Title
Distinct Physical Function Profiles in Older Adults Receiving Cancer Chemotherapy.

Journal
Journal of pain and symptom management, 54(3)

ISSN
0885-3924

Authors
Miaskowski, Christine
Wong, Melisa L
Cooper, Bruce A
et al.

Publication Date
2017-09-01

DOI
10.1016/j.jpainsymman.2017.07.018

Peer reviewed

Original Article

Distinct Physical Function Profiles in Older Adults Receiving Cancer Chemotherapy

Christine Miaskowski, RN, PhD, Melisa L. Wong, MD, Bruce A. Cooper, PhD, Judy Mastick, RN, MN, Steven M. Paul, PhD, Katherine Possin, PhD, Michael Steinman, MD, Janine Cataldo, RN, PhD, Laura B. Dunn, MD, and Christine Ritchie, MD

School of Nursing (C.M., B.A.C., J.M., S.M.P., J.C.), University of California, San Francisco, California; School of Medicine (M.L.W., K.P., M.S., C.R.), University of California, San Francisco, California; and School of Medicine (L.B.D), Stanford University, Palo Alto, California, USA

Abstract

Context. Although physical function is an important patient outcome, little is known about changes in physical function in older adults receiving chemotherapy (CTX).

Objectives. Identify subgroups of older patients based on changes in their level of physical function; determine which demographic and clinical characteristics were associated with subgroup membership; and determine if these subgroups differed on quality-of-life (QOL) outcomes.

Methods. Latent profile analysis was used to identify groups of older oncology patients ($n = 363$) with distinct physical function profiles. Patients were assessed six times over two cycles of CTX using the Physical Component Summary score from the Short Form 12. Differences, among the groups, in demographic and clinical characteristics and QOL outcomes were evaluated using parametric and nonparametric tests.

Results. Three groups of older oncology patients with distinct functional profiles were identified: Well Below (20.4%), Below (43.8%), and Above (35.8%) normative Physical Component Summary scores. Characteristics associated with membership in the Well Below class included the following: lower annual income, a higher level of comorbidity, being diagnosed with depression and back pain, and lack of regular exercise. Compared with the Above class, patients in the other two classes had significantly poorer QOL outcomes.

Conclusion. Almost 65% of older oncology patients reported significant decrements in physical function that persisted over two cycles of CTX. Clinicians can assess for those characteristics associated with poorer functional status to identify high-risk patients and initiate appropriate interventions. J Pain Symptom Manage 2017;54:263–272.

Key Words

Physical function, older adults, chemotherapy, comorbidity, latent class analysis

Introduction

The number of older adults diagnosed with cancer is expected to increase by 67% between 2010 and 2030.[1] However, older adults are less likely to receive the most effective cancer treatments[2] and to complete a standard course of chemotherapy (CTX).[3] To optimize the receipt of cancer treatments in older adults, a significant amount of research has focused on predictors of mortality, dose reductions, and other traditional treatment outcomes (for reviews, see[4–7]). Although prediction of these treatment outcomes is important,[8] virtually nothing is known about the

Address correspondence to: Christine Miaskowski, RN, PhD, Department of Physiological Nursing, University of California, 2 Koret Way – N631Y, San Francisco, CA 94143-0610, USA. E-mail: chris.miaskowski@ucsf.edu

Accepted for publication: July 7, 2017.

0885-3924/$ - see front matter
http://dx.doi.org/10.1016/j.jpainsymman.2017.07.018

impact of CTX on older oncology patients' functional status during the receipt of CTX.[9–12]

The assessment of physical function is an extremely important component of any evaluation of the overall health and physiologic reserves of oncology patients. Although not assessed as consistently as comorbid conditions, functional status is as important as comorbidity in predicting mortality and health care utilization.[13,14] In addition, for many older adults, functional status is an extremely important health outcome that informs treatment decisions.[9]

After a diagnosis of cancer, regardless of age, patient-reported physical function deteriorates at an accelerated rate compared with that of age-matched controls.[4,5,15] However, only two research groups have characterized changes in physical function in older adults receiving cancer treatment, as well as demographic and clinical characteristics associated with functional decline.[16–18] In one large prospective study that recruited a sample of newly diagnosed older adults,[16,17] changes in physical function were evaluated using the physical functioning subscale of the Medical Outcomes Study Short Form 36 (SF-36).[19] In the first report from this study,[16] changes in physical function were assessed from before the diagnosis of cancer to six to eight weeks after initial treatment. In the second report,[17] changes in physical function were evaluated multiple times for up to one year after the cancer diagnosis. In the multivariable analysis, older age and higher number of comorbidities were the only characteristics associated with decreases in physical function in the immediate treatment period.[16] In the 12-month follow-up study,[17] being female, as well as older age and a higher number of comorbidities were associated with declines in physical function. In the most recent study,[18] older adults were evaluated before their first and second cycles of CTX using a different measure of function, namely the Activities of Daily Living scale.[20] In the multivariable model, higher scores on the Geriatric Depression Scale[21,22] and lower scores on another measure of function (i.e., Instrumental Activities of Daily Living scale[23]) at enrollment were associated with increased risk for functional decline. Across these three studies,[16–18] cancer diagnosis, stage of disease, or type of cancer treatment were not associated with either outcome measure. Differences in the functional outcome measures used and the heterogeneous nature of the samples in terms of demographic and clinical characteristics may account for the different predictors that were identified.

