

An Analysis of Shortness of Breath and Survival of Covid-19 Patients: Retrospective Cohort Study from Tertiary Hospital in East Java Indonesia

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Abstract. Indonesia is one of the most affected countries in terms of the number of cases; however, Indonesia is not among the top 10 countries in terms of the number of deaths. Patients experiencing shortness of breath have a higher mortality rate than those without shortness of breath. This study aims to analyze the relationship between shortness of breath and the survival of COVID-19 patients over time. This study used a retrospective cohort design based on secondary data from the Medical Records of "Aisyiyah General Hospital, Ponorogo. The study included 894 COVID-19 patients hospitalized from March to December 2021. The dependent variables were patient status (Deceased or Alive) and Shortness of Breath. Potential confounders of the independent variables were smoking, hypertension, heart disease, lung disease, diabetes mellitus, kidney disease, chronic liver disease, oxygen saturation, anosmia, ARDS, acidosis, septic shock, coagulopathy, and convalescent plasma. Frequency and percentage are descriptive statistics expressed for each component. Survival rates were determined using the Kaplan-Meier method, and differences were assessed using the log-rank test. Hazard ratios with 95% CIs were used to describe the risk of mortality. The impact of factors on the survival rate of COVID-19 patients was examined using single and multiple Cox regression analyses. All statistical analyses were performed with Stata. The result survival analysis showed that there were 273 (32.2%) deaths, which occurred in 53.2% of those with shortness of breath ($P < 0.001$), 22 (2.6%) who smoked, 383 (45.1%) with heart disease ($P < 0.001$), 77 (9.1%) with kidney disease ($P < 0.001$), and 513 (60.4%) with abnormal oxygen saturation. Shortness of breath significantly impacted the survival of COVID-19 patients. COVID-19 patients with shortness of breath had a 1.987-fold greater risk of death than patients without shortness of breath. Shortness of breath significantly impacted the survival of COVID-19 patients.

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1 Introduction

Globally, the healthcare sector is under unprecedented strain due to the new corona virus illness 19 (COVID-19). In order to allocate resources and focus therapies, it is critical to make efforts to stratify clinical outcomes and predict survival [1]. Indonesia has recorded 6,467,189 confirmed cases of COVID-19 since the epidemic started, with a 2.45% case fatality rate (158,398 fatalities as of October 2022) [2]. East Java is one of the provinces with the highest number of confirmed cases in Indonesia, amounting to 98,123 cases or a total of 9.4% nationally as of October 30, 2021 [3]. According to current data, Indonesia is among the most impacted nations in terms of the number of cases; nevertheless, it does not rank among the top 10 countries in terms of case fatalities.

People with COVID-19 also frequently have severe and incapacitating symptoms, such as shortness of breath (18–71%), which can frequently last for a long time [4]. Age and comorbidities are also the main factor of mortality [5]. Even while persons with COVID-19 who experience shortness of breath had a considerably higher death rate (OR = 4.34, 95% CI: [2.68–7.05], $p < 0.001$, I² = 69.2%, $p < 0.001$, random-effects model) [6]. However, given that the disease is still wreaking havoc worldwide, research on variables that influence the risk of death from COVID-19 is critical to combating the pandemic and reducing mortality. Health professionals and decision-makers can utilize life expectancy, a positive indicator of recovery rate, to develop and implement strategies to control and combat the COVID-19 pandemic. Little information is available on the life expectancy of COVID-19 patients and prognostic variables. Therefore, the current study aims to analyze shortness of breath on survival in COVID-19 patients admitted to a tertiary care facility in East Java.

2 Method

We performed a retrospective cohort study using medical records of 849 laboratory-confirmed COVID-19 cases hospitalized at 'Aisyiyah Hospital COVID-19 Treatment Centre from March 1 to December 30, 2021. All patients tested positive using Real-time reverse Transcriptase Polymerase Chain Reaction (RT-PCR) SARS-CoV-2 assay of a nasopharyngeal swab specimen. This study was conducted in "Aisyiyah Hospital COVID-19 treatment centre in Ponorogo Regency. This Regency consists of 21 sub-districts, 26 urban villages, and 281 villages (out of a total of 666 sub-districts, 777 urban villages, and 7,724 villages in East Java), comprises six hospitals with COVID-19 treatment provided in 'Aisyiyah Hospital. This hospital is the largest pilot and referral hospital in Ponorogo, located about 220 km from Surabaya (the capital of East Java). The dependent variable are final status of patients (Die and Live) and Shortness of breath (Shortness and No shortness). The potential confounding of independence variable are smoking variable, hypertension, heart disease, lungs disease, diabetes mellitus, kidney disease, chronic liver, oxygen saturation, anosmia, ARDS, Acidosis, Sepsis Shock, coagulopathy, and convalescent plasma. Frequency and percentage were descriptive statistics that were expressed for every component. The survival rate was determined using the Kaplan Meier technique, and survival rates were compared using the log-rank test. Hazard ratios with a 95% CI were used to illustrate the risk of mortality. The impact of factors on the survival

