Cancer Causes and Control (2005) 16:929–937
DOI 10.1007/s10552-005-4932-9

Breast cancer and dietary factors in Taiwanese women★

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Received 7 October 2004; accepted in revised form 5 April 2005

Key words: breast cancer, early onset, Chinese, diet, Taiwanese.

Abstract

Objectives: To examine the effect of the consumption of dietary factors on the risk of breast cancer in a case–control study in Taiwan.
Methods: Two-hundred-and-fifty cases and 219 age-matched controls between the ages of 25 and 74 were interviewed in person between 1996 and 1999. Usual consumption of dietary habits including 100 foods was assessed using a food frequency questionnaire and a nutrient database developed and validated in Taiwanese populations.
Results: Cases consumed significantly more fat than controls. Cases also consumed statistically significant less supplements such as vitamins and mineral than controls. Food group analyses showed that highest quartile of beef and pork intake significantly increased risk in younger women (OR = 2.5, 95% CI = 1.0–6.0) and all women (OR = 2.5, 95% CI = 1.1–3.3). The age- education- and total calorie-adjusted odds ratio (OR) of breast cancer risk comparing the highest and second highest quartile of fat intake to the lowest quartile was 5.1, 95% confidence interval (CI): 2.1–13 and 3.5, 95% CI: 1.4–8.7 among those younger cases (≤40). A multiple regression model indicates a protective effect of supplements (OR: 0.40, 95% CI: 0.3–07) and a harmful effect of dietary fat (OR: 2.6, 95% CI: 1.4–5.0) for the highest *versus* lowest quartile in all women.
Conclusions: Our results indicate a strong protective effect of dietary supplements and a harmful effect of dietary fats on the risk of breast cancer among women in Taiwan. These findings should be confirmed in future follow-up studies. Specific amount of dietary supplements and dietary fats should be quantified for a more accurate evaluation on the risk for breast cancer in this population.

Introduction

Breast cancer is the most commonly diagnosed cancer among Taiwanese women, contributing to more than 25% of the overall cancer burden in this population. The average annual incidence rate of breast cancer between 1995 and 2000 was about 39.6 per 100,000; approximately two third of the rate of Chinese Americans in the US (59 per 100,000) [1]. Early-onset breast cancer (age ≤40) composed of 30% of all breast cancer patients seen in the Koo Foundation Sun Yet-Sen Cancer Center in Taiwan [2]. Women with breast cancer diagnosed at a younger age have been observed in Asian countries as well. Recent efforts have focused on the role of dietary factors, both the increased risk of dietary fat and fatty acids [3–5], and the protective effect of fruits and vegetables [6–10], and phytoestrogens [11, 12] in the etiology of this hormone-dependent breast cancer. Epidemiological studies on the relationship of macronutrients and micronutrients with breast cancer risk in Taiwanese women are relatively rare. The most recent case–control study by Chie *et al.* [13] showed little association of

★ Supported by the Koo Foundation Cancer Center Research Fund.
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dietary factors with the risk of breast cancer, the sample size of this study was relative small and dietary questions were very limited as well.

This case–control study examined the association between dietary factors and specific foods and breast cancer risk in Taiwan. We determined the risk associated with dietary factors using a nutrient database developed by Taiwanese colleagues [14]. We believed that a more complete assessment of dietary consumption from various food sources and a more specific measurement of the frequency and amount of each food consumed would allow us to gain a better understanding of the risk association between dietary consumption and breast cancer in Taiwan.

