonesia.⁶ It is characterized by chronic airflow obstruction in the lungs. A combination of airway damage, such as chronic bronchitis, and lung parenchymal damage, such as emphysema, causes airflow obstruction. Chronic inflammation causes structural changes, including narrowing of the airways and damage to the lung parenchyma.¹³ The risk factors for COPD include smoking, age, air pollution, sex, infection, occupation, allergies, and genetics.¹⁴ In this study, the risk factors for death in COPD patients who died with sample criteria based on age, sex, comorbidities, and mSOFA score were determined. This study used a total sampling method with a sample of COPD patients who died at Dr. Soetomo General Academic Hospital, Surabaya, throughout 2019, obtained from the patient's medical record status of 31 samples.

Characteristics of the sample by age

The characteristics of the sample in this study were based on age. Most of the samples were elderly patients over 66 years old. This result aligns with previous studies that used data from the Indonesia Family Life Survey-5, showing that being over 40 years old was a risk factor for COPD.¹⁵ Another study from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 report also stated that most COPD patients were above 60 years old.¹⁶

Possible risk factors for death in COPD patients being older age may be due to age being a risk factor for pulmonary function disorder. This means that the older a person is, the higher the risk of experiencing pulmonary function disorder. Age tends to affect the body's resistance to the occurrence of a disease. As a person ages, their immune system tends to weaken. Thus, aging is a process where the ability of tissues to repair or replace and maintain the structure of their normal function gradually decreases.¹⁷

Age-related changes in the intrinsic mechanisms that aid cell regeneration and repair, such as depletion of the adult stem cell reservoir, mitochondrial dysfunction, increased oxidative stress, and telomere shortening, contribute to the inability of lung cells to maintain early homeostasis. Normal lung aging is associated with several structural and functional changes in the respiratory tract, leading to reduced lung function, altered lung remodelling, reduced regeneration, and increased susceptibility to lung disease. Decreased lung function is a predictor of morbidity and mortality, which can promote the development of various diseases. The epithelial surface of the airways is a large and highly vascularized area where gas exchange efficiency and the body's immune system depend on epithelial integrity. Age-related changes in the composition and function of alveolar type I (AEC1), alveolar type II

(AEC2), fibroblasts, endothelial cells, and acid sphingomyelinase (ASM) may contribute to the development and progression of lung disorders in old age. Age-related reductions in the level and composition of lactic acid bacteria (LAB) antioxidants may also underlie the increased susceptibility of the elderly to exposure to environmental toxins, such as ozone, cigarette smoke, and particulate matter.¹⁸

Characteristics of the sample by gender

The characteristics of the sample in this study were based on gender, which showed that more males died from COPD than females. This study aligns with the study conducted by Nurfaizi (2021), which was conducted at Dr. Soetomo General Academic Hospital, Surabaya, from January 2017 to December 2018.¹⁹ The results showed that most of the sex of COPD patients were males compared to females, with a ratio of 91.7% males and 8.3% females.¹⁹ Compared to female COPD patients, male COPD patients did have greater mortality rates.²⁰ Meanwhile, in 2018, the Centers for Disease Control and Prevention (CDC) reported that the number of deaths from COPD was higher in females than males (82,158 vs 73,877).²¹ However, because there are more females than males with COPD, the mortality rate is higher in men (42.9 vs 35.8 per 100,000).²¹

According to this study, males are more at risk of developing COPD than females. It could be related to COPD, theorized to be a disease primarily associated with males. However, this assumption is mainly based on the fact that more males smoke regularly than females. Empirical data also indicates that males usually start smoking earlier than females (several decades). A study demonstrated a differential susceptibility to developing COPD in males and females who smoke regularly.²²

In contrast, COPD, rather than lung cancer or cardiovascular disease, is the main cause of death among female smokers in the United States (US). Nowadays, males no longer predominately suffer from COPD, especially the elderly. Several different phenotypes are present, and certain female phenotypes cannot be ruled out. According to Gut-Gobert, *et al.* (2019), studies showed that females did not seek medical attention for dyspnea but rather for exhaustion, which has serious psychosocial repercussions and a poor quality of life, causing a significant delay in diagnosis. In primary care medicine, underdiagnosis is still widespread.⁹

