Title

Variations in the Co-occurrence of Anxiety and Depressive Symptoms and its Impact on Quality of Life in Women Following Breast Cancer Surgery

Author

Gold, Marshall Lee

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Variations in the Co-occurrence of Anxiety and Depressive Symptoms and its Impact on Quality of Life in Women Following Breast Cancer Surgery

by

Marshall L. Gold

THESIS

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ABSTRACT

Purpose: Little is known about the prevalence of combined anxiety and depressive symptoms (CADS) in patients with breast cancer. The purpose of this study was to evaluate for differences in demographic and clinical characteristics, as well as quality of life (QOL) outcomes prior to breast cancer surgery among women classified into one of four distinct groups with and without CADS.

Methods: A total of 410 patients completed a demographic questionnaire and self-report measures of performance status, comorbidity, anxiety, depression, and QOL prior to and monthly for 6 months following breast cancer surgery. Growth mixture modelling (GMM) was used to identify subgroups of women with distinct trajectories of anxiety and depressive symptoms. Results of these analyses were used to create four groups of patients with and without CADS. Differences in demographic, clinical, and symptom characteristics, among the four groups of women were evaluated using analyses of variance and Chi square analyses.

Results: Women with CADS were younger, non-white, had lower performance status, received neoadjuvant or adjuvant chemotherapy, had greater difficulty dealing with their disease and treatment, and reported less support from others to meet their needs. In addition, these women had lower physical, psychological, social well-being, and total QOL scores. Higher levels of anxiety with or without subsyndromal depressive symptoms were associated with fears of recurrence, hopelessness, uncertainty, loss of control, and a decrease in life satisfaction.

Conclusion: Findings from this study suggest that CADS occurs in a high percentage of women following breast cancer surgery and results in a poorer QOL.

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INTRODUCTION

Population-based studies suggest that depression and anxiety disorders affect about 6.7%[1] and 18%[2] of Americans, respectively. What is less clear, particularly in primary care settings, is the percentage of individuals who have mixed anxiety and depression disorders.[3-5] Part of this uncertainty comes from ambiguity in the definitions of anxiety and depression, each of which refers to several different types and levels of disorders that vary in terms of the severity of the symptoms experienced.[6]

Both depression and anxiety are more common in oncology patients than in the general population. These two symptoms are often assessed together and referred to as psychological distress.[7] Previous psychological treatment, lack of an intimate confiding relationship, younger age, and severely stressful non-cancer life experiences were associated with the co-occurrence of depression and anxiety in women with breast cancer.[8] Additionally, in oncology patients, these two treatable conditions are associated with non-adherence to treatment recommendations; increased time in the hospital; and impaired physical, social, and family functioning.[9] Finally, anxiety and depression are associated with a poorer prognosis and increased mortality.[10]

Several systematic reviews have noted wide variations in the prevalence rates for anxiety and depression in oncology patients.[9,11,12] Although many studies mention the co-occurrence of anxiety and depression in oncology patients, only three studies were identified that provided information on the prevalence of combined anxiety/depressive symptoms (CADS) in patients with breast cancer.[7,13,14] In a large epidemiological study that assessed patients at the time of diagnosis or prior to the initiation of cancer treatment (n=8,175), using the Brief Symptom Inventory,[7] 10.8% of the patients with breast cancer had CADS, 14.9% had only anxiety symptoms, 2.8% had only depressive symptoms, and 71.5% had neither symptom.

In the second study that assessed Chinese patients (n=218) midway through chemotherapy (CTX) or radiation therapy (RT) for breast cancer using the Hospital Anxiety and

Depression Scale (HADS),[14] 15.6% of the sample had CADS. In the third longitudinal study that assessed CADS in patients prior to the diagnosis of breast cancer (n=482) and again at 12 and 24 months after the diagnosis, using the short-form of the State-Trait Anxiety Inventory (STAI) and the Center for Epidemiological Studies-Depression (CES-D) scale,[13] the occurrence rates for CADS were 28%, 14%, and 10%, respectively. The occurrence of CADS at the time of cancer diagnosis was associated with higher levels of fatigue and poorer quality of life (QOL) at 12 and 24 months after the cancer diagnosis.

While findings from these studies suggest that CADS occurs in 10% to 28% of patients with breast cancer depending on the time of the assessment,[7,13,14] the demographic and clinical characteristics associated with CADS and its impact on QOL outcomes have not been evaluated. In addition, single assessments of anxiety and depressive symptoms were used to diagnosis CADS.

Our research team evaluated anxiety (unpublished data) and depressive[15] symptoms in women prior to and for six months following breast cancer surgery (n=398). Using growth mixture modeling (GMM) to evaluate patients' ratings of state anxiety using the STAI, two distinct latent classes were identified. The Lower Anxiety class (36.9%) had state anxiety scores of 31.9 at enrollment that gradually decreased over the 6 months of the study. The Higher Anxiety class (63.1%) had state anxiety scores of 49.5 at enrollment that gradually decreased over the 6 months of the study. In addition, patients in the Higher Anxiety class were significantly younger, had a lower Karnofsky Performance Status (KPS) score, and a higher Trait Anxiety score prior to surgery. When CES-D scores were analyzed using GMM, four distinct latent classes were identified (i.e., Resilient (38.9%), Subsyndromal (45.2%), Delayed (11.3%), and Peak (4.5%). Compared to patients in the Resilient class, patients in the Subsyndromal class were significantly younger and had a lower KPS score.

