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Health and personal resources in older cancer patients undergoing chemotherapy

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Abstract

Objectives—The purpose of this study was to gather preliminary data on both direct and moderating effects of health status, the social environment, and perceived personal control on the older cancer patient's symptom distress and QOL during a treatment regimen of chemotherapy.

Materials and Methods—Participants were cancer patients aged ≥ 65 years being treated with a variety of chemotherapy regimens specific to their particular diagnosis. Using a longitudinal study design, we measured patients at baseline prior to beginning chemotherapy, midpoint in the regimen, and upon discharge (approximately 2 weeks after chemotherapy completion). Outcomes of interest were symptom distress and QOL. Multivariate linear regression was used to determine the association between the predictors and outcomes, controlling for demographic and clinical characteristics.

Results—Our final sample consisted of 94 cancer patients (35 male; 59 female; mean age 73.5 years). In the health status domain, lower body strength was inversely associated with symptom distress ($p=0.025$) and positively associated with QOL ($p=0.015$). In the social environment domain, social support was inversely associated with fatigue ($p=0.001$) and depression ($p<0.001$), and positively associated with QOL ($p=0.016$ and $p=0.029$ at midpoint and endpoint, respectively). Personal control variables, mastery and self-efficacy, were significantly associated with multiple outcomes of interest.

Discussion—Mastery was the best predictor of symptom distress and QOL. Self-efficacy, social support, and lower body functioning are important predictors of these outcomes among older cancer patients undergoing chemotherapy.

Keywords

chemotherapy; older adults; physical function; social support; personal control; fatigue; quality of life

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Introduction

Because age is a major risk factor for cancer, the majority of cancer patients are older adults. This fact, coupled with our aging population, has led researchers to conclude that we will see a substantial increase in cancer incidence in the near future, with some estimates as high as 67% by 2030.(1) Chemotherapy is an effective treatment for cancer, and studies have shown that generally healthy older cancer patients obtain similar benefits from standard chemotherapy treatment as their younger counterparts.(2–5) Nevertheless, age disparities exist in regards to the use of chemotherapy as a cancer treatment in older adults, with older adults less likely to receive chemotherapy for a variety of cancers.(6) Compared to younger adults, older adults are at greater risk of certain complications from chemotherapy resulting in unpleasant and serious side effects, in particular, lower tolerance of the toxicity of the chemotherapy treatment.(7, 8) Therefore, the older adult cancer patient receiving chemotherapy is subject to problems associated with the treatment regimen that are exhibited as physical symptoms and comorbid conditions. These are often considered to be extremely stressful to the patient and may impair both physical and psychological functioning, thereby impacting quality of life (QOL).

While there are many factors of advancing age that can be seen as beneficial to the older adult, including continued creativity and development of wisdom, advancing age is also associated with various factors detrimental to the older adult, which make a cancer diagnosis and associated treatment extremely stressful. Older cancer patients may be negatively affected due to the aging process, which limits their adaptability to the stress of chemotherapy treatment. This may include (a) general health status, in particular, presence of comorbid disease and functional disability; (b) the social or external environment, encompassing social support and social network; and (c) personal or internal resources, such as perceived personal control, generally defined in terms of the perceived influence that individuals have over their lives and environments, Elderly cancer patients tend to have worse outcomes than their younger counterparts; this is thought to be due, at least in part, to the myriad non-cancer chronic diseases that tend to accrue with age, complicate treatment decisions, impose functional limitations, and eventually lead to functional disability. (9, 10) In a typical geriatric series, people aged 65 years and older have been shown to have an average of three different diseases, and multiple studies have shown that comorbidities are relevant to the prognosis of cancer patients(11, 12). Also, while a secondary analysis of epidemiological data has shown presence of comorbid conditions correlating with functional status in older cancer patients,(13) a clinical study of 203 older cancer patients found no correlation between presence of comorbid conditions and functional status, indicating that these constructs may need to be assessed separately. (14)

