Psychometric Evaluation of Two Scales Assessing Functional Status and Peripheral Neuropathy Associated With Chemotherapy for Ovarian Cancer: A Gynecologic Oncology Group Study

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Purpose/Objectives: To evaluate the psychometric properties of two adapted scales, one for functional status and one for peripheral neuropathy secondary to neurotoxic chemotherapy.

Design: Repeated measures methodologic design conducted within a Gynecologic Oncology Group (GOG) phase III clinical trial that randomly assigned patients with advanced epithelial ovarian cancer to cisplatin and cyclophosphamide or cisplatin and paclitaxel.

Setting: 8 GOG institutions participating in the GOG clinical trial.

Sample: 88 evaluable outpatients enrolled in the GOG clinical trial. Sample size at time 1 (T1) was 88 patients and at time 2 (T2) was 67 patients.

Methods: All scales were administered at T1 (prior to initiation of chemotherapy) and T2 (after six cycles of chemotherapy but prior to second-look laparotomy). Internal consistency reliability, criterion validity, and construct validity were evaluated, and clinical application was explored.

Main Research Variables: Self-reported peripheral neuropathy and functional status (comprised of physical function and role function subscales), the GOG performance status scale, and the GOG toxicity criteria.

Findings: Reliability coefficients at T1 were physical function = 0.83, role function = 0.96, and peripheral neuropathy = 0.91; at T2, they were physical function = 0.83, role function = 0.92, and peripheral neuropathy = 0.89. At T1, physical function and role function correlated positively with performance status. Peripheral neuropathy correlated positively with GOG toxicity criteria used at T2. Principal component factor analysis suggested that the functional status scale had a two-factor structure with factors representing general and specific mobility and that the peripheral neuropathy scale also had a two-factor structure with factors representing foot and hand neuropathy.

Conclusions: The physical function, role function, and peripheral neuropathy scales have internal consistency, reliability, criterion validity, and construct validity. However, revision of the scales should address modification of specific questions and consider increasing the Likert scale from a four-point to a five- or seven-point scale to enhance clinical sensitivity and application.

Implications for Nursing: With minor modifications, these scales should be useful in assessing physical function, role function, and peripheral neuropathy in patients who receive agents that may cause peripheral neuropathy.

Key Points . . .

- Peripheral neuropathy is a principal toxic effect of chemotherapy for ovarian cancer.
- Peripheral neuropathy interferes with self-care activities, mobility, and physical and role activities, and this may reduce domains of quality of life related to functional and role status.
- Self-report instruments may be a useful adjunct to measuring the subjective symptoms of peripheral neuropathy just as they have with pain and fatigue.
- With minor modifications and testing, these scales may be useful in assessing peripheral neuropathy symptoms in patients who receive neurotoxic chemotherapy.

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The neurotoxic effects of cisplatin are well recognized, and, at cumulative doses of 300 mg/m^2 or greater, sensory peripheral neuropathy is the principal dose-limiting toxicity (Kedar, Cohen, & Freeman, 1978; LoMonaco et al., 1992; Mollman, Glover, Hogan, & Furman, 1988; Roelofs, Hrushesky, Rogin, & Rosenberg, 1984). Symptoms experienced by patients include tingling and numbness in the hands and feet in a characteristic stocking-glove distribution and a decreased sense of touch or hyperesthesia that causes a burning pain, particularly in the feet. Clinical examination shows a decrease in vibratory sense that usually is greater in the toes and ankles than in the fingers and wrists, a decrease in joint position sense, and a loss of deep tendon reflexes.

Peripheral neuropathy is also one of the principal toxic effects of paclitaxel (McGuire et al., 1989; Rowinsky, Onnetto, Cannetta, & Arbuck, 1992) and seems to be worse with higher doses (Chaudhry, Rowinsky, Sartorius, Donehower, & Cornblath, 1994; Rowinsky, Eisenhauer, Chaudhry, Arbuck, & Donehower, 1993) or when shorter infusion schedules (Connelly et al., 1995) are used. Unlike the sensory peripheral neuropathy induced by cisplatin, paclitaxel causes sensory and motor neuropathy. Combinations of cisplatin and paclitaxel, when administered in less than three-hour infusions, lead to excessive neurotoxicity with as many as 20% of patients experiencing adverse effects that caused a significant reduction of activities of daily living (ADL), as evidenced by Gynecologic Oncology Group (GOG) neurotoxicity scores greater than grade 3 (Connelly et al.; Piccart et al., 1997).

Neurologic toxicity eventually decreases patients' abilities to perform physical functions necessary for ADL. For example, people may report difficulty buttoning shirts or closing zippers, walking without the aid of visual cues, or feeling the shape of objects held in the hands. Role functions in the family and work setting also may be affected as a result of peripheral neuropathy. As examples, an individual's inability to perceive temperatures may hinder safe use of heat-producing kitchen equipment or an impaired ability to feel brake or accelerator pedals in a vehicle can affect driving safety.

