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Distinct Cognitive Function Profiles Are Associated With a Higher Presurgery Symptom Burden in Patients With Breast Cancer

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Abstract

Background: Cancer-related cognitive impairment (CRCI) is a common symptom in patients with breast cancer. In our previous study of 397 women with breast cancer, we identified 3 groups of patients with distinct CRCI profiles (ie, high, moderate, and low-moderate attentional function).

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Compared with the other 2 classes, the low-moderate class was younger, had more comorbidities, and with lower functional status.

Objectives: In this study, we expand on this work and evaluate for differences among these latent classes in the severity of psychological (depression and anxiety) and physical (fatigue, decrements in energy, sleep disturbance, and pain) symptoms before surgery.

Methods: Cancer-related cognitive impairment was assessed using the Attentional Functional Index from before through 6 months after surgery. Lower Attentional Functional Index scores indicate higher levels of CRCI. Psychological and physical symptoms were assessed with valid instruments. Parametric and nonparametric tests were used to evaluate for differences in symptom severity scores among the latent classes.

Results: Approximately 60% of patients experienced CRCI (ie, moderate and low-moderate classes). Significant differences were found among the 3 classes in the severity of trait and state anxiety, depressive symptoms, fatigue, and sleep disturbance (ie, high < moderate < low-moderate). In addition, compared with the other 2 classes, the low-moderate class reported higher pain interference scores.

Conclusions: These findings suggest that women with clinically meaningful levels of persistent CRCI have a relatively high symptom burden before surgery.

Implications for Practice: Clinicians need to routinely perform preoperative assessments of CRCI and associated symptoms and initiate therapeutic interventions.

Keywords

Breast cancer; Cancer-related cognitive; impairment; Cognitive function; Depression; Fatigue; Sleep disturbance

Cancer-related cognitive impairment (CRCI) is defined as deficits in short-term and working memory, verbal fluency, processing speed, and attention span.[1,2] Decrements in concentration and memory loss are two of the most common symptoms of CRCI.[2] Approximately 30% to 35% of patients with breast cancer report CRCI before treatment, and 35% report that it persists after the completion of treatment.[3–5] Cancer-related cognitive impairment has negative effects on patients' abilities to make treatment decisions, adhere to therapy, and maintain optimal work performance.[6]

The fact that CRCI can occur before treatment suggests that inflammatory cytokines induced by the tumor itself trigger inflammatory processes and neuroanatomic changes (eg, white and gray matter loss[5]). However, across 6 cross-sectional studies,[7–12] findings are inconsistent regarding presurgical risk factors for CRCI. Whereas in 3 studies[7,9,11] no association was found with age, in 3 studies,[8,10,12] younger patients reported worse cognitive function scores. In terms of education, whereas in 3 studies[8,10,12] no association was found, in another study,[9] lower levels of education were associated with higher levels of cognitive complaints.

In addition to demographic and clinical risk factors, a limited number of cross-sectional studies have evaluated for associations between CRCI and common psychological (ie,

anxiety and depression) and physical (ie, fatigue, sleep disturbance, and pain) symptoms. Across the 3 studies that evaluated anxiety, whereas no associations were found in one study,[10] in 2 studies,[9,11] higher anxiety scores were associated with worse self-reported cognitive function scores. In terms of depressive symptoms, whereas one study found no association,[10] in the other study,[9] patients with higher levels of depressive symptoms reported more cognitive complaints. In the studies that evaluated for associations between sleep disturbance[9] or physical fatigue,[10] patients with higher levels of both of these symptoms reported more cognitive complaints. In 2 studies that used global measures of symptom distress and total mood disturbance,[7,8] higher scores on both measures were associated with higher levels of cognitive dysfunction.

Only 3 longitudinal studies of CRCI in patients with breast cancer have included a presurgical assessment.[13–15] In the first study that assessed CRCI from before through 24 months after surgery,[13] CRCI worsened the first month after surgery but gradually improved and returned to presurgical levels at 12 months. Although no associations between demographic and clinical characteristics and CRCI were evaluated, at each assessment, higher levels of anxiety, depression, fatigue, and sleep disturbance were associated with worse self-report ratings of cognitive function. In the second study that assessed CRCI from before through 12 months after surgery,[14] cognitive function scores increased slightly over time. The characteristics associated with poorer cognitive function scores included being non-White, having a higher level of comorbidity, receipt of adjuvant chemotherapy, and receipt of hormonal therapy. In addition, patients with higher levels of trait anxiety, fatigue, and sleep disturbance and lower levels of energy reported poorer cognitive function scores before surgery.

