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Original Article

Differences in Composition of Symptom Clusters Between Older and Younger Oncology Patients

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Abstract

Context. Older oncology patients have unique needs associated with the many physical, psychological, and social changes associated with the aging process. The mechanisms underpinning and the impact of these changes are not well understood. Identification of clusters of symptoms is one approach that has been used to elicit hypotheses about the biological and/or psychological basis for variations in symptom experiences.

Objectives. The purposes of this study were to identify and compare symptom clusters in younger (<60 years) and older (≥60 years) patients undergoing cancer treatment.

Methods. Symptom data from one Australian study and two U.S. studies were combined to conduct this analysis. A total of 593 patients receiving active treatment were dichotomized into younger (<60 years) and older (≥60 years) groups. Separate exploratory factor analyses (EFAs) were undertaken within each group to identify symptom clusters from occurrence ratings of the 32 symptoms assessed by the Memorial Symptom Assessment Scale.

Results. In both groups, a seven-factor solution was selected. Four partially concordant symptom clusters emerged in both groups (i.e., mood/cognitive, malaise, body image, and genitourinary). In the older patients, the three unique clusters reflected physiological changes associated with aging, whereas in the younger group the three unique clusters reflected treatment-related effects.

Conclusion. The symptom clusters identified in older patients typically included a larger and more diverse range of physical and psychological symptoms. Differences also may be reflective of variations in treatment approaches between age groups. Findings highlight the need for better understanding of variation in treatment and symptom burden between younger and older adults with cancer. J Pain Symptom Manage 2015;49:1025–1034. © *2015 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

Key Words

Symptom cluster, cancer, factor analysis

Introduction

Older oncology patients have unique health and support needs associated with the many physical, psychological, and social changes associated with the aging process. Although major advances in cancer treatment and supportive therapies have occurred in recent years, outcomes for older oncology patients continue to be suboptimal compared with those for younger adults.[1,2] The disparities in outcomes between older and younger patients are a result in part to our limited understanding of the implications of the aging process for symptom burden, treatment

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responses, and treatment decision making. In fact, available evidence in the emerging field of geriatric oncology is contradictory. Some studies found that the adverse effects of cancer treatment experienced by older patients were no more severe or prolonged than those reported by younger patients.[3] For example, in one study on patients receiving 5-fluorouracil/oxaliplatin, patients aged older than 70 years had similar rates of nonhematological toxicity and overall survival as younger patients.[4] In another study on patients aged75 years and older with Stage III colorectal cancer, adjuvant treatments did not alter these patients' health-related quality of life.[5] In contrast, we reported that although the same symptoms on the Memorial Symptom Assessment Scale (MSAS) were the most common in older (≥60 years) and younger (<60 years) oncology patients, older patients reported significantly lower occurrence rates for 15 (46.9%) of the 32 MSAS symptoms. In addition, a similar pattern was found across ratings of frequency, severity, and distress, with older patients reporting lower ratings compared with younger patients.[6]

Numerous plausible explanations exist for the inconsistent findings related to the symptom experiences in older oncology patients, including systematic biases in the inclusion of older patients in clinical trials, variations in treatment approaches for this group, and the substantial heterogeneity within the older population itself.[7–9] In addition, it is possible that response shifts occur in how patients experience and report symptoms,[6] and differences between studies in samples and the ways in which symptoms are measured. Notwithstanding these explanations, in the absence of large population-based studies or rigorous trials that compare treatment regimens and responses in older and younger patients, the impact of physiological and psychological changes associated with aging on treatment responses are not well understood.

