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Associations among hearing loss, multiple co-occurring symptoms, and quality of life outcomes in cancer survivors

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Abstract

Purpose Evaluate for differences in demographic and clinical characteristics, occurrence of common symptoms, symptom severity scores, and quality of life (QOL) outcomes in survivors with ($n = 155$) and without ($n = 118$) audiometrically confirmed hearing loss.

Methods Survivors, who were recruited from throughout the San Francisco Bay area, completed the self-report questionnaires to obtain the information of demographic and clinical characteristics; the occurrence and severity of depression, anxiety, fatigue, decrements in energy, sleep disturbance, pain, and cognitive impairment; and the general and cancer-specific QOL outcomes. Parametric and non-parametric tests were used to evaluate for differences between the two survivor groups.

Results Survivors with audiometrically confirmed hearing loss were older, more likely to be male, were more likely to be unemployed, report a lower annual household income, and had a higher comorbidity burden. Except for the severity of worst pain, no between-group differences were found in the occurrence rates for or severity of any of the symptoms. Survivors with hearing loss reported worse physical function and general health scores.

Conclusions While no between-group differences in symptom occurrence rates and severity scores were found, across the total sample, a relatively high percentage of survivors who were over 6 years from their cancer diagnosis reported clinically meaningful levels of depression (25%), anxiety (50%), fatigue (40%), decrements in energy (70%), sleep disturbance (58%), cognitive impairment (57%), and pain (60%).

Implications for Cancer Survivors Clinicians need to perform routine assessments of hearing loss, as well as common co-occurring symptoms and initiate individualized symptom management interventions.

Keywords Cancer · Chemotherapy · Depression · Fatigue · Hearing loss · Patient-reported outcomes · Quality of life · Sleep disturbance · Symptoms

Introduction

With an estimated 18 million cancer survivors living in the USA [1], an evaluation of symptoms that can effect these individuals' ability to work, engage in social activities, and experience optimal levels of physical and psychological functioning is of paramount importance. For the majority of survivors who received chemotherapy for breast, gastrointestinal, gynecological, or lung cancer, neurotoxic agents (i.e., platinum and/or taxane compounds) were administered. While chemotherapy-induced peripheral neuropathy (CIPN) is a common adverse effect of neurotoxic chemotherapy [2], emerging evidence suggests that hearing loss is equally problematic.

Studies of hearing loss in oncology patients have focused primarily on children who received platinum [3]. The limited amount of research in adults has evaluated for hearing loss in patients treated with platinum compounds for testicular [4–9] and head and neck [10–12] cancers. However, in our first cross-sectional study of cancer survivors with breast, gastrointestinal, gynecologic, or lung cancers [13], of the 371 survivors who had objectively confirmed CIPN, 41.5% self-reported hearing loss. Compared to the survivors with only CIPN, those with hearing loss had higher state and trait anxiety scores.

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Given the underestimation of hearing loss by self-report [14], in our recent study of survivors with breast, gastrointestinal, gynecologic, or lung cancer who received either a platinum- and/or a taxane-containing chemotherapy regimen [15], hearing loss was confirmed audiometrically. While only 32.9% of the 273 survivors in this study self-reported hearing loss, between 52.3 and 71.4% had hearing loss confirmed with an audiogram. Of note, no statistically significant differences in the occurrence rates for and effects of hearing loss were found among the three chemotherapy regimens (i.e., only platinum, only taxane, both platinum and taxane). While our findings warrant confirmation, this study is the first to provide evidence that audiometrically confirmed hearing loss occurs in a large percentage of survivors with four of the most common solid tumors.

On average, cancer survivors report nine co-occurring symptoms [16]. Some of the most common symptoms include depression, anxiety, sleep disturbance, fatigue, cognitive impairment, and pain [17–19]. While not studied in oncology patients, in the general population, recent evidence suggests that hearing loss is associated with higher levels of depression [20, 21], anxiety [22], cognitive impairment [23], sleep disturbance [24], and fatigue [25, 26]. Therefore, it is reasonable to hypothesize that compared to survivors without hearing loss, cancer survivors with hearing loss would report higher levels of these common symptoms. Given the paucity of research on associations between hearing loss and symptoms and QOL outcomes in cancer survivors, the purposes of this study were to evaluate for differences in demographic and clinical characteristics, occurrence of common symptoms, symptom severity scores, and QOL outcomes in survivors with ($n = 155$) and without ($n = 118$) audiometrically confirmed hearing loss.