Although these 2 longitudinal studies[13,14] provide useful information on changes in CRCI after breast cancer surgery, neither of them used a person-centered analytic approach to identify patients at higher risk for CRCI. In our previous analysis,[15] we used growth mixture modeling to identify subgroups of patients with breast cancer (n = 397) with distinct CRCI profiles from before through 6 months after surgery, using the Attentional Functional Index (AFI)[12] as the measure of CRCI. We identified 3 distinct CRCI profiles, namely, high (41.6%), moderate (25.4%), and low-moderate attentional function (33.0%). Compared with the high class, the low-moderate class was significantly younger. In addition, compared with the other 2 classes, the low-moderate class had a lower annual household income, a higher level of comorbidity, and a lower functional status. However, in this article, differences in presurgical psychological and physical symptom severity scores were not evaluated. Given that the findings from a recent review suggest that psychological and physical symptoms may co-occur and create a cascade effect that further worsens CRCI,[16,17] as well as the paucity of research on co-occurring symptoms in patients with breast cancer with distinct CRCI profiles, the purpose of this study was to evaluate for differences among the 3 CRCI classes in the severity of psychological and physical symptoms before surgery.

Methods

This analysis is part of a larger, longitudinal study that evaluated multiple symptoms in patients who underwent breast cancer surgery.[18] The theory of symptom management

developed by faculty members at the University of California, San Francisco, served as the theoretical framework for the entire study.[19] Patients were recruited from breast care centers in a Comprehensive Cancer Center, 2 public hospitals, and 4 community practices located in the greater San Francisco Bay area. Eligible patients were English-speaking women diagnosed with breast cancer, older than 18 years, scheduled to undergo surgery on 1 breast, and able to provide written informed consent. Patients scheduled to have surgery on both breasts and those with distant metastases at the time of diagnosis were excluded. Of the 516 patients who were approached, 410 enrolled in the study (79.5% response rate), and 397 completed the enrollment assessment. The most common reasons for refusal were being too busy or feeling overwhelmed.

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco, and by the institutional review boards at each of the study sites. During preoperative visits, a clinical staff member explained the study and invited patients to participate. Patients who were willing to participate were introduced to a research nurse who determined their eligibility. After providing written informed consent, patients completed the enrollment questionnaires an average of 4 days before surgery. Follow-up questionnaires were completed each month for 6 months after surgery (ie, 7 assessments over 6 months).

Instruments

Demographic and Clinical Characteristics

Patients completed a demographic questionnaire, the Karnofsky Performance Status scale,[20] and the Self-Administered Comorbidity Questionnaire.[21] Medical records were reviewed for disease and treatment information.

Attentional Function

Changes in attentional function from before through 6 months after surgery were assessed using the AFI.[12] This 16-item instrument assesses an individual's perceived effectiveness in performing daily activities that are supported by attention and working memory in the past week. A higher total mean score on a 0 to 10 scale indicates greater capacity to direct attention. Total scores are grouped into categories of attentional function (ie, <5.0 low function, 5.0–7.5 moderate function, and >7.5 high function).[8] In this study, Cronbach's alpha for the total AFI score was .93.

Psychological Symptoms

ANXIETY—State and trait anxiety were assessed using the 20-item Spielberger State-Trait Anxiety Inventories (STAI-S and STAI-T, respectively). Patients completed the items using the time frame of "right now." Total scores for each scale range from 20 to 80, with higher scores indicating greater anxiety. Scores of 31.8 or higher and 32.2 or higher suggest high levels of trait and state anxiety, respectively.[22] In this study, Cronbach's alphas for the STAI-T and STAI-S were .88 and .95, respectively.

DEPRESSION—The 20-item Center for Epidemiologic Studies–Depression (CES-D) scale was used to assess depressive symptoms in the past week. Total scores can range from 0 to 60, with scores of 16 or higher indicating the need for clinical evaluation of depression. Four subscale scores (ie, somatic, depressed affect, positive affect, and interpersonal problems) were calculated.[23] In this study, Cronbach's alpha for the total CES-D score was .90.

Physical Symptoms

FATIGUE AND ENERGY—The 18-item Lee Fatigue Scale was designed to assess physical fatigue and energy.[24] Each item was rated on a 0 to 10 numeric rating scale (NRS) using the time frame of "right now." Total fatigue and energy scores were calculated as the mean of the 13 fatigue items and the 5 energy items, with higher scores indicating greater fatigue severity and higher levels of energy. Cutoff scores of 4.4 or higher and 4.8 or less indicate clinically meaningful levels of fatigue and decrements in energy levels, respectively.[25] In this study, Cronbach's alphas for the fatigue and energy scales were .96 and .93, respectively.

