

Estimation of Life Function in Coronary Heart Disease Patients to Determine the Best Treatment Method

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Abstract: Based on the observations by the Global Burden of Disease and also by the Institute for Health Metrics and Evaluation (IHME), in 2014-2019, heart disease is the highest cause of death in Indonesia. The BPJS for 2021 states that the biggest expenditure is on heart disease. Due to this conflict, this study was carried out. This study contained survival analysis utilizing exponential distribution for censored data type 1 in patients with coronary heart disease to model a single sample and determine the survival of sufferers of the disease. The data used are secondary data about the patient's lifetime which is included in parametric methods, patient status (alive/dead), and the treatment applied, namely ring and bypass. In analysis uses, the hazard function, the reliability function, and mean time to failure. Then, the result shows that a treatment bypass is better to be applied than a treatment ring since the risk is lower.

Keywords— Survival Analysis, Coronary Heart Disease, Type 1 Censored Data, Exponential Distribution

INTRODUCTION

Coronary Heart Disease (CHD) is a global health problem that is the focus of the health Sustainable Development Goals (SDGs) because it is the main cause of death worldwide, with more than 17 million deaths each year. The Ministry of Health of the Republic of Indonesia (2018) explains Coronary Heart Disease (CHD) is a disorder of heart function due to a lack of blood in the heart muscle due to blockage or narrowing of the coronary arteries. This can happen because the lining of the blood vessel walls (Atherosclerosis) is damaged. Patients with CHD often experience impaired heart function, difficulty in carrying out daily activities, and a high risk of having a heart attack or sudden death. Causes of coronary heart disease include smoking, having an unhealthy diet, or suffering from certain diseases, such as high blood pressure and high cholesterol.

Based on data from the World Health Organization (WHO) in 2021, the prevalence of Coronary Heart Disease (CHD) in Indonesia is around 12.1%. The prevalence of other countries in the world is as follows: Kiribati (18.4%), Afghanistan (16.7%), Indonesia (12.1%), Bangladesh (11.1%), and India (8.7%). So, Indonesia is in 3rd place with the highest CHD prevalence rate in the world.

Based on the Global Burden of Disease and the Institute for Health Metrics and Evaluation (IHME) 2014-2019, CHD is the highest cause of death in Indonesia. Heart disease is the biggest cost burden. Based on BPJS Health data in 2021, the largest health financing is for CHD patients amounting to IDR 7.7 trillion. CHD does not only have an impact on individual health but also has a major economic impact on society and the country.

Therefore, CHD is one of the important topics in the SDGs set by the United Nations (UN) as a global agenda to

achieve sustainable development by 2030. Efforts to prevent and treat CHD are important in achieving the health SDGs goals, especially in achieving targets to reduce mortality from non-communicable diseases, including CHD. Bypass treatment and ring treatment are two types of medical treatment that are effective in treating CHD and improving the patient's quality of life. In this context, discussions about bypass treatment and ring treatment for CHD can provide an overview of global efforts to achieve the health SDGs targets and also provide useful information for the public, health workers, and policymakers in improving the quality of life of patients with CHD.

REVIEW OF LITERATURE

Previous research conducted by Lukitasari et al (2015) regarding the lifetime of patients with coronary heart disease has been carried out. However, it is different from previous studies which used the Weibull distribution and focused on how many patients were still alive while undergoing the treatment given but did not provide conclusions regarding which treatment was best for CHD patients.

Based on the results of these previous studies, future research will be able to see more about the resilience of CHD patients and show the best type of treatment that can be given to CHD patients using an exponential distribution approach. Thus, this research can benefit related parties such as hospitals for further trials to be carried out to ensure the effectiveness of the recommended treatment.

The survival time distribution can be expressed by three functions, namely the probability function, the survival function, and the hazard function. Survival time (T) is a variable that represents the survival time of each object of

observation in the population which is a non-negative continuous random variable or $t > 0$ (Lawless, 1982).