One approach to understanding the symptom experience of patients is to consider groups of co-occurring and related symptoms called symptom clusters.[10] Several authors have proposed that the co-occurrence of symptoms suggests a common biological mechanism that can explain similarities and differences in individual treatment responses.[11,12] For example, some studies have reported associations between specific symptom clusters and underlying biological mechanisms, such as alterations in neuroendocrine hormones and proinflammatory cytokines.[13] However, only two studies have reported on the nature and impact of symptom clusters in older oncology patients. In one study of 220 lung cancer patients aged 65 years and older, a single cluster of seven symptoms (i.e., nausea, fatigue, weakness, appetite loss, weight loss, altered taste, and vomiting) was identified.[14] In a more recent study of 192 breast cancer survivors aged 65 years and older, seven clinically distinct symptom clusters were found that included 36 different symptoms.[15] Although neither of these studies compared symptom clusters between older and younger oncology patients, in the study of breast cancer survivors, two symptom clusters (i.e., neurocognitive and dryness) were identified that are associated with a number of age-related chronic conditions. However, no data were provided to explain the nature and direction of the association between aging and the existence of these clusters.

The rapid growth in the number of older persons with a diagnosis of cancer underscores the importance of gaining a better understanding of older oncology patients' experiences with multiple concurrent symptoms. The purposes of this study were to identify and compare symptom clusters in younger (<60 years) and older (≥60 years) patients undergoing cancer treatment. More specifically, this hypothesis-generating study was designed to explore age-related differences in symptom clusters. If differences are identified, this exploration could guide the development of future studies to investigate biological, psychological, and social responses to cancer and cancer treatments, particularly in older oncology patients.

Methods

Study Samples

Full details of the study samples are reported elsewhere.[6,16] In brief, demographic, clinical, and symptom data from one Australian study (i.e., Symptom Clusters) and two U.S. studies (i.e., Fatigue, Pain, and Sleep Study [FPS study] and Symptom Prevalence Study) were combined to conduct this analysis. To evaluate the effect of age, patients were dichotomized into younger (<60) and older (≥60) groups. This cutoff was based on the findings that indicate cancer mortality rates are increasing in those aged older than 60 years[17] and is consistent with other large studies in this field.[18,19]

Symptom Clusters Study. This prospective, longitudinal study was designed to identify symptom clusters and their effects on physical and psychological functioning of patients with metastatic disease. Data were collected from patients using an interview-administered survey at the time of diagnosis or progression of metastatic disease and again at two months and four months. Data from the first assessment were used in these analyses. Patients were recruited consecutively from two major tertiary referral hospitals in Australia. Patients were eligible to participate if they: were adults (>18 years of age) who could read, write, and understand English; had no cognitive limitations; had a primary cancer of breast, lung, colon/rectum, prostate, upper

gastrointestinal tract, or ovaries; and were diagnosed with metastatic disease in the past month or had clinical evidence of progressive metastatic disease. Patients were excluded if they had local recurrence, but no evidence of metastatic disease; had a prognosis of less than four months as determined by their clinician; or had physical or cognitive impairments that precluded participation in the 15 minute survey. The study was approved by the Ethics Committees of Queensland University of Technology and the two participating hospitals.

FPS Study. This longitudinal study evaluated multiple symptoms in patients who underwent primary or adjuvant radiotherapy (RT). Patients were recruited from two RT departments located in a Comprehensive Cancer Center and a community-based oncology program at the time of the patient's simulation visit. Data used for this study were from this initial visit. Patients were eligible to participate if they: were aged18 years or older; were scheduled to receive primary or adjuvant RT for one of four cancer diagnoses (i.e., breast, prostate, lung, and brain); were able to read, write, and understand English; gave written informed consent; and had a Karnofsky Performance Status (KPS) score of 60 or higher. Patients were excluded if they had: metastatic disease, more than one cancer diagnosis, or a diagnosed sleep disorder. The study was approved by the Committee on Human Research at the University of California, San Francisco (UCSF) and at the second site.

Symptom Prevalence Study. This descriptive, cross-sectional study used self-report questionnaires to obtain information from a convenience sample of oncology outpatients. Patients were recruited from four outpatient settings in Northern California, including a university-based Cancer Center, a Veterans Affairs facility, and two community-based outpatient clinics. Patients were eligible to participate if they were aged 18 years or older; were able to read, write, and understand English; gave written, informed consent; had KPS scores of 50 or higher; and were receiving active cancer treatment. The study was approved by the Committee on Human Research at UCSF and at each of the study sites.