Although physical function is an extremely important patient outcome,[24,25] research on changes in function in older oncology patients is extremely scarce. To begin to address this gap, the purposes of this study, in a sample of older oncology outpatients ($n = 363$; ≥65 years of age) whose physical function was assessed using the physical component summary (PCS) score from the SF-12, six times over two cycles of CTX, were to identify subgroups of older patients (i.e., latent growth classes) based on changes in their level of self-reported physical function; determine which demographic and clinical characteristics were associated with subgroup membership; and determine if these subgroups differed on quality-of-life (QOL) outcomes.

Methods

Patients and Settings

Details regarding the methods for the larger, longitudinal study from which this sample was drawn are published elsewhere.[26,27] In brief, for the larger study, eligible patients were ≥18 years of age; had a diagnosis of breast, gastrointestinal, gynecological, or lung cancer; had received CTX within the preceding four weeks; were scheduled to receive at least two additional cycles of CTX; were able to read, write, and understand English; and gave written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. A total of 2234 patients were approached and 1343 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with their cancer treatment. For this study, data from patients who were ≥65 years of age ($n = 363$) were used in the analysis of changes in physical function.

Instruments

At enrollment, a demographic questionnaire obtained information on age, gender, ethnicity, marital status, living arrangements, education, employment status, and income. The Karnofsky Performance Status (KPS) scale was used to assess patients' overall performance status.[28] Patients rated their functional status using the KPS scale that ranged from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms).[29,30]

Self-Administered Comorbidity Questionnaire (SCQ) consists of 13 common medical conditions simplified into language that can be understood without prior medical knowledge.[31] Patients indicated if they had the condition; if they received treatment for it (proxy for disease severity); and if it limited their activities (indication of functional limitations). Across the 13 conditions, the total SCQ score can range from 0 to 39 with higher scores indicating a worse comorbidity profile. The SCQ has well-established validity and reliability.[32,33]

Physical function over the two cycles of CTX was assessed using the PCS score from the SF-12.[34] 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 that measure physical (i.e., PCS) and psychological (mental component summary [MCS]) function. These scores can range from 0 to 100. Higher PCS and MCS scores indicate better physical and psychological functioning, respectively. The PCS score includes the dimensions of physical functioning, role-physical, bodily pain, and general health perceptions. The individual items on the SF-12 were used to evaluate generic aspects of QOL. The SF-12 has well-established validity and reliability.[34]

Disease-specific QOL was evaluated using the Quality of Life Scale-Patient Version (QOL-PV).[35,36] This 41-item instrument measures four domains of QOL (i.e., physical, psychological, social, and spiritual well-being) in oncology patients, as well as a total QOL score. Each item is rated on a 0−10 numeric rating scale with higher scores indicating a better QOL. The QOL-PV has well-established validity and reliability.[35−38] In the present study, the Cronbach's alpha for the QOL-PV total score was 0.92.

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Board at each of the study sites. Eligible patients were approached by a research staff member in the infusion unit to discuss participation in the study. Written informed consent was obtained from all patients. Depending on the length of their CTX cycles, patients completed questionnaires in their homes, a total of six times over two cycles of CTX (i.e., before CTX administration [i.e., recovery from previous CTX cycle, Assessments 1 and 4], approximately 1 week after CTX administration (i.e., acute symptoms, Assessments 2 and 5), approximately 2 weeks after CTX administration [i.e., potential nadir, Assessments 3 and 6]). Research nurses reviewed patients' medical records for disease and treatment information.

Data Analysis

Descriptive Statistics. Data were analyzed using SPSS version 23.[39] Descriptive statistics and frequency distributions were calculated for demographic and clinical characteristics.

Latent Profile Analysis of Physical Function Scores. As was done for different outcomes,[40] unconditional latent profile analysis (LPA) was used to identify the profiles of physical function scores (i.e., PCS scores) that characterized unobserved subgroups of patients (i.e., latent classes) over the six assessments. Typically, growth mixture modeling or latent class growth modeling would be used to identify latent classes of individuals who change differently over time. However, the data in this study demonstrated a complex pattern of change because a pretreatment assessment, an immediate post-treatment assessment, and a second post-treatment assessment were done over two cycles of CTX. Therefore, LPA is more appropriate for this type of change trajectory. To incorporate expected correlations among the repeated measures, we included covariance parameters among measures that were one or two occasions apart (i.e., a covariance structure with a lag of two). In this way, we retained the within-person correlation among the measures, at the same time that we focused on the patterns of means that distinguished among the latent classes. We limited the covariance structure to a lag of two to accommodate the expected reduction in correlation that would be introduced by two treatments within each set of three measurement occasions and to reduce model complexity.

Estimation was carried out with full information maximum likelihood with standard errors and a chi-square test that are robust to nonnormality and nonindependence of observations ("estimator = MLR"). Model fit was evaluated to identify the solution that best characterized the observed latent class structure with the Bayesian Information Criterion, Vuong-Lo-Mendell-Rubin likelihood ratio test, entropy, and latent class percentages that were large enough to be reliable (i.e., likely to replicate in new samples).[41,42] Missing data were accommodated with the use of the Expectation−Maximization algorithm.[43]

Mixture models, like LPA, are known to produce solutions at local maxima. Therefore, our models were fit with from 1000 to 2400 random starts. This approach ensured that the estimated model was replicated many times and was not due to a local maximum. Estimation was done with Mplus version 7.4 (Muthen and Muthen, Los Angeles, CA).[44]

Evaluation of Differences Among the Latent Classes. Differences among the latent classes in demographic and clinical characteristics and QOL outcomes were evaluated using analysis of variance and Kruskal-Wallis or chi-square tests with Bonferroni-corrected post hoc contrasts. All calculations used actual values. A corrected *P*-value of <0.0167 (i.e., 0.05/3) was considered statistically significant.