Females who have COPD experience different clinical signs and outcomes than males do. Given the same disease severity, females frequently report higher symptoms. Females with COPD are more likely to experience anxiety for a given airflow restriction and age. Females also have more significant impairments in life quality and impact on exercise capacity, dyspnea, and lower quality of life for a given amount of airflow blockage. Still, they are less likely to report cough and phlegm.²³

Sample characteristics by comorbidity

The characteristics of the sample in this study, based on their comorbidities, showed that almost all of the

patients who died had at least one comorbidity, with many having more than one comorbid factor. Furthermore, this study also found that infection was the most common comorbid factor in COPD patients who had died, with pneumonia being the most prevalent.

Lung Foundation Australia reported higher rates of cardiovascular illness, stroke, diabetes, depression, polypharmacy, and mobility issues.²⁴ In primary care, multimorbidity has been debated more and more. Multimorbidity is the co-existence of two or more chronic medical illnesses in the same person, which may or may not interact with one another directly. It affects elderly patients in primary care more frequently than not. Effective multimorbidity management calls for a patient-centered approach to balancing various and occasionally conflicting demands. Obesity, anxiety, depression, osteoporosis, and metabolic disorders are a few of the significant comorbidities faced by those with COPD. These conditions are linked to worse physical performance as determined by the distance covered during the 6-minute walk test (6MWT).

A retrospective cohort analysis of nearly 2,000 male US Army veterans with COPD admissions indicated that comorbidity was linked to lower rates of corticosteroid and antibiotic use while in the hospital, as well as a higher 30-day readmission and mortality rate.²⁵ Additionally, COPD is related to poor health conditions, multiple comorbidities, and natural comorbidities of old age, all of which contribute to a higher mortality risk for COPD in elderly patients.²⁶ In a study conducted by Kim-Dorner, *et al.* (2022), older patient groups also showed more significant age-specific comorbidities than younger patient groups.²⁰ This study also showed a significant number of diverse comorbidities.²⁰

This study slightly aligns with the study conducted by Putra (2019) at Dr. Saiful Anwar General Hospital, Malang, from 2016-2017.²⁷ This study reported that pneumonia was the most common comorbidity, with 58 patients. Chronic obstructive pulmonary disease patients with radiologically established pneumonia, mainly those hospitalized repeatedly, may be susceptible to *Legionella spp.*, gram-negative microorganisms, and anaerobic microorganisms. Therefore, clinical and radiographic factors should be considered when designing initial empiric antibiotic therapy.²⁴

The disruption of innate lung defenses in COPD patients increases their susceptibility to infections. Chronic obstructive pulmonary disease patients suffer from dyspnea, cough, and sputum production and may experience COPD exacerbations, which are often caused by respiratory tract infections.²⁸ More specifically, only 30%-50% of all exacerbations are associated with increased airway eosinophilic inflammation and appear to respond to systemic corticosteroids. In contrast, approximately 50% are triggered by bacterial infection and may react to antibiotics.²⁹

In a population of patients with hospitalized non-exacerbated COPD (NECOPD), it was shown that 7.1% of patients had community-acquired acute kidney injury (CA-AKI), and 12.0% had hospital-acquired AKI (HA-AKI).

Patients with cor pulmonale also had a greater incidence of AKI. Age-related changes in females, the presence of cor pulmonale, the stage of chronic kidney disease, diuretics, exposure to contrast material, and the use of glycopeptide antibiotics before AKI were linked to HA-AKI. After various adjustments towards age, females, Charlson comorbidity index (CCI), and minimum hemoglobin (Hb) level, HA-AKI remained a risk factor for in-hospital death regardless of the presence or absence of cor pulmonale. All kinds of AKI considerably elevated the length of hospital stays and costs in the NECOPD population. Patients with HA-AKI had a considerably higher mortality risk than those with CA-AKI. After the patients were separated into groups based on whether they had cor pulmonale, no other discernible difference was found.³⁰