Instruments

Demographics. Demographic information on age, gender, marital status, and living arrangements were obtained at enrollment. Data on education were recoded into a dichotomous variable (i.e., no post-high school vs. post-high school education). Patients' medical records were reviewed for cancer diagnosis, presence of metastatic disease, and current treatment regimens (i.e., none, chemotherapy [CTX], RT, or both CTX and RT). In the Australian study, patient's functional status was rated by their clinician using the Eastern Cooperative Oncology Group (ECOG) Performance Status score that ranges from zero (fully active) to four (disabled). In the U.S. studies, 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). Based on the recommendations of Verger et al,[20] the KPS scores were converted to ECOG scores for use in subsequent analyses.

Memorial Symptom Assessment Scale. All three studies used the MSAS to evaluate the occurrence, severity, frequency, and distress of 32 symptoms commonly associated with cancer and its treatment.[21] The MSAS is a self-report questionnaire designed to measure the multidimensional experience of symptoms. Using the MSAS, patients were asked to indicate whether or not they had experienced each symptom in the past week (i.e., symptom occurrence). If they had experienced the symptom, they were asked to rate its frequency of occurrence, severity, and distress. Symptom frequency was evaluated using a four-point Likert scale (i.e., 1 = rarely, 2 = occasionally, 3 = frequently, and 4 = almost constantly). Symptom severity was measured using a four-point Likert scale (i.e., 1 = slight, 2 = moderate, 3 = severe, and 4 = very severe). Symptom distress was measured using a five-point Likert scale (i.e., 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, and 4 = very much). The reliability and validity of the MSAS is well established in studies of oncology inpatients and outpatients.[21] Patients' ratings of symptom occurrence were used to create the symptom clusters in this study.

Statistical Analysis

Analyses were conducted using SPSS version 18 (SPSS, Inc., Chicago, IL) and MPlus version 6.0(Muthen & Muthen, Los Angeles, CA).[22] Descriptive statistics of proportions for categorical data and means and standard deviations for continuous data were determined to summarize patients' characteristics and symptom ratings. Differences in demographic and clinical characteristics between the two age groups were determined using independent sample *t* tests and Chi-squared analyses.

Exploratory factor analyses (EFAs) were used to identify symptom clusters from occurrence ratings of the 32 symptoms assessed, assuming that related symptoms result from common underlying factors. Separate EFAs were done within the older (≥60 years) and younger (<60 years) age groups. We assumed that the measurement model from each analysis holds for all cases, despite different treatments and cancer diagnoses. As patients only rate symptoms that are

severe, a zero rating was assigned when a symptom did not occur to retain all cases in the analysis. Tetrachoric correlations were used to create the matrix of associations among symptoms.[23] The estimator was the robust weighted least squares method with mean and variance adjustment suited to binary and categorical data and samples lower than 200.[22,24] As the underlying factors are likely to be related, Geomin (oblique) rotation was conducted to allow for correlated factors, and is the recommended method for the analysis of categorical data.[25] Statistical significance was set at P value lower than 0.05.

Determination of the EFA model is based on statistical criteria and whether the symptom clusters are clinically meaningful (i.e., likely to co-occur in the clinical setting). No consensus exists on what constitutes "good fit" of the model to the data. Fit statistics were developed for confirmatory factor analysis, but are interpreted similarly in EFA, although studies have not tested the suitability of this approach. Hence, the guidelines to determine the number of factors are interpreted cautiously, using several "fit" criteria: a statistically nonsignificant model Chi-squared statistic higher than 0.05, a comparative fit index (CFI) of 0.95 or higher, and a root mean square error of approximation (RMSEA) lower than 0.05.[26] A statistically significant Chi-squared result suggests that the model must be further diagnosed. Improvement in fit with each additional factor is indicated by decreases of 0.01 in CFI, of 0.015 in RMSEA,[27] and of less than 0.001 in standardized root mean square residual.[28] It is desirable that the resultant solution will exhibit simple structure, evident when the structure coefficients (correlations) approach 0 or 1.0, and the associations between factors and sets of symptoms are distinct. A suggested cutoff for interpreting residual correlations is that all absolute residuals are less than 0.05, with values higher than 0.10 indicating poor fit.[29]

