

Assessment of one-year overall survival among stage III breast cancer patients

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ABSTRACT

Background: The results of a comprehensive diagnosis, combined with the individual's general state, establish the appropriate therapeutic care for breast cancer patients. These management disparities have an impact on clinical outcomes, which may influence patient survival. The evaluation process of breast cancer management is essential as a strategy to boost the therapy's effectiveness in the future year.

Objectives: Assessing survival rate, one-year overall survival, among stage III breast cancer patients.

Methods: An observational study was conducted comprising a retrospective cross-sectional study. Data collected retrospectively from the medical record followed a total sampling technique. This study included patients with breast cancer as a main diagnosis with or without comorbidities and aged ≥ 18 years when undergoing their first diagnosis. Moreover, the exclusion criteria were patients who had incomplete medical record data, undergoing breast cancer treatment at other healthcare facilities, unspecified clinical stage, and patients who had been diagnosed with non-stage III breast cancer. The survival time of the participants is defined as the number of months from initial diagnosis to their last status (alive, died, or loss of follow-up). One-year overall survival was projected using the Kaplan-Meier curve and presented as a percentage with a 95% confidence interval.

Results: Of the 23 patients with stage III breast cancer and the mean age was 57.39 ± 10.417 years. The one-year overall survival for stage III breast cancer was 78.3%. In addition, metastases conditions were associated with worse one-year overall survival compared to patients without metastases (40.0% vs 88.9%, $p=0.028$).

Conclusion: The survival rate of breast cancer patients remains lower than in another recent study from Indonesia. This indicates the requirement of treatment strategies evaluation.

INTRODUCTION

Breast cancer is a complex disease that brings about serious health issues for women around the world. According to International Agency for Research on Cancer (IARC) data, in 2022, the global number of patients hit 2.3 million new cases, and it was the trigger of death for 667,000 people.¹ In 2022, the Global Cancer Observatory (GLOBOCAN) recorded 66,271 new cases of breast cancer.² Breast cancer is a serious health concern in Indonesia, with significant morbidity and mortality rates. Breast cancer is the most frequent form of cancer among Indonesian women, accounting for more than 30% of all female cancer diagnoses in 2020 and around 20% of deaths due to cancer that same year. It is also the most frequent variety of cancer, accounting for more than a third of all cancer cases in women and one-fifth of all cancer cases in the general



population.³ In accordance with data from Basic Health Research in 2023, the Special Region of Yogyakarta is known as one of the provinces in Indonesia with the highest incidence rate of breast cancer, achieving 4.86 cases per 1000 population.⁴ This indicates that breast cancer is a pressing health issue, particularly in regions with higher rates of incidence, and requires focused attention.

Breast cancer is likewise a depiction of a complicated disorder. Understanding clinical complexity, encompassing both biological and non-biological aspects, is critical for managing breast cancer treatment.⁵ The severity levels of breast cancer among individuals are determined by the results of their diagnosis. This level can be determined according to the breast cancer stage and the existence of comorbidities or associated disorders. The results of a comprehensive diagnosis, combined with the individual's general state, establish the appropriate therapeutic care for breast cancer patients. These management disparities have an impact on clinical outcomes, which may influence patient survival.⁶ However, many factors influence breast cancer patients' survival, including socio-demographic factors (age, levels of education, financial status, familial history, and social behavior), tumour pathological and clinical characteristics (tumour size, nodal status, the extent of metastatic disease, clinical stage, tumour location, histology grade), the presence of comorbidities, and the type of treatment used.⁷ These factors play a crucial role in determining both prognosis and treatment effectiveness.

Moreover, the management of breast cancer has evolved over the years with the advent of new diagnostic tools and treatment modalities. Surgical interventions, chemotherapy, radiotherapy, and hormonal therapies, along with more targeted approaches such as immunotherapy and targeted therapy, have all contributed to improving survival rates. However, the impact of these therapies varies significantly depending on the patient's specific characteristics, including the tumour's molecular subtype and the stage at which the cancer is diagnosed.

Breast cancer patients' clinical conditions necessitate long-term therapy and rehabilitation due to their complexity. Breast cancer is a catastrophic disease with the highest expenditures when compared to other types of cancer because of the complexities of its therapeutic management. To achieve the most favourable clinical outcomes for breast cancer patients, the treatment must be optimised, especially for new treatment facilities. New treatment facilities require evaluation while in operation. This evaluation process is essential as a strategy to boost the therapy's effectiveness in the future year. Furthermore, stage III breast cancer is the most frequently diagnosed advanced-stage breast cancer in Yogyakarta, Indonesia. This formed a framework for Academic Hospital Universitas Gadjah Mada's research on assessing survival rate, especially one-year overall survival, among stage III breast cancer patients with different characteristics.

