Instruments for Assessing Chemotherapy-Induced Peripheral Neuropathy: A Review of the Literature

Kristin R. Curcio, DNP, AGPCNP-BC, AOCNP

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a common and often dose-limiting side effect of chemotherapy that can result in disability and poorer quality of life. However, no standardized measurement for CIPN exists. Clinicians often base decisions for dose modification or discontinuation of a chemotherapeutic agent on patient report of subjective symptoms and physical examination.

Objectives: This review is designed to identify valid and reliable assessment tools that measure or assess CIPN in adult patients receiving chemotherapy.

Methods: A systematic literature review was conducted using PubMed, CINAHL®, and Cochrane Library. Articles were included if their primary purpose was to evaluate the psychometric properties of scales to measure CIPN in adult patients with cancer receiving neurotoxic chemotherapeutic agents.

Findings: The search yielded 143 results, with 16 articles meeting criteria for inclusion in the review. Seven unique scales and their reduced and modified versions were examined. The majority of the questionnaires were evaluated in a single tumor type, primarily with taxanes and platinum compounds. No consensus exists on the most appropriate patient self-report scale for use in the general oncology population.

Key words: chemotherapy-induced peripheral neuropathy; scales; questionnaires; instruments; psychometric properties

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Chemotherapy-induced peripheral neuropathy (CIPN) is a major dose-limiting side effect of many commonly used chemotherapeutic agents (Hershman et al., 2014; Pachman, Barton, Watson, & Loprinzi, 2011). The reported incidence of CIPN ranges from 0%–70% in patients receiving chemotherapy (Pachman et al., 2011). Common symptoms of CIPN are sensory neuropathies, including paresthesia and pain. These symptoms may resolve completely but, in many instances, are only partially reversible, leading to decreased functional status and disability (Pachman et al., 2011). Multiple pharmacologic agents have been studied for the treatment of CIPN. A randomized clinical trial by Lavoie Smith et al. (2013b), demonstrated a decrease in the mean neuropathic pain score during five weeks when comparing duloxetine (Cymbalta®) 60 mg daily with placebo in patients who had received platinum and taxane agents. However, effective treatment for CIPN remains a challenge underscoring the need for assessment of CIPN accurately and in a timely manner to reduce these side effects.

Although patient self-report scales and questionnaires have been developed to measure CIPN, they are not routinely used in clinical practice. Clinicians often use a combination of patient symptom report and physical examination to assess CIPN. A standardized assessment tool could provide clinicians with a way to identify changes in neuropathy from baseline and, if changes are noted, chemotherapy regimens can be modified with dose reductions, treatment breaks, and/or discontinuation of neurotoxic drugs before symptoms of CIPN become debilitating and potentially irreversible. This review article examines the literature on assessment of CIPN to identify tools that accurately measure or assess CIPN.
Methods

A literature review was conducted in PubMed, CINAHL®, and the Cochrane Library using the following key words and medical subject headings (MeSH) terms: neoplasms with subheading drug therapy, antineoplastic agents, peripheral nervous system diseases with subheading chemically induced, questionnaires, neurotoxicity, neuropathy, severity of illness index, and instrument®. Search terms were combined using the words “AND” and “OR.” A manual search was also performed by reviewing the reference lists of included articles for additional publications.

Articles were included in the review if (a) the primary purpose was to evaluate the psychometric properties of the scale or questionnaire, (b) the sample included patients who had cancer and were either receiving or had received neurotoxic chemotherapeutic agents, and (c) the article included an assessment of CIPN by a patient report scale or questionnaire. Articles were limited to those that included adult patients aged 18 years or older and were published in English. No limits were placed on the date of publication.

Articles were excluded if they were a review, an editorial, or a commentary; if the study was performed in a setting that was other than oncology; the focus of the article was on prevention or treatment of CIPN; or only clinician toxicity scales were evaluated (i.e., the study did not evaluate a patient self-assessment of CIPN).

