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Neuropathic Symptoms, Physical Function, Symptoms and Quality of Life in Hospice Patients with Cancer

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Abstract

The purpose of this cross-sectional, descriptive study was to assess differences in neuropathic symptoms, physical and emotional functioning, and quality of life in cancer patients at the end of life compared to those without neuropathic symptoms. Neuropathic symptoms are defined as numbness and tingling in the hands and/or feet. A secondary analysis of data from two hospices in Central Florida was performed. Adults (n= 717) with a cancer diagnosis, an identified family caregiver, and were receiving hospice services, were eligible. The prevalence of numbness/tingling in the hands or feet was 40% in this sample of hospice patients with cancer. Participants with neuropathic symptoms of numbness/tingling had a significantly higher prevalence of pain (76.7% vs. 67.0%; p=.006), difficulty with urination (29.4% vs.20.3%; p=.007), shortness of breath (64.9% vs.54.1%; p=.005), dizziness/lightheadedness (46.0% vs.28.2%; p<.001), sweats (35.5% vs. 20.3%; p<.001), worrying (50.7% vs. 37.3%; p=.001), feeling irritable (38.5% vs. 28.7%; p=.008), feeling sad (48.2% vs. 37.8%; p=.008), and difficulty concentrating (46.2% vs. 32.5%; p<.001). They also reported significantly higher overall symptom intensity and symptom distress scores (p= <.001) and higher pain severity (p=.001) and distress (p=.002) decreased quality of life (p=.002) compared to those without numbness/tingling. Neuropathic symptoms are emotionally distressing at the end of life and associated higher symptom burden and diminished quality of life.

Keywords

supportive care; palliative care; symptom management

Introduction/Background

Cancer-related neuropathic symptoms result from damage to the peripheral sensory, motor, or autonomic nerves, and can be the result of both cancer treatments and accompanying co-

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Conflict of Interest

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morbid conditions [40]. Neuropathic symptoms consisting of pain, numbness and tingling, decreased proprioception, allodynia, dysesthesia, impaired gait and balance, as well as sexual dysfunction and poor bowel and bladder control have been reported [8, 18]. Diabetes, autoimmune disorders, Vitamin B12 deficiency, chemotherapy drugs, and specific malignant diagnoses are common reasons for neuropathy in cancer populations. Other cancer-related neuropathic syndromes including mononeuropathies, neuropathic pain from spinal cord or vertebral body involvement with radiculopathy, as well as pain stemming from immunosuppression related herpes zoster can also occur. While the presence of neuropathic symptoms has been previously characterized in cancer populations [2, 3, 17], the prevalence of neuropathic symptoms and their effect on physical functioning and quality of life (QOL) at the end of life has not been delineated.

Neuropathic symptoms negatively affect many aspects of quality of life including sleep, physical and role functioning, emotional well-being and enjoyment of life [33, 38]. Numerous studies have examined symptoms and quality of life in association with neuropathic symptoms. Many of these studies have focused on specific types of cancer, particularly ovarian [5, 10, 14], breast [2, 29, 32], and colorectal [24, 25, 34]. These studies were conducted either during cancer treatment or during the survivorship phase, but not in hospice patients. Studies including more diverse cancer populations in treatment or survivorship phases have also described the negative effects of neuropathic symptoms on physical and psychological outcomes such as pain, numbness and tingling in the extremities, depression, anxiety and poor sleep quality [13, 35, 37]. Given that none of the aforementioned studies were conducted in hospice settings, there is a gap in current knowledge related to the impact of neuropathic symptoms at the end of life.

A primary focus of hospice care is to control symptoms and improve quality of life. Understanding neuropathic symptoms at the end of life is an important step toward informing clinical practice, and guiding symptom management efforts. Despite the prevalence of neuropathic symptoms in the general cancer population, neuropathy symptoms remain under-recognized and under-treated in clinical settings [30]. However, the enhanced focus on a multidisciplinary approach to pain, symptom management and quality of life provided by hospice care may offer additional benefit to persons with neuropathic symptoms.

The purpose of this study was to describe differences in symptoms, physical functioning, and quality of life in cancer patients who report neuropathic symptoms at the end of life compared to those who do not report neuropathic symptoms. This information may provide insight into the needs of cancer patients at the end of life that clinicians can begin to address.