SLEEP DISTURBANCE—The 21-item General Sleep Disturbance Scale (GSDS) was designed to assess sleep disturbance in the past week. Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSDS total score is the sum of the 7 subscale scores that can range from 0 (no disturbance) to 147 (extreme sleep disturbance). Each mean subscale score can range from 0 to 7. Higher total and subscale scores indicate higher levels of sleep disturbance.[26] Subscales scores of 3 or higher and a GSDS total score of 43 or higher indicate a clinical meaningful level of sleep disturbance.[27] In this study, Cronbach's alpha for total GSDS score was .86.

PAIN—Breast pain was evaluated using the Breast Symptoms Questionnaire (BSQ). Part 1 of the BSQ obtained information on the occurrence of pain in the affected breast. Patients who reported breast pain were asked to complete part 2 of the BSQ, which assessed pain intensity "right now," average daily pain, and worst pain using 0 (no pain) to 10 (worst imaginable pain) NRSs, as well as number of days per week with pain and number of hours per day in pain in the past week. Patients who reported breast pain rated its level of interference using a 0 (no interference) to 10 (complete interference) NRS. The 8 items that assessed pain interference were adapted from the interference scale of the Wisconsin Brief Pain Inventory.[28] Eight additional items were used to assess pain interference based on studies by Tasmuth et al.[29,30]

Statistical Analyses

Data were analyzed using SPSS 27 (IBM, Armonk, New York) and Mplus 6.11 (Muthen and Muthen, Los Angeles, California). Descriptive statistics and frequency distributions were generated for sample characteristics and symptom scores. Growth mixture modeling with robust maximum likelihood estimation identified latent classes of patient with distinct trajectories of cognitive function. The growth mixture modeling methods are described in detail elsewhere.[15,31]

Parametric and nonparametric tests were used to evaluate for differences in demographic, clinical, and symptom characteristics among the classes. A value of $P < .05$ was considered statistically significant. Post hoc contrasts were done using a Bonferroni corrected $P < .017$ (.05/3 possible pairwise comparisons).

Results

Growth Mixture Modeling Classes

As described previously,[15] among the 397 patients, 3 classes with distinct attentional function profiles were identified. Lower scores on the AFI indicate lower levels of attention and working memory or higher levels of CRCI. As illustrated in the Figure, patients in the high attentional function ("high") class (41.6%) had an estimated AFI score of 7.78 at enrollment, which increased and remained high over the next 6 months. Patients in the moderate attentional function ("moderate") class (25.4%) had an estimated AFI score of 6.58 at enrollment that decreased and then increased significantly but remained moderate over the next 6 months. Patients in the low-moderate attentional function ("low-moderate") class (33.0%) had an estimated AFI score of 5.23 at enrollment that did not change significantly over the next 6 months.

Demographic and Clinical Characteristics

Compared with the high class, the low-moderate class was significantly younger and more likely to self-report a diagnosis of depression. Compared with the other 2 classes, the low-moderate class had a lower annual household income, a higher Self-Administered Comorbidity Questionnaire score, and a lower Karnofsky Performance Status score (Table 1).

Psychological Symptoms

Among the 3 AFI classes, differences in trait and state anxiety followed the same pattern (high < moderate < low-moderate). In terms of depressive symptoms, except for the CES-D interpersonal problems (high < low-Moderate) and CES-D positive affect (high > moderate > low-moderate) subscales, for all the other subscales and total CES-D scores, differences among the AFI classes followed the same pattern (high < moderate < low-moderate; Table 2).

Physical Symptoms

Among the 3 AFI classes, levels of fatigue, worse sleep quality, sleep onset latency, excessive daytime sleepiness, and overall level of sleep disturbance followed the same pattern (high < moderate < low-moderate). Compared with the other 2 classes, the low-moderate class had higher scores for mid sleep awakenings and for all of the pain interference scores. Compared with the high class, the other 2 classes had worse decrements in energy. Compared with the high class, the low-moderate class had higher scores for use of medications for sleep, quantity of sleep (ie, fewer hours of sleep), early awakenings, worst pain, and number of days per week in pain, as well as a higher occurrence rate for breast pain before surgery (Table 2).

Discussion

This study extends our previous work[15] by evaluating for differences in the severity of common psychological and physical symptoms before surgery in 3 groups of patients with breast cancer with distinct CRCI profiles. Compared with previous preoperative prevalence rates of 30% to 35%,[3–5] almost 60% of our patients had decrements in cognitive function. Several plausible explanations exist for these inconsistent findings. First, the definitions for CRCI and criteria used to diagnose CRCI varied across studies. Second, a wide variety of subjective and/or objective measures were used to assess CRCI. Of note, subjective assessments, like the one used in our study, may be better able to detect early and more subtle forms of CRCI than objective measures.[32] In addition, different analytic methods were used to estimate the prevalence rates for CRCI. Rather than use cutpoint or summary scores, in the current study, we used a person-centered analytic approach to identify patients with distinct CRCI profiles.

