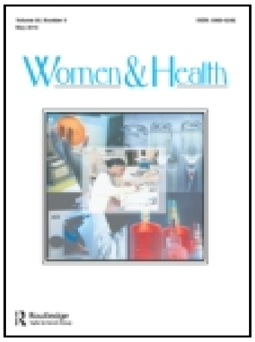


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# The Effects of Perceived Stress and Life Style Leading to Breast Cancer

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*Researchers conducted a study in a Taiwanese medical center from June 2009 to June 2011 to investigate the relations of perceived*

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*stress and lifestyle to breast cancer. A total of 157 cases and 314 controls completed a structured questionnaire. Using multiple logistic regression models, high perceived stress (adjusted odds ratio [AOR] = 1.65; 95% confidence interval [CI], 1.10–2.47), less than 1,000 kcal of physical activity expenditure per week (AOR, 2.17; 95% CI, 1.39–3.39), and high intake of fried and stir-fried food (AOR, 1.86; 95% CI, 1.24–2.77) were positively associated with breast cancer. Breast cancer was related to joint interactions between high perceived stress and alcohol intake of 11.0 g or more per day (AOR, 2.91; 95% CI, 1.23–6.86), smoking at least one cigarette per day (AOR, 2.52; 95% CI, 1.16–5.47), intake of less than 100 ml of green tea per day (AOR, 2.47; 95% CI, 1.40–4.38), physical activity of less than 1,000 kcal per week (AOR, 3.36; 95% CI, 1.77–6.36), high fried and stir-fried food intake (AOR, 3.18; 95% CI, 1.79–5.63), and high meat and seafood intake (AOR, 1.89; 95% CI, 1.09–3.27). Perceived stress, when combined with potentially risky lifestyle behaviors, may be a contributing factor to breast cancer.*

*KEYWORDS breast cancer, perceived stress, lifestyle behavior, dietary habits*

## INTRODUCTION

Like other industrialized countries, the most frequent type of cancer among women in Taiwan is breast cancer. The occurrence of breast cancer has increased steadily in Taiwan in recent years. In 2007, the annual incidence rate of breast cancer was 75.02 per 100,000 women; the rate increased to 81.36 per 100,000 women in 2008 (Taiwan Health Bureau, 2011).

Factors causing breast cancer are many and complex. The circulating level of estrogen in women has been identified as a significant factor contributing to the occurrence of breast cancer (Bernstein & Ross, 1993; Toniolo et al., 1995; Persson, 2000). Research results regarding lifestyle factors in relation to the development of breast cancer have been inconsistent. Alcohol consumption (Zhang et al., 2007; Deandrea et al., 2008; Lew et al., 2009), tobacco smoking (Gram et al., 2005; Brown et al., 2010; Deroo et al., 2011), green tea consumption (Wu et al., 2003; Shrubsole et al., 2009; Iwasaki et al., 2010), physical activity (Lahmann et al., 2007; Howard et al., 2009; Smith et al., 2011), consumption of certain foods (Wang et al., 2008; Li et al., 2009; Trichopoulous et al., 2010), and increased weight (Meyskens et al., 2000; Verkasalo et al., 2001; McTiernan et al., 2006) are lifestyle factors that have been considered in relation to the risk of breast cancer. However, the existence and strength of the relationships of these factors to breast cancer development have been inconsistent. Even though these studies found that certain factors are related to the development of breast cancer, the overall effects observed have been quite small. The lack of agreement in the role of these lifestyle factors affecting breast cancer warrants further study on the matter.

Previous studies have also illustrated a relationship between the risk of breast cancer and psychological stress (Helgesson et al., 2003; Kruk & Aboul-Enein, 2004; Williams et al., 2009). Psychological stress may promote carcinogens through estrogen synthesis and metabolism, as well as changes in the concentration of circulating estradiol (Gunin, 1996; Kam et al., 2000). Estradiol binds to estrogen receptors, activating gene expression and increasing cell proliferation (Pitot & Dragan, 2001). A woman with a lower concentration of estradiol may have a lower risk of breast cancer compared to a woman with a higher estradiol concentration (Cauley et al., 1999).

A prospective case-control study showed an association between stressful life events and breast cancer risk. In this study, more breast cancer patients consumed alcohol and smoked than did healthy controls, but the difference was not statistically significant (Ollonen, Lehtonen, & Eskelinen, 2005). One cohort and two case-control studies have also shown an association of stress with a higher risk of breast cancer (Helgesson et al., 2003; Lillberg et al., 2003; Kruk & Aboul-Enein, 2004). However, these studies only examined stress in relation to breast cancer risk; they did not analyze any further link between stress and other risk factors or whether the strength of the relationship of stress to breast cancer risk was affected by other factors.

