Title

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Publication Date

2019-08-01

DOI

10.1016/j.ejon.2019.07.001

Peer reviewed

HHS Public Access

Author manuscript

Eur J Oncol Nurs. Author manuscript; available in PMC 2020 August 01.

Published in final edited form as:

Eur J Oncol Nurs. 2019 August ; 41: 196–203. doi:10.1016/j.ejon.2019.07.001.

CO-OCCURING SYMPTOMS IN OLDER ONCOLOGY PATIENTS WITH DISTINCT ATTENTIONAL FUNCTION PROFILES

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Abstract

Purpose: Evaluate how subgroups of older adults with distinct attentional function profiles differ on the severity of nine common symptoms and determine demographic and clinical characteristics and symptom severity scores associated with membership in the low and moderate attentional function classes.

Methods: Three subgroups of older oncology outpatients were identified using latent profile analysis based on Attentional Function Index (AFI) scores. Symptoms were assessed prior to the second or third cycle of CTX. Logistic regressions evaluated for associations with attentional function class membership.

Results: For trait anxiety, state anxiety, depression, sleep disturbance, morning fatigue, and evening fatigue scores, differences among the latent classes followed the same pattern (low>moderate>high). For morning and evening energy, compared to high class, patients in low and moderate classes reported lower scores. For pain, compared to moderate class, patients in low class reported higher scores. In the logistic regression analysis, compared to high class, patients with lower income, higher comorbidity, higher CTX toxicity score, and higher levels of state anxiety, depression, and sleep disturbance were more likely to be in low AFI class. Compared to high class, patients with higher comorbidity and trait anxiety and lower morning energy were more likely to be in moderate AFI class.

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Conflicts of interest: Dr. Wong has reported a conflict of interest outside of the submitted work (i.e., immediate family member is an employee of Genentech). The other authors have no conflicts of interest to declare.

Conclusions: Consistent with the hypothesis that an increased risk for persistent cognitive decline is likely related to a variety of physical and psychological factors, for six of the nine symptoms, a “dose response” effect was observed with higher symptom severity scores associated with a progressive decline in attentional function.

Keywords

cognitive function; attentional function; older adult; depression; fatigue; pain; sleep disturbance; anxiety; chemotherapy; cancer

INTRODUCTION

In the United States, of the more than 1.7 million individuals who will be diagnosed with cancer in 2018, approximately two thirds of them will be over 60 years of age (Siegel et al., 2019). While cancer treatments have become more effective, the number of acute and long term adverse effects are increasing. Impairment in cognitive function is one such effect that occurs in 12% to 75% of patients receiving chemotherapy (CTX) (Loh et al., 2016). Recent evidence suggests that older adults may be more vulnerable to this adverse effect (Ahles and Root, 2018; Ahles et al., 2012; Hurria et al., 2006b; Lange et al., 2014). While cancer-related cognitive impairment (CRCI) is one of the most feared adverse effects (Ahles et al., 2012), only a limited amount of information is available on the impact of CTX on older oncology patients’ cognitive function (Joly et al., 2015).

In a longitudinal study of older women (>65 years) with breast cancer (Lange et al., 2016), compared to healthy controls, no differences in cognitive function were found from before to after the completion of CTX or radiation therapy. However, patients who were ≥75 years of age were at the highest risk for cognitive decline following the completion of treatment. In another study of older patients with breast cancer (>65 years) (Hurria et al., 2006a), 51% perceived a decline in memory after CTX, in particular in their ability to learn new information. Neither of these studies evaluated for changes in cognitive function at multiple time points over two cycles of CTX.

Recent evidence suggests that patients receiving CTX experience multiple co-occurring symptoms (Lange et al., 2016; Mandelblatt et al., 2014b; Ritchie et al., 2014). For example, in one study that evaluated for differences in the symptom experience of four older groups of oncology patients (i.e., 60-64, 65-69, 70-74, ≥75 years of age) receiving active treatment (Ritchie et al., 2014), regardless of age group, patients reported an average of 10 symptoms on the Memorial Symptom Assessment Scale (MSAS). The five most common symptoms were pain, lack of energy, feeling drowsy, difficulty sleeping, and difficulty concentrating.

In the two studies that evaluated for associations between changes in cognitive function and common co-occurring symptoms in older adults (Lange et al., 2016; Mandelblatt et al., 2014b), no associations were found between CRCI and fatigue, anxiety, or depression. The authors suggested that this lack of association may be related to the small sample size (Lange et al., 2016) or that subgroups of older patients may be more susceptible to CRCI (Mandelblatt et al., 2014a). As noted in one review on potential mechanisms for CRCI (Janelsins et al., 2014), additional research is needed to understand how co-occurring

symptoms may influence the occurrence and severity of CRCI. In addition, in three reviews (Joly et al., 2015; Loh et al., 2016; Mandelblatt et al., 2014a), it was noted that longitudinal studies of changes in and factors associated with decrements in cognitive function in older adults receiving CTX are urgently needed to inform clinical decisions and follow-up care. In a recent review (Ahles and Root, 2018), Ahles and Root hypothesized that an increased risk for persistent cognitive decline may be related to a variety of physical (e.g., fatigue, comorbidities) and psychological (e.g., anxiety, depression) factors and recommended that research is needed to verify this hypothesis.

