# **Original Article**

# A Prospective Study of the Relationship between Psychological Factors and Breast Cancer

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#### ABSTRACT

**Objective:** This cross-sectional prospective study aimed to explore the relationship between psychological factors and breast cancer incidence. **Methods:** The subjects who scheduled to receive mammography screening were recruited from a medical center's outpatient department in Taiwan. Psychological factors used for measurement were stress, anxiety, and depression. **Results:** A total of 1160 questionnaires were completed, which underwent statistical analysis using independent t-test, Chi-square test, Pearson's correlation, and multiple logistic regression. There were statistically significant differences in the average scores of the two groups with and without breast cancer for psychological factors of anxiety (t = -2.071; P = 0.039), depression (t = -3.035; P = 0.002), and stress (t = -4.087; P < 0.001). The crude odds ratio of the two groups showed that subjects with borderline anxiety were 2.576

times (P=0.001) more likely to have breast cancer as compared to subjects with no anxiety. Subjects with depression were 4.078 times (P=0.03) more likely to have breast cancer as compared to subjects with no depression. Every point added to the average total stress score increased the additional risk of breast cancer by 1.124 times (P<0.001). Conclusions: After making adjustments on educational factors, the results conclude that psychological factors such as stress, anxiety, and depression can be considered predictors of breast cancer risk. To prevent and control breast cancer in women, the findings suggest that nurses should consider adding emphasis on psychological factors in women's health education.

Key words: Anxiety, breast cancer, depression, risk factors, stress

#### Introduction

Breast cancer has become the most common type of cancer among women and was responsible for the second highest

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number of cancer deaths in women in the United States.<sup>[1]</sup> It is estimated that 232,670 women were diagnosed with and

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40,000 women died of breast cancer in 2014.<sup>[2]</sup> The incidence of breast cancer in women was highest among all other cancer types in Taiwan.<sup>[3]</sup> It poses a major threat to the health of women worldwide. There are many risk factors for breast cancer. Currently, the recognized high-risk factors include hormonal replacement, genes, age, diet, and ethnicity.<sup>[4]</sup> Other factors more tentatively elated to breast cancer include psychological factors,<sup>[5]</sup> smoking,<sup>[6]</sup> and exercise.<sup>[7]</sup>

Psychological stress, an emotional factor, might play an important role in the development of breast cancer.[8-12] Some studies have indicated a link between various psychological factors and an increased risk of developing cancer, although other studies have not. [13,14] In vitro, in vivo, and clinical studies show that stress-related processes can impact pathways associated to cancer progression, including immunoregulation, angiogenesis, and invasion. [13] A study found that corticotropinreleasing hormone is related to stress or emotions and increases a human's susceptibility to disease and promotes infections, inflammation, or tumors. [15] Depending on this association, some studies further focused on psychological factors in relation to the elevated risk of specific cancer. [16-20] To demonstrate the relationship between stress and cancer, a population-based sample of 3177 cancer-free adults were followed for 24 years with findings suggesting that major depression was associated with a higher hazard for overall cancer (hazard ratio [HR]: 1.9, 95% confidence interval [CI]: 1.2-3.0) and a significant increased hazard for breast cancer (HR: 4.4, 95% CI: 1.08-17.6).[17] A study followed 33,819 newly diagnosed major depressive disorder (MDD) patients with mean duration of 5.19 years, and the result showed that female MDD patients had higher breast cancer risk.[18] A hospitalbased case-control study consisted of 148 breast cancer patients and 148 health controls and found that women with high levels of stress compared to those reporting low stress had an odds ratio (OR) of 1.92 (95% CI: 0.81-4.55) for breast cancer. [19] A study investigated the relations of perceived stress and lifestyle to breast cancer and found perceived stress, when combined with potentially risky lifestyle behaviors, may be a contributing factor to breast cancer. [20] As presented above, psychological factors are known to contribute to breast carcinomas.

In contrast, several studies have found no relationship between psychological factors and breast cancer. Sun *et al.*<sup>[5]</sup> conducted an updated meta-analysis of cohort studies to assess the association between depression and risk of breast cancer, and concluded that the evidence was insufficient to support a positive association between depression and breast cancer. Heikkilä *et al.*<sup>[21]</sup> conducted a meta-analysis of 12 cohort studies that included 116,056 men and women aged 17-70 years old who were free from cancer at the baseline study and were followed-up after a median of 12 years. The results revealed that no association was observed between work stress and the risk of breast cancer. Lillberg *et al.*<sup>[22]</sup> investigated stress in 10,519 subjects and followed them for 20 years. Their result indicated that stress was not related to breast cancer.

although the report did not provide data on the validity of the measurement tools used. Kroenke *et al.*<sup>[23]</sup> conducted a study of 69,886 nonprofessional patient caregivers who experienced high degrees of stress and followed them for 4-8 years. Among these women, only 1700 were diagnosed with breast cancer; leading the researchers to conclude that stress did not increase the risk of breast cancer in these women.