While stress and lifestyle may be associated with breast cancer, few studies have explored the interaction between stress and lifestyle in relation to breast cancer risk. Researchers in the current study designed a hospital-based, case-control study to assess the relationship between perceived stress and lifestyle, and the potential interaction of these on the odds of breast cancer among women. They hypothesized that perceived stress would increase the odds of breast cancer and that joint effects of perceived stress and specific lifestyle factors might increase the odds of breast cancer among women in Taiwan.

## METHODS

### Study Population

This hospital-based, matched-pair, case-control study was carried out in Chung-Shan Medical University Hospital, a medical center and teaching hospital in central Taiwan. The period of study was from June 2009 to June 2011. A total of 471 participants were involved in the research with two participants in the control group matched on age to each participant in the breast cancer case study group.

Patients in the case study group were diagnosed by physicians of the breast surgical department, with histological confirmation of carcinoma in the breast tissue of all case study participants. These new breast cancer patients were about 2% of all patients seen in the breast surgical department during the period of the investigation. Of the 162 new cases (new cases were defined as cases diagnosed within one month of the study), 5 patients refused to be interviewed, and 157 patients (96.31%) took part in this study. Three hundred fourteen controls were recruited from outpatients seen in the family medicine and physical check-up departments. Two controls were matched to each case study on age (± 2 years). Matched participants were interviewed during the same time period (within one month) as the cases. Participants in the control group were screened by physicians of the family medicine and physical examination center; no control participants had cancer, a previous history of cancer, a previous case of a benign tumor, or a reproductive system disease. Generally speaking, participants in the control group tended to suffer from colds, gastric problems, diabetes, hypertension, coronary disease, liver disease, and nephritis, or they had come to the hospital for a general health check-up. These controls comprised about 4% of all patients visiting the outpatient family medicine and physical check-up departments. Of the 334 participants selected to be in the control group, 20 women did not agree to be interviewed, and 314 women (95.93%) participated in the control group.

## Data Collection

All participants resided in central Taiwan and were personally interviewed face-to-face by an interviewer using a structured questionnaire that collected information about lifestyle and stress. Interviewers were not masked as to which group each interviewee belonged. Participants were asked about their daily routines and stress levels prior to any illnesses. Before interviewing the cases, interviewers would tell respondents to answer all questionnaire questions, including lifestyle and perceived stress, retrospectively—that is how they felt in the past. If the information given by the respondents was incomplete, the questionnaire was excluded from the study. All respondents were clear-minded without any mental impairment.

The study protocol was approved by the ethics committee of Chung-Shan Medical University Hospital. All participants gave their written and signed informed consent.

## Instruments

The structured questionnaire was designed to collect personal information from respondents, including demographic and breast cancer-relevant characteristics, perceived stress level, individual behavior, and dietary habits. Demographic and breast cancer-relevant characteristics included educational level, marital status, self-reported weight and height to calculate body mass index (BMI), age at menarche, age at menopause, family history of breast cancer, and previous use of menopausal hormone therapy. BMI was calculated as weight (kg) per height squared ($m^2$). BMI was categorized into normal/underweight, $<25$ kg/$m^2$; overweight and obese, $\geq 25$ kg/$m^2$ (National Heart Blood Lung Institute, 1998).

### Perceived Stress Level

The survey on perceived stress consisted of 14 questions from the perceived stress scale (PSS) that measured one's perception of stress related to one's daily life (Cohen, Kamarck, & Mermelstein, 1983). The Chinese version of PSS had a test-retest reliability ($r = 0.76$ over a 4-week interval). The construct validity was assessed by factor analysis. Two factors, life being uncontrollable and life being unpredictable and overloaded, were assessed. The total variance accounted for by these two factors was 49.5% (Chen, 1993). The PSS asked respondents to evaluate their lives for stress levels during the preceding month. The PSS items were designed to provide a way for respondents to express how unpredictable, uncontrollable, and overloaded they felt that their lives were. The measure was sensitive to the nonoccurrence of events and ongoing life circumstances, not for a particular situation. On the PSS, a 5-level Likert scale was used to measure perceived stress levels (0 = *Never*; 4 = *Very often*). The total possible range of scores was from 0 to 56. Higher scores indicated higher levels of stress. In this study, the range of PSS scores among participants was assessed as above (high stress) or below (low stress) the median score. The median score of 23 was the cut-off value.

