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Cancer-related cognitive impairment and associated factors in a sample of older male oral-digestive cancer survivors

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Abstract

Objective: This study examines the demographic and clinical variables associated with cancer-related cognitive impairment (CRCI) in a sample of older, male, oral-digestive cancer survivors at VA Medical Centers in Boston and Houston.

Methods: A two-time point, longitudinal design was used, with cognitive assessment conducted at 6 and 18 months post-diagnosis. Using ANCOVA, the cognitive functioning of 88 older adults with head and neck, esophageal, gastric, or colorectal cancers was compared with that of 88 healthy controls. Paired *t*-tests examined cognitive change over time in the cancer group. Hierarchical linear regression examined variables potentially associated with cognitive impairment at 18 months.

Results: Forty-eight percent of cancer patients exhibited cognitive impairment 6 months post-cancer diagnosis, and 40% at 18 months. Cancer survivors were impaired relative to controls on measures of sustained attention, memory, and verbal fluency at 18 months, controlling for age. Older age, low hemoglobin, and cancer-related PTSD were associated with worse cognition at 18 months.

Conclusions: CRCI is more frequent in older adults than reported in studies of younger adults and may be more frequent in men. Potential areas of intervention for CRCI include psychotherapy

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DECLARATION OF CONFLICTING INTERESTS

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from authors A.D.N. and J.M. upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

for cancer-related PTSD, treatment of anemia, and awareness of particularly vulnerable cognitive domains such as sustained attention, memory, and verbal fluency.

Keywords

anemia; attention; cancer; cancer survivorship; cancer-related cognitive impairment; memory; oncology; phonemic fluency; PTSD

1 | BACKGROUND

The number of cancer survivors in the United States is currently estimated at 16.9 million¹ and continues to climb due to advances in cancer treatment. As the number of cancer survivors grows, cancer-related cognitive impairment (CRCI) is a key survivorship issue and potential “late effect” of cancer treatments.^{2,3} The American Cancer Society includes in its definition of CRCI problems in the cognitive domains of memory, attention, executive function, and processing speed,⁴ although research has also found impairment in working memory, new learning, visuospatial skills, and language.⁵ The clinical prevalence of CRCI has primarily been assessed in breast cancer patients and survivors.^{4,6} Longitudinal neuropsychological assessment of breast cancer patients finds that up to 75% of patients experience CRCI during treatment, and up to 35% experience CRCI months or years after completion of treatment.⁴ Long-term prevalence of CRCI post-treatment is estimated at 35% to 60%⁷ and may persist for 20 years following completion of chemotherapy.⁸

The pathogenesis of CRCI is not fully understood and is likely multifactorial. Potential mechanisms include the neurotoxic effects of chemotherapy and radiation therapy (eg, brain damage),⁹ type of chemotherapeutic agent (eg, methotrexate, 5-fluorouracil, carmustine, cisplatin, and cytarabine),¹⁰ circulating cytokines,¹¹ blood-brain barrier (BBB) damage,¹² hormonal changes,¹³ DNA alterations,¹⁴ oxidative stress (eg, telomere shortening),^{11,15} decline in hemoglobin (ie, anemia),¹⁶ reduced synaptic plasticity,¹⁴ altered growth factor levels,¹⁴ and impaired hippocampal neurogenesis.¹⁴

Patient characteristics, including a genetic predisposition (although there is still not a potent biomarker) such as the presence of allele ε4 of the apolipoprotein E (APOEε4),¹¹ genetic variability in transporters of the BBB,¹⁷ age,¹⁴ education,¹⁴ cognitive reserve,¹³ and cancer-related comorbidities (eg, depression, cancer-related post-traumatic stress disorder)^{14,18} may also contribute to cognitive dysfunction after treatment. Of these, age is the most potent risk factor,^{15,18} possibly driven by the fact that older adults have more risk factors for cognitive impairment in general than younger adults and are disproportionately affected by cancer, with 62% of cancers occurring in older patients.¹⁹

Admittedly, it is difficult to discern which outcomes are specific to treatment versus cancer itself; however, several studies have shown cognitive and structural changes due to chemotherapy independent of cognitive alterations directly linked to the cancer process.^{20,21} The importance of delineating the nature of cognitive dysfunction due to cancer treatments and identifying ways to predict, assess, and manage these changes is becoming increasingly emphasized in the literature. However, the majority of studies addressing CRCI utilize samples of young-to-middle-aged female breast cancer patients/survivors.^{4,6} In recent years,

researchers have begun examining CRCI in other cancer types,⁶ although older adults and males are still not well-represented in these samples.

