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Survival Analysis Using Kaplan-Meier and Cox Regression in Hypertension Patients at Kefamenanu Regional Hospital

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A B S T R A C T

Hypertension is a chronic disease with a steadily increasing global prevalence and is one of the leading causes of serious complications. Indonesia is among the countries with a high prevalence of hypertension, necessitating an understanding of the factors influencing patient treatment duration to enhance the effectiveness of healthcare services. This study aims to analyze differences in the survival rates of hypertensive patients at Kefamenanu Hospital based on gender. The Kaplan-Meier method was used to estimate patient survival rates, while Cox Proportional Hazards regression was used to evaluate the influence of gender on survival time. The Kaplan-Meier analysis results showed that female patients had a higher probability of survival than male patients during hospitalization. However, the Cox Proportional Hazards regression analysis indicated that this difference was not statistically significant. These findings suggest that while there are differences in survival patterns, gender is not the primary determinant of the duration of care for hypertensive patients. The results of this study are expected to provide input for hospitals in designing more effective care strategies that focus on other factors that may influence patient survival time.

Keywords: Hypertension, Cox Proportional Hazard, Kaplan-Meier, Survival Time

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1. Introduction

Health is an important aspect of human life. Without a healthy body condition, individuals may find it difficult to carry out daily activities optimally [1]. One of the most common chronic diseases that often goes unnoticed is hypertension. This condition is a concern because it can increase the risk of various serious complications such as stroke, heart failure, and kidney disease [2]. In Indonesia, hypertension is among the top five non-communicable diseases most commonly suffered by the population and requires serious attention in its treatment. Hypertension is a medical condition characterized by an increase in both systolic and diastolic blood pressure above normal, namely > 140/90 mmHg [3].

Hypertension is categorized into two types: essential hypertension, which is the most common, and secondary hypertension, which is caused by kidney disease or other factors [4]. The World Health Organization (WHO) defines hypertension, also referred to as high or elevated blood pressure, as a condition where the blood pressure rises persistently [5]. The prevalence of increasing numbers of hypertension sufferers worldwide, according to the World Health Organization (WHO) in 2015, from around 1.13 billion people estimated to be 1.5 billion people, and in 2025, an estimated 9.4 million people will die from hypertension and its complications [6].

According to the findings of the basic health research (RISKESDAS), the incidence of hypertension in the Indonesian population under 18 years of age increased from 25.8% in 2013 to 34.1% in 2018 [7]. Hypertension (HTN) is considered one of the most significant public health challenges worldwide and is a risk factor for cardiovascular disease, stroke and kidney failure [8]. Hypertension occurs because the heart works harder to circulate blood throughout the body through blood vessels. This can disrupt blood flow, damage blood vessels, even diseases that cause body tissues or organs to deteriorate over time, until death [9].

In addition to being caused by the heart working harder, there are several factors that can also cause hypertension. Hypertension risk factors are classified into two categories: those that are immutable and those that are modifiable [3]. Unchangeable factors include ethnicity, gender, genetics, and age. In contrast, modifiable factors include adherence to medication, salt consumption, smoking habits, obesity, lack of physical activity, unhealthy lifestyle and stress, and others [10].

One commonly used method to analyze survival time is Survival Analysis. It is a statistical approach utilized to study data where the primary focus is on the time elapsed until a particular event occurs. Survival analysis usually refers to a survival time variable, which indicates the time that a person has survived during a period until failure. Survival analysis is divided into two, namely descriptive and inferential survival analysis [1] The Kaplan-Meier method is a non-parametric approach for estimating the survival function, commonly applied to illustrate the survival of a population or to compare the survival rates between two populations [11]. While the Cox regression method or Cox Proportional Hazards Regression is a regression method in survival analysis used to determine the relationship between dependent variables and independent variables.

The Kaplan-Meier method and Cox regression are often used in survival analysis to understand and model the time until an event occurs, such as recovery or death in patients. The Kaplan-Meier method is used to non-parametrically estimate the survival function and can also handle simple censored data, even with a small sample size. This method is considered to provide a better picture of an individual's resistance to a disease so that the picture obtained can be used as material to provide better treatment for patients [12].

