

This material is protected by U.S. copyright law. Unauthorized reproduction is prohibited. To purchase quantity reprints, please e-mail reprints@ons.org or to request permission to reproduce multiple copies, please e-mail pubpermissions@ons.org.

# Peripheral Neuropathy in Patients With Gynecologic Cancer Receiving Chemotherapy: Patient Reports and Provider Assessments

DeLeslie W. Kiser, FNP, AOCNP®, Tara B. Greer, RN, MSN, ANP,  
Margaret C. Wilmoth, PhD, MSS, RN, FAAN, Jacek Dmochowski, PhD,  
and R. Wendel Naumann, MD

**G**ynecologic cancers as a group comprise about 15% of all cancers in women, with 6% ovarian, 6% endometrial, 3% uterine, and less than 1% cervical (National Cancer Institute [NCI], 2007). Chemotherapy regimens for gynecologic cancers typically combine platinum and taxanes after surgical debulking or radiation therapy. Although these drug combinations have increased survival significantly, a high incidence of peripheral neuropathy is associated with these chemotherapy regimens (Pan & Kao, 2007). This particular side effect often is seen as “less important” than life-threatening side effects of chemotherapy, and many times it goes unreported by patients because of its insidious onset (Wickham, 2007). Often patients will only report peripheral neuropathy when it begins to limit their function or has become very painful (Bruner et al., 2007). As survival rates of patients with gynecologic malignancies improve, the immediate and long-term effects of neuropathy on patients are becoming a topic of interest in research.

## Purpose and Objectives

The purpose of this study was to evaluate the incidence and severity of neuropathy in the clinical setting using a broad range of patient- and treatment-related factors as potential influencing factors. All patients with gynecologic cancer receiving chemotherapy in this clinic were included in the study, and multiple variables of hypothesized significance were recorded in a database. Analysis focused on any variables that increased or decreased patients' reporting of neuropathy symptoms. The primary study objective was to identify factors related to patients' experiences of this treatment side effect. Secondary objectives were to analyze the frequency of provider notations of neuropathy in the chart and to

**Purpose/Objectives:** To analyze the incidence of chemotherapy-induced neuropathy in a set of patients with gynecologic cancer who were treated with known neurotoxic agents, to identify correlative factors related to patients' experience of neuropathy, and to analyze providers' assessment and treatment of neuropathy.

**Design:** Observational descriptive study of patient-reported neuropathy using a retrospective chart analysis.

**Setting:** A hospital-based outpatient infusion center in the southeastern United States.

**Sample:** A convenience sample of 171 patients with gynecologic cancer for a total of 302 chemotherapy treatments.

**Methods:** A mixed model and compound symmetry covariance matrix was used to adjust for correlations between neuropathy treatment scores and patients who completed more than one chemotherapy cycle. Backward elimination method was used to determine the final model.

**Main Research Variables:** Functional Assessment of Cancer Treatment/Gynecologic Oncology Group-Neuropathy Treatment scores, patients' demographic information, past medical history, and chemotherapy history.

**Findings:** Patients who were physically shorter and heavier than the average population had the highest rating of neuropathy. Patients who were treated with nontaxane and platinum therapies had less neuropathy than patients who were treated with first-line taxanes and platinums. Neuropathy was noted by providers early in the course of treatment, and providers' grading was consistent with the patients' scoring.

**Conclusions:** First-line treatments for gynecologic malignancies resulted in the highest neuropathy scores; however, patients who had received previous treatment with taxane and platinum therapies had lower neuropathy scores than patients currently receiving taxanes and platinums, suggesting that neuropathy improved after completion of first-line therapy and that second-line therapies were not necessarily correlative with worsening scores.

**Implications for Nursing:** Nurses must educate patients about symptoms of neuropathy and the need to report symptoms. Nurses must recognize patients at highest risk for neuropathy and advocate use of validated assessment tools.

determine whether providers used the NCI Common Terminology Criteria (CTC) scoring of neuropathy or merely implied a subjective scoring of the severity of a patient's neuropathy.