Both pattern and structure coefficients were interpreted. Pattern coefficients are standardized regression coefficients. Structure coefficients are interpreted as correlations between the factor and symptom. They indicate the total effect of the factor on the symptom, accounting for the unique effect of the factor on the symptom while controlling for the influence of other factors (pattern coefficient) and the indirect effect of other related factors.[30] For symptom inclusion in the cluster, we arbitrarily set a cutoff value for structure coefficients ≥0.40,[31,32] such that at least 16% of the variance in each symptom was explained by the factor, directly or indirectly. Cross-loading of symptoms on factors is expected and was allowed. Further refinement of symptom clusters was determined by the contextual relevance of symptoms based on the literature and author experience.

Results

Differences in Demographic and Clinical Characteristics Between Older and Younger Patients

The combined sample included 593 oncology outpatients who were classified as younger and older (i.e., 44.4%:<60 years and 55.6%: ≥60 years). Table 1 presents a summary of the demographic and clinical characteristics of the sample.

As reported in our previous articles,[6,16] some significant differences in demographic characteristics were found between the younger and older groups, with the older patients more likely than younger patients to be male ($P < 0.001$), less likely to have finished high school, more likely to have prostate cancer ($P < 0.001$), more likely to be receiving RT ($P < 0.001$), and more likely to be fully active ($P = 0.04$).[6,16]

Symptom Clusters in Older Versus Younger Patients

Table 2 provides a summary of the occurrence rates for symptoms with severity ratings ≥1 (i.e., slight, moderate, severe, or very severe). In both age groups, the most common symptoms were fatigue, pain,

Table 1
Demographic and Clinical Characteristics of the Total Sample and Differences in Demographic and Clinical Characteristics Between Patients <60 ($N = 263$) and ≥60 Years ($N = 330$)

		Age Group (yrs)		
Demographics	Total (%)	<60 (%)	≥60 (%)	*P*-value
Study project				
Fatigue, Pain, and Sleep	28.8	28.9	28.8	0.170
Prevalence	34.4	38.0	31.5	
Yates	36.8	33.1	39.7	
Gender—female	54.6	70.7	41.8	<0.001
Lives alone	26.4	24.0	28.2	0.260
Partnered/married	60.9	57.3	63.7	0.126
Education—post high school	61.4	68.8	55.5	0.001
Diagnosis				
Breast	33.6	48.3	21.8	<0.001
Prostate	26.0	11.0	37.9	
Lung	13.2	11.4	14.5	
Other	27.3	29.3	25.8	
Metastases	34.9	37.3	32.9	0.297
Treatment				
None	15.5	13.3	17.3	<0.001
Only radiation	43.6	33.8	51.4	
Only chemotherapy	27.4	31.2	24.3	
Both	13.5	21.7	7.0	
ECOG Performance Status				
Fully active	21.4	15.8	26.0	0.043
Ambulatory, light work	48.9	53.1	45.5	
Ambulatory, mobile >50%	21.6	23.5	20.1	
Ambulatory, mobile <50%	7.2	6.5	7.7	
Disabled	0.9	1.2	0.6	
Mean age (y)	61.3 (12.1)	50.3 (7.7)	70.1 (6.5)	<0.0001

ECOG = Eastern Cooperative Oncology Group.