Patients and methods

Survivors and settings

This study is part of a larger study that evaluated for hearing loss, tinnitus, and CIPN in cancer survivors who received neurotoxic chemotherapy. Survivors were recruited from throughout the San Francisco Bay area using a variety of recruitment strategies (e.g., investigator registry, clinician referral, medical record review, emails to participants in the Dr. Susan Love Foundation's Love Research Army® Program). Survivors with and without CIPN were ≥ 18 years of age; had received a platinum and/or a taxane compound; had a Karnofsky Performance Status (KPS) score of ≥ 50 [27]; were able to read, write, and understand English; and were willing to complete questionnaires that took 90 to 150 min over 2 weeks and travel to UCSF for a 3-h study visit.

For the CIPN evaluation, survivors with and without CIPN were excluded if they had peripheral vascular disease, vitamin B12 deficiency, thyroid dysfunction, HIV neuropathy, another condition that was difficult for them to distinguish from their CIPN, a hereditary sensory or autonomic neuropathy [28], and/or a hereditary mitochondrial disorder [29]. For the hearing and tinnitus evaluation, survivors were excluded if they had tinnitus of > 8 on a 0 to 10 numeric rating scale prior to chemotherapy; had hearing loss prior to chemotherapy that prevented understanding a one-to-one conversation; had a history of vestibular schwannoma; had radiation to head or neck; or had diagnosis of cancer to the brain. A detailed history was obtained to evaluate for the presence of these conditions. Of the 1012 survivors who were screened (primary reason for ineligibility was not meeting the inclusion criteria for the CIPN portion of the study), 365 were enrolled and 273 completed the self-report questionnaires and the study visit. Visit completions were interrupted by the COVID-19 pandemic.

Study procedures

Survivors communicated their willingness to participate in the study by phone or email. Research staff phoned survivors and determined their eligibility to participate. For survivors who met our inclusion criteria, the research nurse or audiologist obtained consent over the phone; asked the survivors to complete the self-report questionnaires prior to their study visit either electronically or by hard copy; and scheduled the study visit. During the study visit, the research staff obtained written informed consent, reviewed the study questionnaires for completeness, and performed the audiometric testing. The study visit was conducted by research nurses and audiologists in a large, dedicated research space that contained all the necessary equipment to conduct the study procedures including a double-walled sound-treated unit for hearing testing.

Measures

Demographic and clinical characteristics

Survivors completed a demographic questionnaire, the KPS scale [27], and the Self-Administered Comorbidity Questionnaire (SCQ) [30]. Survivors were interviewed to obtain information on their cancer diagnosis, previous and current cancer treatments, and chemotherapy regimens. Medical records were reviewed for detailed information on cancer diagnosis, previous cancer treatments, and chemotherapy regimens.

Audiometric testing

Prior to the audiometric assessment, survivors underwent video otoscopy (Teslong, Irvine, CA) and tympanometry (Titan, Interacoustics, Eden Prairie, MN). Pure tone air conduction thresholds were obtained bilaterally at frequencies of between 0.25 and 16.0 kHz covering the speech frequency range. An audiometer (Pello Interacoustics, Eden Prairie, MN), with insert earphones, that utilized the GSI-AMTAS automated threshold assessment (Grayson-Sadler, Eden Prairie, MN) was used to perform the audiometric assessment [31]. A bone oscillator, insert earphones, and circumaural high-frequency earphones were used to assess air and bone conduction hearing thresholds.

Co-occurring symptom measures

An evaluation of other common symptoms was done using valid and reliable instruments. The symptoms and their respective measures were depressive symptoms (Center for Epidemiological Studies-Depression scale (CES-D) [32]); state and trait anxiety (Spielberger State-Trait Anxiety Inventories [33]); morning and evening fatigue and morning and evening energy (Lee Fatigue Scale (LFS) [34]); sleep disturbance (General Sleep Disturbance Scale (GSDS) [35]); cognitive impairment (Attentional Function Index (AFI) [36]); and pain (Brief Pain Inventory (BPI) [37]).

QOL measures

QOL was evaluated using generic (i.e., Medical Outcomes Study-Short Form-12 (SF-12) [38]) and disease-specific (i.e., QOL-Patient Version (QOL-PV) [39]) measures. QOL-PV measures four dimensions of QOL (i.e., physical, psychological, social, and spiritual well-being), as well as a total QOL score. The individual items on the SF-12 were evaluated and the instrument was scored into two component scores (i.e., physical component summary (PCS) and mental component summary (MCS)). For both measures, higher scores indicate a better QOL.