Whereas a strong social support system is thought to be advantageous in dealing with stressful situations, advancing age is often accompanied by loss of key contacts due to death, retirement, and relocation. Early studies with cancer patients found emotional support and social exchange predictive of well-being in cancer patients and inadequate support associated with maladjustment to a cancer diagnosis and depression. (15–19) In breast cancer patients, social support has been found to modify the effect of cancer-related intrusive thoughts on QOL, and to have direct effects on mental health. (20, 21) In the context of chemotherapy, lack of emotional support has been associated with higher levels of treatment-related anxiety.(22)

Two elements of personal control, self-efficacy and mastery, are among internal resources integral to coping with cancer. Self-efficacy rests on the expectancy that a sought after outcome is achievable and that an individual can see himself as being capable of engaging in behavior that will produce the desired result. Self-efficacy has been related to coping with cancer (23–25), and research supports the notion that cancer patients who feel more efficacious about their coping capacity are better adjusted and will cope better with the disease and treatment side-effects.(26) Likewise, an impressive body of literature has described the beneficial role of sense of mastery, (27–30) defined as the extent to which individuals perceive having personal power and control over their life and environment. (31, 32) Sense of mastery has also been known to serve as a buffer against the negative consequences that arise from adversity like a medical event or functional disability.(33–35) The positive effects of sense of mastery also have been found among breast cancer survivors such that those with a greater sense of mastery had a better physical and psychological adjustment and a higher quality of life. (36, 37) Little, if any, research on self-efficacy and mastery has been done with older patients in the context of chemotherapy treatment.

The purpose of this study was to gather preliminary data on both direct and moderating effects of health status, the social environment, and perceived personal control on the cancer patient's symptom distress and QOL during a treatment regimen of chemotherapy. The primary aim of the study was to determine the effect of comorbid disease and physical functioning, social support and network, and perceived personal control (both cancer-specific and global) on symptom distress and QOL of older cancer patients undergoing adjuvant/therapeutic chemotherapy, both at regimen midpoint and upon follow-up at the completion of treatment. General hypotheses were as follows:

> H^1: Older cancer patients with more comorbid illness, more functional disability or poorer physical functioning at baseline will exhibit higher levels of symptom distress and poorer QOL during follow-up;
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> H^2: Older cancer patients with more social support and larger social networks at baseline will exhibit lower levels of symptom distress and better QOL during follow-up;
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> H^3: Older cancer patients with higher levels of perceived cancer-specific self-efficacy and global mastery at baseline will exhibit lower levels of symptom distress and better QOL during follow-up.

A second aim of the study was to examine the relative contributions of these domains to the outcomes of interest. While we hypothesized that physical health, social factors and perceived personal control impact an individual's ability to tolerate chemotherapy and maintain QOL, we were interested in discovering which domain best predicted these outcomes.

Methods

Study participants

The sample for this study was drawn from patients seen in the Senior Adult Oncology Program (SAOP) at the H. Lee Moffitt Cancer Center & Research Institute. To become eligible for the study, participants had to: (a) be ≥ 65 years of age; (b) have a score ≥24 on the Mini Mental State Examination; (c) be capable of speaking and reading English; (d) have been seen by a physician in the SAOP; (e) be scheduled for chemotherapy treatment at Moffitt's Infusion Center; and (f) be able to provide informed consent. Once patients were identified as potential study participants by their SAOP physician, the PI or a trained research assistant (RA) was notified and he/she met with the patient in a room adjacent to the examination room where they were being seen. After confirming patient eligibility, the PI/RA provided the patient with a verbal description of the study. Patients who indicated an interest in participation were given an informed consent form to review in the presence of the PI/RA who offered to answer any questions the patient may have. Those patients wishing to participate were asked to sign the informed consent form and were given a copy of the consent form to take home.

All interviews and clinical evaluations took place at the Moffitt Center. In addition to a review of patient medical records upon entering the study, participants were evaluated at three points in time: (a) at baseline, prior to the first chemotherapy treatment, (b) at the midpoint of their chemotherapy regimen, and (c) at discharge, usually 2–3 weeks after completion of chemotherapy. Patient medical records were again reviewed at the time of the discharge evaluation. Demographic information was obtained at baseline through self-report at the pre-chemotherapy assessment and during the initial review of medical records.

