Title

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HEARING LOSS AND TINNITUS IN SURVIVORS WITH CHEMOTHERAPY-INDUCED NEUROPATHY

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Abstract

Purpose—The purpose of this study was to evaluate for differences in demographic, clinical, and pain characteristics, as well as measures of sensation, balance, perceived stress, symptom burden, and quality of life (QOL) among survivors who received neurotoxic chemotherapy (CTX) and who reported only chemotherapy-induced neuropathy (CIN, n=217), CIN and hearing loss (CIN/HL, n=69), or CIN, hearing loss, and tinnitus (CIN/HL/TIN, n=85). We hypothesized that as the number of neurotoxicities increased, survivors would have worse outcomes.

Methods—Survivors were recruited from throughout the San Francisco Bay area. Survivors completed self-report questionnaires for pain and other symptoms, stress and QOL. Objective measures were assessed at an in person visit.

Results—Compared to survivors with only CIN, survivors with all three neurotoxicities were less likely to be female and less likely to report child care responsibilities. In addition, survivors with all three neurtoxicities had higher worst pain scores, greater loss of protective sensation, and worse timed get up and go scores. These survivors reported higher state anxiety and depression and poorer QOL. For some outcomes (e.g., longer duration of CIN, self-reported balance problems), significantly worse outcomes were found for the survivors with CIN/HL and CIN/HL/TIN compared to those with only CIN.

Conclusions—Our findings suggest that compared to survivors with only CIN, survivors with CIN/HL/TIN are at increased risk for the most severe symptom burden, significant problems

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associated with sensory loss and changes in balance, as well as significant decrements in all aspects of QOL.

Keywords

chemotherapy; peripheral neuropathy; hearing loss; tinnitus; balance; survivor

INTRODUCTION

Research on the neurotoxic effects of chemotherapy (CTX) in cancer survivors has focused primarily on an evaluation of somatosensory changes in the upper and lower extremities (i.e., chemotherapy-induced neuropathy (CIN)). While the exact prevalence of CIN in cancer survivors is unknown, estimates range from 38% to 90% (Kerckhove et al., 2017). In addition, limited evidence suggests that CIN results in significant decrements in physical function (Miaskowski et al., 2017), significant psychological distress (Leach et al., 2016; Miaskowski et al., 2017), sleep disorders (Hong et al., 2014; Miaskowski et al., 2017), and increased risk for falls (Bao et al., 2016; Gewandter et al., 2013; Kolb et al., 2016; Tofthagen et al., 2012).

Recently, the prevalence and impact of two additional neurotoxic effects of CTX, namely hearing loss and tinnitus, have begun to be evaluated in cancer survivors. Most of this research, albeit limited, focused on an evaluation of hearing loss and tinnitus in survivors who received platinum for testicular (Frisina et al., 2016; Oldenburg et al., 2007) or head and neck cancer (Huang et al., 2016; Malgonde et al., 2015; Theunissen et al., 2015). Findings from these studies suggest that these problems contribute to significant decreases in quality of life (QOL). Only a few small studies have evaluated for audiovestibular toxicities in patients with breast, gastrointestinal (GI), gynecological (GYN), or lung cancer (Bacon et al., 2003; Jenkins et al., 2009; Ozguroglu et al., 2006; Salvinelli et al., 2003; Skalleberg et al., 2017). In addition, while taxanes are known to produce CIN (Kerckhove et al., 2017), only one clinical study was identified that evaluated the effects of taxanes on the auditory system (Sarafraz and Ahmadi, 2008). While the findings from this study were negative, results of preclinical studies suggest that the administration of taxanes results in hearing loss (Atas et al., 2006; Dong et al., 2014).

Given the paucity of research on the neurotoxic effects of CTX in cancer survivors, we recently evaluated for CIN, hearing loss, and tinnitus in a sample of cancer survivors who received a platinum and/or a taxane (Miaskowski et al., In press). Of these 609 survivors, 18% did not have any of these neurotoxicities and 14.1% had all three neurotoxicities. Compared to the no neurotoxicity group, survivors with all three neurotoxicities (i.e., CIN, hearing loss, and tinnitus) were older, less likely to be employed, had a higher body mass index (BMI), had a higher number of comorbid conditions, and reported a poorer functional status, In addition, these survivors reported higher levels of depressive symptoms, anxiety, fatigue, and sleep disturbance; higher levels of perceived stress; and poorer QOL outcomes. In terms of objective measures of sensation and function, the survivors with all three neurotoxicities had significant decrements in light touch, cold, pain, and vibratory sensations, as well as significant decreases in balance and physical function. Of note, no

between group differences were found in the types of CTX regimens received, the total dose of CTX administered, the length of time since the cancer diagnosis, and the number of metastatic sites.

No studies were found that attempted to determine if the number of neurotoxicities associated with CTX had differential effects on important survivor outcomes. Therefore, the purpose of this study was to evaluate for differences in demographic, clinical, and pain characteristics, as well as measures of sensation, balance, perceived stress, symptom burden, and QOL among adult cancer survivors who received neurotoxic CTX and who reported only CIN, CIN and hearing loss (CIN/HL), or CIN, hearing loss, and tinnitus (CIN/HL/TIN). We hypothesized that as the number of neurotoxicities increased, survivors would have worse outcomes.

METHODS

Survivors and Settings

The methods for this larger study are described in detail elsewhere (Miaskowski et al., 2017). In brief, survivors were recruited from throughout the San Francisco Bay area. Survivors with CIN met the following inclusion criteria: were ≥18 years of age; had received a platinum and/or a taxane compound; had completed their course of CTX ≥3 months prior to enrollment; had changes in sensation and/or pain in their feet and/or hands of ≥3 months duration following the completion of CTX; had a rating of ≥3 on a 0 to 10 numeric rating scale (NRS) for any one of the following sensations from the Pain Qualities Assessment Scale (i.e., numb, tender, shooting, sensitive, electrical, tingling radiating, throbbing, cramping, itchy, unpleasant) (Galer and Jensen, 1997); if they had pain associated with the CIN, had an average pain intensity score in their feet and/or hands of ≥3 on a 0 to 10 NRS; had a Karnofsky Performance Status (KPS) score of ≥50; and were able to read, write, and understand English (Watson and Evans, 1992).