Analysis

Determination of audiometrically confirmed hearing loss

Following the audiogram, to adjust for age- and gender-related changes in hearing, each survivor's audiogram was evaluated using the National Health and Nutrition Examination Survey (NHANES)-modified Occupational Safety and Health Administration (OSHA) age adjustment standards [40, 41]. A survivor was classified as having hearing loss if at any frequency they scored poorer than the 50th percentile for their age and gender.

Data analysis

Study data were collected and managed using the Research Electronic Data Capture (REDCap) system hosted at UCSF [42]. REDCap is a secure, web-based software platform designed to support data capture for research studies. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 28 (IBM Corporation, Armonk, NY). Differences between the survivors with and without hearing loss in demographic and clinical characteristics, symptom occurrence rates, symptom severity scores, and QOL outcomes were evaluated using parametric and non-parametric tests. A p-value of < 0.05 was considered statistically significant.

Results

In this study that evaluated 273 survivors, 56.8% and 43.2% did and did not have audiometrically confirmed hearing loss, respectively.

Demographic and clinical characteristics

As shown in Table 1, compared to survivors without hearing loss, survivors with hearing loss were older, more likely to be male, less likely to be employed, more likely to have a lower annual household income, and less likely to report child care responsibilities. In addition, survivors with hearing loss had a higher number of comorbidities and a higher comorbidity burden, were a longer time since their cancer diagnosis, were less likely to report breast cancer, were more likely to report gastrointestinal cancer, had a higher number of metastatic sites, and were more likely to self-report diagnoses of osteoarthritis and lung disease.

Co-occurring symptoms

As shown in Table 2, no between-group differences were found in the occurrence rates for clinically meaningful levels of depression, state anxiety, morning and evening fatigue, decrements in morning and evening energy, sleep disturbance, or cognitive impairment. No between-group differences were found in the occurrence rates for cancer pain, non-cancer pain, and both cancer and non-cancer pain.

As shown in Table 3, except for worst pain scores, no between-group differences were found in depression, state anxiety, fatigue, energy, sleep disturbance, or cognitive impairment scores. Compared to the survivors without

Table 1 Differences in demographic and clinical characteristics between survivors with and without audiometrically confirmed hearing loss

