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CO-OCCURRENCE OF DECREMENTS IN PHYSICAL AND COGNITIVE FUNCTION IS COMMON IN OLDER ONCOLOGY PATIENTS RECEIVING CHEMOTHERAPY

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Abstract

Purpose: Older adults receiving cancer chemotherapy are at increased risk for decrements in physical (PF) and cognitive (CF) function.

Objectives: Study identified subgroups of patients with distinct PF and CF profiles; risk factors associated with subgroup membership; and impact of subgroup membership on quality of life (QOL).

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Methods: In 366 older oncology patients, PF and CF were assessed using the Physical Component Summary (PCS) of the SF-12 and Attentional Function Index, respectively. Latent profile analysis was used to identify subgroups of older patients with distinct PF/CF profiles.

Results: Three distinct PF/CF profiles were identified (i.e., Very Low PF+Moderate CF (15.6%); Low PF+Low CF (39.3%), Normal PF+Normal CF (45.1%)). Compared to the both Normal class, patients in the other two classes had a lower functional status, a worse comorbidity profile, and were less likely to exercise on a regular basis. Compared to the Both Normal class, patients in the Both Low class were less likely to be married/partnered, more likely to live alone, less likely to be employed, and more likely to report depression and back pain. Compared to the other two classes, patients in the Both Low class had a lower annual household income and were receiving chemotherapy with a worse toxicity profile.

Conclusion: First study to use a person-centered analytic approach to identify subgroups of older adults with distinct PF/CF profiles. Fifty-five percent of the older adults had statistically significant and clinically meaningful decrements in both PF AND CF that had negative effects on all aspects of QOL.

Keywords

older adult; chemotherapy; cancer; physical function; cognitive function; patient reported outcomes

INTRODUCTION

While over 60% of cancers are diagnosed in individuals over 60 years (Siegel et al., 2019), the administration of chemotherapy to older adults is complex due to the high degree of heterogeneity in the aging process and the large amount of inter-individual variability in treatment tolerability (Jolly et al., 2015). In addition, older patients may be at increased risk for chemotherapy-induced decrements in both physical function (PF) and cognitive function (CF) (Kenis et al., 2017; Mandelblatt et al., 2013; Wildiers et al., 2014). While studies have identified risk factors associated with the inability to complete treatment (Puts et al., 2012; Puts et al., 2014), less is known about factors associated with declines in PF and CF in older adults during chemotherapy (Joly et al., 2015; van Abbema et al., 2019).

Limited evidence suggests that compared to age-matched controls, PF deteriorates at an accelerated rate in older adults following a cancer diagnosis (Brown et al., 2016; Puts et al., 2012; Wildiers et al., 2014). For example, in a study that evaluated 364 patients 70 years prior to their first or second cycle of chemotherapy (Hoppe et al., 2013), 17% reported functional decline. In the multivariable model that adjusted for activities of daily living (ADL) and MAX2 scores (i.e., a measure of toxicity of the chemotherapy regimen) (Extermann et al., 2004) at enrollment, higher depression and lower instrumental ADL (IADL) scores were associated with higher rates of functional decline. In another study that assessed 387 patients (i.e., 70 years) 2 to 3 months after initiation of chemotherapy (Kenis et al., 2017), 20% and 41% of them had declines in ADL and IADL, respectively. Lower IADL scores at enrollment were associated with an increased risk for functional decline. These findings (Hoppe et al., 2013; Kenis et al., 2017), as well as our previous work

(Miaskowski et al., 2017b; Wong et al., 2018), suggest that among older adults, a large amount of inter-individual variability exists in the effects of chemotherapy on patients' functional status.

Cancer-related cognitive impairment (CRCI) occurs in 12% to 75% of patients receiving chemotherapy (Loh et al., 2016). While findings regarding age differences in CRCI are inconclusive (Bompaire et al., 2017; Wefel et al., 2015), evidence suggests that compared to healthy controls, older patients undergoing chemotherapy experience a decline in CF (Ahles and Root, 2018; Lange et al., 2014). For example, in a study of patients 65 years with early stage breast cancer who were evaluated for changes in CF before and at the completion of adjuvant treatment (i.e., chemotherapy or radiation therapy) (Lange et al., 2019), five patterns of change were identified. Of the 118 patients evaluated, compared to healthy age-matched controls (n=62), 49% had a cognitive decline. Of these patients, 24% had comparable scores to healthy controls prior to treatment and experienced cognitive decline but did not develop cognitive impairment; 64% had comparable scores to healthy controls prior to treatment and experienced cognitive impairment; and 12% had cognitive impairment prior to treatment that increased following treatment. In another study of older women with breast cancer (i.e., 65 years, n=50) who were assessed prior to and six months after the completion of chemotherapy (Hurria et al., 2006), 51% perceived a decline in memory at 6 months. In addition, 63% of the patients who perceived poor memory prior to chemotherapy were more likely to report further memory deterioration after chemotherapy. Similar to PF, and congruent with our previous studies (Utne et al., 2019; Utne et al., 2018), a large amount of inter-individual variability exists in chemotherapy-induced changes in CF in older adults.