Methods

This descriptive, cross-sectional study is a secondary analysis of from 717 community dwelling cancer patients from two hospices located in west, central Florida. The primary aim of the original study was to determine the efficacy of providing the interdisciplinary team with systematic feedback from standardized assessment tools in improving hospice outcomes [21]. The results and primary methods are published elsewhere [21].

Setting and Sample

The sample was drawn from two private, non-profit, large hospices that offer comprehensive services provided by interdisciplinary teams that include nurses, physicians, social workers/counselors, clergy, and hospice care aides. Patients were identified from admissions data as those who had a cancer diagnosis, had an identified family caregiver, were receiving homecare, were adults (18+ years old), able to read and understand English, and able to pass mental status screening. Patients were excluded if they were confused, excessively debilitated, comatose or actively dying.

Instruments

The instruments used for this study included a revised version of the Memorial Symptom Assessment Scale [22, 27, 36], the Hospice Quality of Life Index-14 [19, 22], Palliative Performance Status[1], and the Katz Activities of Daily Living Index[15]. Demographic data included age, sex, race and ethnicity, marital status, cancer type, and time since diagnosis.

Memorial Symptom Assessment Scale

The Memorial Symptom Assessment Scale (MSAS) is a multidimensional assessment of frequently occurring cancer related symptoms[27]. The original MSAS assesses 33 unique symptoms including frequency, intensity, and distress levels within the previous week. For each symptom that is present, participants provide a severity, distress, and frequency score, ranging from 1–4 with lower scores indicating less severe, distressing or frequent symptoms. A revised MSAS containing 25 items, developed for hospice patients with cancer, was used in this study. Face validity was assessed by a group of hospice experts who reviewed the items and removed those that seemed least likely to be problematic for hospice patients. For this revised version, Internal consistency reliability coefficients between .78-.85 and correlations between MSAS distress scores and Hospice Quality of Life Index (HQLI) scores ($r = -.72$; $p<.001$) in cancer patients at the end of life provide evidence of reliability and validity in this population [20, 36].Total symptom severity and total distress scores range from 0–100. Higher scores correspond with higher symptom intensity or distress.

Hospice Quality of Life Index-14

The Hospice Quality of Life Index-14 (HQLI-14) is a shortened version of the previously used and validated HQLI [22]. The original version has 28 items with each item rated on a 0–10 point numeric rating scale[19]. The shortened version (HQLI-14) is designed for repeated clinical use with hospice patients. Each item is scored on a 0 to 10 scale with 10 being the most favorable response; item scores are added to obtain a total scale score. Total scores can range from 0 (worst quality of life) to 140 (best quality of life). Subscales for three QOL domains include psychophysiological well-being (six items), functional well-being (four items), and social/spiritual well-being (four items). Construct validity of the short form was evaluated by correlation with the original HQLI. The correlation between the two instrument total scale scores was very strong ($r=.94$), providing excellent evidence of the validity of the shortened HQLI. Reliability of the short form was estimated using Cronbach's alpha. Alpha for the total tool was strong ($r=.77$). For the subscales, the alphas

were as follows: psychophysiological well-being (r=.68), functional well-being (r=.72), and social/spiritual well-being (r=.82) [21].

Palliative Performance Scale

The Palliative Performance Scale (PPS) is used to assess the physical condition and functional status of persons receiving palliative care [1]. This instrument measures three broad areas: mobility, intake and level of consciousness in five categories (degree of ambulation; ability to do activities and extent of disease; ability to do self-care; food/fluid intake; and state of consciousness). The PPS is scored from 0–100% at 10% increments, similar to the more commonly used Karnofsky Performance Scale. Validity of this instrument was assessed comparing the PPS score with length of survival, demonstrating shorter survival time with lower PPS scores [21]. Higher scores indicate better functional status and independence in self-care. Reliability of the PPS was evaluated in the parent clinical trial. Inter-rater reliability between two raters was very strong (r=.95).

Katz Activities of Daily Living Index

A revised version of the Katz Activities of Daily Living Index (ADLI) assesses six activities of daily living bathing, dressing, toileting, transfer, continence, and feeding [15]. Independence in 6 key activities of daily living; bathing, dressing, eating, toileting, transfer, continence were evaluated[6] and a summative score was compiled with higher scores corresponding with decreased functional status and increased dependence on others for activities of daily living. Relationships between independence with activities of daily living and health related quality of life demonstrate validity for this approach [7].

