Title

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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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REFERENCES

Aapro M, Extermann M, Repetto L, 2000 Evaluation of the elderly with cancer. Ann Oncol 11 Suppl 3, 223–229. [PubMed: 11079145]

Ahles TA, Root JC, 2018 Cognitive Effects of Cancer and Cancer Treatments. Annu Rev Clin Psychol 14, 425–451. [PubMed: 29345974]

Ando M, Ando Y, Hasegawa Y, Shimokata K, Minami H, Wakai K, Ohno Y, Sakai S, 2001 Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. Br J Cancer 85, 1634–1639. [PubMed: 11742480]

Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG, 2001 AUDIT: The Alcohol Use Disorders Identification Test Guidelines for Use in Primary Care. World Health Organization, Geneva.

Bedillion MF, Ansell EB, Thomas GA, 2019 Cancer treatment effects on cognition and depression: The moderating role of physical activity. Breast 44, 73–80. [PubMed: 30685529]

Bherer L, 2015 Cognitive plasticity in older adults: effects of cognitive training and physical exercise. Ann N Y Acad Sci 1337, 1–6. [PubMed: 25773610]

Blanchet S, Chikhi S, Maltais D, 2018 The benefits of physical activities on cognitive and mental health in healthy and pathological aging. Geriatrie et psychologie neuropsychiatrie du vieillissement 16, 197–205. [PubMed: 29877188]

Bompaire F, Durand T, Leger-Hardy I, Psimaras D, Ricard D, 2017 Chemotherapy-related cognitive impairment or chemobrain: concept and state of art. Geriatrie et psychologie neuropsychiatrie du vieillissement 15, 89–98. [PubMed: 28266346]

Brown JC, Harhay MO, Harhay MN, 2016 Patient-reported versus objectively-measured physical function and mortality risk among cancer survivors. J Geriatr Oncol 7, 108–115. [PubMed: 26907563]

Carvalho A, Rea IM, Parimon T, Cusack BJ, 2014 Physical activity and cognitive function in individuals over 60 years of age: a systematic review. Clin Interv Aging 9, 661–682. [PubMed: 24748784]

Chen H, Ding K, Zhao J, Chao HH, Li CR, Cheng H, 2019a The dorsolateral prefrontal cortex is selectively involved in chemotherapy-related cognitive impairment in breast cancer patients with different hormone receptor expression. Am J Cancer Res 9, 1776–1785. [PubMed: 31497358]

Chen X, He X, Tao L, Li J, Wu J, Zhu C, Yu F, Zhang L, Zhang J, Qiu B, Yu Y, Wang K, 2017 The working memory and dorsolateral prefrontal-hippocampal functional connectivity changes in long-term survival breast cancer patients treated with tamoxifen. Int J Neuropsychopharmacol 20, 374–382. [PubMed: 28177081]

Chen YJ, Li XX, Ma HK, Zhang X, Wang BW, Guo TT, Xiao Y, Bing ZT, Ge L, Yang KH, Han XM, 2020 Exercise training for improving patient-reported outcomes in patients with advanced-stage cancer: A systematic review and meta-analysis. J Pain Symptom Manage 59,734–749. [PubMed: 31546002]

Cimprich B, So H, Ronis DL, Trask C, 2005 Pre-treatment factors related to cognitive functioning in women newly diagnosed with breast cancer. Psycho-Oncology 14, 70–78. [PubMed: 15386786]

Cimprich B, Visovatti M, Ronis DL, 2011 The Attentional Function Index--a self-report cognitive measure. Psychooncology 20, 194–202. [PubMed: 20213858]

Cohen JA, Verghese J, Zwerling JL, 2016 Cognition and gait in older people. Maturitas 93, 73–77. [PubMed: 27240713]

Collins DM, Downer B, Kumar A, Krishnan S, Li CY, Markides KS, Karmarkar AM, 2018 Impact of multiple chronic conditions on activity limitations among older Mexican-American care recipients. Prev Chronic Dis 15, E51.