Results

The PubMed and CINAHL searches yielded 143 results. No articles from the Cochrane Library search were used. Sixteen of the 143 articles met the criteria for inclusion (see Table 1). The articles described seven scales or questionnaires to assess CIPN and their reduced or modified versions. The instruments included the Peripheral Neuropathy Scale (PNS); Functional Assessment of Cancer Therapy/Gynecologic Oncology Group (FACT/GOG)–Neurotoxicity (Ntx), –Taxane, and –Neurotoxicity 12 (Ntx12) subscales; the Total Neuropathy Score (TNS) and its other versions (reduced, clinical, modified, and reduced short form); the Patient Neurotoxicity Questionnaire (PNQ); the Scale for Chemotherapy-Induced Long-Term Neuropathy (SCIN); the Quality of Life Questionnaire-CIPN20 (QLQ-CIPN20); and the CIPN Assessment Tool (CIPNAT).

Peripheral Neuropathy Scale

One article reported psychometric testing of the PNS questionnaire (Almadrones, McGuire, Walczak, Florio, & Tian, 2004), a self-report, 11-item Likert-type scale developed based on common complaints expressed by patients receiving neurotoxic chemotherapy for ovarian cancer. Questions on the PNS pertain to physical function (e.g., eating, dressing, ability to walk short distances, bending) and role function (e.g., ability to work outside the home, ability to perform household chores). Content validity was established by an expert panel of patients and physicians familiar with the symptoms (Ostchega, Donohue, & Fox, 1988). The reliability of the PNS was acceptable, with Cronbach alphas of 0.91 and 0.89 at T1 (baseline) and T2 (after six cycles of chemotherapy), respectively (Almadrones et al., 2004). In addition, the questionnaire was clinically sensitive in that the scores changed significantly from T1 to T2 (p < 0.05) (Almadrones et al., 2004).

Functional Assessment of Cancer Therapy

Four articles reported psychometric testing of the FACT/GOG-Ntx, FACT/GOG-Taxane, and FACT/GOG-Ntx12 subscales. The FACT/GOG-Ntx contains 11 items scored from 0–4, and scores are summed for a range of 11–44. Questions on the Ntx subscale pertain to the feeling of weakness all over, numbness or tingling in the hands or feet, and difficulty buttoning their buttons. The FACT/GOG-Ntx was initially developed with the input of expert clinicians and patients who reported symptoms of CIPN within the past month (Calhoun et al., 2003). The questionnaire was validated with patients diagnosed with gynecologic malignancies who received taxanes and platinum compounds, well-known neurotoxic drugs (Calhoun et al., 2003; Huang, Brady, Cella, & Fleming, 2007). Reliability was measured using Cronbach alpha of greater than 0.7, which is acceptable (Calhoun et al., 2003; Huang et al., 2007). Of note, coefficient alphas tended to be higher for sensory symptoms than for motor symptoms. Construct and/or criterion validity of the scale were measured by comparing the scores of two groups of patients, one with known CIPN and one without neuropathy. A significant difference was found between the groups (p < 0.05–0.001) (Calhoun et al., 2003). Huang et al. (2007) evaluated the questionnaire for ability to discriminate between the presence and absence of neurotoxicity by plotting a receiver operating characteristic curve. The area under the curve for the Ntx subscale was 0.81, indicating that this scale has good accuracy for a diagnostic test.

Cella, Peterman, Hudgens, Webster, and Soccinski (2003) examined the psychometric properties of the FACT-Taxane questionnaire. This questionnaire is similar to the FACT/GOG-Ntx, but this questionnaire contains 16 items in the Taxane subscale—the 11-item Ntx subscale and five additional questions that assess symptoms related to arthralgias, myalgias, and skin discoloration. The FACT/GOG-Taxane has been used with patients with non-small cell lung cancer who received platinum compounds and taxanes. The questionnaire had good reliability (Cronbach alpha = 0.84–0.88). The scale was also responsive to the change in CIPN over time (p < 0.05).