Cox Proportional Hazard Regression is a semi-parametric method used to analyze the effect of independent variables on survival time. Unlike other types of regression, this method does not require any specific assumptions regarding the nature or shape of the data distribution. Survival analysis with this method is often applied in various studies to evaluate factors that influence the duration until an event occurs [1].

This aligns with prior studies conducted by [13]. Employing the Kaplan-Meier test and Cox regression analysis to evaluate the recovery time of patients with moderate Covid-19 symptoms in the Jember region, at RSD dr. Soebandi Jember. The results of the study showed that : 1) the survival function of patients with moderate symptoms of Covid-19 at RSD dr Soebandi Jember, for female patients, the recovery time was faster than male patients, 2) the survival function of patients with moderate symptoms of Covid-19 at RSD dr Soebandi Jember, for patients who do not have comorbidities, the recovery time is faster than patients who do have comorbidities, and 3) the variables of gender and comorbid status affect the recovery time of patients with moderate symptoms of Covid-19 at RSD dr Soebandi Jember. The likelihood ratio (LRT) value of 3.5255 for the gender variable, and 16.5221 for the comorbid status variable.

Another study by [14] examined the survival rates of breast cancer patients using the Cox Proportional Hazards regression and Kaplan-Meier methods. The findings revealed that the two-year survival probability was 73.7%, with the highest rate observed in patients aged 51–60 years (80.1%) and the lowest in those aged 31–40 years (65.6%). Survival outcomes were notably better among patients diagnosed at an early stage (94.4%), with tumor sizes ≤ 5 cm (87.7%), without metastasis (90.7%), and those who received radiotherapy (79.2%). The Cox regression analysis indicated that age, cancer stage, and tumor size were significant predictors of survival. Patients aged 51–60 years, with early-stage cancer and smaller tumors, demonstrated a higher likelihood of survival compared to other groups. These findings have encouraged researchers to apply similar methods in a study titled "Survival Analysis Using Kaplan-Meier and Cox Regression in Hypertension Patients at Kefamenanu Regional Hospital".

2. Research Methods (Optional)

This quantitative study uses secondary data from a thesis entitled Analysis of Survival in Hypertensive Patients Using the Kaplan-Meier Method (Case Study: Kefamenanu Regional General Hospital). The purpose of the Kaplan-Meier test is to calculate the estimated survival function and create a survival function graph showing the recovery time of hypertensive patients at Kefamenanu Regional General Hospital. Data on Table 1 The following data was collected from 164 sample patients [15].

Table 1. Data on the recovery time of patients suffering from hypertension at Kefamenanu Regional Hospital

Patient Name	Gender	Length of Stay	Status
A	M	141	1
AA	M	39	0
AB	M	3	0
AD	M	1	0
AF	F	11	1
⋮	⋮	⋮	⋮
YPN	M	6	0
YS	M	11	1
YSF	M	7	0
YT	F	6	0
Z	M	6	0

The amount of time spent by patients with hypertension at Kefamenanu Regional General Hospital ranged from one to more than one hundred days, as shown in Table 1. Some patients experienced death (status = 1), while others were classified as censored (status = 0) because they did not experience death by the end of the observation period or were removed from the observation before death. In the Kaplan-Meier analysis, the survival curve varies depending on patient status and length of hospitalization. Each death reduces the survival function value, while censored data maintain the survival function value until the end of the observation period. As a result, the cumulative probability of patients surviving at each point in time during hospitalization is based on this data. This potential is then illustrated in the Kaplan-Meier survival function graph.

2.1. Survival Analysis

Survival time can be expressed in units of years, months, weeks, days, hours, minutes, seconds, or other units [16]. Suppose T is a non-negative random variable that shows the survival time of individuals in the population. Since T is a non-negative variable, all functions related to T will only be defined in intervals. These functions consist of the probability density function, the cumulative distribution function, and the survival function [17]. The survival function, $S(t)$ is defined as the probability of survival over time t where

$$S(t) = \Pr[T > t] = 1 - \Pr[T \leq t] = 1 - F(t) = 1 - \int_0^t f(x)\,dx = \int_t^\infty f(x)\,dx. \tag{1}$$

In this case the survival function $S(t)$ is a continuous descending function which has the following properties.