Characteristic	No hearing loss 43.2% ($n=118$)	Hearing loss 56.8% ($n=155$)	Statistic, p-value
	Mean (SD)	Mean (SD)	
Age (years)	54.6 (11.7)	66.1 (9.4)	$t=-8.79$, $p<.001$
Education (years)	16.4 (2.3)	16.2 (2.4)	$t=0.91$, $p=.364$
Body mass index (kg/m^2)	27.4 (7.2)	27.6 (6.4)	$t=-0.77$, $p=.783$
Karnofsky Performance Status score	88.0 (10.4)	86.4 (10.6)	$t=1.28$, $p=.203$
Number of comorbidities	1.4 (1.5)	2.1 (1.4)	$t=-3.65$, $p<.001$
Self-Administered Comorbidity Questionnaire score	3.2 (3.7)	4.3 (3.3)	$t=-2.54$, $p=.012$
Years since cancer diagnosis	6.6 (5.6)	8.7 (7.4)	$t=-2.59$, $p=.010$
Number of prior cancer treatments	3.1 (0.7)	3.1 (0.9)	$t=-0.11$, $p=.916$
Number of current cancer treatments	0.5 (0.6)	0.4 (0.6)	$t=1.53$, $p=.128$
Number of metastatic sites (out of 7)	0.7 (0.8)	0.9 (0.9)	$t=-2.53$, $p=.012$
Number of metastatic sites without lymph node involvement (out of 6)	0.2 (0.6)	0.3 (0.7)	$t=-2.15$, $p=.033$
Dose of platinum compounds for patients who received only a platinum (mg/m^2)	1092.9 (598.5)	1534.9 (1071.4)	$t=-1.22$, $p=.231$
Dose of taxane compounds for patients who received only a taxane (mg/m^2)	1194.7 (540.7)	1390.2 (1783.9)	$t=-0.85$, $p=.395$
Dose of drugs for patients who received both a platinum and a taxane compound			
Platinum dose (mg/m^2)	3502.29 (1071.69)	3534.9 (1613.53)	$t=-0.10$, $p=.923$
Taxane dose (mg/m^2)	1331.1 (791.36)	1887.1 (2444.4)	$t=-1.25$, $p=.217$
	% (n)	% (n)	
Female (% yes)	96.6 (114)	87.1 (135)	FE, $p=.008$
Married/partnered (% yes)	65.0 (76)	66.9 (103)	FE $p=.796$
Lives alone (% yes)	25.6 (30)	26.1 (40)	FE, $p=1.000$
Employed	62.7 (74)	38.8 (59)	FE, $p<.001$
Ethnicity			
White	65.3 (77)	76.0 (117)	$X^2=9.11$, $p=.058$
Black	5.1 (6)	1.9 (3)	
Asian or Pacific Islander	15.3 (18)	9.7 (15)	
Hispanic	4.2 (5)	7.8 (12)	
Mixed or other	10.2 (12)	4.5 (7)	
Annual household income			
< $20,000	5.3 (6)	6.1 (9)	U, $p=.003$
$20,000–$59,999	18.4 (21)	27.9 (41)	
$60,000–$99,999	14.0 (16)	25.2 (37)	
> $100,000	10.2 (12)	4.5 (7)	
Child care responsibilities (% yes)	26.4 (29)	10.1 (15)	FE, $p<.001$
Adult care responsibilities (% yes)	10.0 (11)	6.8 (10)	FE, $p=.367$
Smoker (ever)	30.1 (34)	39.9 (59)	FE, $p=.118$
Comorbid conditions (% yes)			
Osteoarthritis	22.9 (27)	41.6 (62)	FE, $p=.002$
Back pain	28.4 (33)	33.8 (50)	FE, $p=.423$
Depression	14.8 (17)	18.8 (28)	FE, $p=.414$
High blood pressure	22.4 (26)	29.6 (45)	FE, $p=.210$
Heart disease	1.7 (2)	6.6 (10)	FE, $p=.074$
Diabetes	3.4 (4)	6.8 (10)	FE, $p=.274$
Lung disease	1.7 (2)	7.2 (11)	FE, $p=.044$
Anemia or blood disease	5.1 (6)	4.6 (7)	FE, $p=1.000$
Ulcer or stomach disease	2.5 (3)	4.0 (6)	FE, $p=.735$
Kidney disease	0.0 (0)	0.7 (1)	n/a
Liver disease	0.9 (1)	1.3 (2)	FE, $p=1.000$
Rheumatoid arthritis	1.8 (2)	6.8 (10)	FE, $p=.074$

Table 1 (continued)

Characteristic	No hearing loss 43.2% ($n=118$)	Hearing loss 56.8% ($n=155$)	Statistic, p-value
	Mean (SD)	Mean (SD)	
Type of cancer			$X^2=12.82$, $p=.013$
Breast	80.5 (95)	61.9 (96)	1 > 2
Gastrointestinal	5.1 (6)	14.8 (23)	1 < 2
Gynecological	10.2 (12)	14.2 (22)	NS
Lung	0.8 (1)	3.2 (5)	NS
Other	3.4 (4)	5.8 (9)	NS
Any metastatic disease (% yes)	53.8 (54)	67.1 (50)	FE, $p=.032$
Type of prior cancer treatment			
Only CTX, surgery, or RT	1.7 (2)	1.3 (2)	$X^2=0.89$, $p=.640$
CTX and surgery, or CTX and RT, or surgery and RT	33.9 (40)	39.4 (61)	
CTX, surgery, and RT	64.4 (76)	59.4 (92	
Type of CTX			
Only taxane	62.7 (74)	52.3 (81)	$X^2=4.52$, $p=.104$
Only platinum	8.5 (10)	16.1 (25)	
Both taxane and platinum	28.8 (34)	31.6 (49)	

Abbreviations: *CTX* chemotherapy, *FE* Fisher's exact, *kg* kilograms, *mg* milligrams, m^2 meters squared, *n/a* not applicable, *NS* not significant, *RT* radiation therapy, *SD* standard deviation, *U* Mann–Whitney *U* test

Table 2 Differences in symptom occurrence rates between survivors with and without audiometrically confirmed hearing loss

