Survival Rate of Chronic Obstructive Pulmonary Disease Patients with Type II Respiratory Failure at Haji Adam Malik Hospital

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ARTICLE INFO	ABSTRACT
	Introduction: Chronic obstructive pulmonary disease is associated with acute exacerbations that can lead to respiratory failure and as major cause of morbidity and mortality worldwide. The Aim of study was to explore survival rate of COPD patients with type II respiratory failure **Methods**: Observational research with retrospective cohort design using data from medical records of chronic obstructive pulmonary disease patients with type II respiratory failure treated at H. Adam Malik General Hospital Medan for 10 months from November 2021 to September 2022. Analyzed of independent and dependent variables used Chi Square test. To obtain most dominant independent variable that influence dependent variable, a multiple logistic regression test is used. **Results**: There were 21 patients (50%) who alived until end of research but also 21 deaths occured. Survival rate was 50% with a median survival time 14 days (CI 95%: 7.178-20.822 days). Survival rate of COPD patients with type II respiratory failure who do not routinely received therapy was 16.7% with a median survival time 4 days (CI 95%: 42.962-5.039). Survival rate of COPD patients with type II respiratory failure who routinely received therapy was 75%. Based on log rank test, there was a significant difference median length of life between patients who did not and who routinely received therapy (p <0.001). **Conclusion**: The survival rate in COPD patients who regularly use inhaler therapy is significantly higher than patients who do not routinely use inhaler therapy.
Keywords	

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is third most common cause of death worldwide, with continuing increasement mortality rates for both short and long term due to acute exacerbations.[1] Respiratory failure is a clinical condition that occurs when respiratory system fails to maintain its main function, namely air exchange and arterial partial pressure of oxygen (PaO2) is < 60 mmHg and/or the arterial partial pressure of carbon dioxide (PaCO2) is > 50 mmHg.[2] Hypercapnic respiratory failure is most commonly found in COPD patients.[3,4]

COPD continues to be a leading cause of morbidity and mortality in United States and worldwide. Hypercapnic respiratory failure is a phenomenon that may occur during acute and chronic COPD exacerbations as the disease progresses. Patients with COPD and hypercapnic respiratory failure have a poorer prognosis, are more likely to be hospitalized, and experience a more rapid decline in pulmonary and non-pulmonary function. Once hypercapnia develops, the two-year mortality rate for COPD patients increases to 30-40%.[5]

A multicenter prospective cohort study before noninvasive ventilation (NIV) era showed that COPD patients who admitted to ICU for acute exacerbations and who were >65 years old had mortality rate 30%, which doubled after 1 year to 60%.[6] Another retrospective study aimed to evaluating long-term survival of patients treated with NIV for the first time found survival rates at 1, 2 and 5 years were 72%, 52% and 26%, respectively [7]. This survival rate is also influenced by readmission needs, where patients who require readmission have 20% chance of surviving at 5 years.[6]

METHODS

This research was an observational study with a cross-sectional design using data from medical records of chronic obstructive pulmonary disease patients with type II respiratory failure who treated at H. Adam Malik General Hospital, Medan. The research was carried out over a 10 month period from November 2021 to September 2022.

The number of patients required based on the calculation for the hypothesis of different proportions is 50 patients. Inclusion criteria include diagnosed chronic obstructive pulmonary disease patients with acute exacerbation and type II respiratory failure based on clinical symptoms, blood gas analysis results, and treatment in ICU; while patients with incomplete medical record data and patients diagnosed with malignancy were excluded from this research.

Collected data will be processed using statistical software. Data will be processed and analyzed descriptively to evaluate the frequency distribution of research subjects based on characteristics. Then proceed with inferential analysis. Analyze of correlation between independent and dependent variables using Chi-Square test. To obtain most dominant independent variable that influence dependent variable, a multiple logistic regression test is used. The significance level is obtained if p-value <0.05.

RESULTS

This research was conducted on 42 patients diagnosed as chronic obstructive pulmonary disease with type II respiratory failure at Haji Adam Malik Teaching General Hospital, Medan, from November 2021 to September 2022.

Most of patients were male as much as 33 people (78.6%). There were 22 patients aged <60 years old (52.4%). The most common comorbidities were pneumonia and DM type 2, as much as 6 people (14.3%). The number of patients with 2 comorbid diseases was 26 people (61.9%).
A total of 17 patients each were active smokers and former smokers. A total of 18 patients (42.9%) did not received routine treatment. Most subjects experienced exacerbations > 1 x a year. Mean length of stay for patients was 9.6 days with shortest 2 days and longest 25 days. A total of 21 patients died.