- $S(0) = 1$, meaning the probability of an individual surviving longer than zero time is 1.
- $S(\infty) = 0$, meaning the probability of an individual surviving an infinite time is 0.

2.2. Kaplan-Meier and Cox Regression

The Kaplan-Meier method is a non-parametric approach for estimating the survival function, designed to manage incomplete data and effectively handle small sample sizes. One of the good statistical methods is the Kaplan-Meier method to measure an individual's likelihood of survival within a certain period of time, which is generally used to summarize survival experiences. The Kaplan-Meier method offers benefits compared to the life table approach (time grouping), namely its ability to provide a precise survival proportion because it utilizes exact survival times, rather than relying on interval classes. In addition, the Kaplan Meier method can produce a survival estimation curve and record the median survival time. This method is a statistical computation to calculate survival chances. The Kaplan-Meier method relies on the survival time of each individual and assumes that censored data are independent of the survival duration, where the reason for the censored observation is unrelated to the cause of the failure time [18]. The formula of Kaplan Meier is

$$S(t) = \prod_{j=1}^{k} \left(1 - \frac{d_j}{n_j}\right), \quad t \geq 0 \tag{2}$$

where

$S(t)$	:	survival probability at time i,
n_j	:	he number of individuals at risk of failure,
d_j	:	number of individuals who failed at time j.

2.3. Cox Regression Method

The Cox proportional hazard regression model is a technique used to identify the relationship between survival time and factors that are believed to influence survival. This model presumes that the hazard functions for different individuals are proportional, implying that the ratio of hazard functions between two individuals stays consistent over time [16].

The Cox Proportional Hazard model is a nonparametric model that is often used in survival analysis. One of its advantages is that it does not require assumptions about the nature or shape of the distribution, as is usually required in other regression models, where the independent variables must follow a certain distribution. Generally, the Cox PH regression model is expressed as

$$h(t,x) = h_0 \exp\left(\beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_p x_p\right). \tag{3}$$

The form of the cox PH model in equation 4 has the property that if all $x = 0$, then the formula is reduced to the baseline hazard function. Based on equation 3, $h_0(t)$ is considered as the initial or basic function of the hazard function and can be written as

$$\begin{aligned} h(t,x) &= h_0(t)\exp\left(\beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_p x_p\right) \\ &= h_0(t)\exp\left(\beta_1 \times 0 + \beta_2 \times 0 + \cdots + \beta_p \times 0\right) \\ &= h_0(t)\exp(0) \\ &= h_0(t)\cdot 1 \\ &= h_0(t) \end{aligned} \tag{4}$$

where

$h(t,x)$	:	The risk of death of an individual at time (t) with characteristics x,
$h_0(t)$	:	Basic hazard function / baseline hazard function,
$\beta_1, \beta_2, \cdots, \beta_p$	:	Parameters of the regression model,
$x_1, x_2, \cdots, x_p$	:	The independent variable.

2.4. Research Stages

This research stage includes several important steps designed to ensure a systematic and valid analysis process. The stages shown in Figure 1.

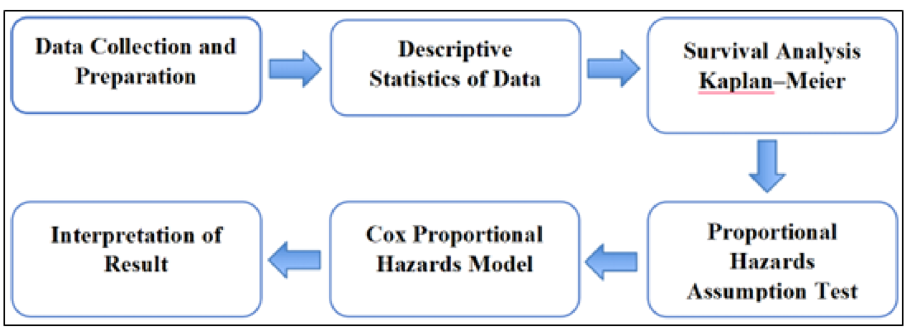

Figure 1. Research Stages Flowchart

The following is an explanation of the flow diagram in Figure 1.