As noted in reviews from the geriatric literature (Bherer, 2015; Carvalho et al., 2014; Cohen et al., 2016; Kirk-Sanchez and McGough, 2014; Montero-Odasso et al., 2019; Montero-Odasso et al., 2015; Montero-Odasso et al., 2012), an accumulating body of evidence suggests that decrements in PF and CF are highly related and often co-occur as people age. However, as noted in one review (Montero-Odasso et al., 2019), most geriatricians and geriatric researchers have evaluated and managed impairments in PF and CF separately. The same statement can be made for research in geriatric oncology. Given this gap in knowledge, as well as the fact that older adults are heterogeneous in terms of their levels of PF and CF (Santoni et al., 2017), it is extremely important to evaluate which demographic and clinical characteristics place older patients at higher risk for poorer PF and/or CF during chemotherapy.

In this paper, in order to evaluate the effects of decrements in BOTH PF and CF, we used a person-centered analytic approach, namely, latent profile analysis (LPA) (Jung and Wickrama, 2008) to identify subgroups of older adults with distinct PF AND CF profiles. In addition, to identify modifiable and nonmodifiable risk factors associated with these PF/CF profiles, we evaluated how these subgroups differed on demographic and clinical characteristics and QOL outcomes.

METHODS

Patients and Settings

Details on the larger study are published elsewhere (Miaskowski et al., 2017a; Miaskowski et al., 2014). In brief, in the larger study, eligible patients were 18 years; had a diagnosis of breast, gastrointestinal, gynecological, or lung cancer; had received chemotherapy within the preceding four weeks; were scheduled to receive at least two additional cycles of chemotherapy; were able to read, write, and understand English; and gave written informed consent. Recruitment occurred at two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. Of the 2234 patients approached during their first or second cycle of chemotherapy, 1343 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with their cancer treatment. For this paper, data from patients who were 65 years of age (n=362) were used in the LPA.

Instruments

Patients completed a demographic questionnaire; Karnofsky Performance Status scale (Ando et al., 2001; Schnadig et al., 2008); Self-Administered Comorbidity Questionnaire (SCQ) (Sangha et al., 2003); and Alcohol Use Disorder Identification Test (AUDIT) (Babor et al., 2001).

Changes in PF were assessed using the physical component summary (PCS) score from the Medical Outcomes Study-Short Form 12 (SF-12) (Ware et al., 1996). The SF-12 consists of 12 questions about physical and mental health as well as overall health status. The SF-12 was scored into two components (i.e., physical component summary (PCS) score and mental component summary (MCS) score) that evaluate physical and psychological function, respectively. These scores can range from 0 to 100 with higher scores indicating better function.

Changes in CF were assessed using the 16-item Attentional Function Index (AFI) that evaluates attention and executive function (Cimprich et al., 2011). A higher total mean score on a 0 to 10 numeric rating scale (NRS) indicates better CF (Cimprich et al., 2011). Total scores are grouped into categories of attentional function (i.e., <5 low function, 5.0 to 7.5 moderate function, >7.5 high function) (Cimprich et al., 2005). The Cronbach's α for the total AFI score was 0.93.

Disease-specific QOL was evaluated using the Quality of Life Scale-Patient Version (QOL-PV) (Padilla et al., 1990; Padilla et al., 1983). This 41-item instrument measures four domains of QOL (i.e., physical, psychological, social, spiritual well-being) and overall QOL. Each item was rated on a 0 to 10 NRS with higher scores indicating a better QOL. The Cronbach's α for the total QOL score was 0.92.

Study Procedures

This study was approved by the Committee on Human Research at the University of California, San Francisco and the Institutional Review Board at each study site. Eligible

patients were approached, during their first or second cycle of chemotherapy, by a research staff member in the infusion unit to discuss participation in the study. Written informed consent was obtained from all patients. Patients completed questionnaires in their homes, a total of six times over two cycles of chemotherapy (i.e., prior to their next cycle of chemotherapy, Assessments 1 and 4; approximately 1 week after chemotherapy administration, Assessments 2 and 5; and approximately 2 weeks after chemotherapy administration, Assessments 3 and 6).