METHODS

Study design

An observational study was conducted comprising a retrospective cross-sectional study design focusing on individuals who were first diagnosed with stage III at the Academic Hospital Universitas Gadjah Mada.

Population and sample

The population was patients diagnosed with breast cancer between April 2022 and October 2022. Patient's data were accessed from the electronic medical record. The participants were recruited using total sampling methods based on the inclusion and exclusion criteria. The inclusion criteria included patients with breast cancer as a main diagnosis with or without comorbidities and aged ≥ 18 years when undergoing first diagnosis. Moreover, the exclusion criteria were patients who had incomplete medical record data, undergoing breast cancer treatment at other healthcare facilities, unspecified clinical stage, and patients who had been diagnosed with non-stage III breast cancer.

Data collection

Data collected retrospectively from the electronic medical record. Patients were followed up until 31st October 2023 to assess their last status (alive, died, and loss of follow-up). The details of the patient's information, diagnosis, and clinical data were extracted from electronic medical records. In the beginning, the medical record units provided the population list based on research needs. The total sample obtained from this population was 23 participants. The following relevant patients' characteristics data were collected, including age, BMI (body mass index), comorbidity, breast cancer stage, tumour size, immunohistochemistry results, recurrent and metastatic status, and types of surgical intervention performed.

The primary outcome of this study was one-year overall survival. The survival time of the participants is defined as the number of months from initial diagnosis to their last status (alive, died, and loss of follow-up) for one year period. To determine predictors of overall survival, the dataset was designated as lifespan data, with the span of survival provided as the time variable. The cancer stage in this study was determined based on the 8th edition of the American Joint Committee on Cancer (AJCC), as recorded in the medical records.⁸ Additionally, tumour size refers to the largest diameter of the tumour as determined from the examination results that categorised into ≤ 2 cm, 3 – 5 cm, and > 5 cm, which are recorded in the medical records. Meanwhile, the recurrence and metastasis status were obtained from the doctor's assessment and statement within the patient note in the medical record during the one-year treatment period, starting from the patient's initial diagnosis, as recorded in the medical records.

Data analysis

A complete dataset was exported into SPSS for analysis. The continuous data were analyzed using univariate analysis and reported as means and standard deviations. The number for ordered categorical data was calculated, and the results were displayed as percentages. Clinical and histological features were documented using frequency and percentage. One-year overall survival was projected using the Kaplan-Meier curve and presented as a percentage with a 95% confidence interval. Cox proportional hazard model regression was utilized to identify variables of survival time which reported with a hazard ratio. A significance level of 5% was adopted.

Ethical statement

This research was conducted in full compliance with ethical standards and was approved by the Faculty Ethics Committee of Medicine, Public Health, and Nursing (FKKMK) at Universitas Gadjah Mada. The ethical approval for this study was granted under the approval number KE/FK/0816/EC, issued on May 15th, 2023. The approval process ensured that the research adhered to ethical guidelines designed to protect the rights, dignity, and well-being of all participants involved in the study. Before the data collection process, permission to access the records was obtained from the research ethics committee and medical record units.

RESULTS

This study included a total of 23 patients with stage III breast cancer with different characteristics (Table 1). Of the 23 patients with stage III breast cancer, the mean age was 57.39 ± 10.417 years, with the mean of BMI was 24.17 ± 3.821 kg/m². It was estimated that 4.3% of stage III breast cancer patients were diagnosed at <40 years of age, 21.7% were diagnosed between 40 and 50 years of age, and the remaining were diagnosed at >50 years of age in our study. Thus, those above 50 years of age accounted almost three-quarters of all participants. Nearly four out of five patients diagnosed with stage IIIB breast cancer, and most presented tumours size between 3 – 5 cm (52.2%), while stage IIIA breast cancer only diagnosed in around 20% patients. Greater than one-half of the patients had human epidermal growth factor receptor 2 (HER2) overexpression, while the other subtype is below 20%, Luminal B, triple negative breast cancer (TNBC), and Luminal A, 17.4%, 13.0%, and 8.7%, respectively.

