

Factors Associated with Malignant Breast Tumors Among Women Diagnosed with Breast Tumors at Campur Darat Hospital, Tulungagung

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Article Info

Article history:

Received: April 24, 2026

Revised: July 19, 2026

Accepted: July 28, 2026

Published : July 31, 2026

Keyword:

Menstruation; Body Mass Index;
Breast Neoplasm; Breast Cancer;
Menopausal status

How to cite:

Putra YD, Tristifany A, Rai WG.
Factors Associated with
Malignant Breast Tumors Among
Women Diagnosed with Breast
Tumors at Campur Darat
Hospital, Tulungagung. Jurnal
Bedah PABI : The Indonesian
Journal of Surgery. 2026;1(1):1–
9.

ABSTRACT

Background : Breast tumor pathology is influenced by multiple factors, including menopausal status and body mass index (BMI). Menopausal status is associated with changes in endogenous estrogen exposure, while excess BMI is associated with chronic inflammation, altered adipokine secretion, and insulin resistance, all of which may contribute to breast tumor malignancy. This study aimed to identify factors associated with malignant breast tumors among women diagnosed with breast tumors at Campur Darat Hospital, Tulungagung.

Methods : This descriptive analytical study employed a cross-sectional design. Data were collected from electronic medical records of female patients with histopathologically confirmed breast tumors treated at Campur Darat Hospital, Tulungagung, between March 2023 and October 2025. Bivariate analysis was performed using the chi-square test or Fisher's exact test, as appropriate. Multivariable binary logistic regression analysis using the Enter method was performed to identify factors independently associated with breast tumor type (benign versus malignant).

Results and Discussion: In the multivariable analysis, age was independently associated with malignant breast tumors (adjusted OR [aOR] = 1.220, 95% CI: 1.155–1.290; $p < 0.001$). BMI also remained significantly associated with malignant breast tumors, with each 1 kg/m² increase associated with a 31.5% increase in the odds of malignancy (aOR = 1.315, 95% CI: 1.120–1.545; $p = 0.001$). Menopausal status remained significantly associated with breast tumor type after adjustment (aOR = 0.214, 95% CI: 0.051–0.898; $p = 0.035$), whereas hormonal contraception history and family history of malignancy were not significantly associated with breast tumor type.

Conclusion : Age, BMI, and menopausal status were independently associated with breast tumor type among women diagnosed with breast tumors. These findings suggest that both metabolic and reproductive factors contribute to the differentiation between benign and malignant breast tumors.



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INTRODUCTION

A tumor (neoplasm) is an abnormal mass caused by a higher rate of cell division than cell death. Tumors can be classified as benign and malignant. Benign tumors are primary tumors that do not invade other parts of the body and tend to grow slowly. Malignant tumors (cancer) are tumors that grow uncontrollably and can spread rapidly to surrounding areas or areas far from their primary location.¹ Breast tumors are a fairly common complaint, although the majority of reported cases are benign.² Palpable breast tumors are highly likely to be malignant.³

Breast cancer is one of the most common types of malignant tumors found in women. This tumor originates from uncontrolled cell growth in the ductal and lobules of the breast.⁴ In 2022, an estimated 2.3 million women will be diagnosed with breast cancer after puberty, with the number increasing with age. Data from 2022 indicate that breast cancer is known to cause 670,000 deaths

worldwide.⁵ In Indonesia, breast cancer ranks first among cancers in women, with 66,271 (30.1%) cases. This disease ranks third in mortality with 22,598 (9.3%) deaths.⁶

Breast cancer risk is closely linked to estrogen exposure. A study of 263 breast cancer patients and 457 non-breast cancer patients in China from 2009 to 2011 found that short menstrual cycles and postmenopausal status were positively associated with breast cancer incidence ($P < 0.001$). Perimenopausal women had a three-fold higher risk of breast cancer, while postmenopausal women had a five-fold higher risk compared to premenopausal women.⁷ A meta-analysis and systematic review of reproductive and menstrual factors on breast cancer risk in Iran also found a positive association between menopausal status and breast cancer incidence (OR = 1.60 95% CI: 1.18–2.17).⁸

