ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ)* 2021, Volume 10, Number 1: 320-324
P-ISSN.2089-1180, E-ISSN: 2302-2914

Bali Medical Journal
www.BaliMedicalJournal.org
Published by Bali Medical Journal

Fat intake in Javanese breast cancer patients: any difference?

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ABSTRACT

Background: Breast cancer is the second most prevalent women's malignancy in Central Java. The risk of breast cancer incidence drops by 2.5 times for breast cancer if fat consumption is reduced by 50%, although not all types of fat intake increase the risk of breast cancer incidence. Fat consumption in Indonesia increased by 11% in the last 7 years. The study aims to analyze the differences in fat intake between breast cancer subjects and healthy subjects.

Methods: This study is a cross-sectional study. We invited 45 outpatients diagnosed with breast cancer in Kariadi Hospital from January to August 2019 as well as 45 healthy subjects who are relatives or friends of the patients who met the inclusion criteria to participate in this study. Various types of fat intake were measured with quantitative food frequency questionnaires. The statistical analysis employed a chi-square test and Mann-Whitney test for non-parametric tests and an independent t-test for parametric data.

Results: There was a significant difference in polyunsaturated fatty acid (PUFA) intake between breast cancer patients and healthy subjects (p=0.022). This study found no significant differences in total fat intake (p=0.677), saturated fatty acid (SFA) (p=0.368), monounsaturated fatty acid (MUFA) (p=0.593), omega 3 (p=0.095), omega 6 (p=0.092), and TFA (p=0.669) between breast cancer patients and healthy subjects.

Conclusion: There is a significant difference in PUFA intake, but not in the other types of fat between breast cancer patients and healthy subjects. For further study, more precise and objective fat intake measurements may be achieved in studies with animal models.

Keywords: nutrition, fat, breast cancer, intake.
Cite This Article: Christian., Puruhita, N., Himawan, A., Muis, S.F., Fasitasari, M., Pangarsa, E.A., Panigoro, S.S., Sutandyo, N. 2021. Fat intake in Javanese breast cancer patients: any difference?. *Bali Medical Journal* 10(1): 320-324. DOI: 10.15562/bmj.v10i1.2173

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Received: 2021-01-06
Accepted: 2021-04-20
Published: 2021-04-30

INTRODUCTION

Breast cancer (BC) is a malignant tumor that mainly occurs in women. In Western Europe, North America, and other developed countries breast cancer ranks first as the most common type of cancer in women. In China 40,000 women have died due to breast cancer.[1] A GLOBOCAN study in 2012 found that breast cancer was the second most common cancer with 1.7 million cases (11.9%) and the fifth leading cause of death in the world with 522,000 deaths (6.4%).[2] Based on the estimated number of patients with any type of cancer in 2013, Central Java was the second most estimated cancer patient at 61,230 people.[3]

Saturated fat consumption in Indonesia was found at 18.2% or 38.1 grams/capita/day higher than the World Health Organization (WHO) recommendation of less than 10%, which increases cancer risk.[4,5]

The risk of breast cancer incidence drops by 2.5 times for breast cancer if fat consumption is reduced by 50%. It is associated with fat consumption and fatty tissue that produces estrogen, as well as with metabolic syndromes and tumorigenesis pathways involving IGF-1 and insulin.[6-8]

Nine cohort studies and 16 case-control studies have shown that as fat intake increases, so does breast cancer risk. However, other studies with 350,000 subjects and 7300 cases of breast cancer have shown that breast cancer is not significantly associated with fat intake. The WCRF/AIC (World Cancer Research Fund/American Institute of Cancer) therefore recommends that fat intake be categorized as being "limited-suggestive" which requires further research.[9] Inconclusive evidences regarding correlation between intake of various types of fat and breast cancer incidence and the

recommended classification from WCRF/AIC of fat intake as "limited-suggestive" provide a reason for this study.

METHOD

This cross-sectional study took place at an outpatient oncology clinic in Dr. Kariadi Semarang Hospital. The center hosted the second-highest number of incidence after Yogyakarta which met our inclusion and exclusion criteria from January to August 2019. The inclusion criteria for BC subjects are women diagnosed with breast cancer at any stage, aged 19 and above, receiving chemotherapy and/or radiotherapy, willing to participate in the study, and having a complete medical record. The inclusion criteria for healthy subjects are female, close relatives or friends of the patients, aged 19 and above, and willing to participate in the study.

