

The Role of Psychosocial Factors in the Development of Breast Carcinoma: Part II

Life Event Stressors, Social Support, Defense Style, and Emotional Control and Their Interactions

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BACKGROUND. The evidence supporting an association between life event stress and breast carcinoma development is inconsistent.

METHODS. Five hundred fourteen women requiring biopsy after routine mammographic breast screening were interviewed using the Brown and Harris Life Event and Difficulties Schedule. Other psychosocial variables assessed included social support, emotional control, and defense style. Biopsy results identified 239 women with breast carcinoma and 275 women with benign breast disease. Multiple logistic regression analysis was used to distinguish between breast carcinoma subjects and benign breast disease controls based on these psychosocial variables and their interactions.

RESULTS. The findings of the current study revealed a significant interaction between highly threatening life stressors and social support. Women experiencing a stressor objectively rated as highly threatening and who were without intimate emotional social support had a ninefold increase in risk of developing breast carcinoma.

CONCLUSIONS. Although there was no evidence of an independent association between life event stress and breast carcinoma, the findings of the current study provided strong evidence that social support interacts with highly threatening life stressors to increase the risk of breast carcinoma significantly. [See also accompanying article on pages 679–85, this issue.] *Cancer* 2001;91:686–97.

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Renewed debate regarding the association between stress and the development of breast carcinoma has coincided with the recent publication of three studies, two of which report a significant association between antecedent life events and breast carcinoma and a third that found no association.^{1–3} The series of commentaries concerning the topic of stress and the development of breast carcinoma also reflect the inconsistency of research findings.^{4–8} Assessments of existing findings include the opinion that stress or other emotional factors play a “relatively minor” role in the etiology of breast carcinoma,⁴ that the question is clinically insignificant,⁵ that major life events in the presence of other psychosocial factors increase the risk of breast carcinoma,⁶ and that an adequate test of the hypothesis has yet to be performed.^{7,8} Despite this, there is widespread belief in the community that stress is a risk factor for cancer,⁹ in particular breast carcinoma.^{9,10}

Population-based studies examining widowhood and divorce have found no association with breast carcinoma.^{11,12} Early childhood losses or separation from parents also have been studied, with some studies reporting no increased risk of breast carcinoma¹³ whereas others report a significantly higher risk of cancer (including breast carcinoma) in individuals who have experienced such events.¹⁴

The majority of life event studies have used event checklists, an approach prone to underreporting of events, bias by mood state,^{15,16} and "insensitivity" due to lack of specificity and contextual details.¹⁷ It therefore is not surprising that studies using this approach have yielded mixed results: four negative findings,^{2,18-20} three positive findings,^{3,21,22} and two cases in which the breast carcinoma group experienced significantly less stress than the control group.^{23,24}

Use of the Life Events and Difficulties Schedule (LEDS)²⁵ to assess life event stress objectively has produced somewhat more consistent results. This interview enables precise event definition and encompasses contextual information in independent ratings of event severity. Two studies have reported that recent events rated as the highest category of severity of threat were reported to occur two to three times more often in women diagnosed with breast carcinoma than in those women with benign breast disease.^{1,16} However, a recent study using this approach failed to replicate these findings.²⁶

However, the study of life events alone may be a somewhat incomplete approach. It may be that life event stressors, when examined in conjunction with vulnerability factors such as coping style, emotional and behavioral patterns, and social support, will enable the relative impact of components of psychosocial "stress" to be teased apart.^{8,27} To our knowledge only a few studies reported to date have assessed these multiple factors;^{1,16,19,28} this perhaps is due to the large samples required for sufficient power with which to assess the interaction of these psychosocial variables adequately.

A significant weakness in this area of research is the essentially atheoretic approach to examining clearly interrelated psychosocial concepts in a multifactorial disease such as breast carcinoma, despite models being available.²⁹ Both Greer and Watson³⁰ and Temoshok³¹ described a cancer prone personality that is believed to predispose an individual to developing cancer. This personality is related to stress, and purported to be maladaptive under conditions of prolonged or severe stress, increasing rather than reducing the impact of stressors^{30,31}; however, life event stress and personality rarely are considered together.

Based on existing evidence, Hilakivi-Clarke et al. outlined a comprehensive model in which life event stress, personality, and social support influenced an individual's ability to cope, which in turn mediated breast carcinoma risk via alterations in neuroendocrine and immune functioning.³² The crucial factor in this model is not the stressor, but the complex interaction between stressors, personality, and social support that affect an individual's ability to cope. This model is compatible with more general models of stress and illness.¹⁷ In the Brown and Harris model,¹⁷ life events are conceptualized as provoking agents for illness, are influenced by specific vulnerability factors such as social support, and are proposed to increase the impact of life events and consequently the resulting stress and strain.

