

Research

The Effect of Body Mass Index on Five Years Progression Free Survival in Breast Cancer

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Abstract

Background Breast cancer is the type of cancer that has the highest prevalence. Breast cancer growth is related to nutritional status. Nutritional status is assessed based on measurements of BMI Body Mass Index (BMI) and obesity is a factor that plays a role in the growth of cancer cells.

Objective To investigate the effect of BMI on the five-year progression-free survival (PFS) of breast cancer patients

Methods A retrospective cohort study using observational methods on 82 female patients with breast cancer at Bethesda Hospital, Yogyakarta.

Results A total of 82 medical records of breast cancer patients were collected at Bethesda Hospital Yogyakarta. A total of 71 patients (86.6%) were still alive, while 11 have died. This study found an average progression-free survival of BMI category $<25 \text{ kg/m}^2$ 78,5 months while the BMI $\geq 25.0 \text{ kg/m}^2$ 80,9 months (HR 2,057, 95% CI: .457–2.491). In addition, BMI and other prognostic variables did not have a significant relationship with progression-free survival in breast cancer patients ($p = 0.114$).

Conclusion In this study, Body Mass Index was not associated with the 5-year progression-free survival of breast cancer patients.

Keywords: BMI, breast cancer, progression-free survival

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Introduction

Cancer is one of the non-communicable diseases with a high prevalence in the world and in Indonesia. The prevalence of breast cancer reached 11.6% of all cancer cases in 2018. The prevalence of breast cancer deaths reached 6.6% of all cancer deaths. Data from the Indonesian Ministry of Health in 2019, breast cancer cases in Indonesia had 42.1 cases per 100,000 population, and the incidence of death was 17 cases per 100,000 population.¹

The nutrition status measured by Body Mass Index (BMI) of more than 25 is related to breast cancer risk factors.² Body Mass Index is one of nutritional status measurement that calculated from weight in kilograms divided

with the height in meter square. In previous research found that the overweight and obesity patient is a predictor of breast cancer risk in post menopause women although it can be a protective factor in premenopausal. Obesity is a body condition in which there is an excessive accumulation of fat in body tissues.³ Obesity is one of the factors that play a role in the growth of cancer cells.² The prevalence of obesity increased from 2010 to 2013, reaching 15.4%, while the prevalence of cancer caused by obesity reached 7-41%.³ Numerous studies have examined the relationship between the BMI with the survival of patient with breast cancer. Many of these studies found that higher BMI associated with low survival.⁴ This study we presented analysis

association between BMI with progression free survival in breast cancer.

Methods

A retrospective cohort study, with an observational method on all female patients with breast cancer at Bethesda Hospital Yogyakarta from January 1, 2013, to December 31, 2016. Research was started in May 2021 to September 2021 at Bethesda Hospital Yogyakarta, we have eighty-two patients that met our criteria.

Inclusion criteria was breast cancer patients under 85 years of age. Exclusion criteria was incomplete medical record data. The independent variables in this study were all breast cancers progression free survival. The dependent variable of this study that would be analyzes was Body Mass Index. BMI classified as $<25\text{kg/m}^2$ and $\geq 25\text{kg/m}^2$. It is count from the weight divided with the height in meter square. While the progression free survival is the duration of time between the time treatment starts to the first assessment of disease progression or death. If patient die or cure it will note as an event. This study used univariate, bivariate, and multivariate data analysis. The distribution of each variable described by a univariate analyzes. The relationship between BMI and the independent

variables of breast cancer patients analyzes with bivariate analyzes. The trend of disease progression related to the BMI analyzed using Kaplan Meier. Multivariate analyzes using cox regression survival to analyzes PFS with the variables in this study.

Health Research Ethics Committee Bethesda Hospital Yogyakarta have approved this study, number 52/KEP-RSB/VI/21.

Results

A total of 182 medical records of breast cancer patients at Bethesda Hospital Yogyakarta in the last 5 years, only eighty-two of medical records could be followed up. The rest could not be included in the study due to the lack of complete data on stage, grade, molecular subtype, and loss of follow-up.

Of the 82 subjects, most of the patients were > 50 years old (65.9%). About 51 people (62.2%) had stage III cancer and 31 people (37.8%) had stage II cancer. The BMI most found is the normal category at 47.6%. The most subtypes were luminal A by 32.9%, the most histological type was ductal type at 89.0%, the most grade was grade 3 at 62.2%. Of the 82 subjects, 71 people (86.6%) were still alive, while 11 people (13.4%) had died (Table 1).