Materials and methods

Study subjects

Cases were newly diagnosed with pathologically confirmed breast cancer (ICD-9 code 174) between 1996 through 1999, who were treated in either out-patient clinic or in patient Koo Foundation Cancer Center (KFCC) in Taipei. KFCC is the leading Cancer hospital in Taiwan. For each index case, one healthy control subject matched to the case by five year age group was recruited from out-patient mammography screening clinic and medical annual check up clinic at KFCC. Eligibility criteria for both cases and controls were age between 25 and 79, and alive at the time of contact for the study. Controls were excluded if they were diagnosed with cancer, gastric problems or heart diseases. The overall response rate was 87% (89% for cases and 84% for controls). The final study sample for this analysis was 250 cases and 219 controls, of which 99 cases and 89 controls were under or equal to 40 years of age. We present this group stratification because early onset of breast cancer especially before age 40 is the unique feature in Taiwan. Among cases in the younger age group (≤40), 14% were *in situ* cases, and 28%, 32%, 21% and 4% were at stage 1, 2, 3 and 4, respectively; among cases in the older age group (>40), 10% were *in situ* cases, and 31%, 36%, 21% and 2% were at stage 1, 2, 3, and 4, respectively

Data collection

Face-to-face interviews were conducted in the out-patient clinic at KFCC for both cases and controls. Interviewers were trained in survey and dietary assessment methods. The same interviewer interviewed both cases and the age-matched controls to reduce information bias. Information on demographic characteristics (ethnicity, residence), marital and reproductive history, weight and height, dietary and physical activity habits, medical history, and family history of breast cancer was ascertained directly from the subjects. The period of reference in assessing diet and other lifestyle factors was one year before diagnosis for cases and last year prior interviews for controls. The development of the food frequency questionnaire is described in detail elsewhere [14]. Questions included the frequency (times per day, week, or year during the reference period) and quantity of consumption of 100 food and food items. Three-dimensional food models were used to assist subjects in estimating the portion size.

Data analysis

Dietary data was first estimated by nutrients intake. Nutrient database of Taiwanese foods provided 19 macro and micro nutrients for each food and food items. We excluded women whose total daily caloric intake was higher than 5000 kcal, or lower than 500 kcals, because those intakes were judged to be over- or under-reported, respectively. A total of 21 cases and 14 controls were excluded which give us 250 cases and 219 controls for the analysis. All analyses were modeled separately for different age stratifications: One group by menopausal age i.e. younger than age 50 or over than age 50; and the other group by early onset i.e. younger (≤40) and older (>40); and all age groups. The comparisons of distribution or mean levels of demographic factors between cases and controls were performed by chi-square or two-tailed *t*-test. Odds ratios (OR) and 95% confidence interval (CI) were obtained by unconditional logistic regression for traditional reproductive variables and some lifestyle characteristics.

The 100 food items were regrouped into 20 food groups. The food groups were categorized based on their similar nutrient contents. For example: High fat food includes pork, beef, lamb, smoked meat, ice cream, cheese, cream, salad dressing, cooking oil, peanuts and walnuts, cake and pie, croissant and donut, chocolate, potato chips and instant noodles. High vitamin C food includes papaya, mango, kiwi, guava, citrus fruits, strawberry, cherry, green leafy vegetables, broccoli, radish, green peas, tomato, cucumber, sprouts and potato. Soy rich food consists of soy beans, dried soy bean curd, fried soy bean curd, soy milk, soy drink, miso soup and other soy products. Allium includes green onion, onion, ginger and garlic.

Since most nutrients and some food items were not normally distributed among cases and controls, the Wilcoxon rank-sum test was used to test for differences in levels of these food items and nutrients between cases and controls. Univariate analyses using unconditional logistic regression were performed to find the OR and 95% CI associated with each quartile of foods and nutrients adjusted for age, education and total calories. The cut-offs of the quartile levels for each of the nutrients were based on the distributions among control subjects. The *p*-value for test for linear trend was computed by including one term for the nutrient in its ordinal form (i.e. four levels for the nutrients or food groups). To examine if the association between food groups and breast cancer could be confounded by other factors, multivariate analyses were conducted to adjust the effects of other factors. Covariates were included in the multivariate models using several approaches: if they were determined to be independently associated with breast cancer in univariate analysis, if their inclusion in the multivariate model significantly altered the log-likelihood statistic of the nested model [15], and if they affected the magnitude of the nutrient ORs by more than 10%. In all of the models, odds ratios were presented for each quartile, adjusted for multi-factors including at least age and total calories other than fat.