Recently, Loh and colleagues¹⁴ identified several research priorities to improve the study of cognitive impairment in older patients with cancer, beginning with longitudinal studies evaluating the prevalence of cognitive impairment exclusively in older patients with cancer. Consequently, the present study aims to address this priority as well as the dearth of male patients in current study samples. We do so through a two-time point longitudinal assessment of the effects of several adjuvant therapies on late cognitive effects in a population of older, male cancer survivors with a variety of cancer types. Additionally, we seek to identify demographic, medical, and cancer-related variables associated with cognitive impairment. This article builds on the literature evaluating cognitive impairment in men with genitourinary cancers^{22,23} and other cancers (eg, colorectal cancer²⁴), which demonstrates impaired cognition in the short term.

2 | DESIGN AND METHODS

2.1 | Study design and setting

We conducted an observational cohort study of Veterans with head and neck, gastric, esophageal, or colorectal cancer. The current analysis is of 88 male patients who completed cognitive testing at both 6 and 18 months after diagnosis; one outlier with cognitive impairment in the moderate-to-severe range at 18 months was excluded from analyses. Veterans completed in-person assessments lasting approximately 2 hours each. Participants were compensated \$30 for each interview. The study received ethical approval from the Boston Veterans Affairs Medical Center (VAMC) and Houston VAMC Institutional Review Boards (IRB) (Houston IRB #25446; Boston IRB #2317). Prior to participation, Veterans completed a written consent form, which became part of their permanent medical records in the VA Computerized Patient Records System. Complete protocol methods, including efforts to address potential sources of bias and determination of study size, have previously been described in extensive detail.²⁵

2.2 | Participants

Potential participants were identified from the Boston VAMC and Houston VAMC tumor registries. Inclusion criteria were diagnosis of head and neck, esophageal, gastric, or colorectal cancers, stages I-IV. Exclusion criteria were referral to hospice care at any point within 6 months post-cancer diagnosis, diagnosis of dementia, and diagnosis of psychotic spectrum disorder.

2.2.1 | Controls—Participants were compared with a sample of normal controls recruited for a separate validation study.²⁶ Raw data were provided to the authors by the PI of that study. Normal controls were 88 older volunteers with no memory or cognitive complaints and normal baseline neuropsychological performance as described elsewhere.²⁶ As the normal controls were older ($M = 72.85$, $SD = 6.77$) than the patient sample ($t = -5.62$, $P < .001$), statistical comparisons in our analyses controlled for age.

2.3 | Measures

2.3.1 | Demographics—Participants reported their age, gender, racial and ethnic status, and level of education. For analytic purposes, we dichotomized age at less than 70 ($n = 62$) and 70 or more ($n = 28$), to characterize older age as a risk factor.

2.3.2 | Cognition—Cognitive performance was assessed via the Montreal Cognitive Assessment (MoCA),²⁶ a cognitive screener sensitive to mild cognitive impairment. This measurement tool has been suggested in place of others such as the Mini-Mental State Examination²⁷ due to its sensitivity in detecting cognitive impairment in cancer survivors.^{28,29} The MoCA includes items susceptible to cognitive changes after cancer, including copy of a complex figure, trail-making, verbal fluency, list learning, and sustained attention tasks. Items were scored according to standard criteria and summed to create a total score ranging from 0 to 30. Per instructions, we added one point to the total score for participants with a high school education or less. The MoCA has evidenced strong validity (sensitivity = 90%, specificity = 87%, positive predictive values = 89%, negative predictive values = 91%) and reliability (ICC = 0.92, $\alpha = 0.83$).²⁶ Per scoring guidelines, a cutoff score of 26 and above was used to indicate “not impaired.”²⁶ As is standard practice, an alternate version of the MoCA was administered upon retest to avoid practice effects.

At each site, the MoCA was administered by one experienced research interviewer with a bachelor’s degree who was trained to administer this measurement tool through teaching and observation by a geropsychologist. Each assessment was discussed in weekly interdisciplinary team meetings for quality assurance.

2.3.3 | Cancer variables—Cancer site, stage, and treatment (surgery, radiation, and/or chemotherapy) were recorded from the medical record. Participants were assigned a score of 1 if they received either chemotherapy or radiation; if they were solely treated with surgery, they were assigned a score of zero.

