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Survival analysis in heart failure patient using the Kaplan Meier methods

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Abstract

Heart failure is one of the biggest health problems worldwide, causing increased mortality, morbidity, and financial problems, especially in elderly patients. Survival analysis is a collection of statistical methods used to answer questions relating to whether and when an event occurs. The Kaplan-Meier method is a nonparametric estimation method in survival functions that is commonly used to describe the survival of a population or compare the survival of two or more populations. This study aims to estimate the survival of a patient with heart failure. The data for this study was obtained from the BMC Chicco and Jurman Medical Informatics and Decision Making website in 2020. The data consisted of medical records of 299 patients diagnosed with heart failure during the follow-up period of the study. Based on the results of the analysis, it was found that the results of the calculation of the product limit estimator or Kaplan-Meier and the survival plot of Heart Failure patients who survived for 4 days had a greater chance of survival than Heart Failure patients who survived for 285 days. In addition, based on the analysis, heart failure patients with male gender have a higher estimated average survival than heart failure patients with female gender. This cannot escape the influence of various factors. Therefore, this study is expected to help develop more effective treatment strategies and provide more accurate predictions regarding the prognosis of Heart Failure patients.

Keywords: Censored Data; Heart Failure Patients; Kaplan-Meier Method; Length of Life Data; Survival Analysis; Survival Function

1. Introduction

Heart failure has become a major urgency in the world of health internationally [4]. The potential for heart failure in Southeast Asia is up to three times when compared to European and American countries, namely percent rates of 4.5-6.7% and 0.5-2% [7]. Basic Health Research (Riskesdas) data in 2023 shows the potential for heart failure disease of 0.85% or with an estimated 877,531 people. Heart failure is a disease with significant mortality and morbidity at all levels of the country. The disease is still a significant health issue at the global level with an estimated potential of around 38 million patients internationally especially in Asia. The potential of heart failure in Asia is between 1-3%. The potential for heart failure in Indonesia is 5% [16]. In Asia, patients with heart failure typically spend between 5-12.5 days in hospital and the re-hospitalization rate within 30 days of treatment is between 3% to 15%. In Indonesia, the 30-day readmission rate is 7% and the average hospitalization cost for heart failure treatment is approximately USD 813 [16]. Heart failure patients have limited activities in their daily lives, which makes them vulnerable to depression and anxiety in controlling emotions. They also consider treatment administration, disease diagnosis, and recovery duration, which can reduce the quality of life of heart failure patients [3]. The influence of the quality of life of heart failure patients is determined by physical symptoms such as shortness of breath, fatigue, oedema, loss of appetite, and other psychological symptoms [1]. In addition, a person's level of knowledge correlates with the quality of life of patients with heart failure [10].According to the World Health Organization (WHO) in 2016, states that 17.5 million people died from cardiovascular disease. The prevalence of Heart Failure disease continues to increase in both developed and developing countries. Heart failure that occurs in developed countries, one of which is the United States with a prevalence of

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5,700,000 cases. Heart failure cases in Australia amounted to 2.0%. A developing country that experiences Heart Failure is Indonesia. According to RISKADES 2018, the prevalence of Heart Failure in Indonesia is 1.5%. The prevalence of CHD in West Kalimantan is estimated at 1.3%.

A statistical method that focuses on variables that influence the time between initial and final events is survival analysis. This analysis uses survival time as a variable, i.e. death is considered a failure. One method that is often used in nonparametric survival analysis is Kaplan Meier analysis followed by the Log Rank test. Kaplan Meier analysis is used to estimate the survival function. Then from the estimated survival function, a Kaplan Meier survival curve can be formed. While the Log Rank test is used to test whether there is a difference or not in the Kaplan Meier survival curve on variables that have two or more categories. (Nasution et al.) conducted previous research entitled Kaplan Meier Survival Curve Analysis Using the Log Rank Test (Case Study: Coronary Heart Disease Patients at Undata Palu Hospital). The results of the study explained that descriptively based on the Kaplan Meier survival curve and the Log Rank test on stage variables, complications and anemia status showed that there were no differences in survival curves, which means that each category in the variable is not different and will not affect the probability of survival of CHD patients [3].

