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Predictors of the multidimensional symptom experience of lung cancer patients receiving chemotherapy

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Abstract

Purpose—Few studies have examined inter-individual variability in the symptom experience of lung cancer patients. We aimed to identify the most prevalent, severe, and distressing symptoms, and risk factors associated with increased symptom burden.

Methods—Lung cancer patients (n=145) reported occurrence, severity, and distress for 38 symptoms on the Memorial Symptom Assessment Scale one week after chemotherapy. Using

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multidimensional subscales, risk factors for higher global distress, physical, and psychological symptoms were evaluated using simultaneous linear regression.

Results—Mean age was 64.0 years and 56.6% were female. Mean Karnofsky Performance Status score was 79.1 (SD 14.6) and mean Self-Administered Comorbidity Questionnaire score was 7.3 (SD 3.9). The most distressing and prevalent symptom was fatigue. Problems with sexual interest/activity had the highest mean severity rating. Patients with lower functional status (p=0.001) and higher comorbidity (p=0.02) reported higher global distress. Similarly, lower functional status (p=0.003) and higher comorbidity (p=0.04) were associated with a higher physical symptom burden along with lower body mass index (p=0.02). Higher psychology symptom burden was associated with lower functional status (p=0.01), younger age (p=0.02), non-metastatic disease (p=0.03), higher number of prior treatments (p=0.04), and income (p=0.03).

Conclusions—Fatigue was the most distressing and prevalent symptom among lung cancer patients receiving chemotherapy. Lower functional status was associated with a higher burden of global distress, physical, and psychological symptoms. Younger age and non-metastatic disease were additional risk factors for increased psychological symptoms. Together, these risk factors can help clinicians identify lung cancer patients at increased need for aggressive symptom management.

Keywords

lung cancer; chemotherapy; symptom burden; multiple symptoms; distress; fatigue

INTRODUCTION

Lung cancer, the leading cause of cancer mortality in the U.S.[1] , is associated with a high symptom burden from both the disease and its treatment [2]. Chemotherapy (CTX) is associated with numerous physical and psychological symptoms. These symptoms can result in functional decline and poor quality of life (QOL) [3,4]. Furthermore, there is significant inter-individual variability in patients' symptom experience with some reporting few mild symptoms and others reporting numerous severe symptoms [5,6].

In addition, individual symptoms may differ in their occurrence, severity, and associated distress. Most studies of lung cancer patient symptoms focus on one symptom dimension such as severity [7,8]. A few studies have included multiple dimensions but were conducted in heterogeneous groups of patients undergoing different types of treatments [9,10]or with different types of cancer [11,12]. For example, a study of patients with inoperable lung cancer found that symptom occurrence, severity, and distress ratings differed, especially earlier in the disease trajectory [10]. However, these patients received a variety of cancer treatments and symptom assessments were not timed consistently in relation to CTX cycles [10].

Given the paucity of research on the multidimensional symptom experience of lung cancer patients receiving CTX, we aimed to identify the most prevalent, severe, and distressing symptoms, and risk factors associated with an increased multidimensional symptom burden

in the week following CTX administration. We hypothesized that lower functional status and higher comorbidity would be associated with higher symptom burden.

MATERIALS AND METHODS

Patients and Settings

This cross-sectional analysis is part of a parent study that evaluated the symptom experience of oncology outpatients receiving CTX [5]. The parent study enrolled adults age 18 years with lung, breast, gastrointestinal, or gynecological cancer. The current analysis evaluated only patients with lung cancer. All patients received CTX within the preceding four weeks and were scheduled to receive at least two additional cycles. Patients were required to read, write, and understand English and provided written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veterans Affairs hospital, and four community-based oncology programs. In the parent study, a total of 2,234 patients were approached and 1,343 consented to participate (60.1% response rate; lung cancer specific response rate is not available because cancer type was not collected from patients who did not consent to participate). The major reason for refusal was being overwhelmed with cancer treatment.

Instruments

Patients completed a demographic questionnaire and rated their functional status using the Karnofsky Performance Status (KPS) scale from 30 (severely disabled) to 100 (normal) [13]. The Self-Administered Comorbidity Questionnaire (SCQ)evaluated 13 common comorbidities that were simplified into language that could be understood without any prior medical knowledge [14]. Patients indicated if they had the condition, if they received treatment for it, and if it limited their activities , for a maximum of 3 points per condition resulting in an overall score of 0 to 39. The SCQ has well-established validity and reliability[15].