When peripheral neuropathy develops, assessment of impairment in physical and role function requires objective clinical and subjective patient assessment and, when appropriate, intervention. Most objective measures of peripheral neuropathy, such as vibratory sense, joint position sense, and deep tendon reflexes, are difficult to perform in the clinical setting because of time, cost, and lack of experience by healthcare providers. A subjective assessment of changes in physical and role function and peripheral sensations may add valuable information to the accuracy of assessment and assisting selection and implementation of interventions.

Few valid and reliable instruments exist that nurses can use to help patients report their own perceptions of physical and role function impairment related to peripheral neuropathy caused by neurotoxic drugs. Thus, the purpose of this study was to adapt and evaluate two existing scales to measure functional status (comprised of physical and role function subscales) and peripheral neuropathy in a population of patients with ovarian cancer receiving potentially neurotoxic chemotherapy. The long-term goal of the research is to produce a clinically feasible instrument that might be used by nurses to more comprehensively assess peripheral neuropathy and its effects on selected aspects of quality of life (QOL).

Background and Conceptual Framework

The proliferation of aggressive cancer treatment strategies with increasing types and severity of adverse effects has led, in part, to an increased interest in evaluating QOL in addition to traditional outcomes such as survival time. Cella and Bonomi (1995) defined QOL to reflect its multidimensionality: "Health-related QOL refers to the extent to which one's usual or expected physical, emotional, and social well-being are affected by a medical condition or its treatment" (p. 48). Schipper (1990) defined QOL in the context of clinical trials as ". . . a pragmatic, day-to-day functional representation of a patient's physical, psychological, and social response to a disease and its treatment" (p. 52). Aaronson (1989, 1990), Aaronson et al. (1987), Cella and Cherin (1988), and Cella and Tulsky (1990) suggested that assessment of QOL should include, at a minimum, four domains: (a) physical functional status, (b) physical symptoms, (c) psychological functioning, and (d) social and role functioning. The conceptual framework used in this methodologic study is derived from these definitions and domains of QOL.

Functional status refers to the capacity to perform a variety of activities that are normal for most people (Aaronson, 1990). Four commonly measured categories are (a) self-care activities (feeding, dressing, bathing, using the toilet), (b) mobility (ability to move around indoors, outdoors, or in the community), (c) physical activities (walking, climbing stairs, lifting, bending), and (d) role activities (ability to carry out social roles associated with work, school, or household activities). Thus, functional status encompasses physical and role function.

Careful assessment of peripheral neuropathy as a toxicity in trials can help to detect intergroup differences in QOL, including functional status (Aaronson, 1990). Because peripheral neuropathy is predominantly subjective, use of questions that elicit patients' perceptions and relate them to physical and role function aspects of QOL can enhance assessment and ultimately lead to effective interventions.

Ostchega, Donohue, and Fox (1988) were the first oncology nurses to demonstrate the importance of assessing long-term effects of peripheral neuropathy symptoms on overall ability to perform ADL and work responsibilities. They conducted a descriptive, retrospective study of 30 patients who had received high-dose (> 720 mg/m^2) cisplatin for testicular or ovarian cancer and had been free of cancer and off all treatment for more than one year. They used the QOL Questionnaire (QOLQ) developed by Aaronson et al. (1987) of the European Organization for the Treatment of Cancer (EORTC). The QOLQ contained subscales assessing ADL and work limitations, fatigue and malaise, psychological distress, sense of well-being, and social support. Ostchega et al. also developed and added an eight-item scale assessing symptoms of peripheral neuropathy. They found that peripheral neuropathy symptoms were significantly correlated ($p < 0.05$) with increased fatigue, malaise, and psychological distress and decreased sense of well-being, satisfaction with life, ADL, and ability to work. Ostchega et al.'s approach guided this methodologic study.

Methods

Design

A repeated measures design was used to assess the psychometric properties (reliability, concurrent validity, construct

validity) of the two scales: functional status (with physical and role function subscales) and peripheral neuropathy. Scales were administered before treatment (time 1 [T1]) and at the end of treatment (time 2 [T2]). End of treatment was defined as assessment at cycle 6 or within four weeks of cycle 6. End-of-treatment assessment always occurred prior to second-look laparotomy.

The study was initiated by a group of nurses within the context of the GOG phase III clinical trial that compared two regimens for first-line treatment (McGuire et al., 1996). Patients in this trial were assigned randomly to receive either six cycles of IV cisplatin (75 mg/m^2) with cyclophosphamide (750 mg/m^2) or six cycles of IV cisplatin (75 mg/m^2) with paclitaxel (135 mg/m^2). Although the principal objective of the trial was to determine patients' response rates, response duration, and survival, another objective was to compare relative toxicities and, in particular, the neurotoxicity of the two regimens. This article is related to the latter objective and reports the psychometric evaluation of two scales designed to measure peripheral neuropathy and functional status.

Setting and Sample

The GOG phase III clinical trial described previously was conducted at numerous GOG member institutions and their affiliates. Eight of the institutions that participated in the GOG trial also took part in this study. These eight institutions participated because historically they had the highest numbers of patients entering GOG ovarian trials and the GOG study nurses expressed a willingness to participate. The institutional review boards of all eight participating institutions approved the study.