Results

LCA of Physical Function

As shown in Table 1, a three-class solution was selected because the VLMR was significant, indicating that three classes fit the data better than two classes and the VLMR was not significant for the four-class solution, indicating that too many classes had been

Table 1
Latent Profile Analysis Solutions and Fit Indices for One Through Four Classes for SF-12 Physical Component Scores

Model	LL	AIC	BIC	VLMR	Entropy
1 Class	−1927.82	3897.64	3979.42	n/a	n/a
2 Class	−1800.19	3656.37	3765.41	255.27[a]	0.79
3 Class[b]	−1725.57	3521.14	3657.44	149.23[c]	0.82
4 Class	−1684.82	3453.64	3617.20	81.50[d]	0.81

LL = log-likelihood; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; VLMR = Vuong-Lo-Mendell-Rubin likelihood ratio test for the K versus K-1 model.
[a]$P < 0.001$.
[b]The three-class solution was selected because the VLMR was significant, indicating that three classes fit the data better than two classes, and the VLMR was not significant for the four-class solution, indicating that too many classes had been extracted.
[c]$P < 0.05$.
[d]Not significant.

extracted. The classes were named based on a mean reference PCS score of 44.9 identified in the 2001 Utah Health Status Survey as the age-based normative score for individuals aged between 65 and 74 years.[45] As shown in Fig. 1, 35.8% of the sample had PCS scores that were above the normative score at enrollment (i.e., 50.6, "above"). The largest class (43.8%) had PCS scores at enrollment that were slightly below the normative score (i.e., 39.8, "slightly below"). The third class (20.4%) had PCS scores at enrollment that were well below the normative score (i.e., 26.2, "well below"). Across all three classes, the PCS scores remained relatively stable over the two cycles of CTX.

Differences in Demographic and Clinical Characteristics

As shown in Table 2, across the three latent classes, KPS scores (i.e., well below < slightly below < above), as well as number of comorbidities and SCQ scores (i.e., well below > slightly below > above), were in the expected directions. In addition, compared to the above class, patients in the slightly below and well below classes were more likely to be unemployed, to report a lower income, and to have heart disease. Compared to the slightly below and above classes, patients in the well below class were less likely to exercise on a regular basis and more likely to report back pain. Finally, compared to the above class, patients in the well below class had lower hemoglobin and hematocrit levels and were more likely to report depression.

No age or gender differences were found among the latent classes. In addition, none of the disease (i.e., cancer diagnosis, time since cancer diagnosis, number of metastatic sites) or treatment (i.e., number of prior cancer treatments, types of prior cancer treatments, CTX cycle length) characteristics were associated with latent class membership.

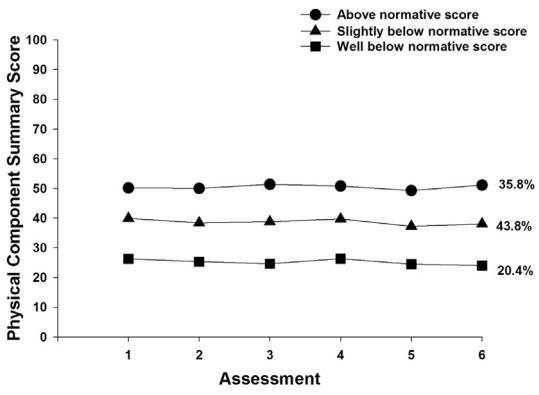

Fig. 1. Trajectories of physical component summary function scores for the three physical function latent classes.

Differences in Generic QOL Outcomes

As shown in Table 3, for the SF-12 physical function, role-physical, bodily pain, general health, vitality, and social functioning scores, the differences among the latent classes followed the same pattern (i.e., well below < slightly below < above). For the role emotional score, compared to patients in the slightly below and above classes, patients in the well below class reported lower scores. In terms of the PCS and MCS scores, the PCS scores followed the expected direction (i.e., well below < slightly below < above). No differences were found among the latent classes in MCS scores.

Differences in Disease-Specific QOL Outcomes

As shown in Table 3, for the QOL-PV at enrollment, the physical well-being, psychological well-being, social well-being, and total QOL scores, the differences among the latent classes followed the same pattern (i.e., well below < slightly below < above). No differences were found among the latent classes in the spiritual well-being scores.

Discussion

This study is the first to use LPA to identify groups of older oncology patients with distinct physical function profiles over two cycles of CTX. In this relatively large sample of 363 patients, with a mean age of 71.4 (±5.5) years, three groups of older adults with distinct physical function profiles were identified. When the mean PCS scores at enrollment for these three groups were compared to age-based normative data for individuals between 65 and 74 years from the 2001 Utah Health Status Survey (i.e., a mean PCS score of 44.9),[45] 64.2% of our sample was slightly or well below this normative score. As a validity check, compared to the "above normative score" class, the differences in PCS scores at enrollment for the slightly

Table 2
Differences in Demographic and Clinical Characteristics Among the Physical Function Latent Classes