Excessive Body Mass Index (BMI), also known as overweight or obesity, is also a risk factor for breast cancer in women. Increased BMI and increased adipose tissue can lead to chronic inflammation and insulin resistance. This inflammatory condition leads to increased circulating cytokines, leptin, and insulin. These factors play a role in the development of breast cancer.⁹ From 1990 to 2022, the prevalence of obesity in women increased from 4.8% to 18.5%. An estimated 504 million women are obese.¹⁰ A population-based cohort study of 15,055 women in China concluded that women with a BMI $> 24 \text{ kg/m}^2$ and a family history of cancer had a 2.06-fold increased risk of developing breast cancer.¹¹

Risk factor analysis plays a role in preventing and raising awareness of breast tumors, particularly in women. Understanding risk factors is expected to improve preventive efforts, which in turn can reduce the incidence of breast cancer in women. The purpose of this study was to determine the association between menopausal status, BMI, and breast tumor type (benign versus malignant) among female patients diagnosed with breast tumors at Campur Darat Hospital, Tulungagung.

RESEARCH METHODS

This descriptive analytical study employed a cross-sectional design. The aim of this study was to identify factors associated with malignant breast tumors among women diagnosed with breast tumors at Campur Darat Hospital, Tulungagung, with a particular focus on menopausal status and body mass index (BMI). The study population comprised all female patients with breast tumors confirmed by histopathological examination who were treated at Campur Darat Hospital, Tulungagung, between March 2023 and October 2025. Additional clinical data were obtained from medical records. Samples were selected using purposive sampling. The inclusion criteria were female patients with breast tumors who had complete information on age, BMI, hormonal contraception history, menopausal status, family history of malignancy, physical activity, and histopathological findings. Patients with incomplete data for any of these variables were excluded.

Data were analyzed using SPSS version 27.0. Bivariate analysis for categorical variables was performed using the chi-square test when its assumptions were met; otherwise, Fisher's exact test was used. Variables considered clinically relevant or potential confounders, including age, body mass index (BMI), menopausal status, hormonal contraception history, and family history of malignancy, were entered simultaneously into a multivariable binary logistic regression model using the Enter method to identify factors independently associated with breast tumor type (benign versus malignant). Age and BMI were analyzed as continuous variables. Breast tumor type was the dependent variable and was coded as benign (1) and malignant (2). A two-sided p value of < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Total sample size of 282 patients meeting the inclusion criteria. Table 1 shows the frequency distribution of characteristics based on age, BMI, contraceptive use history, menopausal history, family history of malignancy, physical activity history, breast tumor location, and breast tumor classification (benign/malignant).

In this study, there were 55 (91.7%) benign tumor patients aged <30 years, while there were 5 (8.3%) malignant tumor patients. In the 31- 40 age group, there were 12 (41.4%) benign tumor patients, while there were 17 (58.6%) malignant tumor patients. In patients aged 41 - 50 years, there were 9 (13.6%) benign tumor sufferers and 57 (86.4%) malignant tumor sufferers. In patients aged 51 - 60 years, there were 4 (6.3%) benign tumor sufferers and 60 (93.8%) malignant tumor sufferers. Malignant tumors were most commonly found in those over 60 years of age, namely 61 (96.8%), while this age group had the fewest number of benign tumors, only 2 (3.2%). The results of this study differ from previous studies. Research at Cipto Mangunkusumo Hospital from 2010 to 2014 showed that the highest number of breast cancer cases was found in the 40-49 age group.¹² Similar research results were also obtained in Norway, where the age range of breast tumor sufferers was 40-49 years (75%).¹³ A cross-sectional study of breast cancer incidence in Yogyakarta from 2008 to 2018 found that the average age of cancer patients was 50-53 years, with less than 10% of cases found in those under 30 years of age. The peak incidence of breast cancer was in the 60-64 age group.¹⁴