### Alcohol Consumption, Habitual Smoking, Green Tea Consumption, and Physical Activity

To assure content validity in the questionnaire section on alcohol consumption, habitual smoking, green tea consumption, and physical activity, the questionnaires were reviewed by three experts in the fields of epidemiology, nutrition, and health education. The content validity (correlation coefficient) was 0.90 and the test-retest reliability was 0.93 in this section. Alcohol consumption was measured as average alcohol consumption (times per day or week) and amount of alcohol ingested (dependent upon the type of beverage). Total alcohol intake was 11.0 g of ethanol for 120 ml of wine, 14.0 g for 45 ml of liquor, 12.8 g for 360 ml of regular beer, or 11.3 g for 360 ml of light beer (Zhang et al., 2007). Alcohol consumption was categorized as "no" if a participant's average ingested alcohol amount was less than the above criterion every day and "yes" otherwise. Habitual smoking was measured as number of cigarettes smoked per day and intensity of inhalation. Habitual smoking was categorized as "no" if it was less than once daily on average and "yes" otherwise. Green tea intake was categorized as "no" if it was less than one cup per day on average and "yes" otherwise. The volume of a cup of green tea was assumed to be 100 ml (Kuriyama et al., 2006). Physical activity was measured by calculating a given activity's metabolic equivalent by multiplying the number of physical activities each week with the duration of the activity and the person's weight (Ainsworth et al., 2000). In this study, a physically active individual was defined as one who had physical energy consumption of more than 1,000 kcal/week.

### Dietary Habits

To assure content validity for food intake, the questionnaires were reviewed by three experts in the fields of epidemiology, nutrition, and health education. The content validity (correlation coefficient) was 0.89 and the test-retest reliability was 0.92. The food-frequency questionnaire estimated the frequency of an individual person's normal intake of food. The food items included 18 different types of food: rice, pasta, cake, poultry, red meat, processed meat (sausage/bacon), fried meat, stir-fried meat, fish, fried fish, stir-fried fish, seafood (shrimp/clams/oysters), eggs, soybean products, dairy products, green/leafy vegetables, dark yellow vegetables, and fruits. The response consisted of food items in 5 frequency of consumption categories, which were separated as *never*, *seldom* (2–3 times/month), *occasionally* (1–2 times/week), *usually* (4–6 times/week), and *always* (at least one time/day). The responses were scored from 0 (*never*) to 4 (*always*). Factor analysis was used to analyze the frequencies of food intake for these food items. Researchers used an orthogonal rotation to identify dietary factor groupings using eigen values, the scree plot, and interpretability. Factor loadings above 0.6 were considered to be the factors. With 61.06% of variance explained, three food categories were formed: fried/stir-fried foods, meat/seafood, and vegetables/fruits. The fried/stir-fried foods group included the following foods and factor loadings: stir-fried fish, 0.88; fried fish, 0.83; stir-fried meat, 0.80; and fried meat, 0.78. The meat/seafood group included foods and factor loadings as follows: poultry, 0.85; red meat, 0.84; seafood (shrimp/clams/oysters), 0.67; and fish, 0.60. The vegetables/fruits group included the following foods with these factor loadings: green/leafy vegetables, 0.91; dark yellow vegetables, 0.90; and fruits, 0.71. By summing the frequency of consumption scores for each food in each food category weighted by its factor loading, researchers were able to calculate food group scores. They distributed participant food scores for each food category into percentiles. Using the 50th percentile (median) of the distribution as a cut-off point, they separated frequency of intake into low and high intake. The fried/stir-fried foods and meat/seafood groups thus each contained four food items, and the total possible sum of scores for each of these two food groups was 16. Three food items were in the vegetables/fruits group, which produced a total possible summed score of 12. The median cut-off scores and ranges for each of these three food groups were fried/stir-fried foods, median = 3.44 and range = 0–11.45; meat/seafood, median = 6.27 and range = 0–11.17; and vegetables/fruits, median = 9.00 and range = 2.52–10.08.

### Statistical Analysis

Data were analyzed using SPSS17.0 (Chicago, IL, USA). Univariate logistic regressions were used to test the association of breast cancer and demographics with relevant characteristics comparing cases and controls. Crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each variable. Variable(s) significantly differing between cases and controls were considered to be confounding factor(s), using statistical significance as $p < 0.10$. The main effect in conditional multiple logistic regression analysis was used to examine the differences of perceived stress and lifestyle factors between breast cancer cases and controls, considering statistical significance to be $p < 0.05$. Spearman correlation coefficients were used to assess the relation of perceived stress and each lifestyle variable. After identification of the main effects in the logistic regression models, two-way interaction factors (perceived stress and lifestyle factors) were tested with multiple logistic regression models. Variables eligible for inclusion in the models included those with variable(s) significant at $p < 0.10$ in Spearman correlations between perceived stress and each lifestyle factor and demographic characteristics. The final models were checked for goodness of fit with the Hosmer and Lemeshow test to ensure the models fit the data well.