Although the potential benefits of social support on health, quality of life, and immunity are well established,³³⁻³⁵ consideration of the role of social support in breast carcinoma generally has focused on its ability to mitigate the impact of diagnosis, adjustment to illness, and prognosis.³⁶⁻⁴¹

To our knowledge, only a few studies to date have considered social support in relation to the development of breast carcinoma. Using an unspecified self-report measure of social support, Bleiker et al. reported no association with breast carcinoma.⁴² Cooper et al.²⁸ and Edwards et al.¹⁹ reported no differences in the number of social supports available in a crisis between breast carcinoma cases and controls. In what to our knowledge is one of the few studies in this research area with a theoretic basis, the Brown and Harris model was used to examine the modifying effect of social support on stressful life events in the development of breast carcinoma.^{15,16} However, a high correlation between "lack of social support" and "life events" precluded the inclusion of support in the model. To overcome the difficulty of assessing the components of stress, Tennant et al. suggested that stress-related variables such as life events, social support, personality, and coping should be assessed as distinct concepts.⁴³

The aim of the current study was to examine the role of antecedent life stressors, together with psychosocial "vulnerability" factors including social support, coping style, and emotional control, in the diagnosis of breast carcinoma in asymptomatic women attending a community-based mammographic breast carcinoma screening program. This study design was chosen to minimize selection bias and enabled assessment to be performed with both subjects and researchers blind to disease status.

MATERIALS AND METHODS

Subjects

Eligible subjects were asymptomatic women requiring fine-needle biopsy for the diagnosis of breast disease after routine breast screening. Women attending the Northern Sydney and Lower Central Coast Breast Screening Program between April 1994 and April 1997 and who were recalled on radiologic grounds were invited to participate in research examining the psychosocial factors in the development of breast carcinoma. Participation involved completing a self-report questionnaire. Life event stress and social support details were collected by personal interview. The ideal of interviewing all subjects was not feasible; instead, a subset of the sample, those women undergoing breast biopsy, were selected for interview. This group shared similar conditions of testing and were expected to experience similar apprehension prior to diagnosis. The current study focuses on interview and questionnaire data from women undergoing biopsy.

The inclusion criteria were: 1) undergoing breast biopsy after routine breast screening; 2) age \geq 40 years; and 3) adequate command of English. The exclusion criteria were: 1) prior history of breast carcinoma; 2) breast symptoms prompting screening; 3) knowledge of results of biopsy; and 4) physical or psychiatric impairment inhibiting completion of the questionnaire and/or the interview.

Procedure

The complete assessment procedure, from mammography to ultrasound, physical examination, and biopsy, usually occurred on the same day. On arrival at the clinic, consenting women completed a self-administered questionnaire while waiting for assessment. After consenting to the biopsy procedure, subjects were interviewed prior to their test results being available. Approval for the study was granted by the Royal North Shore Hospital Medical Research Ethics Committee.

Measures

Demographic and somatic risk factor variables were collected by self-report and included age, marital status, education, employment, family history of breast carcinoma, history of benign breast disease, parity, age at the birth of the first child, lactation, menopausal status, age at the onset of menopause, oral contraceptive use, use of hormone replacement therapy, height, weight, and alcohol and cigarette consumption.

Self-report psychologic questionnaires assessed features of Temoshok's "cancer prone personality."³¹ Emotion-focused coping was assessed using the DSQ-

40, yielding scores for mature, immature, and neurotic defense styles.⁴⁴ Problem-focused coping was assessed by the Locus of Control of Behaviour (LCB) scale yielding a single factor reflecting internal/external locus of control.⁴⁵ The Emotional Expression and Control (EEC) scale measured the expression and control of anger, anxiety, and depression resulting in three factor scores: emotional expression-in, emotional expression-out, and emotional control.⁴⁶ Rosenberg's Self-Esteem scale measured the self-acceptance aspect of self-esteem.⁴⁷ Trait anxiety was assessed using the State-Trait Personality Inventory (STPI).⁴⁸ State anxiety and state depression was assessed using the Hospital Anxiety and Depression (HAD) scale.⁴⁹ Detailed analysis of these data were reported separately.

An abbreviated version of the Henderson Social Support Interview Schedule was administered to assess social support.⁵⁰ Independent ratings of intimate and nonintimate support for both emotional and instrumental support were made to reflect availability and quality. Ratings were made on a three-point scale (poor, adequate, and good), in which a "good" rating reflected support generally available and comforting, an "adequate" rating reflected support available but with some form of restriction, and a "poor" rating reflected limited availability and/or uncertainty in the quality of support. Subjective appraisal of support also was recorded using this three-point scale and subjective evaluation of change in support during the past 2 years was recorded (better, worse, and no change).

The Bedford College LEDS²⁵ was used to collect details regarding life stressors occurring during the previous 2 years. This semistructured interview allows details of life stressors and the context in which they occurred to be recorded. A vignette of each subject's personal circumstances and stressors was presented to independent raters, without reference to the subject's emotional responses or diagnosis. Of prime interest in this study was the ongoing impact of stressors reflected in the ratings of long-term "threat."

Long-term threat defines the degree of impact of a stressor 1 week after the occurrence. The severity of long-term threat was rated for each stressor on a five-point scale. Ratings were based on the criteria described and detailed examples provided by the authors of the schedule, with the addition of categories (none and extreme) to allow further distinction of stressors at the extremes. For example, the death of a spouse or child would be rated at the highest level of threat (extreme) and the death of an elderly parent living in the same home would be rated a degree lower (severe), whereas the death of a parent-in-law not living in the same home but with regular contact

would be rated another degree lower (highly threatening).