Survivors with CIN were excluded if they had: peripheral vascular disease, vitamin B12 deficiency, thyroid dysfunction, HIV neuropathy, another painful condition that was difficult for them to distinguish from their CIN, a hereditary sensory or autonomic neuropathy (Rotthier et al., 2009), and/or a hereditary mitochondrial disorder (McFarland and Turnbull, 2009). A detailed patient history was obtained to evaluate for the presence of these conditions. Of the 1450 survivors who were screened, 754 were enrolled, and 609 completed the self-report questionnaires and the study visit. To answer the aims of this study, data from 371 survivors (i.e., 58.5% (n=217) with only CIN, 18.6% (n=69) with CIN/HL, 22.9% (n=85) with CIN/HL/TIN) were evaluated.

Study procedures

Research nurses screened and consented the survivors over the phone; sent and asked them to complete the self-report questionnaires prior to their study visit; and scheduled the in person assessment. At this assessment, written informed consent was obtained, questionnaires were reviewed for completeness, and objective measurements were done.

Study Measures

Demographic and Clinical Characteristics—Survivors provided information on demographic characteristics and completed the Karnofsky Performance Status (KPS) scale (Karnofsky, 1977; Karnofsky et al., 1948; Schnadig et al., 2008) and the Self-Administered Comorbidity Questionnaire (SCQ) (Brunner et al., 2008; Cieza et al., 2006).

Hearing Loss and Tinnitus—Two items from the Functional Assessment of Therapy/Gynecologic Oncology Group Neurotoxicity (FACT/GOG-Ntx) subscale were used to evaluate hearing loss (i.e., I have trouble hearing) and tinnitus (i.e., I get ringing or buzzing in my ears) (Huang et al., 2007). Each item was rated on a 0 (not at all) to 4 (very much) scale. Survivors with CIN who reported a score of 0 were classified in the only CIN group. Survivors with CIN who reported a score of >0 on these questions were classified into either the CIN/HL group or the CIN/HL/TIN group.

Pain Characteristics—Survivors completed the Brief Pain Inventory (Daut et al., 1983) and the Pain Qualities Assessment Scale (Victor et al., 2008).

Sensation—Light touch was evaluated using Semmes Weinstein monofilaments (Bell-Krotoski, 2002). Cold sensation was evaluated using the Tiptherm Rod (Papanas and Ziegler, 2011; Viswanathan et al., 2002). Pain sensation was evaluated using the Neurotip (Papanas and Ziegler, 2011). Vibration threshold was assessed using a vibrometer (Duke et al., 2007). For all of the measures of sensation, the upper and lower extremities on the dominant side were tested.

Balance—Self-report questions from the Chemotherapy-Induced Peripheral Neuropathy Assessment Tool (CIPNAT) were used to assess balance (Tofthagen et al., 2011). The objective measures of balance were the timed get up and go test (TUG) (Mathias et al., 1986) and the Fullerton Advanced Balance (FAB) test (Hernandez and Rose, 2008; Rose et al., 2006).

Symptom Burden—Survivors completed self-report questionnaires that evaluated trait and state anxiety (Spielberger et al., 1983), depressive symptoms (Radloff, 1977), diurnal variations in fatigue and energy (Lee et al., 1991), sleep disturbance (Lee, 1992), and changes in attentional function (Cimprich et al., 2011).

Perceived Stress—Stress associated with the cancer and its treatment was evaluated using the Impact of Event Scale – Revised (IES-R) (Weiss and Marmar, 1997). A global evaluation of perceived stress due to life circumstances was evaluated using the Perceived Stress Scale (PSS) (Cohen et al., 1983).

QOL—A generic evaluation of QOL was done using the Medical Outcomes Study-Short Form (SF12) (Ware et al., 1996). The disease specific measure of QOL was the QOL Scale-Patient Version (QOL-PV) (Ferrell, 1995; Ferrell et al., 1995; Padilla et al., 1990; Padilla et al., 1983).

Data Analysis

Data were analyzed using SPSS version 23 (SPSS, 2015). Descriptive statistics and frequency distributions were calculated for survivors' demographic and clinical characteristics. For the four measures of sensation (i.e., light touch, cold, pain, vibration), composite scores, over all of the sites that were tested on the dominant upper and lower extremities, were created. For light touch, cold, and pain, the number of sites with loss of each sensation were summed. For vibration, the mean score across the sites was calculated. Differences among the three neurotoxicity groups in phenotypic characteristics, balance, and levels of perceived stress, symptom burden, and QOL were evaluated using analyses of variance, Chi square analyses, and Kruskal-Wallis tests with Bonferroni corrected post hoc contrasts. A p-value of <0.05 was considered statistically significant.

RESULTS

Differences in Demographic and Clinical Characteristics

As shown in Table 1, compared to survivors with only CIN, survivors with CIN/HL/TIN were less likely to be female, more likely to report a lower annual household income, and less likely to report having child care responsibilities. In addition, compared to survivors with only CIN, survivors with CIN/HL were older. As shown in Figure 1, compared to survivors with CIN/HL, a higher percentage of survivors with all three neurotoxicities reported more severe hearing loss.

In terms of clinical characteristics (Table 2), compared to survivors with only CIN, survivors in the other two groups reported a higher number of comorbidities and had a higher comorbidity burden; had cancer longer; were more likely to report kidney disease; and were more likely to report that they had non-cancer related pain. In addition, compared to survivors with only CIN, survivors with CIN/HL/TIN had a lower KPS score; were more likely to report an injury to their arm; and were more likely to report back pain and depression. Compared to survivors with only CIN, survivors with CIN/HL were more likely to report osteoarthritis and more likely to report ulcer or stomach disease. In terms of CTX regimens, compared to the other two groups, a higher percentage of survivors with CIN/HL/TIN received a CTX regimen with only a platinum compound. Compared to survivors with all three neurotoxicities, a higher percentage of survivors with CIN/HL received a CTX regimen with both a platinum and a taxane compound. In addition, in terms of the specific platinum drugs, compared to the CIN/HL group, survivors with CIN/HL/TIN were more likely to have received cisplatin. Of note, no differences were found among the three groups in number of prior cancer treatments, cancer diagnoses, number of metastatic sites, and doses of platinum and/or taxane compounds received.

Differences in Pain Characteristics

As shown in Table 3, differences among the three neurotoxicity groups in various pain characteristics varied depending on whether the upper or lower extremity was evaluated. In terms of duration of CIN, for both the upper and lower extremities, compared to survivors with only CIN, survivors with CIN/HL/TIN had CIN for a longer duration. In terms of pain interference in the upper extremity, all of the items on this scale were rated higher by

survivors with CIN/HL/TIN compared to survivors with only CIN and the same relationships were found for balance, normal work, mood, relations with other people, and mean interference with function items for the lower extremity.