Our detailed evaluation of anxiety and depressive symptoms provided an opportunity for us to evaluate for differences in demographic and clinical characteristics, as well as QOL

outcomes prior to breast cancer surgery among women who were classified into one of four distinct groups with and without CADS (i.e., Lower Anxiety and Resilient; Lower Anxiety and Subsyndromal depressive symptoms; Higher Anxiety and Resilient; Higher Anxiety and Subsyndromal depressive symptoms).

METHODS

Patients and Settings

This descriptive, longitudinal study is part of a larger study that evaluated for neuropathic pain, lymphedema, and other symptoms in a sample of women who underwent breast cancer surgery. A detailed description of the methods are published elsewhere.[15-18] In brief, patients were recruited from Breast Care Centers located in a Comprehensive Cancer Center, two public hospitals, and four community practices.

Patients were eligible to participate if they were $\geq$18 years of age; would undergo breast cancer surgery on one breast, were able to read, write, and understand English; agreed to participate; and gave written informed consent. Patients were excluded if they were having breast cancer surgery on both breasts or had distant metastasis at the time of diagnosis.

A total of 516 patients were approached and 410 were enrolled in the study (response rate 79.5%). For those who declined participation, the major reasons for refusal were: too busy, overwhelmed with the cancer diagnosis, or insufficient time available to do the assessment prior to surgery.

Study Procedures

The Committee on Human Research at the University of California, San Francisco and the Institutional Review Boards at each of the study sites approved the study. During the patient's preoperative visit, a staff member explained the study to the patient and introduced the patient to the research nurse who met with the women, determined eligibility, and obtained written informed consent prior to surgery. After providing consent, patients completed the enrollment questionnaires. Patients were contacted two weeks after surgery to schedule the first

post-surgical appointment. The research nurse met with the patients either in their home or in the Clinical Research Center at one, two, three, four, five, and six months after surgery.

Instruments

A demographic questionnaire obtained information on age, education, ethnicity, marital status, employment, and financial status. Medical records were reviewed to obtain information on disease and treatment characteristics.

Patient's functional status was assessed using the KPS scale, which ranges from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal, I have no complaints or symptoms). The KPS has well established validity and reliability.[19]

The Self-Administered Comorbidity Questionnaires (SCQ) is a short and easily understood instrument that was developed to measure comorbidity in clinical and health service research settings.[20] The questionnaire consists of 13 common medical conditions. Patients were asked to indicate if they had the condition; if they received treatment for it; and did it limit their activities (indication of functional limitations). For each condition, a patient can receive a maximum of 3 points. The SCQ has well-established validity and reliability and was used in studies of patients with a variety of chronic conditions.[21-23]

The Spielberger State-Trait Anxiety Inventories (STAI-T, STAI-S) consist of 20 items each that are rated from 1 to 4. Scores for each scale are summed and can range from 20 to 80. A higher score indicates greater anxiety. The STAI-T measures an individual's predisposition to anxiety determined by his/her personality and estimates how a person generally feels. The STAI-S measures an individual's transitory emotional response to a stressful situation. It evaluates the emotional responses of worry, nervousness, tension, and feelings of apprehension related to how a person feels "right now" in a stressful situation. Cutoff scores of $\geq$31.8 and $\geq$32.2 indicate high levels of trait and state anxiety, respectively.[24,25] In this study, Cronbach's alphas for the STAI-T and STAI-S were .88 and .95, respectively.

The CES-D consists of 20 items selected to represent the major symptoms in the clinical syndrome of depression. Scores can range from 0 to 60, with scores of ≥16 indicating the need for individuals to seek clinical evaluation for major depression. The CES-D has well-established concurrent and construct validity.[26,27] In this study, Cronbach's alpha for the CES-D was 0.90.

The Quality of Life Scale-Patient Version (QOL-PV) is a 41-item instrument that measures four dimensions of QOL in cancer patients (i.e., physical well-being, psychological well-being, spiritual well-being, social well-being), as well as a total QOL score. Each item was rated on a 0 to 10 NRS with higher scores indicating a better QOL. The QOL-PV has well established validity and reliability.[28-30] In this study, Cronbach's alpha for the QOL-PV total score was .86. For the physical, psychological, social, and spiritual well-being subscales, the coefficients were 0.70, 0.79, 0.75, and 0.61, respectively.

Selected items from the QOL-PV were used to assess a number of psychosocial adjustment characteristics. Singular items asked patients to provide ratings of life satisfaction, sense of purpose/mission in life, and hopefulness. In addition, patients were asked to rate the amount of isolation caused by their illness and the degree of uncertainty they felt about the future. Fear was assessed with three questions: fear of future diagnostic tests, fear of a second cancer, and fear of metastasis. One question asked patients to rate the level of control they felt over their lives and another asked patients to rate their difficulty coping as a result of the cancer and its treatment. The final item asked patients to rate whether the amount of support they received from others was sufficient to meet their needs. Each item was rated using a 0 to 10 NRS with higher scores indicating a more positive appraisal of a particular characteristic. The specific items were chosen based on the review of the literature of psychosocial adjustment and depression and anxiety in women with breast cancer.[31-38]

Data Analysis

GMM Analyses of the Anxiety and Depression Classes - Data were analyzed using SPSS Version 20[39] and Mplus Version 6.11.[40] The specific details regarding the identification of

the anxiety (unpublished data) and depression[15] latent classes using GMM are published elsewhere. In brief, for each symptom, a single growth curve that represented the "average" change trajectory was estimated for the total sample. Then the number of latent growth classes that best fit the data were identified using published guidelines.[41-43] Separate GMM analyses were done for anxiety and depressive symptoms.