1. Data collection and preparation.
   The dataset used in this study consists of medical records of hypertensive patients who underwent inpatient treatment at the hospital. The data contains important information related to patient characteristics and treatment history. The available variables include: patient_name (patient name), which serves as a unique identifier for each individual; gender (sex), used as a categorical variable for comparative analysis; Length_of_Stay (length of stay in days), which represents the duration of the patient's stay in treatment until an event occurs or the observation period ends; and status, which indicates the patient's final condition—death (represented as an event) or a condition other than death, such as not recovered or recovered (represented as censored). The dataset was originally stored in Excel format and then imported into the Python environment

using the pandas library for further processing. During the preparation stage, key variables relevant to survival analysis were identified and defined, namely duration variables as time-to-event and status variables as event occurrences. This step ensured that the data was in the appropriate format for use in Kaplan–Meier analysis and Cox Proportional Hazards models.

2. Descriptive Statistics of Data.
   Descriptive statistics were performed to provide an overview of the characteristics of the hypertensive patient data analyzed in this study. Descriptive statistics were calculated based on the variables of gender and status (event and censored) to summarize the distribution of patients between the two categories. The results include the number and percentage of patients in each status category in each gender group, as well as the overall total. This analysis aims to highlight proportional differences in outcomes between male and female patients, serving as initial descriptive insights prior to conducting more in-depth survival analysis.
3. Survival analysis using Kaplan-Meier.
   The Kaplan-Meier method was used to estimate the survival function of patients based on gender. This survival function indicates the probability of patients remaining under care up to a certain time during the observation period. Using this method allows for a more detailed view of patient survival patterns, including the point at which survival begins to decline and the magnitude of differences between male and female groups. The survival function graph is presented for each gender group, enabling a visual comparison of survival patterns and trends. This presentation helps in understanding the distribution of treatment duration and provides an initial overview of the potential differences in survival rates between the two groups.
4. Proportional harzards assumption testing.
   The reliability of the Cox Proportional Hazards model largely relies on the fulfillment of the proportional hazards (PH) assumption. This test is performed using the Schoenfeld residual, and the results are summarized for each variable in the model. If the PH assumption is met, the interpretation of the analysis results can be done with more confidence.
5. Cox proportional hazard model construction.
   A Cox Proportional Hazards model was developed using the Lifelines library to assess the relationship between gender and length of stay with the risk of death. The categorical variable gender was converted into dummy variables for regression purposes. This model was fitted to the variables length_of_stay(days) as the duration and event as the event status. After the model was completed, the results were displayed through a summary table that included hazard ratio (HR) values, p values, and confidence intervals.
6. Interpretation of results and visualization.
   After the PH assumption test, the Cox regression results for each year are visualized in the form of a graph showing the hazard ratio and its confidence interval. This graph provides easy-to-understand information about the relative risk based on the predictor variables. The regression results table offers an in-depth view of the correlation between the independent variables and the likelihood of death in hypertensive patients.

3. Result and Discussion

The length of treatment for hypertension patients at Kefamenanu Regional Hospital varies greatly. The patient data include patient name, gender, length of stay, and status. This can be seen from the data summary presented in Table 2.

Table 2. Data on the recovery time of patients suffering from hypertension at Kefamenanu Regional Hospital

Gender		Status		Total
		Event	Censored	
F	Count	8	67	75
	% of Total	10.67%	89.33%	100%
M	Count	20	69	89
	% of Total	22.48%	77.52%	100%
Total	Count	28	136	164
	% of Total	17.07%	82.93%	100%

Based on Table 2, the largest percentage of hypertensive patients who experienced a death event were male patients, namely 22.5% or 20 people, and the highest recovery rate (censored) was female patients, namely 89.3% or 67 people. Meanwhile, 77.5% of male patients recovered and 10.7% of female patients died.