## Literature Review

### Defining Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is hypothesized to occur when neuronal fibers are damaged by toxic agents and are unable to meet their metabolic needs of axonal regeneration. This causes a disruption of myelination, which results in the interruption of axonal transport of nervous impulses (Visovsky, 2005). Peripheral neuropathy can be categorized as causing motor deficits, sensory deficits, or mixed deficits. Motor neuropathy ranges from transient asymptomatic muscle weakness to weakness that interferes with functioning to total paralysis. Sensory neuropathy is characterized by paresthesia, decreased deep tendon reflexes, and in extreme cases may result in a total loss of sensation (Visovsky, 2005). Most chemotherapy-induced neuropathy is sensory in nature (Argyriou et al., 2005), although rare cases of motor neuropathy leading to complete paralysis have been reported (Martino, Miller, & Grendys, 2005).

### Measurement of Neuropathy

No scientific consensus currently exists for grading peripheral neuropathy resulting from chemotherapy or on the optimal scale used for self-reporting of neuropathy by patients. A number of self-reporting and provider-assessment scales are used, and most combine subjective patient rating of sensory and motor neuropathy. The largest study to date that has included an assessment of CIPN is the Scottish Randomized Trial in Ovarian Cancer (SCOTROC) (Vasey et al., 2004). In this trial, neuropathy was graded by a neuropathy assessment consisting of 12 questions and five neurologic tests to create a neuropathy score in addition to the CTC scoring of neuropathy grade during treatment (Vasey et al., 2004). Several other studies have used the CTC scoring, including the Multicenter Italian Trial in Ovarian Cancer (Pignata et al., 2006) and a retrospective study in Japan (Fujiwara et al., 2005).

Two studies (Argyriou et al., 2005; Pan & Koa, 2007) looked at objective measurement of neuropathy through the use of electrophysical measurement and nerve conduction studies. Pan and Koa (2007) found a difference between "objective" neuropathy, as measured by changes in electrophysical nerve conduction, and reports by providers that the neuropathy was "tolerated well by the patient." Missing from the study were patient self-reports of neuropathy. Argyriou et al. (2005) found contradictory data; despite improvement of neu-

ropathy according to electrophysical measurements, patients' symptoms did not improve. Therefore, it appears that electrophysical scores do not correlate with patients' subjective symptoms and, therefore, have little value in assessing the effect of peripheral neuropathy on patients. Consensus is needed for a standardized assessment and grading of neuropathy to facilitate future collaboration of research efforts and to improve quality of patient care.

### Incidence of Neuropathy

Reports of the incidence of peripheral neuropathy vary widely in the literature, likely because of the use of varied chemotherapy regimens as well as different measurement tools. Although, in theory, the rate of residual neuropathy decreases after treatment, only one long-term study with a median follow-up of 28 months was found (Pignata et al., 2006). In it, 11% of patients experienced residual neuropathy. In all of the reviewed studies, sensory neuropathy was the most common type of neuropathy represented, with rare occurrences of motor neuropathy. In the SCOTROC trial, the rates of sensory neuropathy were 8% in the docetaxel and carboplatin arm and 30% in the paclitaxel and carboplatin arm (Vasey et al., 2004). Bruner et al. (2007) reported that in the chemotherapy arm of a clinical trial treating endometrial cancer with doxorubicin and cisplatin, 41% of patients experienced sensory neuropathy at the end of treatment, 61% at the three-month follow-up, and 56% at six months after completion of chemotherapy. In the Multicenter Italian Trial in Ovarian Cancer (Pignata et al., 2006), 56% of patients experienced neurologic toxicity during chemotherapy and the rate of any grade of residual neuropathy was 23% at a median follow-up of 48 months.