Symptom*	No hearing loss 43.2% ($n=118$)	Hearing loss 56.8% ($n=155$)	Statistic, p-value
	% (n)	% (n)	
Depression (≥ 16.0)	22.6 (26)	26.8 (41)	FE, $p=.478$
State anxiety (≥ 32.2)	54.8 (63)	44.1 (67)	FE, $p=.086$
Morning fatigue (≥ 3.2)	49.6 (57)	39.9 (61)	FE, $p=.136$
Evening fatigue (≥ 5.6)	44.6 (50)	37.7 (57)	FE, $p=.310$
Morning energy (≤ 6.2)	78.4 (91)	67.3 (103)	FE, $p=.054$
Evening energy (≤ 3.5)	71.2 (79)	65.1 (99)	FE, $p=.351$
Sleep disturbance total score (≥ 43.0)	59.5 (69)	57.5 (88)	FE, $p=.803$
Attentional function total score (< 7.5)	62.5 (65)	52.5 (73)	FE, $p=.150$
Type of pain			
None	25.2 (29)	15.1 (23)	$X^2=6.11$, $p=.106$
Only non-cancer pain	20.9 (24)	23.0 (35)	
Only cancer pain	27.8 (32)	25.0 (38)	
Both cancer and non-cancer pain	26.1 (30)	36.8 (56)	

*Percentage of survivors who scored above the clinically meaningful cut point for each of the symptoms. Clinically meaningful cut point for each symptom measure is listed in parentheses

hearing loss, survivors with hearing loss reported higher worst pain intensity scores.

QOL outcomes

As shown in Table 4, no between-group differences were found for any of the QOL-PV subscale or total scores. In terms of the SF-12, survivors with hearing loss had lower physical functioning, role physical, general health, and PCS scores.

Discussion

This study is the first to evaluate for differences in demographic and clinical characteristics, occurrence and severity of common co-occurring symptoms, and QOL

Table 3 Differences in symptom severity scores between survivors with and without audiometrically confirmed hearing loss

Symptom	No hearing loss 43.2% ($n=118$)	Hearing loss 56.8% ($n=155$)	Statistic, p-value
	Mean (SD)	Mean (SD)	
Depression (≥ 16.0)	10.9 (8.8)	10.0 (8.7)	$t=.078$, $p=.434$
State anxiety (≥ 32.2)	35.4 (10.5)	33.7 (12.4)	$t=1.21$, $p=.228$
Morning fatigue (≥ 3.2)	3.2 (2.3)	2.8 (2.3)	$t=1.22$, $p=.225$
Evening fatigue (≥ 5.6)	5.0 (1.9)	4.9 (2.1)	$t=0.62$, $p=.534$
Morning energy (6.2)	4.2 (2.2)	4.7 (2.4)	$t=-1.78$, $p=.076$
Evening energy (≤ 3.5)	2.8 (2.1)	2.8 (2.2)	$t=-0.09$, $p=.933$
Sleep disturbance total score (≥ 43.0)	49.9 (18.5)	47.8 (20.6)	$t=0.84$, $p=.401$
Quantity of sleep (≥ 3.0)	5.0 (1.4)	4.9 (1.4)	$t=0.57$, $p=.570$
Quality of sleep (≥ 3.0)	3.6 (1.8)	3.3 (1.9)	$t=1.27$, $p=.205$
Sleep onset latency (≥ 3.0)	2.6 (2.1)	2.7 (2.3)	$t=-0.24$, $p=.811$
Mid-sleep awakenings (≥ 3.0)	5.0 (2.1)	4.9 (2.4)	$t=0.58$, $p=.560$
Early awakenings (≥ 3.0)	3.6 (2.5)	3.3 (2.4)	$t=0.86$, $p=.393$
Excessive daytime sleepiness (≥ 3.0)	2.1 (1.3)	2.0 (1.3)	$t=0.73$, $p=.468$
Use of sleep medications (≥ 3.0)	0.5 (0.6)	0.6 (0.7)	$t=-0.66$, $p=.510$
Attentional function total score (< 5.0 = low, 5.0 to 7.5 = moderate, > 7.5 = high)	6.9 (1.6)	7.1 (1.7)	$t=-1.28$, $p=.200$
Effective action	6.9 (1.7)	7.1 (1.9)	$t=-1.14$, $p=.257$
Attentional lapses	6.8 (2.0)	7.0 (2.0)	$t=-0.57$, $p=.567$
Interpersonal effectiveness	7.0 (1.7)	7.4 (1.9)	$t=-1.61$, $p=.109$
For patients with pain			
Pain now	2.4 (2.1)	2.6 (2.1)	$t=-0.98$, $p=.327$
Average pain	2.9 (1.8)	3.4 (1.9)	$t=-1.94$, $p=.053$
Worst pain	5.7 (2.4)	6.4 (2.2)	$t=-2.17$, $p=.031$
Number of days in pain	2.5 (2.4)	2.9 (2.8)	$t=-1.25$, $p=.212$
Hours per day in pain	6.1 (7.4)	7.7 (8.1)	$t=-1.41$, $p=.162$
Percent relief from pain medication	5.4 (3.8)	5.1 (3.3)	$t=0.52$, $p=.606$
Satisfaction with pain management	5.7 (3.4)	5.3 (3.0)	$t=0.76$, $p=.447$