## RESULTS

### Characteristics of Participants

The mean age of participants was 54.67 ± 10.95 years, and ages ranged from 32 to 76 years. Due to matching, the age distributions were very similar for cases and controls (Table 1). No significant differences between breast cancer cases and controls were observed in education level, marital status, BMI, late menopause, family history of breast cancer in first degree relatives, or use of hormone therapy. However, the OR for education level ≤ 9 years (OR = 1.40; 95% CI, 0.95–2.06), menarche before age 12 years (OR = 1.84; 95% CI, 1.21–2.81), and past hormone therapy for ≥ 3 months (OR = 1.59; 95% CI, 0.97–2.61) were increased and were retained in the main effect model and interaction model as confounding variables per the selection criterion ($p < 0.10$).

**TABLE 1** Unadjusted OR and 95% CI for Demographic and Breast Cancer-Relevant Characteristics in Breast Cancer Patients as Compared with Control Participants

| Characteristics | Cases ($n$ = 157) | Controls ($n$ = 314) | Total ($n$ = 471) | OR (95% CI) |
|---|---|---|---|---|
| Education level ≤ 9 years; $n$ (%) | 91 (58.0) | 156 (49.7) | 247 (52.4) | 1.40 (0.95–2.06) |
| Married/live together vs. single; $n$ (%) | 117 (74.5) | 236 (75.2) | 353 (74.9) | 0.97 (0.62–1.50) |
| BMI ≥ 25/overweight & obese vs. normal weight; $n$ (%) | 45 (28.7) | 73 (23.2) | 118 (25.1) | 1.33 (0.86–2.05) |
| Menarche before age 12 years; $n$ (%) | 34 (21.7) | 41 (13.1) | 75 (15.9) | 1.84 (1.11–3.04) |
| Age at menopause ≥ 55 years; $n$ (%) | 16 (10.2) | 38 (12.1) | 54 (11.5) | 0.82 (0.49–1.68) |
| First-degree family history of breast cancer; $n$ (%) | 13 (8.3) | 23 (7.3) | 36 (7.6) | 1.14 (0.56–2.32) |
| Past hormone therapy for ≥ 3 months; $n$ (%) | 33 (21.0) | 45 (14.3) | 78 (16.6) | 1.59 (0.97–2.61) |

## Main Effects of Perceived Stress and Risk Factors in Breast Cancer Patients Compared with Controls

Fifty-four percent ($n$ = 252) of the population reported high levels of perceived stress. High level of perceived stress was significantly positively associated with risk of breast cancer (Table 2). The AOR for high perceived stress, adjusted for education level, age at menarche, and past hormone therapy was 1.65 (95% CI, 1.10–2.47) and for being less physically active (<1,000 kcal/week) was 2.17 (95% CI, 1.39–3.39). Among the dietary factors, consumption of fried/stir-fried foods was associated with a significantly increased odds of breast cancer (AOR = 1.86; 95% CI, 1.24–2.77). No association was found between breast cancer and any of the following: alcohol consumption, habitual smoking, green tea consumption, or consumption of meat/seafood or vegetables/fruits.

**TABLE 2** Unadjusted OR and AOR and 95% CI for Perceived Stress and Behavioral and Dietary Risk Factors in Breast Cancer Patients Compared with Control Participants

| Characteristics | Cases ($n$ = 157) | Controls ($n$ = 314) | OR (95% CI) | AOR (95% CI) |
|---|---|---|---|---|
| Perceived stress (PSS) high level | 99 (63.1) | 153 (48.7) | 1.80 (1.21–2.66) | 1.65 (1.10–2.47) |
| Behavioral factors | | | | |
| Alcohol drinking; $n$ (%) | 16 (10.2) | 20 (6.4) | 1.67 (0.84–3.32) | 1.50 (0.74–3.03) |
| Habitual smoking; $n$ (%) | 20 (12.7) | 25 (8.0) | 1.69 (0.91–3.14) | 1.46 (0.77–1.02) |
| Green tea drinking; $n$ (%) | 64 (40.8) | 166 (52.9) | 0.61 (0.42–0.90) | 0.65 (0.44–0.97) |
| Physical inactivity; $n$ (%) | 118 (75.2) | 190 (60.5) | 1.97 (1.29–3.03) | 2.17 (1.39–3.39) |
| Dietary factors | | | | |
| Fried/stir-fried foods | 99 (63.1) | 147 (46.8) | 1.94 (1.31–2.87) | 1.86 (1.24–2.77) |
| Meat/seafood | 84 (53.5) | 146 (46.5) | 1.32 (0.90–1.94) | 1.38 (0.94–2.08) |
| Vegetables/fruits | 73 (46.5) | 172 (54.8) | 0.72 (0.49–1.05) | 0.71 (0.48–1.06) |