Table 1. Baseline Characteristics of Respondents

	Variable	Frequency	Percentage
Age	<50 years	28	34.1
	>50 years	54	65.9
Stage	Stadium II	31	37.8
	Stadium III	51	62.2
BMI	Underweight ($< 18,5\text{ kg/m}^2$)	3	3.7
	Normal ($\geq 18.5 - < 24.9\text{ kg/m}^2$)	39	47.6
	Overweight ($\geq 25.0 - < 27\text{ kg/m}^2$)	23	28.0
	Obese ($> 27,5\text{ kg/m}^2$)	17	20.7
Molecular Subtype	Luminal A	27	32.9
	Luminal B	22	26.8
	HER2+	23	28
	TNBC	10	12.2
Grade	Grade 1	4	4.9
	Grade 2	27	32.9
	Grade 3	51	62.2
Histological type	Ductal	73	89.0
	Lobular/ND	9	11
Disease progress	Censored	71	86,6
	Event	11	13,4

Histological type	Ductal	65	79,2	8	9,7	14,508
	Lobular/ND	6	7,3	3	3,6	
Stage	Stage II	30	36,5	1	1,2	2,479
	Stage III	41	50	10	12,1	

Because patients with a BMI <18.5 kg/m² were very few, in the next analysis the BMI category was divided into <25 kg/m² (for underweight and normal categories) and ≥25.0 kg/m² (for overweight and obese categories). It is found that among the prognostic variables, neither BMI nor other prognostic variables have a significant relationship with progression free survival in

breast cancer patients. This study obtained an average PFS of BMI category <25 kg/m² 78,5 months while the BMI ≥ 25.0 kg/m² 80,9 months (HR 2,057, 95% CI: .457–2.491). Figure 1 shows the progression free survival that the event mostly occurs in the ≥ 25.0 kg/m² category and the cum survival is lower than the <25 kg/m² category.

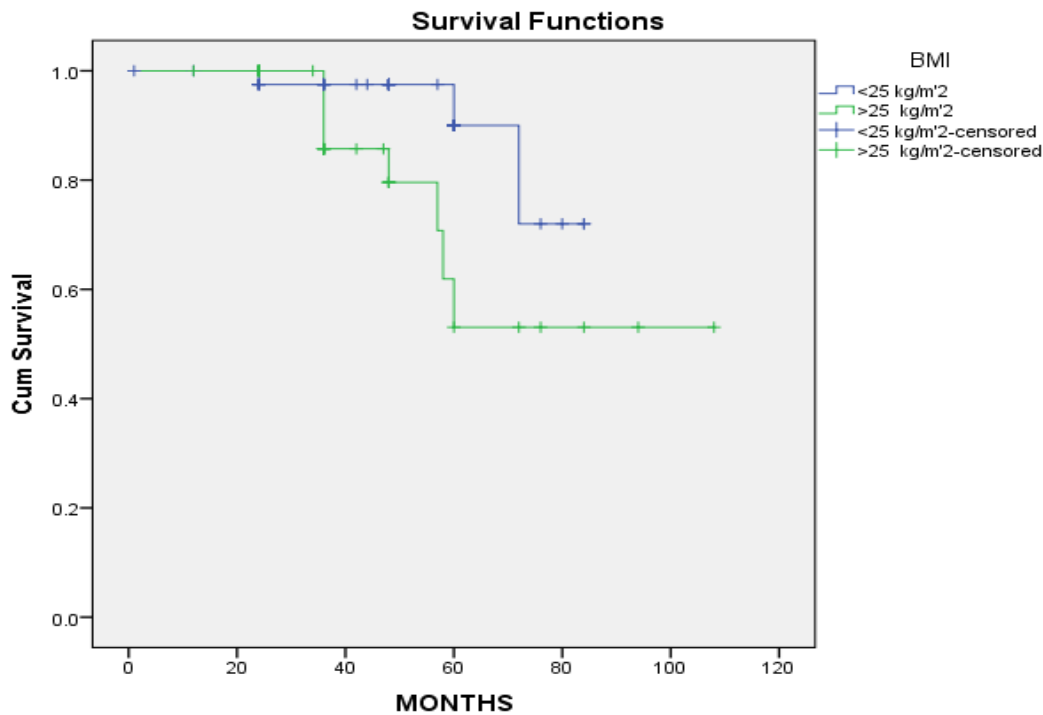


Figure 1. The trend of diseases progression with Body Mass Index

Discussion

Currently, research related to progression-free survival continues to be intensified because it is associated with the duration of time in which the disease does not progress after therapy, and it affects the quality of life and the follow-up of therapy in patients with cancer. Many studies have been conducted to look for the relationship between breast cancer and obesity. Several studies have shown that a low BMI increases the risk of breast cancer in the pre-menopausal period, while an excess BMI

increases the risk of breast cancer in the postmenopausal period. In addition, several studies have also investigated the relationship between BMI and breast cancer prognosis/survival but have got different results.⁵

