pISSN 1598-2998, eISSN 2005-9256

Cancer Res Treat. 2017;49(4):990-1000

https://doi.org/10.4143/crt.2016.488

Original Article

Open Access

Risk Factors of Female Breast Cancer in Vietnam: A Case-Control Study

Phuong Dung (Yun) Trieu, MDR[1,2]
Claudia Mello-Thoms, PhD[1]
Jennifer K. Peat, PhD[3]
Thuan Doan Do, PhD[4]
Patrick C. Brennan, PhD[1]

[1]*Faculty of Health Sciences, The University of Sydney, New South Wales, Australia,* [2]*University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam,* [3]*Australian Catholic University, Queensland, Australia,* [4]*Department of Diagnostic Imaging, Vietnam National Cancer Hospital, Hanoi, Vietnam*

Correspondence: Phuong Dung (Yun) Trieu, MDR
Faculty of Health Sciences, The University of Sydney, Room 504, M Building, 75 East Street, Lidcombe, New South Wales 2141, Australia
Tel: 61-290367454
Fax: 61-90367394
E-mail: phuong.trieu@sydney.edu.au

Received October 10, 2016
Accepted December 28, 2016
Published Online February 20, 2017

Purpose

Rates of women with breast cancer have increased rapidly in recent years in Vietnam, with over 10,000 new patients contracting the disease every year. This study was conducted to identify demographic, reproductive and lifestyle risk factors for breast cancer in Vietnam.

Materials and Methods

Breast density, demographic, reproductive and lifestyle data of 269 women with breast cancer and 519 age-matched controls were collected in the two largest oncology hospitals in Vietnam (one in the north and one in the south). Baseline differences between cases and controls in all women, premenopausal and postmenopausal women were assessed using chi-squared tests and independent t tests. Conditional logistic regression was used to derive odds ratios (OR) for factors that had statistically significant associations with breast cancer.

Results

Vietnamese women with breast cancer were significantly more likely to have a breast density > 75% (OR, 1.7), be younger than 14 years at first menstrual period (OR, 2.2), be postmenopausal (OR, 2.0), have less than three pregnancies (OR, 2.1), and have less than two babies (OR, 1.7). High breast density (OR, 1.6), early age at first menstrual period (OR, 2.6), low number of pregnancies (OR, 2.3), hormone use (OR, 1.8), and no physical activities (OR, 2.2) were significantly associated with breast cancer among premenopausal women, while breast density (OR, 2.0), age at first menstrual period (OR, 1.8), number of pregnancies (OR, 2.3), and number of live births (OR, 2.4) were the risk factors for postmenopausal women.

Conclusion

Breast density, age at first menarche, menopause status, number of pregnancies, number of babies born, hormone use and physical activities were significantly associated with breast cancer in Vietnamese women.

Key words
Breast neoplasms, Risk factors, Case-control studies, Demography, Reproductive behaviour, Life style

Introduction

Breast cancer affected 1.7 million women worldwide in 2012 [1]. In low-income countries such as Vietnam, breast cancer was traditionally found to have a low incidence rate (less than 20 per 100,000 women) compared with Westernized populations [2], but recently reported increases demand attention. For example, in 2012 over 10,000 cases of female breast cancer were diagnosed in Vietnam, which is a 30% increase compared with 10 years ago [3]. At the time of writing, breast cancer was the most common cancer amongst women in Vietnam.

In response to this increase in breast cancer incidence, the Vietnamese government is promoting breast self-examination as a method of breast cancer screening. However,

Copyright © 2017 by the Korean Cancer Association
This is an Open-Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

focused primary prevention is significantly hindered by limited data pertaining to risk factors associated with the disease. While demographic, reproductive and lifestyle factors linked to breast cancer are reasonably well understood in developed countries [4], the relevance of these parameters to Vietnamese women is much less understood. Two previous studies relating to breast cancer in Vietnam exist. The first, which focused only on *BRCA* mutations, found an insignificant association between genetic profiles and breast cancer due to low BRCA positivity in Vietnam [5]. The second investigation did not find any association of breast cancer with body mass index (BMI), age of menarche, total months of lactation, and family history of breast cancer [6]; however, this sample included only premenopausal women in Vietnam and China, which limited its scope in general and specifically its relevance to Vietnam. Other potentially important agents such as breast density and lifestyle parameters have been under-explored. Therefore, this study was conducted to explore the association of breast density, demographic, reproductive and lifestyle factors with female breast cancer in Vietnam.

Materials and Methods

Ethical approval was obtained from the Research Ethics Board of the University of Sydney, the Biomedical Research Board of Ethics at the University of Medicine and Pharmacy in Ho Chi Minh City and site permission from two hospitals involved in this study.

1. Data collection

A prospective study was conducted in the two largest cities of Vietnam, Ha Noi (National Cancer Hospital) and Ho Chi Minh City (Oncology Hospital) in 2015. These hospitals are the main cancer centers providing screening and treatment services for residents in the two regions.

Participants were recruited from X-ray departments. Women who came for mammography either for screening or diagnostic purposes were invited to participate in the study and informed consent was obtained from the participants. Data collected for each woman included a self-administered questionnaire and a radiology report. For each cancer case, we selected one to two controls matched on a single year of age to the cases. Cancer cases were defined as women diagnosed with breast cancer that was biopsy confirmed, while controls were women who did not have breast cancer based on negative breast clinician and radiology reports. Females with a prior history of breast cancer who received cancer treatment or women with a breast biopsy of unknown outcome were excluded. Overall, there were 283 cancers and 527 controls fulfilling these criteria (138 cancer cases and 276 controls from the Vietnam National Cancer Hospital in Hanoi; 145 cancer cases and 251 controls from the Oncology Hospital in Ho Chi Minh City). The ages of cases ranged from 27 to 74 years and Kinh ethnicity accounted for 97% of the participants.