Table 2
Occurrence Rates for Symptoms within MSAS Severity Ratings of ≥1 for Younger and Older Oncology Patients ($N = 593$)

Age Group (yrs)			
<60		≥60	
Symptom	Prevalence (%)	Symptom	Prevalence (%)
Lack of energy	81.3	Lack of energy	65.8
Pain	73.0	Pain	54.9
Difficulty sleeping	63.9	Feeling drowsy	51.2
Feeling drowsy	63.5	Difficulty sleeping	42.7
Worrying	57.8	Dry mouth	39.7
Difficulty concentrating	56.6	Difficulty concentrating	34.9
Feeling irritable	52.3	Cough	33.4
Feeling sad	52.1	Problems with urination	33.4
Sweats	44.4	Worrying	30.6
Dry mouth	41.8	Feeling irritable	29.7
Feeling nervous	39.1	Constipation	29.1
Cough	38.8	Sweats	28.8
Nausea	37.6	Lack of appetite	28.5
Lack of appetite	37.6	Feeling sad	28.2
Skin changes	37.6	Diarrhea	28.0
Shortness of breath	36.8	Numbness/tingling in hands/feet	27.6
Numbness/tingling in hands/feet	35.7	Changes in food tastes	27.6
Problems with sexual interest/activity	34.9	Feeling nervous	25.8
I do not look like myself	34.6	Nausea	24.6
Itching	33.4	Itching	20.9
Constipation	33.0	Weight loss	20.3
Feeling bloated	31.1	Problems with sexual interest/activity	20.2
Changes in way food tastes	30.1	Shortness of breath	20.0
Dizziness	26.2	Dizziness	19.4
Hair loss	23.2	Do not look like myself	18.8
Weight loss	22.8	Skin changes	18.5
Diarrhea	20.6	Feeling bloated	16.7
Problems with urination	20.5	Hair loss	15.8
Vomiting	16.4	Swelling of arms/legs	14.3
Swelling of arms/legs	15.9	Difficulty swallowing	13.1
Difficulty swallowing	15.2	Mouth sores	10.6
Mouth sores	14.0	Vomiting	8.8

MSAS = Memorial Symptom Assessment Scale.

difficulty sleeping, and feeling drowsy. Occurrence rates for all of the symptoms were consistently lower for older people. These symptoms were included in the EFA to determine the number and types of symptom clusters in each of the age groups.

Results of the EFA for those younger than 60 years and those aged 60 years or older are presented in Table 3 ($\chi^2 = 333.01$, $P = 0.05$, RMSEA = 0.02, CFI = 0.99) and Table 4 ($\chi^2 = 310.72$, $P = 0.04$, RMSEA = 0.02, CFI = 0.99), respectively. The initial analysis for the older age group resulted in a negative residual variance analysis for vomiting, so the results presented in Table 4 are from a second EFA with vomiting excluded. In both groups, a seven-factor solution was selected based on interpretation of pattern and structure coefficients, examination of statistical criteria previously specified, and clinical meaning. Symptom cluster names are descriptive and reflect the core symptoms with larger structure coefficients.

In both groups, four partially concordant symptom clusters emerged, indicated by similar items and structure coefficients, namely a mood/cognitive cluster, a malaise cluster, a CTX toxicity cluster, and a genitourinary cluster (Table 5). For the mood/cognitive cluster, common symptoms for both groups included worry, feeling sad, nervous, irritable, lack of energy, and difficulty concentrating. For younger patients, related symptoms were difficulty sleeping and problems with sexual interest. In the older age group, a number of additional somatic symptoms loaded on this factor, including lack of appetite, nausea, and feeling drowsy. The malaise cluster included a number of common symptoms across age groups, namely feeling drowsy, lack of energy, difficulty concentrating, difficulty sleeping, and feeling nervous. In older patients, additional symptoms that loaded on this cluster included a number of mood-related symptoms (feeling sad or irritable). In younger patients, a range of gastrointestinal-related symptoms including nausea, lack of appetite, diarrhea, and feeling bloated loaded on the malaise cluster. For both older and younger groups, the genitourinary cluster included problems with urination and sexual interest/activity, with diarrhea and irritability loading on this cluster for the older age group. Symptoms that were common to both age groups in the CTX toxicity cluster included hair loss, not looking like oneself, and swelling of the arms/legs. For the younger group, this cluster included a number of other bodily changes including mouth sores, taste changes, dry mouth, and constipation, with skin changes loading on this cluster for older patients.