Creation of the Four Groups of Patients - For the purposes of this study, the results of the GMM analyses for anxiety (i.e., Lower and Higher Anxiety latent classes) and depressive symptoms (i.e., Resilient and Subsyndromal latent classes) were used to create the four groups of patients with or without CADS (i.e., Lower Anxiety and Resilient; Lower Anxiety and Subsyndromal depressive symptoms; Higher Anxiety and Resilient; Higher Anxiety and Subsyndromal depressive symptoms).

Evaluation of differences among the anxiety/depression groups – Descriptive statistics and frequency distributions were generated on the sample characteristics using the Statistical Package for the Social Sciences (SPSS) version 20.[39] Differences in demographic, clinical, and psychological adjustment characteristics and QOL outcomes, among the four groups, were evaluated using analyses of variance and Chi Square analyses. Adjustments were not made for missing data. Therefore, the cohort for each analysis was dependent on the largest set of available data across groups. A p-value of $<.05$ was considered statistically significant. Post hoc contrasts were done using the Bonferroni correction to control the overall family alpha level of the six possible pairwise contrasts for the four anxiety/depression groups at .05. For any one of the six pairwise contrasts, a p-value of $\leq .008$ (.05/6) was considered statistically significant.

RESULTS

Creation of the four anxiety/depression groups

Four groups of patients with or without CADS were created by combining the results from the GMM analyses for anxiety (unpublished data) and depressive[15] symptoms. The largest percentage of patients was classified in the Higher Anxiety and Subsyndromal group (n=149,

44.5%). The second largest group was called the Lower Anxiety and Resilient group (n=109, 32.5%). The third largest group was called the Higher Anxiety and Resilient group (n=46, 11.6%). The smallest percentage of patients were in the Lower Anxiety and Subsyndromal group (n=31, 9.3%). The CES-D, and Trait Anxiety and State Anxiety scores prior to surgery, for each of the groups are shown in Figures 1A and 1B, respectively.

Differences in demographic characteristics among the anxiety and depression groups

As shown in Table 1, except for age and ethnicity, no significant differences were found among the four groups in any demographic characteristics. Patients in the Higher Anxiety and Subsyndromal group were younger than those in the Lower Anxiety and Resilient group. Compared to the Lower Anxiety and Resilient group, a higher percentage of Non-white women were in the Higher Anxiety and Resilient and Higher Anxiety and Subsyndromal groups.

Differences in clinical characteristics among the anxiety and depression groups

As shown in Table 2, except for the KPS score, the occurrence of high blood pressure, the receipt of neoadjuvant or adjuvant CTX, and the use of complementary therapies, no significant differences in clinical characteristics were found among the four groups. In terms of KPS scores, patients in both Subsyndromal groups had lower KPS scores than those in the Lower Anxiety and Resilient group.

For both receipt of neoadjuvant and adjuvant CTX, compared to the Lower Anxiety and Resilient group, a higher percentage of patients in the Higher Anxiety and Subsyndromal group received these treatments. For both high blood pressure and the use of complementary therapy, while the overall Chi square test was significant, none of the post hoc contrasts were significant.

Differences in psychosocial adjustment characteristics among the anxiety and depression groups

For each of the psychosocial adjustment characteristics (Table 3), statistically significant differences were found among the groups. Patients in both of the Higher Anxiety groups reported less life satisfaction than those in the Lower Anxiety and Resilient group. In addition,

patients in the Higher Anxiety and Subsyndromal group reported the lowest life satisfaction scores of all four groups. A lesser degree of purpose in life was reported by patients in the Higher Anxiety and Resilient group than by those in the Lower Anxiety and Resilient group. Patients in both Higher Anxiety groups were less hopeful than patients in the Lower Anxiety and Resilient group.

More isolation caused by illness was reported by patients in the Higher Anxiety and Subsyndromal group than by patients in both Lower Anxiety groups. Greater uncertainty about the future was expressed by both Higher Anxiety groups when compared to the Lower Anxiety and Resilient group. In addition, patients in the Higher Anxiety and Subsyndromal group reported more uncertainty about the future than those in the Lower Anxiety and Subsyndromal group.

Results for fears of future diagnostic tests, second cancers, recurrence, and metastasis were identical and consistent with findings for uncertainty about the future. Both Higher Anxiety groups reported greater fears than the Lower Anxiety and Resilient group. In addition, patients in the Higher Anxiety and Subsyndromal group reported more fears than those in the Lower Anxiety and Subsyndromal group.

Patients in the Higher Anxiety and Resilient group felt less in control of things in their life than those in the Lower Anxiety and Resilient group. In addition, patients in the Higher Anxiety and Subsyndromal group felt less in control than the other three groups. Patients in the Higher Anxiety and Subsyndromal group reported greater difficulty coping as a result of their disease and treatment than patients in the other three groups. When compared to patients in the Lower Anxiety and Resilient group, patients in the Higher Anxiety and Subsyndromal group reported less support from others to meet their needs.