Intraperitoneal (IP) is another method of delivering chemotherapy that has been used more frequently after studies showed significant survival benefits. However, little data exist on the relationship of IP chemotherapy and the rate of neuropathy. Fujiwara et al. (2005) reported on a retrospective study analyzing the toxicities of IV paclitaxel (dose = 175 mg/m<sup>2</sup>) followed by IP carboplatin (dose = area under the curve [AUC] 5–7.5). As the dose of IP carboplatin increased, the incidence of sensory neuropathy also increased. At the recommended dose of AUC 6.5, 44% of patients had a loss of deep tendon reflexes or paresthesia (grade 2 neurotoxicity) and 11% had neuropathy that interfered with function (grade 3 neurotoxicity). Therefore, more research should be conducted on the effect of IP carboplatin and rates of persistent effects of neuropathy and their effect on patients' ability to function. Although incidence rates vary greatly according to different regimens and dose intensities, what is clear is that neuropathy is a problem for patients with gynecologic cancer receiving chemotherapy.

## Neuropathy and Preexisting Conditions

A paucity of data exist about patients with preexisting conditions that put them at high risk for neurologic toxicity when they are treated with platinum and taxane chemotherapies. The few known risk factors are diabetes mellitus, history of alcohol abuse, or preexisting neuropathy (Wickham, 2007). In all of the large trials mentioned in this article, patients with preexisting diabetes or neurologic deficits were excluded from data collection. One case does report on a woman aged 60 years with Charcot-Marie tooth disease who was diagnosed with ovarian cancer and who developed severe neuropathy with paclitaxel and carboplatin. The patient was changed to docetaxel and carboplatin and was able to complete six cycles without further exacerbation of her neuropathy (Martino et al., 2005). Although this is a single case study, it suggests that docetaxel may be preferred to paclitaxel in patients with preexisting neuropathy. Additional research is needed to find appropriate treatment for patients with preexisting neuropathy.

The primary purpose of this study was to describe the incidence and severity of peripheral neuropathy in a diverse population of patients with gynecologic cancer receiving different types of neuropathy-inducing chemotherapy. All eligible patients were included in the study to examine the impact of various comorbid conditions on the experience of neuropathy. Analysis focused on the severity of patient-reported neuropathy comparing different regimens. A secondary aim of the study was to learn whether provider scoring of neuropathy correlated with patient reports.

## Conceptual Framework

The Theory of Unpleasant Symptoms (Lenz, Pugh, Miligan, Gift, & Suppe, 1997) served as the conceptual framework for the analysis of peripheral neuropathy. Symptoms have characteristics (intensity, duration, distress, quality), influencing factors (physical, psychological, situational), and consequences (functional and cognitive). The correlation between the conceptual framework and data collection can be seen in Table 1. The Theory of Unpleasant Symptoms provides a comprehensive structure to assess the global effect of peripheral neuropathy on patients receiving chemotherapy.

## Methods

### Design

This study was an observational descriptive analysis of patient-reported peripheral neuropathy. After the institutional review board of the affiliated hospital approved the study, charts of all patients with gynecologic cancer who had received outpatient chemotherapy from June 2006–December 2007 were reviewed. Beginning

**Table 1. Integration of Theoretical Framework and Neuropathy Variables**

Theory of Unpleasant Symptoms Category	Symptoms as Measured by the NCI CTC Scale [v.2.0]
<b>Symptom characteristics</b>	
Distress	Scale weight (0–4)
Duration	During the past seven days
Intensity	Descriptive terms: “not at all,” “a little bit,” “somewhat,” “quite a bit,” “very much”
Quality	Numbness, tingling, discomfort, joint pain, cramps, weak, ringing, buzzing
<b>Influencing factors</b>	
Physical	Age, race, gender, body surface area, diabetes, preexisting neuropathy, neurotoxic medications, preexisting chemotherapy-induced neuropathy
Psychological	History of depression
Situational	Alcohol use
<b>Consequences</b>	
Functional	Trouble hearing, buttoning buttons, feeling small objects, or walking

NCI CTC—National Cancer Institute Common Terminology Criteria

in June 2006, the cancer center had begun to ask patients to complete the Functional Assessment of Cancer Treatment/Gynecologic Oncology Group-Neuropathy Treatment (FACT/GOG-NTX) scoring tool (Calhoun et al., 2000) at each chemotherapy infusion. This tool was filed in patients' charts to give providers a better understanding of patients' neuropathy; 171 patients completed at least one scoring tool and all were included in this study.

