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Modeling Survival Analysis and Risk Factors in Breast Cancer Patients

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Abstract— *Breast cancer is the most common cancer suffered by women worldwide, including in Indonesia, and is still an important public health problem due to the high incidence rate and lack of prevention efforts. This study aims to analyze the survival data of breast cancer patients using the Kaplan-Meier method. This method is used to estimate patient survival curves, compare groups based on clinical and demographic variables, and identify the main factors that affect patient survival. The data used were secondary data from breast cancer patients at a hospital in California, with a total of 317 patients. The analysis showed that the survival probability of patients decreased over time, with the highest value on day 1 (0.99685) and the lowest on day 2763 (0.154459). The Kaplan-Meier survival curve shows a decreasing pattern that illustrates the chances of patient survival during the observation period. This study is expected to contribute to the understanding of survival patterns of breast cancer patients and help the development of more effective treatment strategies.*

Keywords— *Breast cancer; kaplan-meier; survival analysis; tumor stage.*

I. Introduction

Breast cancer is one of the most common types of cancer faced by women worldwide, including in Indonesia [1]. This disease falls into non-communicable diseases caused by genetic changes that control cell growth and differentiation [2]. As a result, these cells can grow and proliferate uncontrollably. According to information from the World Health Organization (WHO) and the Indonesian Ministry of Health, breast cancer significantly contributes to morbidity and mortality rates among women related to cancer [3]. In 2020, Indonesia reported 68,858 new breast cancer cases, equivalent to 16.6% of the total 396,914 new cancer cases reported [4]. Despite advances in diagnosis and treatment that have improved patient survival rates, breast cancer remains a serious threat, requiring an in-depth understanding to enhance management and treatment outcomes [5]. The exact causes of breast cancer remain not fully understood [6]. However, it is suspected to be multifactorial, involving a combination of environmental factors and mutations in various genes [7].

One statistical approach that can be used to evaluate patient survival is survival analysis. This approach analyzes data to identify survival patterns over time [8]. In the context of breast cancer, this analysis can provide insights into how clinical and demographic variables are related to patient survival. One of the most commonly used methods in survival analysis is the Kaplan-Meier method. This method is highly popular due to its simplicity in estimating survival curves without requiring specific distributional assumptions [9]. Kaplan-Meier allows researchers to estimate the probability of survival over various time intervals and compare patient groups based on variables such as cancer stage, age, or treatment methods [10]. Additionally, this method provides an intuitive depiction of survival patterns, making it highly beneficial for clinical and research applications.

Several previous studies have revealed various factors affecting the survival of breast cancer patients. Research conducted by Suganda et al [11]. Dr. H. Abdul Moeloek Regional General Hospital in Lampung showed that the five-year survival rate for patients with grade 1 breast cancer reached 100%. On the other hand, patients with grade 3 had lower survival rates. Furthermore, Wulandari et al. examined factors influencing patient survival at Dr. M. Djamil General Hospital in Padang. Their findings revealed that age and cancer stage significantly influenced patient survival. These studies utilized the Kaplan-Meier method to analyze survival curves and compare patient groups based on relevant variables [12].

This study aims to analyze the survival data of breast cancer patients using the Kaplan-Meier method. It focuses on estimating patient survival curves, comparing groups based on clinical and demographic variables, and identifying the main factors affecting patient survival. Through this approach, this research is expected to contribute significantly to understanding the survival patterns of breast cancer patients and assist healthcare practitioners in developing more effective treatment strategies [13]. Ultimately, this study aims to bridge the gap between statistical analysis and clinical practice, hoping to improve breast cancer patient's quality of life and survival rates through better decision-making and more precise care.

II. Literature Review and Hypothesis

A. *Breast Cancer*

Breast cancer is a condition where a complex, immovable lump forms in the breast, caused by damage to genes regulating cell growth and differentiation. This damage leads to uncontrolled cell growth, spreading through the axillary lymph nodes and potentially metastasizing to other organs such as the brain, lungs, and liver [14].

According to [15], breast cancer occurs when cells in breast tissue undergo uncontrolled growth, invading surrounding healthy tissue. These cells divide faster than normal cells, forming a lump or mass due to cell accumulation.

Breast cancer can be summarized as the abnormal, uncontrolled growth of cells in breast tissue, which invades healthy tissue, resulting in the formation of a lump or mass.