Instruments and measures

The Mini Mental State Examination (MMSE),(38) a widely-used 30-item questionnaire for assessing cognitive mental status, was used during participant screening to establish participant eligibility. In the health status/physical functioning domain, the Cumulative Index Rating Scale – Geriatric (CIRS-G),(39, 40) which allows for severity grading of any comorbidities, was used to assess the presence of comorbid medical conditions; and two self-report measures, Activities of Daily Living (ADLs)(41) and Instrumental Activities of Daily Living (IADLs),(42) were used to assess moderate to severe functional limitations in the participants. Two performance-based measures were used to assess upper and lower body strength: the grip strength test,(43) which uses a dynamometer to measure manual strength, and the "get-up-and-go" test,(44) a timed measure of lower body strength and walking. It should be noted that ADL and get-up-and-go scores are reverse coded, such that higher scores indicate higher functional limitation and disability, respectively. The social environment domain was measured using the Interpersonal Support Evaluation List-Short Form (ISEL-SF),(45) a 15-item self-report measure addressing perceived social support, and the Lubben Social Network Scale,(46) which examines the size and composition of the individual's social network. In the personal control domain, the Cancer Behavior Inventory-Long Form (CBI-L),(24) a cancer-specific measure of perceived self-efficacy, and the

Mastery Scale,(47) a brief measure of perceived global mastery with excellent psychometric characteristics, were used to assess perceived personal control in the patients.

Outcomes of interest were symptom distress and quality of life (QOL). Symptom distress was measured by the 33-item Memorial Symptom Assessment Scale (MSAS), which reflects symptoms commonly associated with cancer, and is designed to differentiate among frequency, intensity, and distress from these symptoms.(48, 49) Three instruments were used to evaluate QOL. The Functional Assessment of Cancer Therapy-Geriatric (FACT-G) scale, a widely used QOL scale in oncology that has been validated in older cancer patients, was used to assess physical, social/familial, emotional, and functional well-being.(50, 51) The severity, frequency, and daily pattern of fatigue as well as its perceived interference with quality of life was measured using the Fatigue Symptom Inventory.(52) Depressive symptomatology was measured using the Center for Epidemiological Studies–Depression (CES-D), a widely used scale that has proven useful both as a screening instrument to detect individuals at risk for depression and to measure the symptoms of depression.(53)

Statistics

Correlation analysis and both simple and multivariate linear regression were performed. The direction of effect between predictors and outcomes was ascertained by examining correlation coefficients (r) and slopes from linear regression. Correlation coefficients were used to assess whether a predictor was associated with an outcome. If the corresponding p-value was less than 0.05, a significant relationship was inferred to exist. Simple linear regression was used to confirm the results of the correlation analysis. Multivariate linear regression was performed to obtain adjusted measures of effect between predictors and outcomes. Demographic and clinical characteristics were perceived as important predictors of symptom distress and QOL of cancer patients undergoing chemotherapy. Stepwise model selection was performed to determine which of these characteristics to include in the final models for each outcome. The relevant covariates were then entered into the final model with the main predictors. Coefficients of determination (r^2) were examined to assess which domains and exposures best predicted each outcome.

This research was approved by the Institutional Review Board of Moffitt Cancer Center.

Results

Participants

The final sample consisted of 94 older cancer patients (35 male, 59 female; mean age 73.5 years) undergoing chemotherapy at the H. Lee Moffitt Cancer Center & Research Institute. The majority of patients were being treated for stage III or stage IV cancers, with lung cancer being the most common tumor site among participants. Demographics and clinical characteristics are detailed in Table 1.

Physical Health

Table 2 shows all of the significant associations between predictors and outcomes based on simple linear regression. The number of co-morbidities at baseline was associated with symptom distress at midpoint of chemotherapy (p=0.030). Symptom distress increased as the patient's number of co-morbidities increased. This effect remained significant in the multivariate linear regression analysis (Table 3). Table 4 displays the covariates included in the final models predicting each outcome. Performance of ADLs was associated with depression at midpoint (p=0.025). Depression increased with increasing functional limitation in performing ADLs, even after controlling for relevant confounders in the multivariate analysis. Lower body functioning, as measured by the get-up-and-go test, was associated with symptom distress (p=0.025) and QOL (p=0.015) at midpoint of chemotherapy. As lower body functioning became more limited, symptom distress increased, while QOL decreased. This deleterious effect of lower body functional limitation persisted after adjusting for confounders.