Medical records were reviewed for disease and treatment information. Toxicity of each patients' chemotherapy regimen was rated using the MAX2 index. A MAX2 score is the average of the most frequent grade 4 hematologic toxicity and the most frequent grade 3 to 4 nonhematologic toxicity reported in publications of a regimen and correlates well with overall risk of severe toxicity for that regimen (Aapro et al., 2000; Extermann et al., 2004; Extermann et al., 2002; Extermann et al., 2015).

Data Analysis

Latent profile analysis (LPA) was used to identify subgroups of older patients with distinct PF/CF profiles. This LPA was done with the combined set of variables (i.e., PCA AND AFI scores) over time (i.e., using the PCS and AFI scores obtained during the six assessments in a single LPA). This approach provides a profile description of **two outcomes** with parallel profiles over time. The LPA was done using Mplus version 8-4 (Muthen and Muthen, 1998–2020).

In order to incorporate expected correlations among the repeated measures of the same variable and cross-correlations of the series of the two variables (i.e., PCS and AFI scores), we included covariance parameters among measures at the same occasion and those that were one or two occasions apart. Covariances of each variable with the other at the same assessments were included in the model and autoregressive covariances were estimated with a lag of two with the same measures and with a lag of one for each variable's series with the other variable. We limited the covariance structure to a lag of two to accommodate the expected reduction in the correlations that would be introduced by two chemotherapy cycles within each set of three measurement occasions and to reduce model complexity (Jung and Wickrama, 2008).

Data were analyzed using SPSS version 23 (IBM Corporation, Armonk, NY). Descriptive statistics and frequency distributions were calculated for demographic and clinical characteristics. Differences among the PF/CF classes in demographic and clinical characteristics and QOL outcomes were evaluated using parametric and nonparametric tests. A Bonferroni corrected p-value of <0.017 (i.e., 0.05/3) was considered statistically significant for the pairwise contrasts.

RESULTS

Results of the LPA

As shown in Table 1, the three-class solution was chosen because it fit better than the two-class solution and the profiles of means for the PCS and AFI scores within each class were

clinically meaningfully different. As shown in Figure 1, the trajectories for the PF and CF scores differed among the latent classes. Using the normative score for the PCS (i.e., 50) (Ware et al., 1996) and the clinically meaningful cutoff scores for the AFI (i.e., <5 low function, 5.0 to 7.5 moderate function, >7.5 high function) (Cimprich et al., 2005), the three PF/CL classes were named: Very Low PF and Moderate CF (15.6%, Very Low PF + Moderate CF); Low PF and Low CF (39.3%, Both Low), and Normal PF and Normal CF (45.1%, Both Normal). Within each of the three classes, both the PF and CF trajectories remained relatively stable over the two cycles of chemotherapy (Figure 1).

Differences in Demographic and Clinical Characteristics

Compared to the Both Normal class, patients in the Very Low PF + Moderate CF class were older, had lower hemoglobin and hematocrit levels, were a longer time from their initial cancer diagnosis, and were more likely to report lung disease. Compared to the Both Normal class, patients in the other two classes had lower KPS scores, a worse comorbidity profile, and were less likely to exercise on a regular basis. Compared to the Both Normal class, patients in the Both Low class were less likely to be married or partnered, more likely to live alone, less likely to be employed, and more likely to report depression and back pain. Compared to the other two classes, patients in the Both Low class had a higher MAX2 score and a lower annual household income. No differences in gender or education were found among the three PF/CF classes (Table 2).

Differences in Generic QOL Outcomes

Compared to the Both Normal class, patients in the other two classes reported lower scores on the role physical, bodily pain, vitality, and social functioning subscales of the SF-12. For the physical functioning and general health subscales and the PCS scores, significant differences were found among the three classes (i.e., Very Low PF + Moderate CF < Both Low < Both Normal). For the mental health subscale and the MCS, compared to the other two classes, patients in the Both Low class reported lower scores (Table 3).

Differences in Disease-specific QOL

For the QOL-PV physical well-being, social well-being, and total QOL scores, compared to the Both Normal class, patients in the other two classes reported lower scores. For the psychological well-being subscale, significant differences were found among the three classes (i.e., Both Low < Very Low PF + Moderate CF < Both Normal). No differences were found among the three classes in the spiritual well-being scores (Table 3).