Table 1. Characteristics of research participants

Characteristics	Total study population (n=23)	
	n	%
Age (year)	57.39 ± 10.417	
BMI (kg/m ²)	24.17 ± 3.821	
Comorbidity		
With comorbidity	7	30.4
Without comorbidity	16	69.6
Stage		
IIIA	5	21.7
IIIB	18	78.3
Tumour Size (cm)		
≤2	5	21.7
3 - 5	12	52.2
> 5	6	26.1
Immunohistochemistry		
Luminal A	2	8.7
Luminal B	4	17.4
TNBC	3	13.0
HER2 overexpression	14	60.9
Recurrent		
Yes	5	21.7
No	18	78.3
Metastatic		
Yes	5	21.7
No	18	78.3
Surgical intervention		
Mastectomy	15	65.2
Lumpectomy	8	34.8

Based on the patient's characteristics (Table 2), patients having larger tumour sizes represent worse one-year overall survival, 100%, 75.0%, and 66.7% for patients with ≤2 cm, 3 – 5 cm, and > 5 cm tumour size, respectively (p=0.202), even though they did not contribute significantly. In addition, metastases conditions were associated with worse one-year overall survival compared to patients without metastases (40.0% vs 88.9%, p=0.028).

Table 2. One-year overall survival of the participants based on patient' characteristics

Characteristics	One year OS (n=23)		HR (95% CI)
	N (%)	p	
Comorbidity			
With comorbidity	6 (85.7)	0.645	11.286
Without comorbidity	12 (75.0)		(9.990 – 12.582)
Stage			
IIIA	4 (80.0)	0.846	11.800
IIIB	14 (77.8)		(11.449 – 12.151)
Tumour Size			
≤2	5 (100.0)	0.202	4.462
3 - 5	9 (75.0)		(4.226 – 5.642)
> 5	4 (66.7)		
Immunohistochemistry			
Luminal A	2 (100.0)	0.460	5.418
Luminal B	2 (50.0)		(0.753 – 39.003)
TNBC	2 (66.7)		2.260
HER2 overexpression	12 (85.7)		(0.205 – 24.924)

Characteristics	One year OS (n=23)		HR (95% CI)
	N (%)	p	
Recurrent			
Yes	3 (60.0)	0.251	10.800 (9.100 – 12.500)
No	15 (83.3)		
Metastatic			
Yes	2 (40.0)	0.028*	5.760 (0.961 – 34.521)
No	16 (88.9)		
Surgical intervention			
Mastectomy	13 (86.7)	0.122	11.867 (11.695 – 12.039)
Lumpectomy	5 (62.5)		

*p < 0.05; OS: Overall Survival; HR: Hazard Ratio

Our study indicated that patients with Luminal B hormone receptor had a lower survival rate (HR 5.418, 95% CI 0.753 - 39.003) than those with TNBC hormone receptor status (HR 2.260, 95% CI 0.205 - 24.924) (Figure 1D). Patients with metastatic breast cancer had a worse survival result (HR 5.760, 95% CI 0.961 - 34.521). Meanwhile, patients who underwent mastectomy surgery had a higher survival rate than those who underwent lumpectomy (HR 11.867, 95% CI 11.695-12.039) (Figure 1G). The one-year OS among stage III breast cancer patients with Luminal A immunohistochemistry results was 100.0%, which was twofold the survival rate of those with Luminal B immunohistochemistry at 50.0% (Figure 1D). Patients with tumour size ≤2 cm had an OS of 100.0%, while tumour size > 5 cm decreased OS to 66.7% (Figure 1E).

DISCUSSION

Our study indicated that patients with Luminal B hormone receptor had a lower survival rate than those with TNBC hormone receptor status. The one-year OS among stage III breast cancer patients with TNBC immunohistochemistry results was 66.7%. TNBC is a particular subtype of breast cancer, accounting for around 10-20% of all breast cancer subtypes worldwide.¹⁶ The TNBC is characterised by the lack of estrogen receptors (ER), progesterone receptors (PR), and HER2 amplification, making it more challenging to treat compared to other subtypes. The previous study showed an association between TNBC subtype and greater tumour size, greater number of positive axillary lymph nodes, worse clinical stage, and advanced histological grade that significantly shortened the survival of TNBC patients, which were inconsistent with a recent study.¹⁶ These discrepancies can be brought about by a variety of variables, including the therapy used and the patient's health status. Clinical outcomes among TNBC patients improve as treatment is intensified, including greater polychemotherapy and immunotherapy. Immunotherapy, in particular, is a promising avenue for TNBC, as it targets the immune system to recognise and fight cancer cells more effectively. The use of checkpoint inhibitors, which block proteins that prevent immune cells from attacking cancer cells, has demonstrated encouraging results in improving survival in patients with advanced TNBC. As a result, personalised treatment plans based on the specific clinicopathological features of each patient are becoming increasingly important in improving survival rates, especially for aggressive subtypes like TNBC.^{11,12}