It has been established that lung cancer and COPD are closely connected diseases. In some cases, COPD, especially in cases of squamous cell cancer, may operate as a primary risk factor for lung cancer. The high rate of lung cancer in COPD was thought to be caused by a shared pathogenic mechanism between the two, such as early aging of the lungs, genetic susceptibility to either condition, or shared pathogenic factors such as growth factors, activation of intracellular pathways, or epigenetics. Age and smoking are two risk factors that are common to both cancer and COPD. It is well known that the trend in COPD fatalities and lung cancer deaths rose from 1975 to 2015. The risk of COPD-related death was the highest among patients between the ages of 40-45 years old. Adenocarcinoma was shown to be associated with the lowest risk among all histological types in analyses stratified by lung cancer. Compared to other anatomic sites in the lung, a tumor in the main bronchus had the highest risk.³¹

Females and males also have different comorbidities. Due to increased weight points given to cardiovascular comorbidities, males had higher Elixhauser-vW index scores than women. In addition, men experienced more significant sleep disturbances than women. Given that inadequate sleep has negative effects on cardiovascular health. One of the most important determinants of quality of life and health status in COPD patients is anxiety and depression. Chronic illnesses that impact mental health are more common in females, and these illnesses are known to lower the quality of life.^{20,32}

Sample characteristics based on Modified Sequential Organ Failure Assessment score

Based on the mSOFA score, the sample's characteristics showed that the total score of 0-7 was more than those who died, with a total score of 8-11. The results obtained on the sample mSOFA score in this study could not describe the risk of COPD patients dying because the results received many mSOFA scores of 0-7. In contrast, in this study, the samples were those who died during treatment. Several factors may have influenced the results of the mSOFA score of this study. Likewise, in the study conducted by El-Naggar, *et al.* (2018), between COPD and pneumonia cases at admission and after 48 hours in the

hospital, the SOFA score was not significant.³³ It was unable to forecast patient mortality or length of stay.³³

According to Jentzer, *et al.* (2018), in general, in critically unwell patients, the SOFA score, a straightforward measure of illness severity, is used to forecast mortality.³⁴ The mSOFA score is measured to determine the severity of the patient, especially to check organ functions based on measurements using the mSOFA score at the time of admission to the hospital. The mSOFA score used more specific sampling criteria in this study to minimize reliance on laboratory resources. In this mSOFA score, creatinine laboratory values were used.

The mSOFA score is a simplified form of the SOFA score, which was initially used to predict death in sepsis patients. However, there is concern that the SOFA score does not accurately predict death when used for patients with isolated respiratory failure.³⁵

Strength and Limitations

This study provided valuable insights into the prevalence and risk factors associated with mortality in COPD patients, offering a comprehensive analysis of a sample over one year. The retrospective study design allowed examining historical data from medical records, providing a practical and cost-effective approach to investigating the subject. However, certain limitations should be considered. The single-center focus of the study at Dr. Soetomo General Academic Hospital, Surabaya, might limit the generalizability of findings to broader populations. Furthermore, this study predominantly relied on quantitative data, potentially overlooking qualitative aspects that could provide a more nuanced understanding of patient experiences and outcomes. Despite these limitations, this study offers valuable contributions to the knowledge of COPD in a hospital setting. Future research endeavors may benefit from addressing these limitations to enrich the knowledge in this field further.

Conclusion

The results of this study indicated that most of the samples were aged above 60 years old, the gender ratio between males and females was 9:1, most of the comorbidities experienced were pneumonia infection, and most of the total initial mSOFA scores entered were 0-7. We suggest further analyzing the relationship between risk factors (age, gender, environment, occupation, comorbidities, SOFA score, and others) and COPD patient mortality. It is expected that further research can be performed with an enormous amount of data collection to describe the mortality outcomes in COPD patients more thoroughly.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Ethical Clearance

This study was approved by the Research Ethic Commission, Dr. Soetomo General Academic Hospital (No. 0853/LOE/301.4.2/IV/2022) on 01-04-2022.

Authors' Contributions

Designed the study: HIW, AB, EK, and ANR. Collected data, conducted a background literature review, designed the manuscript, and performed a statistical analysis: HIW. Supervised the results and discussions: AB, EK, and ANR. All authors reviewed and approved the final version of the manuscript.

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