A distinction was made according to the duration of the stressor. Stressors were regarded as acute if < 6 months in duration and chronic if they continued for ≥ 6 months. Both acute and chronic stressors were categorized according to type (health of self, health of others, death, role/interaction, crisis/news, employment, financial, marital, and miscellaneous).

Training of the interviewers and raters for this study was conducted by an expert in the field (C.T.). Interviews were conducted prior to results being available to either the subject or interviewer. The content of the interviews were rated independently with both the interviewer and rater blind to the disease status of the women. Interrater reliability for this study was 0.92.

The choice of time frame for the assessment of stressors involved a difficult balance between the time period during which the impact of stressors is believed to influence tumor development and that of optimizing reliability in recalling life event stressors. The time from etiology to the early detection of breast carcinoma is difficult to determine, but has been approximated at 18 years.⁵¹ The majority of reports suggesting a relation between life event stressors and the diagnosis of breast carcinoma refer to a relatively short time frame, most commonly between 2–5 years, suggesting that any impact of stressors would be related to promoting tumor growth. Accuracy of recall using the checklist approach to examining life events rapidly decreases over 6 months, particularly for less severe events, although the most severe events are least affected.⁵² However, using the LEDS approach, the decrease in the reporting of events is approximately 5% per year and is similar for severe and nonsevere events.¹⁷ Given these data, a 2-year time frame for life events in our asymptomatic sample approximates the longer recall period of symptomatic women in previous studies, and ensures a high degree of reliability in recall.

Diagnosis of Breast Carcinoma

The diagnosis of breast carcinoma was confirmed by histopathologic results of breast tissue biopsy. Those women without malignancy were classified as benign controls.

Statistical Analysis

Data were analyzed using logistic regression to distinguish between subjects with breast carcinoma and control subjects with benign breast disease. Age was included as a confounder in all analyses. The final model included other confounders selected on both

statistical and theoretic grounds.⁵³ All variables were entered simultaneously. Results were reported in terms of the Wald statistic, odds ratio (OR), and 95% confidence intervals (95% CI). Variables initially were examined as “main effects.” Interaction between the main effect variables were examined regardless of the individual significance of each main effect. All analyses were performed using SPSS for Windows (SPSS Inc., Chicago, IL). Correlations are reported as Pearson's *r* (two-tailed) for continuous variables and Spearman's ρ (two-tailed) for categorical variables.

RESULTS

Sample Characteristics

Of 2821 women recalled for assessment on radiologic grounds after routine breast screening, 848 underwent needle biopsy and were invited to participate in this part of the study. One hundred eight women (12.7%) declined to participate and an additional 48 women who initially agreed to participate later declined to be interviewed (6%), representing a response rate of 81.6%. Of the 692 women participating, 176 (25.4%) were unable to be interviewed for logistical reasons including the preliminary biopsy results being given to the subject prior to the interview, the subject leaving the clinic while the other subjects were being interviewed, and no private space being available for the interview to be conducted. Five hundred sixteen women were interviewed prior to biopsy results being available. One woman who was diagnosed with lymphoma and one woman whose final diagnosis was outstanding were excluded from analyses. Interview data were available for 239 women who later were confirmed to have breast carcinoma (46.5%) and 275 women who were diagnosed with benign breast disease (53.5%). Of all the women requiring biopsy after breast screening during 1994–1996 inclusive, 47.2% were diagnosed with breast carcinoma, suggesting our sample is representative of our region. The benign to malignant biopsy ratio was consistent with other screening programs.^{54–57}

The mean age of the breast carcinoma group was 61.3 years (standard deviation [SD] of 9.4), which was significantly older than benign controls, who had a mean age of 57.0 years (SD of 9.8), giving an OR of 1.05 (95% CI, 1.03–1.07). No differences were detected based on marital status, occupational status, family history of breast carcinoma, history of benign breast disease, parity, age at menopause, or obesity. There were increased odds of breast carcinoma with increasing level of education, increasing age at first birth for parous women, being postmenopausal, ever use of oral contraceptives, current use of hormone replace-

ment therapy, and daily alcohol consumption (Table 1).

Acute Stressors

Our first hypothesis was that there was a threshold at which acute stressors may trigger or at least promote tumor growth. This being the case, we expected that significantly more women diagnosed with breast carcinoma would have experienced a highly threatening acute stressor compared with benign controls. One thousand four hundred fifty-three acute stressors were recorded in the 2-year period prior to biopsy. The mean number of acute stressors experienced was 2.82 for the breast carcinoma group and 2.84 for the benign group (OR = 1.04; 95% CI, 0.94–1.16). Table 2 shows the numbers of subjects reporting acute stressors according to severity ratings for long-term threat. More of the women in the breast carcinoma group did report an acute stressor that was rated as extremely threatening (4.6%) compared with the benign group (2.9%), although, after adjusting for age, the difference failed to reach statistical significance (OR = 1.06; 95% CI, 0.37–3.02). Combining stressors rated as extremely and severely threatening for long-term threat, the percentage of women experiencing such stressors was similar across groups (OR = 0.89; 95% CI, 0.49–1.62). The numbers of women experiencing an acute stressor rated as being of high, moderate, and mild degree of threat also were similar across the groups.