Survival Analysis (Kaplan-Meier) of COPD Patients with Type II Respiratory Failure

Based on the time from admission ICU until death, survival rate for COPD patients with type II respiratory failure were obtained using Kaplan-Meier survival analysis method. In this research, 21 patients (50%) survived until the end of research, with 21 deaths out of 42 patients. Survival rate was 50% with median survival time 14 days (CI 95%: 7.178-20.822 days).

Survival rate and Median Life Length of COPD Patients with Type II Respiratory Failure Based on Gender

Survival rate of COPD patients with type II respiratory failure in men was 42.4% with a median survival time 12 days (CI 95%: 4.937-19.027). Survival rate of COPD patients with type II respiratory failure in women was 77.8% with a median survival time 6 days (CI 95%: 4.312-7.688). The log rank test shows that there is no significant difference in median length of life between men and women (p = 0.110). There is no significant relationship between gender and survival rate of COPD patients with type II respiratory failure. The

Proportional Hazard assumption is not met, which means that the ratio of survival rate between male and female patients was not constant.

Table 1. Demographic characteristics of research subjects

Demographic characteristics	n = 42
Gender, n (%)	
Male	33 (78,6)
Female	9 (21,4)
Age, n (%)	
≥ 60 years old	20 (47,6)
< 60 years old	22 (52,4)
Comorbidity, n (%)	
CHF	1 (2,4)
CKD and DM type 2	1 (2,4)
DM type 2	2 (4,8)
Hypertension	3 (7,1)
Hypertension and DM type 2	3 (7,1)
Hypertension and SOL	1 (2,4)
Pneumonia	1 (2,4)
Pneumonia and CKD	3 (7,1)
Pneumonia and DM type 2	6 (14,3)
Pneumonia and ICH	1 (2,4)
Pneumonia and Stroke	1 (2,4)
SOL	1 (2,4)
SOL and DM type 2	1 (2,4)
Stroke	2 (4,8)
Stroke and CHF	2 (4,8)
Stroke and DM type 2	1 (2,4)
Stroke and Encephalopathy	1 (2,4)
Stroke and Hypertension	4 (9,5)
TB Pulmonal	5 (11,9)
TB Pulmonal and DM type 2	1 (2,4)
None	1 (2,4)
Total Comorbid Disease, n (%)	
0	1 (2,4)
1	15 (35,7)
2	26 (61,9)
Smoking habit, n (%)	
Active smoker	17 (40,5)
Former smoker	17 (40,5)
Not a smoker	8 (19)
Inhaler therapy, n (%)	
Not Routine	18 (42,9)
Routine	24 (57,1)
History of exacerbation, n (%)	
> 1x in a year	27 (64,3)
1 x in a year	1 (2,4)
None	14 (33,3)
Length of stay, n (%)	
Mean (SD)	9,6 (5,82)
Median (Min – Mak)	8,5 (2 – 25)
Outcome, n (%)	
Death	21 (50)
Alive	21 (50)

Survival rate and Median Life Length of COPD Patients with Type II Respiratory Failure Based on Age

Survival rate of COPD patients with type II respiratory failure aged > 60 years old was 45% with a median survival time 18 days (CI 95%: 5.637-30.363). Survival rate of COPD patients with type II respiratory failure

aged ≤ 60 years was 54.5% with a median survival time 14 days (CI 95%: 7.178-20.822). The log rank test showed that there was no significant difference in median length of survival between patients aged > 60 years and ≤ 60 years (p = 0.664). It can be seen on curve in Fig.3 intersect each other, which means there is no significant relationship between age and survival time of COPD patients with type II respiratory failure. The Proportional Hazard assumption is not met, which means that the comparison of survival time between patients aged > 60 years and ≤ 60 years was not constant.

Table 2. Median Length of Life and survival rate based on Subject Characteristics of COPD Patients with Type II Respiratory Failure

Subject Characteristics	n	Event	Median length of life		Survival Rate		p*
			Days	95% CI	n	%	
Gender							
Male	33	19	12	4,937-19,027	14	42,4	0,110
Female	9	2	6	4,312-7,688	7	77,8	
Age							
> 60 years old	20	11	18	5,637-30,363	9	45	0,664
≤ 60 years old	22	10	14	7,178-20,822	12	54,5	
Total Comorbid Disease, n (%)							
0	1	0	-	-	1	100	0,512
1	15	9	-	-	6	40	
2	26	12	-	-	14	53,8	
Smoking habit, n (%)							
Active smoker	17	10	14	3,995-24	7	41,2	0,369
Former smoker	17	9	12	1,506-22,494	8	47,1	
Not a smoker	8	2	18		6	75	
Inhaler therapy, n (%)							
Not Routine	18	15	4	2,962-5,039	3	16,7	<0,001
Routine	24	6	-	-	18	75	
History of exacerbation,							
Yes	28	12	18	7,614-28,386	16	57,1	0,437
No	14	9	8	6,185-9,815	5	35,7	
Length of stay							
≤ 12 days	21	21	-	-	0	0	<0,001
> 12 days	21	0	-	-	21	100	

log rank

Survival rate and Median Life Length of COPD Patients with Type II Respiratory Failure Based on Total of Comorbid Diseases