2.3.4 | Laboratory variables—We extracted hemoglobin and albumin lab values from the electronic medical record at 18 months post-diagnosis as proxy indicators of hypoxia and inflammation, respectively. Following conventional reference ranges for mild, moderate, and severe anemia for adults,³⁰ we dichotomized the sample into those with normal or mild anemia (hemoglobin ≥ 11.0 g/dL) ($n = 82$) versus moderate-to-severe anemia (< 10.9 g/dL) ($n = 8$). Serum albumin values were dichotomized at normal to mildly depleted (≥ 3.1 g/dL) ($n = 85$) versus moderately to severely depleted (< 3.0 g/dL) ($n = 5$).³¹

2.3.5 | Post-traumatic stress disorder—Cancer-related PTSD (CR-PTSD) and combat-related PTSD were assessed for three reasons: cancer diagnosis and treatment can be distressing and traumatic for patients,^{32,33} participants were recruited from VAMCs, and some studies find that post-traumatic stress is a risk factor for dementia.³⁴ The 17-item Posttraumatic Stress Disorder Check List-Stressor-Specific version (PCL-S)³⁵ measured CR-PTSD in the past week ($\alpha = .95$ in this sample). To orient respondents to cancer as the traumatic event, each item was amended to refer to cancer (eg, “repeated, disturbing memories, thoughts, or images of cancer, your diagnosis, or treatment?”), as similarly

adapted for breast cancer survivors.³⁶ A total score was created by summing items rated on a five-point scale (1 = “not at all” to 5 = “extremely”); a standard cut score of 50 or more indicated the presence of CR-PTSD.³⁵

To control for possible influence of combat-related PTSD, we administered the four-item Primary Care PTSD Screen³⁷ with participants who endorsed combat experience ($\alpha = .90$ in this sample). This four-item measure uses a yes/no response format to assess the occurrence of nightmares or intrusive thoughts about the military, avoidance of thoughts or situations that are reminders of the military, feeling on guard or easily startled, and feeling numb or detached from others in the past month. For analytic purposes, participants were assigned a score of 1 if they endorsed any combat-related PTSD symptoms; otherwise, they were assigned a score of zero.

2.3.6 | Comorbidity—To control for comorbidity burden, we extracted outpatient ICD-9 data using the Charlson Comorbidity Index (CCI).^{37,38} The CCI is the most widely used clinical index for a variety of disorders and cancers³⁹ and sums the weighted scores of 19 medical conditions. For analytic purposes, the index was dichotomized at the median.

2.4 | Statistical methods

Cognitive impairment was evaluated using normative cut-offs.²⁶ Cognitive functioning in cancer patients was compared with normal controls (raw, original MoCA data) using ANCOVA, controlling for age at both the total score and item level. Change over time in the cancer group was examined using paired *t*-tests. Hierarchical linear regression examined variables potentially associated with impairment at 18 months, in three steps: (a) comorbidity and combat-related PTSD scores were entered as a control; (b) categorical variables were entered to indicate four potential risk factors (older age, treatment with chemotherapy or radiation, abnormal hemoglobin, abnormal albumin); and (c) cancer-related PTSD total scaled score as reported at 6 months post-diagnosis was entered to determine if it predicted cognitive dysfunction over and above other risk factors. All independent variables were dichotomized and scored as 1 = presence of risk factor, 0 = absence. All significance tests were twosided using a significance level of $P < .05$. Analyses were conducted using SPSS software version 21.0 (IBM, New York).

3 | RESULTS

3.1 | Participants and descriptive data

Participants were 88 men with a mean age of 65.93 years ($SD = 9.36$, range 41–88). The majority of participants were White (73.9%), and 53.4% had some college education or were college graduates (Table 1). Participants had head/neck, esophageal or gastric cancer (39.8%), or colorectal cancer (60.2%). The stage distribution was as follows: stage I (34.1%), II (26.1%), III (20.5%), or IV (19.3%). Treatment received included surgery (75.0%), chemotherapy (51.1%), and radiation (37.5%), and 28.4% received both chemotherapy and radiation; 14.8% of participants ($N = 13$) were undergoing active treatment. Mean comorbidity score was 6.31 ($SD = 3.91$); mean hemoglobin (18 months) was 13.05 ($SD = 1.84$); and mean albumin (18 months) was 3.79 ($SD = 0.45$).

