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Psychological Responses to Cancer Recurrence:

A Controlled Prospective Study

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Abstract

BACKGROUND—There is a dearth of knowledge regarding the psychological responses to a diagnosis of cancer recurrence.

METHODS—An ongoing randomized clinical trial provided the context for prospective study. Women with Stage II/III breast carcinoma (N = 227) were initially assessed after their diagnosis/surgery and before adjuvant therapy and then reassessed every 6 months. Eight years into the trial, 30 patients had recurred (R) and were assessed shortly after receiving their second diagnosis. Their data were compared with a sample of trial patients who had no evidence of disease (disease free [DF]; n = 90). The groups were matched on study arm, disease stage, estrogen receptor status, menopausal status, and time since initial diagnosis.

RESULTS—As hypothesized, patients' cancer-specific stress at recurrence in the R group was higher ($P < 0.05$) than stress levels for the DF group at the equivalent point in time. Importantly, the R group reported stress for their recurrent diagnosis equivalent to that reported for their initial diagnosis. Identical results were found for measures of health status and symptomatology. In contrast, analyses for emotional distress and social functioning showed no pattern of disruption for the R group at cancer recurrence and levels equivalent to that of the DF group.

CONCLUSIONS—To the authors' knowledge, this was the first controlled, prospective psychological analysis of patients' responses to cancer recurrence. The findings were consistent with a learning theory conceptualization of the cancer stressor. Patients' stress was "compartmentalized" and did not, at least in the early weeks, result in diffuse emotional distress and quality of life disruption, underscoring the resilience of patients when confronted with cancer recurrence.

Keywords

cancer recurrence; stress; quality of life; cancer; psychological; behavioral; longitudinal; prospective

Each year, over 1.2 million individuals are diagnosed with cancer recurrence and more than one-half will progress rapidly and die of their disease.[1] Despite the prevalence of cancer recurrence, psychosocial research on patients who recur is very limited. Moreover, the

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prospects for expansion in the coming years may be dim, as new funding initiatives focus on cancer survivors rather than on those recurring and dying of the disease. As biobehavioral research has advanced our knowledge of patients' responses to the initial cancer diagnosis, understanding the psychological and behavioral aspects of cancer recurrence is similarly important.

The literature provides a clinical picture. Psychological responses to cancer recurrence appear to include depressive symptoms, such as the loss of hope for recovery,[2] anxieties and fears of death, and difficulties with disability.[3–5] Morbidities can include pain,[6] appetitive difficulties (e.g., anorexia, cachexia), [7] poor body image,[8] and others. It has been suggested that psychological factors, such as social support,[5,9,10] emotional control,[11] or spirituality[12] may be moderators of patient distress.

There are few empirical reports, however, to document the accuracy of this clinical picture. Typical for emerging research areas, methodologies of the studies have been limited and the results descriptive, without a priori conceptual or theoretic predictions (see Northouse et al. [13] for an exception). Reports have small sample sizes, assessments occurring months or even years after the cancer recurrence diagnosis, and heterogeneous samples, with diagnoses of Stage IV included with recurrent cases, for example. More problematic is the absence of research designs, per se, as many are reports of one group completing one assessment. Some are studies of patients at the time of the diagnosis,[3,11,14–19] whereas others assessed patients at variable times since diagnosis.[9,10,20]

We consider two conceptual frameworks for understanding patients' responses to cancer recurrence. The classic notion of existential plight,[21] a term characterizing the emotional trauma of the initial diagnosis of cancer, may have some similarities to patients' responses to a diagnosis of cancer recurrence. Individuals may again have fears of what is to come: treatments, life disruption, just feeling "sick," and the expectation that one's trajectory is decline and death. Would friends and families provide support once again? Hopes for the future may evaporate and a premature death is no longer a remote possibility.

An alternative conceptualization considers principles of learning.[22,23] Habituation, for example, would predict that responses to cancer recurrence may be difficult, but less so than those experienced at the initial diagnosis, and certainly not worse. Many experiences and circumstances would be familiar ones (e.g., disruption of daily routines, immersion in the medical system, knowledge of cancer treatments and the symptoms they produce) and consequently, less distressing. Other circumstances—such as having established relations with oncologists and nurses—might lessen stress and anxiety and even offer the opportunity for early social support. Having experienced this once, the patient would be more knowledgeable of the type and availability of his/her existing resources (e.g., insurance coverage, finances), and problem solving could be focused and, possibly, more successful. Experiencing a cancer recurrence diagnosis would not be a repeat of a traumatic event that elicits "conditioned" emotional sequelae. Instead, emotional responses would be different, and dampened by fewer, less severe stressors and the addition of other neutral (i.e., familiar) to positive (supportive) experiences.