Social Environment

Social support was associated with fatigue (p=0.001) and depression (p<0.001) at midpoint of chemotherapy and QOL at both time points (p=0.016, p=0.029 at midpoint and endpoint, respectively). As social support increased, disruptive fatigue and depression decreased. On the other hand, patients with more support at baseline exhibited higher QOL during chemotherapy. This effect in particular appeared to diminish over time, based on the change in the correlation coefficient from midpoint to endpoint. With the exception of endpoint QOL, these relationships remained significant in the multivariate linear regression analysis. Social network was associated with QOL at midpoint (p=0.029). Patients with a larger social network at baseline had better QOL during chemotherapy. However, the effect of social network size on QOL lost significance after adjusting for marital status.

Personal Control

Self-efficacy was negatively associated with fatigue (p=0.034) and depression (p=0.001) at midpoint and positively associated with QOL at both time points (p=0.001, p=0.006). All of these effects remained significant in the multivariate analysis. Mastery was associated with symptom distress (p=0.014, p=0.010), QOL (p<0.001, p=0.001), and depression (p=0.016, p=0.028) both during and after a chemotherapy regimen. Patients with a greater sense of mastery at baseline exhibited lower symptom distress, better QOL, and less depression during follow-up. After controlling for relevant demographic and clinical characteristics, these relationships remained significant.

Best predictors of symptom distress and QOL

Table 5 displays the coefficients of determination (r^2) for all of the significant relationships between predictors and outcomes. These values were used to assess which predictor and its corresponding domain best explained the variation in each outcome. Mastery, a predictor from the personal control domain, explained the most variation in symptom distress at both midpoint and endpoint of chemotherapy. Additionally, mastery was the best predictor of QOL, as measured by FACT-G, at both midpoint and endpoint of chemotherapy. Thus, the personal control domain best predicts symptom distress and QOL during and immediately following a chemotherapy regimen. Social support explained the most variation in fatigue and depression at midpoint of follow-up, demonstrating the importance of the social environment for these subsets of QOL. However, by the end of treatment, social support was no longer significantly associated with fatigue or depression, indicating a diminishing effect of social support over time. Mastery was the only significant predictor of depression at the end of chemotherapy, and interestingly, none of the predictors were significantly associated with fatigue immediately following a chemotherapy regimen.

Discussion

Of the five predictors in the physical health domain, performance of IADLs and upper body strength, as measured by maximum grip strength, were not associated with symptom distress or QOL at either time point, nor were they associated with fatigue and depression. Thus, based on the results of this study, public health action planning to address physical health should focus on the other three predictors in the physical health domain (i.e. presence of comorbidities, performance of ADLs, and lower body functioning). Specifically, our study suggests that interventions that help older cancer patients maintain lower body functioning would be the most effective in reducing symptom distress and improving QOL during chemotherapy.

Social support seems to be more important in minimizing symptom distress and maximizing QOL than the size of one’s social network. Had fatigue and depression not been examined, the importance of social support would not have been fully realized. It accounts for more variation in fatigue and depression during chemotherapy than any other predictor variable investigated in this study. Social support explains almost one fifth of the variation in depression during chemotherapy. Interventions that include ways to increase social support will have much success in reducing depression, thereby improving QOL.