The three clusters that were unique to the older group included what was defined as a broad aging-related cluster, a nutritional symptoms cluster, and an aerodigestive cluster (Table 5). In the younger group, the three unique clusters were all considered treatment-related; one included a wide ranging group of treatment-related toxicities, one focused on nausea and vomiting, and one reflected symptoms associated with hormonal changes. For the younger age group, skin changes and numbness/tingling of the hands or feet were not identified in any cluster; and for the older age group, itching and mouth sores were not in any cluster.

Discussion

Symptom clusters provide an opportunity to examine biological and/or psychological mechanisms that underlie common co-occurring symptoms in

Table 3
Symptom Clusters[a] for Younger (<60 Years) Patients

Treatment-Related Symptom Cluster	Mood/Cognitive Symptom Cluster	Malaise Symptom Cluster	Treatment-Related GI Symptom Cluster	Genitourinary Symptom Cluster	Hormonal Symptom Cluster	Chemotherapy Toxicity Symptom Cluster
Dry mouth	**Worrying**	**Lack of energy**	**Vomiting**	**Problems with urination**	**Sweats**	**Hair loss**
Difficulty swallowing	**Feeling sad**	**Feeling drowsy**	**Nausea**	Problems with sexual interest	Difficulty sleeping	**Change in food tastes**
Shortness of breath	**Feeling nervous**	**Lack of appetite**	NOT itching		Pain	**I do not look like myself**
Lack of appetite	**Feeling irritable**	**Nausea**			NOT weight loss	**Mouth sores**
Nausea	**Difficulty concentrating**	**Difficulty concentrating**				Constipation
Vomiting	**Lack of energy**	**Diarrhea**				Feeling bloated
Lack of energy	Difficulty sleeping	Feeling bloated				Swelling of arms/legs
Change in food tastes	Problems with sexual interest	Feeling nervous				Dry mouth
Feeling dizzy	I do not look like myself	Difficulty sleeping				
Cough						
Weight loss						
Constipation						
Pain						
Feeling drowsy						
Mouth sores						
Feeling nervous						
I do not look like myself						
Difficulty concentrating						
Feeling bloated						

GI = gastrointestinal.
NOT means this had a negative loading.
[a]Structure coefficients >0.40. Bold indicates symptoms with structure coefficients >0.50.

oncology patients receiving treatment.[12,33,34] Although the sample in this study represents a heterogeneous group of patients in terms of tumor sites and stages of disease, all patients were receiving active treatment for their cancer. Moreover, as older and younger patients were recruited as part of the same study using the same instrument and data collection procedures, the similarities and differences in patterns of symptom clusters observed in this study raise important theoretical and practical considerations that warrant further investigation.

First, our analyses confirmed four clusters that have partial concordance in older and younger groups, including mood/cognitive, malaise, body image, and genitourinary clusters. These clusters are similar to those identified clinically and from empiric evidence in patients with various types of cancers.[34] Such clusters are typically viewed as being common responses to the disease process and to the multifaceted experience of undergoing cancer treatment. However, although some concordance existed, notable differences were found between older and younger patients in terms of the specific symptoms within each of these common clusters. Specifically, the symptom clusters identified in older patients typically included a larger and more diverse range of physical and psychological symptoms than were found in the clusters for younger patients. This finding was most evident in the mood/cognitive cluster where a number of additional somatic symptoms, including lack of appetite, nausea, and feeling drowsy, loaded on this factor for older patients. Similarly, the malaise cluster in older patients included additional mood-related items, including feeling sad and irritable. Theoretically, the more diffuse nature of the symptom clusters identified in older patients could reflect the multiple risk factors and organ systems that are often involved in how older patients present in clinical practice.[35] The existence of geriatric-type syndromes, representing links exist between particular symptoms and a number of underlying co-occurring etiological factors or diseases associated with aging,[35,36] could explain some of the cluster differences observed in this study. That is, some empirical evidence to support this notion exists in the case of mood-related disorders, whereby older cancer patients often present with a variety of symptoms in addition to depressed mood and anhedonia.[37] These additional symptoms can include general malaise or dissatisfaction, diffuse somatic complaints, general aches and/or stomach aches, hopelessness, late insomnia, variations in mood throughout the course of a day, and loss of sexual