The epidemiological data used in this study were gathered from three sources: a clinical mammographic assessment form completed by a radiologist, a pathologist's report if a biopsy test was undertaken and a self-administered questionnaire completed by the participant. The questionnaire was developed based on Canadian and Australian studies that focused on well-known risk factors of breast cancer related to demographic, reproductive and lifestyle information [7,8].

2. Study variables

Breast density, which represents the amount of fibro-glandular tissues on the mammograms, was assessed using Breast Imaging-Reporting and Data System (BI-RADS) scores from the radiology report as follows: BI-RADS 1, mostly fatty breast (0%-24% dense); BI-RADS 2, scattered fibroglandular breast (25%-50% dense); BI-RADS 3, heterogeneously dense breast (51%-75% dense); BI-RADS 4, extremely dense breast (76%-100% dense). The BI-RADS fourth edition [9] was used was in line with clinical practice in Vietnam.

The information collected from the women who completed questionnaires included age, height and weight (BMI=weight in kg/[height in meters]^2), residency, age at menarche, age at menopause, age at having first child, age at having last child, number of pregnancies, number of babies born, and how many months on average individuals had breastfed each of their children. Women were defined as postmenopausal if they did not have menstrual periods within the previous 12 months. Women with bilateral oophorectomy or hysterectomy were also considered to be postmenopausal. Family history of breast cancer was established if they had a mother, sister or daughter (first degree) or a relative (second degree) ever diagnosed with breast cancer. Participants were also asked about their hormone use (hormone replacement therapy and daily oral contraceptive). A positive response for alcohol consumption and smoking was identified when participants reported having ever consumed at least 125 mL of wine, 250 mL of beer or 30 mL of spirits per week in a 6-month period or smoked a cigarette at least once a day over a 3-month period.

Physical activity questions were designed to estimate how many minutes per week were spent in light (e.g., walking), moderate (e.g., swimming and badminton) and vigorous

Table 1. Distribution of cases and controls of all women

Factor	No. (%)[a]		p-value[b]	Unadjusted OR (95% CI)[c]	Adjusted OR (95% CI)[d]
	Case (n=269, 34.1%)	Control (n=519, 65.9%)			
Age					
Mean±SD (yr)	49.2±9.7	48.8±8.5	0.37		
Breast density (%)					
≤ 75	181 (67.2)	382 (73.6)	0.04	1.0 (reference)	1.0 (reference)
> 75	88 (32.8)	137 (26.4)		1.7 (1.3-2.4)*	1.5 (1.1-2.2)*
Height (cm)					
Mean±SD	154.2±5.3	154.0±5.5	0.70		
< 155	138 (51.3)	268 (51.6)	0.93	1.0 (reference)	
≥ 155	131 (48.7)	251 (48.4)		1.0 (0.8-1.4)	
Weight (kg)					
Mean±SD	54.1±8.2	53.8±7.7	0.60		
≤ 54	144 (53.4)	288 (55.5)	0.56	1.0 (reference)	
> 54	125 (46.6)	231 (44.5)		1.1 (0.8-1.5)	
BMI					
Mean±SD	22.8±3.1	22.6±2.9	0.60		
< 23	146 (54.3)	303 (58.3)	0.29	1.0 (reference)	
≥ 23	123 (45.7)	216 (41.7)		1.2 (0.9-1.6)	
Age at first menstrual period (yr)					
Mean±SD	15.3±2.0	15.6±2.0	0.04		
< 14	58 (22)	58 (11.4)	< 0.001	2.2 (1.5-3.3)*	2.1 (1.4-3.2)*
≥ 14	205 (78)	453 (88.6)		1.0 (reference)	1.0 (reference)
Menopause status					
Pre	121 (45.1)	324 (62.5)	< 0.001	1.0 (reference)	1.0 (reference)
Post	148 (54.9)	195 (37.5)		2.0 (1.5-2.7)*	2.5 (1.8-3.4)*
Age at menopause					
Mean±SD	48.6±4.8	49.1±4.8	0.38		
< 50	74 (50.3)	84 (43.3)	0.20	1.3 (0.9-2.0)	
≥ 50	74 (49.7)	111 (56.7)		1.0 (reference)	
Age at first birth (yr)					
Mean±SD	24.5±4.4	23.9±4.5	0.09		
< 23	99 (36.9)	234 (45.5)	0.08	1.0 (reference)	
23-29	136 (50.8)	229 (44.5)		1.4 (1.0-2.0)	
≥ 30	33 (12.3)	51 (10)		1.5 (0.9-2.5)	
Age at last birth (yr)					
Mean±SD	30.3±5.5	30.1±5.3	0.65		
< 30	124 (46.4)	251 (48.8)	0.55	1.0 (reference)	
≥ 30	144 (53.6)	263 (51.2)		1.1 (0.8-1.5)	
No. of pregnancies					
Mean±SD	3.1±2.0	3.7±2.0	< 0.001		
< 3	119 (44.4)	144 (28)	< 0.001	2.1 (1.5-2.8)*	2.2 (1.6-3.0)*
≥ 3	149 (55.6)	370 (72)		1.0 (reference)	1.0 (reference)
No. of babies born					
Mean±SD	2.1±1.3	2.4±1.3	0.001		
< 2	73 (27.3)	91 (17.7)	0.002	1.7 (1.2-2.5)*	1.0 (0.6-1.5)
≥ 2	195 (72.7)	423 (82.3)		1.0 (reference)	1.0 (reference)
No. of months of breast feeding					
Mean±SD	15.0±6.4	15.1±6.1	0.79		
< 15	131 (48.9)	238 (46.4)	0.53	1.1 (0.8-1.5)	
≥ 15	137 (51.1)	276 (53.6)		1.0 (reference)	