Most of the studies of CRCI in older oncology patients are cross-sectional and tended to categorize patients as impaired or not impaired (Ahles and Root, 2018). The absence of longitudinal studies, with multiple assessments, precludes any evaluation of changes in CRCI over time and the identification of subgroups of patients with distinct CRCI profiles. This analysis builds on our previous work that used latent profile analysis (LPA) to identify three subgroups of older oncology patients with distinct attentional function profiles (i.e., low function (36.7%), moderate function (37.3%), and high attentional function (26.0%)), using the Attentional Function Index (AFI) (Utne et al., 2018). This instrument assesses two of the key components of CRCI, namely attention and executive function (Cimprich et al., 2011). In our previous analysis, we evaluated for demographic and clinical characteristics that were associated with worse attentional function. Compared to the high class (i.e., better attentional function scores), older adults in the low and moderate attentional function classes had lower functional status scores, a worse comorbidity profile, and were more likely to be diagnosed with depression. In this paper, we extend these findings and evaluate how these subgroups of older adults differed on the severity of nine of the most common co-occurring symptoms (i.e., trait anxiety, state anxiety, depression, sleep disturbance, morning fatigue, evening fatigue, morning energy, evening energy, pain) in oncology patients. In addition, we evaluated which demographic and clinical characteristics, as well as symptom severity scores, were associated with membership in the low and moderate attentional function classes.

METHODS

Sample Characteristics

Details about the larger, longitudinal study are reported elsewhere (Miaskowski et al., 2017). Details on the older adults (n=365) included in this analysis are reported in our previous publication (Utne et al., 2018). In brief, patients were adults with one of four cancer diagnoses (i.e., breast, lung, gastrointestinal (GI), gynecological (GYN)) who were receiving CTX.

Instruments

Information was obtained on age, gender, ethnicity, education, marital status, employment, and annual household income. In addition, patients completed the Karnofsky Performance Status (KPS) scale (Karnofsky et al., 1948) and Self-Administered Comorbidity Questionnaire (SCQ).

Symptoms were assessed using the (AFI) (Cimprich et al., 2011), the Lee Fatigue Scale (LFS) (Lee et al., 1991), the Spielberger State-Trait Anxiety Inventories (STAI-T and STAI-S) (Spielberger et al., 1983), the Center for Epidemiological Studies-Depression scale (CES-D) (Radloff, 1977), and the General Sleep Disturbance Scale (GSDS) (Lee, 1992). The occurrence and severity of pain was assessed using the Brief Pain Inventory (Daut et al., 1983).

Study Procedures

The Committee on Human Research at the University of California, San Francisco and the Institutional Review Boards at each site approved this study. During their second or third cycle of CTX, eligible patients were approached in the infusion unit by a research staff member to assess interest in the study. Written informed consent was obtained from all patients. Patients filled out questionnaires in their homes, a total of six times over two cycles of CTX (i.e., over a period of two months). Patients' medical records were reviewed for disease and treatment information. The toxicity of the CTX regimen was rated using the MAX2 index (Aapro et al., 2000; Extermann et al., 2004; Extermann et al., 2002; Extermann et al., 2015).

Data Analysis

As described in detail in our previous paper (Utne et al., 2018), LPA was used to identify the profiles of AFI scores (i.e., latent classes) over the six assessments. Descriptive statistics and frequency distributions were calculated for demographic, clinical, and symptom characteristics. Differences among the latent classes in symptom severity scores were evaluated using analysis of variance and Kruskal-Wallis or Chi Square tests with Bonferroni corrected post hoc contrasts. A corrected p-value of <.0167 (i.e., .05/3) was considered statistically significant for the three possible post hoc contrasts.

In order to evaluate the associations between select phenotypic characteristics and the nine common co-occurring symptoms (i.e., trait anxiety, state anxiety, depression, sleep disturbance, morning fatigue, evening fatigue, morning energy, evening energy, pain) and AFI latent class membership, a hierarchical stepwise regression analysis was done using the Wald criteria. Separate logistic regression analyses were done between the low versus the high AFI latent classes and between the moderate versus high AFI latent classes to predict membership in the low and moderate classes, respectively.

Each regression analysis proceeded in two stages. For the low versus the high AFI latent class analysis, the phenotypic characteristics that differed between the two classes (i.e., age, KPS score, SCQ16 score, hemoglobin (Hgb), hematocrit (HCT), MAX2 index score, married/partnered, lives alone, employment status, income, regular exercise; see Table 1) were entered into Block 1. Then, the symptom severity scores (i.e., trait anxiety, state anxiety, depression, total sleep disturbance score, morning fatigue, evening fatigue, morning energy, evening energy, presence of pain (yes/no)) were entered into Block 2. The same approach was used for the moderate versus the high latent class analysis with the following phenotypic characteristics being entered into Block 1: age, KPS score, SCQ16 score, income, regular exercise, and previous treatment groups (see Table 2). After controlling for

the phenotypic characteristics, it is possible to evaluate the relative contribution of co-occurring symptoms to AFI latent class membership. In order to include MAX2 index scores in the regression analyses, this variable was multiple by 100. A p-value of <0.05 was used to determine statistical significance.