The literature provides three relevant studies. None offered a conceptual model, but each evaluated psychological responses among recurrent patients by contrasting groups—comparing patients with an initial diagnosis with those with cancer recurrence. Munkres et al. [4] reported no group differences in emotional distress, per se, yet the patients with recurrent disease reported greater distress with symptoms and burden from their own self-care. Both Given and Given[24] and Kissane et al.'s[25] comparison employing diagnostic psychiatric interviews reported no group differences. Similarly, there is no consistency of findings in

retrospective studies, in which recurrent patients are assessed and then asked to recall their level of distress at their initial diagnosis. Some patients recall cancer recurrence as less distressing than their initial diagnosis,[13] but others believe the experiences were similar.[5,6] Cella et al.[14] and Mahon and Casperson[26] reported cancer recurrence as more difficult, with concerns of death common and overwhelming. In summary, the nature and magnitude of psychological responses to cancer recurrence are unknown.

Examining this issue is difficult. Obviously, patients cannot be randomized to "recurrent" and "non-recurrent" groups. A longitudinal design—following patients from the time of their initial diagnosis until cancer recurrence—is the best alternative. Further, diagnostically similar patients remaining disease free and followed for an equivalent interval would provide an important comparison, as even survivors of cancer remaining disease free report adjustment difficulties such as poorer health status and continuing fatigue.[27–29] The quality of life (QOL) trajectory of patients with cancer who became survivors would provide a relevant comparison with a recurrent group.

We are conducting a randomized trial to test the efficacy of a psychological intervention for patients with breast cancer on biobehavioral outcomes and disease end points.[30,31] Accrued after surgery and before beginning adjuvant therapy, the sample is large and homogeneous, and a range of measures assesses cancer-specific stress, emotional distress, social adjustment, functional status, and health status. After 8 years of follow-up, some women have recurred while the majority have no evidence of disease. A comparison of these two groups of women at the time of their initial diagnoses and the time at which one group recurred provides an unprecedented circumstance for a controlled, prospective analysis of patients' responses to cancer recurrence.

MATERIALS AND METHODS

Study Design and Patients

Clinical trial sample—Trial patients were consecutive cases at a university-affiliated National Cancer Institute-designated Comprehensive Cancer Center. Women with newly diagnosed, surgically treated regional breast carcinoma were eligible. Details of informed consent procedures, accrual, and randomization have been published.[31] The sample is similar to those in the Ohio Cancer Incidence Surveillance System[32] and the Surveillance, Epidemiology, and End Results program[33] databases for patients with breast carcinoma.

Before clinical trial randomization and beginning adjuvant therapy, women completed face-to-face interviews and questionnaires assessing cancer stress, mood, and QOL. A nurse also completed a health status evaluation. Study arms were assessment only or psychological intervention and assessment. By the 12-month follow-up, all cancer therapies were completed and the intervention sessions had ended. For those randomized to the intervention, there were significant reductions in emotional distress, improvements in health behaviors, and higher immune responses at 4 months[31] and 12 months (unpublished data). Follow-up continues with assessments every 6–12 months for 10 years.

Recurrent (R) group Accrual for this substudy began within 6 months of the opening of the trial. Cancer recurrence refers to the clinical detection of metastatic breast disease in the same area, adjacent to, or distant from the original site. Women diagnosed with a second primary tumor (e.g., contralateral breast, endometrial) and those recurring < 12 months after the initial diagnosis were excluded. The latter criterion effectively excludes women with rapid disease progression. Also, 12 months is an important milestone for patients with cancer, as many then view themselves as survivors and cancer recurrence would be more unexpected.

R cases were identified through notification from clinic staff, routine tracking, and/or patients' own notification. As soon as feasibly possible, typically before the start of any cancer therapies and after informed consent was obtained, patients completed a shortened version of the routine assessment. Data analyses for the current study began 8 years after the start of the trial. By then, 43 of 227 patients (18%) had recurred. Of these, 2 recurred before 12 months, 1 recurred after 12 months but rapidly progressed and died, 6 dropped out of the trial before their cancer recurrence, and 4 declined participation in the substudy. Thus, 30 of 43 (70%) women diagnosed with recurrent cancer were included in the R group.