Procedures

The project was approved by the administrators of the two involved hospices and by the University of South Florida Institutional Review. Eligible patient/caregiver dyads who were potential study subjects for the parent study were identified initially by hospice admission staff and referred to study staff, who contacted the caregivers to arrange visits. During this visit, the study was explained, consent of both patient and caregiver obtained, the mental status of the patient and caregiver were assessed, and the functional status of the patient was evaluated. Baseline data was collected at that visit from patients and caregivers who met eligibility criteria. Only patient data collected at baseline was included in this analysis.

Data Analysis

Participants with numbness/tingling in the hands or feet were compared with participants who denied numbness or tingling in the hands or feet, using a single item from the MSAS. Data were analyzed using SPSS 25. Demographic data are presented as frequencies, percentages, means, and standard deviations (Table 1). In univariate analysis, mean values of symptoms, function, and quality of life were compared between persons with numbness and tingling (n=279) and those without (n=418) by use of student t tests and Mann Whitney U tests. Similarly, chi-square tests were used to compare presence of symptoms between those

with numbness and tingling and those without. To account for multiple comparisons, a p level of p<.01 was used to define statistical significance for all analyses.

Results

The total sample consisted of 717 hospice patients with a cancer diagnosis. Forty percent of the sample (n=279) affirmed the presence of numbness/tingling in the hands and/or feet. There were 20 participants who did not complete the MSAS, who were excluded from analysis, resulting in a sample size of 697 for the univariate analysis. The demographic characteristics were similar between groups (Table 1) with no statistically significant differences identified upon analysis. Participants with neuropathic symptoms of numbness/tingling had higher prevalence of numerous physical, psychologic, and cognitive symptoms including pain (76.7% vs. 67.0%; p =.006), difficulty with urination (29.4% vs.20.3%; p =.007), shortness of breath (64.9% vs.54.1%; p =.005), dizziness/lightheadedness (46.0% vs. 28.2%; p<.001), sweats (35.5% vs. 20.3%; p<.001), worrying (50.7% vs. 37.3%; p =.001), feeling irritable (38.5% vs. 28.7%; p =.008), feeling sad (48.2% vs. 37.8%; p =.008), and difficulty concentrating (46.2% vs. 32.5%; p<.001) (Table 2).

Participants who reported numbness/tingling had lower quality of life scores (p =.002), significantly higher overall symptom severity (p<.001) and symptom distress scores (p<.001), and significantly higher pain severity (p=.001) and pain distress (p=.002) than those without neuropathic symptoms (Table 3). There were no significant differences in performance status according to PPS and Katz ADL scores.

Discussion

Our findings suggest that neuropathic symptoms are present and persistent in patients with cancer nearing the end of life, and may continue to negatively impact both physical and emotional well-being and quality of life. Participants with neuropathic symptoms had higher overall symptom severity, symptom distress, more pain, and lower quality of life than patients who did not report neuropathic symptoms. Although the etiology of neuropathic symptoms in our study sample is unknown, it is likely that many patients were experiencing peripheral neuropathy, due to its high prevalence in cancer survivors [2, 10, 35, 39]. Therefore, we have compared our findings mainly to those reported in papers focused on neuropathy.

The prevalence of neuropathic symptoms in this sample of 40% was congruent with previous studies demonstrating rates of neuropathy ranging from 36–58% in person undergoing cancer treatment as well as cancer survivors up to 12 years post-treatment [2, 10, 35, 39].

Increased pain, dizziness, difficulty concentrating, feeling sad, worried and irritable were more common in those with neuropathic symptoms, which is consistent with previous studies [10, 13, 16]. Other researchers have also demonstrated that neuropathic symptoms negatively impact emotional, physical and cognitive functioning, and impair quality of life in patients with cancer [3, 25, 35, 37]. For example, examination of the effects of neuropathy on psychological distress and sleep quality in patients receiving chemotherapy identified

significant correlations between neuropathy symptoms and depression, anxiety and poor sleep quality[13]. Neuropathy, pain, sleep disturbance, and psychologic distress have been previously described as a symptom cluster [26, 28]. Additional studies of neuropathic symptoms are needed in patients with advanced cancer at the end of life.

The findings of higher incidence of difficulty with urination, sweating, and shortness of breath in people with neuropathic symptoms were unexpected. It is possible that these symptoms were the result of autonomic neuropathy [8, 18]. There have been case reports of dyspnea in at least 3 patients receiving bortezomib [11], a highly neurotoxic monoclonal antibody, for treatment of amyloidosis. Dyspnea has been proposed as a potential sign of autonomic dysfunction in persons with COPD [23]. While it may be the case that autonomic symptoms are more common in people with neuropathic symptoms at the end of life, to our knowledge this has not been reported in the literature. Future studies should be done to further evaluate these findings.