Characteristic	Well Below Normative Score (0) 20.4% ($n = 74$) Mean (SD)	Below Normative Score (1) 43.8% ($n = 159$) Mean (SD)	Above Normative Score (2) 35.8% ($n = 130$) Mean (SD)	Statistics
Age (yrs)	72.7 (6.0)	71.2 (5.4)	70.7 (5.4)	$F = 2.96$, $P = 0.053$
Education (yrs)	16.6 (3.6)	16.0 (2.9)	17.0 (3.1)	$F = 3.43$, $P = 0.034$; $1 < 2$
Body mass index (kg/m^2)	27.1 (5.9)	26.2 (5.1)	25.5 (5.3)	$F = 2.09$, $P = 0.125$
Karnofsky Performance Status score	68.7 (12.1)	83.3 (10.6)	89.6 (8.0)	$F = 97.22$, $P < 0.001$; $0 < 1 < 2$
Number of comorbidities	3.6 (1.6)	2.9 (1.5)	2.3 (1.2)	$F = 17.01$, $P < 0.001$; $0 > 1 > 2$
SCQ score	8.2 (3.9)	6.4 (3.4)	4.7 (2.4)	$F = 30.09$, $P < 0.001$; $0 > 1 > 2$
Hemoglobin (gm/dL)	11.1 (1.6)	11.4 (1.4)	11.8 (1.3)	$F = 6.15$, $P = 0.002$; $0 < 2$
Hematocrit (%)	33.5 (4.7)	34.2 (4.1)	35.3 (4.0)	$F = 4.96$, $P = 0.008$; $0 < 2$
Time since cancer diagnosis (yrs)	4.4 (7.9)	2.4 (4.3)	2.6 (4.2)	KW, $P = 0.212$
Time since cancer diagnosis (median)	1.05	0.5	0.5	
Number of prior cancer treatments	2.0 (1.6)	1.7 (1.5)	1.7 (1.6)	$F = 1.11$, $P = 0.329$
Number of metastatic sites including lymph node involvement	1.4 (1.3)	1.4 (1.2)	1.3 (1.1)	$F = 0.76$, $P = 0.471$
Number of metastatic sites excluding lymph node involvement	1.1 (1.1)	0.9 (1.1)	0.8 (0.9)	$F = 1.71$, $P = 0.183$
	% (n)	% (n)	% (n)	
Gender				$\chi^2 = 6.00$, $P = 0.199$
Female	78.4 (58)	67.3 (107)	63.8 (83)	
Male	21.6 (16)	32.1 (51)	36.2 (47)	
Transgender[a]	0.0 (0)	0.6 (1)	0.0 (0)	
Ethnicity				$\chi^2 = 1.48$, $P = 0.961$
White	80.8 (59)	78.5 (124)	81.5 (106)	
Asian or Pacific Islander	6.8 (5)	7.6 (12)	4.6 (6)	
Black	6.8 (5)	6.3 (10)	6.9 (9)	
Hispanic, mixed, or other	5.5 (4)	7.6 (12)	6.9 (9)	
Married or partnered (% yes)	58.3 (42)	55.8 (87)	63.6 (82)	$\chi^2 = 1.80$, $P = 0.407$
Lives alone (% yes)	27.8 (20)	35.5 (55)	24.0 (31)	$\chi^2 = 4.59$, $P = 0.101$
Childcare responsibilities (% yes)	2.8 (2)	6.3 (10)	3.9 (5)	$\chi^2 = 1.63$, $P = 0.442$
Care of adult responsibilities (% yes)	6.5 (4)	6.3 (9)	2.5 (3)	$\chi^2 = 2.30$, $P = 0.317$
Currently employed (% yes)	9.6 (7)	17.6 (28)	33.9 (43)	$\chi^2 = 18.90$, $P < 0.001$; 0 and $1 < 2$
Income				KW, $P = 0.002$; 0 and $1 < 2$
<$30,000+	31.3 (20)	25.2 (34)	18.3 (21)	
$30,000 to <$70,000	25.0 (16)	31.1 (42)	18.3 (21)	
$70,000 to <$100,000	12.5 (8)	20.0 (27)	17.4 (20)	
≥$100,000	31.3 (20)	23.7 (32)	46.1 (53)	
Specific comorbidities (% yes)				
Heart disease	17.6 (13)	15.7 (25)	3.1 (4)	$\chi^2 = 14.45$, $P = 0.001$; 0 and $1 > 2$
High blood pressure	56.8 (42)	45.9 (73)	40.0 (52)	$\chi^2 = 5.33$, $P = 0.070$
Lung disease	31.1 (23)	22.0 (35)	11.5 (15)	$\chi^2 = 11.85$, $P = 0.003$; $0 > 2$
Diabetes	20.3 (15)	14.5 (23)	10.8 (14)	$\chi^2 = 3.47$, $P = 0.176$
Ulcer or stomach disease	4.1 (3)	5.0 (8)	3.8 (5)	$\chi^2 = 0.27$, $P = 0.875$
Kidney disease	1.4 (1)	3.8 (6)	0.0 (0)	$\chi^2 = 5.55$, $P = 0.062$
Liver disease	8.1 (6)	6.3 (10)	7.7 (10)	$\chi^2 = 0.34$, $P = 0.845$
Anemia or blood disease	8.1 (6)	10.7 (17)	7.7 (10)	$\chi^2 = 0.89$, $P = 0.642$
Depression	24.3 (18)	20.1 (32)	10.8 (14)	$\chi^2 = 7.18$, $P = 0.028$; $0 > 2$
Osteoarthritis	33.8 (25)	21.4 (34)	20.0 (26)	$\chi^2 = 5.64$, $P = 0.059$
Back pain	47.3 (35)	23.9 (38)	16.9 (22)	$\chi^2 = 23.27$, $P < 0.001$; $0 > 1$ and 2
Rheumatoid arthritis	5.4 (4)	2.5 (4)	3.8 (5)	$\chi^2 = 1.26$, $P = 0.532$
Exercise on a regular basis (% yes)	36.6 (26)	68.4 (106)	79.8 (103)	$\chi^2 = 38.80$, $P < 0.001$; $0 < 1$ and 2
Smoking, current or history of (% yes)	47.9 (35)	48.4 (76)	46.0 (58)	$\chi^2 = 0.17$, $P = 0.920$
Cancer diagnosis				$\chi^2 = 11.50$, $P = 0.074$
Breast	20.3 (15)	23.9 (38)	23.8 (31)	
Gastrointestinal	20.3 (15)	35.2 (56)	36.9 (48)	
Gynecological	28.4 (21)	18.2 (29)	22.3 (29)	
Lung	31.1 (23)	22.6 (36)	16.9 (22)	