In our previous report,[15] the demographic and clinical characteristics associated with latent class membership were described. This discussion focuses on differences among the classes in the severity of the common psychological and physical symptoms that were evaluated before surgery.

Psychological Symptoms

Consistent with previous reports,[9,11,13,14] progressively higher levels of anxiety were associated with worse levels of cognitive function. Not surprising, for all 3 classes, state anxiety scores exceeded the clinically meaningful cutoffs. Anxiety increases when individuals encounter high levels of threat like a cancer diagnosis and impending surgery. According to the theory of attentional control, increased anxiety may decrease one's ability to flexibly focus and shift attention to current goals, which impairs working memory and allocation of attentional resources.[33,34] Our findings suggest that early assessments of preoperative levels of anxiety and appropriate interventions warrant consideration.[35]

Similar to anxiety and consistent with previous reports,[9,13] progressively higher levels of depressive symptoms were associated with worse levels of cognitive function. Whereas the moderate class reported subsyndromal levels of depressive symptoms (ie, 13.7),[36,37] the low-moderate class had total CES-D scores (ie, 19.4) that warrant clinical evaluation. In addition, compared with the other 2 classes, the low-moderate class reported higher somatic symptom and lower positive affect scores. These findings suggest a possible interdependence between somatic symptoms and negative affect. One possible explanation for this interdependence is that external stressors (eg, cancer diagnosis) activate the hypothalamic-pituitary-adrenal axis, which leads to decreased activity in the prefrontal cortex as a result of changes in serotonin metabolism.[38] In turn, these changes impair one's ability to control negative elaborative processes (eg, rumination) and results in increased depressive symptoms and an exacerbation of negative affect.[38] Consistent with previous reports in older, community-dwelling adults[39] and patients with breast cancer after the initiation of chemotherapy,[40] compared with the high class, the low-moderate class reported higher interpersonal problems. One possible explanation for this finding is that social and

family support may act as buffers for depressive symptoms and partially moderate the association between depressed affect and CRCI.[41–43]

Physical Symptoms

Comparable to previous reports of fatigue in patients with breast cancer before surgery,[10,13] 33% of patients in the low-moderate class reported fatigue scores that approached the clinically meaningful cutoff. One possible explanation for the co-occurrence of fatigue and CRCI is that the tumor itself triggers the release of proinflammatory cytokines.[5,44] Given that our previous work demonstrated that fatigue and energy are distinct but related symptoms,[45,46] it is interesting to note that almost 60% of our sample reported clinically meaningful decrements in energy. Given that this study is the first to report on this association, additional research is warranted on diurnal variations in both fatigue and energy to confirm those findings and evaluate for underlying mechanisms.

Consistent with a study of patients undergoing surgery for lung cancer,[47] almost 60% of our patients reported clinically meaningful levels of sleep disturbance before surgery. The total GSDS scores reported by the low-moderate class are higher than those reported by postpartum mothers (ie, 55.5),[48] equivalent to those reported by permanent night shift workers (ie, 60.5),[26] but lower than those reported by patients with non–central nervous system cancer (ie, 74.4)[49] or breast cancer during chemotherapy (ie, 69.3).[50] An evaluation of the GSDS subscale scores provides insights into the types of sleep disturbance our patients were experiencing. All 3 classes reported clinically meaningful decrements in the quantity of their sleep and a higher level of midsleep awakenings. However, whereas the moderate class reported problems primarily with sleep maintenance (ie, higher scores for early and mid-sleep awakenings), the low-moderate class had problems with both sleep initiation (ie, longer sleep onset latency) and sleep maintenance. Of note, the use of sleep medications was very low across all 3 groups.