Results

Since early onset of breast cancer is the unique feature in Taiwan, we decided to present the results by grouping this younger than or equal to 40 and older than 40 groups in addition to all women. We also performed all the analyses based on menopausal age groups, i.e. Younger than 50 and equal or older than 50, but found results of these two groups were not very striking; and results of the older than 50 group were similar to findings from the group of older than 40. Thus, we presented results stratification by the early onset group (younger or equal to 40) and the older women group (age older than 40).

The distributions of weight, height, body mass index, age, and residence (rural *versus* urban), region (South *versus* North), dialect spoken (Taiwanese *versus* others) were similar between cases and controls, *p*-value greater than 0.05 (Table 1). Education level was different, although not significant, that cases were more likely to report less education than controls. Among the younger group (≤40), more cases were married; and the controls were slightly younger than their corresponding cases. Table 2 shows risk associated with traditional known risk factors, such as age at menarche, menopause, age at first pregnancy, and parity, and a few factors that we hypothesized such as housework, life satisfaction, supplement use and use of bras. Consistent with previous findings, women having their menopause at later age were more likely to be diagnosed with breast cancer. Women doing more than two hours housework per week, taking supplements were significantly at lower risk of breast cancer. Contrary to previous findings, young women (≤40) having their menarche at higher age or having more full-term pregnancies were more likely to be diagnosed with breast cancer.

The adjusted OR and 95% CI for each quartile level of nutrient intake are presented in Table 3. The highest quartile of energy intake and total fat intake were significantly associated with about 100% increase in breast cancer risk among all women, compared to the corresponding lowest quartiles; the risks were even more noticeable within young age group, especially for the highest quartile of dietary fat intake the risk was five

Table 1. Demographic characteristics by case control status and by age groups

	Age ≤40			Age >40			All women		
	Case (n = 99)	Control (n = 89)	*p* value	Case (n = 151)	Control (n = 130)	*p* value	Case (n = 250)	Control (n = 219)	*p* value
Mean age	35.3 ± 3.7	34.0 ± 4.4	0.03	54.9 ± 9.5	55.0 ± 9.6	0.98	47.2 ± 12.4	46.4 ± 13	0.54
Mean weight	54.8 ± 7.4	54.0 ± 6.9	0.46	57.3 ± 8.7	56.7 ± 6.7	0.48	56.3 ± 8.3	55.6 ± 6.9	0.3
Mean height	158.7 ± 4.7	159.2 ± 5.5	0.49	156 ± 5.3	156.3 ± 4.4	0.64	157.1 ± 5.3	157.5 ± 5.1	0.41
Mean BMI	21.8 ± 2.8	21.3 ± 2.5	0.25	23.6 ± 3.6	23.2 ± 2.7	0.34	22.9 ± 3.4	22.4 ± 2.8	0.15
Education									
≤12	45 (45.5)	30 (33.7)	0.2	110 (72.9)	84 (64.6)	0.26	155 (62)	114 (52.0)	0.07
13–16	47 (47.5)	49 (55.1)		39 (25.8)	42 (32.3)		86 (34.4)	91 (41.6)	
≥17	7 (7.1)	10 (11.2)		2 (1.3)	4 (3)		9 (3.6)	14 (6.4)	
Marital status									
Single	10 (10.1)	20 (22.5)	0.02	7 (4.6)	2 (1.5)	0.14	17 (6.8)	22 (10.1)	0.2
Married	89 (89.9)	69 (77.5)		144 (95.4)	128 (98.5)		233 (93.2)	197 (89.9)	
Living place									
Urban	56 (56.6)	58 (65.2)	0.23	104 (68.9)	89 (68.5)	0.94	160 (64)	147 (67.1)	0.48
Rural	43 (43.4)	31 (34.8)		47 (31.1)	41 (31.5)		90 (36)	72 (32.9)	