In terms of pain qualities for both the upper and lower extremities, significantly higher scores were reported by survivors with CIN/HL/TIN compared to survivors with only CIN. The qualities that were rated higher in the lower extremities were: sharp, hot, throbbing, and itchy. The qualities that were rated higher in the upper extremities were: unpleasant, sharp, aching, tender, and throbbing.

Differences in Sensation

Detailed information on all of the sensory testing is provided in Supplemental Tables 1 through 5. As summarized in Table 4, compared to survivors with only CIN, survivors in the other two groups had a higher number of lower extremity sites with loss of light touch and a higher number of upper extremity sites with loss of cold sensation. For both the upper and lower extremities, compared to the survivors with only CIN, vibration thresholds were significantly higher for both of the other groups.

Differences in Balance

Compared to the survivors with only CIN, a higher percentage of survivors in the other two groups reported trouble with balance. In addition, compared to survivors with only CIN, survivors with CIN/HL/TIN reported high severity scores for balance problems and worse TUG scores (see Table 4).

Differences in Symptom Burden

As shown in Table 4, compared to survivors with only CIN, survivors in the other two groups reported higher trait anxiety scores. In addition, compared to survivors with only CIN, survivors with CIN/HL/TIN reported higher state anxiety and depressive symptoms scores as well as lower morning energy and attentional function scores.

Differences in Perceived Stress

No differences were found among the three groups for any of the IES-R or PSS scores (Table 4).

Differences in QOL

For all of the SF-12 subscale scores, as well as for the physical component summary (PCS) and mental component summary (MCS) scores, compared to the survivors with only CIN, survivors with CIN/HL/TIN reported lower scores. Except for the spiritual well-being subscale, the same group differences were seen for the subscale and total scores on the QOLS-PV (see Table 4).

DISCUSSION

This study is the first to determine if the number of neurotoxicities (i.e., CIN, HL, tinnitus) reported by survivors who received platinum and taxane compounds has differential effects

on important survivor outcomes. Our pre-specified hypothesis was only partially supported. For the majority of the outcomes evaluated, survivors with all three neurotoxicities reported worse outcomes than survivors with only CIN. For some outcomes, significant differences were found between the survivors with only CIN and the other two neurotoxicity groups.

Compared to survivors with only CIN, survivors with CIN/HL were older. While the association between increased age and hearing loss is known (Bainbridge and Wallhagen, 2014), prospective studies are needed that evaluate for pre-existing hearing loss in older oncology patients prior to the receipt of neurotoxic CTX. Compared to the only CIN group, survivors with CIN/HL/TIN were more likely to be males; to have a lower annual household income; and less likely to report child care responsibilities. While no studies of cancer survivors were identified, in studies of the general population, while findings regarding gender differences in tinnitus are inconclusive (McCormack et al., 2016; Paulin et al., 2016; Wu et al., 2015), a higher percentage of males have hearing loss (Feder et al., 2015; Pinto et al., 2014a). In terms of income, in a large, cross-sectional survey of the general population, hearing loss was associated with economic hardship including both lower income and unemployment/underemployment (Emmett and Francis, 2015).

In terms of clinical characteristics, a number of findings warrant consideration. Compared to the only CIN group, survivors in the other two groups reported a higher number of comorbidities, a higher comorbidity profile, and were more likely to report the occurrence of chronic non-cancer pain (CNCP). These findings are consistent with cross-sectional studies of the general population that found that individuals with hearing loss and/or tinnitus reported higher levels of comorbidity and worse functional outcomes (Holgers et al., 2000; Hsu et al., 2016; Pattyn et al., 2016; Tseng et al., 2016). The specific comorbid conditions that warrant additional investigation in cancer survivors with CIN include: osteoarthritis, back pain, depression, and kidney disease. Given that over 50% of these survivors reported CNCP, prospective studies are needed that determine if a pre-existing CNCP condition is a risk factor for the development of CIN.

While findings from previous studies suggest that ototoxicity occurs in a dose dependent manner (Landier, 2016), consistent with our findings for the total sample (Miaskowski et al., 2017), no differences were found among the three groups in the total doses of the platinum and/or taxane compounds administered (Table 2). However, differences were found among the three survivor groups in the type of CTX regimen received. Compared to the other two groups, for survivors who had CIN/HL/TIN, a higher percentage of them had received only a platinum containing regimen as well as cisplatin specifically. In addition, compared to survivors with all three toxicities, for survivors who had CIN/HL, a higher percentage of them had received both a platinum and a taxane. Of note, no differences were found among the three neurotoxicity groups in the percentage of patients who received only a taxane. Taken together, these findings suggest that the mechanisms by which these CTX drugs and/or regimens produce neurotoxic effects may depend on a number of factors other than cumulative dose of the drug (e.g., phenotypic characteristics of the patient, genetic and epigenetic factors, methods and timing of drug administration).

In terms of differences in pain characteristics (Table 3), most of the differences occurred between the only CIN and CIN/HL/TIN groups. Across the three groups, for both the upper and lower extremities, these survivors were experiencing pain from CIN for over three years. The pain was of moderate to severe intensity (Paul et al., 2005) and persisted for most of the day. In addition, the pain was associated with mild to moderate levels of interference with function (Shi et al., 2017).

While the PQAS was used to evaluate the qualities of pain associated with a number of neuropathic pain conditions (Galer and Jensen, 1997; Gammaitoni et al., 2004; Jensen et al., 2005; Jensen et al., 2006), this study is the first to evaluate for differences in pain qualities in survivors with CIN. For all three neurotoxicity groups, as well as for both the upper and lower extremities, numbness, unpleasant, and tingling were the qualities with the highest severity scores.

For the objective measures of sensation, for both the upper and lower extremities, compared to survivors with only CIN, survivors with CIN/HL/TIN reported significant decrements in light touch, cold, and vibration. One potential explanation for this finding is that these survivors had CIN for a significantly longer duration.

Recent evidence suggests that balance problems and falls are significant problems for survivors with CIN (Gewandter et al., 2013). In our study, compared to the only CIN group, a higher percentage of survivors in the other two groups reported problems with balance. In addition, compared to the only CIN group, survivors with CIN/HL/TIN reported more severe balance problems. These findings suggest that additional studies are warranted to determine the relative contribution of changes in sensory and vestibular function to the balance problems associated with CIN.