Our association between higher levels of sleep disturbance and worse cognitive function is consistent with previous studies.[9,13] For example, in one study of older adults in the general population,[51] an inverted U-shaped association was found between sleep quantity and cognitive decline. The authors noted that compared with individuals who had an adequate number of hours of sleep (7 hours), cognitive decline was faster in those individuals who had an insufficient (<4 hours) or excessive (>10 hours) sleep duration per night. In another study that examined the sleep-wake patterns of elderly women,[52] sleep fragmentation and longer average sleep latency were associated with neurodegeneration and cognitive decline. Given that sleep plays an important role in memory consolidation[53] and restorative process,[54] clinicians need to assess for this symptom and initiate appropriate interventions (eg, sleep hygiene, medication, cognitive-behavioral therapy).[55]

Although only 30% of the women had pain in their breast before surgery, the low-moderate class had worst pain intensity scores in the moderate range. Based on our previous analyses,[56,57] this preoperative breast pain may be related to inflammatory changes associated with the total number and/or timing of the previous breast biopsies. In terms of its association with CRCI, in one conceptual model of pain-related cognitive impairment,[58] pain may have negative effects on cognition through changes in brain networks (eg,

prefrontal cortex, hippocampus, amygdala). Additional research is warranted on the effects of acute and chronic pain on CRCI in women before and after breast cancer surgery.

In summary, for the majority of the symptoms, the severity scores increased in a stepwise fashion across the CRCI classes. These findings suggest additive or synergistic interactions among these symptoms and that they may share common underlying mechanisms. For example, the default mode network (DMN), a brain network composed of the medial prefrontal cortex, the posterior cingulate cortex, inferior parietal lobule, hippocampus, and the precuneus, are all associated with cognitive function (eg, implicit learning, memory retrieval, prospection).[59–61] Findings from functional magnetic resonance imaging (fMRI) studies suggest that the DMN is deactivated when attention is focused on the external environment and during the formation of working memory. In contrast, it is highly activated when a person is not engaging with specific behavioral tasks and in self-referential processing.[61,62] In a recent fMRI study,[63] compared with nonfatigue patients, fatigued patients with breast cancer had increased DMN activity. In addition, decreased connectivity between the DMN and other brain structures was associated with higher levels of depressive symptoms in patients with breast cancer receiving chemotherapy. Taken together, these fMRI findings suggest that the co-occurrence of these symptoms may be the result of prolonged activation of the DMN network.

Another possible explanation for these findings is that the release of tumor-induced inflammatory cytokines leads to increased concentrations of various neurotransmitters (eg, serotonin, dopamine).[5] Alterations in levels of these neurotransmitters contribute to the development of these common symptoms.[5] In recent studies,[64,65] whereas higher levels of IL-6 and serotonin were associated with increases in DMN activity, increases in dopamine had the opposite effect on DMN activity. Future research needs to examine the interrelationships among various biomarkers, DMN activity, CRCI, and other common symptoms to increase our understanding of their common and distinct underlying mechanisms.

Limitations

Although this longitudinal study has numerous strengths including a relatively large sample size and a comprehensive evaluation of associations between common symptoms and CRCI, several limitations need to be acknowledged. First, most of the women were well educated and diagnosed with early-stage breast cancer, which limits the generalizability of our findings. Second, our assessment of CRCI was based on an instrument that primarily evaluates attention and executive function. Although some studies have included healthy controls,[10,66] this study aimed to identify groups of patients with breast cancer with distinct CRCI profiles from before through 6 months after breast cancer surgery.

Implications for Research and Practice

Future studies need to evaluate for distinct CRCI profiles, using both subjective and objective measures in patients with other types of cancer who are undergoing different types of cancer treatment. In addition, longitudinal studies that use analytic techniques like parallel process growth modeling[67] are needed to determine which symptom(s) are driving

or influencing the severity of the other common symptoms. These types of studies will aid in the development and testing of interventions for CRCI.

Given the high rates of CRCI, as well as the clinically meaningful levels of common physical and psychological symptoms before surgery, clinicians need to perform comprehensive symptom assessments and initiate appropriate pharmacologic and nonpharmacologic interventions. Nonpharmacologic interventions that are effective for multiple symptoms (eg, mindfulness-based stress reduction, cognitive-behavioral therapy) can be prescribed.[2,68] Some patients may warrant referrals to psychological or symptom management services.