Kopiec et al. (2006) modified the FACT/GOG-Ntx by adding one item specific to oxaliplatin (Eloxatin®) and renamed this version the FACT/GOG-Ntx12. The revised version was tested in patients with colon cancer. Reliability was good (Cronbach alpha = 0.85), and the questionnaire scores were correlated with the National Cancer Institute-Sanofi criteria. The FACT/GOG-Ntx12 was also shown to be sensitive to changes in CIPN over time.

Total Neuropathy Score

Five studies examined the psychometric properties of the TNS and its other versions. The TNS was initially designed to evaluate diabetic neuropathy (Cornblath et al., 1999) and was later validated in patients with cancer experiencing neuropathy (Cavaletti et al., 2003). The TNS includes objective measures, such as pin prick, vibration threshold, and nerve conduction...
### TABLE 1. CIPN Scales and Psychometrics Evidence Review

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<th>Study</th>
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<tr>
<td>Almadrones et al., 2004</td>
<td>PNS</td>
<td>Sample included women with ovarian cancer with a mean age of 58 years (SD = 11.2). 88 women participated at T1, and 67 participated at T2. Women were chemotherapy naïve at baseline and given neurotoxic chemotherapy. CIPN was measured at baseline and at cycle 6 of chemotherapy.</td>
<td>Results showed a Cronbach alpha of 0.91, clinical sensitivity from T1 to T2 (p &lt; 0.05), and a correlation between CIPN and function (p &lt; 0.05).</td>
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<td>Calhoun et al., 2003</td>
<td>FACT/GOG-Ntx</td>
<td>Sample for study A included 56 women with epithelial ovarian cancer with a mean age of 57.15 years (SD = 12.78). Women were chemotherapy naïve at baseline and given neurotoxic chemotherapy. CIPN was measured at baseline; during chemotherapy; at the end of chemotherapy; and at 3, 6, 9, and 12 months postchemotherapy. Sample for study B included 43 women with ovarian cancer who were older than age 18 years. The women had known CIPN (grade 2 or higher). CIPN was measured at baseline and at 6, 9, and 12 months postchemotherapy.</td>
<td>For group A, Cronbach alpha for FACT/GOG-Ntx was greater than 0.8 for all time points. For group B, Cronbach alpha for FACT/GOG-Ntx was greater than 0.79 for all time points. The Ntx subscale significantly differentiated groups A and B at baseline (p &lt; 0.001) and at 3 (p &lt; 0.01) and 6 months (p &lt; 0.05).</td>
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<td>Cavaletti et al., 2003</td>
<td>TNS, TNSr</td>
<td>Sample included 60 women with squamous cervical carcinoma who received neurotoxic chemotherapy. Age was not reported.</td>
<td>TNS scores increased during chemotherapy from 2.91 (95% CI [2.43, 3.4]) at baseline to 6.66 (95% CI [5.62, 7.7]), respectively; p &lt; 0.0001 and was more sensitive in severe cases of CIPN. TNSr and TNS had a correlation (r = 0.98).</td>
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<td>Cavaletti et al., 2006</td>
<td>TNSr, TNSc</td>
<td>Sample included 218 women and 210 men with a mean age of 55 years (range = 18–77). Chemotherapy drugs included cisplatin (Platinol®)/carboplatin (Paraplatin®) (n = 172), thalidomide (Thalomid®) (n = 162), paclitaxel (Abraxane®)/docetaxel (Taxotere®) (n = 146), and vincristine (Oncovin®)/vinblastine (n = 95).</td>
<td>A highly significant correlation was found between the TNSr (r = 0.516–0.738, p &lt; 0.0001) and TNSc (r = 0.491–0.747, p &lt; 0.00001) scores and NCI CTC.</td>
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<td>Cavaletti et al., 2007</td>
<td>Study 1: TNS</td>
<td>Sample included 122 female patients ranging in age from 32–74 years. Patients received platinum/taxane combination chemotherapy.</td>
<td>Cronbach alpha ranged from 0.82–0.86 for the neurotoxicity subscale and from 0.84–0.88 for the taxane subscale. Mean score change from baseline to week 12 was 7 (p &lt; 0.001).</td>