As shown in Table 3, in terms of symptom burden, all three groups of survivors reported moderate levels of evening fatigue and sleep disturbance, as well as decrements in morning and evening energy. Of note, compared to survivors with only CIN, survivors with CIN/HL/TIN reported higher anxiety and depression scores, as well as lower attentional function scores. These findings are consistent with studies in the general population that found associations with hearing loss and/or tinnitus and anxiety (Pinto et al., 2014b), depression (Al-Swiahb et al., 2016; Davis et al., 2016; Huang et al., 2010), and decrements in cognitive function (Peelle and Wingfield, 2016; Tegg-Quinn et al., 2016; Wongrakpanich et al., 2016). While the relative contribution of CIN versus hearing loss versus tinnitus to the symptom burden of these survivors warrants additional investigation, our findings suggest that clinicians need to assess for multiple symptoms and initiate appropriate interventions.

While previous research demonstrated positive associations between stress and pain (Thieme et al., 2015; Woda et al., 2016), as well as tinnitus (Vanneste and De Ridder, 2013; Ylikoski et al., 2017), our previous study was the first to demonstrate that compared to survivors without CIN, survivors with CIN/HL/TIN had higher IES-R and PSS scores (Miaskowski et al., In press). In the current study, no differences were found among the three survivor groups on either stress measure. The PSS is a widely used measure that evaluates non-specific stress that exceeds a person’s coping abilities (Cohen et al., 1983). The PSS scores

in our study are slightly higher than those reported by breast cancer survivors (i.e., 11.6 (±7.9)) (Xiao et al., 2017). The IES-R was used in this study to measure the survivors response to their cancer and its treatment (Weiss and Marmar, 1997). None of the survivor groups exceeded the clinically meaningful IES-R cutoff score of ≥33.

While we hypothesized that differences would be found among the three survivor groups in the generic and disease specific measures of QOL, significant decrements in QOL outcomes were found between the CIN/HL/TIN and only CIN groups. Of note, all of the between group differences found on Table 4 represent not only statistically significant but clinically meaningful (i.e., Cohen's d = 0.37 to 0.73) decrements in the physical, psychological, and social domains of QOL (Osoba, 1999; Sloan et al., 2006). It should be noted that across all three groups, the physical component summary (PCS) score for the SF-12 was below 50 which is the normative score for the general United States population (Ware et al., 1996). Future studies need to evaluate the relative contribution of each type of neurotoxicity to these significant decrements in QOL.

A number of limitations warrant consideration. Given that only survivors who received a platinum and/or a taxane regimen were recruited for this study, our findings may not generalize to other survivors who received other types of neurotoxic CTX. While hearing loss and tinnitus are common neurotoxicities in patients with head and neck cancer (Huang et al., 2016; Lastrucci et al., 2017; Malgonde et al., 2015; Theunissen et al., 2015), only four patients in this study had this diagnosis. Therefore, additional studies are needed with this important diagnostic group. In addition, a pretreatment assessment of hearing loss and tinnitus was not obtained for these survivors. Therefore, one cannot rule out the relative contribution of factors other than the neurotoxic effects of CTX (e.g., age-related changes, noise exposure) to these two symptoms. Future studies need to perform a detailed clinical assessment of pretreatment hearing loss and tinnitus as well as an audiometric evaluation. The use of more precise measures of balance may allow for the determination of the relative contributions of sensory and vestibular changes to the balance problems reported by cancer survivors.

Despite these limitations, our findings suggest that compared to survivors with only CIN, survivors with CIN/HL/TIN are at increased risk for the most severe symptom burden, significant problems associated with sensory loss and changes in balance, as well as significant decrements in all aspects of QOL. Additional research, with larger samples, is needed to evaluate the common and distinct mechanisms associated with these three neurotoxicities, as well as the relative contribution of each of these neurotoxicities to balance problems, risk for falls, and decrements in physical and cognitive function.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Hearing loss and tinnitus warrant assessment in survivors who received neurotoxic chemotherapy.
- Survivors with chemotherapy-induced neuropathy, hearing loss, and tinnitus report a higher symptom burden.
- Survivors with chemotherapy-induced neuropathy, hearing loss, and tinnitus report significant decrements in functional status and quality of life.

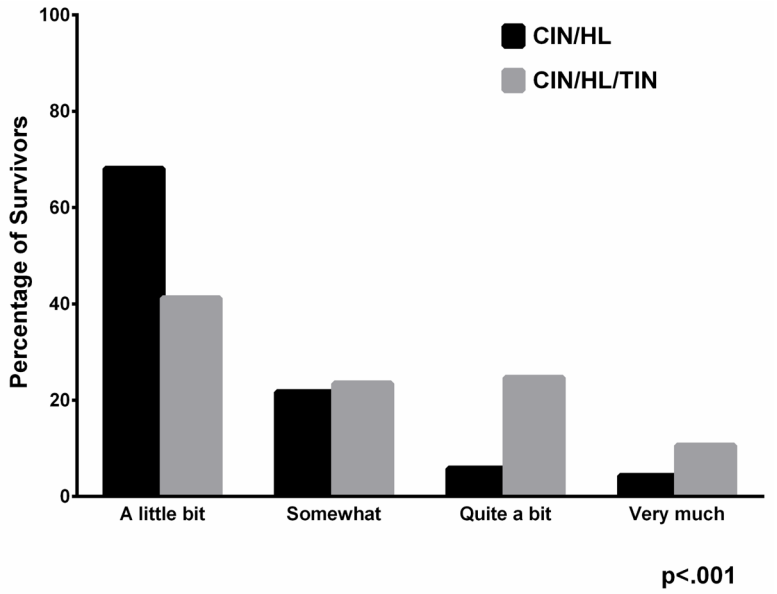

Figure 1.

Differences in the percentages of survivors with chemotherapy-induced neuropathy (CIN) and hearing loss versus the percentage of survivors with CIN, hearing loss, and tinnitus.

Table 1

Differences in Demographic Characteristics Among the Neurotoxicity Groups

Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	59.68 (10.39)	64.13 (9.16)	62.50 (9.78)	F=6.15, .002 0<1
Education (years)	16.54 (2.84)	16.64 (2.66)	15.92 (2.47)	F=1.85, .158
	% (n)	% (n)	% (n)	
Female	90.3 (196)	89.7 (61)	75.3 (64)	χ^2=12.64, .002 0>2
Married/partnered (% yes)	64.5 (138)	60.0 (39)	62.2 (51)	χ^2=0.47, .789
Lives alone (% yes)	25.8 (55)	32.8 (22)	28.6 (24)	χ^2=1.29, .525
Employed (% yes)	46.3 (100)	37.7 (26)	36.5 (31)	χ^2=3.20, .202
Ethnicity				
White	76.5 (166)	81.2 (56)	77.6 (66)	
Asian/Pacific Islander	8.3 (18)	7.2 (5)	4.7 (4)	χ^2=3.66, .722
Black	3.7 (8)	4.3 (3)	7.1 (6)	
Hispanic/Mixed/Other	11.5 (25)	7.2 (5)	10.6 (9)	
Annual household income				
<$30,000	17.0 (34)	20.3 (13)	33.3 (27)	
$30,000 – $69,999	19.0 (38)	23.4 (15)	23.5 (19)	KW, .011 0>2
$70,000 – $99,999	20.0 (40)	17.2 (11)	11.1 (9)	
>$100,000	44.0 (88)	39.1 (25)	32.1 (26)	
Child care responsibilities (% yes)	17.3 (37)	13.0 (9)	6.0 (5)	χ^2=6.53, .038 0>2
Adult care responsibilities (% yes)	4.0 (8)	6.1 (4)	0.0 (0)	χ^2=4.13, .127