Table 1. Continued

Factor	No. (%)[a]		p-value[b]	Unadjusted OR (95% CI)[c]	Adjusted OR (95% CI)[d]
	Case (n=269, 34.1%)	Control (n=519, 65.9%)			
Hormone use					
No	190 (70.5)	385 (74.1)	0.40	1.0 (reference)	
Yes	79 (29.5)	134 (25.9)		1.2 (0.8-1.7)	
Family history of breast cancer					
No	252 (93.7)	485 (93.4)	0.14	1.0 (reference)	
1st degree	6 (2.2)	22 (4.3)		0.5 (0.2-1.3)	
2nd degree	11 (4.1)	12 (2.3)		1.8 (0.8-4.1)	
Smoking					
No	265 (98.5)	509 (98.1)	0.66	0.8 (0.2-2.5)	
Yes	4 (1.5)	10 (1.9)		1.0 (reference)	
Alcohol drinking					
No	268 (99.6)	515 (99.2)	0.51	1.0 (reference)	
Yes	1 (0.4)	4 (0.8)		0.5 (0.05-4.3)	
Soy drinking					
< 1 Cup per day	227 (84.4)	449 (86.5)	0.46	1.0 (reference)	
≥ 1 Cup per day	42 (15.6)	70 (13.5)		1.2 (0.7-1.8)	
Coffee drinking					
< 1 Cup per day	224 (83.1)	457 (88)	0.09	1.0 (reference)	
≥ 1 Cup per day	45 (16.9)	62 (12)		1.5 (0.9-2.4)	
Vegetable consumption (servings)					
≤ 1	32 (11.9)	44 (8.5)	0.16	1.0 (reference)	
2-3	144 (53.5)	313 (60.3)		0.6 (0.4-1.1)	
≥ 4	93 (34.6)	162 (31.2)		0.8 (0.4-1.4)	
Physical activities					
No (inactive)	27 (10.1)	41 (7.9)	0.35	1.3 (0.7-2.3)	
Yes (insufficient and sufficient)	242 (89.9)	478 (92.1)		1.0 (reference)	

OR, odds ratio; CI, confidence interval; SD, standard deviation; BMI, body mass index. *Statistically significant ($p < 0.05$). [a]Number of participants (%), [b]Obtained from t test for continuous variables and chi-squared test for categorical variables, [c]Unadjusted OR (95% CI)—obtained from binary logistic regression, [d]Multivariable adjusted OR (95% CI)—obtained from multiple logistic regression.

activities (e.g., weight-lifting, aerobics, gardening, and farming). Activity level classification followed the Active Australia Survey where: inactive indicates not engaged in any physical activity during the preceding month; insufficient indicates spending less than 150 minutes per week doing physical activities; sufficient indicates spending ≥ 150 minutes per week exercising [exercise time=walking time+moderate activity time+(2×vigorous activity time)] [10].

Short questions regarding diet about were also included. Specifically, women were asked to report the frequency of drinking soy and coffee over the last 12 months and rate their daily servings of vegetables (1 serving=one-half cup of cooked vegetables or one cup of salad or vegetables).

3. Statistical methods

The statistical methods used in this study were primarily as described in a similar study of an Asian population [11]. Baseline differences in the features of women with and without breast cancer were assessed using the chi-squared test for categorical variables and an independent t test for continuous variables. For continuous variables (age, age at menarche, age at menopause, BMI, age at having first child, age at having last child, number of pregnancies, number of babies born, number of months in breast feeding), we used an optimal cut-off point obtained from a receiver operating characteristic (ROC) curves with area under the curve values above 0.5 (the highest diagnostic accuracy point closest to the upper left corner of the ROC curve) to allocate these variables