Docking RE, Fleming J, Brayne C, Zhao J, Macfarlane GJ, Jones GT, 2011 Epidemiology of back pain in older adults: prevalence and risk factors for back pain onset. Rheumatology (Oxford) 50, 1645–1653. [PubMed: 21606130]

Extermann M, Bonetti M, Sledge GW, O'Dwyer PJ, Bonomi P, Benson AB 3rd, 2004 MAX2--a convenient index to estimate the average per patient risk for chemotherapy toxicity; validation in ECOG trials. Eur J Cancer 40, 1193–1198. [PubMed: 15110883]

Extermann M, Chen H, Cantor AB, Corcoran MB, Meyer J, Grendys E, Cavanaugh D, Antonek S, Camarata A, Haley WE, Balducci L, 2002 Predictors of tolerance to chemotherapy in older cancer patients: a prospective pilot study. Eur J Cancer 38, 1466–1473. [PubMed: 12110492]

Extermann M, Reich RR, Sehovic M, 2015 Chemotoxicity recurrence in older patients: Risk factors and effectiveness of preventive strategies-a prospective study. Cancer 121, 2984–2992. [PubMed: 26033177]

Feng Y, Zhang XD, Zheng G, Zhang LJ, 2019 Chemotherapy-induced brain changes in breast cancer survivors: evaluation with multimodality magnetic resonance imaging. Brain Imaging Behav 13, 1799–1814. [PubMed: 30937827]

Hoppe S, Rainfray M, Fonck M, Hoppenreys L, Blanc JF, Ceccaldi J, Mertens C, Blanc-Bisson C, Imbert Y, Cany L, Vogt L, Dauba J, Houede N, Bellera CA, Floquet A, Fabry MN, Ravaud A, Chakiba C, Mathoulin-Pelissier S, Soubeyran P, 2013 Functional decline in older patients with cancer receiving first-line chemotherapy. J Clin Oncol 31, 3877–3882. [PubMed: 24062399]

Hu L, Smith L, Imm KR, Jackson SE, Yang L, 2019 Physical activity modifies the association between depression and cognitive function in older adults. J Affect Disord 246, 800–805. [PubMed: 30634111]

Hurria A, Goldfarb S, Rosen C, Holland J, Zuckerman E, Lachs M, Witmer M, van Gorp W, Fornier M, D'Andrea G, Moasser M, Dang C, Robson M, Currie V, 2006 Effect of adjuvant breast cancer chemotherapy on cognitive function from the older patient's perspective. Breast Cancer Res Treat 98, 343–348. [PubMed: 16541322]

Jolly TA, Deal AM, Nyrop KA, Williams GR, Pergolotti M, Wood WA, Alston SM, Gordon BB, Dixon SA, Moore SG, Taylor WC, Messino M, Muss HB, 2015 Geriatric assessment-identified deficits in older cancer patients with normal performance status. Oncologist 20, 379–385. [PubMed: 25765876]

Joly F, Giffard B, Rigal O, De Ruiter MB, Small BJ, Dubois M, LeFel J, Schagen SB, Ahles TA, Wefel JS, Vardy JL, Pancre V, Lange M, Castel H, 2015 Impact of Cancer and Its Treatments on Cognitive Function: Advances in Research From the Paris International Cognition and Cancer Task Force Symposium and Update Since 2012. J Pain Symptom Manage 50, 830–841. [PubMed: 26344551]

Jung T, Wickrama KAS, 2008 An Introduction to Latent Class Growth Analysis and Growth Mixture Modeling. Social and Personality Psychology Compass 2, 302–317.