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Abbreviations: CIN = chemotherapy-induced neuropathy, KW = Kruskal Wallis test, SD = standard deviation

Table 2

Differences in Clinical Characteristics Among the Neurotoxicity Groups

Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Karnofsky Performance Status score	84.35 (10.08)	83.43 (10.52)	80.73 (10.03)	F=3.76, .024 0>2
Body mass index (kg/m^2)	26.56 (5.59)	27.02 (6.28)	26.83 (5.62)	F=0.19, .826
Number of comorbidities	1.72 (1.33)	2.46 (1.70)	2.36 (1.54)	F=9.94, <.001 0<1 and 2
Self-Administered Comorbidity Questionnaire score	3.57 (2.90)	4.96 (4.01)	5.06 (3.66)	F=8.59, <.001 0<1 and 2
Alcohol Use Disorders Identification Test score	2.19 (2.25)	2.43 (2.12)	1.96 (1.95)	F=0.94, .393
Years since cancer diagnosis	4.09 (3.90)	5.98 (5.80)	5.60 (5.85)	F=5.64, .004 0<1 and 2
Number of prior cancer treatments	3.15 (0.97)	3.19 (1.00)	3.01 (0.99)	F=0.77, .464
Number of current cancer treatments	0.48 (0.63)	0.29 (0.49)	0.35 (0.55)	F=3.32, .037 No significant pairwise contrasts
Number of metastatic sites (out of 7)	0.74 (0.79)	0.87 (0.89)	0.69 (0.72)	F=0.99, .372
Number of metastatic sites without lymph node involvement	0.23 (0.60)	0.35 (0.68)	0.15 (0.48)	F=2.11, .123
	% (n)	% (n)	% (n)	
Smoker (ever)	35.2 (76)	42.6 (29)	41.7 (35)	χ^2=1.83, .401
Exercise on a regular basis (% yes)	87.6 (190)	88.9 (62)	77.6 (66)	χ^2=6.09, .048 No significant pairwise contrasts
Born prematurely (% yes)	7.1 (14)	6.3 (4)	6.3 (5)	χ^2=0.09, .956
Surgery on arms (% yes)	19.9 (43)	18.8 (13)	23.8 (20)	χ^2=0.72, .697

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Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Surgery on hands (% yes)	9.3 (20)	13.0 (9)	15.5 (13)	χ^2=2.55, .279
Surgery on legs (% yes)	26.5 (56)	30.9 (21)	23.8 (20)	χ^2=0.97, .616
Surgery on feet (% yes)	15.6 (33)	18.8 (13)	20.5 (17)	χ^2=1.15, .564
Injury to arms (% yes)	22.5 (48)	27.5 (19)	37.3 (31)	χ^2=6.69, .035 0<2
Injury to hands (% yes)	28.2 (59)	38.8 (26)	41.0 (34)	χ^2=5.54, .063
Injury to legs (% yes)	21.8 (46)	23.2 (16)	27.7 (23)	χ^2=1.16, .559
Injury to feet (% yes)	23.9 (50)	36.2 (25)	32.9 (27)	χ^2=4.97, .083
Comorbid conditions (% yes)				
Cancer	49.3 (107)	55.1 (38)	47.1 (40)	χ^2=1.04, .594
Osteoarthritis	24.0 (52)	43.5 (30)	36.5(31)	χ^2=11.30, .004 0<1
Back pain	27.6 (60)	39.1 (27)	47.1 (40)	χ^2=11.12, .004 0<2
Depression	18.9 (41)	26.1 (18)	32.9 (28)	χ^2=7.04, .030 0<2
High blood pressure	24.4 (53)	30.4 (21)	29.4 (25)	χ^2=1.39, .500
Heart disease	7.4 (16)	8.7 (6)	7.1 (6)	χ^2=0.17, .919
Diabetes	6.9 (15)	5.8 (4)	3.5 (3)	χ^2=1.26, .534
Lung disease	2.8 (6)	5.8 (4)	7.1 (6)	χ^2=3.18, .204
Anemia or blood disease	5.5 (12)	8.7 (6)	2.4 (2)	χ^2=3.02, .220
Ulcer or stomach disease	1.4 (3)	8.7 (6)	5.9 (5)	χ^2=9.06, .011 0<1
Kidney disease	0.0 (0)	4.3 (3)	8.2 (7)	χ^2=16.68, <.001 0< 1 and 2
Liver disease	2.3 (5)	4.3 (3)	3.5 (3)	χ^2=0.88, .643

Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Rheumatoid arthritis	1.8 (4)	1.4 (1)	5.9 (5)	χ^2=4.30, .116
Pain not related to cancer	50.9 (110)	71.0 (49)	69.0 (58)	χ^2=13.42, <.001 0<1 and 2
Type of cancer				
Breast	59.4 (129)	49.3 (34)	48.2 (41)	
Colon	10.1 (22)	7.2 (5)	10.6 (9)	
Lung	1.8 (4)	1.4 (1)	1.2 (1)	χ^2=15.16, .056
Ovarian	9.7 (21)	18.8 (13)	5.9 (5)	
Other	18.9 (41)	23.2 (16)	34.1 (29)	
Any metastatic disease (% yes)	59.5 (128)	63.2 (43)	59.8 (49)	χ^2=0.31, .858
Chemotherapy regimen				χ^2=16.73, .002
Only a platinum compound	18.4 (40)	14.5 (10)	36.5 (31)	0 and 1<2
Only a taxane compound	49.8 (108)	44.9 (31)	42.4 (36)	NS
Both a platinum and a taxane compound	31.8 (69)	40.6 (28)	21.2 (18)	1>2
Platinum drugs				
Cisplatin	13.4 (29)	7.2 (5)	22.4 (19)	X^2=7.46, .024 1<2
Carboplatin	27.6 (60)	42.0 (29)	25.9 (22)	X^2=6.02, .049 No significant pairwise contrasts
Oxaliplatin	14.7 (32)	10.1 (7)	15.3 (13)	X^2=1.07, .586
	Mean (SD)	Mean (SD)	Mean (SD)	
Dose of platinum compound for patients who received only a platinum (mg/m^2)	694.67 (330.67)	681.03 (368.33)	633.00 (585.12)	F=0.16, .855
Dose of taxane compound for patients who received only a taxane (mg/m^2)	711.41 (294.62)	1088.51 (1573.83)	649.54 (290.01)	KW, .165

Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Dose of drugs for patients who received both a platinum and a taxane compound				
Platinum dose (mg/m^2)	1762.15 (808.40)	2105.47 (850.03)	1721.74 (517.23)	F=2.01, .139
Taxane dose (mg/m^2)	950.27 (50.15)	915.76 (407.94)	699.26 (345.82)	F=1.98, .143
Patients who had a dose reduction or delay due to neuropathy (% (n))	15.0 (31)	10.8 (7)	11.1 (9)	χ^2=1.20, .549

Abbreviations: CIN = chemotherapy-induced neuropathy, kg = kilograms, m^2 = meters squared, mg = milligrams, SD = standard deviation

Table 3

Differences in Pain Characteristics Among the Neurotoxicity Groups

Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Pain Characteristics – Lower Extremity				
Duration of CIN (years)	3.19 (3.24)	4.70 (5.01)	4.98 (5.27)	F=7.00, .001 0<1 and 2
Pain now	3.52 (2.21)	3.42 (1.99)	3.72 (2.43)	F=0.35, .703
Average pain	3.91 (2.16)	3.97 (1.70)	3.97 (2.19)	F=0.03, .966
Worst pain	5.81 (2.56)	6.32 (2.23)	6.22 (2.71)	F=1.37, .256
Days per week in pain	3.49 (3.03)	3.26 (3.01)	4.56 (2.91)	F=4.34, .014 0 and 1<2
Hours per day in pain	14.48 (9.54)	15.58 (8.89)	15.54 (9.35)	F=0.55, .580
Pain Characteristics – Upper Extremity				
Duration of CIN (years)	3.03 (3.24)	3.96 (4.32)	4.67 (5.22)	F=4.18, .016 0<2
Pain now	2.68 (1.96)	2.56 (2.17)	3.22 (2.26)	F=1.87, .156
Average pain	2.82 (1.94)	3.24 (2.31)	3.64 (2.24)	F=3.69, .026 0<2
Worst pain	4.33 (2.49)	5.04 (2.85)	5.09 (2.73)	F=2.59, .077
Days per week in pain	3.41 (3.03)	3.26 (3.17)	4.54 (2.81)	F=3.74, .025 0<2
Hours per day in pain	12.29 (9.83)	15.03 (9.61)	13.35 (9.99)	F=1.31, .272
Pain Interference Scale – Lower Extremity				
Balance	3.26 (3.04)	3.89 (3.08)	4.27 (3.14)	F=3.41, .034 0<2
Walking ability	3.17 (3.00)	3.80 (3.18)	3.81 (3.05)	F=1.83, .161
Enjoyment of life	2.63 (2.70)	3.11 (2.76)	3.40 (3.12)	F=2.36, .096
Normal work	2.35 (2.65)	3.08 (3.01)	3.31 (3.06)	F=3.97, .020 0<2
Sleep	2.54 (2.75)	2.85 (2.93)	3.37 (3.16)	F=2.38, .094
General activity	2.32 (2.50)	2.98 (3.06)	3.15 (2.67)	F=3.50, .031 No significant pairwise contrasts

Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Mood	2.10 (2.25)	2.62 (2.40)	3.05 (2.92)	F=4.60, .011 0<2
Relations with other people	1.29 (2.17)	1.71 (2.22)	2.03 (2.51)	F=3.27, .039 0<2
Sexual activity	0.77 (1.85)	1.09 (2.13)	1.49 (2.94)	F=2.79, .063
Mean interference score	2.30 (2.06)	2.78 (2.17)	3.13 (2.52)	F=4.46, .012 0<2
Pain Interference Scale – Upper Extremity				
Routine activities [+]	2.09 (2.46)	2.93 (2.88)	3.12 (2.96)	F=4.21, .016 0<2
Walking ability	0.17 (0.61)	0.53 (1.36)	0.97 (2.30)	F=8.12, <.001 0<2
Enjoyment of life	1.76 (2.39)	2.27 (3.06)	2.89 (2.99)	F=4.24, .015 0<2
Normal work	2.38 (2.52)	2.91 (3.19)	3.58 (2.81)	F=4.65, .010 0<2
Sleep	1.04 (1.77)	1.87 (2.41)	2.49 (3.18)	F=9.73, <.001 0<2
General activity	2.04 (2.45)	2.60 (3.01)	3.53 (2.82)	F=7.21, .001 0<2
Mood	1.61 (1.93)	1.80 (2.37)	2.89 (2.94)	F=7.24, .001 0 and 1<2
Relations with other people	0.55 (1.23)	0.96 (2.02)	1.22 (2.01)	F=4.25, .015 0<2
Sexual activity	0.38 (1.21)	0.73 (2.04)	1.56 (3.01)	F=7.82, .001 0<2
Mean interference score	1.36 (1.50)	1.88 (2.09)	2.49 (2.27)	F=9.11, <.001 0<2
Pain Qualities Assessment Scale Scores – Lower Extremity				
Numb	5.34 (2.99)	5.20 (2.84)	6.10 (3.16)	F=2.20, .113
Unpleasant	4.26 (2.39)	4.81 (2.47)	4.86 (2.64)	F=2.33, .099
Tingling	4.19 (3.00)	3.94 (2.83)	5.00 (3.01)	F=2.75, .065
Intense	3.08 (2.53)	3.23 (2.10)	3.68 (2.56)	F=1.58, .208
Dull	3.16 (2.80)	2.97 (2.52)	3.29 (2.74)	F=0.25, .781