DISCUSSION

This study is the first to characterize three classes of older oncology patients with distinct PF and CF profiles. Using valid and reliable self-report measures of PF and CF with well-established clinically meaningful cutpoints, 55% of our sample had deficits in both of these extremely important patient-reported outcomes. At enrollment, the Both Low class had a mean PCS score of 38.0 and a mean AFI score of 5.0 which when compared to the scores of the older adults in the Both Normal class represent not only statistically significant, but clinically meaningful decrements in both PF ($d = 0.87$) and CF ($d = 1.56$). In addition,

compared to the Both Normal class, patients in the Very Low PF + Moderate CF class had clinically meaningful decrements in both PF ($d = 1.70$) and CF ($d = 0.57$).

In the geriatric literature, evidence suggests that the coexistence of declines in PF and CF are associated with pathophysiologic changes within the central nervous system, even in the absence of overt neurological disorders (Cohen et al., 2016; Montero-Odasso et al., 2019; Montero-Odasso et al., 2012; Rosso et al., 2013). The brain areas and networks that are involved in both gait control and navigation (i.e., prefrontal cortex, hippocampus) are essential for higher levels of CF. As individuals age, these areas are susceptible to white matter changes and cerebral infarcts (Montero-Odasso and Hachinski, 2014). While associations between changes in brain structure and function and chemotherapy-induced changes in balance and gait have not been evaluated, recent findings suggest that chemotherapy-induced changes in the prefrontal cortex and hippocampus are associated with CRCI (Chen et al., 2019; Chen et al., 2017; Feng et al., 2019; Zhang et al., 2019). Research is warranted to determine the underlying mechanisms for chemotherapy-induced decrements in both PF and CF in older adults. Clinicians need to assess for both problems because evidence in the geriatric literature suggests that the co-occurrence of mobility and cognitive impairments place older adults at increased risk for falls and fractures, as well as dementia syndromes (Montero-Odasso et al., 2019).

While no studies were found in oncology patients, our finding that 45.1% of our older adults had normal levels of both PF and CF is consistent with a previous report from a large cohort study that found that before age 85 at least half of the older adults evaluated had no disabilities, although they had chronic disorders and some functional impairment (Santoni et al., 2017). However, high levels of inter-individual variability in health status were identified that markedly increased after age 70. Given that changes in health status occur more rapidly in older adults, the identification of characteristics that place older oncology patients at higher risk for worse PF and CF may assist patients and clinicians to make more informed decisions about treatment options and management strategies.

Health status is determined not only by biological factors, but by complex interactions among social, cultural, and economic factors; one's physical environment; and individual's choices regarding health behaviors. In addition, based on their social status, individuals experience differences in exposure and vulnerability to health-compromising conditions (McGilton et al., 2018). Therefore, it is interesting to note that compared to the Both Normal class, a number of demographic characteristics were associated with being in either the Very Low PF + Moderate CF (i.e., older age) or Both Low (i.e., less likely to be married or partnered, more likely to live alone, being unemployed) classes. Although each of these risk factors can place older adults in a vulnerable position, it is possible that in our two classes with lower levels of PF and CF, these factors are inter-related and mediate the effects of the socio-economic health gradient.

In terms of clinical characteristics, compared to the older adults in the Both Normal class, patients in the other two classes had a higher number of comorbidities, a higher comorbidity burden, and a lower KPS score. While the authors of a recent paper called for the adaptation of clinical trials to account for comorbidities in oncology patients (Williams et al., 2016), in

a recent systematic review of predictors of chemotherapy intolerance in older oncology patients (van Abbema et al., 2019), in 3 of 9 studies, a higher number of comorbidities was associated with worse chemotherapy toxicity and in 5 of 11 studies, a higher level of comorbidity was associated with chemotherapy discontinuation. However, no studies were identified that examined the association between the administration of chemotherapy and functional decline. In another study that aimed to identify modifiable factors that affected older adults functional status during cancer treatment (Kirkhus et al., 2019), while a higher number of comorbidities was associated with functional decline in the univariate analysis, it was not a significant predictor in the multivariable model. These inconsistent findings in older oncology patients contrast with the geriatric literature that suggests that a worse comorbidity profile is associated with declines in both PF and CF (Collins et al., 2018; Snowden et al., 2017; Steeves et al., 2019). These inconsistent findings may be related to the fact that in previous studies of older oncology patients changes in PF and CF were evaluated separately or patients with decrements in PF were excluded from participation.