The demographic data of age, address, education, occupation, and menopause status were taken in the questionnaires. We obtained the diagnosis from medical records that report histopathological features of breast cancer. We measured the weight with calibrated scales and height with stadiometry for both subject groups to obtain obesity status based on body mass index with a threshold value of ≥ 25 kg/m^2. Intake data were collected using semiquantitative food frequency questionnaires (FFQ). The FFQs collected standardized intake portion numbers or specific portion choices using 66 questions with 54 questions on saturated fat, 49 questions on trans fat consisting of 14 questions on ruminant, 19 on deep frying, 16 on cakes, and 8 on unsaturated fat. The standard portion was based on the standard guidelines for household size in Indonesia stipulated in the Minister of Health Regulation No. 41 of 2014 on Balanced Nutrition Guidelines and complemented with a food photo book. The answers were processed using a computer application; if the food was not available in the application, it was added manually for further analysis.

The data were analyzed using several different tests to determine the differences in intake of various fat types between BC and healthy subjects, including categorical and numerical data. Non-normally distributed data were analyzed in Mann-Whitney test or chi-square test. The significance limit of p-value was set at < 0.05. All data analysis was performed using a computer program.

Table 1. General characteristics

Variable	BC Subjects (n=45)	Healthy Subjects (n=45)
	n (%)	n (%)
Age		
< 30 years old	1 (2.2)	5 (11.1)
31-40 years old	2 (4.4)	14 (31.1)
41-50 years old	20 (44.4)	11 (24.4)
51-60 years old	13 (28.9)	14 (31.1)
> 60 years old	9 (20)	1 (2.2)
Education		
Uneducated	1 (2.2)	1 (2.2)
Primary School	2 (4.4)	0
Junior High School	6 (13.3)	0
Senior High School	19 (42.2)	5 (11.1)
Undergraduate	16 (35.6)	39 (86.7)
Postgraduate	1 (2.2)	0
Occupation		
Unemployed	1 (2.2)	0
Housewife	21 (46.7)	4 (8.9)
Government employee	13 (28.9)	28 (62.2)
Private employee	3 (6.7)	3 (6.7)
Entrepreneur	7 (15.6)	3 (6.7)
Other	0	7 (15.6)

Table 2. Specific characteristics

Variable	BC Subjects (n=45)	Healthy Subjects (n=45)
	n (%)	n (%)
Menopausal Status		
Not Menopause	24 (53.3)	33 (73.3)
Menopause	21 (46.7)	12 (26.7)
Body Mass Index		
< 18,5 kg/m^2	2 (4.4)	0
18,6-22,9 kg/m^2	7 (15.6)	10 (22.2)
23-24,9 kg/m^2	15 (33.3)	9 (20)
25-29,9 kg/m^2	15 (33.3)	10 (22.2)
> 30 kg/m^2	6 (13.3)	16 (35.6)

RESULTS

This study was conducted on 90 subjects with 45 BC subjects and 45 healthy subjects. Table 1 shows that the mean age of BC subjects was 51.7 ± 8.96, while the age at cancer diagnosis was 48.82 ± 9.07 years. Most subjects were highly educated (61.1%) with more than 40% having higher education degrees. The most considerable proportions of subjects were government employees (45.6%) and housewives (46.7%).

Table 2 shows that more BC subjects were diagnosed with breast cancer during pre-menopause (53.3%) than after menopause. According to the Asia Pacific BMI classification, both BC patients and healthy subjects were classified as obese grade I based on subjects' BMI.