Women with pathologically verified stage III epithelial ovarian cancer who had more than 1 cm of residual disease after surgery or stage IV disease were eligible. Eligible patients also provided written informed consent, entered the GOG trial within six weeks of surgery, had not received previous chemotherapy or radiation therapy for cancer except nonmelanoma skin cancer, had a GOG performance status of 0, 1, or 2 (Blessing, 1990), and had a normal white blood cell count, normal serum creatinine levels, and serum bilirubin and serum aspartate aminotransferase values no more than twice the upper level of institutional normal.

Instruments

This study used data from standard GOG forms completed in the clinical trial, including patient registration, surgical and pathologic descriptions, chemotherapy and toxicity assessment information for each cycle of chemotherapy, and response and ongoing follow-up. Side effects were graded using the GOG toxicity criteria (Blessing, 1990).

The **GOG Performance Status Scale** was used for criterion validity analysis of the scales tested in this study. It was completed by clinicians prior to study entry, at each chemotherapy cycle, and at the end of the trial prior to second-look laparotomy. The five-point (0–4) scale rates patients' abilities to perform activities (0 = fully active; 1 = restricted in strenuous physical activity but ambulatory; 2 = ambulatory, capable of self-care, unable to work, up 50% of waking hours; 3 = limited self-care, confined to bed or chair 50% of waking hours; 4 = completely disabled, no self-care). Higher scores indicate poorer function.

The functional status and peripheral neuropathy scales tested in this study were combined into one questionnaire to facilitate completion. The functional status scale was comprised of physical and role function subscales that were adapted from the EORTC QOLQ developed in 1987 and validated by Aaronson et al. (1991). The original QOLQ was a 36-item multidimensional core instrument that assessed four major domains: physical, role, emotional, and social functioning. The instrument was tested initially in 537 patients with nonresectable lung cancer from western Europe, Asia, and North America. It demonstrated evidence of internal consistency, construct validity, sensitivity to differences in clinical status, and clinical feasibility (Aaronson et al., 1991). Overall, results indicated that the psychometric characteristics were similar across various languages and cultures with the exception of the Japanese subsample, in which the reliability of several of the subscales was lower (Aaronson et al., 1991). The QOLQ provided a dichotomized (yes or no) response format for the physical and role function subscales. In the present study, this format was revised (with permission) into a four-point Likert-type scale ranging from 1 (not at all) to 4 (very much). The physical function subscale consisted of six items, with a total score range of 6–24. The role function subscale consisted of two items, with a total score range of 2–8 (see Figure 1). The functional status total score is the sum of item scores from both subscales and has a potential range of 8–32. Cumulative functional status scores were used if at least six of the eight items were answered with the mean response used to impute scores for the missing items. On both subscales and the total scale, higher scores indicated more limitations or needs for assistance. In addition to the change in answer format, the authors slightly modified the wording of several items to increase readability.

The **Peripheral Neuropathy Scale** used in this study was adapted from a self-report, eight-item, Likert-type scale developed by Ostchega et al. (1988). The original instrument was based on the common complaints expressed by patients who experienced peripheral neuropathy while receiving cisplatin. Ostchega et al. established content validity by using an expert panel of two patients who had experienced peripheral neuropathy and two physicians familiar with peripheral neuropathy symptoms. They did not report additional validity data or any reliability data in their sample of 30 patients.

The original eight-item instrument was expanded (with permission) in the present study to 11 items. Ostchega et al.'s (1988) items, which grouped hands and feet, were separated to fully characterize neuropathy. Additionally, minor changes in wording were made for clarity and some items were written in the present tense. Ostchega et al.'s response format of 1 (not at all) to 4 (very much) was retained. The scale was

Physical Function

1. Do you need help with eating, dressing, washing, or using the toilet?
2. Do you have to stay indoors most or all of the day?
3. Are you in bed or a chair most of the day?
4. Do you have trouble either walking a short distance or climbing one flight of stairs?
5. Do you have trouble bending, lifting, or stooping?
6. Do you have trouble either taking a walk or climbing a few flights of stairs?

Role Function

7. Does your condition keep you from working at a job or doing household jobs?
8. Are you limited in any way doing your work or household jobs?

Figure 1. Functional Status Scale

scored by summing the 11 items for a score range of 11–44, provided that at least 8 of the 11 items were answered with the mean response used to impute scores for the missing items. Higher scores indicated a higher degree of patient-reported peripheral neuropathy (see Figure 2).

Procedures

To familiarize nurses with the study and to standardize data collection, the authors conducted two educational sessions at the semiannual GOG meeting just before the trial opened. One session dealt with peripheral neuropathy in general, and the other focused on performing a neurologic assessment and helping patients to complete the self-report scales. The importance of reviewing the assessments for completeness at the time of assessment was stressed, and rules were established for ensuring that all questionnaires were completed before patients left the clinic. The GOG nurse was responsible for ensuring that patients completed the scales at both assessment times.