Butow *et al.*<sup>[8]</sup> reviewed 16 studies focusing on the relationship between stress events and breast cancer incidence, and not only concluded the individual studies had methodological limitations, but also suggested future study should apply theoretical models, develop a clear hypothesis, use a prospective study design, and clearly define the control group to enhance the validity of the results. Since available research on the issue face a number of methodological difficulties, [17] this study planned to address some methodological issues. In addition, to the best of our knowledge, most of the existing findings from the investigation of relationships between psychological factors and breast cancer were obtained from Western societies. This is problematic as Asian and Western cultures differ notably in cancer incidence and lifestyle. [24] Therefore, this study aimed to explore the relationship between psychological factors and breast cancer incidence in patients who were going to receive mammography screening.

# **Methods**

# Study design and sample

A prospective cross-sectional research design was used in this study. All subjects who were going to receive mammography screening were recruited from outpatient departments in a 1820-bed medical center in Taiwan. A total of 1326 questionnaires were distributed and 1215 were returned. Of the 1215 questionnaires received, 55 were invalid due to missing data and 1160 (95.3%) were valid to analyze. Until diagnosis was assured, the subjects were divided into a breast cancer group (n = 54) and a nonbreast cancer group (n = 1106) according to the results of the mammography.

#### **Measures**

Demographic characteristics that were measured included age, educational level, marital status, height, weight, employment status, family income, habits of smoking, drinking, and exercise, medical history, reasons for examination, age at menarche, age at menopause, age of first maternity, postmenopausal hormone use, and family history of breast cancer.

The Perceived Stress Scale (PSS) with a reliability Cronbach's  $\alpha$  of 0.82 was used to measure general, life, and work-related stress perception.  $^{[25]}$  Questions 3, 4, 6, 7, and 10 were reverse questions on a 4-point scale with higher scores representing greater stress. The Hospital Anxiety and Depression Scale (HADS) screens for symptoms of anxiety and depression combined.  $^{[26]}$  The HADS consists of 7 questions measuring

anxiety (HAD-A) and 7 questions measuring depression (HAD-D). The scale primarily uses a 4-point Likert scale (0-3 points). The result score of HAD-A or HAD-D questionnaire can range from 0 to 21, with a higher score representing greater anxiety or depression. A HAD-A or HAD-D score within the range of 0-7 points represents no anxiety or depression; a score within 8-10 points represents borderline anxiety or borderline depression, and a score within 11-21 points represents anxiety or depression. The Cronbach's  $\alpha$  was 0.74 and 0.70 for HAD-A and HAD-D, respectively.

#### Procedures and statistical analysis

First, ethical approval for this study was obtained from the Institutional Review Board of the study hospital (TSGHIRB: 097-05-008). Second, subjects who were waited to have a mammography examination in the outpatient department and met inclusion criteria were invited to participant this study. All subjects were made aware that personal data collected for the study would remain confidential. Subjects had the right to withdraw themselves from the study at any time. Third, on the

day prior to mammography, researchers explained the study protocol and asked subjects to complete the demographic sheet, PSS, and HADS. Grouping subjects into breast cancer or not was based on the result of pathological biopsy. Statistical analysis was performed using SPSS (Statistical Product and Service Solutions) version 18.0. A level of significance of 5% was used to confirm the validity of the data. Student's t-test,  $\chi^2$  test, OR, and multiple logistic regression were examined.