RESULTS

Patient Characteristics

Differences in demographic and clinical characteristics among the AFI latent classes are described in our previous publication (Utne et al., 2018). In brief, across the three AFI latent classes, KPS scores (i.e., low < moderate < high) were in the expected direction. Compared to the high class, patients in the other two classes had higher SCQ scores and were more likely to be diagnosed with depression. Compared to the high class, patients in the low class were less likely to be married or partnered, less likely to be employed, more likely to report back pain, and had a higher MAX2 index score. Compared to the other two classes, patients in the low class reported a lower annual household income. Finally, compared to the high class, patients in the moderate class were less likely to exercise on a regular basis and were less likely to not have received a previous cancer treatment. No age, education, or gender differences were found among the latent classes. In addition, except for MAX2 index scores, none of the disease or treatment characteristics were associated with latent class membership.

Differences in demographic, clinical, and symptom characteristics between the low versus the high and the moderate versus the high AFI classes are summarized in Tables 1 and 2, respectively.

Differences in symptom severity scores

For the AFI total scores, as well as for the three subscale (i.e., effective action, attentional lapses, interpersonal effectiveness) scores measured at enrollment, the differences among the latent classes followed the same expected pattern (i.e., low < moderate < high) (Figure 1). As shown in Table 3, for the trait anxiety, state anxiety, depression, sleep disturbance, morning fatigue, and evening fatigue scores, the differences among the latent classes followed the same expected pattern (i.e., low > moderate > high). For the morning and evening energy scores, compared to the high class, patients in the low and moderate classes reported lower scores. In terms of pain, compared to patients in the moderate class, patients in the low class reported higher worst pain intensity scores. In addition, compared to the high class, a higher percentage of patients in the low class reported both cancer and non-cancer pain.

Contribution of co-occurring symptoms to AFI latent class membership

Low versus the high AFI classes—As shown in Table 4, six variables were retained in the final logistic regression model (i.e., income, SCQ16 score, MAX2 index score, and state anxiety, depression, and total sleep disturbance scores). The overall model was significant ($X^2 = 120.84$, $p<.001$). Compared to the high class, patients with a lower income, a higher

level of comorbidity, a higher CTX toxicity score, and higher levels of state anxiety, depressive symptoms, and sleep disturbance were more likely to be in the low AFI class.

Moderate versus the high AFI classes—As shown in Table 5, four variables were retained in the final logistic regression model (i.e., SCQ16 score, type of prior cancer treatment, and trait anxiety and morning energy scores). The overall model was significant ($X^2 = 62.45$, $p<.001$). Compared to the high class, patients with a higher level of comorbidity, higher trait anxiety, and lower levels of morning energy were more likely to be in the moderate AFI class. In addition, compared to patients who did not receive any previous cancer treatments, patients who received only surgery, CTX, or RT or patients who received surgery and CTX, or surgery and RT, or CTX and RT were more likely to be in the moderate AFI class.

DISCUSSION

This study is the first to evaluate the effects of multiple co-occurring symptoms on CRCI in three subgroups of older oncology patients with distinct attentional function profiles. Consistent with Ahles' and Root's hypothesis that an increased risk for persistent cognitive decline is likely related to a variety of physical and psychological factors (Ahles and Root, 2018), for six of the nine symptoms (i.e., trait anxiety, state anxiety, depressive symptoms, sleep disturbance, morning fatigue, evening fatigue), a "dose response" effect was observed with higher symptom severity scores associated with a progressive decline in attentional function (Table 3). For the two remaining symptoms, compared to the high AFI class, older adults in the low and moderate AFI classes had lower levels of morning energy and were more likely to have pain.

In previous studies of older adults in the general population and/or in older oncology patients, associations between cognitive decline and higher levels of anxiety (Fung et al., 2018; Gulpers et al., 2019), depression (Ezzati et al., 2019; Hu et al., 2019; Morin and Midlarsky, 2018), fatigue (Lin et al., 2013), sleep disturbance (Dzierzewski et al., 2018; Tsapanou et al., 2018), and pain (van der Leeuw et al., 2016; Veronese et al., 2018; Whitlock et al., 2017) have been reported. However, our study is the first measure all of these symptoms at the same time and in the same sample and relate them to distinct attentional function profiles in older oncology patients undergoing CTX.

While statistically significant differences were found among the three attentional function classes in the majority of the symptom severity scores, it should be noted that with the exception of worst pain, all of the symptom severity scores in the low AFI class were at or above the clinically meaningful cutpoints. Coupled with the lack of support (i.e., living alone, lower household income), higher level of comorbidity, and poorer functional status, as well as our previous findings of significant decrements in quality of life outcomes (Utne et al., 2018), this subgroup of older adults needs to be identified and have appropriate symptom management interventions (e.g., cognitive-behavioral therapy) and appropriate referrals (e.g., physical therapy) initiated. This recommendation is supported by previous studies that demonstrated an association between increased levels of comorbidity and declines in

functional status and subsequent impairments in older adults' ability to perform routine activities of daily living (Grov et al., 2009, 2010, 2017).