3.2 | Cognitive findings

3.2.1 | Cognitive functioning—Mean MoCA score for cancer survivors at 6 months post-diagnosis was 25.14 ($SD = 3.21$), with 48% scoring below the impairment cut score. At 18 months post-diagnosis, the mean MoCA score improved to 26.39 ($SD = 2.80$), which was statistically significant ($t_{(87)} = -3.48, P = .001$). However, 40% of the sample still scored in the impaired range. Only 13% of controls scored in the impaired range. Cancer survivors were significantly impaired relative to controls at both 6 months ($F_{(2,174)} = 21.54, P < .001$) and 18 months post-diagnosis ($F_{(2,174)} = 7.07, P = .001$), controlling for age.

On individual items (Table 2), at 6 months post-diagnosis, cancer patients were impaired relative to controls on mini-trials, serial 7s, phonemic fluency, similarities, and memory. By 18 months, cancer survivors had improved on phonemic fluency ($t = -2.52, P = .01$) and memory ($t = 2.55, P = .01$), but remained impaired relative to controls on serial 7s ($F_{(2,174)} = 219.56, P < .001$), phonemic fluency ($F_{(2,174)} = 9.06, P = .003$), and memory ($F_{(2,174)} = 18.04, P < .001$), controlling for age.

3.2.2 | Predictors of cognitive impairment—In bivariate analyses, only older age was negatively associated with total MoCA score at 18 months ($t = 3.80, P < .001$) (Table 1); disease type and stage were not associated with MoCA score. Regarding relationships among predictors, older age was negatively associated with total cancer-related PTSD score ($r = -.39, P = .001$); hemoglobin and albumin values were positively correlated with each other ($r = .53, P < .001$).

For the linear regression analyses, in the final model (Step 3) older age ($\beta = -.42, P < .001$), low hemoglobin ($\beta = -.25, P < .05$), and CR-PTSD ($\beta = -.21, P < .05$) were associated with worse cognition ($R^2 = .25, F_{(7,80)} = 3.72, P = .002$) (Table 3). The addition of CR-PTSD to the model in the last step was significant ($F_{(1,80)} = 4.13, P < .05$). We also ran this model entering chemotherapy and radiation independently. In these models, neither chemotherapy nor radiation alone was associated with decrements in cognition.

4 | CONCLUSIONS

Nearly half (48%) of the 88 middle-aged and older males treated for head and neck, esophageal, gastric, and colorectal cancers in this sample were cognitively impaired at 6 months post-diagnosis, decreasing to 40% at 18 months. These findings are consistent with those of other studies that find a range of 12% to 75% of survivors of other cancers (mostly breast) have cognitive problems post-treatment.⁴ Furthermore, the impaired cognitive domains—sustained attention, memory, and verbal fluency—have previously been identified as domains encompassed by the term CRCI.^{4,5} Importantly, there was improvement in several cognitive domains between the two time periods, particularly phonemic fluency and memory. This is encouraging, given the role of memory and executive cognitive functions on performance of instrumental activities of daily living among older adults.⁴⁰

The rate of impairment found in this study falls in the middle of those reported elsewhere, possibly due to the older age of our sample. In addition, this finding may indicate that female and male patients are differentially affected by CRCI. The extent of cognitive

impairment in this sample cannot be explained by dementia, as we carefully excluded those with dementia, although incipient cognitive impairment cannot be ruled out. Somewhat surprisingly, and unlike other studies, we did not find that impairment varied by the presence or absence of chemotherapy. It may be that, in this older, multimorbid population, who received a range of treatment modalities (half received chemotherapy and more than one-third radiation), the combined effects of cancer and its treatments present the greatest risk to cognition rather than the effect of chemotherapy alone. However, anemia at 18 months was associated with impaired cognition, consistent with suggestions of a potential role for anemia and cerebral hypoxia in cognitive dysfunction in cancer survivors,^{16,41} although other mechanisms of action are generally viewed as more influential.

4.1 | Study limitations

The present study has several limitations. First, participants were homogeneous in terms of race/ethnicity and Veteran status, which may limit generalizability. Although Veteran status is common (one in two men over age 65 are Veterans), the extent to which the Veterans sampled are different from other Veterans or non-Veterans on the characteristics measured here is unknown. Second, the sample size limited the ability to do subgroup and interaction analyses, such as examining potential differential effects of CR-PTSD at different age groups. Additionally, although there were no specific associations among treatment type or cancer-related factors in these analyses, the sample was not adequately powered to test all determinants, such as dose effects of chemotherapy or radiation as potential predictors of impairment.