The exponential distribution is a special case of the gamma distribution with $\alpha=1$. continuous random variable T is said to have an exponential distribution with parameters if it has the following probability density function. According to Lawless (1982), the probability density function of the exponential distribution of type I censored parameters is:

$$f(t; \theta) = \begin{cases} \frac{1}{\theta} \exp\left(-\frac{t}{\theta}\right) & \text{for } t \geq 0 \\ 0 & \text{for } t < 0 \end{cases}, \theta > 0$$

As for the cumulative distribution function, survival function, hazard function, and Mean Time to Failure (MTTF) is given by the following equation:

$$F(t) = \int_0^t \frac{1}{\theta} \exp\left(-\frac{x}{\theta}\right) dx = 1 - \exp\left(-\frac{t}{\theta}\right)$$

$$S(t) = 1 - F(t) = \exp\left(-\frac{t}{\theta}\right)$$

$$h(t) = \frac{f(t)}{S(t)} = \frac{1}{\theta}$$

$$E(t) = \hat{\theta}$$

Data with each observation unit $1, 2, \dots, n$ are each given a period or observation time limit denoted is called L_1, L_2, \dots, L_n called observed only if $(t_i \leq L_i)$ (Lee & Wang, 2003). Type 1 censored data has a value of $t_i = \text{Min}(t_i, L_i)$. The censorship indicator (δ_i) is defined as follows.

$$\delta_i = \begin{cases} 1, & \text{if } t_i \leq L_i \text{ called uncensored} \\ 0, & \text{if } t_i > L_i \text{ called censored} \end{cases}$$

Where θ is the average parameter. According to Balakrishnan (1990) in Dwiramadhan (2015), the equation for finding the estimator value for parameter θ in type I censored survival data is :

$$\hat{\theta} = \frac{\sum_{i=1}^n t_i}{\sum_{i=1}^n \delta_i}$$

The probability that an individual will survive for a certain time is known as the survival function. Assuming that the data has a one parameter exponential distribution, the survival function for $S(t)$ according to Lawless (1982) is :

$$\hat{S}(t_i) = \exp\left(-t_i \left(\frac{\sum_{i=1}^n \delta_i}{\sum_{i=1}^n t_i}\right)\right)$$

Then the hazard function is formulated as follows :

$$\hat{h}(t_i) = \frac{\sum_{i=1}^n \delta_i}{\sum_{i=1}^n t_i}$$

The log rank test was conducted to find out whether there were differences in survive opportunities between several treatments.

The hypothesis test is :

$H_0: S_1(t) = S_2(t)$ or there is no difference between two treatments

$H_1: S_1(t) \neq S_2(t)$ or there is a difference between two treatments

For example, t is the number of research units that experience events during t and n_{1t} and n_{2t} are the number of research units that are at risk of experiencing events on at for each group. The hope value of the event when t for each group is:

$$e_{it} = \frac{n_{1t}}{n_{1t} + n_{2t}} \times d_t \quad ; \quad i = 1, 2$$

Test statistics:

$$W = \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2}$$

Which :

O_1 and O_2 are the number of unsorted observations for each group

E_1 and E_2 are Value of Expectations for Event in each group

H_0 is rejected if $W > X^2_{(\alpha, df=1)}$ or $p\text{value} < \alpha(5\%)$ if using calculations with software.

MATERIALS AND METHODS

The data used is secondary data from research previously conducted by Lukitasari et al (2015) regarding the lifetime of patients with coronary heart disease. However, it is different from previous studies which focused on how many patients were still alive while undergoing treatment. This research only focuses on the variable type of treatment, survival time, and whether the status includes censored data or not. The analysis technique used in this research is survival analysis using an exponential distribution with a type I censored parametric method. Survival data are generally described and modeled in terms of two related probabilities namely survival and hazard.

Because based on previous research conducted and validated by the Indonesian Doctors Association (IDI), where the survival of patients with coronary heart disease is estimated to last up to 10 years or about 12 months. Therefore, this study was limited to a treatment time of around 120 months. If there are patients who can survive more than 120 months, then it is assumed that the data is censored. The samples in this study were coronary heart disease (CHD) patients who underwent treatment in 2015 with the ring treatment and bypass treatment methods with a total sample of 60 patients.