Kenis C, Decoster L, Bastin J, Bode H, Van Puyvelde K, De Greve J, Conings G, Fagard K, Flamaing J, Milisen K, Lobelle JP, Wildiers H, 2017 Functional decline in older patients with cancer receiving chemotherapy: A multicenter prospective study. J Geriatr Oncol 8, 196–205. [PubMed: 28330581]

Khosravi N, Stoner L, Farajivafa V, Hanson ED, 2019 Exercise training, circulating cytokine levels and immune function in cancer survivors: A meta-analysis. Brain Behav Immun 81, 92–104. [PubMed: 31454519]

Kirk-Sanchez NJ, McGough EL, 2014 Physical exercise and cognitive performance in the elderly: current perspectives. Clin Interv Aging 9, 51–62. [PubMed: 24379659]

Kirkhus L, Harneshaug M, Saltyte Benth J, Gronberg BH, Rostoft S, Bergh S, Hjermstad MJ, Selbaek G, Wyller TB, Kirkevold O, Borza T, Saltvedt I, Jordhoy MS, 2019 Modifiable factors affecting older patients' quality of life and physical function during cancer treatment. J Geriatr Oncol 10, 904–912. [PubMed: 31444088]

Lange M, Heutte N, Noal S, Rigal O, Kurtz JE, Levy C, Allouache D, Rieux C, Lefel J, Clarisse B, Leconte A, Veyret C, Barthelemy P, Longato N, Tron L, Castel H, Eustache F, Giffard B, Joly F, 2019 Cognitive changes after adjuvant treatment in older adults with early-stage breast cancer. Oncologist 24, 62–68. [PubMed: 29934409]

Lange M, Rigal O, Clarisse B, Giffard B, Sevin E, Barillet M, Eustache F, Joly F, 2014 Cognitive dysfunctions in elderly cancer patients: a new challenge for oncologists. Cancer Treat Rev 40, 810–817. [PubMed: 24713425]

Loh KP, Janelsins MC, Mohile SG, Holmes HM, Hsu T, Inouye SK, Karuturi MS, Kimmick GG, Lichtman SM, Magnuson A, Whitehead MI, Wong ML, Ahles TA, 2016 Chemotherapy-related cognitive impairment in older patients with cancer. J Geriatr Oncol 7, 270–280. [PubMed: 27197918]

Magnuson A, Mohile S, Janelsins M, 2016 Cognition and cognitive impairment in older adults with cancer. Cur Geriatr Rep 5, 213–219.

Magnuson A, Sattar S, Nightingale G, Saracino R, Skonecki E, Trevino KM, 2019 A Practical Guide to Geriatric Syndromes in Older Adults With Cancer: A Focus on Falls, Cognition, Polypharmacy, and Depression. Am Soc Clin Oncol Educ Book 39, e96–e109. [PubMed: 31099668]

Malva JO, Bousquet J, 2016 Operational definition of active and healthy ageing: Roadmap from concept to change of management. Maturitas 84, 3–4. [PubMed: 26704254]

Mandelblatt JS, Hurria A, McDonald BC, Saykin AJ, Stern RA, VanMeter JW, McGuckin M, Traina T, Denduluri N, Turner S, Howard D, Jacobsen PB, Ahles T, Thinking, Living With Cancer, S., 2013 Cognitive effects of cancer and its treatments at the intersection of aging: what do we know; what do we need to know? Semin Oncol 40, 709–725. [PubMed: 24331192]

McGilton KS, Vellani S, Yeung L, Chishtie J, Commisso E, Ploeg J, Andrew MK, Ayala AP, Gray M, Morgan D, Chow AF, Parrott E, Stephens D, Hale L, Keatings M, Walker J, Wodchis WP, Dube V, McElhaney J, Puts M, 2018 Identifying and understanding the health and social care needs of older adults with multiple chronic conditions and their caregivers: a scoping review. BMC Geriatr 18, 231. [PubMed: 30285641]

Meneses-Echavez JF, Gonzalez-Jimenez E, Ramirez-Velez R, 2015 Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: a systematic review and meta-analysis. BMC Cancer 15, 77. [PubMed: 25885168]

Miaskowski C, Cooper BA, Aouizerat B, Melisko M, Chen LM, Dunn L, Hu X, Kober KM, Mastick J, Levine JD, Hammer M, Wright F, Harris J, Armes J, Furlong E, Fox P, Ream E, Maguire R, Kearney N, 2017a The symptom phenotype of oncology outpatients remains relatively stable from prior to through 1 week following chemotherapy. Eur J Cancer Care (Engl) 26.