A modified version of the Memorial Symptom Assessment Scale (MSAS) [16] evaluated occurrence, frequency, severity, and distress of 38 symptoms commonly associated with cancer and its treatment. In addition to the original 32 MSAS symptoms, the following six symptoms were assessed: chest tightness, difficulty breathing, increased appetite, weight gain, abdominal cramps, and hot flashes. Patients indicated if they experienced each symptom in the past week (symptom occurrence), and if yes, they rated its frequency, severity, and distress. Symptom frequency was measured using a 4-point Likert scale (1 = rarely, 2 = occasionally, 3 = frequently, 4 = almost constantly). Symptom severity was measured using a 4-point Likert scale (1 = slight, 2 = moderate, 3 = severe, 4 = very severe). Symptom distress was measured using a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much).

Three MSAS subscale scores—global distress index(MSAS-GDI), physical(MSAS-PHYS), psychological (MSAS-PSYCH)—were calculated. Each subscale score incorporates two or more dimensions of the symptom experience with higher scores reflecting higher symptom burden. The MSAS-GDI is the average of the distress ratings for 6 physical symptoms (lack

of energy, feeling drowsy, pain, lack of appetite, dry mouth, constipation) and the frequency ratings for 4 psychological symptoms (worrying, feeling sad, nervous, irritable). The MSAS-PHYS is the average of the distress, frequency, and severity ratings for 12 physical symptoms (lack of energy, feeling drowsy, pain, nausea, vomiting, change in the way food tastes, lack of appetite, dry mouth, constipation, feeling bloated, dizziness, weight loss). The MSAS-PSYCH is the average of the distress, frequency, and severity ratings for 6 psychological symptoms (worrying, feeling sad, nervous, irritable, difficulty sleeping, difficulty concentrating). The reliability and validity of the MSAS and its subscales are well established in studies of cancer patients [16].

Study Procedures

The study was approved by the Institutional Review Board at the University of California, San Francisco and at each study site. For this analysis, patients completed the symptom questionnaires approximately one week after CTX administration to capture acute symptoms. Medical records were reviewed for clinical information.

Data Analysis

Data were analyzed using Stata/SEversion 14.1 (StataCorp, College Station, TX). Descriptive statistics and frequency distributions were calculated for patient characteristics as well as symptom occurrence , severity, and distress ratings. For each symptom, mean severity scores were calculated for patients who did and did not report the symptom (severity rating0 = not present to 4 = very severe) and for patients who reported each symptom (severity rating1 = slight to 4 = very severe). Mean distress scores were calculated for only those patients who reported the individual symptom.

Simultaneous linear regression was used to evaluate the associations of patient characteristics with the MSAS-GDI, MSAS-PHYS, and MSAS-PSYCH subscale scores. Sixteen characteristics (age, gender, race, income, employment status, education, marital status, smoking status, body mass index (BMI), KPS, SCQ score, type of lung cancer, months since cancer diagnosis, metastatic disease at time of study (selected instead of stage at diagnosis to reflect current disease status), CTX regimen, number of prior treatments) were included in bivariable analyses based on previous studies of cancer patients [7,11,17,18]. Only those characteristics associated with any subscale score in the bivariable analyses with a p-value <0.20 were included in the multivariable analyses. Results were considered statistically significant at a two-sided p-value of 0.05.

RESULTS

Demographic and clinical characteristics

Of the 157 lung cancer patients enrolled, 145 completed the MSAS and were included in the analysis. Mean age was 64.0 years (SD 11.1), 56.6% were female, and 71.8 % were white (Table 1). Most were current or former smokers (69.7%). Mean KPS score was 79.1 (SD 14.6) and mean SCQ score was 7.3 (SD 3.9). The most common comorbidities were lung disease (60.0%), hypertension (40.0%), and back pain (36.6%). Most patients had non-small cell lung cancer (88.1%). Median time since lung cancer diagnosis was 4.2 months(IQR

2.5–14.5). Patients received a mean of 1.4 prior cancer treatments (i.e, surgery, CTX, or radiation received prior to the current course of CTX). At enrollment, 76.9% of patients had metastatic disease and 77.9% received a platinum-doublet CTX regimen.