Survival rate of COPD patients with type II respiratory failure with 0 comorbidities was 100%. Survival rate of COPD patients with type II respiratory failure with 1 comorbidity was 40%. Survival rate of COPD patients with type II respiratory failure with 2 comorbidities was 53.8%. The log rank test showed that there was no significant difference in survival rates based on total comorbidities (p=0.512). There is no significant relationship between total comorbidities and survival rates of COPD patients with type II respiratory failure. The Proportional Hazard assumption is not met, which means that the comparison of survival rates based on total comorbidities was not constant.

Survival rate and Median Life Length of COPD Patients with Type II Respiratory Failure Based on Smoking habits

Survival rate of COPD patients with type II respiratory failure as active smokers was 41.2% with median survival time 14 days (CI 95%: 3.995-24). Survival rate of COPD patients with type II respiratory failure who were former smokers was 47.1% with median survival time 12 days (CI 95%: 1.506-22.494). Survival rate of COPD patients with type II respiratory failure who are non-smokers was 75%. The log rank test showed that there was no significant difference in survival rates based on smoking habits (p = 0.369). There is no significant

relationship between smoking habits and survival rates of COPD patients with type II respiratory failure. The Proportional Hazard assumption is not met, which means that the comparison of survival rates based on smoking habits was not constant.

Survival rate and Median Life Length of COPD Patients with Type II Respiratory Failure Based on Inhaler Therapy

Survival rate of COPD patients with type II respiratory failure who do not routinely received treatment was 16.7% with median survival time 4 days (CI 95%: 42.962-5.039). Survival rate of COPD patients with type II respiratory failure who routinely received therapy was 75%. The log rank test showed that there was a significant difference in median length of life between patients who did not routinely received therapy and patients who routinely received therapy (p <0.001). There is a significant relationship between routine treatment and survival rates of COPD patients with type II respiratory failure. The Proportional Hazard assumption is met, which means that the ratio of survival rates based on routine treatment is constant.

Survival rate and Median Life Length of COPD Patients with Type II Respiratory Failure Based on history of exacerbation

Survival rate of COPD patients with type II respiratory failure with a history of exacerbations was 57.1% with median survival time 18 days (CI 95%: 7.614-28.386). Survival rate of COPD patients with type II respiratory failure without history of exacerbation was 35.7%. The log rank test showed that there was no significant difference in survival rates based on history of exacerbation (p = 0.4437). There is no significant relationship between history of exacerbation and survival rates of COPD patients with type II respiratory failure. The Proportional Hazard assumption is not met, which means that the comparison of survival rates based on history of exacerbation was not constant.

Survival rate and Median Life Length of COPD Patients with Type II Respiratory Failure Based on length of stay

Survival rate of COPD patients with type II respiratory failure with a length of stay ≤12 days was 0%. Survival rate of COPD patients with type II respiratory failure with a length of stay > 12 days was 100%. The log rank test showed that there was no significant difference in survival rates based on length of stay (p=0.4437). There is a significant relationship between length of stay and survival rates of COPD patients with type II respiratory failure. The Proportional Hazard assumption is met, which means that the comparison of survival rates based on length of stay was constant.

DISCUSSION

COPD is one of the leading causes of death worldwide. In addition, COPD is associated with high morbidity and has socioeconomic impacts.[8] Acute exacerbations of COPD are generally life-threatening with high hospital mortality rates, ranging from 11.5-24%. High in-hospital mortality rates of up to 17% are observed in COPD patients with acute respiratory failure.[9]

Type 2 respiratory failure (hypercapnic) is defined as $PaCO_2$ levels > 50 mmHg, and PaO_2 levels can be within normal limits, or can be low in conditions of respiratory pump failure.[10] Hypercapnic respiratory failure, a state of reduced alveolar ventilation with respiratory acidosis, is often caused by common respiratory diseases such as chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome, obstructive sleep apnea (OSA) and COPD overlap syndrome with OSA.[11]

In this research, there were 33 men (78.6%). There were 22 patients aged <60 years (52.4%). The most common types of comorbidities were pneumonia and DM type 2 as much as 6 people (14.3%). The number of patients with 2 comorbid diseases was 26 people (61.9%). A total of 17 patients each were active smokers and former smokers. A total of 18 patients (42.9%) did not received routine treatment. Most subjects experienced exacerbations > 1 x a year. The mean length of stay for patients was 9.6 days with shortest 2 days and longest

25 days. A total of 21 patients died. The majority of patients with a total of 14 patients (33.3%) with length of stay 1-5 days, followed by 12 patients (28.6%) with a length of stay 6-10 days, 9 patients (21.4%) with a length of stay 11 -15 days, 5 patients (11.9%) with a length of stay 16-20 days and 2 patients (4.8%) with a length of stay >20 days.