## Correlation Coefficients for Perceived Stress and Each Risk Factor

Perceived stress was positively correlated with alcohol consumption ($r$ = 0.092, $p$ = 0.046), habitual smoking ($r$ = 0.109, $p$ = 0.017), physical inactivity ($r$ = 0.118, $p$ = 0.010), fried/stir-fried food ($r$ = 0.114, $p$ = 0.013) and meat/seafood ($r$ = 0.091, $p$ = 0.048), and inversely correlated with green tea consumption ($r$ = –0.103, $p$ = 0.026), and vegetables/fruits ($r$ = –0.093, $p$ = 0.044). Alcohol drinking was correlated with habitual smoking ($r$ = 0.131, $p$ = 0.004) and fried/stir-fried food ($r$ = 0.133, $p$ = 0.004). Habitual smoking was correlated with fried/stir-fried food ($r$ = 0.161, $p < 0.001$) and meat/seafood ($r$ = 0.119, $p$ = 0.010). Physical inactivity was correlated with fried/stir-fried foods ($r$ = 0.099, $p$ = 0.033) and meat/seafood ($r$ = 0.127, $p$ = 0.006) and inversely correlated with green tea ($r$ = –0.194, $p < 0.001$) (Table 3). In this study, all variables were not collinear.

## Interaction Effects of Breast Cancer Associated with Risk Factors and Perceived Stress

The ORs for the interactions of perceived stress and lifestyle factors were adjusted for menarche before age 12 years in the multiple logistic regression models (Table 4). Compared to those with low perceived stress who abstained from excessive alcohol consumption, those with high perceived stress and high amounts of alcohol intake had higher odds of breast cancer (AOR, 2.91; 95% CI, 1.23–6.86). An interaction was also observed between stress and smoking behavior, with those having high perceived stress and habitual smoking habits having higher odds of breast cancer (AOR, 2.52; 95% CI, 1.16–5.47). Stress and green tea intake also showed an interaction: Those with low green tea intake and high levels of perceived stress had a higher odds of breast cancer (AOR, 2.47; 95% CI, 1.40–4.38). Another interaction, one for stress and physical activity, was observed such that those who were less active physically and reported higher levels of perceived stress had a higher odds of breast cancer (AOR, 3.36; 95% CI, 1.77–6.36) than those who were more physically active and reported lower levels of perceived stress. Finally, stress and food showed an interaction: Those who ate large amounts of fried or stir-fried food and reported high levels of stress had higher odds of breast cancer (AOR, 3.18; 95% CI, 1.79–5.63) than those with low stress and low fried food intake, as did those who reported high stress and ingested high amounts of meat and seafood (AOR, 1.89; 95% CI, 1.09–3.27) compared to those who reported low stress and lower intake of meat and seafood. Model fit of the data in each model was not significant ($p > 0.05$); therefore, the null hypothesis was not rejected.

**TABLE 3** Correlation Coefficients for Perceived Stress and Behavioral and Dietary Risk Factors ($n$ = 471)

| | Perceived stress | Alcohol drinking | Habitual smoking | Green tea drinking | Physical inactivity | Fried/stir-fried foods | Meat/seafood | Vegetables/fruits |
|---|---|---|---|---|---|---|---|---|
| Perceived stress | 1 | | | | | | | |
| Alcohol drinking | .092* | 1 | | | | | | |
| Habitual smoking | .109* | .131† | 1 | | | | | |
| Green tea drinking | −.103* | −.084 | −.049 | 1 | | | | |
| Physical inactivity | .118* | .009 | .049 | −.194‡ | 1 | | | |
| Fried/stir-fried foods | .114* | .133† | .161‡ | −0.86 | .099* | 1 | | |
| Meat/seafood | .091* | .047 | .119* | −.011 | .127† | .056 | 1 | |
| Vegetables/fruits | −.093* | −.007 | −.051 | .049 | −.066 | −.084 | −.050 | 1 |

*$p < .05$, †$p < .01$, ‡$p < .001$.