Symptom Occurrence, Severity, and Distress

Patients reported a mean of 14.3 symptoms (SD 7.1, range 1–37). Mean MSAS-GDI score was 1.08 (SD 0.73, range 0–2.92), MSAS-PHYS score was 0.93 (SD 0.59, range 0–2.36), and MSAS-PSYCH score was 0.82 (SD 0.67, range 0–2.52).

Symptom occurrence , mean severity, and mean distress ratings are summarized in Table 2. The five most prevalent symptoms were lack of energy (79.3%), feeling drowsy (66.2%), difficulty sleeping (65.5%), pain (61.4%), and nausea (53.1%). Among only patients who reported the individual symptom , problems with sexual interest or activity, lack of energy, constipation, hair loss, and change in the way food tastes had the highest mean severity ratings. The most distressing symptoms were lack of energy, “I do not look like myself,” pain, nausea, and constipation.

Predictors of multidimensional MSAS subscale scores

Of the 16 characteristics included in the bivariable analyses, 9 were retained for the multivariable analyses (age, gender, income, smoking status, BMI, KPS, SCQ score, metastatic disease, number of prior treatments). For MSAS-GDI, patients with lower functional status ($p = 0.001$) and higher comorbidity ($p = 0.02$) had a higher burden of global symptom distress. KPS and SCQ score uniquely explained 8.0% and 3.7% of the variance in MSAS-GDI score, respectively. Overall, the model explained 31.8% of the variance (large model effect size).

For MSAS-PHYS, patients with a lower BMI ($p = 0.02$), lower functional status ($p = 0.003$), and higher comorbidity ($p = 0.04$) had a higher burden of physical symptoms in the multivariable model. BMI, KPS, and SCQ score uniquely explained 3.6%, 6.4%, and 3.1% of the variance in MSAS-PHYS score, respectively. Overall, the model explained 26.2% of the variance (large model effect size).

For MSAS-PSYCH, patients with younger age, ($p = 0.02$) lower functional status ($p = 0.01$), non-metastatic disease ($p = 0.03$), and a higher number of prior cancer treatments ($p = 0.04$) had a higher burden of psychological symptoms in the multivariable model. Income was also associated with MSAS-PSYCH scores ($p = 0.03$) with patients in the $30,000–69,999 income group having lower MSAS-PSYCH scores than patients in the <$30,000 reference group. However, the protective effect disappeared for patients with income >$70,000. The percentages of uniquely explained variance in MSAS-PSYCH score for individual characteristics were 5.3% (functional status), 4.0% (income), 3.8% (age), 3.2% (metastatic disease status), and 2.9% (prior number of cancer treatments). Overall, the model explained 27.0% of the variance (large model effect size).

DISCUSSION

This study provides a comprehensive symptom assessment of lung cancer patients in the week following CTX. Of note, patients reported an average of 14 symptoms, which is higher than previous reports of 8.8 to 11.5 symptoms in heterogeneous samples of cancer patients [19,20]. Our assessment of occurrence, severity, and distress captured different dimensions of the symptom experience. Of the 38 symptoms assessed, lack of energy was the most distressing, most prevalent, and second most severe symptom. While problems with sexual interest or activity were reported by only 25.5% of patients, it was rated as the most severe symptom. Constipation was a distressing and severe symptom while pain and nausea were distressing and common. When examining risk factors for the three multidimensional MSAS subscales, poor functional status was consistently associated with a higher burden of global distress, physical, and psychological symptoms. Higher comorbidity was associated with higher global distress and physical symptoms but not psychological symptoms. While younger age, non-metastatic disease, and a higher number of prior cancer treatments were associated with increased psychological symptoms, lower BMI was associated with increased physical symptoms.

By assessing the multidimensional symptom experience of lung cancer patients, we found that fatigue is distressing, near universal, and severe. Fatigue was reported by 79.3% of patients, which is consistent with prior studies estimating its prevalence at up to 95% among those treated with CTX [21]. The co-occurrence of fatigue, pain, and difficulty sleeping, which were the most prevalent symptoms reported by our cohort, has been linked to increased mortality and other symptoms [12]. Because fatigue may be under recognized by clinicians, it is important to regularly screen patients and acknowledge the emotional distress fatigue can cause. The National Comprehensive Cancer Network has set forth management guidelines for fatigue including energy conservation, increased physical activity, and psychosocial interventions [22].