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<tr>
<td>Cavaletti et al., 2007</td>
<td>Study 2: TNSc</td>
<td>Sample included 27 male and 24 female patients ranging in age from 44–68 years. 29 patients received thalidomide, and 32 received platinum/taxane combination chemotherapy.</td>
<td>Cronbach alpha ranged from 0.8–0.85. Correlation coefficient was 0.6–0.8 for the sensory neuropathy scores. Area under the curve of the receiver operating characteristic for the Ntx subscale was 0.81.</td>
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<td>Cella et al., 2003</td>
<td>FACT/GOG-Taxane</td>
<td>Sample included 80 males and 63 females with non-small cell lung cancer with a mean age of 62.1 years (SD = 10.3). Patients received carboplatin/paclitaxel. CIPN was measured at baseline and at weeks 6, 12, and 26.</td>
<td>Cronbach alpha ranged from 0.82–0.86 for the neurotoxicity subscale and from 0.84–0.88 for the taxane subscale. Mean score change from baseline to week 12 was 7 (p &lt; 0.001).</td>
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<td>Huang et al., 2007</td>
<td>FACT/GOG-Ntx</td>
<td>Sample included women with advanced endometrial cancer who were chemotherapy naïve at baseline. 92% of women were aged 50 years or older. 129 women received doxorubicin (Doxil®)/cisplatin, and 134 women received doxorubicin/cisplatin/paclitaxel. CIPN was measured at baseline (cycle 1) and at cycles 2 and 7.</td>
<td>Cronbach alpha ranged from 0.8–0.85. Correlation coefficient was 0.6–0.8 for the sensory neuropathy scores. Area under the curve of the receiver operating characteristic for the Ntx subscale was 0.81.</td>
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<tr>
<td>Kopczynski et al., 2006</td>
<td>FACT/GOG-Ntx12</td>
<td>Sample included patients with colon cancer. CIPN was measured at baseline, week 4 of treatment, and at 6, 12, and 18 months post-treatment. 129 males and 77 females received 5-fluorouracil (5-FU) (Adrucil®)/leucovorin. 103 participants were aged 59 years or younger, and 103 were aged 60 years or older. 240 males and 155 females received 5-FU/leucovorin/oxaliplatin (Eloxatin®). 202 participants were aged 59 years or younger, and 193 were aged 60 years or older.</td>
<td>Cronbach alpha was 0.86 at 6 months. Scores had a strong, nonlinear relationship with the NCI-Sanofi criteria at 6 months. Spearman’s rank correlation coefficient between self-reported neurotoxicity and clinical assessment was 0.53 at 6 months, and the Kruskal-Wallis test was highly significant (p &lt; 0.0001). Mean scores increased during chemotherapy from 2.91 (95% CI [2.43, 3.4]) at baseline to 6.66 (95% CI [5.62, 7.71]) in cycle 2 and 7.26 (95% CI [5.91, 8.62]) at 6 months. (Continued on the next page)</td>
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Cl—confidence interval; CIPN—chemotherapy-induced peripheral neuropathy; CIPNAT—CIPN Assessment Tool; CTC—Common Toxicity Criteria; ECOG—Eastern Cooperative Oncology Group; FACT/GOG-Ntx12—Functional Assessment of Cancer Therapy/Gynecologic Oncology Group–Neurotoxicity 12 subscale; FACT/GOG-Taxane—Functional Assessment of Cancer Therapy/Gynecologic Oncology Group–Taxane subscale; FACT/GOG-Ntx—Functional Assessment of Cancer Therapy/Gynecologic Oncology Group–Neurotoxicity subscale; mTNS—modified Total Neuropathy Score; NCI—National Cancer Institute; NPS—CIN—chemotherapy-induced neuropathy specific pain scale; PNQ—Patient Neurotoxicity Questionnaire; PNS—Peripheral Neuropathy Scale; QLQ-CIPN20—Quality of Life Questionnaire–CIPN20; TNS—Total Neuropathy Score; TNS—Total Neuropathy Score–clinical; TNSr—Total Neuropathy Score–reduced; TNSr—SF—Total Neuropathy Score–reduced short form; SCIN—Scale for Chemotherapy Induced Long-Term Neuropathy
TABLE 1. CIPN Scales and Psychometrics Evidence Matrix (Continued)