This research is in line with the 3rd sustainability development goal which aims to ensure healthy living and promote well-being for all people. This study aims to provide an analysis of several factors that cause length of hospitalization that affect the survival of patients with heart failure. Data on patients who survive during the observation period is considered an “event”, while data on patients who die during the observation is considered censored data. With this background, this study focuses on analyzing the survival of heart failure patients using the Kaplan-Meier method. This study has another purpose to provide an update on the research that has been done before and increase our understanding of several factors that affect the duration of hospitalization on the survival of heart failure patients. The results of this study are expected to help improve the quality of care provided to patients suffering from heart failure.

2. Literature Review

2.1. Survival Analysis

Survival analysis is a collection of statistical methods used to analyze data where the outcome variable under study is the time until an event occurs. Three things that must be considered in determining the time of failure namely the starting point in the study is unambiguous, the measurement scale as part of the passage of time is consistent, and the clarity of the definition of the ending event of interest in the study.

2.2. Censored Data

Censoring is one of the steps that must be taken to overcome the incompleteness of an observation data. Censoring occurs when we have information about an individual's survival time, but the exact survival time is unknown, so the data is censored data. There are three causes of censored data, namely:

- Individuals do not experience the event under study until the end of observation
- Individuals who are missing from observation during the study
- Individuals withdrew from the study due to death (if death was not the event under study) or any other reason

Censored data is a term for incomplete data. Censoring is a way to overcome the incompleteness of observation data in a study. It is said to be censored data if the survival time observation does not reach failure time. In a study called censored data, namely if the length of life of a person observed only occurs at a predetermined time (observation interval. There are 3 types of censoring commonly used in life test analysis, namely:

- Type I censorship, where the study of all n individuals entering at the same time must be terminated after reaching a predetermined time T. If there are no individuals who suddenly disappear, then the censored observation survival time is the same as the length of observation time
- Type II censoring, censoring where the rth sample is the smallest observation in a random sample of size $1 \leq r \leq n$.
- Type III censorship, when individuals or observation units enter the experiment at different times during a certain time period.

2.3. Kaplan-Meier Method

The Kaplan-Meier method is used most often to describe or compare the survival of one or more populations. This is because it is one of the best statistical methods for measuring the probability of survival. In its estimation calculation,

this method involves the probability of an event occurring until a certain time, which is then multiplied by the previous probability to produce the final estimate. After that, the Kaplan Meier curve is used to calculate the event, censored data, and survival probability (Ethics).As follows, the estimation of the survival function of the Kaplan-Meier method is given.

$$\begin{aligned}\hat{S}(t) &= \hat{p}_1 \times \hat{p}_2 \times \dots \times \hat{p}_k \\ &= \prod_{j=1}^{k} \hat{p}_j \\ &= \prod_{j=1}^{k} \left(\frac{n_j - d_j}{n_j}\right)\end{aligned} \quad \dots. (1)$$

For $t_k \leq t \leq t_{k+1}, k = 1,2,3, \dots, m$ and $\hat{S}(t) = 1$ for $t \leq t_1$, where, $\hat{p}_j$ denotes the probability of survival at time j, n_j denotes the number of individuals at risk of failure, and d_j denotes the number of individuals who fail at time j. In 1972, Cox defined the hazard function. According to him, the hazard function is the probability of an object experiencing failure, for example death and others at time *t*, provided that the object has survived at time *t*.

$$h(t) = \lim_{\delta t \to 0} \frac{P(t \leq T \leq t + \delta t)}{\delta t} \dots\dots\dots\dots\dots\dots (2)$$

Normality test is a statistical test conducted to determine how the data is distributed. There are various techniques for testing the normality of data distribution developed by experts. One of the frequently used normality testing techniques is Kolmogorov-Smirnov. The advantage of this test is that it is simple. The basic concept of the Kolmogorov Smirnov normality test is to compare the data distribution with the standard normal distribution. If the significance value obtained is more than α = 5% or 0.05, it means that there is no significant difference between the data we test normally and the standard normal or in other words the data is normally distributed.