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Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Cramping	2.67 (3.15)	2.76 (3.20)	3.42 (3.29)	F=1.61, .201
Electrical	2.37 (3.01)	2.35 (3.19)	2.99 (3.19)	F=1.19, .305
Shooting	2.25 (2.78)	2.79 (3.11)	2.79 (3.19)	F=1.40, .248
Sharp	1.95 (2.55)	2.54 (2.96)	2.91 (3.37)	F=3.56, .030 0<2
Aching	2.02 (2.58)	2.45 (2.94)	2.55 (2.87)	F=1.36, .258
Heavy	1.95 (2.62)	2.11 (2.87)	2.65 (3.06)	F=1.80, .166
Cold	1.85 (2.75)	2.05 (2.91)	2.51 (3.00)	F=1.45, .235
Radiating	1.87 (2.60)	2.23 (2.73)	2.25 (2.90)	F=0.77, .462
Hot	1.72 (2.52)	1.65 (2.37)	2.64 (3.12)	F=3.74, .025 0<2
Tender	1.79 (2.38)	2.15 (2.72)	2.09 (2.72)	F=0.74, .476
Sensitive skin	1.59 (2.06)	2.06 (2.31)	1.94 (2.75)	F=1.35, .260
Throbbing	1.52 (2.42)	1.56 (2.46)	2.56 (3.07)	F=4.87, .008 0<2
Itchy	0.77 (1.66)	0.95 (1.98)	1.56 (2.56)	F=4.62, .010 0<2
Intense – surface pain	3.06 (2.64)	3.20 (2.62)	3.58 (2.93)	F=1.04, .355
Intense – deep pain	2.85 (2.67)	3.61 (2.65)	3.95 (3.06)	F=5.18, .006 0<2
Pain Qualities Assessment Scale Scores – Upper Extremity				
Numb	3.67 (2.83)	4.23 (2.86)	4.18 (2.90)	F=1.13, .326
Unpleasant	3.30 (2.32)	4.07 (2.71)	4.22 (2.77)	F=3.91, .021 0<2
Tingling	3.07 (2.79)	2.67 (2.71)	3.64 (2.93)	F=1.67, .191
Intense	2.38 (2.15)	2.91 (2.35)	3.02 (2.56)	F=2.23, .110
Dull	2.35 (2.52)	2.41 (2.62)	2.44 (2.39)	F=0.03, .970
Cramping	1.59 (2.44)	1.50 (2.61)	2.40 (3.02)	F=2.54, .081
Electrical	1.58 (2.53)	1.81 (2.82)	2.30 (2.89)	F=1.69, .187
Shooting	1.48 (2.43)	1.33 (2.33)	2.08 (2.70)	F=1.67, .191

Characteristic	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Test, p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Sharp	1.13 (2.01)	1.27 (2.30)	2.08 (2.78)	F=4.08, .018 0<2
Aching	1.43 (2.24)	1.93 (2.72)	2.56 (2.90)	F=4.81, .009 0<2
Heavy	1.20 (2.20)	0.95 (2.01)	1.89 (2.68)	F=2.84, .060
Cold	1.24 (2.30)	1.20 (2.00)	2.03 (2.58)	F=2.90, .057
Radiating	1.03 (2.02)	1.34 (2.22)	1.57 (2.55)	F=1.52, .221
Hot	0.82 (1.83)	0.93 (1.88)	1.48 (2.39)	F=2.58, .077
Tender	1.34 (2.13)	1.64 (2.42)	2.27 (2.60)	F=3.80, .024 0<2
Sensitive skin	1.18 (2.01)	1.36 (2.28)	1.66 (2.31)	F=1.18, .310
Throbbing	0.97 (1.91)	1.27 (2.20)	1.85 (2.72)	F=3.85, .023 0<2
Itchy	0.57 (1.56)	1.18 (2.47)	0.98 (2.00)	F=2.47, .087
Intense – surface pain	2.77 (2.41)	3.05 (2.59)	3.29 (2.93)	F=0.99, .372
Intense – deep pain	2.08 (2.47)	2.52 (2.62)	3.35 (2.97)	F=5.43, .005 0<2

[+] Dressing, toileting, typing

Abbreviations: CIN = chemotherapy-induced neuropathy, SD = standard deviation

Table 4

Differences in Sensation Measures, Balance Measures, Symptom Severity Scores, Stress Measures, and Quality of Life Outcomes Among the Neurotoxicity Groups

Characteristic**	**Only CIN (0) 58.5% (n=217)**	**CIN and Hearing Loss (1) 18.6% (n=69)**	**CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)**	**Statistic; p-value**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
Sensation Measures[+]				
Light touch – upper extremity sites (out of 7)[a]	0.12 (0.57)	0.23 (0.71)	0.39 (1.41)	F=3.91, .021 0<2
Light touch – lower extremity sites (out of 9)[b]	1.84 (2.16)	2.74 (2.56)	2.63 (2.46)	F=5.95, .003 0<1 and 2
Cold – upper extremity sites out of 4[c]	0.69 (0.96)	1.07 (0.99)	1.01 (1.02)	F=5.90, .003 0<1 and 2
Cold – lower extremity sites out of 4[d]	2.08 (1.22)	2.57 (1.14)	2.44 (1.18)	F=5.57, .004 0<2
Pain – upper extremity sites (out of 7)[e]	0.99 (1.33)	1.38 (1.57)	1.40 (1.58)	F=3.57, .029 No significant pairwise contrasts
Pain – lower extremity sites (out of 9)[f]	3.20 (2.19)	3.64 (2.31)	3.79 (1.88)	F=2.75, .065
Vibration – upper extremity sites (volts)[g]	8.35 (4.00)	10.19 (6.62)	10.35 (4.25)	F=7.75, .001 0<1 and 2
Vibration – lower extremity sites (volts)[h]	25.07 (11.69)	29.41 (11.56)	30.26 (12.00)	F=8.34, .<.001 0<1 and 2
Balance Measures				
Trouble with balance (% yes (n))[i]	58.5 (127)	81.2 (56)	76.2 (64)	χ^2=16.44, <.001 0<1 and 2
Severity of balance trouble (0 to 10)[j]	4.42 (2.76)	4.72 (2.49)	5.61 (2.50)	F=4.30, .015 0<2
Frequency of balance trouble (0 to 10)[k]	4.16 (2.87)	4.73 (3.26)	5.13 (2.59)	F=2.50, .084
Distress from balance trouble (0 to 10)[l]	4.87 (2.90)	5.31 (2.88)	5.91 (3.01)	F=2.66, .072
Timed get up and go test (>13.5 seconds = higher risk for falls)	7.56 (2.22)	7.68 (1.97)	8.36 (3.41)	F=3.17, .043 0<2
Fullerton Advanced Balance test (≤25 is associated with a higher risk of falls)	33.98 (5.79)	32.16 (8.13)	32.20 (7.36)	F=3.20, .042 No significant pairwise contrasts
Symptom Severity Scores				