Problems with sexual interest or activity was the most severe symptom reported in our study. Cancer and CTX can impact a patient’s sexual functioning through a variety of physical and emotional changes. Symptoms such as fatigue, pain, nausea, and alopecia may affect a patient’s QOL, mood, and sexual desire [23]. Lung cancer patients with shortness of breath and emotional distress may be more likely to report sexual concerns [24]while older patients may be less likely to report such concerns [20]. Changes in body image, the second most distressing symptom in this study, may impact a patient’s self-identity and willingness to engage in social relationships [23]. Focus groups with cancer patients and survivors found that 74% of participants valued discussing sexual problems with oncology professionals but only 23% of lung cancer patients reported ever receiving information about sexual function from a clinician [25]. Open communication between clinicians and cancer patients about their sexual concerns needs to be improved.

Constipation was reported by over 50% of patients in our study and was the third most severe and fifth most distressing symptom. Constipation is a well-recognized side effect of opioid analgesics and serotonin receptor antagonist anti-emetics. In fact, assessing for constipation following an opiate prescription is a core quality metric of the American

Society of Clinical Oncology Quality Oncology Practice Initiative, a practice-based quality assessment program [26]. Given the high prevalence, severity, and associated distress from constipation, effective prevention and management of constipation should be a clinical priority. Increased patient education on constipation prophylaxis for opiates and anti-emetics and aggressive symptom management once constipation develops is needed to reduce the burden of this symptom.

In addition to evaluating individual symptoms using multiple dimensions, we found that lung cancer patients with lower functional status, who are less likely to benefit from CTX [27], were more likely to report higher global distress, physical, and psychological symptoms one week after CTX administration. Functional status is associated with several important outcomes in cancer patients including CTX toxicity, benefit from CTX, and overall survival [27–29]. Previous studies have demonstrated an association between patient-reported functional status and increased morning and evening fatigue [18,30], cancer pain [31], and a subgroup of patients who reported higher occurrence rates for multiple symptoms [5]. Of note, our study did not include physician-reported functional status, which has moderate agreement with patient-reported functional status with weighted kappa statistic of 0.30 to 0.53 [32,33]. While studies of older adults with cancer found that physician-reported KPS is not predictive of severe grade ≥3 CTX toxicity [28], it remains unknown whether physician-reported KPS is associated with a higher symptom distress in lung cancer patients.

While patients in this study with higher comorbidity were more likely to report a higher global distress and physical symptoms, no association was found with psychological symptoms. Higher physical symptom burden with increasing comorbidity is consistent with previous studies of cancer patients [5,34]. In contrast, studies on the association between comorbidity and global distress in cancer patients are more limited. For example, in a study of cancer patients age ≥65, having more than three comorbid conditions was associated with a higher level of distress [35]in bivariable but not multivariable analysis, where physical function was a stronger predictor [36]. Of note, our sample of lung cancer patients had higher comorbidity scores than other samples of patients with different cancer types [5], highlighting the importance of evaluating the impact of comorbidity on outcomes in lung cancer.

While no other associations with age were found, younger age was associated with higher MSAS-PSYCH scores, reflecting a higher burden of psychological symptoms. These findings are consistent with prior studies that found higher levels of anxiety [37]and depressive symptoms [38]in younger patients undergoing a variety of cancer treatments. These differences may be due to an age-related response shift in the perception of symptoms or aging-related biological or psychological changes [39]. For instance, some have proposed that older adults may have had time to develop and learn to utilize more adaptive coping strategies in dealing with cancer and its treatment [40]. Another possible explanation for our age-related findings is that older patients who agreed to participate in the study may have been relatively healthier or less distressed than older patients who did not participate [41]. While age is not a modifiable risk factor for psychological distress, it is likely that younger age—in combination with other modifiable factors such as coping strategies and behaviors

—could help identify those patients in greatest need for targeted interventions to reduce the severity and impact of psychological symptoms.