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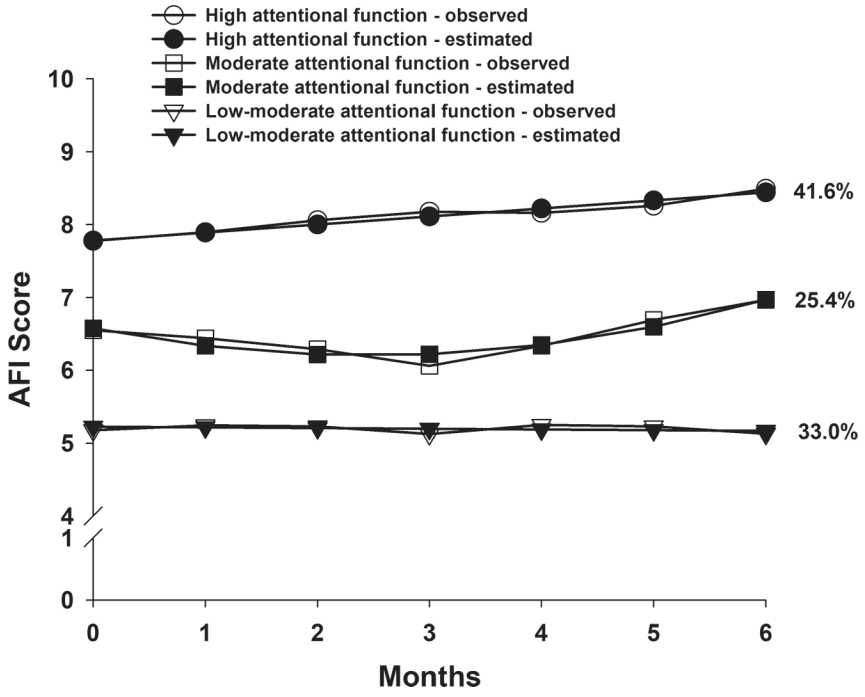

Figure.

Observed and estimated attentional function latent classes from before through 6 months after breast cancer surgery. Adapted from Merriman JD, Aouizerat BE, Cataldo JK, et al. Association between an interleukin 1 receptor, type 1 promoter polymorphism and self-reported attentional function in women with breast cancer. *Cytokine* 2014;65:192–201.

Table 1 •

Differences in Demographic and Clinical Characteristics Among the Attentional Function Classes at Enrollment

Characteristic	High Attentional Function (1) n= 165 (41.6%) Mean (SD)	Moderate Attentional Function (2) n = 101 (25.4%) Mean (SD)	Low-Moderate Attentional Function (3) n = 131 (33.0%) Mean (SD)	Statistics
Age y	56.7 (11.2)	55.2 (10.3)	52.6 (12.6)	F = 4.87, *P* = .008 1 > 3
Education, y	15.8 (2.7)	15.8 (2.9)	15.6 (2.4)	F = 0.25, *P* =.780
Self-Administered Comorbidity Questionnaire score	3.8 (2.5)	4.0 (2.6)	5.1 (3.2)	F = 8.84, *P* <.001 1 and 2 < 3
Body mass index, kg/m^2	25.9 (5.7)	27.6 (6.6)	27.4 (6.3)	F = 3.43, *P* =.033 No significant pairwise contrasts
Karnofsky Performance Status score	95.7 (8.6)	94.9 (6.9)	88.8 (12.8)	F = 19.57, *P* < .001 1 and 2 > 3
	n (%)	n (%)	n (%)	
Race/ethnicity				
White	113 (69.3)	70 (69.3)	72 (55.0)	χ^2 = 9.46, *P* =.149
Black	15 (9.2)	7 (6.9)	18 (13.7)	
Asian/Pacific Islander	17 (10.4)	14 (13.9)	19 (14.5)	
Hispanic/ mixed/ other	18 (11.0)	10 (9.9)	22 (16.8)	
Live alone (% yes)	39 (23.9)	19 (19.2)	36 (27.7)	χ^2 = 2.23, *P* = .328
Married or partnered (% yes)	69 (42.1)	36 (36.0)	60 (46.2)	χ^2 = 2.40, *P* = .301
Currently employed (% yes)	84 (51.5)	52 (51.5)	53 (40.8)	χ^2 = 4.03, *P* = .133
Household income level				KW= 13.22, *P* =.001
<$30 000	19 (14.3)	15 (16.7)	36 (34.0)	1 and 2 > 3
$30 000–$99 999	61 (45.9)	33 (36.7)	40 (37.7)	
≥$100 000	53 (39.8)	42 (47.6)	30 (28.3)	
Regular exercise (% yes)	118 (71.5)	74 (74.0)	82 (63.6)	χ^2 = 3.42, *P* =.181
Occurrence of comorbid conditions				
Heart disease	9 (5.5)	1 (1.0)	5 (3.8)	χ^2 = 3.44, *P* =.179
High blood pressure	54 (32.7)	29 (28.7)	40 (30.5)	χ^2 = 0.49, *P* = .783