Testing the hypothesis that the type rather than the severity of an acute stressor was more important (for example bereavement rather than employment), we proposed that women diagnosed with breast carcinoma would have experienced more bereavements prior to diagnosis compared with benign controls. However, there were no significant differences between the groups with regard to any of the 10 categories of acute stressors reported and, specifically, the number of women widowed in the previous 2 years was not significantly different across the 2 groups.

Chronic Stressors

Examining the possibility that chronic stressors were more important in promoting tumor growth, we hypothesized that women diagnosed with breast carcinoma would have more chronic stressors and more threatening stressors prior to diagnosis compared with benign controls. We recorded 852 chronic difficulties impacting on the past 2 years, with no group differences detected in number (OR = 1.08; 95% CI, 0.94–1.24). Chronic stressors in the highest two severity ratings of long-term threat were rare and similar across groups (Table 3). Women with breast carcinoma did report significantly more chronic stressors

in the lowest (mildly threatening) severity group (OR = 1.72; 95% CI, 1.19–2.49); however, the benign group reported more chronic stressors in both the moderate and high severity ratings, albeit a nonsignificant difference. The most common chronic stressor reported were related to the women's own health and there were no differences in the types of chronic stressors reported between the groups.

Cumulative Stressors

We examined a model of stress that proposed a cumulative impact of life stressors, hypothesizing that women diagnosed with breast carcinoma would have experienced more cumulative stress than women with benign breast disease. To test this theory, we calculated scores to estimate cumulative degree of stressors, separately for acute and chronic stressors as well as a combination of acute and chronic stressors. Each stressor was allocated a weight according to its severity rating, and the weighted scores were totaled. Weightings of stressors were assigned according to Brown et al.⁵⁸ Stressors rated as mild or nonthreatening were weighted zero. Extreme stressors were weighted 5, severe stressors were weighted 4, high stressors were weighted 3, and moderate stressors were weighted 1. No differences were noted with regard to weighted acute, weighted chronic, or weighted combined stressors scores (Table 4).

Vulnerability Factors

Despite finding no evidence of an independent effect for life stressors, we proceeded to examine the effect of other psychosocial factors that we hypothesized would impact on the development of breast carcinoma through their interaction with life stressors. The "vulnerability factors" proposed in our model were a less mature coping style, higher emotional control, and poor emotional social support.

Full analysis of psychologic questionnaire data is reported separately. Selected variables, namely mature defense style and emotional control, are hypothesized in the current study as vulnerability factors, increasing or decreasing the impact of life event stress, without individual etiologic significance.^{16–25} These variables are summarized in Table 5. There were no significant differences detected between groups based on scores of mature defense style or emotional control.

Although breast carcinoma subjects reported "no intimate emotional support" (29.3%) slightly more often than control subjects (24.7%), after adjusting for age the differences were not found to be significant (OR = 0.87; 95% CI, 0.57–1.34). For those who did have an intimate social support system, the groups were

TABLE 1
Demographic and Risk Factor Variables for Breast Carcinoma

Variable	Benign disease (n = 275) No. (%)	Breast carcinoma (n = 239) No. (%)	Odds ratio 95% CI (age-adjusted)
Mean (SD) age (yrs)	57.0 (9.8)	61.3 (9.4)	1.05 (1.03-1.07)
Education			
Primary	14 (5.2)	7 (3.0)	1-
3-4 years secondary	109 (40.7)	86 (36.6)	1.98 (0.74-5.30)
5-6 years secondary	41 (15.3)	41 (17.4)	2.46 (0.87-7.00)
Diploma/certificate	68 (25.3)	58 (24.7)	2.67 (0.96-7.43)
University/college	36 (13.4)	43 (18.3)	3.78 (1.31-10.91)
Marital status			
Married/defacto	189 (70.3)	156 (66.4)	1-
Single	20 (7.4)	15 (6.4)	0.74 (0.38-1.52)
Widowed	27 (10.0)	36 (15.3)	0.93 (0.51-1.70)
Divorced/separated	33 (12.3)	28 (11.9)	0.97 (0.55-1.70)
Age at birth of first child			
Nulliparous	44 (17.3)	31 (14.1)	1-
< 20 yrs	10 (3.9)	7 (3.2)	1.40 (0.46-4.22)
20-24 yrs	84 (33.1)	47 (21.4)	0.88 (0.48-1.60)
25-29 yrs	72 (28.3)	84 (38.2)	1.77 (1.00-3.15)
30+ yrs	44 (17.3)	51 (14.1)	1.81 (0.96-3.40)
Parity			
Nulliparous	44 (17.1)	31 (13.8)	1-
1-2	113 (44.0)	103 (46.0)	1.55 (0.89-2.69)
3+	100 (38.9)	90 (40.2)	2.31 (0.75-2.28)
Family history			
No	222 (80.7)	188 (78.7)	1-
Diagnosed at age < 50 yrs	11 (4.0)	22 (9.2)	2.14 (0.99-4.61)
Diagnosed at age 50+ yrs	27 (9.8)	16 (6.7)	0.64 (0.33-1.25)
Unknown	15 (5.5)	13 (5.4)	0.96 (0.44-2.11)
H/O benign breast disease			
No	223 (84.5)	188 (83.2)	1-
Yes	41 (15.5)	38 (16.8)	1.14 (0.70-1.87)
Menopausal status			
Premenopausal	83 (30.2)	31 (13.0)	1-
Postmenopausal	192 (69.8)	208 (87.0)	1.85 (1.05-3.25)
Age at onset of menopause ^a			
< 45 yrs	52 (32.1)	51 (27.9)	1-
46-50 yrs	58 (35.8)	76 (41.5)	1.41 (0.84-2.39)
> 50 yrs	52 (32.1)	56 (30.6)	1.16 (0.67-2.00)
Ever use of oral contraceptives			
No	102 (42.0)	90 (42.3)	1-
Yes	141 (58.0)	123 (57.7)	1.67 (1.08-2.59)
Current use of hormone replacement therapy			
No	194 (74.6)	149 (66.2)	1-
Yes	66 (25.4)	76 (33.8)	1.51 (1.01-2.25)
Alcohol consumption			
None	58 (22.5)	47 (21.1)	1-
Occasional	73 (28.3)	54 (24.2)	1.03 (0.61-1.77)
Weekly	83 (32.2)	42 (18.8)	0.78 (0.45-1.36)
Daily	44 (17.1)	80 (35.9)	2.58 (1.49-4.48)
(BMI)			
< 25	145 (59.7)	111 (52.9)	1
≥ 25	98 (40.3)	99 (47.1)	1.28 (0.87-1.87)