(*Continued*)

Table 2
Continued

	% (*n*)	% (*n*)	% (*n*)	
Type of prior cancer treatment				$\chi^2 = 7.46$, $P = 0.280$
No prior treatment	21.1 (15)	22.2 (34)	27.1 (35)	
Only surgery, CTX, or RT	28.2 (20)	37.3 (57)	35.7 (46)	
Surgery & CTX, or Surgery & RT, or CTX & RT	29.6 (21)	30.1 (46)	23.3 (30)	
Surgery & CTX & RT	21.1 (15)	10.5 (16)	14.0 (18)	
Length of CTX cycle				$\chi^2 = 2.12$, $P = 0.714$
14 days	32.4 (24)	37.3 (59)	31.8 (41)	
21 days	54.1 (40)	52.5 (83)	58.9 (76)	
28 days	13.5 (10)	10.1 (16)	9.3 (12)	

SCQ = Self-Administered Comorbidity Questionnaire; KW = Kruskal-Wallis; CTX = chemotherapy; RT = radiation therapy.
[a]Chi-square analysis and post hoc contrasts done without the transgender patient include in the analyses.

below (i.e., Cohen's d = 1.0) and well below (i.e., Cohen's d = 2.3) classes represent not only statistically significant but clinically meaningful differences in physical function.[46,47] In addition, the PCS scores for the two lower classes were below those reported in studies of older cancer survivors.[48,49]

It is interesting to note that although previous studies reported a decline in self-reported physical function in the immediate treatment period,[16,18] the PCS scores within each of our latent classes remained relatively stable over the two cycles of CTX. One potential explanation for these differences is that mean scores were used in the previous studies to evaluate changes over time. This approach does not allow for the identification of subgroups with distinct physical function profiles. Similar to our findings, Given and colleagues reported that when assessments of average change in physical functioning scores for patients who remained within the same quartile over two assessment were made, these patients scores did not deteriorate over time.[17] Additional research is warranted to confirm the latent classes identified in our study.

Although consistent with previous reports,[16–18] an interesting finding from this study is that none of the cancer or treatment characteristics were associated with latent class membership. Given that metastatic disease is associated with decrements in physical function, a reasonable hypothesis would be that older adults in the slightly below and well below classes would have a higher number of metastatic sites and/or would have received a higher number of cancer treatments. Perhaps, these patients did not report their functional decline to their oncologists or they were receiving lower doses of CTX compared to those in the above class. Our finding of a lack of an association between cancer burden and functional status warrants confirmation in future studies.

Of note, and consistent with two reports from the same cohort,[16,17] both a higher number of comorbid conditions and a more severe comorbidity profile were associated with membership in the two lower

Table 3
Differences in Quality-of-Life Scores at Enrollment Among the Physical Function Latent Classes

Characteristic	Well Below Normative Score (0) 20.4% (*n* = 74) Mean (SD)	Below Normative Score (1) 43.8% (*n* = 159) Mean (SD)	Above Normative Score (2) 35.8% (*n* = 130) Mean (SD)	Statistics
Medical Outcomes Study—Short Form 12				
Physical functioning	9.6 (15.4)	42.7 (26.9)	81.1 (22.6)	$F = 223.92$, $P < 0.001$; 0 < 1 < 2
Role-physical	25.2 (19.2)	46.0 (24.0)	73.6 (22.3)	$F = 114.77$, $P < 0.001$; 0 < 1 < 2
Bodily pain	55.6 (33.1)	78.1 (24.7)	94.0 (13.6)	$F = 61.24$, $P < 0.001$; 0 < 1 < 2
General health	35.9 (27.8)	64.8 (23.1)	75.7 (22.8)	$F = 63.71$, $P < 0.001$; 0 < 1 < 2
Vitality	26.4 (22.6)	40.5 (25.6)	62.6 (22.5)	$F = 58.78$, $P < 0.001$; 0 < 1 < 2
Social functioning	43.2 (33.9)	66.7 (30.6)	82.0 (25.5)	$F = 39.56$, $P < 0.001$; 0 < 1 < 2
Role emotional	68.7 (34.1)	72.4 (27.8)	85.8 (20.8)	$F = 12.24$, $P < 0.001$; 0 and 1 < 2
Mental health	73.8 (20.3)	73.2 (22.0)	78.5 (17.9)	$F = 2.69$, $P = 0.069$
Physical component summary score	26.2 (6.6)	39.8 (6.5)	50.6 (5.9)	$F = 325.23$, $P < 0.001$; 0 < 1 < 2
Mental component summary score	49.9 (11.9)	49.2 (11.5)	51.8 (9.3)	$F = 1.92$, $P = 0.148$
Quality of Life Scale—Patient Version				
Physical well-being	6.0 (1.6)	6.9 (1.6)	8.0 (1.3)	$F = 44.23$, $P < 0.001$; 0 < 1 < 2
Psychological well-being	5.0 (1.8)	5.8 (1.9)	6.4 (1.8)	$F = 13.52$, $P < 0.001$; 0 < 1 < 2
Social well-being	5.4 (1.8)	6.4 (1.8)	7.3 (1.6)	$F = 25.44$, $P < 0.001$; 0 < 1 < 2
Spiritual well-being	4.9 (2.3)	5.0 (2.1)	4.8 (2.1)	$F = 0.25$, $P = 0.776$
Total quality-of-life score	5.3 (1.5)	6.0 (1.4)	6.7 (1.3)	$F = 23.04$, $P < 0.001$; 0 < 1 < 2