Differences in QOL subscale and total scores among the anxiety and depression groups

For three of the four QOL subscales (Figure 2), statistically significant differences were found among the four groups. Patients in the Higher Anxiety and Subsyndromal group reported

lower physical, psychological, and social well-being scores compared to patients in the other three groups. No significance differences were found among the four groups in spiritual well-being scores.

Patients in the Higher Anxiety and Subsyndromal group reported lower physical well-being scores than those in the Higher Anxiety and Resilient group and the Lower Anxiety and Resilient group. Psychological well-being scores for patients in the Higher Anxiety and Subsyndromal group were the lowest of the four groups. In contrast, patients in the Lower Anxiety and Resilient group reported the highest psychological well-being scores. The social well-being scores of patients in the Higher Anxiety and Subsyndromal group were the lowest of the four groups.

Total QOL scores for the patients in the Higher Anxiety and Subsyndromal group were significantly lower than for patients in the other three groups. In contrast, the Lower Anxiety and Resilient group had the highest total QOL scores.

Discussion

This study is the first to combine data from the GMM analyses of anxiety and depressive symptoms in patients with breast cancer to characterize women with and without CADS. In our previous reports on these GMM analyses, as well as in analyses done for pain,[17] fatigue,[44] sleep disturbance,[45] and attentional function,[46] we suggest that the use of this analytic approach with longitudinal data identifies patients with persistent phenotypes. Therefore, this novel approach to the identification of four groups of women with distinct profiles for anxiety and depressive symptoms provides new insights into risk factors for CADS in women with breast cancer. In the current study, 44.5% of the patients were classified in the Higher Anxiety and Subsyndromal depressive symptoms group which represented the largest group in this sample. Of note, prior to surgery, these patients CES-D and STAI-S were 18.0 ($\pm$8.7) and 47.2 ($\pm$12.1), respectively. In addition, this percentage is higher than the three previous reports of CADS in patients with breast cancer where prevalence estimates ranged from 10.8%[7] to 28%.[13] These differences

may be related to differences in the measures used to assess anxiety and depressive symptoms, the timing of the measures, the definitions of CADS, and the characteristics of the patients who were evaluated.

Only two demographic characteristics (i.e., age, ethnicity) distinguished among the anxiety and depression groups. Consistent with previous studies,[8,47-52] patients with Higher Anxiety and Subsydromal depression symptoms were younger than women with neither symptom. This association in younger women may be explained by a number of factors including concerns about disfigurement and feelings of loss of womanhood.[52] In addition, younger women may have more concerns about their sexuality, their ability to become pregnant, and their ability to care for their children.[53]

In terms of ethnicity, our findings are consistent with those of Sheppard and colleagues[53] who found that about one third of their sample of African American women with breast cancer met cut-off criteria for either depression or anxiety. Of note, younger age, distrust of the medical system, and barriers to care were associated with higher levels of both anxiety and depression in this sample. In addition, Yoo and colleagues[54] noted that in women of color, increased anxiety and depression were associated with more advanced breast cancer at the time of diagnosis, as well as increased mortality. However, additional research is warranted because several studies failed to identify racial/ethnic differences in the occurrence of CADS.[55-57]

In terms of clinical characteristics, only functional status and receipt of neoadjuvant or adjuvant CTX were associated with anxiety and depression group membership. In terms of functional status, women in both Subsyndromal depressive symptom groups had lower KPS scores than women in the Resilient groups. Of note, the differences in KPS scores between the two Subsyndromal groups versus the Lower Anxiety and Resilient group represent not only statistically significant, but clinically meaningful differences in functional status (i.e., for both comparisons the effect size was d=0.5).[58,59] Our finding is consistent with work by Lansky et al.[60] who found that performance status and a history of depression were the strongest predictors of

the severity of depressive symptoms in women with cancer. More recently, Hong and Tian[48] reported that performance status, measured using the Eastern Cooperative Oncology Group scale, and younger age were risk factors for both depression and anxiety.

In our study, receipt of neoadjuvant or adjuvant CTX was associated with CADS. Findings regarding the associations between receipt of CTX prior to or following breast cancer surgery and depression and anxiety are inconclusive. While some studies found associations between these treatments and psychological symptoms,[14,61,62] other studies failed to demonstrate these associations.[63,64]

Several interesting patterns are worth noting from our evaluation of the differences among the anxiety and depression groups in the scores for the various psychosocial adjustment characteristics. For all of the characteristics listed in Table 4, except purpose and mission in life, patients who were classified in the Higher Anxiety and Subsyndromal Depressive symptoms group reported significantly lower scores than patients in the Lower Anxiety and Resilient group. In addition, for the majority of the psychosocial adjustment characteristics, patients classified in the Higher Anxiety and Resilient group had lower scores than patients in the Lower Anxiety and Resilient group. These findings suggest that higher levels of anxiety with or without Subsyndromal depressive symptoms are associated with fears of recurrence, hopelessness, uncertainty, loss of control, and a decrease in life satisfaction.

An evaluation of the four fear of recurrence items (see Table 4) suggests that regardless of anxiety or depression group membership, all of the women had fears regarding recurrence. This finding is consistent with two recent reviews that noted that fear of recurrence is a significant problem for oncology patients.[65,66] In addition as noted in these reviews, anxiety and depression are well-established correlates of fear of recurrence. In the current study, women in the two Lower Anxiety groups reported moderate severity scores for the four fear of recurrence items. However, patients in both Higher Anxiety groups reported severity scores in the severe range for these same four items.