Interestingly, lung cancer patients receiving CTX for non-metastatic disease were more likely to have higher MSAS-PSYCH scores than those with metastatic disease. Patients with non-metastatic disease likely received CTX adjuvantly after surgery or in combination with radiation, both potential approaches for curative intent. The higher psychological symptom burden among these patients may be related to fear of recurrence [42], highlighting the need for psychosocial interventions for lung cancer patients of all stages, not just those with metastatic disease.

Several patient characteristics were not associated with any MSAS subscales. Our study did not find differences in these symptom indices based on gender, race, or education, which prior studies have found to differentiate between latent classes of patients with distinct symptom experiences [5,43]. Additionally, the lack of association between CTX regimen and symptoms in our study may be due to differences in clinicians' choice of CTX agent and/or dose based on anticipated tolerance.

Several limitations need to be acknowledged. Patients were enrolled at various time points during their CTX treatment so some heterogeneity existed in the number of CTX cycles already received. Our cohort did not include lung cancer patients receiving only targeted therapy or immunotherapy without CTX, which are important patient groups for future studies. While the multivariable models for the three MSAS subscales demonstrated large effect sizes, the remainder of unexplained variance may be related to unmeasured factors such as symptom management interventions or patients' symptom experience prior to CTX.

In conclusion, our study confirmed the high symptom burden experienced by lung cancer patients receiving CTX and identified differences in symptoms by prevalence, severity, and distress. Fatigue (the most distressing and prevalent symptom) and problems with sexual activity or interest (the most severe symptom) are both often overlooked or incompletely addressed during lung cancer patient care and require greater attention. Lower functional status and higher comorbidity are important risk factors for increased global symptom distress and physical symptoms, while lower functional status, younger age, and non-metastatic disease are important risk factors for increased psychological symptoms. These risk factors can help clinicians identify lung cancer patients at increased need for early, aggressive symptom management.

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Table 1

Demographic and clinical characteristics of lung cancer patients receiving CTX (N = 145).

Characteristic	No. (%)
Age in years, mean (SD)	64.0 (11.1)
Gender	
Female	82 (56.6)
Male	63 (43.4)
Race/ethnicity	
White	102 (71.8)
Asian or Pacific Islander	14 (9.9)
Black	14 (9.9)
Hispanic, mixed, or other	12 (8.5)
Annual household income	
<$30,000	37 (27.6)
$30,000 to $69,999	31 (23.1)
$70,000 to $99,999	21 (15.7)
>$100,000	45 (33.6)
Currently employed	36 (24.8)
Education in years, mean (SD)	16.1 (3.4)
Married or partnered	93 (64.6)
Lives alone	36 (25.0)
Smoking history	
Current or former smoker	99 (69.7)
Never smoker	43 (30.3)
BMI kg/m^2, mean (SD)	25.3 (4.6)
Patient-reported KPS score, mean (SD)	79.1 (14.6)
SCQ score, mean (SD)	7.3 (3.9)
No. of comorbidities, mean (SD)	3.2 (1.6)
Comorbidities	
Lung disease	87 (60.0)
Hypertension	58 (40.0)
Back pain	53 (36.6)
Depression	26 (17.9)
Osteoarthritis	21 (14.5)
Heart disease	20 (13.8)
Diabetes	18 (12.4)
Anemia or other blood disease	12 (8.3)
Liver disease	12 (8.3)
Rheumatoid arthritis	12 (8.3)
Ulcer or stomach disease	9 (6.2)
Kidney disease	1 (0.7)
Type of lung cancer	

Characteristic	No. (%)
Non-small cell lung cancer	126 (88.1)
Small cell lung cancer	17 (11.9)
Months since cancer diagnosis, mean (SD)	15.1 (31.7)
Months since cancer diagnosis, median (IQR)	4.2 (2.5–14.5)
Metastatic disease at time of study	110 (76.9)
Number of prior cancer treatments, mean (SD)	1.4 (1.4)
Prior treatment	
No prior treatment	54 (38.9)
Surgery only	17 (12.2)
CTX only	12 (8.6)
Radiation only	18 (13.0)
Surgery and CTX	5 (3.6)
Surgery and radiation	3 (2.2)
CTX and radiation	13 (9.4)
Surgery, CTX, and radiation	17 (12.2)
CTX regimen at time of study	
Platinum-doublet	113 (77.9)
Single agent CTX	29 (20.0)
Monoclonal antibody alone	3 (2.1)
Mean number of MSAS symptoms (out of 38, SD)	14.3 (7.1)
MSAS-GDI score (mean, SD)	1.08 (0.73)
MSAS-PHYS score (mean, SD)	0.93 (0.59)
MSAS-PSYCH score (mean, SD)	0.82 (0.67)