In Chen et al.'s study, the duration of patient stay in ICU and hospital was 8.5 ± 6.8 days (median: 8 days, IQR: 3-12) and 24.6 ± 25.4 days (median, 18 days, IQR: 10-33) respectively. A total of 56 patients died during hospitalization and in hospital mortality rate was 32.4% [12]. Hong et al showed that mean duration of mechanical ventilation, length of stay in ICU, and length of stay in hospital were 9.2 ± 10.4, 11.2 ± 16.5, and 24.8 ± 16.8 days respectively and the 30-day hospital mortality rate was 20.1% (77/384).[9]

George et al over a 12 month period found 256 patients initiated on mechanical ventilation for incident hypercapnic acidosis (based on arterial blood gas sampling), of which 212 patients had a diagnosis of COPD (83%) of which 89% of COPD patients were treated in a ward, with 11% of patients then requires critical care. Only 3% of patients received invasive mechanical ventilation. Mortality was higher in 9% with respiratory and metabolic acidosis vs 91% with respiratory acidosis (45% vs 18%).[13]

The proportion of patients who died and lived in this research was found to be equal, namely 21 people each (50%). Morbidity rates appear particularly high after discharge among COPD patients treated as inpatients with non-invasive ventilation (NIV) which is 80% of patients readmitted and 49% of patients dying within 12 months. Another study found that 40% of patients were readmitted and 11% of patients died [11]. Hirtum et al showed that 5, 10 and 15 year survival of COPD patients after clinical exacerbation was 43.7%, 19.9% and 7.3%, respectively. Long-term mortality after clinical exacerbation of COPD appears to increase to 82% compared to the general population [8]. Reported in-hospital mortality associated with COPD exacerbations ranges from 11% to 32% [14].

The mortality rates of all COPD patients within 1 and 5 years after diagnosis were 9.5% and 25.4%, respectively. The 5-year death rate grouped by age was 3.1%, 7.8%, 14.1%, 30.4%, and 55.1%. in the age group 40 - 49, 50 - 59, 60 - 69 , 70 - 79, and 80 - 89 respectively [15].

The research results show that there is a difference in survival rate between subjects who routinely and non-routinely received treatment with a ratio of 75% versus 16.7%. Based on length of stay, there is a significant difference in survival rate between length of stay >12 days and <12 days, namely 100% versus 0%.

The aim of therapy in COPD patients is to improve quality of life where the priority management is to prevent disease progression, reduce level of exacerbations and focus on managing comorbidities. Adherence to inhalation therapy has a significant impact on treatment goals [16].

Survival is improved with long-term oxygen therapy (LTOT). LTOT has also been shown to improve survival by approximately 3.5 years in patients with hypoxemic chronic obstructive pulmonary disease (COPD), but survival is worse if there is more severe airflow limitation when oxygen therapy is initiated. In a 2-year study of 140 patients with severe hypercapnic COPD, two-year survival rate was higher in patients with mechanical ventilation compared with patients without mechanical ventilation (1 year, 87.7% versus 56.7%; 2 years, 71 .8% versus 42%, $p = 0.001$) [17].

Humberger et al showed that effect of inhalation therapy adherence was seen in 33.6% patients and was higher among patients with more severe COPD. In previous studies, better therapy adherence in COPD patients was associated with reduced risk of exacerbations and health care utilization [16].

Moreira et al showed that mortality was associated with non-adherence, presence of symptoms and previous hospitalization. After adjustment, patients who were not adherence to treatment were almost twice as likely to die compared with patients who were adherence to treatment (Hazard Ratio (HR) 1.86; CI 1.16–2.98, $p = 0.01$). Nonadherence to treatment is associated with higher mortality among patients with moderate to severe COPD. Strategies for monitoring and optimizing adherence should be improved to reduce COPD-related mortality [18].

CONCLUSION

The survival rate in COPD patients who regularly use inhaler therapy is significantly higher than in patients who do not routinely use inhaler therapy.

DECLARATIONS

CONSENT FOR PUBLICATION
The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS
The authors declare that there is no conflict of interest in this report.

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