

# The Relationship Between Cancer Stage, Tumor Size and Five-year Survival Rate of Breast Cancer Patients at Dharmais Cancer Hospital

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## ABSTRACT

The result of breast cancer therapy is usually evaluated using the five-year survival rate. Besides therapeutical aspects, several factors also determine the five-year survival rate, e.g. the stage of cancer and tumor size. The goal of this study is to determine the probability of 5-year survival among breast cancer patients at Dharmais Cancer Hospital Jakarta, and the relationship between cancer stage, tumor size, and 5-year survival rate.

The design was a longitudinal study. Data were collected from the medical records of breast cancer patients admitted to Dharmais Cancer Hospital between 1993 and 1996. The sample was 137 women. Data was collected from the medical record as well as by telephoning or sending post mail to establish how long each breast cancer patient survived.

The results show that the 5-year survival rate for breast cancer patients at Dharmais Cancer Hospital was 48%, with a median survival rate of 54 months. The 5-year survival rate of patients of early operable stages was 72%, while that of those from late stages was 12%. By using patients from early operable stages for baseline comparison, the risk-ratio of death in the late stage was 6.612 (95% CI: 4.014; 10.78). Moreover, the 5-year survival rate of patients with tumors that were less than 5 cm in size was 81%, whilst the 5-year survival rate of patients with tumors larger than 5 cm was 24%. If compared to patients with a tumor size < 5 cm, the risk-ratio of death among patients with tumors over 5 cm in size was 6,612 (95% CI: 5.50; 12.48).

**Keywords :** stages tumor size, 5-year survival rate, breast cancer

## INTRODUCTION

Breast cancer is one of the most common cancers to cause death among women. Breast cancer is frequently found all over the world, with a high relative incidence rate of 20% out of all malignancies. In developed nations, breast cancer is the most frequent carcinoma and is also the greatest cause of death among women.<sup>1</sup> In the United States, breast cancer is the most common form of cancer among adult women. There is an estimated 180,000 women diagnosed with breast cancer each year, representing 32% of all cancers among women, with 46,000 deaths each year.<sup>2</sup> In Indonesia, breast cancer is the second most common form of cancer among women after cervical cancer.<sup>3</sup> In addition, the malignancy rate of breast cancer is quite high. Data from the General Directory for Medical Services of the Department of Health of the Republic of Indonesia in the year 2000 demonstrated a 7.5 case fatality rate (CFR) due to breast cancer according to the cause of illness.

The year survival rate is an important measurement to determine the success of cancer treatment. Life survival greatly depends on the level of malignancy and the probability of death for the particular type of cancer. Data from the National Cancer Institute demonstrate a lower 5-year survival rate among breast cancer patients compared to patients with melanoma, uterine cancer, and thyroid cancer. The data also demonstrate a difference in 5-year survival rate of white and black breast cancer patients in the different states of the United States of America. The probability of 5-year survival among whites was higher (78%) compared to 63% among the African-Americans (data from 1981 to 1987).<sup>2</sup>

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The clinical stage of breast cancer greatly determines the patient's survival rate, and is also used as a reference to the choice of treatment. A study by Cutler (1974) of breast cancer patients with radical mastectomy demonstrated a 5-year survival rate of 85%, 66%, 41%, and 10%, for patients in stage I, II, III, and IV respectively.<sup>4</sup> Tjindarbumi (1995) in coordination with researchers from Japan found a 5-year survival rate of 82.3%, 69.2%, and 63.6% respectively among stage I, II, and III breast cancer patients in Jakarta.<sup>5</sup> Vaidya and Shukla reported a correlation between the size of the breast tumor and 5-year survival rate. A tumor over 2 cm in size has a probability of survival of 73% compared to a probability of survival of 47% for tumors 3 to 6 cm in size.<sup>6</sup>

According to data from the medical records of Dharmais Cancer Hospital from the year 2000, breast cancer is the most common form of cancer among hospitalized patients, and the second most common form for ambulatory patients. This hospital was built in 1993, and up to now it has never conducted a study on the probability of 5-year survival among its breast cancer patients and its correlation with cancer stage and tumor size.