Characteristic	High Attentional Function (1) n= 165 (41.6%) Mean (SD)	Moderate Attentional Function (2) n = 101 (25.4%) Mean (SD)	Low-Moderate Attentional Function (3) n = 131 (33.0%) Mean (SD)	Statistics
Lung disease	4 (2.4)	2 (2.0)	6 (4.6)	χ^2= 1.66, P = .436
Diabetes	9 (5.5)	8 (7.9)	14 (10.7)	χ^2 = 2.78, P = .249
Ulcer	4 (2.4)	1 (1.0)	10 (7.6)	χ^2 = 8.35, P =.015
				No significant pairwise contrasts
Kidney disease	2 (1.2)	0 (0.0)	1 (0.8)	χ^2= 1.23, P = .541
Liver disease	5 (3.0)	1 (1.0)	4 (3.1)	χ^2= 1.29, P = .525
Anemia	11 (6.7)	8 (7.9)	12 (9.2)	χ^2 = 0.63, P = .729
Depression	26 (15.8)	22 (21.8)	38 (29.0)	χ^2 = 7.56, P = .023 1 < 3
Osteoarthritis	25 (15.2)	19 (18.8)	25 (19.1)	χ^2 = 0.98, P =.613
Back pain	40 (24.2)	25 (24.8)	46 (35.1)	χ^2 = 4.98, P = .083
Rheumatoid arthritis	3 (1.8)	5 (5.0)	6 (4.6)	χ^2 = 2.45, P = .295
Postmenopausal (% yes)	106 (65.4)	64 (66.7)	78 (60.9)	χ^2 = 0.95, P =.621
Stage of disease				
Stage 0	33 (20.0)	18 (17.8)	22 (16.8)	KW = 4.20, P =.122
Stage I	67 (40.6)	42 (41.6)	42 (32.1)	
Stage II	54 (32.7)	35 (34.7)	52 (39.7)	
Stage III and IV	11 (6.7)	6 (5.9)	15 (11.5)	
Receipt of neoadjuvant therapy (% yes)	27 (16.4)	17 (17.0)	35 (26.7)	χ^2 = 5.63, P =.060
HRT before surgery (% yes)	22 (13.3)	24 (24.0)	21 (16.2)	χ^2 = 5.12, P =.077
Type of surgery				
Breast conservation	135 (81.8)	77 (76.2)	106 (80.9)	χ^2= 1.31, P = .521
Mastectomy	30 (18.2)	24 (23.8)	25 (19.1)	
Sentinel node biopsy (% yes)	140 (84.8)	88 (87.1)	100 (76.3)	χ^2 = 5.60, P =.061
Axillary lymph node dissection (% yes)	52 (31.5)	38 (38.0)	58 (44.3)	χ^2 = 5.10, P =.078
Receipt of adjuvant chemotherapy (% yes) [a]	48 (29.1)	40 (39.6)	45 (34.3)	χ^2 = 3.17, P =.205
Receipt of radiation therapy (% yes)[a]	95 (57.6)	52 (51.5)	77 (58.8)	χ^2 = 1.39, P =.500

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Characteristic	High Attentional Function (1) n= 165 (41.6%) Mean (SD)	Moderate Attentional Function (2) n = 101 (25.4%) Mean (SD)	Low-Moderate Attentional Function (3) n = 131 (33.0%) Mean (SD)	Statistics
Receipt of hormonal therapy (% yes)	78 (47.3)	38 (37.6)	52 (39.7)	$\chi^2 = 2.94$, $P = .230$
Estrogen receptor positive (% positive)	137 (83.5)	74 (73.3)	96 (73.3)	$\chi^2 = 5.81$, $P = .055$
Progesterone receptor positive (% positive)	124 (75.6)	70 (69.3)	85 (64.9)	$\chi^2 = 4.11$, $P = .128$
HER2/neu (% positive)	21 (14.3)	15 (17.0)	23 (18.7)	$\chi^2 = 0.98$, $P = .614$

Abbreviations: HER2/neu, human epidermal growth factor receptor; HRT, hormone replacement therapy; KW, Kruskal-Wallis test; SD, standard deviation.

[a]Receipt of treatment in the 6 months after surgery.

Table 2 •

Differences in Psychological and Physical Symptom Severity Scores Among the Attentional Function Classes at Enrollment