One of the goals of the regression analyses was to identify common and unique characteristics associated with membership in the low and moderate AFI classes. In terms of demographic and clinical characteristics, a higher level of comorbidity was the only common characteristic. Our association is congruent with a study that assessed older patients with breast cancer prior to the initiation of systemic therapy (Mandelblatt et al., 2014b). Compared to healthy controls, in the older patients with breast cancer, comorbidity burden was strongly associated with cognitive impairment. In contrast, in a study that assessed older breast cancer patients prior to and at the end of adjuvant CTX (Lange et al., 2016), a higher level of comorbidity was not associated with cognitive decline. This lack of association may be related to the relatively small sample size and low level of comorbidity in this sample. Additional longitudinal studies are warranted to examine the relationships between changes in cognitive function and specific comorbid conditions and concurrent medications, as well as overall level of comorbidity in older adults undergoing a variety of cancer treatments.

The only demographic characteristic associated with membership in the low AFI class was income. As we noted in our previous paper (Utne et al., 2018), this relationship may be partially explained by interactions between medical and social determinants of health because a lower socioeconomic status increases an individual's risk for chronic conditions (Solar and Irwin, 2010). In fact, in a recent review (Pickett and Wilkinson, 2015), it was noted that income inequality in developed countries leads to an increasing frequency of health problems. Given that compared to other developed countries, the United States has the highest rates of health and social problems related to income inequality (Wilkinson and Pickett, 2009), our findings regarding lower income and higher levels of comorbidity being associated with membership in the low AFI class may be partially explained by this concept.

In terms of treatment characteristics, while a higher MAX2 index score was associated with membership in the low AFI class, the type of previous cancer treatments was associated with membership in the moderate AFI class. While previous studies demonstrated an association between MAX2 index scores and increased incidence of grade 3 or 4 non-hematologic toxicities (Extermann et al., 2004; Extermann et al., 2002) and functional decline (Hoppe et al., 2013), this study is the first to describe an association with this index and cognitive decline in older adults receiving CTX. As for previous cancer treatments, compared to no treatment, older adults who had received a single treatment (i.e., surgery, CTX, or RT) or any combination of two of these treatments were more like to be in the moderate AFI class. This finding supports the hypothesis that any type of cancer treatment can result in changes in cognitive function (Ahles and Root, 2018; Merriman et al., 2013). Whether the receipt of multiple types of cancer treatment results in cumulative decrements in cognitive function remains to be determined.

After controlling for demographic and clinical characteristics, the impact of nine symptom severity scores on AFI group membership was determined. Anxiety was the only symptom that was associated with membership in the low (i.e., state anxiety) and moderate (i.e., trait anxiety) AFI classes. Our association is congruent with two previous prospective reports that

evaluated anxiety as a risk factor for cognitive decline in older adults (Fung et al., 2018; Gulpers et al., 2019). Compared to younger adults, in the older individuals (>65 years), higher levels of anxiety at the time of enrollment were associated with a decline in verbal memory (i.e., immediate and delayed recall) twelve years later (Gulpers et al., 2019). In another study of older adults (≥60 years) with anxiety symptoms (Fung et al., 2018), compared with healthy controls, anxiety symptoms at enrollment predicted a subsequent decline in delayed recall three years later. In contrast, in a study of predictors of mild cognitive impairment in community-dwelling older adults (≥55 years) (Freire et al., 2017), a diagnosis of anxiety at enrollment was not associated with significant cognitive decline two years later. This lack of association may be related to the younger age of this sample. For example, in a study that evaluated for differences in anxiety among three older groups of oncology patients (i.e., 60-69, 70-79, ≥80 years of age), the highest anxiety scores were reported by the oldest patients (Cohen, 2014). Additional longitudinal studies are warranted to examine the relationship between changes in cognitive function and anxiety in different age groups of older oncology patients.

Lower levels of morning energy was the only other symptom associated with membership in the moderate AFI class. Of note, this classes morning energy scores (i.e., 3.9 ± 2.3) were well below the clinically meaningful cutoff score of ≤6.2. One possible explanation for this finding is that older adults are at greater risk of early morning awakenings than younger individuals (Ohayon et al., 2004) or are on medications that may influence morning energy levels.

In terms of the low AFI class, in addition to state anxiety, higher depressive symptom and higher sleep disturbance scores were associated with membership in this class. This finding is consistent with a previous study of older oncology patients from the Health Retirement Study whose cognitive function was evaluated from prior to through four years after their cancer diagnosis (Morin and Midlarsky, 2018). Using latent class analysis, three subgroups of older oncology patients with fairly stable cognitive function trajectories were identified (i.e., lower recall class (30%), middle recall class (52%), and high recall class (18%)). Depressive symptoms after diagnosis was associated only with membership in the low class. In a population based study, that examined the association between depression and cognitive functioning among older adults (≥60 years) (Hu et al., 2019), moderate to severe depressive symptoms were associated with poorer cognitive function primarily in older women.

The association between higher sleep disturbance scores and membership in the low AFI class is consistent with findings from a study that evaluated two cohorts of cognitively healthy elderly (≥65 years) and found that increased sleep problems were associated with increased subjective cognitive decline, independent of demographic and clinical characteristics (Tsapanou et al., 2018). However, in a cross-sectional study of older oncology patients (≥55 years) (Loh et al., 2017), sleep disturbance was not associated with screening positive for possible cognitive impairment. The lack of association may be related to the fact that the presence of sleep problems was based on a dichotomous question “Do you have a sleep problem now?”.