rate of COVID-19 patients was examined using both single and multiple Cox regression analysis. All statistical analysis were performed with Stata.

3 Results

The results of the descriptive analysis of 849 patients who were confirmed with COVID-19 can be seen in **Table 1**. Patients with final status died after hospitalization by 32.16%.

Table 1. Demographic and clinical characteristics

Variable		Frequency	Percentage (%)
Final Status	Die	273	32.16
	Live	576	67.84
Shortness of breath	Shortness of breath	452	53.24
	No shortness of breath	397	46.76
Other factors			
Smoking status	Smoking	22	2.59
	No Smoking	827	97.41
Hypertension	Hypertension	189	22.26
	No Hypertension	660	77.74
Heart disease	Heart disease	383	45.11
	No Heart disease	466	54.89
Lungs disease	Lungs disease	163	19.20
	No lungs disease	686	80.80
Diabetes Mellitus	Diabetes Mellitus	249	29.33
	No Diabetes Mellitus	600	70.67
Kidney disease	Kidney disease	77	9.07
	No Kidneys disease	772	90.93
Chronic liver	Chronic Liver	3	0.35
	No Chronic Liver	846	99.65
Oxygen Saturation	Abnormal	513	60.42
	Normal	336	39.58
Anosmia	Anosmia	25	2.94
	No Anosmia	824	97.06
ARDS	ARDS	55	6.48
	No ARDS	794	93.52
Acidosis	Acidosis	11	1.30
	No Acidosis	838	98.70
Sepsis shock	Sepsis shock	9	1.06
	No Sepsis Shock	840	98.94
Coagulopathy	Coagulopathy	250	29.45
	No Coagulopathy	599	70.55
Convalescent plasma	Convalescent plasma	42	4.95
	No Convalent Plasma	807	95.05

Based on bivariable analysis using the Kaplan-Meier method and Cox Regression to the survival of COVID-19 patients, it can be seen in **Table 2**.

Table 2. Investigation characteristics in relation to final status

Variable		HR	p-value	95% CI (HR)
Main factor				
Shortness of breath	Shortness of breath	2.390	0.000	1.809 - 3.157
	No shortness of breath	1		
Other factors				
Smoking status	Smoking	2.289	0.004	1.305 - 4.013
	No Smoking	1		
Hypertension	Hypertension	1.041	0.786	0.775 - 1.401
	No Hypertension	1		
Heart disease	Heart disease	2.091	0.000	1.603 - 2.728
	No Heart disease	1		
Lungs disease	Lungs disease	1.229	0.190	0.903 - 1.672
	No lungs disease	1		
Diabetes Mellitus	Diabetes Mellitus	1.214	0.162	0.925 - 1.595
	No Diabetes Mellitus	1		
Kidney disease	Kidney disease	2.074	0.000	1.442 - 2.985
	No Kidneys disease	1		
Chronic liver	Chronic Liver	0.808	0.832	0.113 - 5.768
	No Chronic Liver	1		
Oxygen Saturation	Abnormal	2.560	0.000	1.877 - 3.492
	Normal	1		
Anosmia	Anosmia	0.250	0.051	0.062 - 1.007
	No Anosmia	1		
ARDS	ARDS	1.161	0.534	0.726 - 1.856
	No ARDS	1		
Acidosis	Acidosis	1.165	0.792	0.373 - 3.642
	No Acidosis	1		
Sepsis shock	Sepsis shock	2.660	0.031	1.095 - 6.462
	No Sepsis Shock	1		
Coagulopathy	Coagulopathy	1.548	0.001	1.195 - 2.006
	No Coagulopathy	1		
Convalent plasma	Convalent plasma	1.512	0.062	0.979 - 2.336
	No Convalent Plasma	1		

The results of the bi variable analysis showed that the variables of hypertension, lungs diseases, Diabetes Mellitus, chronic liver, anosmia, ARDS, acidosis, and convalescent plasma did not affect the survival of COVID-19 patients. Furthermore, multi variable analysis was carried out to establish the magnitude of the relationship between independent and dependent variables based on the results of bi variable analysis selection. Full model modelling is carried out in the multi variable, issuing one-by-one variables whose $p > 0.05$ values start from the largest p-value. The selection is seen from the change in the Hazard Ratio. If the change in hazard ratio is more than 10%, then the variable has the potential to be a confounding variable. The results of the multi variable analysis can be seen in **Table 3**.