Age is a risk factor for breast cancer, especially in women under 50.¹⁵ Research at Wengaya Hospital, Denpasar, from 2019 to 2022 found a significant association between age and the incidence of benign and malignant breast tumors. With age, an imbalance occurs in DNA repair and damage mechanisms, resulting in the accumulation of damaged DNA. The longer a person is exposed to carcinogens, the lower the amount of IFN- γ . Consequently, NK cells and cytotoxic T cells use the ineffective perforin pathway to detect and fight cancer cells.¹⁶ Aging also causes epigenetic changes, such as DNA methylation, histone modification, and chromatin remodeling. These processes are crucial for regulating gene expression and cell function. Aging also leads to "stem cell exhaustion," which disrupts tissue regeneration and repair. This condition allows tumor cells to more easily proliferate, invade, and develop resistance to therapy. With age, autophagy function, particularly in lysosomes, also declines. This leads to increased cell damage and genomic instability.¹⁷

In the benign tumor group, the BMI results showed that 61 people (41.8%) were in the normal category and 21 people (15.4%) were overweight/obese. This condition is slightly different from the malignant tumor group, where 85 people (58.2%) were found to be overweight/obese. A study at Dr. Soetomo Hospital in Surabaya was conducted to compare the BMI of normal patients with 59 breast cancer respondents and 59 controls. In the breast cancer group, 50.8% were found to be overweight, 30.5% had a normal BMI, and 11.9% were obese. These results are in contrast to the control group, where 55.95% were found to have a normal BMI, 32.2% were overweight, and 10.2% were obese.¹⁸

BMI is closely related to lifestyle factors, such as diet and physical activity. This study found that 182 (70.8%) patients with malignant tumors did not exercise regularly, while only 18 (72%) did. This condition was also found in patients with benign tumors, where 75 (29.2%) did not exercise regularly, while only 7 (28%) did. A literature review on the impact of physical activity in reducing mortality in postmenopausal breast cancer patients concluded that physical activity is associated with a better prognosis. Physical activity has a positive impact on general health and fitness, as well as specifically in cases of breast tumors. Physical activity guidelines recommend 75–150 minutes per week of moderate to vigorous intensity. Physical activity plays a role in preventing the emergence of cancer cells through cellular mechanisms, namely mitochondrial repair and reduced oxidative stress. Resistance physical activity helps eliminate and repair damaged mitochondria, increasing their volume and activity, and protecting against cancer cell progression and metastasis. Physical activity also increases the effectiveness of antioxidant enzymes, thereby preventing the effects of cellular damage.¹⁹

In breast cancer patients, physical activity can improve quality of life and reduce mortality rates through several mechanisms, 1) increasing mitochondrial biogenesis and function which leads to a decrease in the cardiotoxic effects of cancer therapy, 2) increasing oxygen transport throughout the body, thereby increasing fatty acid oxidation and reducing chronic inflammation, 3) strengthening bones by increasing osteoblasts through decreasing sclerostin expression in bones during endocrine therapy.²⁰

In the benign tumor group, 43 people (26.2%) were using contraception, while in the malignant tumor group, 121 people (73.8%) were. In the benign tumor group, only 33 people (33.1%) were not using contraception, while in the malignant tumor group, 79 people (66.9%). A six-month study at the

Oncology Teaching Hospital in Baghdad concluded that breast cancer patients were mostly users of oral contraceptives (combination pills) (49%). The risk of breast cancer was also found to be 73% higher in users of oral contraceptives compared to those who did not use oral contraceptives.²¹

A total of 75 people (42.6%) in the benign tumor group were still menstruating, only 7 people (6.6%) had gone through menopause. In the malignant tumor group, 101 people (57.4%) were still menstruating and 99 people (93.4%) had gone through menopause. The pathogenesis of breast cancer is closely related to estrogen. This hormone plays a role in the development of ductal components, fat deposition, and connective tissue in the breast.²² Breast cells that have been exposed to mutagens can undergo a progressive process that ultimately leads to invasion and metastasis.²³ Breast cancer incidence data indicate that women who have not entered menopause have a greater risk of breast cancer than those who have.¹⁵

A family history of malignancy is also frequently associated with breast cancer. In this study, a family history of malignancy was found in 18 (25.7%) patients in the benign tumor group and 52 (74.3%) in the malignant tumor group. Meanwhile, 64 (30.2%) patients with benign tumors had no family history of malignancy. In the malignant tumor group, 148 (69.8%) patients had no family history of malignancy. This finding is similar to a 2021 study at Dr. Mohammad Hoesin General Hospital in Palembang, which found that the majority (63%) had no family history of malignancy.²³