Table 2. Distribution of cases and controls of pre-menopausal women

Factor	Pre-menopausal women				
	No. (%)[a]		p-value[b]	Unadjusted OR (95% CI)[c]	Adjusted OR (95% CI)[d]
	Case (n=121, 27.2%)	Control (n=324, 72.8%)			
Age					
Mean±SD (yr)	43.3±7.2	43.1±6.8	0.72		
Breast density (%)					
≤ 75	67 (55.4)	212 (65.4)	0.04	1.0 (reference)	1.0 (reference)
> 75	54 (44.6)	112 (34.6)		1.6 (1.1-2.3)*	1.2 (0.6-2.2)
Height (cm)					
Mean±SD	154.7±5.4	154.6±5.6	0.95		
< 155	56 (46.3)	151 (46.6)	0.95	1.0 (reference)	
≥ 155	65 (53.7)	173 (53.4)		1.0 (0.7-1.5)	
Weight (kg)					
Mean±SD	54.2±8.2	54.0±7.9	0.80		
≤ 54	69 (57)	180 (55.6)	0.78	1.0 (reference)	
> 54	52 (43)	144 (44.4)		0.9 (0.6-1.4)	
BMI					
Mean±SD	22.6±3.0	22.5±3.0	0.83		
< 23	70 (57.5)	199 (61.4)	0.46	1.0 (reference)	
≥ 23	51 (42.5)	125 (38.6)		1.2 (0.8-1.8)	
Age at first menstrual period (yr)					
Mean±SD	15.1±1.8	15.5±1.9	0.06		
< 14	27 (22.7)	32 (10.1)	0.001	2.6 (1.5-4.5)*	2.3 (1.2-4.6)*
≥ 14	89 (77.3)	285 (89.9)		1.0 (reference)	1.0 (reference)
Age at first birth (yr)					
Mean±SD	23.8±3.8	23.6±4.3	0.80		
< 23	49 (39.1)	151 (46.7)	0.32	1.0 (reference)	
23-29	63 (50)	147 (45.4)		1.3 (0.8-2.1)	
≥ 30	14 (10.9)	26 (7.9)		1.6 (0.7-3.5)	
Age at last birth (yr)					
Mean±SD	29.5±5.2	29.4±5.3	0.90		
< 30	64 (50.5)	173 (53.3)	0.61	1.0 (reference)	
≥ 30	62 (49.5)	151 (46.7)		1.1 (0.7-1.7)	
No. of pregnancies					
Mean±SD	2.9±1.8	3.4±1.8	0.005		
< 3	64 (51.2)	103 (31.8)	< 0.001	2.3 (1.5-3.6)*	2.6 (1.6-4.4)*
≥ 3	62 (48.8)	221 (68.2)		1.0 (reference)	1.0 (reference)
No. of babies born					
Mean±SD	2.0±1.0	2.1±0.9	0.12		
< 2	30 (24)	62 (19.1)	0.26	1.3 (0.8-2.2)	
≥ 2	96 (76)	262 (80.9)		1.0 (reference)	
No. of months of breast feeding					
Mean±SD	15.9±6.0	15.4±6.2	0.48		
< 15	52 (41.3)	135 (41.8)	0.93	1.0 (0.6-1.5)	
≥ 15	74 (58.7)	189 (58.2)		1.0 (reference)	
Hormone use					
No	75 (62.2)	244 (75.2)	0.02	1.0 (reference)	1.0 (reference)
Yes	46 (37.8)	80 (24.8)		1.8 (1.1-3.0)*	2.3 (1.3-3.9)*

Table 2. Continued

Factor	Pre-menopausal women				
	No. (%)[a]		p-value[b]	Unadjusted OR (95% CI)[c]	Adjusted OR (95% CI)[d]
	Case (n=121, 27.2%)	Control (n=324, 72.8%)			
Family history of breast cancer					
No	112 (92.5)	304 (93.8)	0.22	1.0 (reference)	
1st degree	3 (2.5)	13 (4)		0.6 (0.2-2.3)	
2nd degree	6 (5)	7 (2.2)		2.3 (0.8-7.1)	
Smoking					
No	120 (99.2)	317 (97.8)	0.35	1.0 (reference)	
Yes	1 (0.8)	7 (2.2)		0.4 (0.05-3.1)	
Alcohol drinking					
No	121 (100)	323 (99.7)	0.54	1.0 (reference)	
Yes	0 (0)	1 (0.3)		0.7 (0.7-0.8)	
Soy drinking					
< 1 Cup per day	106 (87.6)	283 (87.3)	0.99	1.0 (reference)	
≥ 1 Cup per day	15 (12.4)	41 (12.7)		1.0 (0.5-2.0)	
Coffee drinking					
< 1 Cup per day	98 (81.1)	285 (87.9)	0.11	1.0 (reference)	
≥ 1 Cup per day	23 (18.9)	39 (12.1)		1.7 (0.9-3.2)	
Vegetable consumption (servings)					
≤ 1	15 (12.8)	26 (8)	0.38	1.0 (reference)	
2-3	69 (57.4)	191 (59)		0.6 (0.3-1.3)	
≥ 4	37 (29.8)	107 (33)		0.6 (0.2-1.3)	
Physical activities					
No (inactive)	15 (12.4)	20 (6.2)	0.04	2.2 (1.0-4.9)*	2.6 (0.8-8.0)
Yes (insufficient and sufficient)	106 (87.6)	304 (93.8)		1.0 (reference)	1.0 (reference)

OR, odds ratio; CI, confidence interval; SD, standard deviation; BMI, body mass index. *Statistically significant ($p < 0.05$). [a]Number of participants (%), [b]Obtained from t test for continuous variables and chi-squared test for categorical variables, [c]Unadjusted OR (95% CI)—obtained from binary logistic regression, [d]Multivariable adjusted OR (95% CI)—obtained from multiple logistic regression.

into two groups: above or below the cut-off point [12]. The independent effects of univariate risk factors for breast cancer were evaluated using conditional logistic regression. Multivariate conditional logistic regression was used to derive adjusted risk estimates for factors significantly linked with breast cancer upon univariate analysis [13]. A forward sequential method was used to identify and remove confounders and non-significant variables from the model. Risk estimates are presented as odds ratios (OR). This analytic procedure was applied for all women, then stratified by menopausal status. Due to the low number of participants from other ethnicities (3%), we excluded eight control and fourteen cases from the data analysis.

p-values were based on two-tailed tests, and a $p < 0.05$ was considered to be significant. Data were analyzed using the IBM SPSS statistical software package ver. 22 (IBM Corp., Armonk, NY).