Table 3. Multi variable Analysis to predict factor influencing final status

Variable		B	SE β	p-value	HR	95% CI
Main factor						
Shortness of breath	Shortness of breath	0.687	0.144	0.000	1.987	1.50 - 2.64
	No shortness of breath					
Other factors						
Smoking status	Smoking	0.525	0.288	0.069	1.689	0.96 - 2.97
	No Smoking					
Heart disease	Heart disease	0.582	0.138	0.000	1.790	1.36 - 2.35
	No Heart disease					
Kidney disease	Kidney disease	0.403	0.189	0.033	1.496	1.03 - 2.17
	No Kidneys disease					
Oxygen Saturation	Abnormal	0.680	0.162	0.000	1.973	1.44 - 2.71
	Normal					

Based on the analysis of **Table 3**, the variable shortness of breath has the greatest influence on the survival of COVID-19 patients. COVID-19 patients who experience shortness of breath have a 1.987 times greater risk of dying than patients who do not experience shortness of breath. Patients who had abnormal saturation had a risk of dying 1.973 times compared to patients with normal saturation. Based on comorbidities, patients who had a history of heart disease had a 1.790 times chance of dying compared to patients without heart comorbidities. In comparison, patients with comorbidities of the kidneys have a 1.496 times chance of dying compared to patients without concomitant kidney disease. In COVID-19 patients with a history of smoking, they had a 1.689 times risk of dying compared to patients with no smoking history.