Disease-free (DF) group Each case with recurrent disease was matched to three other cases from the trial that had no evidence of disease and without a second primary diagnosis. R and DF cases were matched on the following: study arm, disease stage at diagnosis (Stage II vs. III), menopausal status (premenopausal/perimenopausal vs. postmenopausal) before diagnosis, estrogen receptor status (positive vs. negative), presence/absence of spouse/significant other, and duration of disease-free follow-up. For example, if a woman recurred at 24 months (at which time a cancer recurrence assessment was conducted), only DF individuals who met the above criteria and who had completed their 24-month assessments could be selected as matches for that woman. The initial and 24-month data for the 3 DF matches were used for comparison with the R patient's data at initial and cancer recurrence diagnoses assessments.

Measures

Cancer-specific stress—The Impact of Events Scale (IES)[34] evaluates stress-related intrusive thoughts (Intrusion scale) and denial of thoughts and avoidant behaviors (Avoidance scale) relevant to cancer diagnosis and treatment. For the current sample, the coefficient alpha reliability is 0.87 and the 4-month test-retest reliability is 0.78 for the IES total score. Reliability data were calculated similarly for the measures below.

Quality of life: distress and mental health Three measures were used.

Emotional distress The Profile of Mood States (POMS)[35] assesses negative mood. A Total Mood Disturbance score is the sum of five scales (Anxiety, Depression, Anger, Fatigue, and Confusion) minus the score of a Vigor scale. The Cronbach alpha reliability for the POMS is 0.92 and the test-retest reliability is 0.78.

Depressive symptoms A standardized self-report measure, the short form[36] of the Center for Epidemiological Studies-Depression Scale (CES-D),[37] was used to identify symptoms occurring during the previous week. Scores can range from 0 to 22, and ≥ 10 is used as a cutoff value for clinical symptomatology. The internal consistency of the CES-D is 0.81 and the 4-month test-retest reliability is 0.53.

Mental health The Medical Outcomes Study–Short Form[38,39] has 36 items contributing to 8 subscales for assessing psychological and physical QOL. The mental and physical health component scores are computed by their differential weighting of the scales. The component scores are converted to T scores relative to the population, with a mean (M) of 50 and a standard deviation (SD) of 10. The mental health component (SF-36 MHCS) has higher weights for the following: mental health, role functioning related to emotional health, social functioning, and vitality. The test-retest reliability for the MHCS is 0.60 and the internal consistency is 0.88.

Quality of life: social adjustment This construct is evaluated with four measures.

Social network The Social Network Index (SNI)[40,41] documents an individual's direct contact with family, friends, and the community. The test-retest reliability of the SNI is 0.71.

Social support The Perceived Social Support Scales for Friends (PSS-Fr) and Family (PSS-Fa)[42] assess an individual's need for and perception of receiving support. The alpha reliability values are 0.82 and 0.88 and the test-retest reliability values are 0.79 and 0.80 for the PSS-Fr and PSS-Fa, respectively.

Dyadic satisfaction The satisfaction item (DS) from the Dyadic Adjustment Scale (DAS)[43] assesses relationship satisfaction among couples. The test-retest reliability of the DAS is 0.64.

Functional status, symptoms, and evaluations of health—Three measures were used. A research nurse completed the first two after patient evaluation and physician consultation.

Performance status The Karnofsky performance status (KPS)[44] measure was used. Ratings ranged from 0 to 100 with interrater reliability ranging from 0.70 to 0.97.[45,46]

Symptoms, signs, and illnesses A rating scale[47] documented the type and severity of toxicities from cancer treatments as well as other common symptoms/signs and illnesses (e.g., infection). Developed by the Southwest Oncology Group (SWOG), items are grouped within 22 body categories (e.g., hematologic, gastrointestinal, neurosensory). The internal consistency of the SWOG rating scale is 0.83.

Self-evaluation of health The Medical Outcomes Study – Short Form[38] is described above. The score of the Physical Health component (SF-36 PHCS) uses higher weights for the physical functioning, role functioning related to physical health, bodily pain, and general health scales. The test-retest reliability of the SF-36 PHCS is 0.63 and the internal consistency is 0.93.