It is interesting to note that patients in the Higher Anxiety and Subsyndromal depressive symptoms group reported the worst scores for the items related to loss of control, difficulty coping, and social support. These associations are consistent with previous reports that found that decreases in sense of control,[33,34,67] alterations in coping mechanisms,[32,68] and decrements in social support[33] were associated with CADS in women following breast cancer surgery. Additional research is warranted to determine which types of pharmacologic (e.g., anti-anxiety or antidepressant medications) and nonpharmacologic (e.g., cognitive-behavioral therapy) interventions would be most effective to decrease psychological distress in these patients.

As shown in Figure 2, compared to patients in the Lower Anxiety and Resilient group, patients with CADS reported significantly lower physical, psychological, and social well-being, as well as, total QOL scores. This observation is consistent with a number of studies in patients with breast cancer that found that increased severity of each of these psychological symptoms is associated with significant decrements in various dimensions of QOL.[14,69-71]

Several limitations need to be acknowledged. Self-report measures were used to evaluate for anxiety and depressive symptoms. Future studies need to use a Structured Clinical Diagnostic Interview to confirm the co-occurrence of anxiety and depressive symptoms in these patients. In addition, previous psychiatric conditions, as well as the use of medications for anxiety and depressive symptoms, were not evaluated at enrollment. Lastly, since the majority of the patients were well-educated, Caucasian women, the findings from this study may not generalize to more ethnically diverse samples of women with breast cancer.

Despite these limitations, findings from this study suggest that CADS occurs in a high percentage of women prior to breast cancer surgery. Patients with CADS reported increased fear of recurrence; decreased ability to cope as a result of their disease and treatment; a greater sense of isolation; and less life satisfaction. In addition, their QOL was relatively poor. Clinicians need to assess breast cancer patients for the co-occurrence of anxiety and depressive symptoms and refer these patients for mental health services. Successful treatment of

psychological symptoms may lead to improvements in patients' QOL, as well as reductions in hospitalizations and associated health care costs.

Table 1 - Differences in Demographic Characteristics Among the Depression and Anxiety Groups (N=335)

Characteristic	Lower Anxiety and Resilient (0) % (N) 32.5 (109)	Lower Anxiety and Subsyndromal (1) % (N) 9.3 (31)	Higher Anxiety and Resilient (2) % (N) 11.6 (46)	Higher Anxiety and Subsyndromal (3) % (N) 44.5 (149)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	58.3 (11.2)	53.6 (12.6)	54.9 (10.1)	52.8 (11.8)	F=4.97, p=.002 3<0
Education (years)	15.8 (2.3)	16.2 (3.2)	15.9 (2.8)	15.8 (2.7)	F=.25, p=.864
	% (N)	% (N)	% (N)	% (N)	
Ethnicity					X^2=15.92
White	76.9 (83)	80.6 (25)	52.2 (24)	58.8 (87)	p=.001
Non-white	23.1 (25)	19.4 (6)	47.8 (22)	41.2 (61)	0< 2 and 3
Lives alone					
Yes	18.3 (20)	32.3 (10)	31.1 (14)	21.1 (31)	X^2=4.84
No	81.7 (89)	67.7 (21)	68.9 (31)	78.9 (116)	p=.184
Marital status					
Married/partnered	31.2 (34)	51.6 (16)	44.4 (20)	45.9 (68)	X^2=7.44
Single, separated, widowed, divorced	68.8 (75)	48.4 (15)	55.6 (25)	54.1 (80)	p=.059
Currently working for pay					
Yes	54.1 (59)	38.7 (12)	41.3 (19)	48.3 (71)	X^2=3.53
No	45.9 (50)	61.3 (19)	58.7 (27)	51.7 (76)	p=.317
Total annual household income	13.6 (12)	17.9 (5)	20.0 (8)	26.8 (33)	X^2=10.59
<$30,000	37.5 (33)	46.4 (13)	52.5 (21)	37.4 (46)	p=.102
$30,000 to $99,999	48.9 (43)	35.7 (10)	27.5 (11)	35.8 (44)	
≥$100,000					

Abbreviations: SD = standard deviation

Table 2 - Differences in Clinical Characteristics Among the Depression and Anxiety Groups