The specific comorbidities that differed between the Both Normal and the Both Low classes were depression (9.1% vs 29.1%) and back pain (18.2% vs 32.6%). Within the geriatric literature, findings from several reviews suggest that relationships exist among depression, cognitive impairments, and decrements in physical activity (Blanchet et al., 2018; Hu et al., 2019; Shimada et al., 2014). While less well studied in older oncology patients, similar associations are being identified (Bedillion et al., 2019; Magnuson et al., 2016; Magnuson et al., 2019). Recent evidence suggests that exercise has beneficial effects on brain health which contributes to decreased risks for dementia, depression, and stress (Pedersen, 2019; Phillips, 2017; Phillips and Fahimi, 2018). While the benefits of exercise for cancer-related fatigue are well documented (Meneses-Echavez et al., 2015; Tomlinson et al., 2014), recent reviews and meta-analyses suggest that it has beneficial effects on other common symptoms associated with cancer and its treatments (Chen et al., 2020; Khosravi et al., 2019; Nadler et al., 2019; Stout et al., 2017). It should be noted that compared to the Both Normal class (76.8%), a significantly lower percentage of older adults in the other two classes reported that they exercised on a regular basis (44.6% and 62.2%). Oncology clinicians need to assess older patients' level of physical activity and exercise regimen, recommend regular exercise, and make appropriate referrals to physical therapy.

In both classes of older adults with lower levels of PF and CF, 33% of the patients reported back pain. This prevalence rate is consistent with an epidemiologic study of back pain in older adults that found that non-disabling back pain occurred in 23% of participants (Docking et al., 2011). Risk factors for the occurrence of back pain included: poorer self-rated health, previous episode of back pain, and depressive symptoms. Our findings of significant decrements in general health and high occurrence rates for depression in the Both Low class are consistent with these findings in the general population. Oncology clinicians need to do a comprehensive review of co-occurring comorbidities as well as their impact on older patients' levels of PF and CF.

An interesting finding from this study is that the majority of clinical characteristics associated with PF/CF class membership were identified in the older adults in the Very Low PF + Moderate CF class (i.e., lower hemoglobin and hematocrit levels, longer time since

initial cancer diagnosis, higher number of metastatic sites). However, older adults in the Both Low class were more likely to receive chemotherapy regimens that had the potential to be more toxic (i.e., had higher MAX2 scores) and more emetogenic. Our findings are not consistent with a previous study of older oncology patients (≥ 65 years) that examined clinical factors associated with disability (Pamoukdjian et al., 2017). In the multivariable analyses, while impaired mobility, poor functional status, and CRCI were independently associated with disability, none of these outcomes were associated with cancer diagnosis or presence of metastatic disease. Additional studies are warranted to determine which disease and treatment characteristics have the greatest impact on older adults PF and CF.

Consistent with our hypothesis, compared to the Both Normal class, older adults in the other two classes reported statistically significant and clinically meaningful decrements in most of the domains of QOL, except spiritual well-being, that were assessed using both the generic and disease-specific measures. In addition, patients in the Very Low PF + Moderate CF (17.4) and Both Low (37.4) classes, reported PCS scores that were well below the clinically meaningful cutoff of 50 for the general population. Similarly, older adults in the Both Low class reported an MCS score (43.3) that was below the normative score of 50 (Ware et al., 1996). These findings are consistent with a previous report on the effects of age on health-related QOL that found that compared to the general population, oncology patients had a worse QOL and that as patients aged PF decreased (Quinten et al., 2015).

In a recent systematic review of qualitative studies that explored the meaning of QOL to older adults (van Leeuwen et al., 2019), participants noted that one important aspect of QOL was that they felt healthy and not limited by their physical condition. They stated that unrelieved symptoms, side effects of medications, and functional limitations significantly decreased their QOL. Given that international action plans on ageing endorse the importance of QOL (Malva and Bousquet, 2016), and the maintenance of QOL is one of the most important outcomes of care services for older adults (van Leeuwen et al., 2019), our findings suggest that older patients with impairments in both PF and CF need additional support from clinicians during chemotherapy.

A number of limitations warrant consideration. While we used valid and reliable self-report measures to assess PF and CF, future studies need to assess both outcomes using objective measures and examine associations among these measures. In addition, while we assessed both outcomes over two cycles of chemotherapy, additional research is warranted that evaluates both of these patient-reported outcomes in older adults from the initiation to the completion of chemotherapy, as well as their relationships to biomarkers of aging. Finally, additional research is warranted that evaluates the impact of family, social relationships, and community resources on older adults' PF and CF.

Despite these limitations, our findings provide new insights into the occurrence of and impact from deficits in PF and/or CF in older adults receiving chemotherapy. Our findings suggest that over 50% of older adults are at risk for decrements in both outcomes. Clinicians need to monitor both outcomes in older adults on an ongoing basis and initiate appropriate interventions and referrals.