Abbreviations: BMI, body mass index; CTX, chemotherapy; GDI, global distress index; IQR, interquartile range; kg/m^2, kilogram per meter squared; KPS, Karnofsky Performance Status; MSAS, Memorial Symptom Assessment Scale; PHYS, physical symptom subscale; PSYCH, psychological symptom subscale SCQ, Self-Administered Comorbidity Questionnaire; SD, standard deviation.

Table 2

Symptom occurrence, severity, and distress in lung cancer patients during the week after CTX administration.

		Severity among those with and without the symptom[a]			Severity among those with the symptom[b]			Distress among those with the symptom[c]		
Symptom	**Occurrence (%)**	**Mean**	**SD**	**Rank**	**Mean**	**SD**	**Rank**	**Mean**	**SD**	**Rank**
Lack of energy	79.3	1.87	1.17	1	2.38	0.74	2	2.06	1.16	1
Feeling drowsy	66.2	1.26	1.12	4	1.92	0.79	15	1.45	1.17	26
Difficulty sleeping	65.5	1.30	1.10	3	2.00	0.68	10	1.63	1.09	13
Pain	61.4	1.31	1.22	2	2.16	0.76	6	2.04	1.17	3
Nausea	53.1	1.01	1.15	7	1.96	0.82	12	1.99	1.11	4
Change in the way food tastes	51.7	1.10	1.25	6	2.18	0.85	5	1.86	1.21	7
Constipation	50.3	1.13	1.30	5	2.27	0.89	3	1.93	1.23	5
Dry mouth	50.3	0.86	1.04	10	1.71	0.84	27	1.10	1.08	36
Worrying	49.7	0.85	1.04	11	1.75	0.81	25	1.62	1.24	15
Difficulty concentrating	49.7	0.82	0.99	12	1.65	0.77	30	1.56	1.16	19
Lack of appetite	49.0	1.01	1.22	8	2.15	0.85	7	1.56	1.13	18
Cough	46.2	0.73	0.96	15	1.63	0.75	34	1.45	1.08	25
Shortness of breath	45.5	0.87	1.10	9	1.94	0.79	13	1.73	1.22	10
Feeling irritable	44.1	0.73	0.93	16	1.69	0.62	28	1.47	1.02	23
Numbness/tingling in hands/feet	43.5	0.81	1.05	13	1.87	0.76	18	1.48	1.14	21
Feeling sad	41.4	0.70	0.96	19	1.75	0.67	26	1.66	1.12	11
Dizziness	38.6	0.56	0.84	25	1.51	0.67	37	1.26	1.05	32
Difficulty breathing	35.2	0.70	1.09	18	2.04	0.84	9	1.78	1.26	8
I do not look like myself	34.5	0.72	1.18	17	2.12	1.05	8	2.04	1.35	2
Chest tightness	34.5	0.59	0.97	21	1.79	0.83	21	1.64	1.19	12
Hair loss	34.5	0.73	1.22	14	2.21	1.10	4	1.61	1.46	16
Feeling nervous	34.5	0.57	0.87	24	1.64	0.66	32	1.34	1.09	28
Weight loss	33.1	0.52	0.90	26	1.64	0.83	31	1.30	1.25	30
Feeling bloated	31.0	0.57	0.97	23	1.88	0.79	16	1.61	1.26	17
Changes in skin	31.0	0.58	1.03	22	1.93	0.96	14	1.47	1.32	24
Increased appetite	26.9	0.42	0.77	28	1.64	0.59	33	0.78	1.16	38
Problems with sexual interest or activity	25.5	0.59	1.17	20	2.43	1.07	1	1.86	1.36	6