Miaskowski C, Cooper BA, Melisko M, Chen LM, Mastick J, West C, Paul SM, Dunn LB, Schmidt BL, Hammer M, Cartwright F, Wright F, Langford DJ, Lee K, Aouizerat BE, 2014 Disease and treatment characteristics do not predict symptom occurrence profiles in oncology outpatients receiving chemotherapy. Cancer 120, 2371–2378. [PubMed: 24797450]

Miaskowski C, Wong ML, Cooper BA, Mastick J, Paul SM, Possin K, Steinman M, Cataldo J, Dunn LB, Ritchie C, 2017b Distinct Physical Function Profiles in Older Adults Receiving Cancer Chemotherapy. J Pain Symptom Manage 54, 263–272. [PubMed: 28716620]

Montero-Odasso M, Almeida QJ, Bherer L, Burhan AM, Camicioli R, Doyon J, Fraser S, Muir-Hunter S, Li KZH, Liu-Ambrose T, McIlroy W, Middleton L, Morais JA, Sakurai R, Speechley M, Vasudev A, Beauchet O, Hausdorff JM, Rosano C, Studenski S, Verghese J, Canadian G, Cognition N, 2019 Consensus on Shared Measures of Mobility and Cognition: From the Canadian Consortium on Neurodegeneration in Aging (CCNA). J Gerontol A Biol Sci Med Sci 74, 897–909. [PubMed: 30101279]

Montero-Odasso M, Bherer L, Studenski S, Gopaul K, Oteng-Amoako A, Woolmore-Goodwin S, Stoole P, Wells J, Doherty T, Zecevic AA, Galinsky D, Rylett RJ, Jutai J, Muir-Hunter S, Speechley M, Camicioli R, 2015 Mobility and Cognition in Seniors. Report from the 2008 Institute of Aging (CIHR) Mobility and Cognition Workshop. Can Geriatr J 18, 159–167. [PubMed: 26495050]

Montero-Odasso M, Hachinski V, 2014 Preludes to brain failure: executive dysfunction and gait disturbances. Neurol Sci 35, 601–604. [PubMed: 24366243]

Montero-Odasso M, Verghese J, Beauchet O, Hausdorff JM, 2012 Gait and cognition: a complementary approach to understanding brain function and the risk of falling. J Am Geriatr Soc 60, 2127–2136. [PubMed: 23110433]

Muthen LK, Muthen BO, 1998-2020 Mplus User's Guide (8th ed.), 8th ed. Muthen & Muthen, Los Angeles, CA.

Nadler MB, Desnoyers A, Langelier DM, Amir E, 2019 The effect of exercise on quality of life, fatigue, physical function, and safety in advanced solid tumor cancers: A meta-analysis of randomized control trials. J Pain Symptom Manage 58, 899–908. [PubMed: 31319105]

Padilla GV, Ferrell B, Grant MM, Rhiner M, 1990 Defining the content domain of quality of life for cancer patients with pain. Cancer Nurs 13, 108–115. [PubMed: 2331691]

Padilla GV, Presant C, Grant MM, Metter G, Lipsett J, Heide F, 1983 Quality of life index for patients with cancer. Res Nurs Health 6, 117–126. [PubMed: 6556698]

Pamoukdjian F, Aparicio T, Zelek L, Boubaya M, Caillet P, Francois V, de Decker L, Levy V, Sebbane G, Paillaud E, 2017 Impaired mobility, depressed mood, cognitive impairment and polypharmacy are independently associated with disability in older cancer outpatients: The prospective Physical Frailty in Elderly Cancer patients (PF-EC) cohort study. J Geriatr Oncol 8, 190–195. [PubMed: 28236586]

Pedersen BK, 2019 Physical activity and muscle-brain crosstalk. Nat Rev Endocrinol 15, 383–392. [PubMed: 30837717]

Phillips C, 2017 Brain-Derived Neurotrophic Factor, Depression, and Physical Activity: Making the Neuroplastic Connection. Neural Plast 2017, 7260130.