Abbreviation: *SD* standard deviation

Clinically meaningful cut point for each symptom measure is listed in parentheses

outcomes in cancer survivors with and without audiometrically confirmed hearing loss. Contrary to our a priori hypothesis, except for worst pain scores, no between-group differences in the symptom occurrence rates and severity scores were found. These findings are somewhat surprising given the between-group differences in some of the demographic and clinical characteristics.

While our evaluation of hearing loss accounted for age and gender, consistent with findings in the general population, survivors with hearing loss were older [43] and more likely to be male [44]. Equally important, survivors with hearing loss were less likely to be employed and to report a lower annual household income. While not reported in cancer patients, this later finding warrants additional investigation given that a recent meta-analysis found a positive association between adult onset hearing loss and unemployment [45]. This relationship is attributed to high levels of fatigue associated with an increased requirement for intense listening efforts in both work and social situations [46].

In terms of clinical characteristics, survivors with hearing loss had a longer time since their cancer diagnosis, had a higher comorbidity burden, and were more likely to have metastatic disease. However, no between-group differences were found in the types of chemotherapy regimens or doses of neurotoxic chemotherapy. The positive association between hearing loss and a higher comorbidity burden is consistent with studies in the general population [47].

While no between-group differences were found in the occurrence and severity of common symptoms, the findings from this study provide important and clinically useful information on depression, anxiety, fatigue, decrements in energy, cognitive impairment, sleep disturbance, and pain in a relatively large sample of cancer survivors who were over 6 years since their cancer diagnosis. As noted in one review [48], estimates suggest that while 30 to 60% of patients with

Table 4 Differences in quality of life scores between survivors with and without audiometrically confirmed hearing loss

Symptom	No hearing loss 43.2% ($n=118$)	Hearing loss 56.8% ($n=155$)	Statistic, p-value
	Mean (SD)	Mean (SD)	
Multidimensional quality of life scale–cancer			
Physical well-being	7.6 (1.7)	7.7 (1.7)	$t=-0.45$, $p=.651$
Psychological well-being	5.7 (1.7)	5.9 (1.7)	$t=-0.97$, $p=.334$
Social well-being	6.2 (2.0)	6.5 (2.0)	$t=-1.13$, $p=.261$
Spiritual well-being	5.5 (1.8)	5.7 (2.0)	$t=-0.88$, $p=.379$
Total quality of life score	6.1 (1.3)	6.3 (1.4)	$t=-1.14$, $p=.256$
Medical Outcomes Study–Short Form 12			
Physical functioning	74.8 (28.6)	61.7 (34.5)	$t=3.39$, $p<.001$
Role physical	70.0 (27.9)	62.8 (28.3)	$t=2.08$, $p=.038$
Bodily pain	78.4 (24.4)	73.0 (26.1)	$t=1.73$, $p=.085$
General health	73.3 (19.9)	65.4 (23.6)	$t=2.78$, $p=.006$
Vitality	52.2 (21.3)	53.6 (24.5)	$t=$-0.50, $p=.615$
Social functioning	80.4 (24.3)	79.9 (25.1)	$t=0.16$, $p=.870$
Role emotional	79.8 (21.8)	78.0 (23.6)	$t=0.66$, $p=.508$
Mental health	67.7 (17.2)	70.0 (19.6)	$t=-1.04$, $p=.298$
Physical component summary score	48.4 (9.9)	44.0 (10.9)	$t=3.28$, $p=.001$
Mental component summary score	48.0 (9.2)	50.0 (9.4)	$t=-1.66$, $p=.098$

Abbreviation: *SD* standard deviation

cancer have psychological problems, only 10% are referred for treatment. In the current study, approximately 25% of the survivors reported clinically meaningful levels of depressive symptoms; 15% reported a diagnosis of depression on the SCQ; and almost 50% reported clinically meaningful levels of anxiety. Possible reasons for these high levels of psychological symptoms, particularly anxiety, include fear of recurrence [49] and/or financial toxicity associated with the costs of medical management of cancer and other chronic conditions [50–54].