Table 2. Breast cancer risk factors by age groups

Age group	≤40 OR (95 % CI)	> 40 OR (95 % CI)	All OR (95 % CI)
Age at menarche			
≤12	1.0	1.0	1.0
13–14	1.2 (0.5–2.7)	0.7 (0.3–1.7)	1.0 (0.5–1.7)
15–16	1.8 (0.7–4.7)	0.6 (0.2–1.5)	1.0 (0.5–1.9)
≥17	1.2 (0.2–6.4)	1.2 (0.4–3.4)	1.5 (0.7–3.5)
Age at menopause			
< 45	–	1.0	1.0
45–50	–	2.0 (0.9–4.4)	2.0 (0.9–4.4)
51–54	–	2.3 (0.9–6.0)	2.3 (0.9–6.0)
≥55	–	4.3 (1.3–14.1)	4.3 (1.3–14.1)
Age at first full-term pregnancy (FTP)			
< 20	1.0	1.0	1.0
20–24	2.5 (0.4–17)	0.6 (0.3–1.3)	0.7 (0.4–1.4)
25–29	3.4 (0.5–23)	0.8 (0.3–1.8)	1.0 (0.5–2.1)
≥30	1.9 (0.2–15)	1.0 (0.3–3.2)	0.9 (0.4–2.2)
Number of FTP			
Nulliparous	1.0	1.0	1.0
1–2	1.9 (0.9–4.3)	0.6 (0.2–1.5)	1.4 (0.8–2.6)
≥3	2.1 (0.6–6.7)	0.6 (0.2–1.7)	1.4 (0.7–2.8)
Oral contraceptive use			
No	1.0	1.0	1.0
Yes	1.9 (0.9–3.7)	0.8 (0.4–1.4)	1.1 (0.7–1.7)
Do ≥2 h/week housework			
No	1.0	1.0	1.0
Yes	0.5 (0.1–2.4)	0.1 (0.01–0.8)	0.27 (0.09–0.8)
Supplement use			
No	1.0	1.0	1.0
Yes	0.5 (0.3–0.9)	0.4 (0.3–0.7)	0.5 (0.3–0.7)
Family history of breast cancer in first-degree female relative (s)			
No	1.0	1.0	1.0
Yes	3.7 (0.4–3.5)	1.7 (0.7–3.9)	1.9 (0.9–4.1)
Satisfy with your life			
No	1.0	1.0	1.0
Yes	0.4 (0.2–0.7)	0.6 (0.4–1.1)	0.5 (0.4–0.8)
Wear bras per day			
≤12 h	1.0	1.0	1.0
> 12 h	1.3 (0.6–2.5)	2.7 (1.5–4.7)	2 (1.3–3.0)
Wear bras at sleep			
No	1.0	1.0	1.0
Yes	1.6 (0.8–2.9)	1.5 (0.9–2.4)	1.5 (1.0–2.2)

times higher. Intake of vitamins A, E and C showed protective effects to breast cancer in all age groups except younger women group for vitamin E intake. Both vitamin A intake for 1.7–2.6 RE/day/kcal and vitamin C intake for more than 121 mg/day/kcal were significantly and inversely associated with breast cancer risk, OR = 0.6 and OR = 0.5, respectively, compared to their lowest quartile intake levels. The protective effect was not obvious for vitamin E intake.

Table 4 presents adjusted odds ratios for food groups by quartile. High fat food consumption at the highest quartile level significantly increased breast cancer risk from 2.6 times to 3.6 times higher for different age groups, compared to the lowest quartile. Although high vitamin C food group did not show significant protective effect, the fat-and-vitamin C combined food group indicated significant increased risk for high fat and low vitamin C combination for younger women (OR = 3.0) and all age groups (OR = 1.7). Beef and pork intake was also significantly associated with increased risk for the same age groups. Allium at the highest quartile level and soy rich food at the second quartile level

Table 3. Odds ratios associated with selected nutrients by quartiles and by age groups (adjusted for age and education)