A study on the survival rate of breast cancer patients using the Kaplan Meier method would be greatly beneficial to evaluate cancer management at treatment centers. Complete information on factors that influence survival would be greatly beneficial not only to improve the treatment of breast cancer patients especially in Indonesia, but also to provide adequate information for the public about breast cancer, especially on the development of treatment and the prognosis of the disease in the future.

## MATERIALS AND METHOD

### Study Design

This study was a longitudinal study. The study design is time-lined, allowing for more than one data collection. Collection was conducted retrospectively by following subjects to determine events that have not occurred from when the breast cancer patient first came to Dharmais Cancer Hospital for medical attention up to a surveillance time of 5 years. This design was used with the aim of determining the time of death among breast cancer patients.

### The Population and Study Sample

The population in this study consisted of breast cancer patients that come to Dharmais Cancer Hospital for medical attention. The sample consisted of breast cancer patients who came to Dharmais Cancer

Hospital for the first time between 1993 and 1996. The criteria of inclusion were women who have received treatment for breast cancer who were not residual/recurrent cases who have received treatment elsewhere. For analysis purposes, the minimum number of sample is 96 for each of the 2 groups. The sample formula used for each group is as follows:<sup>7</sup>

$$n = \frac{[Z_{1-\alpha} \sqrt{2 f(\lambda)} + Z_{1-\beta} \sqrt{f(\lambda_1) + f(\lambda_2)}]^2}{(\lambda_1 + \lambda_2)^2}$$

$$f(\lambda) = \frac{\lambda^3 T}{\lambda T - 1 + e^{-\lambda T}}$$

n = 47.5 → 48 samples in each group

Note:

- $Z_{1-\alpha}$  = Level of significance 5% (1.645)
- $Z_{1-\beta}$  = Power of the test 90% (1.28)
- $I_1$  = The prevalence of death in 5 years among stage I breast cancer patients
- $I_2$  = The prevalence of death in 5 years among stage III breast cancer patients
- T = 5 years

The values of  $\lambda_1$  and  $\lambda_2$  were taken from the study by Tjindarbumi, et al in 1995, where the probability of death in 5 years among stage I patients, representing patients from the early stage of the disease was 16.7%, while the probability of death in 5 years among stage III breast cancer patients was 36.4%.

### Data Collection

Initial data was collected from the medical records of Dharmais Cancer Hospital, while data on patient survival was obtained via telephone and questionnaires or letters by post.

The source of data was the medical records of Dharmais Cancer Hospital. The medical records selected were those of breast cancer patients who came for their initial visit between 1993 and 1996. Survival data was evaluated after 5 years monitoring.

The data was sorted and analyzed using SPSS 10. The data was analyzed using univariant and bivariate analysis. Univariant analysis was conducted with the aim of determining the distribution of each variable by

portraying the value or central measurement and data variation measurements. Bivariant analysis was conducted with the aimed of determining the correlation and the correlation strength between each dependent variable and independent variable using the Kaplan Meier method. Significance was determined using the log rank test. The odds ratio (OR) was determined using simple Cox regression.

## RESULTS

### The Survival Rate of Breast Cancer Patients

The survival rate of breast cancer patients did not demonstrate normal distribution, but was instead left skewed, with a median of 24 months. For further details on the distribution of 5-year survival among breast cancer patients and the statistical analysis, see Figure 1 and Table 1 as follows.

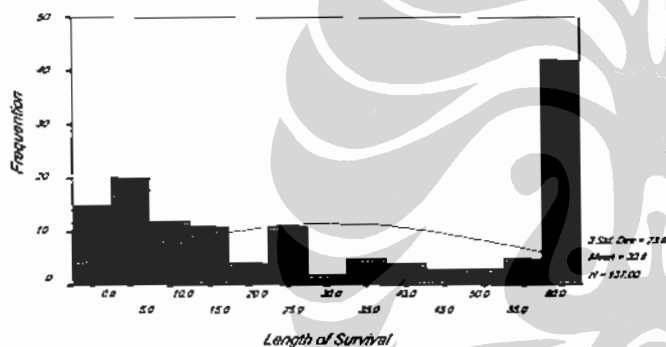


Figure 1. The Distribution of The 5-year Survival Rate of Breast Cancer Patients at Dharmas Cancer Hospital from 1993-1996