Symptom	Occurrence (%)	Severity among those with and without the symptom[a]			Severity among those with the symptom[b]			Distress among those with the symptom[c]		
		Mean	SD	Rank	Mean	SD	Rank	Mean	SD	Rank
Mouth sores	25.5	0.41	0.79	29	1.66	0.68	29	1.31	0.98	29
Swelling of arms or legs	23.5	0.40	0.82	30	1.78	0.75	22	1.23	1.20	34
Abdominal cramps	22.8	0.42	0.87	27	1.88	0.79	17	1.53	0.95	20
Vomiting	22.1	0.33	0.71	32	1.57	0.68	36	1.63	1.01	14
Weight gain	21.4	0.31	0.73	33	1.57	0.84	35	1.24	1.41	33
Sweats	21.4	0.36	0.81	31	1.82	0.82	19	1.21	1.11	35
Difficulty swallowing	18.6	0.28	0.69	35	1.77	0.61	23	1.35	1.07	27
Itching	18.6	0.27	0.62	37	1.44	0.58	38	1.04	1.02	37
Hot flashes	16.6	0.31	0.80	34	2.00	0.87	10	1.48	1.12	22
Diarrhea	15.9	0.27	0.70	36	1.77	0.75	23	1.27	0.83	31
Problems with urination	14.5	0.26	0.70	38	1.81	0.75	20	1.76	1.22	9

Abbreviations: CTX, chemotherapy; SD, standard deviation.

[a] Severity rating range 0 (symptom not present) to 4 (symptom very severe).

[b] Severity rating range 1 (symptom mild) to 4 (symptom very severe); patients without the symptom were omitted.

[c] Distress rating range 0 (not at all) to 4 (very much); only patients with the symptom responded.

Table 3

Multivariable linear regression model of the MSAS subscale scores following CTX administration (n = 110[a]).

	MSAS-GDI		MSAS-PHYS		MSAS-PSYCH	
Characteristic[b]	**beta (95% CI)**	**p**	**beta (95% CI)**	**p**	**beta (95% CI)**	**p**
Age, per 10 years	−0.06 (−0.16 to 0.05)	0.26	−0.04 (−0.13 to 0.04)	0.31	−0.12 (−0.21 to −0.02)	0.02
Male gender	−0.19 (−0.43 to 0.04)	0.11	−0.20 (−0.39 to −0.005)	0.045	−0.18 (−0.40 to 0.03)	0.10
Income (ref: <$30,000)		0.06		0.31		0.03
$30,000 to 69,999	−0.34 (−0.67 to −0.01)		−0.21 (−0.48 to 0.06)		−0.37 (−0.68 to −0.07)	
$70,000 to 99,999	−0.06 (−0.44 to 0.32)		0.04 (−0.27 to 0.35)		−0.10 (−0.45 to 0.25)	
>$100,000	0.07 (−0.25 to 0.38)		−0.03 (−0.30 to 0.23)		0.01 (−0.28 to 0.30)	
Current or former smoker (ref: never smoker)	−0.004 (−0.28 to 0.27)	0.98	0.02 (−0.21 to 0.25)	0.85	0.11 (−0.15 to 0.37)	0.41
BMI	−0.03 (−0.06 to 0.002)	0.07	−0.03 (−0.05 to −0.004)	0.02	−0.01 (−0.04 to 0.01)	0.37
Patient-reported KPS, per 10 units	−0.17 (−0.27 to −0.08)	0.001	−0.12 (−0.20 to −0.04)	0.003	−0.12 (−0.21 to −0.04)	0.01
SCQ score	0.05 (0.01 to 0.08)	0.02	0.03 (0.002 to 0.06)	0.04	0.03 (−0.01 to 0.06)	0.14
Metastatic disease	−0.20 (−0.48 to 0.09)	0.18	−0.11 (−0.35 to 0.12)	0.35	−0.29 (−0.55 to −0.02)	0.03
Number of prior cancer treatments	0.08 (−0.005 to 0.16)	0.07	0.03 (−0.03 to 0.10)	0.33	0.08 (0.004 to 0.16)	0.04
% variance explained	31.8%		26.2%		27.0%	

Abbreviations: BMI, body mass index; CI, confidence interval; CTX, chemotherapy; GDI, global distress index; KPS, Karnofsky Performance Status; MSAS, Memorial Symptom Assessment Scale ; PHYS, physical symptom subscale; PSYCH, psychological symptom subscale; SCQ, Self-Administered Comorbidity Questionnaire.

[a] 35 patients had at least one missing variable so 108patients were included in the linear regression models.

[b] Variables associated with the total number of MSAS symptoms reported with a p-value < 0.20 in the bivariable model were included in the multivariable model.