Two nurses and one nurse practitioner retrospectively reviewed patients' charts, and all study variables were entered into an electronic database. Every cycle of chemotherapy that a patient received during the study time period was recorded. Each rating of neuropathy according to the FACT/GOG-NTX tool was dated and entered with the corresponding cycle information. If the patient did not complete a neuropathy tool, the chemotherapy cycle information was recorded and the neuropathy tool data was left blank. A complete list of main research variables can be found in Figure 1. To score provider determination of neuropathy, the following rubric was used: An explicit statement of a CTC neuropathy grade in the chart was recorded as *graded neuropathy*. If the provider assessed neuropathy but the grade was implied (e.g., the provider noted “tingling and numbness in the fingertips that is intermittent in nature and not interfering with function”), it was recorded as an *implied neuropathy* score. If neuropathy was not noted at all by the provider, it was recorded as *no assessment*.



## Setting

The setting was a hospital-based gynecologic oncology clinic in the southeastern United States that offers surgical debulking, chemotherapy, and radiation treatment. The providers in the clinic include four gynecologic oncologists and one advanced oncology certified nurse practitioner. The most common type of cancer treated with chemotherapy in the practice is ovarian cancer, which also was the most common diagnosis in the study. Typical first-line treatment for ovarian cancer is surgical debulking followed by a course of adjuvant chemotherapy. Paclitaxel with carboplatin is a first-line treatment for ovarian cancer and commonly given in six cycles 3–4 weeks apart. Typical treatment for cervical cancer is a combination of radiation and platin-based chemotherapy. Treatment for endometrial cancer often is a platin-based chemotherapy depending on pathology. If a patient's cancer progresses after first-line therapy, a number of other regimens can be offered.

## Sample

The sample consisted of 171 patients with gynecologic cancer receiving chemotherapy. Inclusion criteria were female gender with a diagnosed gynecologic malignancy requiring chemotherapy for treatment.

### Background Information

- Age
- Alcohol use
- Body surface area
- Chemotherapy regimen
- Current use of antidepressants
- Date of diagnosis
- History of depression
- History of diabetes
- History of preexisting chemotherapy-induced neuropathy
- History of preexisting neuropathy
- Number of cycles of chemotherapy received in current regimen
- Type of cancer
- Use of neurotoxic medications

### Information Collected During Each Cycle of Chemotherapy

- Amifostine use
- Carboplatin dose
- Chemotherapy change because of neuropathy
- Cisplatin dose
- National Cancer Institute Common Terminology Criteria (NCI CTC) grading of neuropathy (stated or implied)
- Dose reduction because of neuropathy
- Glomerular filtration rate
- Grading of neuropathy based on the NCI CTC tool for neuropathy treatment
- Infusion time
- Linear analog scale rating of neuropathy
- Neuropathy described in progress note
- New interventions related to neuropathy
- Paclitaxel dose
- Prescription given for neuropathy

### Figure 1. Main Research Variables Collected From Patients' Medical Records

## Instrument

Neuropathy was graded by the patients using the FACT/GOG-NTX. This tool is a simple 10-question survey that is focused on assessing severity of neuropathy and how it affects the patient's sensation and quality of life. The FACT/GOG-NTX has been shown to be a reliable and valid instrument for assessing the effect of neuropathy on health-related quality of life. The Cronbach alpha score exceeded 0.7 (Calhoun et al., 2000).

## Statistical Methods

FACT-GOG/NTX data were preprocessed according to prorating procedure. If fewer than 6 of the 11 items of the scale were not answered, the score was treated as missing data. If more than six items were answered, the data was prorated according to the following equation: FACT-GOG/NTX score = sum x 11 / (number of nonmissing answers) (Calhoun et al., 2000).

Descriptive statistics and summary graphs were created for all the continuous variables collected in the study. Frequency counts and bar charts were created for categorical variables. Each patient visit for chemotherapy was selected as a unit for analysis. In each treatment regimen, women could have up to six visits for chemotherapy where they could complete a FACT-GOG/NTX tool rating their neuropathy. In the screening phase of analysis, covariates that had more than 50% missing values were excluded from analysis. The variables collected from the medical record were used as potential covariates associated with FACT-GOG/NTX score. Mixed model with compound symmetry covariance matrix to adjust for correlations between FACT-GOG/NTX score from the same woman in the same chemotherapy cycle was used to detect variables associated with FACT-GOG/NTX. Backward elimination method was used to determine the final model (Littell, Milliken, Stroup, & Wolfinger, 1996).