Results

The distribution of cases and controls for all women, premenopausal and postmenopausal women are presented in Tables 1-3. The average age was 49.2 for cancer cases and 48.8 for controls (p=0.37). Premenopausal cancer women had an average age of 43.3 years old, while postmenopausal women diagnosed with breast cancer had a mean age of 55.2 years old. There were no significant differences in ages between cases and controls in either premenopausal (p=0.72) or postmenopausal women (p=0.65).

1. All women

When compared with controls, a significantly increased risk of breast cancer was observed for women with high

Table 3. Distribution of cases and controls of post-menopausal women

Factor	No. (%)[a]		p-value[b]	Unadjusted OR (95% CI)[c]	Adjusted OR (95% CI)[d]
	Case (n=148, 43.1%)	Control (n=195, 56.9%)			
Age					
Mean±SD (yr)	55.2±7.5	55.5±6.5	0.65		
Breast density (%)					
≤ 75	114 (76.9)	170 (87.1)	0.01	1.0 (reference)	1.0 (reference)
> 75	34 (23.1)	25 (12.9)		2.0 (1.2-3.6)*	1.9 (1.0-3.4)*
Height (cm)					
Mean±SD	153.7±5.3	153.0±5.0	0.18		
< 155	82 (55.5)	117 (60.1)	0.39	1.0 (reference)	
≥ 155	66 (44.5)	78 (39.9)		1.2 (0.8-1.9)	
Weight (kg)					
Mean±SD	54.1±8.2	53.5±7.3	0.51		
≤ 54	75 (50.3)	108 (55.4)	0.35	1.0 (reference)	
> 54	73 (49.7)	87 (44.6)		1.2 (0.8-1.9)	
BMI					
Mean±SD	22.9±3.2	22.8±2.8	0.86		
< 23	76 (51.7)	104 (53.2)	0.79	1.0 (reference)	
≥ 23	72 (48.3)	91 (46.8)		1.1 (0.7-1.6)	
Age at first menstrual period (yr)					
Mean±SD	15.4±2.2	15.8±2.1	0.15		
< 14	31 (21.4)	26 (13.2)	0.04	1.8 (1.0-3.2)*	1.7 (0.9-3.1)
≥ 14	116 (78.6)	168 (86.8)		1.0 (reference)	1.0 (reference)
Age at menopause (yr)					
Mean±SD	48.6±4.8	49.0±4.9	0.38		
< 50	74 (50.3)	84 (43.3)	0.20	1.3 (0.9 - 2.0)	
≥ 50	74 (49.7)	111 (56.7)		1.0 (reference)	
Age at first birth (yr)					
Mean±SD	25.1±4.9	24.3±4.8	0.15		
< 23	50 (34.9)	83 (43.5)	0.28	1.0 (reference)	
23-29	73 (51.6)	82 (42.9)		1.5 (0.9-2.4)	
≥ 30	19 (13.5)	25 (13.6)		1.2 (0.6-2.5)	
Age at last birth (yr)					
Mean±SD	31.1±5.7	31.3±5.1	0.66		
< 30	60 (42.9)	78 (41.3)	0.79	1.0 (reference)	
≥ 30	82 (57.1)	112 (58.7)		0.9 (0.6-1.5)	
No. of pregnancies					
Mean±SD	3.3±2.2	4.2±2.2	< 0.001		
< 3	55 (38.8)	41 (21.6)	0.001	2.3 (1.4-3.7)*	2.3 (1.4-3.7)*
≥ 3	87 (61.2)	149 (78.4)		1.0 (reference)	1.0 (reference)
No. of babies born					
Mean±SD	2.2±1.5	2.9±1.7	< 0.001		
< 2	43 (30.1)	29 (15.5)	0.001	2.4 (1.4-4.0)*	1.5 (0.8-2.9)
≥ 2	99 (69.9)	161 (84.5)		1.0 (reference)	1.0 (reference)
No. of months of breast feeding					
Mean±SD	14.3 ±6.7	14.7±6.1	0.51		
< 15	79 (55.6)	103 (54.1)	0.79	1.1 (0.7-1.7)	
≥ 15	63 (44.4)	87 (45.9)		1.0 (reference)	
Hormone use					
No	115 (78)	141 (71.9)	0.28	1.0 (reference)	
Yes	33 (22)	54 (28.1)		0.7 (0.4-1.3)	

Table 3. Continued

Factor	No. (%)[a]		p-value[b]	Unadjusted OR (95% CI)[c]	Adjusted OR (95% CI)[d]
	Case (n=148, 43.1%)	Control (n=195, 56.9%)			
Family history of breast cancer					
No	140 (94.6)	181 (92.8)	0.40	1.0 (reference)	
1st degree	3 (2)	9 (4.6)		0.4 (0.1-1.6)	
2nd degree	5 (3.4)	5 (2.6)		1.3 (0.4-4.5)	
Smoking					
No	145 (98)	192 (98.5)	0.73	1.0 (reference)	
Yes	3 (2)	3 (1.5)		1.3 (0.3-6.7)	
Alcohol drinking					
No	147 (99.3)	192 (98.5)	0.46	1.0 (reference)	
Yes	1 (0.7)	3 (1.5)		0.4 (0.05-4.2)	
Soy drinking					
< 1 Cup per day	121 (81.8)	166 (85)	0.52	1.0 (reference)	
≥ 1 Cup per day	27 (18.2)	29 (15)		1.2 (0.6-2.3)	
Coffee drinking					
< 1 Cup per day	126 (84.6)	172 (88.2)	0.37	1.0 (reference)	
≥ 1 Cup per day	22 (15.4)	23 (11.8)		1.4 (0.7-2.7)	
Vegetable consumption (servings)					
≤ 1	17 (11.4)	18 (9.2)	0.14	1.0 (reference)	
2-3	75 (50.4)	122 (62.6)		0.6 (0.3-1.4)	
≥ 4	56 (38.2)	55 (28.2)		1.1 (0.5-2.5)	
Physical activities					
No (inactive)	12 (8.3)	21 (10.6)	0.52	1.0 (reference)	
Yes (insufficient and sufficient)	136 (91.7)	174 (89.4)		0.8 (0.3-1.7)	