			≤40			> 40			All		
		Quartile	Case (n = 99)	Control (n = 89)	OR (95 % CI)	Case (n = 151)	Control (n = 130)	OR (95 % CI)	Case (n = 250)	Control (n = 219)	OR (95 % CI)
Total energy (kcal/d)	1	< 1721	11	17	1.0	36	37	1.0	47	54	1.0
	2	1721–2106	18	26	1.1 (0.4–3.0)	30	29	1.1 (0.6–2.2)	48	55	1.0 (0.6–1.7)
	3	2107–2651	26	17	2.8 (1.0–7.6)	37	38	1.0 (0.5–2.0)	63	55	1.4 (0.8–2.4)
	4	> 2651	44	29	2.9 (1.1–7.3)	48	26	2.1 (1.1–4.2)	92	55	2.1 (1.2–3.6)
Total fat (g/d)	1	< 56	13	27	1.0	37	29	1.0	50	56	1.0
	2	56–71	16	14	2.8 (1.0–7.6)	30	40	0.6 (0.3–1.2)	46	54	0.9 (0.5–1.6)
	3	72–98	31	26	3.5 (1.4–8.7)	41	30	1.1 (0.6–2.2)	72	56	1.5 (0.9–2.6)
	4	> 98	39	22	5.1 (2.1–13)	43	31	1.2 (0.6–2.4)	82	53	1.9 (1.1–3.2)
Vitamin A (RE/d/kcal)	1	< 1.1	35	22	1.0	50	32	1.0	85	54	1.0
	2	1.1–1.6	24	24	0.6 (0.3–1.4)	39	28	0.9 (0.5–1.8)	63	52	0.8 (0.5–1.3)
	3	1.7–2.6	21	24	0.6 (0.2–1.3)	29	36	0.5 (0.3–1.1)	50	60	0.6 (0.3–0.9)
	4	> 2.6	19	19	0.6 (0.3–1.4)	33	34	0.7 (0.3–1.3)	52	53	0.7 (0.4–1.1)
Vitamin E (α-TE/d/kcal)	1	< 2.4	25	23	1.0	42	27	1.0	67	50	1.0
	2	2.4–3.1	37	31	1.2 (0.5–2.5)	35	36	0.6 (0.3–1.1)	72	67	0.8 (0.5–1.3)
	3	3.2–3.9	20	20	1.0 (0.4–2.4)	32	23	0.8 (0.4–1.7)	52	43	0.9 (0.5–1.5)
	4	> 3.9	17	15	1.1 (0.5–2.8)	42	44	0.6 (0.3–1.2)	59	59	0.8 (0.4–1.3)
Vitamin C (mg/d/kcal)	1	< 88	40	25	1.0	50	30	1.0	90	55	1.0
	2	88–121	26	20	0.9 (0.4–1.9)	38	34	0.7 (0.4–1.3)	64	54	0.7 (0.4–1.2)
	3	122–168	19	20	0.6 (0.2–1.3)	29	35	0.5 (0.3–1.0)	48	55	0.5 (0.3–0.9)
	4	> 168	14	24	0.3 (0.1–0.7)	34	31	0.7 (0.3–1.3)	48	55	0.5 (0.3–0.9)

significantly decreased in risk compared to the lowest quartile for about 40–50% (OR = 0.4, OR = 0.5, respectively) in older age group but not in the younger group.

Results of multiple logistic regression models were shown in Tables 5, 6 and Table 7. The results confirmed the study hypothesis that dietary fat, and fat rich food items were associated with two to three folds increase in breast cancer risk especially among younger women. Vitamin and minerals supplements were consistently shown to offer 50–60% reduction in breast cancer risk among the two age groups, however, engaging in at least two hours of housework was more protective among women after age 40 (90% reduction).

Discussion

Our study supports the findings of previous investigations in other populations showing a protective effect of vitamins and minerals supplements [16, 17], and engaging in physical exercise, such as housework, [18–21] on breast cancer risk, and an increased risk of high fat consumption [3–5]. In our study, the total fat consumption in the highest quartile showed a significant 3-fold increase in breast cancer risk compared to the lowest quartile in all women, as well as among women at younger age. Most literature refers young age group as women under 50; only a few have ever addressed breast cancer risk factors for those under age 40. Our study provides an opportunity to present the finding for this younger age group. Most studies on breast cancer risk factors traditionally address menopausal status as a major factor. We found that results on post-menopausal women were almost identical to the findings with the older women and all women combined. In addition, the highest quartile of vitamin C rich foods also showed a significant reduction in breast cancer risk compared to the lowest quartile. Our study also showed that allium has a potential in reducing breast cancer risk, although the result was not statistically significant.