3. Methodology

3.1. Research Method

The research in this study is a quantitative data on survival analysis of patients with heart failure using the Kaplan-Meier method. The study data were obtained through the BMC Medical Informatics website with the study population being the medical records of 299 patients with heart failure collected at the Faisalabad Institute of Cardiology during April to December 2015. The data is a set of survival data for heart failure patients. This research analysis uses the Kaplan Meier method. The method is a method that describes or compares the survival of one or more populations. This method is most often used because it is one of the best statistical methods in measuring the probability of survival. In the estimation calculation, this method involves the probability of the event occurring until a certain time, then successively multiplied by the previous probability to produce the final estimate. Then the next step Kaplan Meier curve is used to determine the event, censored data, and survival probability. Some of the variables used in this study include age, gender, active smokers, anemia, diabetes, high blood pressure, length of treatment, and patient status.

4. Results

4.1. Normality Assumption Test

Before conducting the Kaplan-Meier test, it is necessary to conduct a normality assumption test to determine whether the data is normally distributed or not.

Table 1 Normality Assumption Test

One-Sample Kolmogorov-Smirnov Test		
		Lama_Perawatan
N		**299**
Normal Parameters[a,b]	Mean	130,26
	Std. Deviation	77.614
Most Extreme Differences	Absolute	0.105

	Positive	0.090
	Negative	-0.105
Test Statistic		0.105
Asymp. Sig. (2-tailed)		0.000[c]

Based on Table 1, it can be seen that the significance value is 0.000 where the value is < α (5%). So it can be concluded that the data is not normally distributed and can be tested with nonparametric analysis methods.

4.2. Data Analysis

After testing the normality assumption, it was found that the data was not normally distributed. So that data testing can be done using the nonparametric survival analysis method with the Kaplan-Meier method. The following table shows the results of the analysis of survival of Heart Failure patients with the Kaplan-Meier method.

Table 2 Survival Analysis of Heart Failure Patient

i	t_i	R_i	δ_i	C_i	q_i	p_i	$S(t)$	$h(t)$
1	4	299	1	0	0.003	0.996	0.996	0.003
2	6	298	1	0	0.003	0.996	0.993	0.006
3	7	297	2	0	0.006	0.993	0.986	0.006
4	8	295	2	0	0.006	0.993	0.979	0.020
5 ⋮	10 ⋮	293 ⋮	6 ⋮	0 ⋮	0,020 ⋮	0,979 ⋮	0,959 ⋮	0,006 ⋮
144	270	6	0	2	0,000	1,000	0,571	0,000
145	271	4	0	1	0,000	1,000	0.571	0,000
146	278	3	0	1	0,000	1,000	0.571	0,000
147	280	2	0	1	0,000	1,000	0.571	0,000
148	285	1	0	1	0,000	1,000	0.571	1,000

Table Description: i : observation *i.;* t_i: survival time of Heart Failure patients; R_i: number of individuals alive at observation *I;* δ_i: number of individuals that died in observation *I;* C_i : number of individuals censored at observation *I;* q_i : estimated probability of individual death at observation *I;* p_i : estimate of the probability of individual resilience at the *i*th observation; $S(t)$: estimate of the survival function for each individual included in the observation; $h(t)$: estimate of the survival failure rate of each individual included in the observation.

In Table 2, it can be seen that the estimated chance of survival of Heart Failure patients who survive for 4 days is 0.996. While the estimated chance of survival of Heart Failure patients who survive for 285 days is 1.000. The estimated survival failure rate of Heart Failure patients who survive for 4 days is 0.003, while Heart Failure patients who survive for 285 days have an estimated survival failure rate of 1.000.

Figure 1 shows an overview of the characteristics of the survival plot of Heart Failure patients. Based on the figure, it can be seen that the plot moves downward and the estimated chance of survival of Heart Failure patients ranges from 0.571 to 1.000. Where 0.571 is the estimated chance of survival of Heart Failure patients who survive for 285 days and 1,000 is the estimated chance of survival of lung cancer patients who survive for 4 days..