Several study limitations warrant consideration. While the assessment of cognitive function took place after the patients had received their first or second cycle of CTX, these older adults were not assessed prior to the initiation of CTX. Additional research is warranted on changes in cognitive function from prior to through and following the completion of CTX and on its association with co-occurring symptoms. Second, our evaluation of cognitive function was limited to a self-report measure that primarily evaluated changes in executive function. Therefore, our findings regarding changes in attentional function over time, as well as associated demographic, clinical, and co-occurrence of symptoms associated with decrements in attentional function warrant confirmation using subjective and objective measures of various domains of cognitive function. The exact relationships among the symptoms and decrements in cognitive function are undoubtedly complex and warrant investigation in future studies.

Despite these limitations, this study is the first to identify how subgroups of older adults with distinct attentional function profiles differed on the severity of nine common symptoms, as well as which demographic and clinical characteristics and symptom severity scores were associated with membership in two groups with different degrees of cognitive function. While the demographic and clinical characteristics associated with membership in the low and moderate classes are not modifiable, effective symptom management interventions may improve cognitive function in older oncology patients. Clinicians need to assess patients for decrements in attentional function and multiple co-occurring symptoms and prescribe evidenced-based interventions to decrease patients' overall symptom burden. Longitudinal studies are needed to evaluate the timing of the occurrence and severity of common symptoms to determine which symptom or symptoms is driving the occurrence and severity of these co-occurring symptoms.

Acknowledgements:

This work was supported by the National Cancer Institute (R01CA134900 and K05CA168960), the National Institute on Aging (T32AG000212) and the National Center for Advancing Translational Studies (KL2TR001870). Dr. Miaskowski is an American Cancer Society Clinical Research Professor.

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Highlights

Older adults experience numerous concurrent symptoms.

Worsening attentional function is associated with a higher symptom burden.

A “dose response effect” was observed with higher symptom scores and a progressive decline in attentional function.

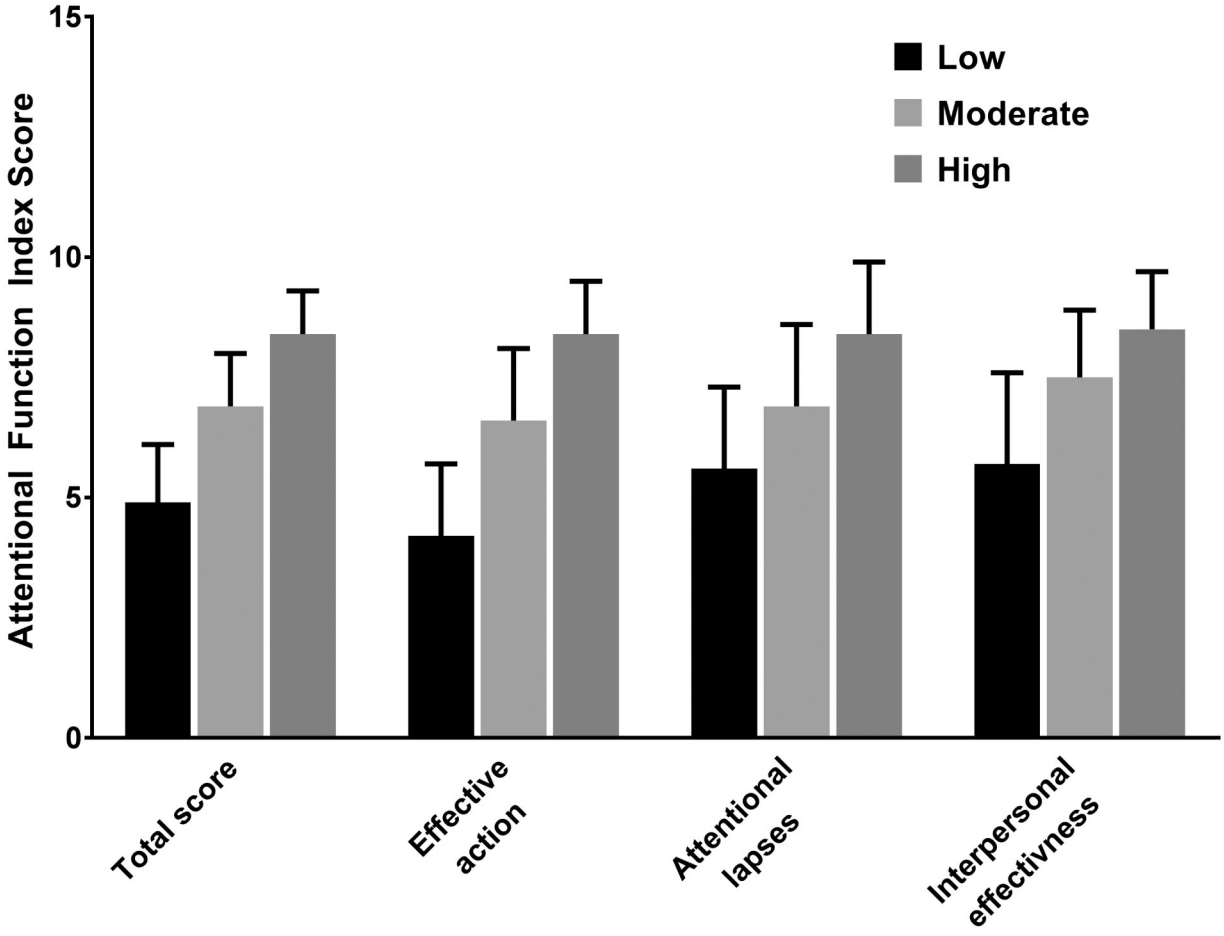

Figure 1.