One must be aware of several limitations when interpreting results from this study. Selection bias could be resulted when participation rate was low, and our study attempted to interview all of available cases, and in fact, the refusal is about 10% for cases and 15% for controls. By examining percentage of cases in various stages at diagnosis, we noticed that 12% were *in situ* cases, over 80% are at early stage, and only 4% are at advanced stage. This distribution of *in situ*, and more advanced stage are slightly lower than those reported in the literature in the West, however, this should not bias our assessment of risk in Taiwanese women.

Table 4. Odds ratios associated with selected food groups by quartiles and age groups (adjusted for age and education)

	Quartile		≤40			> 40			All		
			Case (n = 99)	Control (n = 89)	OR (95 % CI)	Case (n = 151)	Control (n = 130)	OR (95 % CI)	Case (n = 250)	Control (n = 219)	OR (95 % CI)
High fat food (g/week)	1	< 282	13	20	1.0	34	38	1.0	47	58	1.0
	2	282–460	14	18	1.2 (0.4–3.4)	41	35	1.3 (0.7–2.6)	55	53	1.3 (0.7–2.2)
	3	461–661	22	22	1.9 (0.7–4.8)	26	33	0.9 (0.5–1.9)	48	55	1.2 (0.7–2.1)
	4	> 661	50	29	3.6 (1.5–8.8)	50	24	2.6 (1.3–5.1)	100	53	2.7 (1.6–4.6)
High vit C food (g/week)	1	< 1206	31	18	1.0	49	36	1.0	80	54	1.0
	2	1206–1868	21	24	0.5 (0.2–1.2)	33	31	0.8 (0.4–1.6)	54	55	0.7 (0.4–1.1)
	3	1869–2786	25	26	0.6 (0.3–1.3)	33	30	0.8 (0.4–1.6)	58	56	0.7 (0.4–1.2)
	4	> 2786	22	21	0.6 (0.2–1.3)	36	33	0.9 (0.5–1.7)	58	54	0.8 (0.5–1.3)
Total fat (g/d) and vitamin C (mg/d)	1	Low fat high C	11	20	1.0	27	29	1.0	38	49	1.0
	2	Low fat low C	18	21	1.3 (0.5–3.6)	40	40	1.0 (0.5–2.0)	58	61	1.1 (0.6–1.9)
	3	High fat high C	33	23	3.2 (1.2–8.3)	41	26	1.6 (0.8–3.4)	74	49	2.0 (1.1–3.4)
	4	High fat low C	37	25	3.0 (1.2–7.7)	43	35	1.4 (0.7–2.8)	80	60	1.7 (1.0–3.0)
Beef and pork (g/week)	1	< 51	13	18	1.0	35	34	1.0	48	52	1.0
	2	51–106	16	23	1.2 (0.4–3.1)	32	37	0.9 (0.5–1.8)	48	60	1.0 (0.5–1.7)
	3	107–196	28	19	2.3 (0.9–5.8)	36	32	1.2 (0.6–2.3)	64	51	1.5 (0.9–2.6)
	4	> 196	42	29	2.5 (1.0–6.0)	48	27	1.8 (0.9–3.6)	90	56	1.9 (1.1–3.3)
Allium (g/week)	1	< 9.5	41	38	1.0	75	40	1.0	116	78	1.0
	2	9.5–24.7	21	15	1.2 (0.5–2.8)	33	36	0.5 (0.3–0.9)	54	51	0.7 (0.4–1.2)
	3	24.8–52.2	17	16	0.9 (0.4–2.1)	18	23	0.4 (0.2–1.0)	35	39	0.7 (0.4–1.1)
	4	> 52.2	20	20	1.0 (0.5–2.1)	25	31	0.4 (0.2–0.9)	45	51	0.6 (0.4–1.0)
Soy rich food (g/week)	1	< 114	14	15	1.0	43	40	1.0	57	55	1.0
	2	114–191	15	17	0.9 (0.3–2.5)	21	38	0.5 (0.3–1.0)	36	55	0.6 (0.4–1.1)
	3	192–341	33	29	1.2 (0.5–2.9)	46	26	1.8 (0.9–3.5)	79	55	1.6 (0.9–2.6)
	4	> 341	37	28	1.5 (0.6–3.6)	41	26	1.6 (0.8–3.2)	78	54	1.6 (0.9–2.7)
Green tea (g/week)	1	< 16	23	22	1.0	75	56	1.0	98	78	1.0
	2	16–91	23	15	1.5 (0.6–3.6)	10	17	0.5 (0.2–1.1)	33	32	0.9 (0.5–1.6)
	3	92–664	27	29	0.9 (0.4–2.1)	35	30	0.9 (0.5–1.6)	62	59	0.9 (0.5–1.4)
	4	> 664	26	23	1.0 (0.5–2.4)	31	27	0.9 (0.5–1.8)	57	50	1.0 (0.6–1.6)