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Highlights

- Older oncology patients have deficits in both physical and cognitive function
- Comorbidities increase the risk for decrements in physical and cognitive function
- Depression was associated with decreases in physical and cognitive function

Figure 1. Changes in Attentional Function Index (AFI, left y-axis) scores and Physical Component Summary (PCS, right y-axis) scores over two cycles of chemotherapy for subgroups of older oncology patients with Very Low physical function (PF) and Moderate cognitive function (CF, panel A), Low PF and Low CF (panel B) and Normal PF and Normal CF (panel C).

Table 1 –

Latent Profile Solutions and Fit Indices for One Through Four Class Solutions

Model	LL	AIC	BIC	Entropy	VLMR
1 Class	–4950.33	10016.66	10243.01	n/a	n/a
2 Class	–4741.60	9625.20	9902.29	.82	417.46 ^{**}
3 Class ^a	–4666.88	9501.75	9829.57	.83	149.45 [*]
4 Class	–4597.91	9389.82	9768.37	.83	137.93 ^{ns}

Baseline LL is not applicable for the one class solution

^{*}
p < .05;^{**}
p < .01

^a The three class solution was selected because the BIC for that solution was lower than the BIC for the 2-class and 4-class solutions. In addition, the VLMR was significant for the 3-class solution, indicating that three classes fit the data better than two classes. While the BIC was smaller for the 4-class solution, the VLMR was not significant for the 4-class solution, indicating that too many classes were extracted.

Abbreviations: AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; LL = log-likelihood; n/a = not applicable; ns = not significant, VLMR = Vuong-Lo-Mendell-Rubin likelihood ratio test for the K vs. K-1 model

Table 2 –
Differences in Demographic and Clinical Characteristics Among the Latent Classes of Older Oncology Patients at Enrollment

Characteristic	Very Low PF + Moderate CF (1) 15.6% (n=57)		Low PF + Low CF (2) 39.3% (n=144)		Normal PF + Normal CF (3) 45.1% (n=165)		Statistics
	Mean (SD)		Mean (SD)		Mean (SD)		
Age (years)	72.8 (6.2)		71.6 (5.4)		70.7 (5.3)		F=3.36, p=.036 1 > 3
Education (years)	16.7 (3.7)		16.2 (3.0)		16.7 (2.9)		F=1.03, p=.357
Body mass index (kg/m ²)	26.8 (5.2)		26.1 (5.5)		25.9 (5.3)		F=0.71, p=.490
Karnofsky Performance Status score	75.2 (12.5)		78.4 (13.1)		88.9 (8.7)		F=45.27, p<.001 1 and 2 < 3
Number of comorbidities out of 13	3.2 (1.6)		3.1 (1.6)		2.5 (1.3)		F=9.68, p<.001 1 and 2 > 3
SCQ score out of 13 conditions	7.3 (3.8)		7.0 (3.6)		5.1 (2.7)		F=17.37, p<.001 1 and 2 > 3
AUDIT score	3.0 (3.2)		3.0 (2.8)		2.9 (2.0)		F=0.01, p=.986
Hemoglobin	11.1 (1.6)		11.3 (1.4)		11.7 (1.3)		F=5.04, p=.007 1 < 3
Hematocrit	33.4 (4.4)		34.0 (4.4)		35.1 (3.9)		F=4.75, p=.009 1 < 3
Time since cancer diagnosis (years)	5.0 (8.1)		2.2 (4.1)		2.8 (4.6)		KW, p=.035 1 > 3
Median time since diagnosis (years)	1.33		0.47		0.46		
Number of prior cancer treatments	2.1 (1.6)		1.7 (1.5)		1.6 (1.5)		F=2.08, p=.127
Number of metastatic sites including lymph node involvement	1.9 (1.2)		1.2 (1.3)		1.3 (1.1)		F=6.06, p=.003 1 > 2 and 3
Number of metastatic sites excluding lymph node involvement	1.4 (1.0)		0.8 (1.1)		0.8 (1.0)		F=8.24, p<.001 1 > 2 and 3
MAX2 score	0.14 (0.07)		0.17 (0.09)		0.14 (0.08)		F=3.36, p=.036 2 > 1 and 3
Attentional Function Index score	6.8 (1.3)		5.0 (1.3)		7.8 (1.2)		F=196.85, p<.0001 2<1<3
	% (n)		% (n)		% (n)		