physical function classes. In addition, similar to findings from a large epidemiologic study,[50] the most common comorbid conditions in this sample were high blood pressure, back pain, osteoarthritis, lung disease, depression, and diabetes. In the present study, the four comorbid conditions that differentiated between the well below and the above normative score classes were as follows: heart disease, lung disease, depression, and back pain. These findings support the need to evaluate not only the number but also the impact of specific comorbid conditions on older oncology patients' functional status as part of a comprehensive geriatric assessment.[51–53]

Anemia is a common problem in older adults.[54,55] Recently, anemia was defined as a hemoglobin level of <12 g/dL in both older men and women.[56] Using this definition, not unexpectedly in patients undergoing CTX, all three classes of older patients were anemic. This problem is important to evaluate in older adults because anemia is associated with decreased physical performance,[57] an increase in the number of falls,[58] frailty,[57,59,60] increase in depressive symptoms,[61,62] increase in the number of hospitalizations,[63] and increased mortality.[64,65] Although the level of anemia observed in this study may not warrant routine treatment in oncology patients, clinicians need to monitor older adults receiving CTX more carefully to evaluate the impact of anemia on their ability to function.

In terms of demographic characteristics, a higher percentage of older adults in the two lower physical function classes were not employed and reported a lower annual household income. This finding is consistent with work by Owusu and colleagues who found that older women newly diagnosed with nonmetastatic breast cancer, who had a median household income of <$35,000 were 2.5 times more likely to have functional disability at the time of their initial diagnosis.[66] These findings suggest that financial and social factors warrant evaluation and interventions to mitigate their negative impact on physical function.

Of note, although in the other two classes approximately 70% of the patients reported that they exercised on a regular basis, only 37% of the patients in the well below class indicated this level of exercise. Given that older adults who engage in 150 minutes of moderate intensity aerobic exercise per week can reduce the risk of functional impairments by 50%,[67] clinicians need to assess patients' level of exercise before and during CTX and prescribe exercise interventions.

In terms of generic- and disease-specific domains of QOL, as shown in Table 3, significant differences were found among the three physical function classes for almost all of the subscales on the SF-12 and the QOL-PV. With the exception of the mental health, MCS, and spiritual well-being subscales, decrements in physical function were associated with lower scores on all domains of QOL. All of the differences in the various QOL subscales represent not only statistically significant but clinically meaningful decrements in the various QOL domains (i.e., Cohen's d's that ranged between 0.3 and 2.0).[46,47] Given the findings from recent interventions studies in older adults and cancer survivors that suggest that physical activity interventions improve patients' functional status and QOL,[68–72] additional research is warranted to evaluate the use of these types of interventions in older adults during CTX. The lack of significant differences among the classes on the mental health and MCS scores may indicate that these items on the SF-12 are not specific enough to capture depressive symptoms.

Several study limitations warrant consideration. Objective measures of physical function were not assessed in this study. However, the PCS score of the SF-12 is a valid and reliable measure of physical function and normative scores are available for comparative purposes. In addition, it is important to note that patients' self-reported KPS scores, a commonly used measure of functional status in oncology patients, differentiated among the latent classes. Sampling bias may result in an underestimation of the physical function of older adults receiving CTX because patients with lower levels of function may have declined participation. Other measures included in a comprehensive geriatric assessment (e.g., nutritional status, frailty) were not evaluated in this study. Future studies need to compare the latent classes identified in this study to other subgroups identified using other measures of function (e.g., frail vs. vulnerable vs. fit[73]). Although patients were assessed over two cycles of CTX, an assessment before the initiation of the current CTX regimen was not performed. In addition, future studies should determine which components of physical function (i.e., individual items on the SF-12) have the most impact on latent class membership.

Despite these limitations, the findings from this study provide new insights into the percentage of older adults receiving CTX who reported decrements in physical function that are below normative values for older adults in the general population. Given the negative impact of comorbidity on physical function observed in our study and other studies,[16,17] additional research is warranted on the impact of specific comorbidities and whether optimal management of these comorbidities affects physical function. Future intervention studies to improve physical function in older adults undergoing CTX need to account for demographic, clinical, behavioral, and social characteristics that influence physical function.

Disclosures and Acknowledgments

This work was supported by the National Cancer Institute (R01CA134900 and K05CA168960) and the National Institute on Aging (T32AG000212). Dr. Miaskowski is an American Cancer Society Clinical Research Professor. The authors have no conflicts of interest to declare.

References

1. Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of cancer incidence in the United States: burdens upon an aging, changing nation. J Clin Oncol 2009;27:2758–2765.

2. Extermann M, Aapro M, Bernabei R, et al. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol 2005;55:241–252.

3. Fairfield KM, Murray K, Lucas FL, et al. Completion of adjuvant chemotherapy and use of health services for older women with epithelial ovarian cancer. J Clin Oncol 2011;29:3921–3926.

4. Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol 2014;32:2595–2603.

5. Puts MT, Hardt J, Monette J, et al. Use of geriatric assessment for older adults in the oncology setting: a systematic review. J Natl Cancer Inst 2012;104:1133–1163.

6. Puts MT, Santos B, Hardt J, et al. An update on a systematic review of the use of geriatric assessment for older adults in oncology. Ann Oncol 2014;25:307–315.