B. Factors Suspected to Influence the Survival of Breast Cancer Patients

(a) Age

Age is one of the main risk factors in the development of breast cancer. Research shows that the risk of breast cancer increases with age, with the highest incidence in women over 50 years old, particularly after menopause. This is due to cumulative exposure to estrogen hormones throughout a person's life, which can trigger the growth of abnormal cells in breast tissue [16].

Women over 50 years old are at higher risk of developing breast cancer. Women who experience their first menstruation (menarche) before the age of 12 and women who reach menopause after the age of 55 are also at greater risk. This is due to prolonged exposure to estrogen hormones [17].

Age is also related to awareness and early detection. Younger women tend to be less aware of the risk of breast cancer, often resulting in a diagnosis at an advanced stage. Conversely, in older age groups, delays in diagnosis often occur because symptoms such as lumps are considered a natural part of aging [18]. Therefore, a targeted approach to education and early detection based on age groups is crucial to improve treatment outcomes and patient survival.

(b) Sex

According to Hungu [19], sex is the biological difference between males and females determined at birth. Sex relates to physical characteristics, where males produce sperm while females produce eggs and have the biological ability to menstruate, conceive, and breastfeed. These biological differences and functions are fixed and cannot be exchanged between genders, regardless of race. Fakih [20] adds that sex is a biological classification inherent to a specific gender. Nugraha [21] explains that sexual activity involves physical or mental stimulation and physical satisfaction. At the same time, Andarmoyo [22] broadly defines sexuality as the drive to form relationships involving warmth, love, and interaction, which may be expressed with individuals of the same or opposite gender and encompasses thoughts, experiences, values, and emotions. The main difference between sex and sexuality lies in the focus on physical aspects for the former, while the latter includes broader emotional and social dimensions.

Sex also influences attitudes toward health and healthy lifestyles. Lawrence Green in Soekidjo Notoadmodjo [23], sex predisposes individual behavior. Gibney et al. [24] state that women tend to have better knowledge about nutrition, food safety, and weight management due to social and cultural norms that often consider women less deserving of consuming large quantities of food. Additionally, Allport reveals that behaviors based on positive attitudes are more enduring than those based on negative attitudes. Morgan and King [25] reinforce that attitudes and behaviors are generally consistent, meaning a positive attitude toward health encourages individuals to adopt healthy lifestyles.

(c) Tumor Stage

Stage refers to determining the tumor size, local invasion, and its spread to broader areas. Tumor staging uses the TNM system, where T represents the size or extent of the primary tumor, N refers to lymph node involvement, and M describes the extent of metastasis. Tumors are classified into stages 0, I, II, III, and IV. Stages II and III include a broader spectrum of breast cancer, further divided into stages IIA, IIB, IIIA, IIIB, and IIIC. The factors determining the stage include the number and characteristics of axillary lymph nodes, the involvement of other regional lymph nodes, and the condition of the underlying skin or muscles [26].

(d) Types of Breast Cancer

Breast cancer consists of several types, including invasive and non-invasive breast cancer. Invasive breast cancer refers to cancer that has spread beyond the milk ducts and into other organs, while non-invasive breast cancer affects the ducts or lobules without spreading. Below are several types of breast cancer:

1. *Ductal Carcinoma In Situ* (DCIS)

DCIS is a non-invasive breast cancer. Cancer cells remain within the milk ducts and have not spread beyond the walls. Women with this type of cancer have a higher chance of recovery. Detection can be performed through mammography [27].

2. *Lobuar Carcinoma In Situ* (LCIS)

LCIS is a non-invasive type of breast cancer occurring in milk-producing glands but does not spread beyond the lobules. Women with this type are at high risk of developing invasive breast cancer. Regular mammography is recommended to monitor breast health [28].

3. *Infiltrating Ductal Carcinoma* (IDC)

This type of cancer originates from the ducts and invades the duct walls, progressing into the fatty tissue of the breast. It can metastasize to other organs through blood or lymphatic systems [29].

4. *Infiltrating Lobular Carcinoma* (ILC)

ILC spreads from the lobules to the surrounding breast tissue and can metastasize to other body parts, such as lymph nodes, bones, liver, or lungs. This type of cancer is often complex to detect during physical examination or mammography, as the cancer cells tend to spread diffusely without forming a distinct mass or lump [30].