We also wanted to assure that the controls were selected unbiased; comparisons of demographic characteristics between cases and controls are reassuring. Since we interviewed subjects retrospectively, there is always the possibility of recall bias. It is also possible that subjects could have changed their dietary pattern over time, but one can only assume that the dietary pattern in the reference period was similar to the promotional stage of breast cancer. Misclassification of the dietary pattern could also occur with respect to the instrument used and the reference time period, again this would only have biased our results toward null.

Because of the limitation in nutrient data base in Taiwan lacking the detailed fatty acids values, this study would not be able to estimate breast cancer risks associated with saturated, mono and poly unsaturated fat in this unique population.

In a meta-analysis study by Gandini *et al.*, the protective effect of anti-oxidant vitamins achieved statistical significance [22]; similar findings for high vitamin C food were not observed in our study. A study by Cho *et al.*, the increased risk of dietary fat was only significant in those that consumed in the highest quintile [23], but our study showed the increased risk was consistent not just in the highest quartile but also at the third and second quartiles. Additionally, the study by Toniolo *et al.* [24], only women in the upper quintile of meat consumption had significant increased risk associated with breast cancer, the similar association was also seen in our study.

The increased risk of dietary fat in development of breast cancer can be an effective behavior modification strategy for public health message in Taiwan. Consistent finding of regular exercise, like doing housework and taking vitamin supplements showing a protective effect against breast cancer could be a surrogate measure of a healthy lifestyle. It may be more realistic to teach the public to engage in a healthy lifestyle by performing regular exercise, doing house work, consuming some protective amount of high C fruits and vegetables and avoid high consumption of dietary fat and red meat. However, it is critical then to establish the recommended amounts of fat, high C food group consumption level for prevention of breast cancer. Future studies aiming in this direction is recommended.

We did not observe any protective effect of soy consumption against breast cancer in this study. One possible explanation could be due to the soy consumption levels in Taiwan is so homogeneous, thus our study does not have enough power to detect the differences between cases and controls in all age groups.

Our study showed wearing bra at sleep and more than 12 h could have resulted in increased breast cancer risk among older women. The interpretation could only be by speculation that due to breast physiology, absorption and secretion of breast fluid [25], the accumulation of potential carcinogenic compounds remain in breast tissues could be much longer for those women wearing bra for a longer period of time.