7. Ramjaun A, Nassif MO, Krotneva S, Huang AR, Meguerditchian AN. Improved targeting of cancer care for older patients: a systematic review of the utility of comprehensive geriatric assessment. J Geriatr Oncol 2013;4:271–281.

8. Hurria A, Mohile SG, Dale W. Research priorities in geriatric oncology: addressing the needs of an aging population. J Natl Compr Canc Netw 2012;10:286–288.

9. Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. N Engl J Med 2002;346:1061–1066.

10. Meropol NJ, Egleston BL, Buzaglo JS, et al. Cancer patient preferences for quality and length of life. Cancer 2008;113:3459–3466.

11. Chouliara Z, Kearney N, Stott D, Molassiotis A, Miller M. Perceptions of older people with cancer of information, decision making and treatment: a systematic review of selected literature. Ann Oncol 2004;15:1596–1602.

12. Chouliara Z, Miller M, Stott D, et al. Older people with cancer: perceptions and feelings about information, decision-making and treatment–a pilot study. Eur J Oncol Nurs 2004;8:257–261.

13. Chen C, Sia I, Ma HM, et al. The synergistic effect of functional status and comorbidity burden on mortality: a 16-year survival analysis. PLoS One 2014;9:e106248.

14. Anderson G, Horvath J. The growing burden of chronic disease in America. Public Health Rep 2004;119:263–270.

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

16. Given B, Given C, Azzouz F, Stommel M. Physical functioning of elderly cancer patients prior to diagnosis and following initial treatment. Nurse Res 2001;50:222–232.

17. Given CW, Given B, Azzouz F, Stommel M, Kozachik S. Comparison of changes in physical functioning of elderly patients with new diagnoses of cancer. Med Care 2000;38:482–493.

18. Hoppe S, Rainfray M, Fonck M, et al. Functional decline in older patients with cancer receiving first-line chemotherapy. J Clin Oncol 2013;31:3877–3882.

19. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–483.

20. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The Index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963;185:914–919.

21. Montorio I, Izal M. The Geriatric Depression Scale: a review of its development and utility. Int Psychogeriatr 1996;8:103–112.

22. Sheikh JI, Yesavage JA, Brooks JO 3rd, et al. Proposed factor structure of the Geriatric Depression Scale. Int Psychogeriatr 1991;3:23–28.

23. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179–186.

24. Inouye SK, Peduzzi PN, Robison JT, et al. Importance of functional measures in predicting mortality among older hospitalized patients. JAMA 1998;279:1187–1193.

25. Mayer-Oakes SA, Oye RK, Leake B. Predictors of mortality in older patients following medical intensive care: the importance of functional status. J Am Geriatr Soc 1991;39:862–868.

26. Miaskowski C, Cooper BA, Aouizerat B, et al. The symptom phenotype of oncology outpatients remains relatively stable from prior to through 1 week following chemotherapy. Eur J Cancer Care (Engl) 2017;26.

27. Miaskowski C, Cooper BA, Melisko M, et al. Disease and treatment characteristics do not predict symptom occurrence profiles in oncology outpatients receiving chemotherapy. Cancer 2014;120:2371–2378.

28. Karnofsky D, Abelmann WH, Craver LV, Burchenal JH. The use of nitrogen mustards in the palliative treatment of carcinoma. Cancer 1948;1:634–656.

29. Schnadig ID, Fromme EK, Loprinzi CL, et al. Patient-physician disagreement regarding performance status is associated with worse survivorship in patients with advanced cancer. Cancer 2008;113:2205–2214.

30. Ando M, Ando Y, Hasegawa Y, et al. Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. Br J Cancer 2001;85:1634–1639.

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

32. Brunner F, Bachmann LM, Weber U, et al. Complex regional pain syndrome 1—the Swiss cohort study. BMC Musculoskelet Disord 2008;9:92.

33. Cieza A, Geyh S, Chatterji S, et al. Identification of candidate categories of the International Classification of Functioning Disability and Health (ICF) for a Generic ICF Core Set based on regression modelling. BMC Med Res Methodol 2006;6:36.

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

35. Padilla GV, Presant C, Grant MM, et al. Quality of life index for patients with cancer. Res Nurs Health 1983;6:117—126.

36. Padilla GV, Ferrell B, Grant MM, Rhiner M. Defining the content domain of quality of life for cancer patients with pain. Cancer Nurs 1990;13:108—115.

37. Ferrell BR, Dow KH, Grant M. Measurement of the quality of life in cancer survivors. Qual Life Res 1995;4:523—531.

38. Ferrell BR. The impact of pain on quality of life. A decade of research. Nurs Clin North Am 1995;30:609—624.

39. SPSS. IBM SPSS for Windows (Version 23). Armonk, NY: SPSS, Inc, 2015.

40. Kober KM, Cooper BA, Paul SM, et al. Subgroups of chemotherapy patients with distinct morning and evening fatigue trajectories. Support Care Cancer 2016;24:1473—1485.

41. Muthen LK, Muthen BO. Mplus User's Guide, 7th ed. Los Angeles, CA: Muthen & Muthen, 1998-2012.

42. Nylund KL, Asparouhov T, Muthen BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: a Monte Carlo simulation study. Struct Equ Modeling 2007;14:535—569.

43. Muthen B, Shedden K. Finite mixture modeling with mixture outcomes using the EM algorithm. Biometrics 1999;55:463—469.