95% CI: 95% confidence interval; SD: standard deviation; H/O: history of; BMI: body mass index.

^a Numbers for each variable do not add up to total due to missing values.

TABLE 2
Number of Subjects Reporting at Least 1 Acute Stressor for Each Severity Rating of Long Term Threat in the 2-Year Period Prior to Interview

Severity rating of long term threat for acute stressors (rating)	Benign No. (%)	Breast carcinoma No. (%)	Odds ratio (95% CI) ^a
Extreme (5)	8 (2.9)	11 (4.6)	1.06 (0.37–3.02)
Severe (4)	24 (8.7)	20 (8.4)	0.95 (0.48–1.87)
High (3)	61 (22.2)	47 (19.7)	0.94 (0.59–1.50)
Moderate (2)	151 (54.9)	115 (48.1)	0.75 (0.51–1.10)
Mild (1)	164 (59.6)	140 (58.6)	1.15 (0.77–1.72)
Extreme/severe (4, 5)	32 (11.6)	28 (11.7)	0.89 (0.49–1.62)
Extreme/severe/high (3, 4, 5)	84 (30.5)	70 (29.3)	0.92 (0.61–1.39)

95% CI: 95% confidence interval.

^a Adjusted for age.**TABLE 3**
Number of Subjects Reporting at Least 1 Chronic Stressor for Each Severity Rating (Long Term Threat) in the 2-Year Period Prior to Interview

Severity ratings of long term threat for chronic stressors	Benign No. (%)	Breast carcinoma No. (%)	Odds ratio (95% CI) ^a
Extreme (5)	1 (0.4)	0 (0.0)	
Severe (4)	6 (2.2)	5 (2.1)	1.03 (0.30–3.50)
High (3)	42 (15.3)	24 (10.0)	0.70 (0.41–1.22)
Moderate (2)	110 (40.0)	76 (31.8)	0.77 (0.53–1.13)
Mild (1)	141 (51.3)	159 (66.5)	1.23 (1.04–1.44)

95% CI: 95% confidence interval.

^a Adjusted for age.**TABLE 4**
Weighted Scores for Acute and Chronic Stressors in the 2-Year Period Prior to Biopsy

Weighted stressor scores	Benign Mean (SD)	Breast carcinoma Mean (SD)	Odds ratio (95% CI) ^a
Acute stressors	5.09 (4.17)	4.85 (4.01)	1.00 (0.95–1.05)
Chronic stressors	3.29 (3.08)	3.00 (2.90)	0.97 (0.91–1.04)
Acute and chronic stressors	8.38 (5.53)	7.85 (5.19)	0.99 (0.96–1.03)

SD: standard deviation; 95% CI: 95% confidence interval.

^a Adjusted for age.

comparable in terms of the quality of this support (Wald chi-square (2) = 0.09, $P = 0.96$). Nonintimate support ratings generally were good, with similar percentages of adequate ratings across the groups. It is interesting to note that more of the benign group reported having poor or no nonintimate support, al-

though the numbers were small in this category and overall this variable was found to be nonsignificant (Wald chi-square (2) = 6.68; $P = 0.35$). There were no differences in subjective ratings of support (Wald chi-square (2) = 4.03; $P = 0.13$) or in recent changes in the subjective quality of support available (Wald chi-square (2) = 1.04; $P = 0.59$).