Our study findings reveal a worse one-year overall survival among patients with Luminal B hormone receptors, followed by TNBC hormone receptors. However, other studies clearly stated that breast cancer with TNBC expression has the worst impact and severity compared with other types, including Luminal A, Luminal B, and HER2 overexpression.¹³ Triple-negative breast cancer (TNBC) is a breast cancer subtype without the estrogen receptor, progesterone receptor, and HER-2 expression. Hence, they are not responsive to endocrine and targeted HER-2 treatment. Moreover, the TNBC subtype demonstrates poor prognosis, is highly invasive, and is potent for metastasis. Additionally, these poor conditions are coupled with limited therapeutic options in breast cancer patients with TNBC subtypes. This condition describes why TNBC subtypes have a shortened survival time and lower quality of life.¹⁴

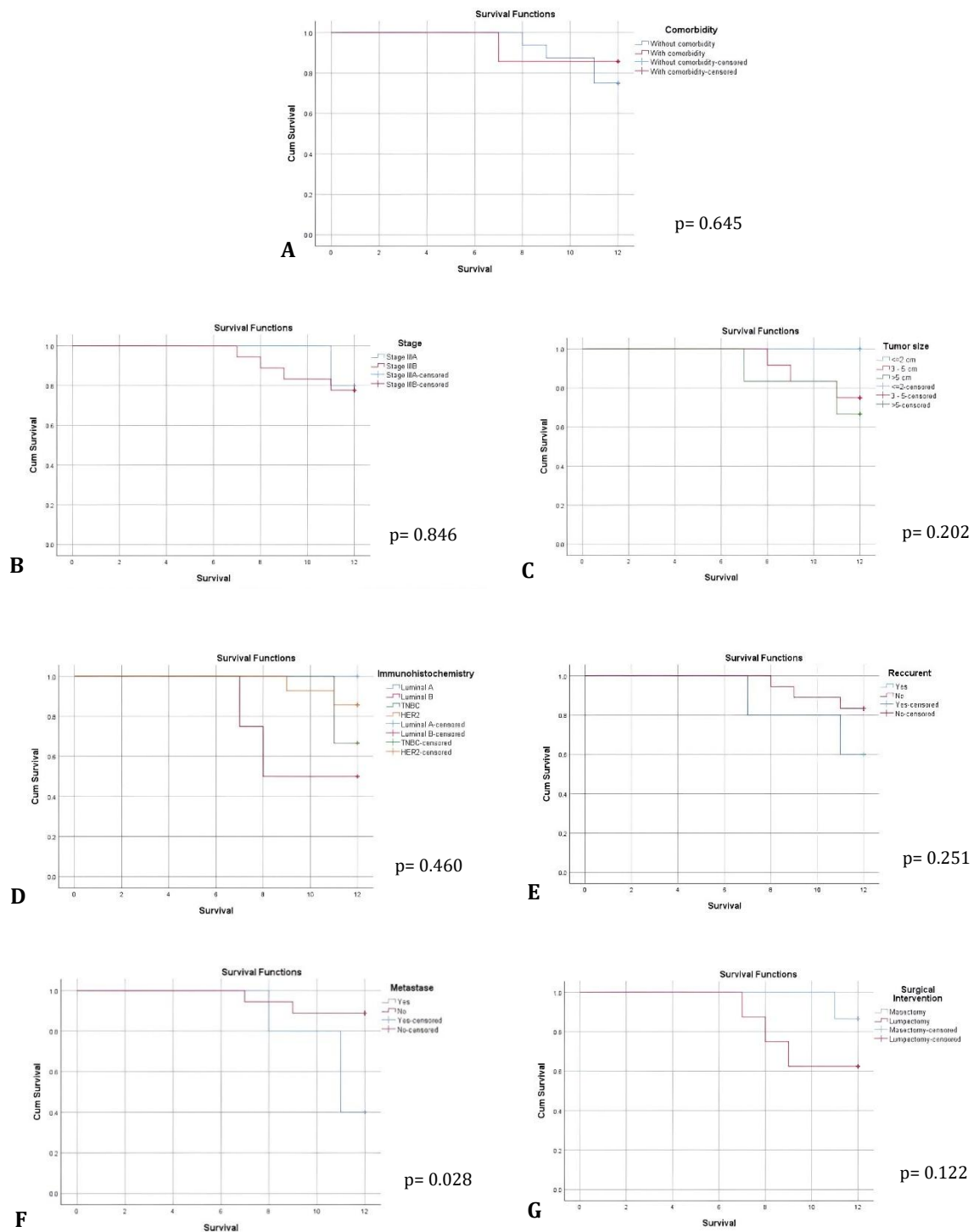


Figure 1. Graph of statistical analysis results with Kaplan-Meier method that shows survival probability by participants' characteristics. A. Survival analysis within comorbidity characteristics; B. Survival analysis within cancer stage characteristics; C. Survival analysis within tumour size characteristics; D. Survival analysis within immunohistochemistry characteristics; E. Survival analysis within recurrent status characteristics; F. Survival analysis within metastases characteristics; G. Survival analysis within surgical intervention characteristics.

In this study, a total of 4.3% stage III breast cancer patients were diagnosed at <40 years of age, 21.7% were diagnosed between 40 and 50 years of age, and the remaining were diagnosed at >50 years. Thus, those above 50 years of age accounted almost three-quarters of all participants. However, this result differs from findings described by previous studies from Korea, despite being similar to a previous study report from Indonesia.^{15,16} The recent study demonstrated the negative impact of young age on recurrence-free survival (RFS) and overall survival (OS), especially for the luminal subtype.^{16,17} There have been several studies on the impact of aging on breast cancer, particularly in the Asian area. Young age at diagnosis has frequently been recognised as a poor prognostic factor, linked to poor differentiation, a high proliferation index, an increased risk of lymphovascular invasion (LVI), and reduced estrogen receptor expression. This consistently leads to a poor prognosis for young people who have been diagnosed with cancer, particularly breast cancer.¹⁶ In fact, the majority of breast cancer patients in Asian countries are diagnosed at a younger age of 40-50 years old, while Westerners are diagnosed at 60-70 years old. This certainly raises concerns of a poorer prognosis for the Asian breast cancer patient population.¹⁸