Differences among the three attentional function classes in total and subscale scores for the Attentional Function Index. All values are expressed as means ± standard deviations. All post hoc comparisons are significant at the p <.001 level (i.e., low < moderate < high).

Table 1

Differences in Demographic, Clinical, and Symptom Characteristics Between the Low (n=134) and High (n=95) Attentional Function Latent Classes

Characteristic	Low Mean (SD)	High Mean (SD)	Statistics
Age (years)	71.8 (5.4)	70.2 (5.1)	$t = 2.29$, p=.023
Education (years)	16.3 (3.0)	16.4 (3.0)	$t = -0.25$, p=.800
Body mass index (kg/m^2)	26.3 (5.4)	25.7 (6.0)	$t = 0.85$, p=.398
Karnofsky Performance Status score	77.7 (13.3)	87.8 (10.0)	$t = -6.36$, p<.001
Number of comorbidities out of 16	3.7 (1.9)	2.8 (1.7)	$t = 3.44$, p=.001
SCQ score out of 16 conditions	8.2 (4.3)	5.6 (3.3)	$t = 4.98$, p<.001
AUDIT score	3.1 (3.0)	2.7 (1.5)	$t = 0.94$, p=.350
Hemoglobin	11.3 (1.4)	11.7 (1.3)	$t = -2.03$, p=.044
Hematocrit	33.9 (4.2)	35.1 (3.8)	$t = -2.23$, p=.027
Time since cancer diagnosis (years)	2.4 (4.4)	3.1 (5.2)	U, p=.543
Time since cancer diagnosis (median)	0.5	0.5	
Number of prior cancer treatments	1.8 (1.6)	1.6 (1.6)	$t = 1.10$, p=.273
Number of metastatic sites including lymph node involvement	1.3 (1.3)	1.4 (1.2)	$t = -0.13$, p=.900
Number of metastatic sites excluding lymph node involvement	0.9 (1.1)	0.9 (1.0)	$t = -0.15$, p=.884
MAX2 score	0.17 (0.09)	0.14 (0.08)	$t = 2.69$, p=.008
	% (n)	**% (n)**	
Gender			
Female	73.5 (97)	60.0 (57)	FE, p=.030
Male	25.8 (34)	40.0 (38)	
Transgender *	0.8 (1)	0.0 (0)	
Ethnicity			
White	77.1 (101)	77.9 (74)	
Asian or Pacific Islander	7.6 (10)	6.3 (6)	X^2=1.13, p=.771
Black	7.6 (10)	10.5 (10)	
Hispanic, Mixed, or Other	7.6 (10)	5.3 (5)	
Married or partnered (% yes)	50.8 (66)	69.6 (64)	FE, p=.006
Lives alone (% yes)	36.2 (47)	20.9 (19)	FE, p=.017
Child care responsibilities (% yes)	3.9 (5)	6.4 (6)	FE, p=.533
Care of adult responsibilities (% yes)	6.2 (7)	2.3 (2)	FE, p=.304
Currently employed (% yes)	14.5 (19)	29.0 (27)	FE, p=.011
Income			
< $30,000	37.7 (43)	14.7 (11)	
$30,000 to <$70,000	28.9 (33)	12.0 (9)	U, p<.001
$70,000 to < $100,000	9.6 (11)	28.0 (21	
≥ $100,000	23.7 (27)	45.3 (34)	
Exercise on a regular basis (% yes)	63.0 (80)	76.8 (73)	FE, p=.029
Smoking, current or history of (% yes)	48.8 (63)	44.7 (42)	FE, p=.588

Characteristic	Low Mean (SD)	High Mean (SD)	Statistics
Cancer diagnosis			
Breast	25.0 (33)	18.9 (18)	
Gastrointestinal	28.0 (37)	42.1 (40)	X^2=5.18, p=.159
Gynecological	20.5 (27)	18.9 (18)	
Lung	26.5 (35)	20.0 (19)	
Type of prior cancer treatment			
No prior treatment	22.5 (29)	36.2 (34)	
Only surgery, CTX, or RT	36.4 (47)	24.5 (23)	X^2=6.13, p=.106
Surgery & CTX, or Surgery & RT, or CTX &RT	25.6 (33)	24.5 (23)	
Surgery & CTX & RT	15.5 (20)	14.9 (14)	
Trait anxiety	40.5 (11.0)	26.2 (6.2)	t = 12.27, p<.001
State anxiety	38.9 (13.2)	24.7 (6.9)	t = 10.35, p<.001
Attentional function	16.8 (10.0)	4.6 (4.0)	t = −26.24, p<.001
Depressive symptoms	58.8 (17.2)	36.4 (15.3)	t = 12.49, p<.001
Sleep disturbance	3.8 (2.2)	1.3 (1.5)	t = 9.91, p<.001
Morning fatigue	5.6 (2.0)	3.7 (2.1)	t = 10.20, p<.001
Evening fatigue	3.6 (2.0)	5.7 (2.9)	t = 6.41, p<.001
Morning energy	3.3 (2.0)	4.7 (2.1)	t = −5.907, p<.001
Evening energy	16.8 (10.0)	26.2 (6.2)	t = −5.08, p<.001
Presence of pain	75.6 (99)	49.5 (46)	FE, p<.001