Interactions

For the examination of interactions between life stressors and these other psychosocial factors, acute and chronic stressors were considered together to increase the power of these analyses. Therefore the term “major stressor” in these analyses was used to identify subjects reporting at least one acute or chronic stressor rated as either severe or extreme for long-term threat in the previous 2 years. Experiencing a major stressor was correlated with intimate emotional support (chi-square (2) = 10.3; $P = 0.01$), but was not correlated with mature defense style ($\rho = -0.04$; $P = 0.38$) or emotional control ($\rho = 0.08$; $P = 0.06$).

The results of interactions between vulnerability factors and a major stressor on breast carcinoma risk are summarized in Table 6. There was no evidence that a less mature defense style (Wald chi-square(1) = 2.23; $P = 0.14$) or higher emotional control (Wald chi-square(1) = 0.02; $P = 0.90$) were interacting with the impact of a major stressor on the development of breast carcinoma.

However, there was a significant interaction between a major stressor and intimate emotional support (Wald chi-square (2) = 10.19; $P = 0.006$). For subjects who had experienced a major stressor within the past 2 years, those rated as having “no intimate emotional support” had an age-adjusted OR for breast carcinoma of 7.46 (95% CI, 1.84–30.22) compared with those rated as having “good” intimate emotional support. Of note, only 26 subjects (5.1% of sample) were in this category, 19 (73.1%) of whom were diagnosed with breast carcinoma. Of the subjects who had experienced a major stressor, those rated as having “poor or adequate” intimate emotional support were not found to be significantly different from those rated as having good intimate emotional support in the OR for breast carcinoma (OR = 1.15; 95%CI, 0.28–4.70).

We hypothesized that mature defense style and/or emotional control may be important in the face of a major stressor when no social support was available. However, we found no evidence to support these higher order interactions (Table 6).

Potential Confounders

A number of variables were considered to be potential confounders for inclusion in the multivariate model

TABLE 5
Descriptives for Vulnerability Factors, Wald Statistic, Odds Ratios, and Corresponding 95% CI

	Benign Mean (SD)	Breast carcinoma Mean (SD)	Wald chi-square (χ^2)	Odds ratio (95% CI) ^a
Mature defense style	6.26 (1.10)	6.44 (1.05)	$\chi^2(1) = 1.82$ ($P = 0.18$)	1.12 (0.95–1.32)
Emotional control	15.72 (3.86)	15.87 (3.53)	$\chi^2(1) = 0.48$ ($P = 0.49$)	0.98 (0.94–1.03)

	Benign No. (%)	Breast carcinoma No. (%)	Wald chi-square (χ^2)	Odds ratio (95% CI) ^a
Intimate emotional support			$\chi^2(3) = 0.46$ ($P = 0.93$)	
Good	130 (47.3)	110 (46.0)		1–
Adequate	45 (16.4)	35 (14.6)		0.95 (0.56–1.60)
Poor	32 (11.6)	24 (10.0)		0.93 (0.51–1.69)
None	68 (24.7)	70 (29.3)		0.86 (0.54–1.38)
Nonintimate emotional support			$\chi^2(2) = 6.68$ ($P = 0.35$)	
Good	227 (82.5)	208 (87.0)		1–
Adequate	31 (11.3)	29 (12.1)		1.07 (0.61–1.85)
Poor/none	17 (6.2)	2 (0.8)		0.14 (0.03–0.63)

95% CI: 95% confidence interval; SD: standard deviation.

^a Adjusted for age.**TABLE 6**
Wald Chi-Square Statistic, Odds Ratios, and Corresponding 95% CI for Interaction Terms between Vulnerability and Major Stressor Variables Predicting Breast Carcinoma Diagnosis

Interaction terms ^a	Wald chi-square (χ^2) (df)	Odds ratio (95% CI) ^b
Stressor X, mature defense style	$\chi^2(1) = 2.23, P = 0.14$	1.57 (0.87–2.82)
Stressor X, emotional control	$\chi^2(1) = 0.02, P = 0.90$	1.01 (0.87–1.17)
Stressor X, intimate social support rating	$\chi^2(2) = 10.2, P < 0.006$	
X Good intimate support		1–
X Poor/adequate intimate support		1.15 (0.28–4.70)
X No intimate support		7.46 (1.84–30.22)
Stressor X, mature defense style X social support	$\chi^2(2) = 0.18, P = 0.91$	
Stressor X, emotional control X social support	$\chi^2(2) = 0.49, P = 0.78$	

95% CI: 95% confidence interval; df: degree of freedom.

^a Each interaction term tested by adding to the main effects only model.^b Age adjusted.

for psychosocial predictors of breast carcinoma. Among sociodemographic and medical variables, age and education were treated as confounding variables, being associated with both stressor variables and with breast carcinoma. Also included were a family history of breast carcinoma, a history of benign breast dis-

ease, age at the onset of menopause, age at birth of the first child, parity, oral contraceptive use, current use of hormone replacement therapy, body mass index, and alcohol consumption. These were chosen based on statistical and empiric grounds.⁵³

Although age was included as a potential confounder, there still was some concern that the impact of age was not controlled adequately.⁷ We hypothesized that age may have affected the likelihood of experiencing certain types or severity of stressors. Analyses were repeated separately on 271 women age < 60 years and on 243 women age \geq 60 years. No differences were noted between the breast carcinoma group and benign controls in each age group, in severity of events and difficulties reported, or in the cumulative stressor scores.