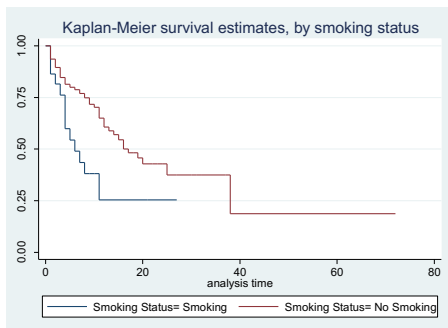


Fig. 1. Cumulative patient survival and shortness of breath

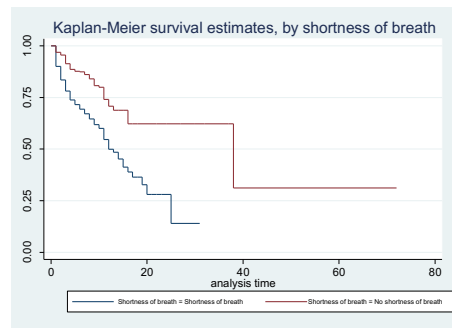


Fig. 2. Cumulative patient survival and smoking status

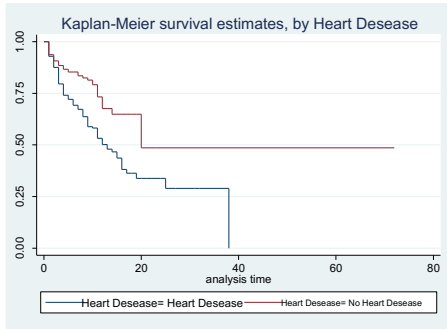


Fig. 3. Cumulative patient survival and heart disease

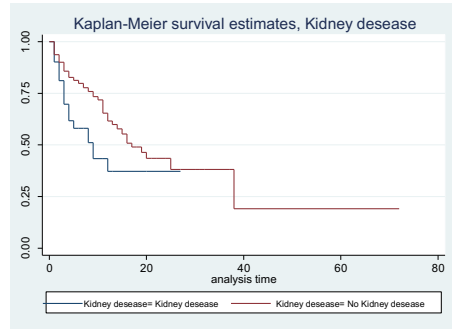


Fig. 4. Cumulative patient survival and kidney disease

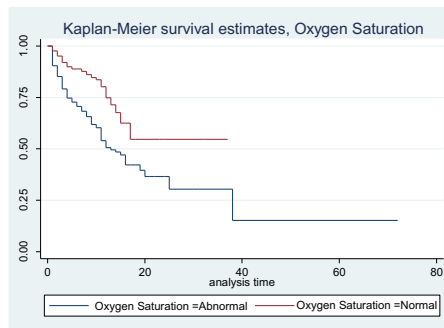


Fig. 5. Cumulative patient survival and oxygen saturation

Based on **Fig. 1**, the survival graph of the final status of COVID-19 patients with shortness of breath shows that on 10th day, 85% of patients survived without shortness of breath. However, of patients with shortness of breath, 60% still survive. In **Fig. 2**, it can be seen that on 10th day, 60% of people who smoke survive, while in patients who do not smoke, there are still 80% who survive. Based on heart disease status (**Fig. 3**), on 10th day it can be seen that 80% of patients without heart disease still survive, while in patients with heart disease there are 65%. In patients with kidney disease (**Fig. 4**), it can be seen that on 10th day, patients without kidney disease survived 80%, while patients with kidney disease survived 55%. **Fig. 5** shows that on 10th day, 90% of patients with normal oxygen saturation survived. While 70% of patients with abnormal oxygen saturation still survive.

4 Discussion

Coronavirus made people died totaled 5,94 million in 2021. In our study, shortness of breath had the greatest impact on the survival of COVID-19 patients. COVID-19 patients who complain of shortness of breath have a higher risk of death of up to 45-85 per cent. When associated with gender, the risk of death for female patients is 1,053 times compared to male patients with complaints of shortness of breath [7]. Female COVID-19 patients who experience shortness of breath experience a worse quality of life than male patients. It is because there are biological factors outside of disease pathology that can increase the severity of symptoms and reduce the quality of life [8]. There is a strong

correlation between shortness of breath and increasing degrees of lung disorders in COVID-19 patients [6].

Table 3 of this study explains that five things have a major effect on the survival of COVID-19 patients: smoking, heart commodities, kidney commodities, oxygen saturation, and shortness of breath. COVID-19 patients with a history of smoking are at a 1,689 times greater risk of dying compared to COVID-19 patients without a history of smoking (*p-value* 0.069 and CI 95% 0.96-2.97). COVID-19 patients with a smoking history had a 1.26 times greater risk of death in hospitals than non-smoking patients with CI: 1.20-1.32; $P < .0,001$ [9]. Smoking is known to cause damage to the pulmonary endothelium, which can hinder lung function [10], and it is known to have a devastating impact on COVID-19 patients [11]. COVID-19 patients who have a history of heart disease have a 1,790 times chance of dying compared to patients without heart disease. Previous studies have also explained that comorbid heart disease is significantly associated with the severity of COVID-19 with an OR of 2.89; CI of 95% 1.98 – 4.21 and COVID-19 deaths with an OR of 3.00; CI of 95 % 1.67 – 5.39 [12]. In COVID-19 patients with concomitant heart disease, there is a possibility of interaction between the *spike* protein spike (S) virus and *angiotensin-converting enzyme 2*, which triggers the virus entry into the host cell. COVID-19 can cause cardiovascular disorders, including myocardial injury, arrhythmia, acute coronary syndrome, and venous thromboembolism [13]. Renal comorbidities/comorbidities are significant to the final status of COVID-19 patients with a P value of 0.033 and CI of 95% 1.03 - 2.17, so the chances of dying are 1,496 times greater than those without kidney disease concomitants. The high mortality rate of COVID-19 patients is significantly higher in CKD patients (23.1 % vs. 10.2 %), with a 1.51 greater chance of death (CI 95 %: 1.19 – 1.90) [14]. Patients who had abnormal saturation had a risk of dying 1.973 times compared to patients with normal saturation. Other studies have also stated that oxygen saturation predicts the severity and outcome of COVID-19 patients with a *p-value* of 0.001 CI 95 % 0.734-0.861 with an OR of 0.795. Oxygen saturation is one of the parameters of breath distress by showing the value of oxygen levels in the blood of COVID-19 patients [15].

5 Conclusion

Health professionals and politicians use survival to plan and execute disease control strategies since it reflects cure rates. The study's conclusions would make it easier to identify individuals who are at risk and to promptly give specialized treatment to avert unfavorable outcomes in the hospital environment.