Abbreviations: AUD IT = Alcohol Use Disorders Identification Test, CTX = chemotherapy, FE = Fisher's Exact test, kg = kilograms, m^2 = meter squared, RT = radiation therapy, SCQ = Self-Administered Comorbidity Questionnaire, SD = standard deviation, U = Mann Whitney U test

*Chi Square analysis done without the transgender patient include in the analyses

Table 2

Differences in Demographic, Clinical, and Symptom Characteristics Between the Moderate (n=136) and High (n=95) Attentional Function Latent Classes

Characteristic	Moderate Mean (SD)	High Mean (SD)	Statistics
Age (years)	71.7 (5.9)	70.2 (5.1)	$t = 2.08$, p=.039
Education (years)	16.7 (3.2)	16.4 (3.0)	$t = 0.57$, p=.572
Body mass index (kg/m^2)	26.2 (4.8)	25.7 (6.0)	$t = 0.75$, p=.455
Karnofsky Performance Status score	83.8 (11.9)	87.8 (10.0)	$t = -2.68$, p=.008
Number of comorbidities out of 16	3.2 (1.6)	2.8 (1.7)	$t = 1.81$, p=.072
SCQ score out of 16 conditions	7.0 (3.9)	5.6 (3.3)	$t = 2.84$, p=.005
AUDIT score	3.1 (2.6)	2.7 (1.5)	$t = 1.16$, p=.250
Hemoglobin	11.5 (1.5)	11.7 (1.3)	$t = -1.14$, p=.257
Hematocrit	34.4 (4.5)	35.1 (3.8)	$t = -1.24$, p=.215
Time since cancer diagnosis (years)	3.3 (5.9)	3.1 (5.2)	U, p=.543
Time since cancer diagnosis (median)	0.6	0.5	
Number of prior cancer treatments	1.8 (1.4)	1.6 (1.7)	$t = 1.08$, p=.282
Number of metastatic sites including lymph node involvement	1.4 (1.1)	1.4 (1.2)	$t = 0.39$, p=.694
Number of metastatic sites excluding lymph node involvement	0.9 (1.0)	0.9 (1.0)	$t = 0.08$, p=.940
MAX2 score	0.15 (0.08)	0.14 (0.08)	$t = 0.70$, p=.484
	% (n)	**% (n)**	
Gender			
Female	69.6 (94)	60.0 (57)	FE, p=.159
Male	30.4 (41)	40.0 (38)	
Ethnicity			
White	84.3 (113)	77.9 (74)	
Asian or Pacific Islander	5.2 (7)	6.3 (6)	X^2=5.98, p=.113
Black	3.0 (4)	10.5 (10)	
Hispanic, Mixed, or Other	7.5 (10)	5.3 (5)	
Married or partnered (% yes)	59.7 (80)	69.6 (64)	FE, p=.159
Lives alone (% yes)	29.9 (40)	20.9 (19)	FE, p=.165
Child care responsibilities (% yes)	4.5 (6)	6.4 (6)	FE, p=.561
Care of adult responsibilities (% yes)	5.8 (7)	2.3 (2)	FE, p=.308
Currently employed (% yes)	23.1 (31)	29.0 (27)	FE, p=.354
Income			
< $30,000	16.9 (21)	14.7 (11)	
$30,000 to <$70,000	29.8 (37)	12.0 (9)	U, p<.001
$70,000 to < $100,000	18.5 (23)	28.0 (21)	
≥ $100,000	34.7 (43)	45.3 (34)	
Exercise on a regular basis (% yes)	61.4 (81)	76.8 (73)	FE, p=.015
Smoking, current or history of (% yes)	48.5 (64)	44.7 (42)	FE, p=.591
Cancer diagnosis			X^2=3.90, p=.272

Characteristic	Moderate Mean (SD)	High Mean (SD)	Statistics
Breast	24.4 (33)	18.9 (18)	
Gastrointestinal	30.4 (41)	42.1 (40)	
Gynecological	25.2 (34)	18.9 (18)	
Lung	20.0 (27)	20.0 (19)	
Type of prior cancer treatment			
No prior treatment	16.3 (21)	36.2 (34)	
Only surgery, CTX, or RT	40.3 (52)	24.5 (23)	X^2=14.2, p=.003
Surgery & CTX, or Surgery & RT, or CTX & RT	31.8 (41)	24.5 (23)	
Surgery & CTX & RT	11.6 (15)	14.9 (14)	
Trait anxiety	32.7 (8.1)	26.2 (6.2)	t = 6.76, p<.001
State anxiety	30.8 (9.9)	24.7 (6.9)	t = 5.45, p<.001
Depressive symptoms	9.9 (7.3)	4.6 (4.0)	t = 7.07, p<.001
Sleep disturbance	47.6 (16.1)	36.4 (15.3)	t = 5.18, p<.001
Morning fatigue	2.3 (1.9)	1.3 (1.5)	t = 4.57, p<.001
Evening fatigue	4.7 (2.0)	3.7 (2.1)	t = 3.32, p=.001
Morning energy	3.9 (2.3)	5.7 (2.9)	t = −5.02, p<.001
Evening energy	3.6 (2.0)	4.7 (2.1)	t = −4.05, p<.001
Presence of pain	71.9 (97)	49.5 (46)	FE, p=.001