Table 3 shows that the mean intake for both groups was 2508.4 kcal ± 691.81 with total fat intake of 49.2% ± 7.91, SFA intake at 18.6% ± 5.74, MUFA intake at 30.5% ± 10.62, PUFA intake at 39.5% ± 14.54, omega 3 intakes at 0.6% ± 0.66, omega 6 intakes at 4.1% ± 8.63, and TFA intake at 1.8% ± 0.81. Our calorie intake analysis

Table 3. Energy and fat intake of subjects

Variable	BC Subjects (n=45)	Healthy Subjects (n=45)
	Mean ± SD	Mean ± SD
Absolute Energy Intake (kcal)	2630.1 ± 684.15	2386.7 ± 685.36
Adjusted Energy Intake [a] (%)	124 ± 32	112 ± 32
Total Fat Intake (g)	139.3 ± 44.47	135.5 ± 40.84
SFA Intake (g)	49.6 ± 20.22	53.5 ± 20.05
MUFA Intake (g)	31.9 ± 10.85	29.9 ± 10.47
PUFA Intake (g)	40.7 ± 14.8	38.3 ± 14.34
Omega 3 Intake (g)	1.8 ± 1.42	1.5 ± 2.34
Omega 6 Intake (g)	13.0 ± 24.72	7.7 ± 16.79
TFA Intake (g)	5.2 ± 2.91	5.0 ± 2.97

[a] using %RDA with mean height correction (156 cm) and age 48 = 2120 kcal

Table 4. Results of bivariate analysis

Variable	BC Subjects Mean ± SD (% energy total)	Healthy Subjects Mean ± SD (% energy total)	p-value
Total Fat Intake	47.2 ± 7.72	51.1 ± 7.68	0.677[a]
SFA Intake	16.9 ± 5.28	20.3 ± 5.77	0.368[a]
MUFA Intake	10.5 ± 2.33	11.3 ± 2.7	0.593[a]
PUFA Intake	13.8 ± 3.9	14.3 ± 4.37	0.022[b*]
Omega 3 Intake	0.6 ± 0.51	0.6 ± 0.78	0.095[c]
Omega 6 Intake	4.7 ± 9.32	3.5 ± 7.94	0.092[c]
TFA Intake	1.7 ± 0.72	1.8 ± 0.89	0.669[b]
Menopausal Age (years)	47.96 ± 4.22	50.5 ± 2.64	0.000[d*]
BMI (kg/m^2)	25.6 ± 4.36	28.2 ± 6.60	0.291[d]

[a] independent *t*-test
[b] transformed data (independent *t*-test)
[c] Mann-Whitney test
[d] chi-square test
*Significant (p<0.05)

found that the average calorie intake in both BC and healthy subjects was similar with an average of 2508.4 kcal ± 691.81. High-calorie intake was in line with high body mass index for both BC and healthy subjects.

Table 4 shows that only PUFA intake had a relationship with breast cancer with p value<0.05. Variables such as BMI, omega 3 intakes, omega 6 intake, PUFA intake, and TFA intake did not indicate significant relationship with p>0.05. Only menopausal status showed a significant value with p<0.05.

DISCUSSION

In this study, the average age of BC subjects was 51.7, and the mean age at breast cancer diagnosis was 48.82. These results are consistent with previous studies that found 83.4% breast cancer incidence in patients aged above 40.[10] Most subjects lived outside Semarang but still in Central Java (53.3%) and were of Javanese origin (89.9%), which confirms that the highest incidence rate in Indonesia is found in Central Java and Yogyakarta.[10] BC subjects were educated (Senior High School 42.2%). As a general knowledge, higher education leads to easier access to health information, hence increased early detection of breast cancer.[11]

Table 1 shows that the proportion of BC subjects experiencing breast cancer during pre-menopause was higher than that of post-menopause subjects. One of the risk factors for breast cancer is late menopause (> 55 years) related to more prolonged exposure to reproductive hormones.[12] In this study, the number of pre-menopausal cases was higher than its post-menopausal counterpart. The exposure to estrogen from food possibly did not affect breast cancer incidence. Menopausal status shows a significant difference in the expression of estrogen receptors in patients with post-menopausal status. Postmenopausal breast cancer patients tend to have positive estrogen receptor expression. Research on histopathology and breast cancer markers has shown that more than 80% of post-menopausal women have positive estrogen receptors correlated with high levels of estrogen in post-menopausal women due to the high uptake of circulating hormones.[13,14] However, after further analysis, the menopause group showed no difference in fat intake between BC and healthy subjects with a p-value >0.05. No difference was found in obesity status between BC subjects and healthy subjects with a p-value >0.05. Thus, menopausal and obesity statuses were not considered confounding variables in this study.