## Results

Table 1 summarizes the demographic characteristics of the two groups. Based on the statistical results of the demographic data, the two groups had statistically significant differences in education level (t = 13.818; P = 0.017), but differences between other variables were not statistically significant (P > 0.05). Table 2 summarizes the results of the t-test on psychological factors in subjects with and without breast cancer. Statistically significant differences were found in the average scores of the two

Demographics	Total	Nonbreast cancer	Breast cancer	$\chi^2$	P
	(n = 1160) n (%)	(n = 1106) n (%)	(n = 54) n (%)		
Age, years					
<40	90 (7.8)	84 (7.2)	6 (11.1)	5.671	0.129
40-50	427 (36.8)	411 (37.1)	16 (29.7)		
51-60	475 (40.9)	456 (41.2)	19 (35.2)		
>60	168 (14.5)	155 (14.5)	13 (24)		
Education level					
Illiterate	17 (1.4)	14 (1.3)	3 (5.5)	13.818	0.017
Primary	123 (10.6)	114 (10.3)	9 (16.7)		
Junior high	120 (10.3)	113 (10.2)	7 (13)		
Senior high	380 (32.8)	370 (33.5)	10 (18.4)		
College	472 (40.7)	451 (40.7)	21 (39)		
Graduate	48 (4.2)	44 (4)	4 (7.4)		
Marital status					
Single	92 (7.9)	88 (7.9)	4 (7.4)	0.854	0.931
Married	994 (85.8)	946 (85.5)	48 (88.9)		
Divorced	69 (5.9)	67 (6.1)	2 (3.7)		
Other	5 (0.4)	5 (0.5)	0 (0)		
Employment status					
No	618 (53.3)	590 (53.3)	28 (51.9)	0.046	0.830
Yes	542 (46.75)	516 (46.7)	26 (48.1)		
Age of menopause					
≤55 years old	519 (59.3)	302 (59.8)	14 (50)	2.352	0.125
>55 years old	217 (40.7)	203 (40.2)	14 (50)		
Hormone replacement therapy					
Yes	184 (15.9)	180 (16.3)	4 (7.4)	0.033	0.082
No	976 (84.1)	926 (83.7)	50 (92.6)		
Breast biopsy					
Yes	170 (14.7)	163 (14.7)	7 (13)	0.719	0.425
No	990 (85.3)	943 (85.3)	47 (87)		
Breast cancer history of first/second-degree relatives					
Yes	78 (6.7)	75 (6.8)	3 (5.6)	0.123	0.725
No	1082 (93.3)	1031 (93.2)	51 (94.4)		

groups for psychological factors of anxiety (t = -2.071; P = 0.039), depression (t = -3.035; P = 0.002), and stress (t = -4.087; P < 0.001). As shown in Table 3, the majority of subjects showed no anxiety (n = 744, 64.1%), followed by borderline anxiety (n = 225, 22%), and anxiety (n = 161, 13.9%). In addition, the majority of subjects showed no depression (n = 985, 85%), followed by borderline depression (n = 142, 12.2%), and depression (n = 32, 2.8%). There was a significant group difference in the anxiety level ( $\chi^2 = 14.778$ ; P < 0.01) and the depression level ( $\chi^2 = 11.089$ ; P < 0.01).

Table 4 summarizes the results of the crude OR of the two groups. Subjects with borderline anxiety were 3.099 times (P < 0.001) more likely to have breast cancer as compared to subjects with no anxiety. Subjects with anxiety were 2.173 times (P = 0.043) more likely to have breast cancer as compared to subjects with no anxiety. Subjects with borderline depression were 1.840 times (P = 0.092) more likely to have breast cancer as compared to subjects with no depression. Subjects with depression were 4.497 times (P = 0.001) more likely to have breast cancer as compared to subjects with no depression. Every point added to the average total stress score increased the additional risk of breast cancer by 1.124 times (P < 0.001). Table 5 shows the results of the goodness-of-fit test for the logistic regression model. The model included anxiety, depression, and stress factors. The overall goodness-of-fittest for psychological factors showed a statistical significance ( $\chi^2 = 25.868$ , P < 0.001).

## **Discussion**

Psychological factors on breast cancer etiology are concerned. In this study, the same tools were used as with Montazeria *et al.*,<sup>[27]</sup> but the average scores for the anxiety levels and depression levels were twice as high as compared to the above-mentioned study. These differences could be due to the fact that subjects in the previous study by Montazeria *et al.*<sup>[27]</sup> suspected that they had breast cancer before diagnosis. Alternatively, the higher scores in the previous study might indicate that Iranian women were experiencing higher levels of anxiety and depression than Taiwanese women. The average age of subjects who developed breast cancer in our study was 47.2 years, which was much younger than the women in the study by Montazeria *et al.*<sup>[27]</sup>

This study showed that breast cancer incidence might be related to psychological factors such as anxiety or depression before educational levels were adjusted, and the results were similar to the some prospective studies. [17,28] However, this study's results were different from the study that had no significant association between a cancer outcome and emotional suppression in a large mammography screened population. [29] The difference may be related to the lifestyle and culture issue between Asian and Western women [24] and