Analytic Strategy

Preliminary analyses compare the R and DF groups at the initial assessment on relevant characteristics using chi-square or analysis of variance (ANOVA) models as appropriate. Primary analyses compare the groups at the cancer recurrence/follow-up time point while taking into account baseline values from the initial diagnosis. A 2 (Group: R vs. DF) × 2 (Time: initial diagnosis vs. cancer recurrence/follow-up) repeated-measures multivariate (MANOVA) and univariate ANOVA models are used. The effect of interest is the two-way, Group × Time interaction. Significant MANOVAs are followed with ANOVAs for individual measures. When relevant, the main effects for Time are provided. An alpha level of 0.05, 2 sided, is used.

RESULTS

Description and Equivalence of the Groups

ANOVAs contrasting the R and DF groups on sociodemographic, prognostic, treatment, and duration of follow-up variables revealed that none of the differences between the groups were statistically significant (all *P*s > 0.05). See Table 1 for a summary. Table 2 provides details regarding the locations of disease for the R group.

Outcomes

Cancer-specific stress—A significant Group × Time interaction for the IES, $F(1, 117) = 13.471$, $P < 0.001$, was observed in the R group (Table 3). R patients reported stress at cancer recurrence equivalent to that reported at their initial diagnoses. Their scores were > 1 SD higher than those reported for a national probability sample of adults (M = 13.02, SD = 6.35)[48] and equivalent to levels reported by women seeking psychiatric treatment for stress disorders.[34] In contrast, cancer-specific stress had decreased significantly across time for DF patients. The IES subscales also revealed significant Group × Time interactions for Avoidance, $F(1, 117) =$

9.843, $P = 0.002$, and Intrusion, $F(1, 117) = 9.509$, $P = 0.003$, with the same pattern of effects as seen with the total score.

Quality of life—A MANOVA with the POMS, CES-D, and the SF-36 MHCS was conducted, and the interaction was not significant ($P = 0.154$). However, there was a significant effect for Time ($P < 0.001$), indicating that emotional distress had lowered and mental health had improved for both groups across time. Likewise, the MANOVA for the PSS-Family and PSS-Friends and the SNI was not significant ($P = 0.243$), indicating no differential change in social adjustment between the groups across time.

Among patients with a romantic partner, there was a significant Group × Time interaction for marital satisfaction, $F(1, 88) = 7.263$, $P = 0.008$. R patients' initial scores were lower than patients who did not recur. After cancer recurrence, patients' DAS values exceeded those of their nonrecurrent counterparts. It is important to note, however, that all marital satisfaction reports were typically positive, with a score of 3 meaning "happy" and a score of 4 meaning "very happy."

Functional status, symptoms, and evaluations of health—The MANOVA interaction for these outcomes was significant, $F(3,114) = 11.037$, $P = 0.001$. Follow-up ANOVAs were conducted. The interaction was significant for the KPS measure, $F(1, 116) = 21.361$, $P = 0.001$. The KPS of R patients significantly declined from their initial to cancer recurrence diagnosis, whereas that for DF patients improved. Ratings of 70 refer to "cares for self: unable to do normal activity/work," 80 refers to "normal activity with effort, some signs/symptoms," and 90 refers to "normal activity, minor signs/symptoms."

There was also differential disruption in QOL due to health status found with the SF-36 Physical Component, $F(1, 116) = 17.642$, $P < 0.001$. R patients reported equivalent levels of disruption for their QOL for both diagnoses, but DF patients reported significantly less interference from health when time passed and they became survivors of cancer. Follow-up ANOVAs revealed significant interactions for three of the four scales comprising the measure and the findings mirror those seen for the total score. Specifically, for the DF group, there was significantly less QOL disruption across time as assessed with the Physical Functioning ($P = 0.001$) and Role Functioning ($P = 0.001$) scales, but the values were equivalent for the R group at both assessments. Also, General Health perceptions for the R group declined significantly from initial to the cancer recurrence diagnosis, whereas they improved slightly for the DF group during the same time period ($P = 0.001$). The Bodily Pain scale was not significant ($P = 0.130$).

In contrast, there was no interaction for symptoms/signs (SWOG; $P = 0.864$), but a main effect for time indicated that both groups were evaluated as having a greater severity of symptoms from initial diagnosis to follow-up, $F(1,116) = 13.053$, $P = 0.001$.