OR, odds ratio; CI, confidence interval; SD, standard deviation; BMI, body mass index. *Statistically significant ($p < 0.05$). [a]Number of participants (%), [b]Obtained from t test for continuous variables and chi-squared test for categorical variables, [c]Unadjusted OR (95% CI)—obtained from binary logistic regression, [d]Multivariable adjusted OR (95% CI)—obtained from multiple logistic regression.

breast density (> 75%) (OR, 1.7; p=0.04), younger than 14 years at the first menstrual period (OR, 2.2; $p < 0.001$), of postmenopausal status (OR, 2.0; $p < 0.001$), having less than 3 pregnancies (OR, 2.1; $p < 0.001$), and having less than two babies born (OR, 1.7; p=0.002). Conversely, age at first giving birth, family history of breast cancer, and drinking coffee did not show significant associations with breast cancer ($p > 0.05$) although the odds ratio for women having cancer with age at first giving birth 30 years old or later was 1.5, while that for women having a second degree family member with breast cancer was 1.8 and that of women who drink a cup of coffee or more per day was 1.5 (Table 1).

The adjusted ORs from multivariable conditional logistic regression with six variables (breast density, age at first menarche, menopausal status, age at first giving birth, number of pregnancies, and number of babies born) are shown in Table 1. The increased risk of breast cancer with high breast density (OR, 1.5; p=0.02), early age at first menstrual period (OR, 2.1; p=0.001), postmenopausal status (OR, 2.5; $p < 0.001$), and low number of pregnancies (OR, 2.2; $p < 0.001$) remained significant when the model was adjusted for other factors (Table 1).

2. Premenopausal and postmenopausal women

Premenopausal women had an increased risk of developing breast cancer with high breast density (OR, 1.6; p=0.04), early age at first menarche (OR, 2.6; p=0.001), low number of pregnancies (OR, 2.3; $p < 0.001$), using exogenous sex hormones (OR, 1.8; p=0.02), and no engagement in physical activities (OR, 2.2; p=0.04) (Table 2). Similar to premenopausal women, breast density > 75% (OR, 2.0; p=0.01), early age at first menarche (OR, 1.8; p=0.04), low number of pregnancies (OR, 2.3; p=0.001), and low number of babies born (OR, 2.4; p=0.001) were found to be related to breast cancer among postmenopausal women (Table 3).

Age at first menstrual period (OR, 2.3; p=0.01), number of pregnancies (OR, 2.6; p < 0.001), and hormone use (OR, 2.3; p=0.003) were significantly associated with breast cancer among premenopausal women in the adjusted model, while breast density (OR, 1.9; p=0.03) and number of pregnancies (OR, 2.3; p=0.001) were consistently important risk factors for postmenopausal women (Tables 2 and 3).

Discussion

To the best of our knowledge, this is the first study to investigate a wide range of breast cancer risk factors in Vietnam. Similar to the results of previous studies conducted in other countries, we found an increased risk of breast cancer associated with high breast density, early age at first menarche, low number of pregnancies, few live births, postmenopausal status, hormone use, and lack of engagement in physical activities, although there are differences in the distribution of risk factors when the analyses are stratified by menopausal status. Additionally, while use of external hormones and no physical activities were associated with breast cancer in premenopausal women, these associations were not found in postmenopausal women whose cancer risks were more influenced by high breast density and low number of pregnancies. Other risk factors reported in Westernized countries, such as BMI, family history of breast cancer, age at first giving birth, and breastfeeding duration were not significant in our study, which might be reflective of the different populations enrolled. Accurate identification of relevant risks helps to frame policies around the most effective strategies to maximize the prevention of breast cancer.

Consistent with case-control studies in other populations, an increased risk of developing breast cancer was observed among women with a breast density > 75% (as reported using BI-RADS scoring) compared to those with less dense breast, although the risk in Vietnam (OR, 1.7) was found to be lower than that reported for westernized countries (OR, 3-5) [14-16]. Moreover, high breast density was more frequent in Vietnamese women than low breast density (BI-RADS 1%-8.3%, BI-RADS 2%-19.9%, BI-RADS 3%-43.2%, BI-RADS 4%-28.6%). This could be explained by the fact that Asian women's breasts are known to be more dense than those of westernized women [17]; therefore, there can be a high degree of density even in non-cancer women when compared with normalized figures from other countries, and the difference between the number of cancer and normal cases in high breast density groups might not be as substantial as in a Caucasian population. Another possible reason is that the cases in this study were retrieved from both screening and diagnostic populations in oncology hospitals, while other studies have often obtained their data from mammographic screening services. Although we would have preferred to have worked with a screening system, the absence of a nationally recognized screening service in Vietnam prevented this.