Table 4
Symptom Clusters[a] for Older (≥60 Years) Patients

Malaise Symptom Cluster	Mood/Cognitive Symptom Cluster	Aerodigestive Symptom Cluster	Genitourinary Symptom Cluster	Nutrition Symptom Cluster	Aging-Related Symptom Cluster	Chemotherapy Toxicity Symptom Cluster
Feeling drowsy	**Worrying**	**Shortness of breath**	**Problems with urination**	**Weight loss**	**Difficulty swallowing**	**Skin changes**
Lack of energy	**Feeling sad**	**Cough**	**Diarrhea**	**Lack of appetite**	**Dry mouth**	**Hair loss**
Difficulty concentrating	**Feeling nervous**	**Dry mouth**	Problems with sexual interest	**Constipation**	**Constipation**	**I do not look like myself**
Difficulty sleeping	**Feeling irritable**	**Difficulty swallowing**	Feeling irritable	**Change in food tastes**	Feeling drowsy	**Swelling of arms/legs**
Feeling nervous	**Lack of energy**	**Lack of appetite**		**I do not look like myself**	Change in food tastes	Feeling sad
Feeling sad	**Difficulty concentrating**	**Feeling bloated**		Lack of energy	Nausea	
Feeling irritable	Lack of appetite	**Feeling nervous**		Feeling drowsy		
Feeling dizzy	Nausea	Lack of energy		Nausea		
Problems with sexual interest	Feeling drowsy	Nausea				
Sweats	Change in food tastes	Swelling of arms/legs				
	Constipation	Feeling dizzy				
	I do not look like myself	Feeling sad				
	Feeling bloated	Pain				
	Numbness/tingling in hands/feet	Feeling drowsy				
		Difficulty sleeping				

[a]Structure coefficients >0.40. Bold indicates symptoms with structure coefficients >0.50.

interest.[38] These additional symptoms may serve as additional important signals to identify depression in the older age group.[37]

In addition to the four partially concordant symptom clusters identified in this study, the unique clusters identified in the older and younger age groups provide further support for the proposition that changes associated with aging or aging-associated multimorbidity can have important influences on how individuals respond to cancer and its treatment. For example, gastrointestinal symptoms in this study loaded differently for the younger and older age groups. For the younger group, a distinct nausea and vomiting cluster was identified, whereas for the older age group, a more diverse cluster was identified that included weight loss, lack of appetite, constipation, and not looking like oneself. This more diffuse clustering could reflect more compromised nutritional reserves that can result from the physiological and psychosocial changes associated with aging.[39] The aerodigestive symptom cluster and the cluster comprising difficulty swallowing, dry mouth, constipation, drowsiness, and taste changes could similarly be explained by age-related decrements in organ function, or possibly the side effects of common pharmacological agents used to treat such physiological changes.

In addition, the differences identified in this study raise the possibility of variations in treatment approaches for older and younger cancer patients. That is, the body image cluster for both groups included hair loss, not looking like oneself, and swelling in arms/legs. However, for the younger group, this cluster also included a number of other bodily changes including mouth sores, taste changes, dry mouth, and constipation. All of these symptoms are likely to be associated with the type and intensity of cancer treatment administered. Similarly, in the genitourinary cluster, one possible explanation for the inclusion of diarrhea in the older patient group is that RT was more commonly used to treat prostate cancer in this cohort. Such age-related differences in treatment approaches were identified in studies from the U.S. and Canada. These studies have reported that older prostate cancer patients are more likely to be treated by RT or no therapy, and younger patients more likely to receive radical prostatectomy than RT or no therapy.[40,41] Although our study is unable to determine the appropriateness of any such variations in treatments, if they do in fact exist, the implications of such variations need to be understood, as treatment outcomes could potentially be compromised.