DISCUSSION

Do patients who recur show qualitatively or quantitatively different psychological responses than those experienced when initially diagnosed? In brief, the answer is yes, and the most unique aspect of patients' responses is their specificity. Patients with recurrent disease report stress about cancer, per se, with intrusive thoughts and avoidance, but importantly, this is not accompanied by global distress or QOL disruption. These data support a learning theory perspective. Clearly, one does not habituate to hearing a cancer diagnosis, but women's previous experiences with a cancer diagnosis may enable them to be emotionally resilient, at least initially, to the sudden change in their disease status. It appears that stress reactions are compartmentalized and focus on cancer, but do not seem to prompt anxious, depressive, or

angry symptoms, as has been suggested.[2–4,14,26,49] This is the case even as patients have a lowered functional status and consequent disruption in activities and roles.

If the magnitude of stress at cancer recurrence diagnosis matches that which women reported when initially diagnosed, some might consider that the same psychosocial services available to the newly diagnosed would also be sufficient for those with cancer recurrence. In considering this issue, we searched the literature for studies providing data on the trajectory of emotional distress for those with recurrent disease. There are only six studies, all with two assessments. Three studies provide data at the time of cancer recurrence diagnosis with one follow-up,[50–52] whereas three others began months/years after diagnosis and then included an additional assessment.[10,53–55] Of these, improvements[10,50,51] and no change[53] in QOL were reported, even as patients approached death.[54] Reports of general declines in QOL have not appeared. Only Pandey et al.[52] reported declines on some measures yet improvements on others. Because there are no studies with more assessments than two, it is difficult to know if these generally positive trends are representative. Historically, very difficult scenarios, with increasing distress, have been described.[56–58]

From another perspective, early reports of traumatic stress symptoms do predict higher levels of emotional distress among patients with cancer with[55] and without[59] advanced-stage disease. If so, the early availability of psychosocial services would be immediately helpful and may be preventive. With stress compartmentalized, a window of opportunity exists. Psychosocial interventions for patients with cancer are generally effective,[31,60] and the strongest effects are achieved when treating anxiety-related problems.[61] Such interventions with recurrent patients could be efficient, focusing on immediate stress and anxiety reduction and also could teach coping strategies to prevent or reduce later emotional distress.

To advance the literature, continued follow-ups with samples such as these are important. The emotional trajectory for those with recurrent disease is unclear. The majority of the patients (80%) studied in the current article were ones with metastatic disease, and some data suggest that their psychosocial course may be more difficult than that for women with local cancer recurrences.[62] We bring a learning perspective to the interpretation of these findings. Although not a rigorous test, per se, it is important to bring conceptual frameworks to this literature as well as to investigate the psychological mechanisms that underlie the potential for resilience among patients with cancer recurrence. Finally, our data speak to the responses of women with breast carcinoma, but in addition, the need for data from men and those with other sites of disease is critical for biobehavioral research in cancer to progress.[60]

In summary, our findings from a controlled, prospective longitudinal study add to the descriptive and empirical literature, but differ from previous retrospective, uncontrolled, or single-assessment studies in which recurrent patients are described as generally distressed. Our data reveal the resiliency with which patients with breast carcinoma respond to a diagnosis of cancer recurrence. Continued follow-up of these and other recurrent patients is needed to understand the biobehavioral trajectory of patients as they cope and live with recurrent disease.