**TABLE 4** Interaction Effects of Breast Cancer Associated with Risk Factors and Perceived Stress

| Variable | Perceived stress | Case (*n*) | Control (*n*) | AOR (95% CI) |
|---|---|---|---|---|
| Alcohol drinking | | | | |
| No | Low | 55 | 153 | 1.00 |
| Yes | Low | 3 | 8 | 0.94 (0.24–3.75) |
| No | High | 86 | 141 | 1.54 (1.01–2.34) |
| Yes | High | 13 | 12 | 2.91 (1.23–6.86) |
| *p* for interaction | | | | 0.05 |
| Habitual smoking | | | | |
| No | Low | 53 | 154 | 1.00 |
| Yes | Low | 5 | 8 | 1.67 (0.51–5.42) |
| No | High | 84 | 135 | 1.63 (1.06–2.50) |
| Yes | High | 15 | 17 | 2.52 (1.16–5.47) |
| *p* for interaction | | | | 0.04 |
| Green tea drinking | | | | |
| Yes | Low | 24 | 96 | 1.00 |
| No | Low | 34 | 65 | 2.04 (1.11–3.78) |
| Yes | High | 40 | 70 | 2.20 (1.20–4.03) |
| No | High | 59 | 83 | 2.47 (1.40–4.38) |
| *p* for interaction | | | | 0.02 |
| Physical inactivity | | | | |
| No | Low | 15 | 74 | 1.00 |
| Yes | Low | 43 | 87 | 2.58 (1.32–5.05) |
| No | High | 24 | 50 | 2.30 (1.08–4.88) |
| Yes | High | 75 | 103 | 3.36 (1.77–6.36) |
| *p* for interaction | | | | 0.00 |
| Fried/stir-fried foods | | | | |
| Low | Low | 23 | 92 | 1.00 |
| High | Low | 32 | 72 | 1.76 (0.94–3.28) |
| Low | High | 35 | 75 | 1.78 (0.96–3.32) |
| High | High | 67 | 75 | 3.18 (1.79–5.63) |
| *p* for interaction | | | | 0.00 |
| Meat/seafood | | | | |
| Low | Low | 29 | 98 | 1.00 |
| High | Low | 30 | 61 | 1.63 (0.89–3.00) |
| Low | High | 44 | 70 | 2.06 (1.16–3.66) |
| High | High | 54 | 85 | 1.89 (1.09–3.27) |
| *p* for interaction | | | | 0.07 |
| Vegetables/fruits | | | | |
| High | Low | 33 | 89 | 1.00 |
| Low | Low | 38 | 70 | 1.46 (0.83–2.58) |
| High | High | 40 | 83 | 1.22 (0.70–2.15) |
| Low | High | 46 | 72 | 1.52 (0.87–2.65) |
| *p* for interaction | | | | 0.45 |

## DISCUSSION

This study explored the relationships of lifestyle behaviors and the perception of stress in women with breast cancer compared to women without breast cancer. Researchers found that women who reported high levels of perceived stress had increased odds of breast cancer. These findings are consistent with previous epidemiological studies (Helgesson et al., 2003; Lillberg et al., 2003; Kruk & Aboul-Enein, 2004). They also found that low physical activity and high fried/stir-fried foods intake were associated with significantly increased odds of breast cancer. Moreover, the combination of higher perceived stress and most lifestyle factors examined (e.g., alcohol, habitual smoking, physical activity, and high fried/stir-fried food consumption) was associated with elevated odds of breast cancer in the Taiwanese women in this study. Previous studies have indicated that persons with high stress levels were more likely to smoke (Rod et al., 2009), drink alcohol (Mulia et al., 2008), engage in less physical activity (Jönsson et al., 2003), lead a sedentary lifestyle (Rod et al., 2009), and have a higher intake of high fat food and sugar than those who report less stress (Habhab, Sheldon, & Loeb, 2009). Unhealthy behaviors coupled with stress-related processes may affect pathways implicated in cancer progression, including immunoregulation, angiogenesis, and invasion (Chida et al., 2008; Lutgendorf, Sood, & Antoni, 2010). A previous study related social isolation to up-regulated mammary gland expression of murine orthologues of several key metabolic genes implicated in human tumor genesis and increased tumor growth in a murine breast cancer model (Williams et al., 2009). In the current study, researchers found that stress was associated with unhealthy behaviors, and together these behaviors and high perceived stress had increased odds of breast cancer.

The mechanism of stress as related to increased risk of breast cancer is complex and not completely understood. When the human body endures stress or stressful events, the production of the stress hormone cortisol may be enhanced. This stress hormone can influence the signals of the hypothalamic-pituitary-adrenal (HPA) axis which in turn can inhibit the function of the hypothalamic-pituitary-gonadal axis by decreasing the synthesis of estrogen (Young & Altemus, 2004; Horst et al., 2011). Although results in some studies have differed in whether stress correlated with increased cancer risk (Schernhammer et al., 2004; Nielsen et al., 2005), these differences may have been due to different methods of measuring stress. Stress was associated in these studies with dysregulation or alterations in various neuroendocrine hormones, particularly cortisol and catecholamines, which may be associated with an increased risk of breast cancer, whether by stimulating cell proliferation, increasing levels of oxidative stress, or workings by some other mechanism (Lutgendorf et al., 2010).

In the present study, researchers found that alcohol consumption alone was not associated with increased odds of breast cancer. This may be due to the fact that most women do not usually drink in Taiwan so that there may have been inadequate statistical power to detect a meaningful association of alcohol with breast cancer as statistically significant, particularly because the magnitude of the associations that some studies have found have been fairly small (Li et al., 2006; Allen et al., 2009; Chen et al., 2011). Nevertheless, current researchers found that high levels of stress in women, combined with drinking alcohol, were associated with an increased odds of breast cancer. Previous studies have demonstrated that moderate consumption of alcohol was associated with an increased odds of breast cancer (Zhang et al., 2007), due to alcohol increasing estrogen levels in the blood. Alcohol could increase the concentration of estrogen (Deandrea et al., 2008; Lew et al., 2009); estrogen might in turn have a carcinogenic effect on breast tissue through estrogen receptors or a direct effect (Suzuki et al., 2005; Seitz et al., 2012). Women with high levels of stress may already have high levels of estrogen existing in their bodies (Figueiredo, Dolgas, & Herman, 2002). Thus, the excess of endogenous estrogen from alcohol could increase a women's probability of contracting breast cancer over women who have lower stress or who are stress-free.