The personal control domain, which consists of self-efficacy and mastery, was the most important domain in explaining variation in the primary outcomes of interest, symptom distress and QOL. Mastery was the most important predictor of symptom distress and QOL in this study. Based on our findings, interventions attempting to increase the older cancer patient’s sense of mastery will have the largest impact on increasing QOL and decreasing adverse health outcomes such as symptom distress, disruptive fatigue, and depression during the course of chemotherapy. It should be noted that fatigue is the most frequently reported side-effect of cancer treatments. Research has identified cancer-related fatigue, differentiated from fatigue healthy individuals may experience, as more severe, more distressing, and less likely to be relieved by rest, and numerous studies have identified a high prevalence of fatigue in patients receiving chemotherapy. Therefore, interventions to address improving mastery with the aim of alleviating fatigue may be of particular importance. However, although mastery explains the most variation in fatigue, it does not account for all of the variation in fatigue and QOL. Self-efficacy, social support, and lower body functioning are also important in maintaining QOL and staving off the aforementioned adverse health outcomes during chemotherapy. Thus, interventions for older cancer patients who are about to receive chemotherapy should include the constructs self-efficacy, social support, and lower body functioning in addition to the central focus of increasing the patient’s sense of mastery.

Limitations

Although the Moffitt Cancer Center & Research Institute vigorously recruits patients from minority populations, our study was limited in racial and ethnic diversity, and there may be some underlying and unrecognized differences in patients that choose to be treated at an NCI-designated comprehensive cancer center versus those patients who choose care at a community-based facility. Also, while we examined predictor variables in three separate domains, i.e. health status, the social environment and personal resources, and their effects on our outcomes of interest, we did not examine the inter-relationship of these domains. We recognize that these variables are almost certainly inter-related on some level, that these relationships may change over time and that these relationships may affect the outcomes of interest. We hope to examine these relationships in a future paper. Additionally, due to our limited sample size we weren't able to fully control for differences in baseline scores in the analyses, and we believe that further study may be needed to rule out alternative explanations of the data. Finally, the sample size precluded stratification by different chemotherapy regimens, thereby limiting the ability to detect subtle differences among these regimens.

Conclusion

Because the exposures were measured at baseline of chemotherapy and used to make predictions about outcome measures at midpoint and endpoint of chemotherapy, the proper temporal progression has been established and reverse causation has been ruled out as an alternative explanation for these detected associations. Further, confounding was addressed through multivariate linear regression, which provided adjusted measures of effect between predictors and outcomes. The only remaining impediment to making causal inferences for all of these associations is the possibility of unknown confounders. Because this was an observational study and the independent variables were not randomly assigned, this is a viable alternative explanation. Future research, particularly randomized controlled trials, is necessary to shed light on the causal nature of these relationships. In these future studies, the treatment will most likely be an intervention designed to alter some of the predictors in this study: mastery, self-efficacy, social support, and lower body strength. Additionally, we believe that interventions in the areas of perceived personal control will be developed using a multidisciplinary approach and collaborative efforts by professionals in the areas of psychology, gerontology and behavioral oncology. It is fortuitous that the factors that are most readily modifiable (i.e. psychosocial factors such as mastery and self-efficacy) are also the most important in determining the symptom distress and QOL of older cancer patients undergoing chemotherapy.

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Table 1

Demographic and clinical characteristics of the study participants

Demographic/Clinical Characteristic	Median or Frequency (percent)
Age	73 years
Time Since Diagnosis	46 days
Sex	
Male	35 (37.2%)
Female	59 (62.8%)
Race/Ethnicity	
Caucasian/White	90 (95.7%)
Black/African American	2 (2.1%)
Hispanic/Latino	2 (2.1%)
Education	
Some high school or less	7 (7.4%)
High school graduate	31 (33.0%)
Some college or technical college	27 (28.7%)
College graduate	29 (30.9%)
Marital Status	
Married	61 (64.9%)
Divorced/Separated	11 (11.7%)
Widowed	22 (23.4%)
Living Arrangements	
Alone	21 (22.3%)
Spouse/Partner	58 (61.7%)
All other living arrangements	15 (16.0%)
Tumor Site	
Gastrointestinal (not colorectal)	15 (16.0%)
Colorectal	17 (18.1%)
Breast	13 (13.8%)
Lung	25 (26.6%)
Gynecologic	13 (13.8%)
All others	11 (11.7%)
Tumor Stage	
Not staged/ill-defined	2 (2.1%)
Stage I	7 (7.4%)
Stage II	11 (11.7%)
Stage III	51 (54.3%)
Stage IV	23 (24.5%)