Characteristic	Very Low PF + Moderate CF (1) 15.6% (n=57)		Low PF + Low CF (2) 39.3% (n=144)		Normal PF + Normal CF (3) 45.1% (n=165)		Statistics
	Mean (SD)		Mean (SD)		Mean (SD)		
Gender							
Female	71.9 (41)		73.8 (104)		62.4 (103)		X ² =5.31, p=.070
Male	28.1 (16)		25.5 (36)		37.6 (62)		
Transgender ^a	0.0 (0)		0.7 (1)		0.0 (0)		
Ethnicity							X ² =3.84, p=.698
White	83.9 (47)		77.3 (109)		81.1 (133)		
Asian or Pacific Islander	5.4 (3)		7.1 (10)		6.1 (10)		
Black	1.8 (1)		7.8 (11)		7.3 (12)		
Hispanic, Mixed, or Other	8.9 (5)		7.8 (11)		5.5 (9)		
Married or partnered (% yes)	60.0 (33)		49.6 (69)		66.9 (109)		X ² =9.24, p=.010 2 < 3
Lives alone (% yes)	27.3 (15)		37.4 (52)		24.1 (39)		X ² =6.56, p=.038 2 > 3
Child care responsibilities (% yes)	7.1 (4)		3.6 (5)		4.9 (8)		X ² =1.10, p=.576
Care of adult responsibilities (% yes)	7.7 (4)		5.8 (7)		3.3 (5)		X ² =1.84, p=.398
Currently employed (% yes)	17.9 (10)		14.2 (20)		29.6 (48)		X ² =10.16, p=.004 2 < 3
Annual household income							KW, p=.001 2 > 1 and 3
<\$30,000+	16.3 (8)		36.8 (46)		15.0 (21)		
\$30,000 to <\$70,000	28.6 (14)		29.6 (37)		20.0 (28)		
\$70,000 to <\$100,000	24.5 (12)		11.2 (14)		20.7 (29)		
>\$100,000	30.6 (15)		22.4 (28)		44.3 (62)		
Specific comorbidities (% yes)							
Heart disease	14.0 (8)		14.2 (20)		8.5 (14)		X ² =2.82, p=.245
High blood pressure	57.9 (33)		43.3 (61)		44.2 (73)		X ² =3.88, p=.144

Characteristic	Very Low PF + Moderate CF (1) 15.6% (n=57)			Low PF + Low CF (2) 39.3% (n=144)			Normal PF + Normal CF (3) 45.1% (n=165)			Statistics
	Mean (SD)			Mean (SD)			Mean (SD)			
Lung disease		29.8 (17)			22.7 (32)			14.5 (24)		$\chi^2=7.12$, $p=.029$ 1 > 3
Diabetes		17.5 (10)			14.9 (21)			12.7 (21)		$\chi^2=0.86$, $p=.650$
Ulcer or stomach disease		3.5 (2)			5.7 (8)			3.6 (6)		$\chi^2=0.88$, $p=.644$
Kidney disease		1.8 (1)			3.5 (5)			0.6 (1)		$\chi^2=3.49$, $p=.175$
Liver disease		8.8 (5)			7.1 (10)			6.7 (11)		$\chi^2=0.28$, $p=.868$
Anemia or blood disease		10.5 (6)			11.3 (16)			6.7 (11)		$\chi^2=2.18$, $p=.336$
Depression		14.0 (8)			29.1 (41)			9.1 (15)		$\chi^2=21.52$, $p<.001$ 2 > 3
Osteoarthritis		29.8 (17)			24.8 (35)			20.0 (33)		$\chi^2=2.54$, $p=.282$
Back pain		33.3 (19)			32.6 (46)			18.2 (30)		$\chi^2=10.00$, $p=.007$ 2 > 3
Rheumatoid arthritis		3.5 (2)			3.5 (5)			3.6 (6)		$\chi^2=.003$, $p=.999$
Exercise on a regular basis (% yes)		44.6 (25)			62.2 (84)			76.8 (126)		$\chi^2=20.87$, $p<.001$ 1 and 2 < 3
Smoking, current or history of (% yes)		51.8 (29)			50.7 (70)			43.2 (70)		$\chi^2=2.18$, $p=.336$
Cancer diagnosis										
Breast		19.3 (11)			25.5 (36)			22.4 (37)		$\chi^2=11.18$, $p=.083$
Gastrointestinal		24.6 (14)			28.4 (40)			39.4 (65)		
Gynecological		31.6 (18)			19.1 (27)			20.6 (34)		
Lung		24.6 (14)			27.0 (38)			17.6 (29)		
Type of prior cancer treatment										
No prior treatment		15.1 (8)			21.7 (30)			28.4 (46)		$\chi^2=9.52$, $p=.147$
Only surgery, CTX, or RT		28.3 (15)			40.6 (56)			32.1 (52)		
Surgery & CTX, or Surgery & RT, or CTX & RT		39.6 (21)			24.6 (34)			25.9 (42)		
Surgery & CTX & RT		17.0 (9)			13.0 (18)			13.6 (22)		