The majority (52.2% and 60.9%) of patients diagnosed with stage III breast cancer had 3 – 5 cm tumour size and HER-2 overexpression type, quite different to the findings in Malaysia and Nigeria regarding the clinicopathological profiles.^{13,14} The clinicopathological profiles are important to determine the prognosis of breast cancer patients. These profiles, which include factors such as tumour size, lymph node involvement, histological grade, and receptor status, are essential for assessing the aggressiveness of the cancer and predicting overall survival. The clinicopathological characteristics of breast cancer not only guide treatment decisions but also provide critical insights into the potential outcomes and long-term prognosis of patients.¹⁹ Additionally, clinicopathological profiles from breast cancer patients remain a dominant factor affecting overall survival.¹⁷ Lastly, subtype-related breast cancer, which is categorised to Luminal A, Luminal B, TNBC, and HER2 overexpression, appears to have distinct effects on disease progression and severity.¹⁷

Our study findings show the age range of our patients was 46–68 years. The mean age at presentation was 57.39 ± 10.417 years. These are comparable with the previous findings. In Indonesia, the age-standardised incidence and death rates for breast cancer are 44 and 15 per 100,000 people, respectively.²⁰ In this nation, breast cancer is frequently discovered in advanced stages with poor survival rates.^{21,22} The incidence of breast cancer varies greatly across Asia and remains considerably lower than in Western countries, although Asia's proportional contribution to global breast cancer rates is growing rapidly in line with socioeconomic development. However, Asia has significantly greater mortality-to-incidence ratios than Western countries.¹⁸ Breast cancer survival rates are heavily influenced by timely and correct diagnoses, as well as the quality of treatment and care provided.²³ This is similar to this study report, where breast cancer cases in Yogyakarta were dominated by stage III breast cancer as an initial diagnosis, with the one-year overall survival for stage III breast cancer was 78.3%. This survival rate remains lower than in another recent study from Indonesia and other countries in the Southeast Asia region. According to a recent annual report from Dharmas Cancer Hospital in Indonesia, the 1-year survival rates for stage III breast cancer were 84.8%.²⁴ In addition, another study reported the survival rate data from five countries in Southeast Asia that present a higher one-year survival rate up to 88.8%, around 70% at five years, and nearly 50% at 10 years for breast cancer individuals.²⁵