The high-calorie intake was in line with the high body mass index of 25-29.9 kg/m^2 (obesity grade 1) for both BC and control subjects. This finding is consistent with previous studies on the association between obesity and breast cancer. The plausible mechanism involves decreased circulating adiponectin in obesity and increased leptin which triggers the proliferation, migration, and invasion of ER-positive and ER-negative cancer cells. The decreased adiponectin also reduces anti-cancer effect, insulin sensitivity, and insulin/IGF-1 secretion.[15] A high intake of PUFA reduces breast cancer risk by 62%.[16] Previous studies have also shown that PUFAs are associated with breast cancer incidence. An increased ratio of omega 6 to omega 3 statistically increased breast cancer risk with RR = 1.63, 95% CI = 1.06-2.41, where p=0.008.[17] Another study also found the effect of PUFA on breast cancer incidence, where a high omega-6 diet increased the risk by 1.2 times (CI = 0.85-1.69).[18] This study found that although PUFA had a significant value in bivariate analysis, the intake of omega 3 and omega 6 which are part of PUFA was not statistically significant due to the risk of recall bias from FFQ data, as well as incomplete and inconsistent food source database for omega 3 and omega 6 due to discrepancies in foodstuff collection,

storage, processing, and cooking. In addition, different types of fish, shrimp, seafood, oil, and avocado have different values. Another factor includes BMI which did not have a significant difference between cases and healthy subjects. It may be due to the development of breast cancer during pre-menopause where the exogenous estrogen factor does not have as much influence as the endogenous estrogen.

Our results are in accordance with previous studies in Poland which also found that PUFA intake > 10% of total energy significantly reduced the risk of breast cancer incidence with OR = 0.4 (95% CI = 0.19-0.85). Previous investigators also did not find a significant association between SFA, MUFA, and cholesterol intake in their study subjects for reasons not yet explained.[19] Menopausal status also affects dietary factors, especially in post-menopausal patients because inflammatory factors are not significantly related to post-menopausal conditions.[20]

The molecular mechanisms by which fatty acids affect carcinogenesis are modifications of cells' structural components (membrane lipids), metabolic effects, translation signals, and gene expression. Modifications of the lipid structure affect the intracellular signaling cascade that controls gene expression and function. Fatty acids associated with membrane phospholipids can be separated by the enzyme phospholipase and modulate another signaling from other pathways. The composition of fat in the cell membrane affects the inflammatory process because PUFAs are the precursors of eicosanoids. Furthermore, lipids are a part of hormones that modulates inflammatory responses and influence cell growth and differentiation.[21] Fat intake also promotes breast cancer growth by increasing circulating estrogen.[22]

The study's limitations lie in the possible bias in respondent selection and the recall process, which depends on the subject's memory. To minimize bias in FFQ collection based on diet habits, the healthy issues were taken from the kin. Subjects were also given a visual description of the food consumed (food models) to improve the recall process. As another limitation, the study did not measure confounding factors such as hormonal status and genetic factors.

CONCLUSION

PUFA intake is significantly different between breast cancer patients and healthy subjects. However, the same conclusion does not apply for other types of fat. We recommend that further study use more objective measurements of fat intake achievable in studies with animal models.

ETHICAL APPROVAL

This study was approved by Kariadi Hospital Ethical Study Committee with ethical clearance reference number: No. 070/EC/KEPK-RSDK-2019.

CONFLICTS OF INTEREST

This research is part of a larger study with Sonar Soni Panigoro as main researcher. There are no other conflicts of interest in this study.

FUNDING

No specific funding was provided for this article.

AUTHOR CONTRIBUTIONS

Supervision: Niken Puruhita, Arientasari Himawan, Siti Fatimah Muis, Minidian Fasitasari, Sonar Soni Panigoro, Noorwati Sutandyo. All author had contributed equally to writing the original draft and had reviewed and agreed for the final version of the manuscript for publication,

ACKNOWLEDGMENTS

This work was supported by the Department of Clinical Nutrition, Faculty of Medicine, Diponegoro University/ Kariadi Hospital Semarang.

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