Data Analysis

Data forms were reviewed, cleaned up, and entered in the GOG statistical office computer system using standard procedures. Data were analyzed using SAS® version 8.2 (SAS Institute Inc., Cary, NC). Measures of central tendency and dispersion were used to profile the sample. Psychometric analyses included Cronbach's coefficient alpha (internal consistency reliability) and confirmatory and explanatory factor analyses with oblique rotation (construct validity). Correlations among the scales and associations with the GOG performance status scale and the GOG toxicity criteria (criterion validity) were examined using the Rank Correlation test (Blessing, 1990). All psychometric analyses were performed at both assessment points. Items were considered highly loaded if their load scores were at least 0.5. Changes in functional status and peripheral neuropathy (from T1 to T2) were examined as indicators of the validity and clinical sensitivity of the scales. Factor analysis of the functional status scale was expected to yield a two-factor solution, with factors distinguishing physical function and role function items. Factor analysis of the peripheral neuropathy scale was exploratory, but the authors anticipated that a two-component solution distinguishing hand and foot items would be consistent with scale construction.

Results

Characteristics of the Patients

A total of 386 women met the eligibility criteria. Of these, 111 patients at eight institutions were eligible to participate in the QOL study based on their performance status and institutional willingness to be involved in the study, because participation was optional. The demographic and baseline clinical characteristics are shown in Table 1. At T1, 88 patients completed all 19 items (6 were treated as missing because of incomplete forms and 17 declined to participate). At T2, 67 patients completed all 19 items (2 were treated as missing, 38 declined to participate, and 4 died before T2). The demographic and clinical characteristics of the women were comparable to the larger sample presented in the report of the phase III trial (McGuire et al., 1996). In brief, patients in this project had a mean age of 58, were predominantly white, and had a good functional status at baseline. The major pathologic type of ovarian cancer was serous adenocarcinoma, predominantly stage III, with a high proportion with grades 2 and 3 and ascites.

Reliability

Cronbach's coefficient alpha was calculated to evaluate internal consistency (see Table 2). Overall, the scales achieved an acceptable level of internal consistency with a coefficient of 0.83 for the physical function subscale, 0.96 for the role function subscale, and 0.91 for the peripheral neuropathy scale at pretreatment (T1) assessment. The coefficients were 0.83, 0.92, and 0.89, respectively, for the assessment at end of treatment (T2). To further check the correct item-total correlation,

Table 1. Demographic and Baseline Clinical Characteristics of Patients Participating in Assessment

Characteristic	n	%
Age (years)		
$\bar{X}$ (SD) = 58 (11.2)	–	–
Median = 60	–	–
Range = 21–77	–	–
Race		
White	78	89
Black	9	10
Other	1	1
Performance status		
0	24	27
1	47	53
2	17	19
Cell type		
Serous adenocarcinoma	67	76
Endometrioid adenocarcinoma	8	9
Mucinous adenocarcinoma	2	2
Clear cell adenocarcinoma	2	2
Other	9	10
Tumor grade		
1	6	7
2	34	39
3	48	55
Measurable disease		
Yes	48	55
No	40	45
Stage		
III	62	70
IV	26	30
Ascites (> 100 ml)		
Yes	74	84
No	14	16

N = 88

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

9. Do you have difficulty buttoning buttons?
10. Do you feel any stiffness or tightness in your hands?
11. Do you feel any stiffness or tightness in your feet?
12. Do you feel clumsy?
13. Do you feel any discomfort in your hands?
14. Do you feel any discomfort in your feet?
15. When holding an object in your hand(s), are you able to feel its shape?
16. Do you have tingling in your hands?
17. Do you have tingling in your feet?
18. Do you have numbness in your hands?
19. Do you have numbness in your feet?

Figure 2. Peripheral Neuropathy Scale

Table 2. Internal Consistency Analyses by Scale at Pretreatment and End of Treatment

Scale and Item	Correct Item—Total Correlation	
	Time 1 (N = 88) r	Time 2 (N = 67) r
Functional status		
Physical function		
1 (need help with eating)	0.40	0.65
2 (have to stay indoors)	0.61	0.58
3 (in bed or chair)	0.61	0.62
4 (trouble working shorter hours)	0.67	0.64
5 (trouble bending)	0.69	0.56
6 (trouble working longer hours)	0.72	0.66
(Coefficient alpha)	0.83	0.83
Role function		
7 (away from job)	0.93	0.86
8 (limited job)	0.93	0.86
(Coefficient alpha)	0.96	0.92
Peripheral neuropathy		
9 (difficulty buttoning)	0.66	0.36
10 (stiffness or tightness in hand)	0.68	0.69
11 (stiffness or tightness in feet)	0.69	0.63
12 (clumsy)	0.49	0.56
13 (discomfort in hand)	0.72	0.69
14 (discomfort in feet)	0.74	0.65
15 (feel object's shape in hand)	0.26	0.31
16 (tingling in hand)	0.82	0.74
17 (tingling in feet)	0.73	0.62
18 (numbness in hand)	0.77	0.66
19 (numbness in feet)	0.74	0.72
(Coefficient alpha)	0.91	0.89

three items were found to be problematic. For the physical function scale, item 1 showed a low correlation (0.40) with the total score at T1, suggesting that this item may not be an appropriate indicator of physical function, at least at T1. Two other questionable items were numbers 9 and 15. Item 9 has a low correlation (0.36) with total score at T2 assessment, and item 15 demonstrated lower item-total correlations (0.26 and 0.31) for peripheral neuropathy at both T1 and T2 assessments.