Most of our other results were also concordant with those of previous observations of reproductive risk factors in westernized and Southeast/East Asian countries [18]. For example, women having their first menstrual period at earlier than 14 years of age were more likely to have breast cancer (OR, 1.7-2.6), while women being pregnant more than two times or having more than one child had a 30%-50% lesser risk of developing breast cancer (although it should be acknowledged that number of babies born was no longer found to be a risk predictor when multivariate logistic regression was used). We also found that women having their first child at 30 years old or older had an increased risk developing breast cancer (OR, 1.5) compared with those who were 23 years old or younger. Although this relationship was not significant (p=0.08), it is relatively similar to a large cohort study in Denmark that showed that women who postpone their first child to after 30 years of age had double the risk of developing breast cancer compared with those who had their first child before they were 20 years old [19]. A number of our findings did not align with those of studies from other countries such as family history of breast cancer or breast feeding duration, neither of which were significantly related to breast cancer in our study. However, the results of breast cancer family history were consistent with those of a previous Hanoi-based investigation [5].

With regard to diet, despite insignificant results (p > 0.05), there was a relationship between breast cancer and consuming one or more cups of coffee per day (OR, 1.5), which is in line with a prospective study in Singapore showing that drinking two or more cups of coffee per day increased the risk of being diagnosed with advanced breast cancer (OR, 2.3) [20]. Similarly, there was no significant relationship between soy intake and breast cancer observed in the present study, which may have been because of the low quantity of soy milk uptake among Vietnamese women; specifically, only 14% of subjects reported that they drank at least one cup of soy milk per day. It seems that the benefit associated with soy milk only occurs in Asian countries in which women begin consuming soy products from early life and in greater amounts [21]. Similar to soy, we did not find any connection between vegetable intake and breast cancer, even though a breast-cancer protective effect of vegetable consumption through antioxidant and fiber content has been reported [22]. Our findings, while consistent with those of a previous U.S. study [23], are at odds with the dose-dependent, decreasing breast cancer trend found to be associated with large quan-

tities of vegetables in postmenopausal Singaporean and Chinese women [22].

Population studies have consistently shown that Western lifestyle patterns such as smoking and drinking alcohol are associated with increased risk of breast cancer; however, no statistical significance was observed in our study. This could be explained by the fact that less than 5% of women in both the control and cancer groups had a history of smoking, and less than 1% consumed alcohol. Whilst in agreement with neighboring countries such as China [11] and Thailand [24], this is in contrast to data from Australia and Japan [25,26].

In this study, a variation of the risk factors for premenopausal and postmenopausal breast cancer was recorded. Having dense breast tissue was a predominant risk factor among all participants, although it had a greater impact on postmenopausal women than premenopausal women as indicated by a higher OR (2.0 vs. 1.6), which was in line with the results of a Korean study [27]. This could be explained by the finding that young women with growing mammary glands often have denser breasts than older women, which make malignant nodules less likely to be detected on mammograms. While having fewer pregnancies was a common risk in both premenopausal and postmenopausal participants, women within menstrual periods were reported to have a higher risk of developing breast cancer (OR, 2.6) than those whose periods had stopped (OR, 2.3). Hormone use and inactivity were only associated with breast cancer in premenopausal women, which illustrate differences in lifestyle between age groups in Vietnam. Premenopausal women tend to have less pregnancies, use more hormone replacements, and participate less in physical activities than postmenopausal women, which makes the risk factors of breast cancer in younger Vietnamese women more similar to those observed in westernized countries [18] where no physical activity is associated with a modest (15%-20%) increased risk [28] and women who have a history of using hormone replacement therapy or regular oral contraceptive pills have an increased risk of breast cancer of 17%-35% [29].

It should be noted that the current study was an exploratory study with several limitations. First, we collected data in a specific period of time; therefore, this study did not allow for changes in behavior over time to be incorporated. Accordingly, a longitudinal study might be needed to confirm these findings. Second, because data were collected through hospital-based systems, participants could not be allocated to a screening or diagnostic route. The inability to consider individually screened and symptomatic women highlights the need for better population-based disease surveillance systems in Vietnam. Nonetheless, this study is the first to investigate key demographic, reproductive and lifestyle factors relating to breast cancer in Vietnam. The findings presented here were similar to and different from those reported elsewhere. Overall, the results of this study will facilitate development of breast cancer prevention strategies specific for the 45 million women who live in Vietnam.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

Acknowledgments

We would like to send special thanks to Prof. Bui Dieu, Dr. Nguyen Van Thi, Dr. Diep Bao Tuan, Dr. Pham Thang Long, Dr. Le Hong Cuc, Ms. Thao Nguyen, Dr. Vo Tan Duc, Mr. Nguyen Hoang Phi Long at the National Cancer Hospital in Ha Noi, the Oncology Hospital and University of Medicine and Pharmacy in Ho Chi Minh City for assisting us in data collection and ethics application.