Demographic/Clinical Characteristic	**Median or Frequency (percent)**
Regimen Type	
Adjuvant	36 (38.3%)
Neo-adjuvant	15 (16.0%)
Therapeutic	40 (42.6%)
Missing/Unknown	3 (3.2%)

Table 2

Significant relationships between exposures and outcomes based on simple linear regression analysis

Predictor	**Outcome**	**r**	**p**
Comorbidities	mid symptom distress	0.228	0.030
ADL	mid depression	0.232	0.025
Get-up-and-go	mid symptom distress	0.235	0.025
	mid QOL	−0.251	0.015
Social Support	mid QOL	0.250	0.016
	end QOL	0.226	0.029
	mid fatigue	−0.328	0.001
	mid depression	−0.434	<0.001
Social Network	mid QOL	0.227	0.029
Self-efficacy	mid QOL	0.348	0.001
	end QOL	0.285	0.006
	mid fatigue	−0.220	0.034
	mid depression	−0.350	0.001
Mastery	mid symptom distress	−0.256	0.014
	end symptom distress	−0.270	0.010
	mid QOL	0.365	<0.001
	end QOL	0.339	0.001
	mid depression	−0.249	0.016
	end depression	−0.228	0.028

Table 3

Significant relationships between exposures and outcomes based on multivariate linear regression

Predictor	Outcome	Slope (95% CI)	p
Comorbidities	mid symptom distress	0.030 (0.003, 0.057)	0.030
ADL	end symptom distress	0.088 (0.000, 0.176)	0.049
	mid depression	1.450 (0.133, 2.767)	0.031
Get-up-and-go	mid symptom distress	0.073 (0.009, 0.136)	0.025
	mid QOL	−2.657 (−4.821,−0.493)	0.017
Social Support	mid QOL	0.735 (0.058, 1.411)	0.034
	mid fatigue	−1.041 (−1.710, −0.371)	0.003
	mid depression	−0.655 (−0.957, −0.354)	<0.001
Self-efficacy	mid QOL	0.110 (0.042, 0.177)	0.002
	end QOL	0.117 (0.039, 0.194)	0.004
	mid fatigue	−0.087 (−0.160, −0.014)	0.021
	mid depression	−0.053 (−0.085, −0.021)	0.002
Mastery	mid symptom distress	−0.021 (−0.038, −0.004)	0.014
	end symptom distress	−0.023 (−0.042, −0.004)	0.017
	mid QOL	1.000 (0.425, 1.575)	0.001
	end QOL	1.091 (0.426, 1.756)	0.002
	mid Depression	−0.312 (−0.596, −0.027)	0.032
	end depression	−0.377 (−0.733, −0.022)	0.038

Table 4

Covariates included in final models predicting each outcome

Outcome	**Covariates**
Mid symptom distress	none
End symptom distress	Regimen type
Mid QOL	Marital status
End QOL	Regimen type
Mid fatigue	Marital status, tumor site, and tumor stage
End fatigue	Regimen type
Mid depression	ADLs, Marital status
End depression	Tumor stage

Table 5

Coefficients of determination to ascertain the best predictors for the outcomes of interest

Outcome	**Predictor**	**r^2**	**Domain**
Mid symptom distress	Co-morbidity	0.052	
	Get-up-and-go	0.055	
	Mastery	0.066	Personal Control
End symptom distress	Mastery	0.073	Personal Control
Mid QOL	Get-up-and-go	0.063	
	Social support	0.063	
	Social network	0.052	
	Self-efficacy	0.121	
	Mastery	0.133	Personal Control
End QOL	Social support	0.051	
	Self-efficacy	0.081	
	Mastery	0.115	Personal Control
Mid fatigue	Social support	0.108	Social Environment
	Self-efficacy	0.048	
End fatigue	None		
Mid depression	ADL	0.054	
	Social support	0.188	Social Environment
	Self-efficacy	0.123	
	Mastery	0.062	
End depression	Mastery	0.052	Personal Control