## Main Research Variables

The main research variables were patient-reported FACT-GOG/NTX scores and the following variables, which were collected from patients' medical records: age, weight, height, race, type of cancer, antidepressant use at baseline, AUC, body surface area, cisplatin dose during cycle 1, depression, diabetes, alcohol use, previous CIPN, preexisting neuropathy, previous treatment with taxane and platinum chemotherapy, amifostine use, any intervention related to neuropathy, chemotherapy change because of neuropathy, creatinine, dose reduction, and glomerular filtration rate. Data from providers included neuropathy grade, provider notations of grade or neuropathy symptoms, and prescriptions written to control neuropathy symptoms.

## Findings

### Sample

The average age of the patients studied was 56 years (range = 23–84); 81% were Caucasian, 14% African American, 4% Hispanic, and 1% Asian. Most of the sample had ovarian cancer (68%), followed by cervical (14%), uterine (8%), ovarian and uterine (1%), and other gynecologic subtypes (8%). Relevant history related to neuropathy was collected and is summarized in Table 2. Data were collected on a total of 302 individual chemotherapy treatments; the mean number of chemotherapy cycles per patient was 4.8 on each regimen. The types of chemotherapy regimens can be seen in Table 3.

Forty-two percent of the patients completed more than six items on the FACT-GOG/NTX scale during the course of six cycles of chemotherapy, making their data eligible for analysis. Each item on the FACT-GOG/NTX scale was considered an observation, and 439 observations were used for the final analysis. A comparison was done between women with missing FACT-GOG/NTX scores in any chemotherapy cycle to women who were not missing any scores. No difference was noted in age ( $p = 0.56$ ), type of cancer ( $p = 0.075$ ), or race ( $p = 0.12$ ) between responders and nonresponders on the FACT-GOG/NTX scales.

Of all of the variables collected in the study, only a few showed a statistically significant relationship with patient rating of neuropathy on the FACT-GOG/NTX tool. Patients who had been previously treated with platinum and taxane chemotherapy had lower neuropathy scores when they received later chemotherapy treatments. Patients with higher neuropathy scores were more likely to have neuropathy noted in the chart, be graded by the provider, and be given written prescriptions for their symptoms. Patients who had received previous taxane and platinum chemotherapy had lower neuropathy scores ( $p = 0.0024$ ). If neuropathy was recorded in the progress note by the provider, then the neuropathy score was higher ( $p = 0.0308$ ). When a prescription was given to

**Table 2. Patients' Medical History Related to Neuropathy**

Patient History	n	%
Previous treatment with taxane- and platinum-based chemotherapy	220	73
Preexisting chemotherapy-induced peripheral neuropathy	136	45
Depression	121	40
Depression (currently on antidepressants)	115	38
Alcohol abuse	33	11
Diabetes mellitus	24	8
Preexisting peripheral neuropathy (unrelated to chemotherapy)	24	8

**Table 3. Chemotherapy Regimens Included in Study**

Regimen	n	%
Carboplatin and paclitaxel	53	18
Topotecan	36	12
Liposomal doxorubicin	23	8
Gemcitabine and cisplatin	11	4
Intraperitoneal cisplatin and paclitaxel	11	4
Gemcitabine and cisplatin	3	1
Docetaxel and gemcitabine	3	1
Intraperitoneal cisplatin and paclitaxel plus other	1	< 1
Other nonspecified regimen	161	53

N = 302

Note. Because of rounding, percentages do not total 100.

the patient for neuropathy symptoms, the neuropathy score was higher ( $p < 0.0001$ ). Rising grades of neuropathy noted by the provider (from grade 0–3) were correlated with sequential rising of neuropathy scoring by the patient ( $p < 0.001$ ) (see Table 4).