References

1. World Health Organization. Global health estimates. Geneva: World Health Organization; 2012.
2. Vuong DA, Velasco-Garrido M, Lai TD, Busse R. Temporal trends of cancer incidence in Vietnam, 1993-2007. Asian Pac J Cancer Prev. 2010;11:739-45.
3. Trieu PD, Mello-Thoms C, Brennan PC. Female breast cancer in Vietnam: a comparison across Asian specific regions. Cancer Biol Med. 2015;12:238-45.
4. Kaminska M, Ciszewski T, Lopacka-Szatan K, Miotla P, Staroslawska E. Breast cancer risk factors. Prz Menopauzalny. 2015;1:196-202.
5. Ginsburg OM, Dinh NV, To TV, Quang LH, Linh ND, Duong BT, et al. Family history, BRCA mutations and breast cancer in Vietnamese women. Clin Genet. 2011;80:89-92.
6. Nichols HB, Trentham-Dietz A, Love RR, Hampton JM, Hoang Anh PT, Allred DC, et al. Differences in breast cancer risk factors by tumor marker subtypes among premenopausal Vietnamese and Chinese women. Cancer Epidemiol Biomarkers Prev. 2005;14:41-7.
7. Boyd NF, Guo H, Martin LJ, Sun L, Stone J, Fishell E, et al. Mammographic density and the risk and detection of breast cancer. N Engl J Med. 2007;356:227-36.
8. Wilson LF, Page AN, Dunn NA, Pandeya N, Protani MM, Taylor RJ. Population attributable risk of modifiable risk factors

associated with invasive breast cancer in women aged 45-69 years in Queensland, Australia. Maturitas. 2013;76:370-6.
9. American College of Radiology. ACR BI-RADS atlas 5 edition changes [Internet]. Reston, VA: American College of Radiology; 2004 [cited 2017 Jan 5]. Available from: http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/BIRADS/BIRADS%20V5%20Changes.pdf.
10. Australian Institute of Health and Welfare. The Active Australia Survey: a guide and manual for implementation, analysis and reporting. Canberra: Australian Institute of Health and Welfare; 2003.
11. Xu YL, Sun Q, Shan GL, Zhang J, Liao HB, Li SY, et al. A case-control study on risk factors of breast cancer in China. Arch Med Sci. 2012;8:303-9.
12. Barton B, Peat J. Medical statistics: a guide to SPSS, data analysis and critical appraisal. 2nd ed. Hoboken, NJ: Wiley BMJ Books; 2014.
13. Peat J, Barton B, Elliott E. Statistics workbook for evidence-based health care. Hoboken, NJ: Wiley-Blackwell; 2009. p. 93-109.
14. Wong CS, Lim GH, Gao F, Jakes RW, Offman J, Chia KS, et al. Mammographic density and its interaction with other breast cancer risk factors in an Asian population. Br J Cancer. 2011; 104:871-4.
15. van Gils CH, Hendriks JH, Holland R, Karssemeijer N, Otten JD, Straatman H, et al. Changes in mammographic breast density and concomitant changes in breast cancer risk. Eur J Cancer Prev. 1999;8:509-15.
16. Harvey JA, Bovbjerg VE. Quantitative assessment of mammographic breast density: relationship with breast cancer risk. Radiology. 2004;230:29-41.
17. Ahmadinejad N, Movahedinia S, Movahedinia S, Holakouie Naieni K, Nedjat S. Distribution of breast density in Iranian women and its association with breast cancer risk factors. Iran Red Crescent Med J. 2013;15:e16615.
18. Anothaisintawee T, Wiratkapun C, Lerdsitthichai P, Kasamesup V, Wongwaisayawan S, Srinakarin J, et al. Risk factors of breast cancer: a systematic review and meta-analysis. Asia Pac J Public Health. 2013;25:368-87.
19. Wohlfahrt J, Andersen PK, Mouridsen HT, Melbye M. Risk of late-stage breast cancer after a childbirth. Am J Epidemiol. 2001;153:1079-84.
20. Zhu L. Coffee consumption increases risk of advanced breast cnacer among Singapore Chinese women [thesis]. Fort Collins, CO: Colorado State University; 2013.
21. Dong JY, Qin LQ. Soy isoflavones consumption and risk of breast cancer incidence or recurrence: a meta-analysis of prospective studies. Breast Cancer Res Treat. 2011;125:315-23.
22. Butler LM, Wu AH, Wang R, Koh WP, Yuan JM, Yu MC. A vegetable-fruit-soy dietary pattern protects against breast cancer among postmenopausal Singapore Chinese women. Am J Clin Nutr. 2010;91:1013-9.
23. Mahoney MC, Bevers T, Linos E, Willett WC. Opportunities and strategies for breast cancer prevention through risk reduction. CA Cancer J Clin. 2008;58:347-71.
24. Jordan S, Lim L, Vilainerun D, Banks E, Sripaiboonkij N, Seubsman SA, et al. Breast cancer in the Thai Cohort Study: an exploratory case-control analysis. Breast. 2009;18:299-303.
25. Protani M, Page A, Taylor R, Glazebrook R, Lahmann PH, Branch E, et al. Breast cancer risk factors in Queensland women attending population-based mammography screening. Maturitas. 2012;71:279-86.
26. Mizota Y, Yamamoto S. Prevalence of breast cancer risk factors in Japan. Jpn J Clin Oncol. 2012;42:1008-12.
27. Park IH, Ko K, Joo J, Park B, Jung SY, Lee S, et al. High volumetric breast density predicts risk for breast cancer in postmenopausal, but not premenopausal, Korean Women. Ann Surg Oncol. 2014;21:4124-32.
28. Monninkhof EM, Elias SG, Vlems FA, van der Tweel I, Schuit AJ, Voskuil DW, et al. Physical activity and breast cancer: a systematic review. Epidemiology. 2007;18:137-57.
29. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. Lancet. 1996;347:1713-27.