Tobacco contains carcinogens, such as polycyclic aromatic hydrocarbons, that are transported into mammary tissues through blood plasma lipoproteins (Rundle et al., 2000), thereby potentially increasing the risk of breast cancer in mammary epithelial cells (Zhang et al., 2011; Keller et al., 2012). Cigarette smoke may also increase breast cancer risk by raising levels of oxidative DNA damage, although a number of studies (Lin et al., 2008; Ahern et al., 2009) have found no association of smoking with breast cancer risk. In this study, researchers found no significant correlation between habitual smoking and breast cancer. This result might be due to the small number of smokers in the study, which reduced the statistical power to detect a meaningful association as statistically significant. However, the results were similar to those of some previous studies (Brown et al., 2010; Deroo et al., 2011). The current researchers found that higher levels of perceived stress in women who smoked was associated with an increased odds of breast cancer. Generally speaking, people who smoke have higher levels of stress in their daily lives (Rod et al., 2009; Childs & De Wit, 2010). Those who are habitual smokers with high levels of stress could increase their potential for developing breast cancer.

In Taiwan, green tea intake is nearly equivalent to coffee intake in the West, particularly at social functions. Green tea contains polyphenols, which are strong antioxidants that help to inhibit the formation of tumors (Chen & Dou, 2008). In previous epidemiological studies, findings have been inconsistent regarding the relationship between green tea and odds of breast cancer (Wu et al., 2003; Shrubsole et al., 2009; Iwasaki et al., 2010). In this study, researchers found that green tea consumption had no association with breast cancer. However, they found that the joint effects of higher perceived stress without drinking green tea were associated with a higher odds of breast cancer. Green tea intake has been associated with lower psychological stress (Hozawa et al., 2009), because green tea contains L-theanine and ascorbic acid, which can reduce the heart rate, blood pressure, and cortisol levels as well as attenuate stress (Brody et al., 2002; Kimura et al., 2007). Green tea consumption may help individuals to cope with stressful events in everyday life.

In this study, researchers found increased physical activity was associated with a reduced odds breast cancer. This finding is similar to the results of some previous studies (Lahmann et al., 2007; Leitzmann et al., 2008). Physical activity may reduce the odds of breast cancer by its effect on weight and estrone among postmenopausal women (Neilson et al., 2009) that depends on the type, dose, and timing of the activity among lean, normal, and overweight women (Friedenreich, 2010), but the literature is inconsistent in the findings with some studies showing no protective effect (Gammon et al., 1998; Smith et al., 2011). Premenopausal and postmenopausal women differ in the relation of developing breast cancer to physical activity. For example, one 20-year prospective investigation indicated that total physical activity was not associated with estrogen and progesterone receptor-positive and breast cancer but suggested that moderate physical activity might reduce the risk of postmenopausal breast cancer risk (Eliassen et al., 2010). Usually, women with higher stress levels have lower amounts of physical activity (Jönsson et al., 2003), which could increase the odds of breast cancer. Physical activity may reduce the accumulation of ovarian estrogen and increases energy consumption, thereby reducing obesity and lipids, which can delay menarche but enhance menstrual cycle changes, augmenting the binding of the sex hormones and enhancing immune function (McTiernan et al., 2006). One previous study identified daily physical activity as being associated with a lower risk of psychological distress (Hamer, Stamatakis, & Steptoe, 2009). Compared with less physical activity, higher amounts of physical activity tended to decrease serum sex hormone concentrations (Monninkhof et al., 2009; Van Gils et al., 2009) and increase sex hormone binding globulin concentrations (Friedenreich et al., 2010), which should be associated with a decrease breast cancer risk. However, under stress women who engaged in less physical activity (Jönsson et al., 2003) would have higher levels of estrone, estradiol, and free estradiol, and lower levels of sex hormone-binding globulin (McTiernan et al., 2006), potentially increasing the odds of breast cancer.