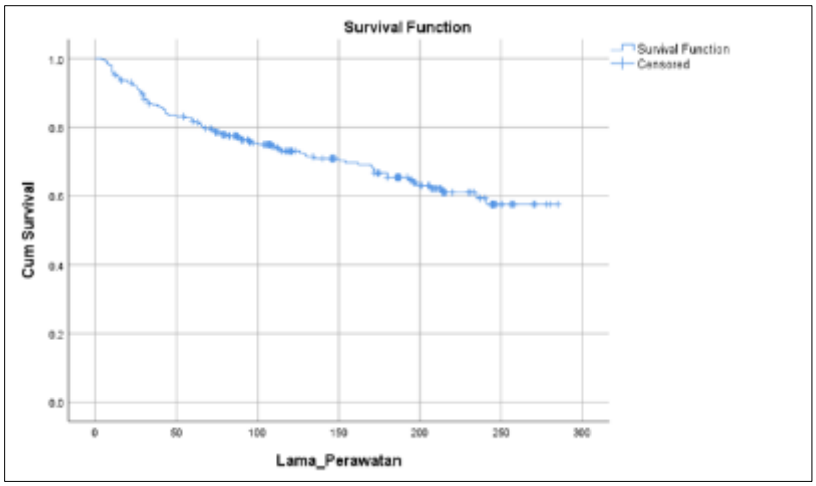

Figure 1 Heart Failure Patient Survival Plot

Table 3 Comparison of Average Survival of Heart Failure Patients by Gender

Means for Survival Time				
Sex	**Mean**		**95% Confidence Interval**	
	Estimate	**Std. Error**	**Lower Bound**	**Upper Bound**
Female	202,024	10,619	181,210	222,838
Male	205,045	8,262	188,852	221,238

Furthermore, in Table 3 when viewed based on gender, it can be seen that the estimated average survival of Heart Failure patients with male gender is around 205 days. While the estimated average survival of Heart Failure patients with female gender is around 202 days. So it can be concluded that the average survival of Heart Failure patients with male gender is higher than Heart Failure patients with female gender.

5. Discussion

Based on the results of the analysis that has been carried out, it can be seen that the data does not meet the normal distribution assumption so that it is continued with the analysis with the Kaplan-Meier method. Based on the analysis with the Kaplan-Meier method, it is known that the longer a patient undergoes treatment, the smaller the chance of survival. This is known from the calculations in Table 2, where after being sorted, out of 299 patients, there is 1 patient who has the shortest length of treatment, namely for 4 days. The patient has a survival chance of 0.996, where the chance can be interpreted that the treatment or care undertaken is successful. Likewise, until the patient who underwent treatment for 285 days had a survival chance of 0.571. Where the chances of successful treatment or care for these patients are quite small. This is also in line with the calculation of the chances of failure in Table 2. However, the success of the treatment or care undergone does not only depend on the length of treatment the patient undergoes. But there may also be other factors that influence it, both external factors and internal factors.

6. Conclusion

Based on the results and discussion obtained previously, it can be concluded that the results of the calculation of the product limit estimator or Kaplan-Meier and the survival plot of Heart Failure patients who survive for 4 days have a greater chance of survival than Heart Failure patients who survive for 285 days. This is also evident through the hazard function value obtained. Namely for Heart Failure patients who survive for 4 days have an estimated survival failure rate of 0.003 while Heart Failure patients who survive for 285 days have an estimated survival failure rate of 1.000. In addition, if the estimated average survival is seen based on gender, then Heart Failure patients with male gender have a higher estimated average survival of about 205 days than Heart Failure patients with female gender who have an estimated average survival of only about 202 days.

Suggestions that we can provide for further research are to use other methods and relevant variables that are thought to affect the estimation of survival of Heart Failure patients in order to help develop more effective treatment strategies and provide more accurate predictions of patient prognosis.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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