While the design is a two-time point longitudinal comparison of cancer survivors with normal controls, the ideal longitudinal design would compare healthy controls, cancer survivors who received systemic therapy, and cancer survivors who did not receive systemic therapy on both standardized neurocognitive testing and self-report measures at time of diagnosis, post-active treatment and follow-up. This study did not use standardized neuropsychological assessments, but rather an established cognitive screening measure, which is not as sensitive to subtle neurocognitive impairments.^{7,42} Although cancer type was not associated with cognition, this study included cancers of various pathologies and was underpowered to evaluate subgroup differences.

Additional data that may be relevant or illuminating was not collected in the original study. For example, 17 participants had stage IV cancer, but it is unknown whether any participants had CNS metastatic disease. It is not known if any participants had metastatic disease to the brain, underwent systemic chemotherapy, or received radiation to the head. A self-report measure for cognitive function was not administered, and analyses could not control for the potential effects of fatigue and depression.

The authors recognize that, when using biomarkers for cancer populations, there are additional valuable panels that provide a clinically relevant perspective of inflammation in the body. However, laboratory values were obtained from blood drawn for routine clinical purposes, which did not include specific markers of inflammation. A final potential limitation is that, although persons with dementia diagnoses were screened out by study criteria, it is possible that some participants with undiagnosed cognitive impairment were

ultimately included and/or that some participants would have become more cognitively impaired over the course of the study regardless of cancer treatment.

4.2 | Future research

To the authors' knowledge, this is one of the few longitudinal studies of cognition in older cancer survivors, although future longitudinal studies should assess for pretreatment baseline functioning. Furthermore, to the authors' knowledge, this is one of the only studies focused specifically on the experience of male survivors, as the literature tends to focus on women after breast cancer. Future research should continue to longitudinally explore the relationship of specific risk factors to cognition in large samples of older adults with various forms of cancer, using direct cognitive assessment and examining other blood markers. Longer periods of follow-up may characterize whether the cognitive decrements after cancer confirms an accelerated cognitive aging hypothesis for some cancer survivors. In order to further examine whether or not male and female patients are differentially affected by CRCI, future longitudinal studies should incorporate, to the extent possible, equivalent sample sizes of both men and women.

4.3 | Clinical implications

These findings represent an important initial contribution to the literature detailing risk factors for CRCI in older men. The potential for cancer-related PTSD to serve as a risk factor for cancer-related cognitive disruption, as found in this and other studies,^{18,32,33} has significant implications for prevention and treatment of cognitive decline. Implementation of effective therapeutic approaches for cancer patients experiencing traumatic stress is critical and may improve both the distressing symptoms of PTSD and the functional/neurological changes associated with cognitive decline. Given the established relationship between PTSD and cognitive dysfunction outside of cancer, and a PTSD prevalence rate range in the literature of up to 52% across all types of cancers,⁴³ our findings merit further study.³³ Additional areas for intervention suggested by our findings include treatment of anemia and awareness of those cognitive domains that may be particularly vulnerable, such as sustained attention, memory, and verbal fluency.

Very shortly, by the year 2020, two-thirds of all cancer survivors are expected to be 65 years of age.² Consequently, more attention must be paid to optimize the care of older adults following cancer treatment. The development of CRCI is likely multifactorial, with numerous potential demographic, clinical, psychosocial, neuropathological, and medical avenues for assessment and intervention. Identifying the etiologies and appropriate treatments for patients with CRCI, particularly older adults, continues to be a clinically important and essential area of research.

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TABLE 1

Participant characteristics and association with MoCA score (18 months)