Table 5. Multiple logistic regression odds ratios and 95% CI for the age group of ≤40

	OR	(95% CI)
Supplement use		
No	1.0	
Yes	0.4	(0.2–0.7)
Education		
< 16	1.0	
≥16	1.6	(0.8–3.0)
High Vit C food (g/week)		
< 1206	1.0	
1206–1868	0.4	(0.2–0.9)
1869–2786	0.5	(0.2–1.1)
> 2786	0.4	(0.2–1.1)
Total kcal-Fat kcal	1.0	(1.0–1.0)
High fat food (g/week)		
< 282	1.0	
282–460	1.2	(0.4–3.4)
461–661	1.9	(0.7–5.5)
> 661	3.2	(1.1–9.6)
Age		
≤30	1.0	
30–40	1.1	(1.0–1.2)

Table 6. Multiple logistic regression odds ratios and 95% CI for the age group of greater than 40

	OR	(95% CI)
Supplement use		
No	1.0	
Yes	0.5	(0.3–0.9)
Education		
≤16	1.0	
> 16	1.3	(0.7–2.4)
Wear bras		
< 13 h/day	1.0	
≥13 h/day	3.0	(1.6–5.7)
Do strenuous housework		
<2 h/week	1.0	
≥2 h/week	0.1	(0.001–0.8)
Total kcal-Fat kcal	1.0	
Allium (g/week)		
< 9.5	1.0	
9.5–24.7	0.6	(0.3–1.2)
24.8–52.2	0.6	(0.3–1.4)
> 52.2	0.4	(0.2–0.9)
High fat food (g/week)		
< 282	1.0	
282–460	1.4	(0.7–2.9)
461–661	0.9	(0.4–2.0)
> 661	2.6	(1.1–6.1)
Age		
41–50	1.0	
51–60	1.0	(1.0–1 0)
> 60	1.0	(1.0–1.0)

Although the study included subjects from only one hospital, this cancer center hospital is a referral hospital and most patients are from wide regions of Taiwan, thus the study is representative of the Taiwanese population. We examined the residence history for both cases and controls, it is reassuring that the study population in deed are drawn from all Taiwan regions, not just locally. Also, to our knowledge, this is the first study that examined the association of breast cancer risk with dietary factors in early on-set age under 40 women in Taiwan. Knowing the specific content of the fat subcomponents, such as saturated or un-saturated fatty acids will help us achieve a more accurate assessment of its harmful role. Additionally, genetic studies by Huang *et al.* [26] with profiling breast tissues in these early onset women may provide clues as where the specific gene deletion or mutations occur in these early onset cases. A study from young Korean women, less than 40 years old, with breast cancer found that the prevalence of BRCA1 and BRCA2 mutations was high [27].

Table 7. Multivariate odds ratios and 95%CI for women of all ages

	OR	(95% CI)
Supplement use		
No	1.0	
Yes	0.4	(0.3–0.7)
Education		
≤16 years	1.0	
> 16 years	1.4	(0.9–2.2)
Wear bras		
< 13 h	1.0	
≥13 h	2.1	(1.3–3.3)
Do strenuous housework		
< 2 h/week	1.0	
≥2 h/week	0.2	(0.1–0.7)
Total kcal-Fat kcal	1.0	(1.0–1.0)
Allium (g/week)		
< 9.5	1.0	
9.5–24.7	0.7	(0.4–1.3)
24.8–52.2	0.8	(0.4–1.4)
> 52.2	0.5	(0.3–0.9)
High fat food (g/week)		
< 282	1.0	
282–460	1.3	(0.8–2.4)
461–661	1.2	(0.7–2.2)
> 661	2.6	(1.4–5.0)
Age		
< 40	1.0	
40–50	1.0	(1.0–1.0)
50 +	1.0	(1.0–1.0)

In conclusion, our results indicate a strong, harmful effect of dietary fat on the risk of breast cancer in Taiwan. These findings should be confirmed in studies in different populations with greater variation in their dietary fat intake. Such study is under-going in European countries. If confirmed, the results can have great public health implication, as there is a potential to reduce a large number of women who could have developed breast cancer; and preventive measure strategies can be achieved through behavior modification and inexpensive means targeting toward them. As Taiwanese women become more westernized, this message of behavior modification is even timelier than before.

Acknowledgements

We like to thank Julie Lin, Chia Wen Kao, Tiffney Chen, and Dr. Chen Chi Ming, for their assistance, and the financial support from Koo Foundation Cancer Research Fund, as well as appreciate all the women for their participation in the study

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