Table 1. Statistical Measurements of The 5-year Survival Rate of Breast Cancer Patients at Dharmas Cancer Hospital from 1993-1996

Statistical measurements	Value (Months)
Mean	30.59
Median	24
Standard deviation	23.5
Minimum	0
Maximum	60

### Stage

The greatest number of breast cancer patients seeking medical attention at Dharmas Cancer Hospital came with stage IV (36 people, 26.3%) and stage IIIB (26 people, 19.0%). The remaining were patients with stages I to IIIA. There were 4 people with stage I (2.9%), 24 people with stage IIA (17.5%), 25 people with stage IIB (18.2%), and 22 people with stage IIIA (16.1%). For further analysis, the clinical stages were grouped into the following 2 categories: operable early stages

(stage I to IIIA), consisting of 75 people (54.7%), and advanced stages (stages IIIB and IV), consisting of 62 people (45.3%).

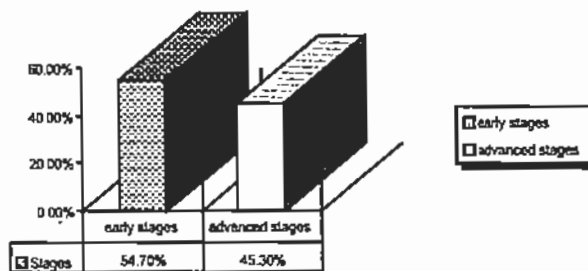


Figure 2. The Distribution of Frequency According to Stage of Breast Cancer Patients at Dharmas Cancer Hospital from 1993-1996

### Tumor Size

The size of the tumor was measured in centimeters (cm). The measurement used was length or width, depending on which is longer. Tumor size was classified into 2 groups, tumors less than 5 cm in diameter and those over 5 cm. The distribution of the frequency of breast cancer patients can be found in figure 3 as follows.

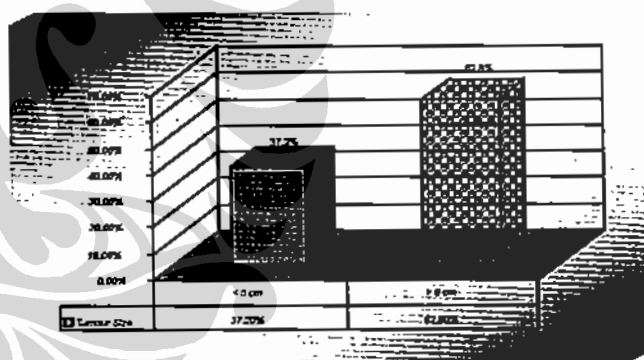


Figure 3. The Distribution of Frequency According to Tumor Size of Breast Cancer Patients at Dharmas Cancer Hospital from 1993-1996

### The 5-year Survival of Breast Cancer Patients

Out of 137 cases of breast cancer patients, 82 people became sensors (59.85%), and from these sensors, 40 cases were lost from observation (29.19%), while 55 patients underwent an event (40.15%). Figure 4 demonstrates the probability of 5-year survival. In this graph, the 5-year survival rate of breast cancer patients is demonstrated in months from 0 to 60 months. The probability value is 0 to 1 or 0 to 100% if read as percentages. In this graph, it can be found that the probability of 5-year survival (60 months) after treatment is 0.4827 (48%) and the median 5-year survival rate is 54 months. Calculations using the Kaplan Meier method are further explained in the following graph.