In this study, there was no relationship between BMI and age, tumor molecular subtype, histopathological type, grade, or stage of breast cancer. The results are different from the research conducted by Cihan in 2014 in Turkey, which found that BMI has a

significant relationship with menopausal status, histological type, and chemotherapy. Research by Turkoz et al. (2013) also found BMI to have a significant relationship with lymph vascular invasion and tumor molecular subtypes.⁶

This study obtained an average PFS of BMI category $<25 \text{ kg/m}^2$ 78,5 months while the BMI $\geq 25.0 \text{ kg/m}^2$ 80,9 months (HR 2,057, 95% CI: .457–2.491). This shows that with a higher BMI the chance of an event occurring was 2 times higher than the event with a lower BMI. Although, Neither BMI nor other prognostic variables had a significant relationship with progression-free survival in breast cancer patients ($p=0,114$). This result is in line with the research obtained by Cihan which showed that there was no effect on BMI ($p = 0.197$). The smaller sample size, genetic characteristics of the patient population, and potential weight changes during follow-up may explain our results regarding PFS.⁷

Although the results were not statistically significant, it was seen that the PFS in the BMI $\geq 25 \text{ kg/m}^2$ group was slightly higher than in the BMI $<25 \text{ kg/m}^2$ group. This result is in line with the research by Safarudin et al. in 2014 but differs from several previous studies which found that a high body mass index has a lower survival rate.^{5,7} In a study involving African TNBC patients, being overweight was significantly associated with breast cancer mortality (HR 2,903, 95% CI: 1,551–5,432) and recurrence (HR 1,899, 95% CI: 1.05–3,433).⁸ The above may be caused by differences in the characteristics of the respondents used in the study. In another study, it was found that most patients with an overweight-obese BMI tend to have worse condition than patients with a low-normal BMI. Whereas in this study, patients with normal-low BMI tend to have high grade, stage III, and luminal B subtypes and more TNBC than those with high BMI. Based on these characteristics, the low BMI group has a greater chance of experiencing recurrence, metastasis, or death.² In review and meta-analysis study, BMI significantly associated with breast cancer breast cancer mortality. Compared to normal BMI obese, overweight, and underweight breast cancer patients for before diagnosis, <

12 month and ≥ 12 month after diagnosis identified have worse mortality relative risk. Co-morbid condition related to worse risk.⁹

Body mass index is predicted to be a prognostic factor/assessment of breast cancer survival through the theory that many metabolic and hormonal pathways are involved in the relationship between obesity and prognosis. Increased peripheral estrogen synthesis in adipose tissue and reduced sex hormone-binding globulin in postmenopausal patients with a higher BMI may be responsible for the poor breast cancer prognosis. This is due to an increase in aromatase activity, which can induce and stimulate the growth of abnormal breast cells. Women with higher BMIs may not fully benefit from aromatase inhibitors in postmenopausal women. Women with higher BMIs and older age may withstand comorbidities and reduced doses of chemotherapy drugs because of concerns about toxicity, and women with higher BMIs may exhibit elevated levels of insulin, insulin-like growth factors, and hormones with strong mitogenic activity. Hyperadiposity, locally associated with chronic low-grade inflammation. The obese patients harbor inflamed adipose tissue, resembles chronic tissue injury.¹⁰ In addition, the paracrine secretion of interleukin-6 and tumor necrosis factor-alpha and the formation of a pro-inflammatory microenvironment can promote tumor growth, metastasis. Several cytokines produced by obese adipose tissue can promote breast cancer progression through upregulation of breast cancer stem cells, inhibit antitumor immunity and stimulate breast tumor angiogenesis. So, a higher BMI can lead to the development of breast cancer.⁵ Another study also reported that obese patients were more likely to receive reduced doses of chemotherapy compared to normal weight women, which was associated with a poorer prognosis.⁷

This study has not been able to prove that BMI has a relationship with the 5-year progression free survival of breast cancer patients at Bethesda Hospital. This study also has limitations. Firstly, there are differences in the definition of BMI categories in various populations regarding overweight and

obesity. Second, changes in body weight may occur during the therapy process, so it needs to be monitored continuously to ensure the effect of changes in BMI on the prognosis of breast cancer. This study has a small sample compared to other studies. It is hoped that in the future, there will be research that can discuss the interaction of BMI with other prognostic factors such as blood tests and other clinical factors.

Conclusions

In this study, Body Mass Index was not associated with the 5-year progression free survival of breast cancer patients.

Conflict of Interest

All authors have no conflict of interest

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