3.1. Survival Analysis Using Kaplan-Meier

The estimates in this analysis focus on examining whether the gender variable has an effect on the length of hospital stay for patients with hypertension. Therefore, in this Kaplan-Meier test, the authors only concentrate on the gender variable. The estimated length of hospital stay for male and female patients based on the Kaplan-Meier method can be seen in Table 3.

Table 3. Kaplan-Meier estimate of length of stay for male and female patients

Gender	Time (t_i)	Hypertension Disease Patient (n_i)	The Number Individuals Who Died (d_i)	Estimation of Individual Death Probability ($h(t_i)$)	Estimation of Individual Survival Probability ($S(t_i)$)
Male	1	89	1	0.0112	0.9888
Male	2	86	2	0.0233	0.9658
Male	3	79	2	0.0253	0.9413
Male	4	69	3	0.0435	0.9004
Male	5	64	0	0.0000	0.9004
Female	1	75	0	0.0000	1.0000
Female	2	74	1	0.0135	0.9865
Female	3	71	1	0.0141	0.9726
Female	4	59	0	0.0000	0.9726
Female	5	53	1	0.0189	0.9542

Based on the Kaplan-Meier estimation results in Table 3, it is seen that male patients have an individual death probability ($h(t_i)$) of 0.0112 on the first day, with a survival probability ($S(t_i)$) of 0.9888. As time passes, the individual death probability increases; for example, on the 4th day it reaches 0.0435, causing the survival probability to decrease to 0.9004, and on the 5th day there are no deaths, so the value remains the same. Meanwhile, female patients on the first day did not experience any deaths ($h(t_i) = 0.0000$), so the survival probability remains at 1.0000, then begins to decrease on the second day to 0.9865, and continues to decrease until it reaches 0.9542 on the 5th day. The rate of decline in survival probability in female patients is relatively slower compared to male patients. Overall, these results indicate a suspicion that gender affects the length of hospital stay for hypertensive patients, where female patients tend to have a higher survival rate during the hospital stay compared to male patients. The difference in estimated survival probability between male and female patients is illustrated in Figure 2, which shows the survival curves of each group based on the gender variable.

In Figure 2, the blue line represents the survival curve for male hypertensive patients, while the orange line represents the survival curve for female hypertensive patients. It can be seen that the two curves do not intersect significantly, with the female patient curve tending to be above the male

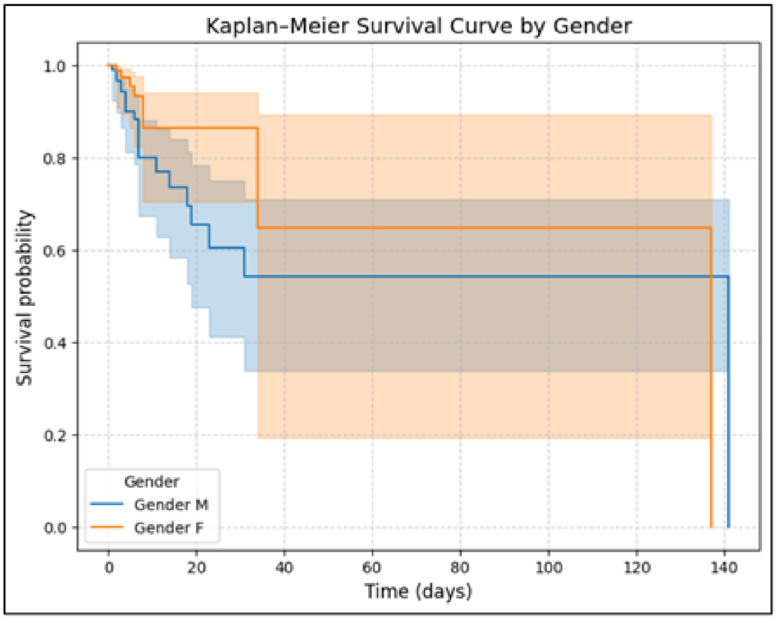

Figure 2. Kaplan-Meier curve of length of stay for male and female patients

patient curve. This indicates that female patients have a higher probability of survival compared to male patients during the hospitalization period. The decline in the male patient curve occurs more rapidly, indicating a higher mortality rate at the beginning of the treatment period.