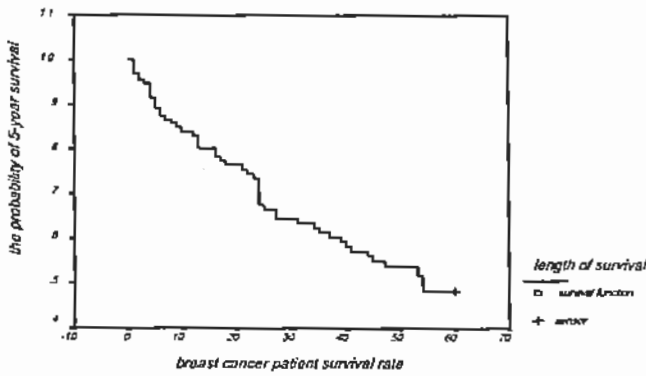


Figure 4. The Probability of 5-year Survival of Breast Cancer Patients at Dharmais Cancer Hospital from 1993-1996 The Survival Rate of 5 Years for each Clinical Stage

Table 2. The 5-Year Survival Rate for Each Clinical Stage

Stage	Sum	Percentage	Cummulative Probability of 5 years	Median (months)
	4	2.9%	100%	60+
I/A	24	17.5%	82%	60+
I/B	25	18.2%	81%	60+
II/A	22	16.1%	46%	54.43
II/B	26	19%	20%	39.34
IV	36	26.3%	5%	18.94

• 60+ = survival rate of over 60 months

**The Correlation Between 5-year Survival Rate and Cancer Stage**

In the operable early stages (stages I to IIIA), the probability of 5-year survival among 75 patients was 0.7169 (72%). In advanced stages (IIIB and IV), the median survival rate was 22 months, and the probability of 5-year survival was 0.1186 (12%). Advanced statistical analysis with the log rank test demonstrated a difference between stage and 5-year survival at  $l = 0.05$  (log rank = 50.53,  $df = 1$ ,  $p = 0.000$ ). Further details on the correlation between 5-year survival of breast cancer patients and cancer stage can be found in the following figure.

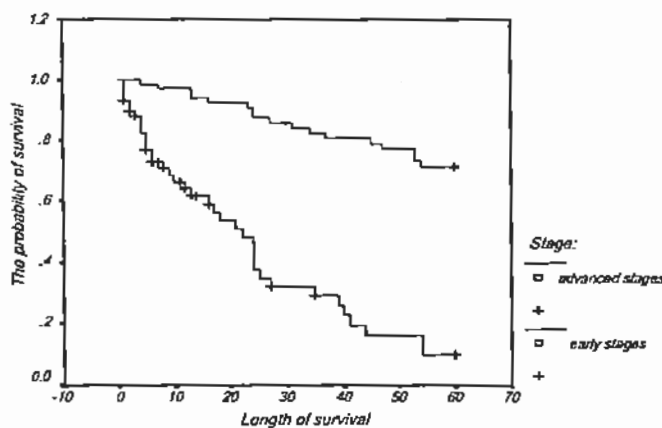


Figure 5. The Probability of 5-year Survival of Breast Cancer Patients According to Stage at Dharmais Cancer Hospital from 1993-1996

**Tumor Size and 5 Year Survival**

According to tumor size, the median survival rate of the group with a tumor size of over 5 cm is 25 months. In addition, the probability of survival in breast cancer patients with a tumor size of less than 5 cm is 0.8091 (81%), and the probability of survival for breast cancer patients with a tumor size of over 5 cm is 0.243 (24%). Statistically, using the log rank test, the difference between tumor size and 5-year survival is at  $l = 0.05$  (logrank = 32.93,  $df = 1$ ,  $p = 0.000$ ). Further details on the correlation between 5-year survival of breast cancer patients and tumor size can be found in the following figure.