Taller patients with larger weight and body surface area had higher FACT-GOG/NTX scores. Deterministic, nonlinear relationships were seen between height and weight and body surface area in relationship to FACT-GOG/NTX scores. To better illustrate the effect of body shape and size on FACT-GOG/NTX score, four imaginary reference patients were created: thin and small (5'1" and 126.5 lbs.), thin and tall (5'6" and 126.5 lbs.), heavy and small (5'1" and 213 lbs.), and heavy and tall (5'6" and 213 lbs.). These heights and weights were selected because they were one standard deviation above and below the mean height and weight of the sample population. The thin and small person was used as a reference person. On average, a short and heavy person had a higher FACT-GOG/NTX score by 5.4 points, the tall and thin person had a higher FACT-GOG/NTX score by 2.7 points, and the tall and heavy person had a higher FACT-GOG/NTX score by 3.7 points.

Demographic factors such as age, race, and type of cancer were not related to neuropathy. Preexisting conditions that were investigated (diabetes, depression, antidepressant use, and alcohol use) did not affect neuropathy scores. Treatment-related factors such as creatinine, glomerular filtration rate, dose reduction, preexisting CIPN, or amifostine use were not associated with increased or decreased patient-reported neuropathy.

## Discussion

The results of this study shed light on two distinct areas of neuropathy: cumulative neuropathy and how providers assess, diagnose, and treat neuropathy. In addition, it is interesting to note the large number of variables that are commonly thought to be related to neuropathy that were not correlated. The relationships

between CIPN and height and weight are interesting new findings that warrant additional research.

Taxane- and platinum-based drugs are first-line treatment regimens for most gynecologic malignancies, and both are known for their cumulative neurotoxicities. Therefore, it was anticipated that patients receiving second- and third-line treatments would report more severe neuropathy. Therefore, the finding that previous treatment with these neurotoxic compounds was correlated with a decreased rating of neuropathy during treatment was surprising. The reduction was significant, scoring 4.38 points lower on the FACT-GOG/NTX than patients who had not been previously treated with taxane and platinum drugs. Therefore, the data suggest that, although second-, third-, and fourth-line treatments for gynecologic malignancies have some neurotoxic side effects, they are less neurotoxic than first-line treatment. The side effect of neuropathy is cumulative during first-line chemotherapy treatments, which is why it often is a dose-limiting side effect (Vivosky, 2005). A limitation of other studies that have examined residual neuropathy after treatment was that they only followed patients during progression-free survival when patients are not receiving additional chemotherapy (Bruner et al., 2007; Pignata et al., 2006). However, with gynecologic cancers, patients often undergo multiple regimens of neurotoxic chemotherapy and little is known about their cumulative effect. Therefore, the finding that patients who had been previously treated with highly neurotoxic regimens had lower neuropathy in later treatments is an encouraging finding for patients who may need multiple treatment regimens.

An interesting secondary finding was the perceptions of providers related to patient reports of neuropathy. The providers in this study were four gynecologic oncologists and one nurse practitioner. They noted neuropathy in their charting when patients rated their neuropathy as mild in two areas of their body (FACT-GOG/NTX score = 1.56). This suggests that these providers were aware of this adverse affect of treatment and were screening patients appropriately. Current study findings reinforced the assertion by Vasey et al. (2005) that, although CTC grading of neuropathy can be subjective, a positive correlation exists between neuropathy grading by providers and patient rating of their symp-

toms. In this study, the fact that gaps exist in providers' neuropathy grading is apparent. Grade 1 appears to be assigned for very mild symptoms; however, a delay then occurs before providers assess neuropathy as grade 2. This gray zone between grades 1 and 2 was where the providers gave prescriptions for neuropathy symptoms ( $\bar{X}$  FACT-GOG/NTX score = 7.34). The fact that prescriptions were given for symptoms implies that patients were troubled enough by their symptoms to take medication. However, at this same score, providers were still not rating this level of neuropathy as a grade 2. Unfortunately, no direct comparisons exist of the CTC grading system and FACT-GOG/NTX rating in the literature. Therefore, determining that grade 2 neuropathy correlates with a specific range of FACT-GOG/NTX scores was not possible. This illustrates some of the inconsistencies with various tools and grading systems with these two widely accepted means of measuring neuropathy and reinforces the need for more psychometric work in this area.