Survival evaluation is commonly utilised in oncology, particularly for breast cancer assessment, because it offers details regarding the efficacy of both diagnosis and therapy. Furthermore, when applied to data from populations, it can help discover particular aspects of disease behaviour and prognostic markers.²⁶ At the same time, it can assist health facilities in evaluating their implemented healthcare services. Breast cancer patients could benefit from the survival rate evaluation from a larger population to support clinicians' decisions on their treatment process. Adequate evaluation findings can serve as a reference for estimating each

survival rate based on patient factors, such as disease characteristics and procedures performed. When a clinician understands a patient's projected survival rate based on their individual characteristics, they can determine the most appropriate actions or treatment plan to optimise the patient's quality of life and overall health for the remainder of their life.

Patients having larger tumour sizes represent worse one-year overall survival, even though they did not contribute significantly. In addition, metastases conditions were associated with worse one-year overall survival compared to patients without metastases (40.0% vs 88.9%, $p=0.028$). The prognosis for patients with metastatic breast cancer varies according to their characteristics, such as hormone receptor status, comorbidities, lymph node involvement, and tumour size. Overall, people with metastatic breast cancer have been shown to have a considerably shorter survival duration compared to individuals without metastatic disease.²⁷ An earlier investigation from Sweden, based on national registry data, reported an approximate overall survival of 2.5 years and a 5-year survival rate of 30% for metastatic breast cancer.²⁸ In contrast, a study from the United States found a 5-year survival rate of 91% for patients with non-metastatic breast cancer.²⁹ Multiple variables, particularly demographics, clinic, histopathological features, and treatment, may contribute to breast cancer patients' survival rates.³⁰

Unfortunately, our study did not involve treatment regimen evaluation between the population due to the limited number of patients undergoing the entire therapy course. Furthermore, despite the difficulty in assessing treatment suggestions due to a lack of available information, the analysis took into account the primary predictive elements that could impact the adoption of these therapies. The results, on the other hand, highlighted the crucial role of information produced by health services, which allows for a better understanding of challenges, particularly in the public health service responsible for the majority of Yogyakarta's cancer care, as well as the establishment of relevant recommendations to support breast cancer control practices and improve service quality.

Although this study shares similar results with previous research in Indonesia, it presents different variables and provides recommendations for overcoming specific barriers and improving healthcare quality, especially in breast cancer therapy. Furthermore, the study's findings are limited to one health facility, the Academic Hospital Universitas Gadjah Mada in Yogyakarta, making it insufficient to generalise the survival rate, especially one-year overall survival, among stage III breast cancer patients, across all health facilities in Indonesia. Further studies with larger sample sizes and longer follow-up periods are recommended to validate these findings and explore other potential prognostic factors, including treatment response, molecular subtypes, and socioeconomic influences.

CONCLUSION

The one-year overall survival of stage III breast cancer patients was 78.3% which remains lower. Among several prognostic factors, metastasis condition was the only significant predictor for a one-year survival outcome. Further studies with a multicenter design and longer follow-up periods are recommended to validate these findings and explore other potential prognostic factors.

CONFLICT OF INTEREST

No existing or potential conflict of interest relevant to this article was reported.

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DATA AVAILABILITY

Authors are required to include a data availability statement in their manuscript. The data

availability statement should clearly explain where the data supporting the research findings can be accessed. If the data are not publicly accessible, the author must provide a clear reason and explain how to obtain access if requested.

SUPPLEMENTAL DATA

Detailed data that are not included in the article may be available upon request from the corresponding author

AUTHOR CONTRIBUTIONS

D, IPS, SW, NAM, and SLA: concepts and design the research. IPS and FR: data analysis and data interpretation. All authors contributed to manuscript preparation, review, and approval. FR: Manuscript editing.

DECLARATION OF USING AI IN THE WRITING PROCESS

The authors did not use artificial intelligence (AI) or AI-assisted technologies in the writing or editing of this manuscript.

LIST OF ABBREVIATIONS

IARC: Agency for Research on Cancer; AJCC: American Joint Committee on Cancer; BMI: Body mass index; CI: Confidence interval; GLOBOCAN: Global Cancer Observatory; HER2: human epidermal growth factor receptor 2; HR: Hazard ratio; IARC: International Agency for Research on Cancer; LVI: lymphovascular invasion; OS: Overall survival; RFS: recurrence-free survival; TNBC: triple negative breast cancer; er: estrogen receptors; PR: progesterone receptors

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