Participant Characteristics			Association with MoCA	
Variable	Category	n	%	P
Age	Younger (range 41–69)	61	69.3	$t = 3.66$
	Older (range 70–88)	27	30.7	$t = -0.60$
Education	High school or less	41	46.6	$t = -0.60$
	College	47	53.4	$t = 0.77$
Race	African American/Other	23	26.1	$t = 0.77$
	Caucasian	65	73.9	$t = 0.55$
Comorbidity	Lower (range 2–4)	43	48.9	$t = 0.55$
	Higher (range 5–17)	45	51.1	$t = -1.30$
Combat PTSD	None (0)	68	77.3	$t = -1.30$
	Any (1–4)	20	22.7	$t = -0.66$
Cancer type	Head and neck/other	35	39.8	$t = -0.66$
	Colorectal	53	60.2	$F = 0.49$
Cancer stage	I	30	34.1	$F = 0.49$
	II	23	26.1	
	III	18	20.5	
	IV	17	19.3	
Treatment type	Surgery	68	75.0	$t = -1.74$
	Chemotherapy	45	51.1	$t = -0.50$
	Radiation	33	37.5	$t = 0.53$
Hemoglobin (18 months)	Low (range 5.4–10.9)	8	9.1	$t = 1.34$
	Mild–WNL (range 11.0–17.3)	80	90.9	
Albumin (18 months)	Low (range 1.9–2.9)	5	5.7	$t = 0.32$
	Mild–WNL (range 3.0–4.7)	83	94.3	
Cancer PTSD (6 months)	No (< 50)	9	10.2	$t = 0.70$
	Yes (50+)	79	89.8	

Note: Student's t-test or ANOVA was used to examine the relationship between demographic category groups and MoCA total score.

TABLE 2

Unadjusted^a mean (SD) item and total scale scores for patients and controls

<i>Item</i>	<u>Cancer Group 6 Months Post-Diagnosis</u>		<u>Cancer Group 18 Months Post-Diagnosis</u>		<u>Normal Controls</u>	
	M	(SD)	M	(SD)	M	(SD)
Mini-trails	0.77	(0.42) [*]	0.83	(0.38)	0.88	(0.33)
Cube copy	0.77	(0.42)	0.94	(0.94)	0.72	(0.45)
Clock drawing	2.78	(0.58)	2.91	(0.33)	2.56	(0.71)
Animal naming	2.92	(0.41)	2.92	(0.41)	2.88	(0.37)
Digits repetition	1.88	(0.37)	1.85	(0.39)	1.82	(0.44)
Letter tapping	0.90	(0.57)	0.94	(0.23)	0.97	(0.18)
Serial 7 subtraction	2.53	(0.84) [*]	2.58	(0.72) [*]	4.55	(0.91)
Sentence repetition	1.92	(0.31)	1.91	(0.33)	1.83	(0.38)
Phonemic fluency ^b	0.55	(0.50) [*]	0.68	(0.47) ^{*,†}	0.86	(0.35)
Similarities	1.61	(0.63) [*]	1.76	(0.53)	1.83	(0.43)
Five-word memory	2.28	(1.67) [*]	2.76	(1.72) ^{*,†}	3.72	(1.28)
Orientation	5.83	(0.79)	5.88	(0.42)	5.99	(0.11)
<i>Total</i>	25.14	(3.21) [*]	26.39	(2.80) [†]	27.35	(2.21)

^a Means shown are not adjusted for age.

^b Fluency is scored as 1 point for 11 or more words, otherwise 0.

^{*} Significantly different than normal controls at $P < .01$, based on ANCOVA controlling for age.

[†] 18-month value significantly improved from 6-month value, based on paired t -tests at $P < .01$.

TABLE 3

Hierarchical linear regression of risk factors on 18-month MoCA total score

Step	Variable	B	Std. Error	β	P	R ²	P (R ²)
1	(Constant)	26.74	0.47			.02	.108
	Comorbidity	-1.00	0.60	-.18	.096		
	Combat-related PTSD	0.71	0.71	.11	.319		
2	(Constant)	27.38	0.59			.25	.004
	Comorbidity	-1.00	0.57	-.18	.080		
	Combat-related PTSD	0.33	0.68	.05	.631		
	Age 70	-2.25	0.62	-.37	<.01		
	Chemotherapy/radiation	0.36	0.58	.06	.537		
	Abnormal hemoglobin (18 mo)	-2.26	1.21	-.23	.065		
3	Abnormal albumin (18 mo)	2.15	1.53	.18	.164		
	(Constant)	27.59	0.58		0	.25	.002
	Comorbidity	-1.01	0.55	-.18	.071		
	Combat-related PTSD	0.65	0.68	.10	.348		
	Age 70	-2.51	0.62	-.42	<.001		
	Chemotherapy/radiation	0.35	0.57	.06	.544		
	Abnormal hemoglobin (18 mo)	-2.39	1.19	-.25	.048		
	Abnormal albumin (18 mo)	2.55	1.52	.21	.097		
	Cancer-related PTSD (6 mo)	-1.93	0.95	-.21	.045		

 $R^2 = .22$, $F(7,80) = 3.72$, $P = .002$.