Characteristic**	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Statistic; p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Trait anxiety (STAI-T score ≥31.8)	33.65 (8.33)	37.76 (9.96)	38.49 (11.06)	F=10.63, <.001 0<1 and 2
State anxiety (STAI-S score ≥32.2)	31.26 (10.18)	34.39 (11.57)	35.53 (13.95)	F=5.07, .007 0<2
Depressive symptoms (CES-D score ≥16)	8.78 (7.49)	11.23 (9.90)	13.47 (11.27)	F=8.86, <.001 0<2
Morning fatigue (LFS score ≥3.2)	2.88 (2.13)	3.20 (2.28)	3.48 (2.39)	F=2.33, .099
Evening fatigue (LFS score ≥5.6)	5.40 (2.09)	5.20 (1.91)	5.39 (1.67)	F=0.26, .768
Morning energy (LFS score ≤6.2)	5.18 (2.17)	4.82 (2.01)	4.43 (2.42)	F=3.68, .026 0<2
Evening energy (LFS score ≤3.5)	3.57 (2.06)	3.41 (1.71)	3.42 (1.95)	F=0.28, .760
Sleep disturbance (GSDS score ≥43)	46.48 (20.20)	46.44 (22.84)	51.40 (19.95)	F=1.87, .156
Attentional function (AFI score <5 is low function, 5.0 to 7.5 is moderate function, >7.5 is high function)	7.00 (1.62)	6.46 (1.80)	6.16 (1.66)	F=8.76, <.001 0<2
Stress Measures				
IES-R Avoidance mean subscale score	0.70 (0.67)	0.72 (0.69)	0.68 (0.79)	F=0.08, .927
IES-R Intrusion mean subscale score	0.68 (0.66)	0.69 (0.63)	0.76 (0.85)	F=0.38, .682
IES-R Hyperarousal mean subscale score	0.46 (0.60)	0.52 (0.67)	0.66 (0.86)	F=2.48, .085
IES-R Total mean score	0.63 (0.57)	0.65 (0.59)	0.70 (0.79)	F=0.38, .685
IES-R Total score (≥33)	13.87 (12.46)	14.41 (13.00)	15.42 (17.45)	F=0.38, .685
Perceived Stress Scale score	17.02 (8.36)	19.33 (9.23)	19.36 (9.99)	F=3.04, .049 No significant pairwise contrasts
MOS - SF12 Scores				
Physical functioning	69.19 (32.62)	59.93 (34.86)	54.46 (35.81)	F=6.37, .002 0>2
Role physical	64.77 (28.44)	64.15 (28.56)	51.49 (30.58)	F=6.67, .001 0 and 1>2
Bodily pain	72.09 (26.92)	71.27 (26.56)	60.06 (31.64)	F=5.70, .004 0 and 1>2
General health	69.55 (24.02)	62.39 (24.78)	56.91 (23.45)	F=8.76, <.001 0>2

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Characteristic**	Only CIN (0) 58.5% (n=217)	CIN and Hearing Loss (1) 18.6% (n=69)	CIN and Hearing Loss and Tinnitus (2) 22.9% (n=85)	Statistic; p-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Vitality	52.76 (24.02)	47.06 (23.47)	40.77 (24.78)	F=7.77, <.001 0>2
Social functioning	82.33 (25.03)	76.84 (27.43)	68.98 (31.62)	F=7.39, .001 0>2
Role emotional	81.54 (21.53)	75.74 (28.64)	72.47 (28.10)	F=4.61, .011 0>2
Mental health	73.33 (17.70)	68.38 (18.89)	65.77 (22.39)	F=5.36, .005 0>2
Physical component summary score (≥50.0)	44.91 (11.08)	43.20 (9.96)	39.74 (11.17)	F=6.51, .002 0>2
Mental component summary score (≥50.0)	51.29 (8.90)	48.65 (9.61)	47.47 (10.69)	F=5.45, .005 0>2
Multidimensional Quality of Life (QOL) Scale – Cancer				
Physical well-being	7.67 (1.47)	7.33 (1.65)	6.78 (1.77)	F=9.70, <.001 0>2
Psychological well-being	5.74 (1.59)	5.22 (1.67)	5.23 (1.70)	F=4.43, .013 0>2
Social well-being	6.23 (2.12)	5.78 (2.05)	5.32 (2.22)	F=5.82, .003 0>2
Spiritual well-being	5.39 (2.18)	5.05 (2.03)	7.23 (2.26)	F=0.68, .507
Total QOL score	6.16 (1.35)	5.71 (1.36)	5.55 (1.53)	F=6.67, .001 0>2

*When available, the clinically meaningful cut-point score is provided in parentheses next to the characteristic.

+Changes in sensation are reported for the dominant extremity

[a]Upper extremity sites for light touch were: pad of thumb, thumb webspace, tip of index finger, tip of little finger, midway base of palm, one third up anterior arm, two thirds up anterior arm

[b]Lower extremity sites for light touch were: pad of great toe, pad of 3rd toe, pad of 5th toe, base of heel, metocarpophalangeal (MP) joint of great toe, MP joint of 3rd toe, MP joint of 5th toe, midway along tibia, patella

[c]Upper extremity sites for cold were: pad of index finger, pad of little finger, dorsal MP area of the hand, wrist

[d]Lower extremity sites for cold were: top of great toe at 1st MP joint, pad of great toe, dorsum of foot midpoint, medial malleolus

[e]Upper extremity sites for pain were: pad of thumb, thumb webspace, tip of index finger, tip of little finger, midway base of palm, one third up anterior arm, two thirds up anterior arm

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[f] Lower extremity sites for pain were: pad of great toe, pad of 3rd toe, pad of 5th toe, base of heel, metocarpophalangeal (MP) joint of great toe, MP joint of 3rd toe, MP joint of 5th toe, midway along tibia, patella

[g] Upper extremity sites for vibration were: dorsal interphalangeal (IP) joint of thumb, dorsal IP joint of index finger, ulnar prominence, lateral epicondyle

[h] Lower extremity sites for vibration were: dorsal IP joint of great toe, medial malleolus, patella

[i] Since your chemotherapy, have you had trouble with your balance?

[j] At its worst, how severe is the trouble with your balance (0 = not at all severe to 10 = extremely severe)?

[k] How often do you have trouble with your balance (0 = never to 10 = always)?

[l] At its worst, how distressing is the trouble with your balance (0 = not at all distressing to 10 = extremely distressing)?

Abbreviations: AFI = Attentional Function Index, CES-D = Center for Epidemiological Studies-Depression Scale, CIN = chemotherapy-induced neuropathy, LFS = Lee Fatigue Scale, GSDS = General Sleep Disturbance Scale, IES-R = Impact of Event Scale-Revised, MOS-SF-12 = Medical Outcomes Study-Short Form 12, QOL = quality of life, SD = standard deviation