Phillips C, Fahimi A, 2018 Immune and neuroprotective effects of physical activity on the brain in depression. Front Neurosci 12, 498. [PubMed: 30093853]

Puts MT, Hardt J, Monette J, Girre V, Springall E, Alibhai SM, 2012 Use of geriatric assessment for older adults in the oncology setting: a systematic review. J Natl Cancer Inst 104, 1133–1163. [PubMed: 22851269]

Puts MT, Santos B, Hardt J, Monette J, Girre V, Atenafu EG, Springall E, Alibhai SM, 2014 An update on a systematic review of the use of geriatric assessment for older adults in oncology. Ann Oncol 25, 307–315. [PubMed: 24256847]

Quinten C, Coens C, Ghislain I, Zikos E, Sprangers MA, Ringash J, Martinelli F, Ediebah DE, Maringwa J, Reeve BB, Greimel E, King MT, Bjordal K, Flechtner HH, Schmucker-Von Koch J, Taphoorn MJ, Weis J, Wildiers H, Velikova G, Bottomley A, 2015 The effects of age on health-related quality of life in cancer populations: A pooled analysis of randomized controlled trials using the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 involving 6024 cancer patients. Eur J Cancer 51, 2808–2819. [PubMed: 26602015]

Rosso AL, Studenski SA, Chen WG, Aizenstein HJ, Alexander NB, Bennett DA, Black SE, Camicioli R, Carlson MC, Ferrucci L, Guralnik JM, Hausdorff JM, Kaye J, Launer LJ, Lipsitz LA, Verghese J, Rosano C, 2013 Aging, the central nervous system, and mobility. J Gerontol A Biol Sci Med Sci 68, 1379–1386. [PubMed: 23843270]

Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN, 2003 The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum 49, 156–163. [PubMed: 12687505]

Santoni G, Marengoni A, Calderon-Larranaga A, Angleman S, Rizzuto D, Welmer AK, Mangialasche F, Orsini N, Fratiglioni L, 2017 Defining health trajectories in older adults with five clinical indicators. J Gerontol A Biol Sci Med Sci 72, 1123–1129. [PubMed: 28329788]

Schnadig ID, Fromme EK, Loprinzi CL, Sloan JA, Mori M, Li H, Beer TM, 2008 Patient-physician disagreement regarding performance status is associated with worse survivorship in patients with advanced cancer. Cancer 113, 2205–2214. [PubMed: 18780322]

Shimada H, Park H, Makizako H, Doi T, Lee S, Suzuki T, 2014 Depressive symptoms and cognitive performance in older adults. J Psychiatr Res 57, 149–156. [PubMed: 25023083]

Siegel RL, Miller KD, Jemal A, 2019 Cancer statistics, 2019. CA Cancer J Clin 69, 7–34. [PubMed: 30620402]

Snowden MB, Steinman LE, Bryant LL, Cherrier MM, Greenlund KJ, Leith KH, Levy C, Logsdon RG, Copeland C, Vogel M, Anderson LA, Atkins DC, Bell JF, Fitzpatrick AL, 2017 Dementia and co-occurring chronic conditions: a systematic literature review to identify what is known and where are the gaps in the evidence? Int J Geriatr Psychiatry 32, 357–371. [PubMed: 28146334]

Steeves JA, Shiroma EJ, Conger SA, Van Domelen D, Harris TB, 2019 Physical activity patterns and multimorbidity burden of older adults with different levels of functional status: NHANES 2003–2006. Disabil Health J 12, 495–502. [PubMed: 30871954]

Stout NL, Baima J, Swisher AK, Winters-Stone KM, Welsh J, 2017 A systematic review of exercise systematic reviews in the cancer literature (2005–2017). PM R 9, S347–S384. [PubMed: 28942909]

Tomlinson D, Diorio C, Beyene J, Sung L, 2014 Effect of exercise on cancer-related fatigue: a meta-analysis. Am J Phys Med Rehabil 93, 675–686. [PubMed: 24743466]