5. *Inflammatory Breast* Cancer (IBC)

IBC is a rare but highly aggressive type of breast cancer characterized by inflammatory symptoms on the breast skin. Unlike other breast cancers, IBC does not typically cause a distinct lump but presents with changes such as redness, swelling, warmth, and thickened skin resembling an orange peel (peau d'orange). Treatment often involves a multimodal approach, including chemotherapy, radiation therapy, mastectomy, and targeted therapy [31].

C. Survival Analysis

Survival analysis is a research method focusing on the survival duration of individuals or experimental units. The primary variable in this approach is the time measured until a specific event occurs, often related to survival or the endurance of an entity from a defined starting point. Based on Lawless [32], the primary objectives of survival analysis are:

1. Identifying suitable statistical models for survival distribution to describe the failure of a unit to function normally.
2. Estimating unknown parameters of the survival distribution model.
3. Calculating confidence intervals for survival estimates.

Survival analysis differs from other statistical fields due to its incorporation of censoring. Survival data is often considered parametric, as it usually relies on assumptions about the survival distribution model. However, the survival data is considered nonparametric if the distribution model is unknown. Survival time T is a non-negative random variable representing the survival duration of individuals in a homogeneous population. The probability distribution of T, representing survival time, can be determined using various methods. In survival analysis, three primary functions are often applied: the probability density function, the survival function, and the hazard function, as described by Kalbfleisch [33].

The survival function is perceived as the probability that an individual will survive until time t. If T is a random variable that represents the length of an individual's lifespan in the interval [0, ∞), then the survival function $S(t)$ can be expressed as:

$$S(t) = P(T \geq t)$$
$$= \int_t^{\infty} f(t)dt$$

Thus an equation emerges that explains the relationship between the survival function and the cumulative distribution function [34], which is represented as follows:

$$S(t) = 1 - F(t)$$

D. Censored Data

Censoring plays a crucial role in survival analysis, giving it uniqueness compared to other statistical methods. This process is implemented for various reasons, including time constraints and budget limitations. The primary purpose of censoring is to reduce the duration of the study, considering that recording survival or failure events often requires significant time and resources. Uncensored observations record the duration of survival from the experiment's start until the subject's death. On the other hand, censored observations occur when the survival duration is not precisely known, limited by time or other factors [35]. Research has three common types of censoring: type I, II, and III censorship.

E. Variable Dummy

Censoring Dummy variables are used to quantify qualitative or dichotomous variables in regression analysis [36]. Dummy variables only have two values, 1 and 0, to indicate the presence or absence of a particular category or condition. Dummy variables, often called indicator variables or binary variables, are a type of variable used to represent categorical variables in data analysis. If the independent variable has more than two categories, then in the regression model, the variable must be expressed as a dummy variable with the number of dummy variables created equal to the categories minus one. Dummy variables are given 1 for specific categories and 0 for others. Dummy variables facilitate the interpretation of regression analysis results and allow hypothesis testing on qualitative variables.

F. Metode Kaplan-Meier

(a) Introduction to Kaplan-Meier

In 1958, Edward L. Kaplan and Paul Meier developed a statistical calculation method named after them, the Kaplan-Meier method. This non-parametric technique estimates survival functions in the presence of incomplete or censored data. It is widely used to estimate the survival probabilities of individuals over specific periods [37]. The Kaplan-Meier model equation is as follows:

$$S(t) = \prod_{t_i<t} (1 - \frac{d_i}{n_i})$$

Description:
$S(t)$ = Probability of survival from the start of the study.
n_i = Number of individuals at risk and still surviving at time *i*.
d_i = Number of individuals experiencing the event at time *i*.

(b) Kaplan-Meier Curves

According to Cleophas, Zwinderman, and Cleophas [38], the Kaplan-Meier curve is a nonparametric estimate derived from a person's survival probability distribution. Each time point t represents the cumulative proportion of individuals who experienced the event. The Kaplan-Meier survival curve itself produces a monotonous downward trend as t increases, some cases are found to be close to zero or even have a value of 0. The value of the Kaplan-Meier curve at time t is denoted by S(t) with the following equation:

$$S(t) = S_{(t-1)} \times (1 - \frac{d_i}{n_i})$$

Description:
n_i = The number of people who are at risk but still survive in time *i*.
d_i = The number of people experiencing an event at a time *i*.