Table 2: Psychological factors in women with/without breast cancer

	Mean±SD			t	P	
Factors	Total (n = 1160)	iotai itomeaniesi				
Anxiety	6.5±3.60	6.4±3.60	7.5±3.42	-2.071	0.039	
Depression	$4.6 \pm 3.04$	$4.5 \pm 3.01$	$5.8 \pm 3.46$	-3.035	0.002	
Stress	$13.7 \pm 4.09$	13.6±4.95	16.4±5.27	-4.087	< 0.001	
SD: Standard	deviation					

Table 3: Psychological factors in women with/without breast cancer

Levels of factor	Total $(n = 1160)$	Noncancer $(n = 1106)$	Cancer ( <i>n</i> = 54)	$\chi^2$	P
	n (%)	n (%)	n (%)		
Anxiety level					
No anxiety	744 (64.1)	722 (65.3)	22 (40.7)	14.78	0.001
Borderline anxiety	255 (22)	233 (21.1)	22 (40.7)		
Anxiety	161 (13.9)	151 (13.7)	10 (18.5)		
Depression level					
No depression	986 (84.9)	947 (85.6)	39 (72.2)	11.09	0.004
Borderline depression	142 (12.2)	132 (11.9)	10 (18.5)		
Depression	32 (2.8)	27 (2.4)	5 (9.3)		

Table 4: Crude OR and 95% CI for psychological factors (n = 1160) 95% CI Variable Р Anxiety Borderline anxiety vs. no anxiety 1.685-5.698 0.001 3.099 Anxiety vs. no anxiety 2.173 1.009-4.684 0.043 Depression Borderline depression vs. no depression 1.840 0.897-3.772 0.092 Depression vs. no depression 4.497 1.643-12.303 Stress 1.124 1.062-1.190 < 0.001 OR: Odds ratio, CI: Confidence interval

Variable	В	Wald	Exp(B)	95% CI
Anxiety				
Borderline anxiety vs. no anxiety	0.69	4.03	1.99*	1.02-3.90
Anxiety vs. no anxiety	-0.12	0.06	0.89	0.34-2.31
Depression				
Borderline depression vs. no depression	0.28	0.54	1.32	0.63-2.79
Depression vs. no depression	0.08	3.95	2.95*	1.02-8.56
Stress	0.96	6.52	1.10*	1.02-1.19

the fact that breast cancer was more prevalent in women aged 40-49 years in Taiwan; and in contrast, invasive breast cancer was more prevalent in women aged 60-69 in the United States based on the statistical data from 1975 to 2003. [30] Women in Taiwan face rapidly changing social patterns, play multiple roles, and have a high level of emotional distress, which may have contributed the

relationship among the risks of breast cancer such as stress, anxiety, and depression, as seen in the results of this study.

The results of this study indicate that whether education level is adjusted or not, stress could be a predictor of breast cancer incidence; and it is the most significant factor among the three psychological factors that correlated with the risk of breast cancer. Every point added to the stress score would increase crude risk 1.124 times. Some studies have suggested that stress increases the risk of breast cancer, [19,20,31] but other studies have not found this. [21,22] Unlike this study, Kroenke *et al.* [23] suggested that stress is not related to breast cancer incidence. Their study recruited 69,886 nonprofessional patient caregivers, with a high degree of pressure, to measure their stress from caring for elderly people or children and their long working hours. After 4-8 years of continued followup, 1700 were diagnosed with breast cancer. Their result concluded that stress did not increase the risk of breast cancer.

This study showed that anxiety, depression, and stress might tentatively be related to breast cancer incidence. These findings suggest that nurses should pay more attention to the mental health of women and provide their female patients, especially those with lower education levels, with more breast cancer prevention information such as more breast cancer prevention information and psychosocial interventions with a well-focused stress reduction and coping skills. Available literature have only a few reports on prospective studies exploring the relationship between breast cancer and psychological factors. This study had some valuable findings, but it might have some unavoidable interference of emotional factors. while awaiting mammograms and the lower proportion of anxiety level participants within the cancer group that goes to the bias that borderline anxiety group were at significantly higher risk, but the group who met a diagnostic score were at a lower statistically significantly increased risk. To reduce this potential bias, future research could investigate subjects undergoing annual regular screening in the community. To increase the generalizability of the results of this study, it is suggested that future studies should conduct investigations nationwide to build up a database for comprehensive analyses.

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#### **Conflicts of interest**

There are no conflicts of interest.

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