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TABLE 1

Equivalence of Disease-Free and Recurrence Groups at Initial Cancer Diagnosis

Variables	Disease-free (DF) *n* = 90 Mean (%)	Recurrence (R) *n* = 30 Mean (%)
Sociodemographic		
Mean age in yrs	51.0 (9.7)	52.0 (11.6)
Race (Caucasian)	(90.0)	(96.7)
Education in no. of yrs	15.1 (2.6)	14.8 (2.4)
Family Income (thousands of dollars/yr))	76.3 (87.9)	59.7 (48.9)
Marital Status (Married)	(72.2)	(76.7)
Significant Other (Yes)	(83.3)	(83.3)
Prognostic		
Months since initial diagnosis	38.0 (17.3)	36.6 (16.9)
Stage II vs. III (II)	(85.6)	(83.3)
Positive nodes	3.1 (4.5)	4.3 (8.5)
Tumor size in cm	3.0 (1.7)	3.6 (1.4)
ER/PR positive	(70.0)	(56.7)
Premenopausal status	(53.3)	(46.7)
Treatment received		
Psychological intervention	(60.0)	(60.0)
Surgery, segmental mastectomy	(53.3)	(66.7)
Radiation therapy	(62.2)	(40.0)
Hormonal therapy	(76.7)	(70.0)
Chemotherapy	(84.4)	(86.7)
Doxorubicin	75.6	73.3
Cyclophosphamide	83.4	86.7
Methotrexate	11.1	16.7
5-fluorouracil	18.8	26.7
Paclitaxel	15.6	23.3
Docetaxol	3.3	3.3
Chemotherapy[a]: Average dose intensity received ($mg/m^2/wk$)		
Doxorubicin, n = 90	19.1 (4.2)	18.8 (7.1)
Cyclophosphamide, n = 101	255.4 (204.6)	210.9 (209.2)
Methotrexate, n 3 15	15.6 (3.3)	11.3 (5.9)
5-Fluorouracil, n = 25	201.3 (64.0)	179.7 (69.9)
Paclitaxel, n = 22	63.6 (12.8)	52.3 (22.5)
Docetaxol, n = 4	21.3 (5.3)	16.3 (NA)

ER/PR: estrogen/progesterone receptor status; NA: not applicable.

[a]Mean based on number of patients who were recommended treatment.

TABLE 2

Location of Recurrent Disease for the Recurrence Group (n = 30)

Location	No. of patients (%)
Viscera	13 (43.3)
Bone	16 (53.3)
Local (n = 6)	
Chest wall	3 (50)
Breast tissue	3 (50)
Regional (n = 1)	
Supraclavicular nodes	1 (100)
Distant (n = 23)	
Lung	9 (39.1)
Liver	6 (26.1)
Bone	16 (69.6)
Pleura	1 (4.3)
Brain	1 (4.3)
Intestine	1 (4.3)

TABLE 3

Initial Diagnosis and Follow-Up (Time of Recurrence for the Recurrence Group) Data for the Groups

	Initial (*N* =120)		Follow-up (*N* = 120)	
	Disease Free (*n* = 90)	**Recurrence (*n* = 30)**	**Disease Free (*n* = 90)**	**Recurrence (*n* = 30)**
Variables	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Cancer Specific Stress				
Impact of Events Scale[a]	25.75 (14.02)[a]	23.28 (12.94)[a]	12.35 (11.98)[b]	21.01 (13.74)[a]
QoL: Distress and Mental Health				
Profile of Mood States	20.78 (21.61)	27.83 (18.89)	12.02 (21.85)	19.92 (21.47)
CES-D	5.48 (3.62)	6.10 (3.57)	3.88 (3.56)	5.83 (4.46)
SF-36 MHCS	43.40 (11.35)	41.95 (11.14)	51.99 (8.20)	46.61 (9.11)
QoL: Social Adjustment				
Social Network Index	6.70 (2.69)	5.83 (2.98)	6.34 (2.95)	6.31 (2.71)
Perceived Social Support				
Family	16.74 (4.07)	17.34 (3.98)	17.22 (3.59)	18.03 (3.92)
Friends	17.54 (3.05)	16.31 (3.31)	17.54 (2.89)	17.19 (3.53)
Dyadic Satisfaction[a]	4.07 (1.08)[a]	3.68 (1.29)[a,b]	3.53 (1.37)[b,c]	3.86 (1.21)[a,b]
Functional Status and Health Evaluation[a]				
Karnofsky Performance[a]	85.80 (7.98)[a]	82.00 (9.61)[b]	90.45 (5.85)[c]	78.00 (9.61)[d]
SWOG[a]	0.20 (0.11)[a]	0.22 (0.11)[a]	0.25 (0.10)[b]	0.27 (0.11)[b]
SF-36 PFCS[a]	40.59 (6.61)[a]	40.54 (6.49)[a]	48.21 (10.07)[b]	39.41 (9.47)[a]

SD: standard deviation; CES-D: Center for Epidemiologic Studies-Depression Scale; SF-36: Medical Outcomes Study Short Form; MHCS: Mental Health Component Score; SWOG: Symptoms, signs, and illnesses measure from the Southwest Oncology Group; PFCS: Physical Functioning Component Score.

[a] $P < 0.05$ for M/ANOVA. For measures with significant group by time interactions, common superscripts indicate no significant differences between means, whereas different superscripts indicate significant differences ($P < 0.05$).