Equally important findings in this study are the high occurrence rates for sleep disturbance and both morning and evening fatigue, as well as decrements in both morning and evening energy. In fact, clinically meaningful decrements in morning and evening energy were reported by 72.1% and 67.7% of the sample, respectively. While research on fatigue in oncology patients and survivors is relatively common [55–57], a growing body of evidence suggests that energy is a distinct symptom from fatigue [58–60]. Energy can be defined as an individual's potential to perform physical and mental activities [60]. Adequate amounts of energy are required to perform routine, as well as work-related activities. One potential explanation for the low levels of morning and evening energy in our sample of cancer survivors is the high rate of sleep disturbance. In the current study, almost 60% of our survivors reported clinically meaningful levels of sleep disturbance. An evaluation of the subscale scores of the GSDS (Table 3) indicates that survivors rated the quantity of their sleep as inadequate on 5 out of 7 days each week. While this sample does not appear to have a problem with sleep initiation (i.e., sleep onset latency scores were < 3.0), findings suggest that they have problems with sleep maintenance (i.e., scores of > 3.0 for mid-sleep awakenings and early awakenings). Given that sleep disturbance, fatigue, and decrements in energy are inter-related, survivors with these symptoms would benefit from education on the benefits of regular exercise, cognitive-behavioral interventions (e.g., mindfulness, yoga), and routine sleep management interventions [61–63].

Consistent with previous reports [64, 65], almost 60% of the survivors in this study had AFI scores that suggest moderate to high levels of cognitive impairment. The AFI assesses an individual's perceived effectiveness in performing daily activities that are supported by attention and working memory [66]. This finding has clinical implications particularly in terms of survivors' work performance; ability to carry out child and/or elder care responsibilities; and ability to adhere with a therapeutic regimen and/or survivorship care plan. Equally important, given the mounting evidence of the occurrence of a neuropsychological symptom cluster that consists of pain, fatigue, sleep disturbance, and depression during and following cancer treatment [67–69], cancer survivors need to be assessed for multiple co-occurring symptoms and have individualized interventions initiated to decrease symptom burden and improve QOL.

While no clinically meaningful cutoff scores exist for QOL-PV, both groups of survivors' total QOL scores were in the moderate range (i.e., 6.1 to 6.3 on a 0 (extremely

poo) to 10 (excellent) scale). However, consistent with the higher comorbidity burden in the hearing loss group, our survivors reported not only statistically significant but clinically meaningful decrements [70, 71] in the physical functioning (Cohen's $d=0.40$), role physical (Cohen's $d=0.25$), and general health (Cohen's $d=0.35$) scales of the SF-12. Of note, both groups of survivors reported PCS and MCS scores that were at or below the normative score of 50 for the general population of the USA. Taken together with the relatively high symptom burden, interventions are needed to decrease symptoms and improve survivors' overall QOL.

Several limitations warrant consideration. Due to the cross-sectional design, future studies need to evaluate for changes in symptoms and QOL outcomes in survivors with and without audiometrically confirmed hearing loss. In addition, future studies need to evaluate for differences in symptom burden among survivors with and without multiple types of chemotherapy-induced neurotoxicities (e.g., hearing loss, tinnitus, CIPN). Given that this study did not collect data on pharmacologic and non-pharmacologic interventions, the impact of symptom management interventions warrant evaluation in future studies.

Despite these limitations, this study provides new information on the relatively high symptom burden associated with cancer survivorship. Clinicians can use this information to guide their ongoing assessment of these individuals and to initiate pharmacologic and non-pharmacologic interventions to reduce symptom burden and improve survivors' QOL.

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Author contribution Dr. Miaskowski designed the study, did the data analysis, and wrote the paper. All of the authors contributed to writing the manuscript and approving the final version of the paper.

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Data availability Data are available from Dr. Miaskowski following the completion of a material transfer agreement with the University of California, San Francisco.

Declarations

Ethics approval This study was approved by the Institutional Review Board at the University of California, San Francisco.

Consent to participate Written informed consent was obtained from all of the survivors who participated in this study.

Competing interests The authors declare no competing interests.

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