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, CTX = chemotherapy, FE = Fisher's Exact test, kg = kilograms, m^2 = meter squared, RT = radiation therapy, SCQ = Self-Administered Comorbidity Questionnaire, SD = standard deviation, U = Mann Whitney U test

Table 3

Differences in Co-Occurring Symptom Severity Scores at Enrollment Among the Attentional Function Latent Classes

Symptoms	Low (0) 36.7% (n=134)	Moderate (1) 37.3% (n=136)	High (2) 26.0% (n=95)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Trait anxiety (STAI-T score ≥31.8)	40.5 (11.0)	32.7 (8.1)	26.2 (6.2)	F=71.71, p<.001 0>1 >2
State anxiety (STAI-S score ≥32.2)	38.9 (13.2)	30.8 (9.9)	24.7 (6.9)	F=50.15, p<.001 0>1 >2
Depressive symptoms (CES-D score ≥16.0)	16.8 (10.0)	9.9 (7.3)	4.6 (4.0)	F=69.89, p<.001 0>1 >2
Sleep disturbance (GSDS score ≥43.0)	58.8 (17.2)	47.6 (16.1)	36.4 (15.3)	F=50.52, p<.001 0>1 >2
Morning fatigue (LFS score ≥3.2)	3.8 (2.2)	2.3 (1.9)	1.3 (1.5)	F=49.22, p<.001 0>1 >2
Evening fatigue (LFS score ≥5.6)	5.6 (2.0)	4.7 (2.0)	3.7 (2.1)	F=21.41, p<.001 0>1 >2
Morning energy (LFS score ≤6.2)	3.6 (2.0)	3.9 (2.3)	5.7 (2.9)	F=23.07, p<.001 0 and 1 < 2
Evening energy (LFS score ≤3.5)	3.3 (2.0)	3.6 (2.0)	4.7 (2.1)	F=14.01, p<.001 0 and 1 < 2
Worst pain	6.4 (2.3)	5.3 (2.5)	5.4 (2.5)	F=4.39, p=.014 0>1
	% (n)	% (n)	% (n)	
Pain				F=25.40, p<.001
No pain	24.8 (32)	28.4 (38)	50.5 (47)	0 and 1 < 2
Only cancer pain	12.4 (16)	17.2 (23)	12.9 (12)	NS
Only non-cancer pain	24.8 (32)	29.9 (40)	20.4 (19)	NS
Both cancer and non-cancer pain	38.0 (49)	24.6 (33)	16.1 (15)	0>2

Abbreviations: CES-D = Center for Epidemiological Studies-Depression Scale, LFS = Lee Fatigue Scale, GSDS = General Sleep Disturbance Scale, SD = standard deviation; STAI-T = Spielberger State Anxiety Inventory, STAI-T = Spielberger Trait Anxiety Inventory

Table 4

Logistic Regression Analysis of Phenotypic Characteristics and Co-occurring Symptoms Associated with Membership in the Low Attentional Function Class

	OR	95% CI	p-value
Income	0.44	0.25 – 0.78	.004
SCQ score out of 16 conditions	1.32	1.10 – 1.58	.003
MAX2 score	1.14	1.04 – 1.24	.007
State anxiety	1.08	1.00 – 1.16	.038
Depressive symptoms	1.19	1.03 – 1.38	.018
Sleep disturbance	1.08	1.03 – 1.13	.002
Overall model fit: degrees of freedom = 6, X^2 = 120.84, p<.001			

Abbreviations: CI = confidence interval, OR = odds ratio, SCQ = Self-administered Comorbidity Questionnaire

Table 5

Logistic Regression Analysis of Phenotypic Characteristics and Co-occurring Symptoms Associated with Membership in the Moderate Attentional Function Class

	OR	95% CI	p-value
SCQ score out of 16 conditions	1.14	1.00 - 1.29	0.04
Type of prior cancer treatment (Ref = No treatment)			
Only surgery, CTX or RT	10.31	3.26 - 32.63	<0.001
Surgery & CTX, or surgery & RT, or CTX and RT	4.35	1.51 - 12.52	<0.001
Surgery & CTX & RT	1.59	0.46 – 5.50	0.462
Trait anxiety	1.15	1.07 – 1.23	<0.001
Morning energy	0.78	0.66 – 0.91	.002
Overall model fit: degrees of freedom = 6, $X^2 = 62.45$, p<.001			

Abbreviations: CI = confidence interval, CTX = chemotherapy, OR = odds ratio, RT = radiation therapy, SCQ = Self-administered Comorbidity Questionnaire