Construct Validity

The functional status scale originally was developed to cover two subscales: physical function and role function. Confirmatory factor analysis was performed to evaluate the fitness of this model (see Table 3). The results suggest poor fitness (Chi-square/df > 2, Comparative Fit Index < 0.9, and Non-Normal Fit Index < 0.9), although the model fitness was slightly improved at T2. Because the confirmatory analysis did not support the original structure, an exploratory factor analysis was conducted to investigate possible other patterns. As shown in Table 4, two latent factors for functional status were identified that can be interpreted as general mobility (items 2, 3, 7, and 8) and specific mobility (items 4, 5, and 6). Item 1 also was problematic here. It had a modestly high loading factor 1 (0.49) at T1 but a high loading factor 2 (0.62) at T2.

According to the original design, the peripheral neuropathy scale was a single scale, but a two-component solution was anticipated. Exploratory factor analysis was conducted to explore the possible subscales. These results (see Table 5) suggest two subscales: hand neuropathy (items 9, 10, 13, 16, and 18) and foot neuropathy (items 11, 14, 17, and 19). Item 12 was loaded on factor 2 (foot) at T1 but changed to factor 1 (hand) at T2. At both T1 and T2, item 15 was the item that was not highly loaded on any factor.

Criterion Validity

No well-established criteria exist to evaluate the validity of the instrument for the present study. Criterion validity was assessed by examining the convergence of the functional status score with the GOG performance at T1. At T2, the peripheral neuropathy criteria in the GOG toxicity criteria, used by GOG to assess toxicity, were used to evaluate the criterion validity of the peripheral neuropathy scale. Logically, the functional status at T1 assessment should be associated with GOG performance level at baseline, and peripheral neuropathy at T2 assessment should relate to the Common Toxicity Criteria level.

Two approaches based on the original structure (6 items for physical function, 2 for role function, and 11 for peripheral neuropathy) and the revised structure (4 items for general mobility, 3 for specific mobility, 5 for hand neuropathy, and 5 for foot neuropathy) were examined. The revised structure was modified based on the exploratory factor analysis results by removing the three questionable items (numbers 1, 12, and 15). Using the Rank Correlation test, an association of the functional status with the GOG performance at T1 for both original and revised structures was confirmed (see Table 6). With the same method, a significant association existed between peripheral neuropathy and the Common Toxicity Criteria level at T2 (see Table 7).

Clinical Sensitivity

Certain chemotherapeutic agents may cause peripheral neuropathy during or after treatment. If peripheral neuropathy develops, it may limit a person's functional status. Table 8 shows the score changes in functional status and peripheral neuropathy related to the treatment regimen used in this study according to the original and the revised scale structures. No significant changes existed for functional status between the

Table 3. Confirmatory Factor Analyses for Functional Status Structure at Pretreatment and End of Treatment

Scale and Item	Correct Item—Total Correlation	
	Time 1 (N = 88) r	Time 2 (N = 67) r
Functional status		
Physical function		
1 (need help with eating)	0.38	0.70
2 (have to stay indoors)	0.65	0.66
3 (in bed or chair)	0.66	0.70
4 (trouble working shorter hours)	0.77	0.73
5 (trouble bending)	0.79	0.63
6 (trouble working longer hours)	0.82	0.72
Role function		
7 (away from job)	0.98	0.91
8 (limited job)	0.94	0.94
Goodness of Fit Index	0.78	0.85
Chi-square/df	4.29	2.16
Comparative Fit Index	0.87	0.92
Non-Normal Fit Index	0.81	0.89

Table 4. Exploratory Factor Analysis[a] for Functional Scale at Pretreatment and End of Treatment

Item	Time 1 (N = 88)		Time 2 (N = 67)	
	Factor 1 (General[b])	Factor 2 (Specific[c])	Factor 1 (General[b])	Factor 2 (Specific[c])
1 (need help with eating)	0.49	–0.05	0.13	0.62
2 (have to stay indoors)	0.60	0.14	0.71	0.02
3 (in bed or chair)	0.84	–0.04	0.73	0.04
4 (trouble working shorter hours)	–0.04	0.85	0.08	0.71
5 (trouble bending)	0.13	0.70	0.06	0.63
6 (trouble working longer hours)	0.01	0.87	0.00	0.80
7 (away from job)	0.83	0.15	0.81	0.08
8 (limited job)	0.86	0.09	0.83	0.08
Inter-factor correlation	0.61		0.64	

[a] Oblique promax rotation method performed; standardized regression coefficient (factor loading) = 0.50 in absolute value underlined