In contrast to findings from studies of persons earlier in the cancer trajectory [2, 3, 9, 39], we found no significant differences in physical function among those with neuropathic symptoms at the end of life. The progressive nature of advanced cancer and the necessity for both hospice services and a caregiver, likely contributed to poor performance in both groups, beyond what would be expected in patients with neuropathy at earlier stages of malignancy.

Limitations

The primary limitation of this study is the use of a single item on the MSAS to assess neuropathic symptoms, which was due to the use of existing data in this secondary analysis. While numbness and tingling in the hands or feet are consistently reported to be the most common symptoms of peripheral neuropathy, [3, 33] measuring symptoms with a single dichotomous item poses limitations as reliability and validity of this approach have not been adequately evaluated [4]. Neuropathic symptoms can be the result of chemotherapy, and/or other neuropathy syndromes or the consequence of comorbidities, such as diabetes, or other inherited or acquired neuropathic syndromes.

Neuropathic symptoms can signify other health concerns in this population including spinal cord compression, radiculopathy, and herniated disks, which may also cause numbness and tingling in the hands and feet. Chemotherapy may be the cause of neuropathic symptoms in this sample of hospice patients with cancer, however we lacked access to data concerning the number of participants who received neurotoxic chemotherapy, and data regarding comorbidities such as diabetes, that could have caused neuropathic symptoms in this sample. The research team acknowledges the lack of data regarding the underlying etiology of neuropathic symptoms experienced as a limitation of these findings. Nevertheless, cancer patients present to hospice with a myriad of symptoms that must be managed to improve or maintain physical functioning and QOL, regardless of underlying etiology

Implications for practice and research

Both oncology and hospice healthcare professionals should be aware of the need for management of neuropathic symptoms at the end of life. While opioids are commonly used to alleviate neoplasm related pain, adjuvant medications, specifically for painful

neuropathies, may improve pain control and increase quality of life in cancer patients nearing the end of life. Neuropathic symptoms, may negatively impact emotional well-being, contributing to sadness, worry, irritability, and symptom distress, even at the end of life. Antidepressants, such as duloxetine, which have been shown to alleviate painful neuropathic symptoms, may be preferred because of the dual effects on both painful neuropathy and mood, and may also improve quality of life [12, 31]. When assessing performance and physical function, beyond evaluation of activities of daily living and performance status, incorporating evaluation of fine motor skills and postural stability and sensation, may identify specific deficits, especially when neuropathic symptoms are present. Interventions aimed at safety, physical rehabilitation, pain control, and improved cognition can be suggested as a way to improve quality of life in patients with advanced disease.

Conclusions

The findings from this study suggest that neuropathic symptoms are associated with diminished physical and emotional well-being in cancer patients at the end of life. Overall symptom burden including total symptom severity and distress was higher in persons with neuropathic symptoms. These findings support a need for enhanced clinical focus on treating neuropathic symptoms and addressing physical and psychological concerns. Future studies should seek to identify and test treatments that will reduce neuropathic symptoms in patients with advanced or end-stage disease so that they can have the best quality of life possible.

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Table 1.

Demographic information.