In this study, the most common location of malignant tumors was on the left side in 121 patients (75.2%), while in 79 patients (66.4%) the right side. Benign tumors were found on the left side in 40 patients, and on the right side in 40 patients, and two patients had benign tumors on both sides of the breast. A study of 881,320 breast cancer patients concluded that breast cancer is more common on the left side than on the right. Although there are no differences in histopathological characteristics, left-sided breast cancer has a worse outcome than right-sided breast cancer. This is because E2F target gene factors, G2M checkpoint, mitotic thread, and MYC target genes are more commonly found on the left side than on the right (Abdou 2022). Another study of 92 breast cancer patients reported a better outcome if cancer affects the right breast. The left breast is known to have excess expression of HER2 (human epidermal growth factor 2), VEGF A (vascular endothelial growth factor), a lower anti-angiogenic ratio, and increased PAI-1 (plasminogen activator inhibitor). Lymph node metastases are also more common in left-sided breast cancer²⁴

Table 1. Respondent Characteristics

Characteristic	Benign Tumor		Malignant Tumor		Total
	n = 82	%	n = 200	%	n
Age					
≤ 30 years	55	91,7	5	8,3	60
31 – 40 years	12	41,4	17	58,6	29
41 – 50 years	9	13,6	57	86,4	66
51 – 60 years	4	6,3	60	93,8	64
>60 years	2	3,2	61	96,8	63
Body Mass Index (kg/m²)					
Normal (<24,9)	61	41,8	85	58,2	146
Overweight/Obesity (≥ 25,0)	21	15,4	115	84,6	136
Contraceptive Use					
Currently using	43	26,2	121	73,8	164
Not using	39	33,1	79	66,9	118
Menopausal Status					
Non menopausal	75	42,6	101	57,4	176
Menopause	7	6,6	99	93,4	106
Family History of Malignancy					
Yes	18	25,7	52	74,3	70
No	64	30,2	148	69,8	212
Location of Breast Tumor					
Left	40	24,8	121	75,2	161
Right	40	33,6	79	66,4	119
Both	2	100	0	0	2

Physical Activity					
Active	7	28	18	72	25
Inactive	75	29,2	182	70,8	257

Histopathological examination revealed benign tumors in 82 patients (29.07%), while malignant tumors were found in 200 patients (70.92%). Histopathological examination revealed that the most common benign tumor was fibroadenoma (18.4%), while the most common malignant tumor was grade 3 invasive ductal carcinoma (40.1%). A similar study at Saveetha Medical College concluded that fibroadenoma was the most common benign tumor (22.4%). The most common malignant tumor was invasive ductal carcinoma (41.9%).²⁵

Table 2. Histopathological Examination Results.

Histopathological Findings	n = 282	%
Benign (n = 82)		
Fibroadenoma	52	18,4
Chronic Inflammatory Suppurative	9	3,2
Other	21	7,4
Malignant (n = 200)		
Invasive/Infiltrate Ductal Carcinoma Grade 2	87	30,9
Invasive/Infiltrate Ductal Carcinoma Grade 3	113	40,1

Table 3 presents the results of the chi-square analysis of factors associated with breast tumor type. Two variables were significantly associated with tumor type ($p < 0.001$): body mass index (BMI) and menopausal status. For BMI, the odds ratio was 3.930 (95% CI: 2.223–6.947), indicating that patients with overweight or obesity had 3.93 times higher odds of having a malignant breast tumor than a benign breast tumor compared with patients with normal BMI. For menopausal status, the odds ratio was 10.502 (95% CI: 4.613–23.910), indicating that postmenopausal patients had 10.50 times higher odds of having a malignant breast tumor than premenopausal patients.