[b] Interpreted as general mobility

[c] Interpreted as specific mobility

T1 and the T2 assessments. Significant changes existed in the peripheral neuropathy status between T1 and T2. The changes were nearly identical for the two regimens (cisplatin plus cyclophosphamide versus cisplatin plus paclitaxel). Table 9 shows the correlations among functional status and the peripheral neuropathy scales. Using the original structure, physical function has a strong correlation with role function. Both of them have a weak but statistically significant correlation with peripheral neuropathy at T1. However, the correlation between role function and peripheral neuropathy became nonsignificant at T2. Using the revised structure, the correlation between general and specific mobility and the correlation between hand and foot neuropathy were strong. At T1, general mobility showed a weak but significant correlation with foot neuropathy; specific mobility had weak but significant correlations with hand and foot neuropathy. At T2, the correlation between general mobility and foot neuropathy became nonsignificant.

Discussion

Reliability

The results of this study indicate that the functional status scale (composed of physical and role function subscales) and peripheral neuropathy scale displayed internal consistency reliability. However, item 1 on the physical function subscale of the functional status scale had a low correlation with the total scale score at T1. Because this item asked about needing help with distinct physical activities such as eating and dressing, separation of these activities into individual items would increase the specificity of the subscale and potentially result in better item-total correlations and higher internal consistency.

Similarly, the peripheral neuropathy scale had two items with particularly low item-total score correlations. Item 9, difficulty buttoning buttons, had an acceptable correlation at T1 but a lower correlation at T2 (0.36). The reason is not clear but may have been the result of the specific nature of the item in comparison to other items. Future revision of the scale might consider some rewording of item 9. Item 15, feeling the shape of an object held in the hand, was lower at T1 (0.26) and T2 (0.31). Because the response scale on this item was reverse coded, patients may have misunderstood it when answering the item. Future revision of the scale might consider rewording this item so that the response coding is the same as the other items on the scale.

Validity

Construct validity of the functional status scale initially was examined using confirmatory factor analysis to evaluate the fitness of the two-subscale model (physical function and role function) that formed the latent structure of the original scale. As noted, the model was not supported, so exploratory factor analysis was conducted. The second analysis yielded two latent factors, interpreted as general mobility (items 2, 3, 7, and 8) and specific mobility (items 4, 5, and 6). Of note is that item 1 had lower factor loadings than other items and loaded on factor 1 at T1 but on factor 2 at T2.

These two factors make sense clinically in that factor 1, general mobility, clearly includes items that related to ability to function in general ways (e.g., staying indoors or in a chair, being limited in doing normal activities). In contrast, factor 2, specific mobility, clearly focuses on specific physical functioning (e.g., walking, lifting, climbing stairs). Given that normal physical and role functioning may require any combination of these general and specific mobility items, the authors are not surprised that the results revealed a different latent structure than the original. Indeed, patients may have viewed role function as not only their ability to work at a job or perform household tasks but also in relation to how and where they spent most of their time (e.g., indoors, in a bed or chair). Similarly, they may have viewed physical function as a combination of general and specific activities.

Exploratory factor analysis of the peripheral neuropathy scale, originally designed as a single scale, was anticipated to produce a two-factor solution because the investigators had separated several items on Ostchega et al.'s (1988) original scale into hand- and foot-specific items. With the exception of

Table 5. Exploratory Factor Analysis[a] for Peripheral Neuropathy Scale at Pretreatment and End of Treatment

Item	Time 1 (N = 88)		Time 2 (N = 67)	
	Factor 1 (Hand[b])	Factor 2 (Foot[c])	Factor 1 (Hand[b])	Factor 2 (Foot[c])
9 (difficulty buttoning)	0.65	0.13	0.54	–0.10
10 (stiffness or tightness in hand)	0.76	0.07	0.68	0.16
11 (stiffness or tightness in feet)	0.11	0.67	–0.04	0.85
12 (clumsy)	0.04	0.53	0.54	0.12
13 (discomfort in hand)	0.72	0.13	0.80	0.04
14 (discomfort in feet)	0.03	0.82	–0.01	0.85
15 (feel object's shape in hand)	0.47	–0.15	0.30	0.07
16 (tingling in hand)	0.67	0.26	0.79	0.09
17 (tingling in feet)	–0.13	0.99	0.02	0.76
18 (numbness in hand)	0.77	0.13	0.85	–0.05
19 (numbness in feet)	0.08	0.79	0.12	0.77
Inter-factor correlation	0.66		0.55	

[a] Oblique promax rotation method performed; standardized regression coefficient (factor loading) = 0.50 in absolute value underlined

[b] Interpreted as peripheral neuropathy at hand

[c] Interpreted as peripheral neuropathy at foot

Table 6. Functional Status Scores by Baseline Gynecologic Oncology Group Performance Status Score at Pretreatment—Criterion Validity Assessment