Symptoms [a]	High Attentional Function (1) n = 165 (41.6%) Mean (SD)	Moderate Attentional Function (2) n = 101 (25.4%) Mean (SD)	Low-Moderate Attentional Function (3) n = 131 (33.0%) Mean (SD)	Statistics
		Psychological symptoms		
Trait anxiety (≥31.8)	31.6 (7.4)	34.9 (8.2)	40.3 (9.2)	F = 38.86, *P* <.001 1 < 2 < 3
State anxiety (≥32.2)	36.7 (12.7)	42.9 (12.9)	47.1 (12.4)	F = 24.60, *P* < .001 1 < 2 < 3
Center for Epidemiological Studies–Depression				
Somatic subscale	3.7 (2.9)	5.9 (4.1)	7.9 (3.7)	F = 51.10, *P* <.001 1 < 2 < 3
Depressed affect subscale	3.3 (3.3)	4.8 (4.2)	6.9 (4.7)	F = 26.64, *P* < .001 1 < 2 < 3
Positive affect subscale	10.0 (2.2)	9.2 (2.7)	7.9 (2.7)	F = 24.46, *P* < .001 1 > 2 > 3
Interpersonal problems subscale	0.14 (0.67)	0.23 (0.92)	0.44 (0.89)	F = 4.70, *P* =.010 1 < 3
Total score (≥16.0)	9.2 (7.1)	13.7 (9.5)	19.4 (9.6)	F = 49.72, *P* < .001 1 < 2 < 3
		Physical symptoms		
Lee Fatigue Scale-Fatigue (≥4.4)	2.1 (2.0)	3.2 (2.1)	4.3 (2.3)	F = 35.51, *P* <.001 1 < 2 < 3
Lee Energy Scale-Energy (≤4.8)	5.8 (2.6)	4.6 (2.2)	4.0 (2.2)	F = 22.56, *P* < .001 1 > 2 and 3
General Sleep Disturbance Scale				
Medications for sleep (≥3.0)	0.3 (0.6)	0.5 (0.6)	0.6 (0.8)	F = 4.21, *P* =.016 1 < 3
Quality of sleep (≥3.0)	2.5 (1.9)	3.5 (1.9)	4.2 (1.7)	F = 30.81, *P* <.001 1 < 2 < 3
Quantity of sleep (≥3.0)	4.6 (1.4)	5.0 (1.6)	5.0 (1.5)	F = 3.95, *P* =.020 1 < 3
Sleep onset latency (≥3.0)	1.6 (2.0)	2.3 (2.2)	3.4 (2.5)	F = 22.48, *P* < .001 1 < 2 < 3

Symptoms [a]	High Attentional Function (1) n = 165 (41.6%) Mean (SD)	Moderate Attentional Function (2) n = 101 (25.4%) Mean (SD)	Low-Moderate Attentional Function (3) n = 131 (33.0%) Mean (SD)	Statistics
Mid sleep awakenings (≥3.0)	3.9 (2.5)	3.9 (2.3)	4.7 (2.2)	F = 4.74, *P* =.009 1 and 2 < 3
Early awakenings (≥3.0)	2.8 (2.5)	3.2 (2.7)	3.9 (2.4)	F = 6.46, *P* =.002 1 < 3
Excessive daytime sleepiness (≥3.0)	1.4 (1.0)	2.1 (1.1)	2.8 (1.3)	F = 50.93, *P* <.001 1 < 2 < 3
Total score (≥43.0)	38.3 (19.0)	49.4 (19.1)	59.5 (19.9)	F = 43.14, *P* < .001
Breast pain	n (%)	n (%)	n (%)	1 < 2 < 3
Occurrence of pain in the affected breast before surgery (% yes)	33 (20.5)	33 (33.0)	43 (33.6)	χ^2 = 7.72, *P* = .021 1 < 3
For patients with breast pain	Mean (SD)	Mean (SD)	Mean (SD)	
Pain right now	1.0 (1.4)	1.8 (2.2)	1.9 (2.1)	F = 2.26, *P* =.110
Current average daily pain	1.5 (1.2)	2.1 (2.2)	2.7 (2.2)	F = 3.00, *P* =.055
Worst pain	2.8 (1.6)	3.1 (2.2)	4.3 (2.6)	F = 4.44, *P* = .014 1 < 3
No. days per week in pain	1.7 (2.3)	3.0 (3.0)	3.5 (2.6)	F = 4.45, *P* = .014 1 < 3
Breast Pain Interference				
Brief Pain Inventory [b]	0.9 (1.9)	1.2 (1.6)	2.5 (2.4)	F = 6.36, *P* = .002 1 and 2 < 3
Additional interference items [c]	0.5 (1.0)	0.8 (1.3)	1.8 (2.1)	F = 6.83, *P* = .002 1 and 2 < 3
All interference items	0.7 (1.4)	1.0 (1.3)	2.1 (2.1)	F = 7.30, *P* = .001 1 and 2 < 3

Abbreviation: SD, standard deviation.

[a] Numbers in parentheses indicate clinically meaningful cutoff scores.

[b] Interference items from the Brief Pain Inventory: walking ability, normal work, mood, sexual activity, general activity, relations with other people, sleep, and enjoyment of life.

[c] Additional interference items: ability to sleep on the affected side, ability to touch the site, ability to reach out in front of you, ability to carry things, ability to get up from bed, ability to do handicrafts, ability to drive a car, ability to write, and ability to reach above your head.