A meta-analysis of 21 studies demonstrated a significant effect of BMI on the risk of breast cancer recurrence. There was a positive linear correlation between BMI and the risk of recurrence (RR = 1.02, 95% CI: 1.01–1.03). For every 1 kg/m² increase in BMI, the risk of recurrence increased by approximately 2%.⁽²⁶⁾ Several studies have linked obesity to an increased risk of breast cancer. Another meta-analysis showed that every 5 kg/m² increase in BMI was associated with a 2% increase in breast cancer risk in women.²⁷ Obesity has more adipose tissue. Increased adipose tissue increases aromatase production, which in turn increases circulating estrogen levels. Furthermore, obesity leads to a decrease in sex-hormone binding globulin (SHBG), which may increase breast cancer risk through hormone receptor positivity.²⁸

Physical activity is closely related to body composition and BMI, both of which are risk factors for breast cancer. Vigorous physical activity is known to reduce the risk of breast cancer, especially in postmenopausal women.²⁹ Physical activity is also known to play an immunomodulatory role. Cells in the immune system can prevent tumor progression by recognizing and destroying tumorigenic cells. This mechanism is achieved through increasing the number and activity of cytotoxic NK cells, increasing CD4⁺ cell proliferation, and increasing lymphokine-activated killer (LAK) activity.³⁰ A study conducted at the Cancer Service Development Center (PPLK) of Dr. Soetomo Hospital in Surabaya analyzed the correlation between physical activity levels and breast cancer incidence. The study, conducted on 106 female patients aged 40–60 years diagnosed with breast cancer, concluded that there was a significant correlation between physical activity intensity between the ages of 8–18 years and breast cancer incidence.³¹

The menstrual cycle is closely related to the function of the hormones estrogen and progesterone. These two hormones are actively produced during a woman's pre-menopause period. A case-control study in Vietnam concluded that menopause age of 50 years or older (OR = 1.71, 95% CI: 1.15–2.57 vs. <50 years) was associated with an increased risk of breast cancer. Earlier age at menarche (<13 years) was associated with a significantly increased risk of breast cancer (OR = 2.66, 95% CI: 1.08–7.51). Later menopause was positively associated with the risk of breast cancer with HER2 overexpression (OR = 2.19, 95% CI: 1.14–4.23).³² Estrogen is known to have mitogenic effects that

increase tumorigenesis. Estrogen receptor- α (ER α) expression is found in 80% of breast cancers, while progesterone receptor expression is found in 55% of cases. This theory later became the basis for the development of endocrine therapy.³³ Estrogen receptor modulator drugs such as tamoxifen and fulvestrant work by blocking estrogen biosynthesis through aromatase inhibition. This therapy has been shown to reduce the risk of breast cancer.³⁴

Women who experience early menstruation (early menarche) or menopause at a relatively late age are exposed to higher amounts of estrogen than those who do not. Furthermore, obese women also have detectable higher estrogen levels than leaner women. Although the mechanisms by which estrogen induces and promotes tumorigenesis in vivo have not been fully elucidated, some evidence suggests that estrogen and its metabolites have genotoxic effects. Another hypothesis is that excess estrogen can trigger hyperplasia to become neoplasia.³³ Menopause itself is not directly related to the risk of breast tumors; it is closely related to other factors, such as age and duration of estrogen exposure.

Estrogen is synthesized from cholesterol through a series of enzymatic reactions, with aromatase catalyzing the final conversion of androgens into estrogens. Aromatase expression is regulated by tissue-specific promoters that maintain low estrogen production under normal physiological conditions. However, in obesity-associated breast cancer, activation of the stronger PII and I.3 promoters markedly increases aromatase expression, resulting in excessive local estrogen production. This elevated estrogen exposure stimulates the proliferation of estrogen receptor-positive breast epithelial cells and may promote breast carcinogenesis.³⁵

Obesity disrupts adipose tissue homeostasis by promoting a pro-inflammatory adipokine profile. This dysregulation has been implicated in breast tumor progression through increased cellular proliferation, migration, and expansion of cancer stem cell (CSC) populations. Obesity promotes a protumorigenic microenvironment characterized by adipocyte hypertrophy, increased leptin secretion, reduced adiponectin levels, insulin resistance, and chronic inflammation. These alterations activate oncogenic signaling pathways, including JAK2/STAT3, PI3K/AKT/mTOR, and NF- κ B, while pro-inflammatory cytokines such as IL-6 and TNF- α released by crown-like structures (CLS) further enhance DNA damage, epithelial-mesenchymal transition (EMT), angiogenesis, and breast tumor progression.^{36,37}

Table 3. Results of Chi Square Analysis of Association Between Patient Characteristics and Breast Tumor Type (Benign vs. Malignant).