Some of the limitations of this study include a retrospective analysis of a convenience sample of patients from one institution. The overall completion rate of the FACT-GOG/NTX tool in all chemotherapy cycles the patient received was low at 42% and could be a result of the study design. It was impossible to calculate true incidence rates of neuropathy because of gaps in the data. It would have been beneficial to code the data in such a way to know the order of treatment regimens to better assess cumulative neuropathy. The authors were able to distinguish whether patients had been previously treated with taxanes and platinum therapy, but did not have data on any additional order of therapy. However, the recurrence rates of gynecologic malignancies are high because of advanced staging at diagnosis and many patients return for more therapy, making residual neuropathy assessments challenging. The Theory of Unpleasant Symptoms framework was loosely applied in developing a comprehensive holistic set of factors to examine in this retrospective analysis; however, the effect of neuropathy on overall quality of life was not assessed. To fully assess the effect of neuropathy, its impact on global quality of life must be addressed.

More prospective research is needed to investigate the severity of neuropathy in patients receiving multiple regimens of chemotherapy and its effect on quality of life. The authors' finding that patients who received previous taxane and platinum therapy had lower rates of neuropathy was surprising and needs additional validation. Further research also is needed in special populations of patients, such as those who are obese or who

**Table 4. Correlation of Neuropathy Grading With Significant Variables**

Variable	Neuropathy Score	Standard Error	p
Previous treatment with platinum and taxane agents	-4.38	± 1.28	0.0024
Neuropathy noted by provider in chart	1.58	± 0.72	0.0308
Prescription given for neuropathy symptoms	7.34	± 1.43	< 0.001
Grade 1 neuropathy as assessed by provider	4.19	± 0.87	< 0.001
Grade 2 neuropathy as assessed by provider	10.59	± 1.41	< 0.001
Grade 3 neuropathy as assessed by provider	14.05	± 3.47	< 0.001



have neurologic disorders, diabetes, or are receiving IP chemotherapy. Consensus in the literature is needed concerning the defining of terms related to neuropathy so that the research community can communicate findings effectively. This could be done by establishing guidelines for the use of specific tools for assessing patient symptoms, a correlating grading scale, adding a global quality-of-life tool, and recommendations for prevention and treatment of symptoms. A prospective study design using the Theory of Unpleasant Symptoms framework and the FACT-GOG/NTX tool to assess the effect of CIPN on patients would add valuable information to the body of knowledge on this topic.

## Implications for Nursing

Oncology nurses must take the lead in examining the effect of peripheral neuropathy on the quality of life of their patients and in validating tools used to measure

this side effect. Oncology nurses must be knowledgeable about patients at highest risk for neuropathy and educate them about early signs and symptoms. The nursing role is essential in the healthcare team to ensure that patients achieve the highest quality of life and most appropriate cancer treatment.

DeLeslie W. Kiser, FNP, AOCNP<sup>®</sup>, is a nurse practitioner in the Gynecologic Oncology Department at the Blumenthal Cancer Center in Charlotte, NC; Tara B. Greer, RN, MSN, ANP, is a medical oncology nurse practitioner at Carolinas Cancer Associates in Monroe, NC; Margaret C. Wilmoth, PhD, MSS, RN, FAAN, is a professor in the School of Nursing and Jacek Dmochowski, PhD, is an associate professor in the Mathematics and Science Department, both at the University of North Carolina at Charlotte; and R. Wendel Naumann, MD, is the director of Minimally Invasive Surgery in Gynecologic Oncology at Blumenthal Cancer Center. No financial relationships to disclose. Kiser can be reached at [deleslie.kiser@carolinashhealthcare.org](mailto:deleslie.kiser@carolinashhealthcare.org), with copy to editor at [ONFEditor@ons.org](mailto:ONFEditor@ons.org). (Submitted October 2008. Accepted for publication November 24, 2009.)