	Median (25th–75th Percentile)[a]						
	n = 24		n = 47		n = 17		
Structure	Score	Range	Score	Range	Score	Range	p[b]
By original structure (8-item)							
Physical function[c]	7	6–9	9	6–13	11	9–15	0.0032
Role function[d]	2	2–4	3	2–6	4	2–6	0.0088
By revised structure (7-item)							
General mobility[e]	4	4–7	6	4–10	7	6–12	0.0061
Specific mobility[f]	3	3–6	4	3–7	6	4–8	0.0051

N = 88

[a] Factor-base scores

[b] Spearman's Rank Correlation test of association

[c] Physical function composite: items 1–6

[d] Role function composite: items 7 and 8

[e] General mobility composite: items 2, 3, 7, and 8

[f] Specific mobility composite: items 4–6

item 12, feeling clumsy, all items loaded clearly on one factor or the other at T1 and T2. Factor 1, hand neuropathy, consisted of items 9, 10, 13, 16, and 18, whereas factor 2, foot neuropathy, consisted of items 11, 14, 17, and 19. Item 12 may have been confusing to some patients because clumsiness could be construed as occurring in the hands or the feet, hence its inconsistent loading on the factors. Future revision might consider changing this item to more specifically indicate hand clumsiness and foot clumsiness.

Criterion validity at T1 was assessed primarily through the extent of convergence between the functional status scale score and the GOG performance status score at T1 (see Table 6) and the peripheral neuropathy scale score and National Cancer Institute Common Toxicity Criteria score at T2. As anticipated at T1, analyses using the original functional status scale structure and the revised structure (new two-factor solution with item 1 deleted) yielded consistent results that provided evidence for criterion validity. At T2, peripheral neuropathy was significantly associated with the Common Toxicity Criteria score, supporting that the peripheral neuropathy scale was a valid measure of peripheral neuropathy.

Clinical sensitivity of the peripheral neuropathy scale was evident in that scores changed significantly between T1 and T2 in both arms of the original trial (McGuire et al., 1996). In other words, the scale proved to be a valid indicator of worsening peripheral neuropathy between baseline (T1) and the end of treatment (T2). Because peripheral neuropathy often increases after completion of cisplatin (Mollman et al., 1988), the T2 assessment may not have captured the full extent of peripheral neuropathy disability in patients receiving cisplatin in the original study. Moreover, this issue could have been part of the reason that no significant difference existed in functional status between T1 and T2. In retrospect, an assessment six months following completion of treatment using the functional status and peripheral neuropathy scales may have yielded a clearer picture of peripheral neuropathy and its effects on functional status and is worth considering in future work with these scales.

The finding that the specific mobility in the revised structure of the functional status was more correlated with peripheral neuropathy suggests that this latent structure was a better reflection of clinical reality. In other words, the worse the peripheral neuropathy became, the more functional ability in specific areas was impaired. The overall usefulness of the peripheral neuropathy scale also might be improved with the addition of items that assess other subjective symptoms associated with peripheral neuropathy, such as pain, which is an important component of peripheral neuropathy (Smith, Whedon, & Bookbinder, 2002). And lastly, increasing the four-point Likert scale used in this study to a five-point or higher scale could improve the peripheral neuropathy scale's ability to detect minor changes in treatment-related neuropathy.

Limitations

The sample in this study included only women being treated for ovarian cancer, a known limitation from the outset because the study was conducted within the GOG. If these scales are revised, they will need psychometric evaluation in samples that include men and patients with other types of cancer who receive neurotoxic chemotherapy. Another important limitation was the decrease in sample size from 88 at T1 to 67 at T2. The reason for the higher refusal rate at T2 (n = 38) is not known but may have been related to cumulative toxicity, fatigue, or other psychosocial or physical factors. The extent to which women who were missing or declined to participate experience less, more, or similar peripheral neuropathy and functional status is unknown. Because a comparison of demographic and clinical characteristics between those who completed the study and those who did not indicated no particular patterns, the analyses were based on those who had complete data at T1 (N = 88) and T2 (N = 67). Also, the extent to which the 21 patients who dropped out may have experienced less, more, or similar peripheral neuropathy and

Table 7. Peripheral Neuropathy Scores at End of Treatment—Criterion Validity Assessment

	Median (25th–75th Percentile)[a]						
	CTC = 0 (n = 47)		CTC = 1 (n = 11)		CTC = 2 (n = 9)		
Structure	Score	Range	Score	Range	Score	Range	p[b]
By original structure (11-item)							
Peripheral neuropathy[c]	14	12–20	18	16–20	21	20–23	0.0116
By revised structure (9-item)							
Hand neuropathy[d]	6	5–9	8	6–9	10	8–10	0.0112
Foot neuropathy[e]	5	4–8	8	5–9	8	5–10	0.0236

N = 67

[a] Factor-base scores

[b] Spearman's rank correlation test of association

[c] Peripheral neuropathy composite: items 9–19

[d] Hand neuropathy composite: items 9, 10, 13, 16, and 18

[e] Food neuropathy composite: items 11, 14, 17, and 19

CTC—Common Toxicity Criteria score

Table 8. Score Changes in Functional Status Scale and Peripheral Neuropathy Scale Before and After Treatments