Of trait personality variables examined (locus of control, emotional expression and control, defense style, self-esteem, and trait anxiety) and their subfactors, none were found to be associated independently with breast carcinoma or with life event variables and therefore these were excluded as confounders. Higher state anxiety was associated with the number of chronic stressors reported ($\rho = 0.16; P < 0.001$) but not the number of acute stressors ($P = 0.26$) or severity of stressors ($P = 0.16$), suggesting that anxiety was due to ongoing stressors rather than anxiety influencing the reporting of stressors generally. With no group

TABLE 7
Final Multiple Logistic Regression Model for Predictors of Breast Carcinoma

Term	β (SE)	Wald chi-square (χ^2) (df), <i>P</i> value	Odds ratio (95% CI) ^a
Stressor	-0.66 (0.58)	$\chi^2(1) = 1.31$	0.52 (0.17-1.60)
Intimate emotional support		$\chi^2(2) = 1.52$	
Good			1-
Poor/adequate	-0.04 (0.27)		0.96 (0.57-1.64)
None	-0.35 (0.29)		0.70 (0.39-1.25)
Stressor X, intimate emotional support		$\chi^2(2) = 11.27$, <i>P</i> = 0.004	
+ Stressor X, good support			1-
+ Stressor X, poor/adequate support	-0.21 (0.81)		1.03 (0.22-4.67)
+ Stressor X, no intimate support	2.24 (0.82)		9.39 (1.90-46.42)

SE: standard error; df: degrees of freedom; 95% CI: 95% confidence interval.

^a Includes main effects of age, education, age at menopause, family history of breast carcinoma, history of benign breast disease, age at birth of first child, parity, body mass index, frequency of alcohol consumption, oral contraceptive use, use of hormone replacement therapy, state depression, and nonintimate emotional support.

differences in levels of state anxiety, it was excluded as a confounder.

State depression scores, although not associated with the number of acute or chronic stressors, were associated with stressors in the highest 2 categories of threat ($\rho = 0.14$; $P = 0.002$); therefore state depression was treated as a potential confounder, despite not being associated with breast carcinoma. Nonintimate social support also was considered as a likely confounder, given the significance of intimate emotional support and the trend toward the control group to have poorer levels of nonintimate support, albeit a nonsignificant difference.

The results of the multiple logistic regression model of psychosocial predictors of breast carcinoma, including as potential confounders age, education, age at the onset of menopause, family history of breast carcinoma, history of benign breast disease, age at birth of the first child, parity, body mass index, alcohol consumption, oral contraceptive use, use of hormone replacement therapy, state depression, and nonintimate social support, are presented in Table 7. The OR for breast carcinoma for subjects reporting a major stressor in the past 2 years with no intimate emotional support was 9.39 (95%CI, 1.90-46.42).

DISCUSSION

The results of the current study revealed a significant increase in the development of breast carcinoma for

women reporting a recent stressor independently rated at the highest levels of threat, but only for those without any intimate emotional support. (An intimate support refers to a partner in life, as opposed to close friend or family). The effect size for this specific group increased somewhat after adjustment for potential confounders including age, education, menopausal status, family history, history of benign breast disease, body mass index, reproductive history, alcohol consumption, oral contraceptive use, use of hormone replacement therapy, and depression, and was in the order of a ninefold increase in risk.

In contrast to past findings, we found no evidence of an independent association between recent life stressors and the development of breast carcinoma. Using the same method of assessing life event stress, both Geyer^{15,16} and Chen et al.¹ reported a significant increase in the risk of breast carcinoma after severely threatening life event stressors. The LEDS interview employed in these studies is a well established, reliable, and comprehensive instrument, enabling independent rating of stressors according to precise definitions and encompassing contextual information.

Despite similarities in designs, the current study does vary from the earlier studies in a number of ways. The population from which our sample was drawn is more homogeneous, being community-based, asymptomatic, and recalled for assessment purely on radiologic grounds. Other studies have used symptomatic women who were assessed by their primary physician and referred for biopsy from multiple sources and for varied reasons. The possibility that "awareness" of their diagnosis affected the reporting of psychosocial variables in the current study is minimal.

As a consequence of targeting a population screened by mammography, our sample were "older"; our breast carcinoma group had an average age of 61 years and the current study controls had an average age of 57 years. The Geyer¹⁶ breast carcinoma group had a mean age of 49 years and the controls had a mean age of 43 years; in the study by Chen et al.¹ the breast carcinoma group had an average age 57 years and the controls had a mean age of 50 years. Although our 2 groups were significantly different with regard to age, in real terms the difference was small and considerably less than the 6-7-year age difference in the smaller studies, enabling us to better control for the influence of age.