Variable		Total [a] (n=717)		Without PN (n=418)		With PN (n=279)	
		M	*SD*	*M*	*SD*	*M*	*SD*
Age (years)		72.7	12.1	73.3	12.4	71.8	11.9
Education (years)		12.7	2.9	12.7	2.9	12.8	3.1
Time since diagnosis (months)		26.8	48.2	24.8	44.4	28.3	47.6
		F	*%*	*F*	*%*	*F*	*%*
Gender	Male	400	55.8	225	53.8	169	60.6
	Female	311	43.4	192	45.9	110	39.4
	Missing	6	0.8	1	0.2		
Race/Ethnicity	White/Caucasian	690	96.2	402	96.2	273	97.8
	African American	11	1.5	8	1.9	3	1.1
	Hispanic	7	1.0	7	1.7	0.0	0.0
	Asian	1	0.1	0	0.0	1	0.4
	Other	3	0.4	1	0.2	2	0.7
	Missing	5	0.7				
Marital status	Single, divorced,separated, or widowed	258	35.9	159	38.0	95	34.0
	Married	451	62.9	256	61.2	184	65.9
	Missing	8	1.1	3	0.7		
Cancer Type	Lung	241	33.6	138	33.0	100	35.8
	Pancreas	65	9.1	47	11.2	15	5.4
	Colon	51	7.1	30	7.2	21	7.5
	Prostate	42	5.9	23	5.5	16	5.7
	Breast	40	5.6	18	4.3	19	6.8
	Liver	28	3.9	14	3.3	14	5.0
	Ovarian	25	3.5	15	3.6	10	3.6
	Head & Neck	24	3.3	13	3.1	11	3.9
	Lymphoma	21	2.9	13	3.1	6	2.2
	Kidney	19	2.6	15	3.6	4	1.4
	Bladder	16	2.2	10	2.4	6	2.2
	Esophagus	15	2.1	10	2.4	5	1.8
	Brain/Nervous system	13	1.8	5	1.2	7	2.5
	Leukemia/MDS	13	1.8	11	2.6	2	0.7
	Stomach	11	1.5	4	1.0	7	2.5
	Multiple Myeloma	8	1.1	6	1.4	2	0.7
	Bone	8	1.1	2	0.5	6	2.2
	Uterine	7	1.0	5	1.2	2	0.7
	Skin	6	0.8	3	0.7	3	1.1
	Cervical	5	0.7	4	1.0	1	0.4
	Sarcoma	5	0.7	2	0.5	3	1.1
	Other	45	6.3	21	5.0	18	6.4

Variable		Total [a] (n=717)		Without PN (n=418)		With PN (n=279)	
		M	*SD*	*M*	*SD*	*M*	*SD*
	Missing	9	1.3				

[a] includes all individuals enrolled in the study, 20 of whom did not provide MSAS data and weren't included in the analysis

Table 2.

Differences in prevalence of symptoms between persons with numbness/tingling and those without

	No numbness/ tingling		Numbness/tingling			
Symptom	***N***	***%***	***N***	***%***	X^2	***P***
Problems with urination	85	20.3	82	29.4	7.5	.007*
Shortness of breath	226	54.1	181	64.9	8.0	.005*
Feeling Sad	158	37.8	134	48.2	7.4	.008*
Worrying	156	37.3	141	50.7	12.3	.001*
Dizziness/lightheadedness	118	28.2	128	46.0	23.2	<.001*
Feeling Irritable	120	28.7	107	38.5	7.3	.008*
Sweats	85	20.3	99	35.5	19.8	<.001*
Difficulty Concentrating	136	32.5	129	46.2	13.3	<.001*
Pain	280	67.0	214	76.7	7.7	.006*
Lack of Energy	352	84.2	250	89.5	4.1	.043
Cough	141	50.5	138	49.5	3.2	.075
Feeling nervous	126	30.1	92	33.0	0.6	.453
Dry mouth	275	65.8	206	73.8	5.1	.030
Nausea	117	28.0	101	36.2	5.2	.024
Vomiting	62	14.8	52	18.6	1.8	.210
Diarrhea	62	14.8	47	16.8	0.5	.523
Feeling drowsy	239	57.2	171	61.3	1.2	.307
Difficulty sleeping	171	40.9	124	44.4	0.9	.390
Feeling bloated	108	25.8	87	31.2	2.4	.123
Problems with sex	49	11.7	47	13.8	3.7	.057
Itching	90	21.5	72	25.8	1.7	.201
Lack of appetite	252	60.3	167	60.1	0.1	.937
Difficulty swallowing	103	24.6	88	31.5	4.0	.047
Constipation	174	41.6	136	48.7	3.4	.074

*=statistically significant p value less than 0.1

Table 3.

Differences between hospice patients with numbness/tingling and those without.

Variable	Group	Mean/SD	t	Z	p
MSAS Distress subscale	without	18.0±11.7		−7.3	<.001*
	with	25.7±15.5			
MSAS Severity subscale	without	18.9±10.9		−8.0	<.001*
	with	26.4±13.6			
ADL score	without	2.3±2.1		−1.7	.091
	with	2.7±2.3			
PPS	without	57.5±10.9	0.7		0.50
	with	56.9±10.7			
HQLI-14	without	103.8±17.5	3.1		.002*
	with	99.7±17.0			
Pain severity	without	1.5±1.3	−3.2		.001*
	with	1.8±1.3			
Pain distress	without	1.5±1.4	−3.1		
	with	1.8±1.5			.002*

*=statistically significant p value less than 0.1