Characteristic	Lower Anxiety and Resilient (0) % (N) 32.5 (109)	Lower Anxiety and Subsyndromal (1) % (N) 9.3 (31)	Higher Anxiety and Resilient (2) % (N) 11.6 (46)	Higher Anxiety and Subsyndromal (3) % (N) 44.5 (149)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Body mass index (kg/m^2)	26.4 (6.3)	27.1 (5.4)	27.7 (6.6)	27.1 (6.3)	F= 53, p=.666
Karnofsky Performance Status score	96.1 (6.6)	90.6 (11.8)	93.9 (8.8)	91.3 (11.0)	F=5.64, p=.001 0>1 and 3
Self-Administered Comorbidity Scale score	3.9 (2.4)	3.9 (2.4)	4.3 (2.6)	4.7 (3.2)	F=2.17, p=.092
Number of breast biopsies	1.4 (0.7)	1.5 (0.7)	1.6 (1.0)	1.6 (0.9)	F=1.19, p=.313
	% (N)	% (N)	% (N)	% (N)	
Occurrence of comorbid conditions (% and number of women who reported each comorbid condition from the Self-Administered Comorbidity Questionnaire)					
Heart disease	5.5 (6)	0.0 (0)	2.2 (1)	2.7 (4)	X^2=3.10, p= 378
High blood pressure	36.7 (40)	16.1 (5)	43.5 (20)	27.5 (41)	X^2=8.89, p=.031 NS post hoc contrasts
Lung disease	0.9 (1)	0.0 (0)	4.3 (2)	4.7 (7)	X^2=4.37, p=.224
Diabetes	3.7 (4)	12.9 (4)	15.2 (7)	8.1 (12)	X^2=7.06, p= 072
Ulcer	2.8 (3)	3.2 (1)	6.5 (3)	4.0 (6)	X^2=1.28, p=.736
Kidney disease	0.0 (0)	0.0 (0)	0.0 (0)	2.0 (3)	X^2=3.78, p=.286
Liver disease	3.7 (4)	0.0 (0)	2.2 (1)	2.0 (3)	X^2=1.83, p=.884
Anemia	8.3 (9)	3.2 (1)	4.3 (2)	10.1 (15)	X^2=2.85, p=.449
Depression	17.4 (19)	12.9 (4)	15.2 (7)	26.2 (39)	X^2=6.44, p=.142
Osteoarthritis	13.8 (15)	22.6 (7)	17.4 (8)	15.4 (23)	X^2=1.51, p=.679
Back pain	23.9 (26)	38.7 (12)	21.7 (10)	30.2 (45)	X^2=3.96, p=.266
Rheumatoid arthritis	2.8 (3)	0.0 (0)	0.0 (0)	4.7 (7)	X^2=3.90, p=.273
Gone through menopause					
Yes	68.5 (74)	58.1 (18)	66.7 (30)	60.8 (88)	X^2=2.29
No	31.5 (34)	41.9 (13)	33.3 (15)	39.4 (59)	p=.515
Received neoadjuvant chemotherapy					X^2=8.58
Yes	12.0 (13)	19.4 (6)	26.3 (13)	25.5 (38)	p=.036
No	88.0 (96)	80.6 (25)	71.7 (33)	74.5 (111)	0<3
On hormonal replacement therapy prior to surgery					
Yes	18.5 (20)	16.1 (5)	8.7 (4)	14.9 (22)	X^2=2.46
No	81.5 (89)	83.9 (26)	91.3 (42)	85.1 (126)	p= 486
Stage of disease					
Stage 0	19.3 (21)	22.6 (7)	10.9 (5)	18.1 (27)	
Stage 1	46.9 (50)	38.7 (12)	39.1 (18)	28.2 (42)	X^2=14.41
Stage IIA and IIB	30.3 (33)	32.3 (10)	37.0 (17)	42.3 (63)	p= 109
Stage IIIA, IIIB, IIIC, and IV	4.6 (5)	6.5 (2)	13.0 (6)	11.4 (17)	
Type of surgery					
Breast conserving	80.7 (88)	83.9 (26)	84.8 (39)	77.9 (116)	X^2=1.41
Mastectomy	19.3 (21)	16.1 (5)	15.2 (7)	22.1 (33)	p=.703
Sentinel lymph node biopsy					
Yes	87.2 (95)	80.6 (25)	82.6 (38)	79.9 (119)	X^2=2.44
No	12.8 (14)	19.4 (6)	17.4 (8)	20.1 (30)	p= 486
Axillary lymph node dissection					
Yes	30.6 (33)	41.9 (13)	41.3 (19)	46.3 (69)	X^2=6.56
No	69.4 (75)	58.1 (18)	58.7 (27)	53.7 (80)	p=.087
Reconstruction at the time of surgery					
Yes	20.4 (22)	25.8 (8)	13.0 (6)	22.1 (33)	X^2=2.34
No	79.6 (86)	74.2 (23)	87.0 (40)	77.9 (116)	p=.506
Received radiation therapy during the 6 months					
Yes	59.6 (65)	51.6 (16)	60.9 (28)	53.0 (79)	X^2=1.61
No	40.4 (44)	48.4 (15)	39.1 (18)	47.0 (70)	p= 614
Received adjuvant chemotherapy during the 6 months	22.9 (25)	35.5 (11)	37.0 (17)	41.6 (62)	X^2=9.94
Yes	77.1 (84)	64.5 (20)	63.0 (29)	58.4 (87)	p=.019
No					0<3
Received hormonal therapy during the 6 months					
Yes	46.8 (51)	38.7 (12)	45.7 (21)	40.3 (60)	X^2=1.46
No	53.2 (58)	61.3 (19)	54.3 (25)	59.7 (89)	p= 692
Received biological therapy during the 6 months					
Yes	9.2 (10)	9.7 (3)	13.0 (6)	12.8 (19)	X^2=1.02
No	90.8 (99)	90.3 (28)	87.0 (40)	87.2 (130)	p=.796
Received complementary therapy during the 6 months	21.1 (23)	38.7 (12)	17.4 (8)	34.2 (51)	X^2=9.76
Yes	78.9 (86)	61.3 (19)	82.6 (38)	65.8 (98)	p=.021
No					NS post hoc contrasts
Received physical therapy during the 6 months	14.7 (16)	9.7 (3)	19.6 (9)	17.4 (26)	X^2=1.72
Yes	85.3 (93)	90.3 (28)	80.4 (37)	82.6 (123)	p= 633
No					
Had breast reconstruction during the 6 months	5.5 (6)	9.7 (3)	0.0 (0)	7.4 (11)	X^2=4.25
Yes	94.5 (103)	90.3 (28)	100.0 (146)	92.6 (138)	p= 236
No					
Had re-excision or mastectomy during the 6 months	27.5 (30)	29.0 (9)	34.8 (16)	25.5 (38)	X^2=1.54
Yes	72.5 (79)	71.0 (22)	65.2 (30)	74.5 (111)	p= 674
No					
Evidence of metastatic disease during the 6 months	0.0 (0)	0.0 (0)	2.2 (1)	0.0 (0)	X^2=6.30
Yes	100.0 (109)	100.0 (31)	97.8 (45)	100.0 (149)	p=.098
No					