44. Muthen LK, Muthen BO. Mplus User's Guide, 8th ed. Los Angeles, CA: Muthen & Muthen, 1998-2017.

45. Utah Department of Health. Interpreting the SF-12-Utah Health Status Survey. Salt Lake City: Utah, 2001.

46. Sloan JA, Frost MH, Berzon R, et al. The clinical significance of quality of life assessments in oncology: a summary for clinicians. Support Care Cancer 2006;14:988—998.

47. Osoba D. Interpreting the meaningfulness of changes in health-related quality of life scores: lessons from studies in adults. Int J Cancer Suppl 1999;12:132—137.

48. Annunziata MA, Muzzatti B, Giovannini L, et al. Is long-term cancer survivors' quality of life comparable to that of the general population? An Italian study. Support Care Cancer 2015;23:2663—2668.

49. Huang MH, Lytle T, Miller KA, Smith K, Fredrickson K. History of falls, balance performance, and quality of life in older cancer survivors. Gait Posture 2014;40:451—456.

50. Smith AW, Reeve BB, Bellizzi KM, et al. Cancer, comorbidities, and health-related quality of life of older adults. Health Care Financ Rev 2008;29:41—56.

51. Carlson C, Merel SE, Yukawa M. Geriatric syndromes and geriatric assessment for the generalist. Med Clin North Am 2015;99:263—279.

52. Jolly TA, Deal AM, Nyrop KA, et al. Geriatric assessment-identified deficits in older cancer patients with normal performance status. Oncologist 2015;20:379—385.

53. Mohile SG, Velarde C, Hurria A, et al. Geriatric assessment-guided care processes for older adults: a delphi consensus of geriatric oncology experts. J Natl Compr Canc Netw 2015;13:1120—1130.

54. Cappellini MD, Motta I. Anemia in clinical practice-definition and classification: does hemoglobin change with aging? Semin Hematol 2015;52:261—269.

55. Rohrig G. Anemia in the frail, elderly patient. Clin Interv Aging 2016;11:319—326.

56. Andres E, Serraj K, Federici L, Vogel T, Kaltenbach G. Anemia in elderly patients: new insight into an old disorder. Geriatr Gerontol Int 2013;13:519—527.

57. Pires Corona L, Drumond Andrade FC, de Oliveira Duarte YA, Lebrao ML. The relationship between anemia, hemoglobin concentration and frailty in Brazilian older adults. J Nutr Health Aging 2015;19:935—940.

58. Dharmarajan TS, Avula S, Norkus EP. Anemia increases risk for falls in hospitalized older adults: an evaluation of falls in 362 hospitalized, ambulatory, long-term care, and community patients. J Am Med Dir Assoc 2007;8:e9—e15.

59. Hirani V, Naganathan V, Blyth F, et al. Cross-Sectional and longitudinal associations between anemia and frailty in older Australian men: the concord health and aging in men project. J Am Med Dir Assoc 2015;16:614—620.

60. Juarez-Cedillo T, Basurto-Acevedo L, Vega-Garcia S, et al. Prevalence of anemia and its impact on the state of frailty in elderly people living in the community: SADEM study. Ann Hematol 2014;93:2057—2062.

61. Pan WH, Chang YP, Yeh WT, et al. Co-occurrence of anemia, marginal vitamin B6, and folate status and depressive symptoms in older adults. J Geriatr Psychiatry Neurol 2012;25:170—178.

62. Stewart R, Hirani V. Relationship between depressive symptoms, anemia, and iron status in older residents from a national survey population. Psychosom Med 2012;74:208—213.

63. Nguyen HQ, Chu L, Amy Liu IL, et al. Associations between physical activity and 30-day readmission risk in chronic obstructive pulmonary disease. Ann Am Thorac Soc 2014;11:695—705.

64. Hirani V, Naganathan V, Blyth F, et al. Multiple, but not traditional risk factors predict mortality in older people: the Concord Health and Ageing in Men Project. Age (Dordr) 2014;36:9732.

65. Denewet N, De Breucker S, Luce S, et al. Comprehensive geriatric assessment and comorbidities predict survival in geriatric oncology. Acta Clin Belg 2016;71:206—213.

66. Owusu C, Schluchter M, Koroukian SM, Mazhuvanchery S, Berger NA. Racial disparities in functional disability among older women with newly diagnosed nonmetastatic breast cancer. Cancer 2013;119:3839—3846.

67. Visser M, Simonsick EM, Colbert LH, et al. Type and intensity of activity and risk of mobility limitation: the

mediating role of muscle parameters. J Am Geriatr Soc 2005;53:762–770.

68. Daum CW, Cochrane SK, Fitzgerald JD, Johnson L, Buford TW. Exercise interventions for preserving physical function among cancer survivors in middle to late life. J Frailty Aging 2016;5:214–224.

69. Hupin D, Roche F, Gremeaux V, et al. Even a low-dose of moderate-to-vigorous physical activity reduces mortality by 22% in adults aged >/=60 years: a systematic review and meta-analysis. Br J Sports Med 2015;49:1262–1267.

70. Morey MC, Blair CK, Sloane R, et al. Group trajectory analysis helps to identify older cancer survivors who benefit from distance-based lifestyle interventions. Cancer 2015;121:4433–4440.

71. Morey MC, Snyder DC, Sloane R, et al. Effects of home-based diet and exercise on functional outcomes among older, overweight long-term cancer survivors: RENEW: a randomized controlled trial. JAMA 2009;301:1883–1891.

72. Smith TM, Broomhall CN, Crecelius AR. Physical and psychological effects of a 12-session cancer rehabilitation exercise program. Clin J Oncol Nurs 2016;20:653–659.

73. Balducci L, Extermann M. Management of cancer in the older person: a practical approach. Oncologist 2000;5:224–237.