Variable		Benign		<i>p value</i>	OR (95% CI)	CI 95%	
		n (%)	n (%)			Min	Max
Body Mass Index (BMI)	Normal (<24.9 kg/m ²)	61 (41.8%)	85 (58.2%)	0.000*	3.930	2.223	6.947
	Overweight/obesity ($\geq$ 25 kg/m ²)	21 (15.4%)	115 (84.6%)				
Contraceptive Use	Yes	43 (26.2%)	121 (73.8%)	0.213	0.720	0.429	1.208
	No	39 (33.1%)	79 (66.9%)				
Menopausal Status	Non menopausal	75 (42.6%)	101 (57.4%)	0.000*	10.502	4.613	23.910
	Menopause	7 (6.6%)	99 (93.4%)				
Family History of Malignancy	Yes	18 (25.7%)	52 (74.3%)	0.475	0.800	0.435	1.475
	No	64 (30.2%)	148 (69.8%)				
Physical Activity	Active	7 (28%)	18 (72%)	0.901	0.944	0.379	2.353
	Inactive	75 (29.2%)	182 (70.8%)				

Table 4 presents the results of the multivariable binary logistic regression analysis. After adjustment for age, body mass index (BMI), hormonal contraception history, family history of

malignancy, and menopausal status, age remained significantly associated with malignant breast tumors. Each one-year increase in age was associated with a 22.0% increase in the odds of having a malignant rather than a benign breast tumor (adjusted OR = 1.220, 95% CI: 1.155–1.290; $p < 0.001$). BMI also remained a significant predictor, with each 1 kg/m² increase associated with a 31.5% increase in the odds of malignant breast tumors (adjusted OR = 1.315, 95% CI: 1.120–1.545; $p = 0.001$). Hormonal contraception history ($p = 0.134$) and family history of malignancy ($p = 0.067$) were not significantly associated with breast tumor type after adjustment. Menopausal status remained significantly associated with breast tumor type (adjusted OR = 0.214, 95% CI: 0.051–0.898; $p = 0.035$).

Table 4. Final Logistic Regression Model of Factors Associated with Malignant Breast Tumors

Variable	B	OR (Exp (B))	95% CI	p value
Age	0.199	1.220	1.115 – 1.290	0.000
Contraceptive Use	0.782	2.187	0.785 – 6.088	0.134
Family History of Malignancy	-1.033	0.356	0.118 – 1.076	0.67
Menopausal Status	-1.540	0.214	0.51 – 0.898	0.035
BMI	0.274	1.315	1.120 – 1.545	0.001

This study has several strengths, including the use of multivariable binary logistic regression analysis to adjust for potential confounding factors, including age, hormonal contraception history, and family history of malignancy, thereby allowing the identification of factors independently associated with malignant breast tumors. In addition, the study utilized medical record data, reflecting real-world clinical practice. However, this study also has several limitations. First, all participants had been diagnosed with breast tumors. Therefore, the findings only describe factors associated with malignant versus benign breast tumors and cannot be generalized as risk factors for the occurrence of breast tumors in the general population. Second, the cross-sectional design precludes causal inference. Finally, although several important confounding factors were adjusted for, other potentially relevant variables, such as parity, breastfeeding history, age at menarche, age at menopause, and hormonal therapy use, were not available in the medical records and therefore could not be included in the analysis. Residual confounding from these unmeasured variables cannot be excluded. Future studies should include women without breast tumors as a comparison group, collect more comprehensive reproductive and hormonal data, and employ prospective cohort designs to better evaluate factors associated with breast tumor development.

CONCLUSION

This study found that age, body mass index (BMI), and menopausal status were independently associated with breast tumor type among women diagnosed with breast tumors. These findings highlight the importance of considering demographic, metabolic, and reproductive factors when evaluating patients with breast tumors. Early detection and timely clinical evaluation should be strengthened, particularly among older women and those with overweight or obesity. Future prospective studies including women without breast tumors and incorporating additional reproductive and hormonal variables are warranted to further clarify factors associated with breast tumor development.

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