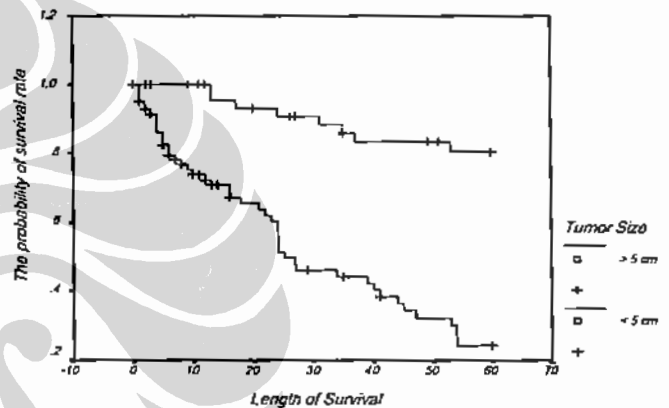


Figure 6. The Probability of 5-year Survival of Breast Cancer Patients According to Tumor Size at Dharmais Cancer Hospital from 1993-1996

**DISCUSSION**

**The Probability of 5-year Survival**

Based on the Kaplan-Meier analysis, the probability of 5-year survival among breast cancer patients receiving treatment in this study was less than that of patients in the different states of the United States from 1981 to 1987,<sup>2</sup> where the probability of survival was 78% among whites and 63% among blacks. This is estimated to be due to the fact that most breast cancer patients in Indonesia come for treatment after the disease has progressed, or in other words during advanced stages, thus reducing the success rate of treatment compared to if they had come earlier (during initial stages). Vaidya and Shukla (1980) from India also reported a survival rate of 60% for breast cancer patients. As in Indonesia, there is a great number of patients in India who come in advanced stages (50%).<sup>6</sup>

The 5-year survival rate obtained here is a relative survival rate, without taking into account factors associated with the survival rate of breast cancer

patients. References state that aside from the treatment aspect, cancer stage and tumor size are important factors that determine the survival of cancer patients in general, specifically breast cancer patients.

### Clinical Stages

The data from this study demonstrated a great percentage of patients that received treatment after late stages. Manuaba (1996) from Denpasar Hospital also reported a great number of patients that came for medical attention during advanced stages (46.6%).<sup>8</sup> Prodjo, et al (1983) also found a great number of patients coming to Gadjah Mada University Hospital for medical attention at stages III and IV (69.23%).<sup>9</sup> Tjindarbumi (1995) also reported that 63.3% of patients who came to Cipto Mangunkusumo Hospital from 1989-1991 had advanced stage cancer.<sup>5</sup> In more developed nations such as Japan, 80 to 85% of patients with stage I and II receive initial treatment, or in other words only 15-20% seek medical attention in advanced stages.<sup>10</sup>

The probability of 5-year survival among patients with advanced stages is only 11.86% (12%), while the probability of 5-year survival for patients with early stages reaches 71.69% (72%). Meanwhile, the median survival time for patients with advanced stage breast cancer is 22.29 months, and the median for those with early stages is 60 months, which means that over 50% of breast cancer patients can survive for over 5 years. This is quite high compared to those with advanced stages, where more than 50% patients can only survive up to 22 or 23 months (approximately 2 years). The study by Langland (1979) found a median survival time of 0.7 to 2.9 years for stage III and IV breast cancer patients, while the median survival time for those in stage I and II was over 6 years (6.6 to 9.7 years).<sup>11</sup> The study by Tjindarbumi (in coordination with researchers from Japan, 1995) also demonstrated a different 5-year survival rate for each cancer stage. The survival rate for breast cancer patients in stage I was 83.3%, 69.2% in stage II and 63.6% in stage III. The study by Cutler, reported by Vorherr (1980) also demonstrated a difference in 5-year survival rate of stages I, II, III, and IV breast cancer patients of 85%, 66%, 41%, and 10%, respectively.<sup>4</sup>

During advanced stages, generally the disease has spread to other organs. This spread cause a bad impact on patients, in the form of organ dysfunction and increase susceptibility to infection. The organs that are often inflicted are lungs, liver, bones, and brain. Patients that enter this phase are more difficult to treat compared to those without metastasis to other organs. Management

during this phase is palliative, aimed to inhibit disease progression and alleviate the patient's suffering.

The correlation between clinical stage and 5-year survival of the patients in this study was significant (statistically tested using log rank) at an alpha of 0.05 ( $p < 0.001$ ). When Cox bivariate regression analysis is used, the mortality risk at advanced stages is 6.584 times (95% CI 4.014: 10.78) greater than those in early stages.