These differences in the ages of the study participants may be important in reconciling differences in reported outcome. Age is an independent risk factor for breast carcinoma and also is associated with the type and number of life events experienced, as well as social support. Although often included in analyses,

McGee et al.⁷ suggest the effects of age may not be controlled adequately by simple statistical means. This difficulty is most marked in smaller studies with larger ranges in age and it is possible that the independent effects of severely threatening events on the development of breast carcinoma reported by Geyer¹⁶ and Chen et al.¹ may in fact have been confounded by age. It also is possible that different psychosocial factors are influential with increasing age. Thus, age differences in samples may explain inconsistent findings, particularly because it is clearly possible that psychoendocrine factors may be the link between stress and breast carcinoma.

A potential limitation of the current study is the relatively short time period covered in assessing life stressors. This time frame was influenced by a desire to obtain an optimal balance between reliability of recall and the presumed time period of tumor growth. Geyer examined the influence of the time period in which severely threatening events were assessed with regard to breast carcinoma risk and found that both those occurring in the 3-year period prior to interview as well as more distant events were similarly predictive of breast carcinoma risk.¹⁵ Likewise, Chen et al.¹ noted that the average annual rate of severely threatening life events did not vary significantly over the 5-year period examined or differ between the groups. This finding notwithstanding, to our knowledge all studies reported to date in fact most likely assess the effect of stressors on tumor growth.

One strength of the current study is the sample size, which includes what we believe to be the largest series of breast carcinoma cases examined prior to diagnosis in this area of research. We believe the power of our study ensures that the likelihood of missing even a modest association between severely threatening stressors and the development of breast carcinoma is minimal. Our sample size also has enabled multiple variables to be assessed simultaneously (life events, coping style, affect, personality, and social support) and more important, for their interactions to be examined.

The progression to exploring the interaction between distinct but interrelating variables is important in this field of research. Although there was no evidence from the current study data of a direct association between social support, coping style, or emotional control and breast carcinoma, the usefulness of examining these variables without consideration of the external stressors with which an individual is coping is questionable. The current study findings concur with the theory of Brown and Harris that "vulnerability factors" (in the current study, social support, coping style, and emotional control) may have no inde-

pendent significant effect, but impact largely through their interaction with provoking agents such as life stressors.²⁵ This theoretic model also is consistent with Temoshok's model of the cancer prone individual, in which the type C coping style interacts with stressors. Under conditions of severe stress, the effectiveness of this coping style breaks down, producing a greater level of strain.³¹

The importance of coping in moderating the impact of stressors is well established,⁵⁹ although to our knowledge few studies to date have examined coping style in conjunction with life event stress and the development of breast carcinoma. Chen et al.¹ reported that confronting stress increased the risk of developing breast carcinoma, independent of life events. However, to our knowledge there was no mention of this interaction being tested or removed from their final model. In what to our knowledge is the only other study to examine the interaction between life event stress and coping style, no significant differences in the development of breast carcinoma were reported for either of these variables or their interaction.¹⁹ We found no evidence that coping style interacted with the impact of life stress in the development of breast carcinoma. It is possible that our measure of coping was not tapping the appropriate concept.

Although there is some evidence of the tendency to control or suppress negative emotions being associated with the development of breast carcinoma,⁶⁰⁻⁶² some studies have failed to support this notion.^{42,63} With one exception,⁶⁰ to our knowledge emotional control has not been considered previously in conjunction with life event stress, and no studies have explored the relation between these two variables. Again, we found no evidence of a role for emotional control in the development of breast carcinoma, nor did we find evidence of an interaction between emotional control and life event stress.

Our finding of an interaction between severely threatening life events and the absence of social support was somewhat unexpected given the absence of independent effects. However, this finding is not without some precedence.¹⁷ Much of the focus on social support and breast carcinoma has been in relation to its role after diagnosis. To our knowledge the only previous study to consider their interaction in the development of breast carcinoma reported no significant differences between breast carcinoma cases and controls in the number or severity of life events, coping style, or social support or their interactions.¹⁹ The results of the current study provide support for the model described by Hilakivi-Clarke et al.³² that emphasizes the interaction between life events and stress-related variables such as social support in me-

diating breast carcinoma risk. Adding credence to our significant interaction between highly threatening stressors and the absence of intimate emotional support is that these two variables, although not totally independent, were assessed and rated quite independently.⁴³

The current study found no evidence of an independent relation between recent life event stress and the development of breast carcinoma. However, examining the interactions between life event stress and a number of vulnerability factors, we identified a small group of women who were at significantly greater risk of breast carcinoma: those experiencing a highly threatening stressor within the previous 2 years and without any intimate emotional support. This group includes, but is not exclusively comprised of, those women recently widowed or divorced. We found no evidence that other vulnerability factors such as coping style and emotional control interacted with life stressors in the development of breast carcinoma. The current study demonstrates the importance of social support, or the lack thereof, as a specific vulnerability factor for the impact of life event stress in the development of breast carcinoma. Although the results of the current study support a multifactorial view of breast carcinoma development, they also suggest that the role of psychosocial factors in the etiology of breast carcinoma in general is small and specific. Women should be reassured that stress per se does not cause breast carcinoma; however, in the absence of intimate emotional support, situations of severe stress may increase a woman's vulnerability to this disease. Health professionals should be encouraged to identify individuals in circumstances of severe stress and if feasible explore avenues for reducing the stress and promoting the use of available support systems, and encourage the utilization of counseling and other supportive services.

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