Measure	n	Median	25th–75th Percentile
By original structure (19-item)			
Physical function[a]			
Cisplatin + cyclophosphamide	25	0	–5–2
Cisplatin + paclitaxel	37	0	–1–3
Role function[a]			
Cisplatin + cyclophosphamide	25	0	–2–2
Cisplatin + paclitaxel	37	0	–2–2
Peripheral neuropathy[b]			
Cisplatin + cyclophosphamide	25	2	1–5
Cisplatin + paclitaxel	34	3	0–9
By revised structure (16-item)			
General mobility[a]			
Cisplatin + cyclophosphamide	25	0	–2–2
Cisplatin + paclitaxel	36	0	–3–3
Specific mobility[a]			
Cisplatin + cyclophosphamide	25	0	–4–1
Cisplatin + paclitaxel	38	0	–1–2
Hand neuropathy[b]			
Cisplatin + cyclophosphamide	25	1	0–3
Cisplatin + paclitaxel	37	0	0–5
Foot neuropathy[b]			
Cisplatin + cyclophosphamide	25	1	0–2
Cisplatin + paclitaxel	37	2	0–4

[a] No significant changes between pretreatment and end of treatment and no significant difference in the score change between two treatment groups; score change defined as score at the end of treatment score at pretreatment

[b] Significant changes between pretreatment and end of treatment ($p < 0.05$, signed-rank test) but no significant difference in the score change between two treatment groups

Table 9. Correlations Among Functional Status Scales and Peripheral Neuropathy Scale

	Correlation Coefficient			
Structure	1	2	3	4
By original structure (19-item)				
Pretreatment				
Physical function	1.00	0.76[a]	0.30[a]	NA
Role function	–	1.00	0.27[a]	NA
Peripheral neuropathy	–	–	1.00	NA
End of treatment				
Physical function	1.00	0.68[a]	0.24[a]	NA
Role function	–	1.00	0.19	NA
Peripheral neuropathy	–	–	1.00	NA
By revised structure (16-item)				
Pretreatment				
General mobility	1.00	0.62[a]	0.11	0.27[a]
Specific mobility	–	1.00	0.25[a]	0.32[a]
Hand neuropathy	–	–	1.00	0.58[a]
Foot neuropathy	–	–	–	1.00
End of treatment				
General mobility	1.00	0.50[a]	0.11	0.02
Specific mobility	–	1.00	0.37[a]	0.28[a]
Hand neuropathy	–	–	1.00	0.58[a]
Foot neuropathy	–	–	–	1.00

[a] Rank Correlation coefficient significantly greater than 0 ($p < 0.05$)

NA—not applicable

functional status is unknown. And lastly, the smaller sample size at T2 may have affected the outcomes of the factor analyses because it allowed an item-to-subject ratio of only 1:6 for peripheral neuropathy and 1:7 for functional status.

Implications

Patient self-report instruments have become a useful adjunct in assessing other subjective symptoms such as pain (Hay, 2002; McGuire, 1997) and fatigue (Piper et al., 1998) and also can be useful for assessing peripheral neuropathy. With minor revisions, the functional status and peripheral neuropathy scales could provide comprehensive, rapid, feasible, and psychometrically sound self-report assessment techniques for clinical purposes. For instance, nurses could use them sporadically to evaluate patients with declining functional status or increasing peripheral neuropathy. Alternatively, they could institute serial clinical assessments to identify specific neurotoxic problems and their impact on functional status as patients progress through treatment and post-treatment follow-up. This knowledge then could guide appropriate interventions, including patient education regarding safety and other issues. When peripheral neuropathy increases in the hands or feet, education can be tailored to patients' specific deficits (Almadrones & Arcot, 1999; Armstrong, Rust, & Kohtz, 1997; DeLaPena & Pyron, 1993; Furlong, 1993; Holden & Felde, 1987; Walker, 1993). And finally, the scales ultimately might be used in quality improvement projects to enhance clinical assessment and management of peripheral neuropathy, leading to better patient outcomes (Smith et al., 2002).

Peripheral neuropathy, although a widespread clinical problem, has received little attention from researchers to date (Smith et al., 2002). The psychometric analyses described build on Ostchega et al.'s (1988) preliminary research that suggested peripheral neuropathy affects physical and role function. These scales offer a feasible and comprehensive method for learning more about the natural history of peripheral neuropathy, its characteristics, and its relationship with functional status. Future research first needs to address the refinement and psychometric evaluation of the instruments. Following revision, the scales then would be appropriate for descriptive longitudinal studies undertaken to better characterize peripheral neuropathy and functional status in various populations receiving neurotoxic cancer treatment regimens. They also may be useful outcome measures in intervention studies conducted to decrease neurotoxicity secondary to chemotherapy.

In conclusion, treatment-induced peripheral neuropathy may have a profound effect on patients' functional status and QOL. Nurses and clinicians must not only have baseline assessment data regarding any preexisting peripheral neuropathy but also perform careful assessment during and after treatment. The scales described in this study, with minor modification and testing, may prove useful in patients who receive neurotoxic chemotherapy.

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