Characteristic	Very Low PF + Moderate CF (1) 15.6% (n=57)	Low PF + Low CF (2) 39.3% (n=144)	Normal PF + Normal CF (3) 45.1% (n=165)		Statistics
	Mean (SD)	Mean (SD)	Mean (SD)		
Cycle length					
14 day cycle	35.1 (20)	33.6 (48)	34.1 (56)		X ² =2.25, p=.691
21 day cycle	49.1 (28)	55.9 (80)	56.7 (93)		
28 day cycle	15.8 (9)	10.5 (15)	9.1 (15)		
Emetogenicity of the CTX regimen					
Minimal/low	35.1 (20)	21.5 (31)	24.4 (40)		X ² =13.33, p=.010 NS
Moderate	63.2 (36)	59.7 (86)	64.6 (106)		NS
High	1.8 (1)	18.8 (27)	11.0 (18)		1 < 2
Antiemetic regimen					
None	10.9 (6)	6.5 (9)	10.0 (16)		X ² =2.71, p=.845
Steroid alone or serotonin antagonist alone	20.0 (11)	18.0 (25)	21.9 (35)		
Serotonin antagonist and steroid	49.1 (27)	54.0 (75)	50.0 (80)		
NK-1 receptor antagonist and two other antiemetics	20.0 (11)	21.6 (30)	18.1 (29)		

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test, CF = cognitive function, CTX = chemotherapy, kg = kilograms, KW = Kruskal Wallis; m² = meter squared, NK = neurokinin, PF = physical function, RT = radiation therapy, SCQ = Self-Administered Comorbidity Questionnaire, SD = standard deviation

^aChi Square analysis done without the transgender patient include in the analyses

[†]Reference group

+Reference group

Table 3 –
Differences in Quality of Life Outcomes Among the Latent Classes of Older Oncology Patients at Enrollment

Characteristic		Very Low PF + Moderate CF (1) 15.6% (n=57)	Low PF + Low CF (2) 39.3% (n=144)		Normal PF + Normal CF (3) 45.1% (n=165)		Statistics
		Mean (SD)	Mean (SD)	Mean (SD)			
Medical Outcomes Study – Short Form-12							
Physical functioning		17.4 (20.7)	37.4 (30.6)	70.9 (29.4)	F=90.73, p<.001 1<2<3		
Role physical		32.1 (25.1)	37.6 (22.8)	70.2 (22.9)	F=95.89, p<.001 1 and 2 < 3		
Bodily pain		65.0 (31.4)	70.7 (29.9)	91.4 (16.4)	F=36.10, p≤.001 1 and 2 < 3		
General health		45.5 (29.1)	57.0 (28.1)	73.8 (22.5)	F=30.51, p<.001 1<2<3		
Vitality		29.5 (24.8)	30.3 (22.3)	64.3 (19.9)	F=109.95, p<.001 1 and 2 < 3		
Social functioning		58.9 (34.2)	51.8 (32.9)	83.4 (23.4)	F=46.05, p<.001 1 and 2 < 3		
Role emotional		81.4 (26.4)	59.6 (29.3)	89.1 (18.0)	F=55.57, p<.001 2 < 1 and 3		
Mental health		79.9 (17.0)	64.7 (22.1)	82.6 (15.6)	F=36.48, p<.001 2 < 1 and 3		
Physical component summary score		29.1 (8.7)	38.0 (9.0)	47.4 (7.8)	F=105.03, p<.001 1<2<3		
Mental component summary score		54.4 (9.0)	43.3 (11.2)	54.8 (7.6)	F=59.58, p<.001 2 < 1 and 3		
Multidimensional Quality of Life Scale – Cancer							
Physical well-being		6.6 (1.6)	6.3 (1.6)	8.0 (1.3)	F=51.34, p≤.001 1 and 2 < 3		
Psychological well-being		5.6 (1.6)	4.9 (1.7)	6.8 (1.7)	F=49.98, p<.001 2<1<3		
Social well-being		6.2 (1.5)	5.6 (2.0)	7.4 (1.5)	F=41.26, p≤.001 1 and 2 < 3		
Spiritual well-being		4.4 (1.9)	5.0 (2.2)	5.1 (2.1)	F=2.51, p=.083		
Total quality of life score		5.7 (1.2)	5.3 (1.4)	6.9 (1.2)	F=54.23, p<.001 1 and 2 < 3		

Abbreviations: CF = cognitive function, PF = physical function, SD = standard deviation