3.2. Survival Analysis Using Cox Proportional Hazard Regression

In this analysis, the main objective is to determine whether gender has an effect on the length of treatment for hypertensive patients at Kefamenanu Regional General Hospital. However, before forming the Cox Proportional Hazard model, the proportional hazard (PH) assumption was tested. The PH assumption is a key requirement in the Cox regression model, which states that the hazard ratio between two or more groups remains constant over time. This assumption was tested using Schoenfeld residuals. The results of the proportional hazard assumption test are presented in Table 4.

Hypothesis :

H_0 : The proportional hazard assumption is met.

H_1 : The proportional hazard assumption is not met.

H_0 accepted if p-value $> \alpha = 0.05$.

Table 4. Proportional Hazard Assumption Test

Variable	**Rank-transformed Time**	**KM-transformed Time**	**Decision**
Gender	0.4355	0.3425	Accept H_0

The results of the proportional hazard assumption test show that the gender variable has a rank-transformed time value of 0.4355 and a km-transformed time value of 0.3425, with the decision to accept the null hypothesis (H_0). Acceptance of H_0 indicates that there is insufficient evidence to reject the proportional hazard assumption for this variable. Thus, the effect of gender on the hazard rate can be considered constant throughout the observation period, meaning that the variable meets the necessary assumptions for the application of the Cox Proportional Hazard model. After the assumption test was conducted, the next step was Cox Proportional Hazard regression analysis. The first step was to estimate the β_i parameter. The parameter estimation results are presented in Table 5.

Table 5. Parameter estimation results β_i

Variable	coef	exp (coef)	se (coef)	z	P-value	log2(p)
Gender	0.6091	1.8388	0.4227	1.4409	0.1496	2.7406

Based on the results in Table 5, a p-value of 0.1496 ($p > 0.05$) was obtained, so H_0 was accepted. This indicates that the gender variable does not have a significant effect on the Cox model. Therefore, the Cox regression model can be written as in equation 5.

$$\begin{aligned} h_i(t) &= h_0(t)\exp\left(\beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_p x_{ip}\right) \\ h_i(t) &= h_0(t)\exp\left(0.6091 \cdot \text{Gender}\right) \end{aligned}. \tag{5}$$

Based on Kaplan-Meier analysis, male patients had a higher tendency to experience death than female patients during the observation period. The results of the Cox regression model estimation show that the gender variable has a coefficient of 0.6091 with $\exp(\beta) = 1.8388$, meaning that male patients have an 83.88% higher risk of occurrence (hazard) compared to female patients during hypertension treatment at Kefamenanu General Hospital, assuming all other variables remain constant. However, the p-value of 0.1496 (> 0.05) indicates that this effect is not statistically significant at the 5% significance level. This condition is likely influenced by other factors not included in the model, as shown in a previous study conducted by [19] in Medan Tenggara Subdistrict, which found that hypertension is influenced by tobacco use (smoking), low fruit and vegetable consumption, the habit of consuming risky foods, processed foods made from flour, and the presence of other medical conditions.

4. Conclusions

Based on the results of the Kaplan-Meier analysis and survival function for hypertensive patients at Kefamenanu Regional Hospital, it was found that male patients tended to die sooner during treatment. In contrast, female patients had longer survival times. Gender variables do not affect the length of treatment for patients with hypertension at Kefamenanu Regional Hospital. Given that gender does not have a significant effect on the length of treatment for hypertension patients, future research is recommended to explore other potential factors that may influence treatment duration. These may include clinical variables such as age, severity of hypertension, presence of comorbidities (e.g., diabetes or kidney disease), type of treatment administered, or patient adherence to therapy. Additionally, expanding the study period or increasing the sample size could provide more robust findings.

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