Table 1. Data Patients Coronary Heart Diseases

Number	Long life (Month)	Treatment Method	Status
1	6	Ring	1
2	7	Ring	1
3	7	Ring	1
4	8	Ring	1
5	11	Ring	1
6	17	Ring	1
7	20	Ring	1
8	21	Ring	1
9	21	Ring	1
10	25	Ring	1
11	26	Ring	1
12	26	Ring	1
13	38	Ring	1
14	51	Ring	1
15	52	Ring	1
16	56	Ring	1
17	57	Ring	1
18	61	Ring	1
19	62	Ring	1
20	62	Ring	1
21	66	Ring	1
22	71	Ring	1
23	71	Ring	1
24	75	Ring	1
25	83	Ring	1
26	106	Ring	1
27	6	Bypass	1
28	6	Bypass	1
29	7	Bypass	1
30	12	Bypass	1
31	12	Bypass	1
32	16	Bypass	1
33	17	Bypass	1
34	17	Bypass	1
35	21	Bypass	1
36	26	Bypass	1
37	32	Bypass	1
38	33	Bypass	1
39	42	Bypass	1
40	42	Bypass	1
41	56	Bypass	1
42	56	Bypass	1
43	60	Bypass	1
44	65	Bypass	1
45	78	Bypass	1
46	87	Bypass	1
47	87	Bypass	1
48	93	Bypass	1
49	102	Bypass	1
50	116	Bypass	1
51	116	Bypass	1

52	123	Ring	0
53	128	Ring	0
54	156	Ring	0
55	183	Ring	0
56	146	Bypass	0
57	161	Bypass	0
58	173	Bypass	0
59	178	Bypass	0
60	182	Bypass	0

Otained status 1 for patients who died before the specified time limit, namely before carrying out treatment for up to 12 months. Furthermore, status 0 is given to patients with coronary heart disease who are still alive and can still carry out treatment for more than 120 months.

DISCUSSION

Parameter Estimations

The method used is a one-parameter exponential distribution. Therefore, there is one parameter that will be estimated for the survival function of coronary heart disease patients, namely θ , which is the average parameter of the length of life of coronary heart disease patients since the last day of receiving treatment.

Parameter Estimations for Treatment Ring

With $n = 30$, the value of the parameter θ for the treatment ring is obtained:

$$\hat{\theta} = \frac{\sum_{i=1}^n t_i}{\sum_{i=1}^n \delta_i} = \frac{\sum_{i=1}^{30} t_i}{\sum_{i=1}^{30} \delta_i} = \frac{6 + 7 + \dots + 156 + 183}{1 + 1 + \dots + 0 + 0} = 65,23$$

Then for MTTF the result is the same as $\hat{\theta}$ which is 65,23 months.

From the results of these calculations, it was obtained that the average longevity of Coronary Heart Disease sufferers since the last day of receiving treatment for the ring treatment method was 65,23 months.

Parameter Estimations for Treatment Bypass

With $n = 30$, the value of the parameter θ for the treatment bypass is obtained:

$$\hat{\theta} = \frac{\sum_{i=1}^n t_i}{\sum_{i=1}^n \delta_i} = \frac{\sum_{i=1}^{30} t_i}{\sum_{i=1}^{30} \delta_i} = \frac{6 + 6 + \dots + 178 + 182}{1 + 1 + \dots + 0 + 0} = 81,8$$

Then for MTTF the result is the same as $\hat{\theta}$ which is 81,8 months.

From the results of these calculations, it was obtained that the average longevity of Coronary Heart Disease sufferers since the last day of receiving treatment for the bypass treatment method was 81,8 months.

Survival function for ring treatment

By using the treatment ring method, the value of $\hat{\theta} = 65.23$ by using equation obtained the estimated survival function of coronary heart disease patients for $S(10) = 0.857869$, $S(20) = 0.735939$, $S(40) = 0.541607$, $S(80) = 0.293338$, $S(160) = 0.0860472$. The interpretation of the value of $S(10) = 0.857869$ is that the survival chance of a patient with Coronary Heart Disease for 10 month is 0.857869. From the value of survival chances, it can be said that the survival chances of patients with Coronary Heart Disease who undergo ring treatment are decreasing for an increasingly long time.

Survival function for bypass treatment

By using the treatment bypass method, the value of $\hat{\theta} = 81.8$ by using equation (7) obtained the estimated survival function of coronary heart disease patients for $S(10) = 0.884928$, $S(20) = 0.783097$, $S(40) = 0.613241$, $S(80) = 0.376064$, $S(160) = 0.141424$. The interpretation of the value of $S(10) = 0.884928$ is that the survival chance of a patient with Coronary Heart Disease for 10 month is 0.884928. From the value of survival chances, it can be said that the survival chances of patients with Coronary Heart Disease who undergo bypass treatment are decreasing for an increasingly long time.