Researchers found that high intake of fried and stir-fried foods was associated with an increased odds of breast cancer. Foods cooked at high temperatures, such as those that are fried or stir-fried, produce carcinogens and heterocyclic amines, especially amino-1-methyl-6-phenylimidazo [4,5-b] pyridine (PhIP) (Sinha et al., 2000). Increased PhIP intake had been correlated with the increased risk of breast cancer in one study (Snyderwine, Venugopal, & Yu, 2002). Current researchers also found that the joint relation of perceived stress and high intake of fried and stir-fried foods was associated with an increased odds of breast cancer. Although there is no direct evidence that people under stress ingest more fried and stir-fried foods, Taiwanese dietary habits have been influenced by Western-style food, and fried and stir-fried foods have gradually become part of the Taiwanese diet. Researchers also found that women who reported high perceived stress levels and high meat and seafood intake had increased odds of breast cancer. It is possible that monounsaturated trans fats may drive the associations between different types of fat and breast cancer (Wang et al., 2008). Obesity and uneven energy intake could affect the secretion and balance of estrogen and thus potentially explain the increased odds of breast cancer (Meyskens et al., 2000; McTiernan et al., 2006). Women with high stress are also often obese (Vicennati et al., 2009). In the current study, researchers did not find a correlation between high perceived stress levels and high vegetable and fruit intake or an increase in the odds of breast cancer. High stress levels have been negatively associated with vegetable and fruit intake (Roohafza et al., 2007). Vegetables and fruits contain antioxidant vitamins, fiber, and folic acid, all of which can help to enhance immune response, inhibit tumor cell proliferation, and reduce DNA oxidative damage to cells (Rock, Lampe, & Patterson, 2000; Li et al., 2009). However, they did not identify any relationship of breast cancer to vegetable and fruit intake in conjunction with high perceived stress.

A number of individual studies have described specific risk factors acting together to produce an increase or decrease in the risk of breast cancer that is greater than a single risk factor acting alone (Suzuki et al., 2005; Li et al., 2009; Sánchez-Zamorano et al., 2011). Few of these interactions have led to more than a moderate change in risk. The current study has established the interactions between multiple lifestyle risk factors and perceived stress in relation to breast cancer.

However, the current study had a number of limitations that must be considered when interpreting the results. First, the main limitation was the potential for recall bias. Patients with breast cancer may have differentially recalled lifestyle behaviors compared to controls and may have been influenced by their disease when reporting perceived stress in the interviews. If breast cancer patients objectively recalled their perceived stress prior to their breast cancer diagnosis, then the bias in this group on this variable would be similar to the bias in the control group on this variable so that no differential misclassification would occur. Interviewers in this study encouraged respondents to remember the exposure to risk factors and stress prior to their illness (for cases) to decrease recall bias, but they cannot be certain that respondents' illness did not influence responses in the cases. A second limitation was that although they had criteria for recruiting cases and controls into this study, the lack of use of a standard instrument to screen the participants for eligibility was a limitation which could have resulted in erroneously including or excluding eligible participants. Third, the lack of inclusion of factors that have been associated with breast cancer in the literature might have resulted residual uncontrolled confounding for such factors as marital status (Kruk & Aboul-Enein, 2004), BMI (McTiernan et al., 2006), age at menopause (Chavez-MacGregor et al., 2005), and family history (Nemesure et al., 2009). Fourth, participants in the case and control groups were from a single Taiwanese medical center, which was not designed to serve a specific group but rather had very similar patient population to other Taiwanese hospitals, thus potentially enhancing the representativeness of the study groups. Taiwanese residents visiting this hospital were not from one specific background (i.e., they came from the general population, not from any one specific group). Because most of participants came from Taichung neighborhood attending a single hospital, local dietary traditions, religious practices, or even genetics of isolated, relatively non-mobile populations could have affected the results such that they would not be representative of women in other Taiwanese areas. Fifth, selection and participation biases may have played a role in this hospital-based study, which included clinic-based participants and thus might not be representative of all women in Taiwan. Finally, participants may have exhibited social acceptability biases when responding to certain questions on the survey (particularly, drinking and smoking habits). However, it was unlikely that the breast cancer patients differed in this regard compared to the controls.

Using the OR to compare breast cancer cases to controls, the 58% prevalence of high stress (Nielsen et al., 2005), the 2:1 ratio of cases to controls (Helgesson et al., 2003), with a two-sided alpha = 0.05, and power of 80%, researchers calculated sample size and found they needed 115 participants in the case group and 230 in the control group. They collected more than these required sample sizes in both case and control groups in anticipation of insufficient expected frequencies in some of the cells for interaction. They did not explore frequencies of lifestyle and perceived stress owing to the restricted sample size. For future studies, examination of dose-response as related to lifestyle and perceived stress would be beneficial.

The study also included a degree of subjectivity regarding lifestyle measurements. Defining the cut-off point of dichotomous groups was somewhat arbitrary, but the study emphasis was on the comparison of groups that were either "high" or "low" with respect to a certain characteristic, not by strictly defining the groups themselves. On the other hand, lifestyle factors may act synergistically and be reinforced by stress, thereby enhancing the odds of breast cancer. To help prevent breast cancer, it would be beneficial to incorporate stress management in high-risk populations to help offset other risk factors.

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