It is notable that the three unique clusters identified for the younger age group can be explained as being treatment-related. That is, one unique cluster for younger patients included a wide-ranging group of treatment-related toxicities, one focused on nausea and vomiting alone, and one reflected symptoms associated with hormonal changes that are potentially related to surgically induced menopausal changes or the use of specific hormonal therapies. Although our analyses revealed no significant differences in whether

Table 5
Core and Unique Symptoms for Older and Younger Patients in Partially Concordant and Age-Specific Symptom Clusters

		Unique Symptoms	
Cluster	Core Symptoms	Younger	Older
Partially concordant clusters			
Mood-cognitive	Worry, feeling sad, nervous, irritable, lack of energy, difficulty concentrating	Difficulty sleeping, problems with sexual interest	Lack of appetite, nausea, feeling drowsy
Malaise	Feeling drowsy, lack of energy, difficulty concentrating, difficulty sleeping, feeling nervous	Nausea, lack of appetite, diarrhea, feeling bloated	Feeling sad, irritable
Chemotherapy toxicity	Hair loss, not looking like oneself, swelling of the arms/legs	Mouth sores, taste changes, dry mouth, constipation	Skin changes
Genitourinary	Urination, sexual interest/activity		Diarrhea, irritability
Unique clusters—older patients			
Aerodigestive			Shortness of breath, cough, dry mouth, difficulty swallowing, lack of appetite, feeling bloated, feeling nervous
Nutrition related			Weight loss, lack of appetite, constipation, change in food taste
			I do not look like myself
Aging related			Difficulty swallowing, dry mouth, constipation
Unique clusters—younger patients			
Treatment-related symptom cluster		Dry mouth, difficulty swallowing, Shortness of breath, lack of appetite, nausea, vomiting, lack of energy, change in food tastes. Feeling dizzy, cough, weight loss, constipation, pain, feeling drowsy, mouth sores, and feeling nervous	
Treatment related—gastrointestinal		Vomiting, nausea	
Treatment related—hormonal		Sweats	

the patients in the younger and older groups received different CTX agents or hormonal therapies, our data do not allow for a more detailed analysis to confirm whether treatment intensity was different in the two groups.

Conclusion

This study is the first to compare the clustering of symptoms in older and younger oncology patients. Although the study was not designed to test specific hypotheses, our approach has provided new insights into differences in the symptom experience of older and younger patients. In doing so, our findings highlight the potential benefits of applying knowledge drawn from the field of gerontology to advance our understanding of the treatment and care of older patients with cancer. Further research is needed to explain how the physiological and psychological changes associated with aging, multimorbidity, or concurrent polypharmacy can alter responses to cancer and its treatment. Understanding such mechanisms will provide important evidence to guide more personalized treatment approaches for this age group.

The implications of the findings from this study for clinical practice are intriguing. Given the multifactorial and complex process required to determine how an individual will respond to cancer treatment, the role of symptom clusters in a comprehensive geriatric assessment and in predicting responses to treatment should be considered. The importance of an individualized clinical assessment that takes into account unique symptom presentations for older patients is recommended, if we are to ensure that the needs of this group are identified and appropriately managed. Lastly, this study has raised the possibility that cancer treatment approaches for younger and older patients may differ. Our study was not designed to determine the appropriateness of any such differences. However, these variations may have potentially serious implications for older patients' treatment outcomes. The findings from this study add to the growing body of evidence in geriatric oncology that highlights the need for more intensive study of the unique issues associated with treatment for this group.

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