### Tumor Size

Theoretically, the size of the tumor at the beginning of treatment is often correlated with the survival rate of cancer patients, particularly those with breast cancer. Tumor size is related to spread of cancer to surrounding tissues. This is often characterized by positive regional lymph node palpation (of the armpits, neck, and chest). The larger the tumor, the greater the chance of spread to other organs. Vaidya and Shukla (1980) reported a correlation between tumor size and positive lymph node palpation, where tumors of over 5 cm in size generally more commonly produce positive regional lymph node palpation.

In addition, patients who are treated after the tumor has enlarged naturally produce a lower success rate compared to if treatment was given when the tumor was a lot smaller (less than 5 cm). This is also often associated with post-surgical residual tumor mass, where the amount of residual tumor mass causes a greater recurrence rate among breast cancer patients.

Out of the 137 cases analyzed in this study, most patients came for medical attention after reaching a tumor size of more than 5 cm (T3), making up 86 patients or 62.8%. While 51 patients or 37.2% came with a tumor of less than 5 cm (T1 and T2) at the initial treatment. Tjindarbumi (1995) also reported a high percentage (50%) of patients that came to Cipto Mangunkusumo Hospital for medical attention with a tumor size of  $> 5$  cm, while only 5.5% came for medical attention with a tumor size of  $< 2$  cm. If compared to the report from Cancer Institute Hospital (Tokyo, 1995), a large number of patients came for medical attention with a tumor size of  $< 5$  cm (83.16%).<sup>5</sup>

The Kaplan Meier analysis demonstrated a difference in 5-year survival rate among breast cancer patients with a tumor size of  $< 5$  cm compared to those with a tumor size of  $> 5$  cm. The probability of 5-year survival rate among breast cancer patients with a tumor size of more than 5 cm was 24.3% (24%) compared to 81% in patients with a tumor size of  $< 5$  cm. The median survival time according to Kaplan Meier in patients with a tumor size of more than 5 cm was 25 months.

According to the study by Fisher in Vaidya and Shukla (1980), there is a difference in the 5-year survival rate of breast cancer patients with smaller tumor size (<2 cm) compared to those with larger size tumors. Patients with a tumor size of less than 2 cm had a 5-year survival rate of 73%, while those with tumor sizes 3-6 cm had a 5-year survival rate of 24%, and those with over 7 cm tumors had a 5-year survival rate of 15 %.

Tabar et al (1992) conducted a study comparing the survival rate of patients with different tumor sizes, stages, and positive lymph node palpation. Tabar (1992) found a difference in the 5-year survival rate of patients with stages I and II cancer with a tumor size of < 15 mm compared to those with stage III cancer and a < 15 mm size tumor, 99% and 90% respectively. Tabar also found that patients with tumor sizes > 15 mm had a 5-year survival rate of 99% in stages I and II, and 70% in stage III. Patients with no lymph node involvement had a 5-year survival rate of 98% if the tumor size was < 15 mm, and 92% if the tumor size was > 15 mm. Patients with lymph node involvement had a 5-year survival rate of 87-91% (< 15 mm) and 70% (> 15 mm).<sup>13</sup>

The correlation between tumor size and 5-year survival rate, after statistical (log rank) analysis was significant at alpha 0.05. This is also in line with the study by McBride et al (1992), who found a correlation between tumor size and survival of breast cancer patients, with a significance of  $p < 0.006$ .<sup>12</sup>

When Cox bivariate regression analysis is used, the mortality risk for patients with a tumor size of more than 5 cm was 6.612 times (95% CI 5.5; 12.48), greater compared to those with tumor size of less than 5 cm.

## CONCLUSION

The probability of 5-year survival after treatment of breast cancer patients at Dharmais Cancer hospital is 48%, with a median survival of 54 months.

There is a correlation between cancer stage and tumor size and 5-year survival rate. The probability of 5-year survival of breast cancer patients with early stages is higher than that of those with advanced stages. The probability of 5-year survival of breast cancer patients with smaller tumor size is higher than that of those with larger tumours.

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