Table 3 - Differences in Psychosocial Adjustment Characteristics Among the Depression and Anxiety Groups

Characteristic	Lower Anxiety and Resilient (0) % (N) 32.5 (109)	Lower Anxiety and Subsyndromal (1) % (N) 9.3 (31)	Higher Anxiety and Resilient (2) % (N) 11.6 (46)	Higher Anxiety and Subsyndromal (3) % (N) 44.5 (149)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
How satisfying is your life? (0 = not at all to 10 = completely satisfied)	8.7 (1.3)	7.8 (1.6)	7.7 (1.4)	6.3 (2.5)	F=30.06, p<.001 2<0, 3<0,1 and 2
Do you have a purpose/mission for your life or a reason for being alive? (0 = none at all to 10 = a great deal)	9.0 (1.8)	8.5 (2.0)	7.8 (3.0)	8.2 (2.2)	F=3.67, p=.013 2<0
How hopeful do you feel? (0 = not hopeful at all to 10 = extremely hopeful)	9.1 (1.2)	8.6 (1.5)	8.3 (1.7)	7.7 (2.2)	F=14.55, p<.001 2 and 3 <0
How much isolation is caused by your illness? (0 = a great deal to 10 = none)	9.0 (1.9)	8.9 (2.3)	8.3 (2.9)	7.2 (2.9)	F=11.81, p<.001 3<0 and 1
How much uncertainty do you feel about your future? (0 = extreme uncertainty to 10 = not at all uncertain)	7.0 (2.7)	5.6 (2.9)	4.5 (3.2)	3.9 (2.9)	F=24.94, p<.001 2<0, 3<0 and 1
To what extent are you fearful of future diagnostic tests? (0 = extreme fear to 10 = no fear)	6.4 (3.1)	5.9 (3.4)	4.0 (3.2)	3.9 (3.1)	F=15.86, p<.001 2<0, 3<0 and 1
To what extent are you fearful of a second cancer? (0 = extreme fear to 10 = no fear)	5.5 (3.2)	4.9 (3.7)	3.9 (3.5)	2.9 (3.0)	F=14.07, p=<.001 2<0, 3<0 and 1
To what extent are you fearful of recurrence? (0 = extreme fear to 10 = no fear)	5.7 (3.2)	4.6 (3.5)	3.7 (3.5)	2.8 (3.1)	F=15.72, p=<.001 2<0, 3<0 and 1
To what extent are you fearful of metastasis? (0 = extreme fear to 10 = no fear)	5.6 (3.5)	4.9 (3.8)	3.6 (3.7)	2.9 (3.4)	F=13.19, p<.001 2<0, 3<0 and 1
Do you feel like you are in control of things in your life? (0 = not at all to 10 = completely in control)	7.8 (1.8)	7.2 (2.0)	6.4 (2.5)	5.1 (2.6)	F=27.34, p<.001 2<0, 3<0,1 and 2
How difficult is it for you to cope as a result of your disease and treatment? (0 = extremely difficult to 10 = not at all difficult)	8.4 (1.8)	7.3 (2.6)	7.3 (2.6)	5.6 (2.5)	F=29.87, p<.001 3 < 0,1 and 2
Is the amount of support you receive from others sufficient to meet your needs? (0 = not at all sufficient to 10 = completely sufficient)	9.3 (1.3)	8.9 (2.1)	8.8 (2.0)	8.1 (2.2)	F=9.26, p<.001 3<0

Abbreviations: SD = standard deviation

Figure legends

Figure 1 – Differences among the four anxiety and depressive symptom groups in Center for Epidemiological Studies Scale (CES-D) scores (A) and Trait and State Anxiety scores (B) at enrollment. All values are plotted as means $\pm$ standard deviations. For CES-D scores, post hoc contrasts revealed that Lower Anxiety and Resilient group scores were significantly lower than the other three anxiety and depression groups (all $p \leq .001$) and that the Lower Anxiety and Subsyndromal group and the Higher Anxiety and Resilient group had lower CES-D scores than the Higher Anxiety and Subsyndromal group (both $p \leq .031$). For State Anxiety scores, post hoc contrasts revealed that the Lower Anxiety and Resilient group scores were significantly lower than the two Higher Anxiety groups (both $p < .0001$) and that Lower Anxiety and Subsyndromal group had lower State Anxiety scores than the two Higher Anxiety groups (both $p \leq .003$). For Trait Anxiety, the Lower Anxiety and Resilient group had lower Trait Anxiety scores than the two Higher Anxiety groups (both $p \leq .004$) and that Lower Anxiety and Subsyndromal group and the Higher Anxiety and Resilient group had lower Trait Anxiety scores than the Higher Anxiety and Subsyndromal group (both $p < .0001$).