The analysis results can be clarified through the Kaplan-Meier survival curve by describing the patient's chance of survival from the start of the study (starting point) until the occurrence of an event (endpoint). In the curve, there is an. Meanwhile, the Y axis states the percentage of a person's chance of living on a scale of 0 to 1. An illustrative example in the following image

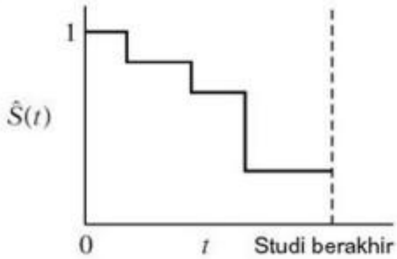

Fig. 1. Kaplan-Meier Survival Curve

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III. METHODOLOGY

This study is a quantitative analysis that aims to model survival in assessing the survival of breast cancer patients using the Cox Regression method. The data source used in this research is secondary data obtained through the kaggle.com site. The data contains information about the population of breast cancer patients at one hospital in California, United States [39]. This study will analyze 317 patients to identify factors that influence the survival of breast cancer individuals. Seven variables are used: five predictor variables and two response variables. A description of each variable is presented in the following table.

TABLE 1. Description of Research Variables

Variable	Variable Name	Variable Definition	Data Type
X_1	Age	The patient's age at the time of breast cancer	Continuous
X_2	Sex	Patients were grouped by gender into two categories: female and male	Categorical
X_3	Tumor Stage	Breast cancer stages are categorized into three levels, stages I, II and III	Categorical
X_4	Types of Cancer	Types of breast cancer are categorized into three, Infiltrating Ductal Carcinoma (IDC), Infiltrating Lobular Carcinoma (ILC), and Mucinous Carcinoma (MC).	Categorical
X_5	Operation Type	The types of surgery for breast cancer patients are categorized into four, Lumpectomy, Modified Radical Mastectomy, Simple Matectomy, and other.	Categorical
Y_1	Period of Suffering from Disease	The period of time a patient suffers from breast cancer is calculated based on days	Continuous
Y_2	Patient Status	Patient status is categorized into two, censored (code 0) if they are still alive and uncensored (code 1) if they die	Categorical

The data analysis procedure in this study includes the following steps: (1) Carrying out descriptive statistical analysis (2) testing data assumptions with a normality test (3) Calculating the estimated survival value for breast cancer patients from each t for the entire data (4) Making a plot Kaplan-Meier survival curve based on the survival estimate value obtained in the previous step.

IV. RESSULTS AND DISCUSSION

A. Descriptive Statistics

The number of samples used was 317 breast cancer patients. The results of the research showed that of the 317 breast cancer patients, 65 of them died and 252 patients were still alive. The period of time they had breast cancer and the ages of the 317 patients are given in Table II below.

TABLE II. Descriptive Statistics for the Time Period of Breast Cancer Patients

Variable	Mean	St.Dev	Median	Max	Min
Time period	442.73	373.633	370	2763	1
Age	58.73	12.827	58	90	29

Based on Table 2, the average time period for patients suffering from breast cancer is 442.73 days, with a standard deviation of 373.633 days and a median of 370 days. The shortest period is 1 day, while the longest is 2,763 days. For the age variable, the average age of breast cancer patients is 58.73 years, with a standard deviation of 12,827 and a median of 58 years. The youngest patient's age was recorded at 29 years, while the oldest was 90 years.

B. Test Data Assumptions

The Kolmogorov-Smirnov Normality Test was carried out to see whether the data met the normal distribution assumption or not. The hypothesis used in testing data assumptions is as follows.

H_0: Data has an exponential distribution
H_1: The data is not exponentially distributed

TABLE III. Kolmogorov-Smirnov Test Results

One-Sample Kolmogorov-Smirnov Test		
N		317
Exponential Parameter	Mean	442.73
Most Extreme Differences	Absolute	0.111
	Positive	0.060
	Negative	-0.111
Kolmogorov-Smirnov Z		1.977
Asymp. Sig. (2-tailed)		0.001

Based on the results of the Kolmogorov-Smirnov test presented in Table III, a p-value of 0.001 was obtained so it was rejected and accepted, so it can be seen that the data on breast cancer patients in one hospital in California, United States does not meet the exponential distribution assumption so that the data can analyzed using the Kaplan-Meier method.

C. Survival Analysis of the Kaplan-Meier Method

The total amount of data is 317 data that will be used for determination (ranking based on the survival time of breast cancer patients). The complete results of the product limit estimator or Kaplan-Meier calculations on breast cancer patient data can be seen in Table IV as follows.