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References

1. G. N. Ioannou *et al.*, “Risk Factors for Hospitalization, Mechanical Ventilation, or Death Among 10 131 US Veterans With SARS-CoV-2 Infection.,” *JAMA Netw. Open*, vol. 3, no. 9, p. e2022310, Sep. 2020, doi: 10.1001/jamanetworkopen, **2020**, 22310.

2. Y. Hartantri *et al.*, “Clinical and treatment factors associated with the mortality of COVID-19 patients admitted to a referral hospital in Indonesia,” *The Lancet Regional Health - Southeast Asia*, vol. 11, no. 38, p. 100167, Apr. **2023**, doi: 10.1016/j.lansea.2023.100167.
3. W. Trisnawati, “Lesson Learned from COVID-19 Pandemic: Optimize 3T Program (Testing, Tracing, and Treatment) for Tuberculosis Elimination in Indonesia,” no. June, **2022**.
4. A. Tong *et al.*, “Core Outcome Measures for Trials in People With Coronavirus Disease 2019: Respiratory Failure, Multiorgan Failure, Shortness of Breath, and Recovery.,” *Crit. Care Med.*, vol. 49, no. 3, pp. 503–516, Mar. **2021**, doi: 10.1097/CCM.0000000000004817.
5. A. F. Mas’udah, L. E. Purwanti, H. Ernawati, N. M. Rohmah, V. A. Muslimah, and V. I. Muslimah, “Age and Comorbidities as The Main Factors of Mortality in Covid-19 Patients : A Retrospective Cohort Study,” *IJNP (Indonesian Journal of Nursing Practices)*, vol. 7, no. 1, pp. 9–17, Jun. **2023**, doi: 10.18196/ijnp.v7i1.17347.
6. L. Hentsch *et al.*, “Breathlessness and COVID-19: A call for research,” ., vol. 100, no. 10, pp. 1016–1026, **2021**, doi: 10.1159/000517400.
7. M. D. Simatupang and M. A. Arcana, “Risiko Kematian Pasien Covid-19 dan Faktor yang Memengaruhinya,” *Seminar Nasional Official Statistics*, **2021**.
8. C. Gut-Gobert *et al.*, “Women and COPD: do we need more evidence?,” *Eur. Respir. Rev.*, vol. 28, no. 151, Mar. **2019**, doi: 10.1183/16000617.0055-2018.
9. R. K. Reddy, W. N. Charles, A. Sklavounos, A. Dutt, P. T. Seed, and A. Khajuria, “The effect of smoking on COVID-19 severity: A systematic review and meta-analysis.,” *J. Med. Virol.*, vol. 93, no. 2, pp. 1045–1056, Feb. **2021**, doi: 10.1002/jmv.26389.
10. Q. Lu, E. Gottlieb, and S. Rounds, “Effects of cigarette smoke on pulmonary endothelial cells.,” *Am. J. Physiol. Lung Cell. Mol. Physiol.*, vol. 314, no. 5, pp. L743–L756, May **2018**, doi: 10.1152/ajplung.00373.2017.
11. M. Y. Abou-Ismaïl, A. Diamond, S. Kapoor, Y. Arafah, and L. Nayak, “Corrigendum to ‘The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management’ [Thromb. Res., 194, October 2020, Pages 101-115].,” *Thromb. Res.*, vol. 204, no. November **2020**, p. 146, Aug. 2021, doi: 10.1016/j.thromres.2020.11.012.
12. P. Mishra, R. Parveen, R. Bajpai, M. Samim, and N. B. Agarwal, “Impact of cardiovascular diseases on severity of COVID-19 patients: A systematic review,” *Ann. Acad. Med. Singap.*, vol. 50, no. 1, pp. 52–60, **2021**, doi: 10.47102/annals-acadmedsg.2020367.
13. M. Nishiga, D. W. Wang, Y. Han, D. B. Lewis, and J. C. Wu, “COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives,” *Nat. Rev. Cardiol.*, vol. 17, no. 9, pp. 543–558, Sep. **2020**, doi: 10.1038/s41569-020-0413-9.
14. N. E. Mohamed *et al.*, “Association between chronic kidney disease and COVID-19-related mortality in New York,” *World J. Urol.*, vol. 39, no. 8, pp. 2987–2993, **2021**, doi: 10.1007/s00345-020-03567-4.
15. N. Shenoy, R. Luchtel, and P. Gulani, “Considerations for target oxygen saturation in COVID-19 patients: are we under-shooting?,” *BMC Med.*, vol. 18, no. 1, p. 260, Dec. **2020**, doi: 10.1186/s12916-020-01735-2.