Digital Object Identifier: 10.1188/10.ONF.758-764

## References

- Argyriou, A., Polychronopoulos, P., Iconomou, G., Koutras, A., Kalofonos, H., & Chroni, E. (2005). Paclitaxel plus carboplatin-induced peripheral neuropathy: A prospective clinical and electrophysiological study in patients suffering from solid malignancies. *Journal of Neurology*, 252, 1459–1464. doi: 10.1007/s00415-005-0887-8
- Bruner, D., Barsevick, A., Tian, C., Randall, M., Mannel, R., Cohn, D., . . . Spirtos, N.M. (2007). Randomized trial results of quality of life comparing whole abdominal radiation and combination chemotherapy in advanced endometrial carcinoma: A gynecologic oncology group study. *Quality of Life Research*, 1, 89–100. doi: 10.1007/s11136-006-9003-5
- Calhoun, E., Fishman, D., Roland, P., Lurain, J., Chang, C., & Cella, D. (2000). Validity and selective sensitivity of the FACT/GOG-NTX [Abstract 1751]. *Proceedings of the American Society of Clinical Oncology*, 19, 446a. Retrieved from [http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=2&abstractID=202320](http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=2&abstractID=202320)
- Fujiwara, K., Suzuki, S., Ishikawa, H., Oda, T., Aotaniy, E., & Kohno, I. (2005). Preliminary toxicity analysis of intraperitoneal carboplatin in combination with intravenous paclitaxel chemotherapy for patients with carcinoma of the ovary, peritoneum, or fallopian tubes. *International Journal of Gynecological Cancer*, 15, 426–431. doi: 10.1111/j.1525-1438.2005.15304.x
- Lenz, E., Pugh, L., Miligan, R., Gift, A., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: An update. *Advances in Nursing Science*, 19(3), 14–27.
- Littell, R., Milliken, G., Stroup, W., & Wolfinger, R. (1996). *SAS system for mixed models*. Cary, NC: SAS Institute, Inc.
- Martino, M., Miller, E., & Grendys, E. (2005). The administration of chemotherapy in a patient with Charcot-Marie tooth and ovarian cancer. *Gynecologic Oncology*, 97, 710–712. doi: 10.1016/j.ygyno.2005.01.017
- National Cancer Institute. (2007). *SEER cancer statistics review, 1975–2005*. Retrieved from [http://seer.cancer.gov/csr/1975\\_2002/2008](http://seer.cancer.gov/csr/1975_2002/2008)
- Pan, Y., & Kao, M. (2007). Discordance of clinical symptoms and electrophysiological findings in taxane plus platinum-induced neuropathy. *International Journal of Gynecological Cancer*, 17, 394–397. doi: 10.1111/j.1525-1438.2006.00766.x
- Pignata, S., De Placido, S., Biamonte, R., Scambia, G., Di Vagno, G., Colucci, G., . . . Perrone, F. (2006). Residual neurotoxicity in ovarian cancer patients in clinical remission after first-line chemotherapy with carboplatin and paclitaxel: The Multicenter Italian Trial in Ovarian Cancer retrospective study. *BMC Cancer*, 6(5), 1–7. doi: 10.1186/1471-2407-6-5
- Vasey, P., Jayson, G., Gordon, A., Gabra, H., Coleman, R., Atkinson, R., . . . Kaye, S.B. (2004). Phase III randomized trial of docetaxel-carboplatin versus paclitaxel-carboplatin as first-line chemotherapy for ovarian carcinoma. *Journal of the National Cancer Institute*, 96, 1682–1691. doi: 10.1093/jnci/djh323
- Visovsky, C. (2005). Measuring oncology nursing sensitive outcomes: Evidence-based summary. Chemotherapy-induced peripheral neuropathy. Retrieved from [http://www.ons.org/Research/Nursing Sensitive/Summaries/Peripheral](http://www.ons.org/Research/NursingSensitive/Summaries/Peripheral)
- Wickham, R. (2007). Chemotherapy-induced peripheral neuropathy: A review and implications for oncology nursing. *Clinical Journal of Oncology Nursing*, 11, 1092–1095. doi: 10.1188/07.CJON.361-376