Figure 2 - Differences among the four anxiety and depressive symptom groups in physical, psychological, social, spiritual, and total quality of life (QOL) scores at enrollment. All values are plotted as means $\pm$ standard deviations. For the physical well-being subscale, post hoc contrasts revealed the following relationships: Lower Anxiety and Resilient group > Lower Anxiety and Subsyndromal group and Higher Anxiety and Subsyndromal group (both $p \leq .003$) and Higher Anxiety and Resilient group > Higher Anxiety and Subsyndromal group (p-.018). For the psychological well-being subscale, post hoc contrasts revealed the following relationships: Lower Anxiety and Resilient group > than the other three anxiety depressive symptom groups (all $p \leq .028$) and Lower Anxiety and Subsyndromal group and Higher Anxiety and Resilient group > the Higher Anxiety and Subsyndromal group (both $p \leq .002$). For the social well-being

subscale, all three anxiety and depressive symptom groups > the Higher Anxiety and Subsyndromal group (all $p \leq .002$). For the total QOL score, all three anxiety and depressive symptom groups > the Higher Anxiety and Subsyndromal group (all $p < .0001$).

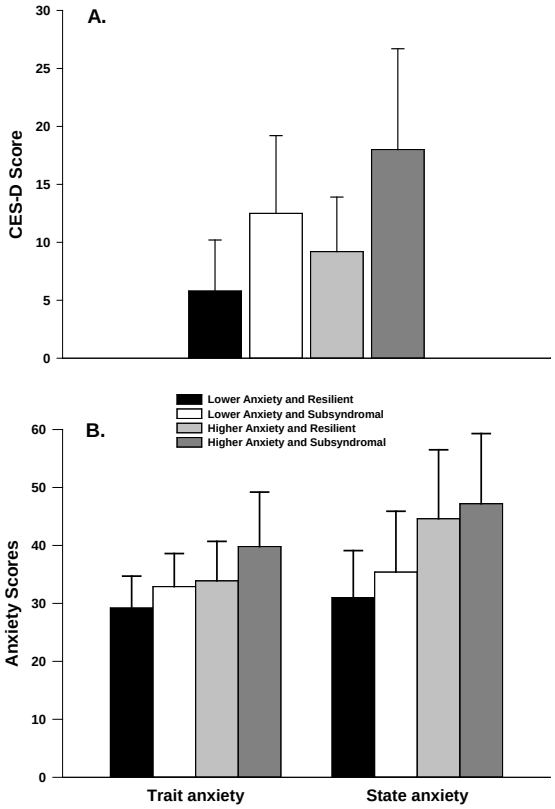
A.
CES-D Score
30
25
20
15
10
5
0
B.
Lower Anxiety and Resilient
Lower Anxiety and Subsyndromal
Higher Anxiety and Resilient
Higher Anxiety and Subsyndromal
Anxiety Scores
60
50
40
30
20
10
0
Trait anxiety
State anxiety

Figure 1

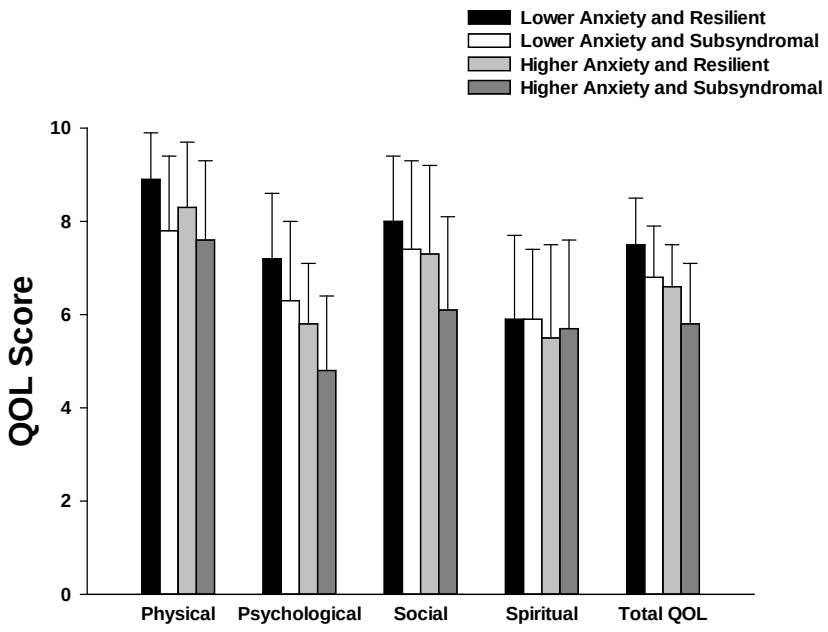
Lower Anxiety and Resilient
Lower Anxiety and Subsyndromal
Higher Anxiety and Resilient
Higher Anxiety and Subsyndromal
QOL Score
10
8
6
4
2
0
Physical
Psychological
Social
Spiritual
Total QOL

Figure 2

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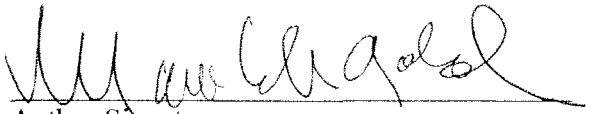

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