Comparison of estimated survival function values of patients with coronary heart disease the two treatment methods can be seen in the following table:

Long life (Month)	Probability of Survival	
	Ring	Bypass
10	0.857869	0.884928
20	0.735939	0.783097
40	0,541607	0,613241
80	0.293338	0.376064
160	0.0860472	0.141424

In table 2. It can be seen that the chances of survival for people with Coronary Heart Disease are decreasing for a greater time (t). The table also shows that the chance of survival for coronary heart disease patients who undergo bypass treatment is greater than that of ring treatment.

Comparison of the survival of the two methods can be seen in the following graph:

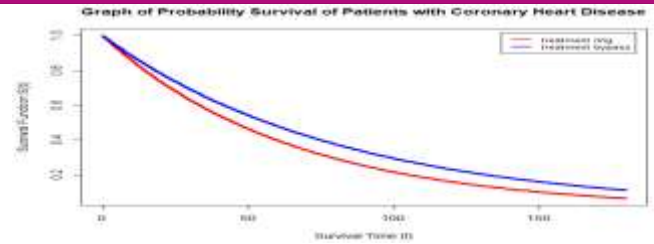


Figure 1. Graphs of Probability Survival of Patients With Coronary Heart Disease

Hazard function for ring treatment

By using the treatment ring method, the value of $\hat{\theta} = 65,23$ by using equation obtained the estimated hazard function of coronary heart disease patients is obtained :

$$\hat{h}(t) = \frac{\sum_{i=1}^n \delta_i}{\sum_{i=1}^n t_i} = \frac{26}{1.696} = 0,01533$$

Hazard function for bypass treatment

By using the treatment ring method, the value of $\hat{\theta} = 81,8$ by using equation (9) obtained the estimated hazard function of coronary heart disease patients is obtained :

$$\hat{h}(t) = \frac{\sum_{i=1}^n \delta_i}{\sum_{i=1}^n t_i} = \frac{25}{2.045} = 0,01222$$

From the results of the calculation of the hazard function, it was found that the bypass treatment produced a smaller value of 0,01222. This means that the death rate in patients with coronary heart disease with bypass treatment is lower than that with ring treatment.

Comparison of the hazard of the two methods can be seen in the following graph:

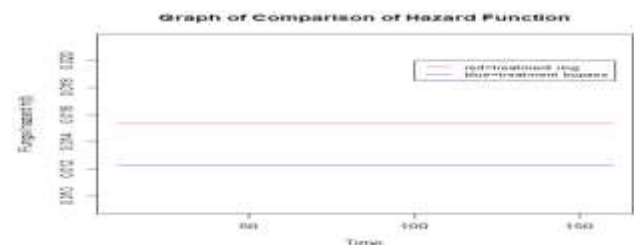


Figure 2. Graphs of Hazard Function of Patients With Coronary Heart Disease

After getting the results of the estimated survival and hazard functions, the next is to conduct a log rank test to find out whether the results obtained are valid or not from two treatment that are tried using RSTUDIO software and obtained as in the following picture:

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survdif(formula = Surv(time, status) ~ treatment)
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	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
treatment=1	30	26	23.7	0.227	0.443
treatment=2	30	25	27.3	0.197	0.443

Chisq= 0.4 on 1 degrees of freedom, p= 0.5

Figure 3. Log rank test results

It is known that the results of the log rank test are 0.5 pvalue which means failed to reject H_0 there is no difference between two treatments.

CONCLUSION

Based on the results of the survival analysis that has been carried out, several conclusions are obtained, namely as follows:

1. Based on the results and discussion, it can be concluded that the bypass treatment more effective than ring treatment. This is seen from the chances of survival for Coronary Heart Disease patients who undergo bypass treatment is greater than patients who undergo treatment ring for all time t. But from the results of the log rank test it turns out there is no significant significant time of life endurance from the two treatment given.
2. Suggestions for future researchers to develop more survival analysis research complex (by adding life tests based on sex, or causative factors) so that other things can be explored from the same case study data or a different case study.

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