Utne I, Loyland B, Grov EK, Paul S, Wong ML, Conley YP, Cooper BA, Levine JD, Miaskowski C, 2019 Co-occuring symptoms in older oncology patients with distinct attentional function profiles. Eur J Oncol Nurs 41, 196–203. [PubMed: 31358253]

Utne I, Loyland B, Grov EK, Rasmussen HL, Torstveit AH, Cooper BA, Mastick J, Mazor M, Wong M, Paul SM, Conley YP, Jahan T, Ritchie C, Levine JD, Miaskowski C, 2018 Distinct attentional function profiles in older adults receiving cancer chemotherapy. Eur J Oncol Nurs 36, 32–39. [PubMed: 30322507]

van Abbema DL, van den Akker M, Janssen-Heijnen ML, van den Berkmortel F, Hoeben A, de Vos-Geelen J, Buntinx F, Kleijnen J, Tjan-Heijnen VCG, 2019 Patient- and tumor-related predictors of chemotherapy intolerance in older patients with cancer: A systematic review. J Geriatr Oncol 10, 31–41. [PubMed: 29706424]

van Leeuwen KM, van Loon MS, van Nes FA, Bosmans JE, de Vet HCW, Ket JCF, Widdershoven GAM, Ostelo R, 2019 What does quality of life mean to older adults? A thematic synthesis. PloS one 14, e0213263.

Ware J Jr., Kosinski M, Keller SD, 1996 A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 34, 220–233. [PubMed: 8628042]

Wefel JS, Kesler SR, Noll KR, Schagen SB, 2015 Clinical characteristics, pathophysiology, and management of noncentral nervous system cancer-related cognitive impairment in adults. CA Cancer J Clin 65, 123–138. [PubMed: 25483452]

Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, Falandry C, Artz A, Brain E, Colloca G, Flamaing J, Karnakis T, Kenis C, Audisio RA, Mohile S, Repetto L, Van Leeuwen B, Milisen K, Hurria A, 2014 International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol 32, 2595–2603. [PubMed: 25071125]

Williams GR, Mackenzie A, Magnuson A, Olin R, Chapman A, Mohile S, Allore H, Somerfield MR, Targia V, Extermann M, Cohen HJ, Hurria A, Holmes H, 2016 Comorbidity in older adults with cancer. J Geriatr Oncol 7, 249–257. [PubMed: 26725537]

Wong ML, Paul SM, Mastick J, Ritchie C, Steinman MA, Walter LC, Miaskowski C, 2018 Characteristics associated with physical function trajectories in older adults with cancer during chemotherapy. J Pain Symptom Manage 56, 678–688 e671. [PubMed: 30144536]

Zhang Y, Chen YC, Hu L, You J, Gu W, Li Q, Chen H, Mao C, Yin X, 2019 Chemotherapy-induced functional changes of the default mode network in patients with lung cancer. Brain Imaging Behav.