TABLE IV. Results of Survival Function Estimation in Breast Cancer Patients

Time (t_i)	n_j	d_j	$1-\frac{d_j}{n_j}$	$\hat{S}(t_i)$	$\hat{H}(t_i)$
1	317	1	0.996845	0.99685	0.00316
4	316	0	1	0.996845	0.00316
6	315	0	1	0.996845	0.00316
7	313	0	1	0.996845	0.00316
9	312	1	0.996795	0.99365	0.00637
10	310	1	0.996774	0.990445	0.009601
12	308	1	0.996753	0.987229	0.012853
14	307	1	0.996743	0.984013	0.016116
19	306	0	1	0.984013	0.016116
21	305	1	0.996721	0.980787	0.0194
23	303	0	1	0.980787	0.0194
24	302	0	1	0.980787	0.0194
30	301	1	0.996678	0.977529	0.022738
31	299	0	1	0.977529	0.022738
35	298	0	1	0.977529	0.022738
40	297	1	0.996633	0.974237	0.026101
45	296	1	0.996622	0.970946	0.029485
⋮	⋮	⋮	⋮	⋮	⋮

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2289	3	1	0.666667	0.308919	1.174676
2317	2	1	0.5	0.154459	1.867824
2763	1	0	1	0.154459	1.867824

Estimated value of the survival function $\hat{S}(t_i)$ in the table above is interpreted as the probability of survival in breast cancer sufferers. Based on the table, it can be seen that the estimated value of the survival probability is getting lower and lower over time and is approaching the value of 0 at the last time t, namely t_{2763}. Based on the table, it can be seen that the lowest survival rate for patients surviving is on day 2, namely $\widehat{H}(1) = 0.00316$ while the highest was on day 2763, namely $\widehat{H}(2763) = 1.867824$

D. Kaplan-Meier Method Survival Curve

The Kaplan Meier survival curve is used to determine the survival characteristics of patients with breast cancer based on factors that are thought to influence survival, including age, gender, tumor stage, type of cancer, and type of surgery. The obtained Kaplan Meier survival curve can be seen in Figure II below.

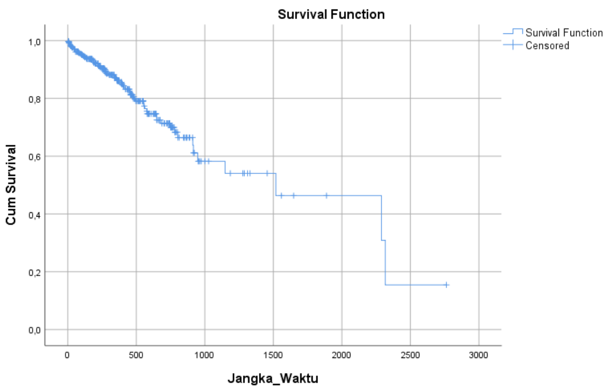

Fig. II. Kaplan-Meier Survival Curve of Breast Cancer Patients

Figure II shows the survival plot of the survival function for breast cancer patients. As t increases during the observation period, the probability of survival $S(t)$ or the chance that the patient continues to be treated/has not gone home will decrease, assuming that as t passes during the inpatient observation period, the patient will have the opportunity to go home in an improved condition. From the Kaplan-Meier survival curve in Figure II and Table IV it is obtained that the largest survival probability value is at $S(1)$ = 0.99685, while the lowest survival probability is at $S(2763)$ = 0.154459. So, it can be concluded that breast cancer inpatients in one of the hospitals in California, United States will quickly experience recovery on day 2763 with a survival probability value that is closest to 0% because the smaller the survival probability value, the more likely the patient will be to go home within things got better.

V. Conclussion and Suggestion

From the results of the survival analysis that was carried out, it was found that the highest probability of survival (patient still undergoing treatment/not yet home) occurred on day 1, namely having a survival probability of 0.99685 and the lowest survival probability occurred on day 2763 with a value of 0.154459. Based on the survival curve, at the beginning of the observation the value of the probability of survival is high, it slowly decreases until at the end of the observation period t reaches the baseline. This shows that the longer the hospital stay, the quicker the patient will go home in improved condition after undergoing treatment.

Based on the analysis carried out, it is recommended that hospitals optimize treatment in the early days of hospitalization to speed up recovery and reduce the duration of treatment. Regular evaluation and monitoring must be carried out to ensure treatment is appropriate for the patient's needs. Resource management, patient and family education, and further research on factors that influence length of stay are also important to improve the efficiency and quality of health care.

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