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

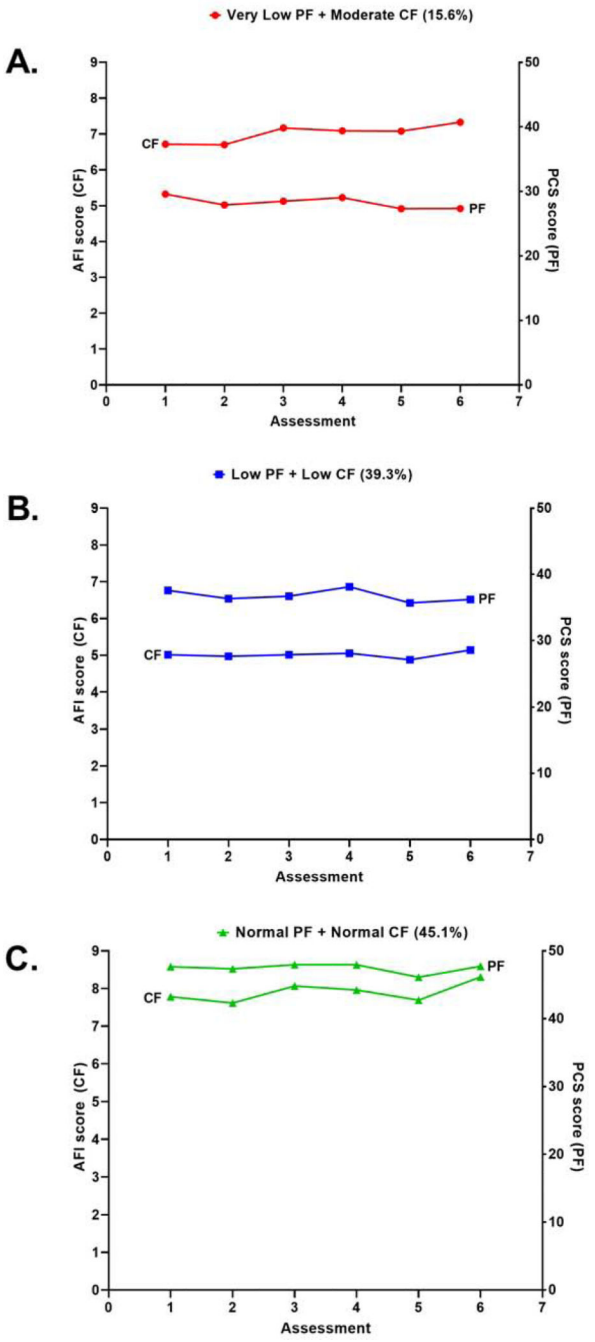

Figure 1.

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	137.93ns

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)	
Male	28.1 (16)	25.5 (36)	37.6 (62)	X^2=5.31, p=.070
Transgender[a]	0.0 (0)	0.7 (1)	0.0 (0)	
Ethnicity				
White	83.9 (47)	77.3 (109)	81.1 (133)	X^2=3.84, p=.698
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				
<$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)	KW, p,.001 2 > 1 and 3
$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)	X^2=7.12, p=.029 1 > 3
Diabetes	17.5 (10)	14.9 (21)	12.7 (21)	X^2=0.86, p=.650
Ulcer or stomach disease	3.5 (2)	5.7 (8)	3.6 (6)	X^2=0.88, p=.644
Kidney disease	1.8 (1)	3.5 (5)	0.6 (1)	X^2=3.49, p=.175
Liver disease	8.8 (5)	7.1 (10)	6.7 (11)	X^2=0.28, p=.868
Anemia or blood disease	10.5 (6)	11.3 (16)	6.7 (11)	X^2=2.18, p=.336
Depression	14.0 (8)	29.1 (41)	9.1 (15)	X^2=21.52, p<.001 2 > 3
Osteoarthritis	29.8 (17)	24.8 (35)	20.0 (33)	X^2=2.54, p=.282
Back pain	33.3 (19)	32.6 (46)	18.2 (30)	X^2=10.00, p=.007 2 > 3
Rheumatoid arthritis	3.5 (2)	3.5 (5)	3.6 (6)	X^2=.003, p=.999
Exercise on a regular basis (% yes)	44.6 (25)	62.2 (84)	76.8 (126)	X^2=20.87, p<.001 1 and 2 < 3
Smoking, current or history of (% yes)	51.8 (29)	50.7 (70)	43.2 (70)	X^2=2.18, p=.336
Cancer diagnosis				
Breast	19.3 (11)	25.5 (36)	22.4 (37)	X^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)	X^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)	
21 day cycle	49.1 (28)	55.9 (80)	56.7 (93)	X^2=2.25, p=.691
28 day cycle	15.8 (9)	10.5 (15)	9.1 (15)	
Emetogenicity of the CTX regimen				X^2=13.33, p=.010
Minimal/low	35.1 (20)	21.5 (31)	24.4 (40)	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)	
Steroid alone or serotonin antagonist alone	20.0 (11)	18.0 (25)	21.9 (35)	X^2=2.71, p=.845
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; m^2 = meter squared, NK = neurokinin, PF = physical function, RT = radiation therapy, SCQ = Self-Administered Comorbidity Questionnaire, SD = standard deviation

[a]Chi 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