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<tr>
<td>Kuroi et al., 2009</td>
<td>PNQ</td>
<td>Sample included 35 women with advanced or metastatic breast cancer with a mean age of 54 years (range = 36–67). Participants received weekly paclitaxel. CIPN was measured at baseline, 8 weeks, and 16 weeks.</td>
<td>Sensory PNQ grade was strongly correlated with the sensory NCI CTC grade (r = 0.58) and the FACT-Taxane (r = 0.51). Motor PNQ grade was poorly correlated with the FACT-Taxane (r = 0.57).</td>
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<td>Lavoie Smith et al., 2013</td>
<td>QIQ-CIPN20</td>
<td>376 participants received neurotoxic chemotherapy and had a mean age of 59.1 years (SD = 10.8). 76% were female and 24% were male. Tumor types were not identified. 575 participants did not receive neurotoxic chemotherapy and had a mean age of 58.2 years (SD = 12). 75% were female and 25% were male. Tumor types were not identified.</td>
<td>Cronbach alphas for the sensory, motor, and autonomic scales were 0.88, 0.88, and 0.78, respectively. Mean scores were significantly higher in individuals who received neurotoxic chemotherapy compared with those who did not (p &lt; 0.0001).</td>
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<td>Oldenburg et al., 2006</td>
<td>SCIN</td>
<td>684 male testicular cancer survivors were included in the total sample, with a mean age at diagnosis of 33.7 years (SD = 10.2) and a mean age at time of survey of 45.1 years (SD = 10.7). Patients had received treatment with surgery alone (n = 146), surgery and radiation (n = 300), or surgery plus cisplatin-based chemotherapy (n = 238). In group A, mean age at diagnosis was 33.6 years (SD = 10.5), and mean age at time of survey was 44.8 (SD = 10.9). In group B, mean age at diagnosis was 33.7 years (SD = 9.9), and mean age at time of survey was 45.3 years (SD = 10.6).</td>
<td>Cronbach alpha was 0.72. The three-factor structure of the SCIN was confirmed with 77% variance explained. Sensory symptom items discriminated between patients who had received cisplatin and those who had received other drugs.</td>
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<td>Postma et al., 2005</td>
<td>QLQ-CIPN20</td>
<td>For phase I, sample included 22 males and 46 females with ovarian cancer, Hodgkin disease, non-Hodgkin lymphoma, digestive tract cancers, leukemia, lung cancer, testicular cancer, bladder cancer, endometrial cancer, brain cancer, and cancer from unknown primary site. Mean age for participants was 53 years (range = 23–79). For phase III, sample included 16 males and 28 females with ovarian cancer, Hodgkin disease, non-Hodgkin lymphoma, digestive tract cancers, breast cancer, leukemia, lung cancer, testicular cancer, and bladder cancer. Mean age for participants was 54 years (range = 32–71). All participants had previously received or were currently receiving neurotoxic chemotherapy agents.</td>
<td>Cronbach alphas for the sensory, motor, and autonomic scales were 0.82, 0.73, and 0.76, respectively.</td>
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<tr>
<td>Shimozuma et al., 2009</td>
<td>PNQ</td>
<td>Sample included 300 women with breast cancer with a mean age of 51.7 (SD = 8.9). Participants had previously received or were currently receiving neurotoxic chemotherapy.</td>
<td>PNQ and sensory and motor scores were correlated with the FACT/GOG-Ntx subscale scores (r = 0.66 and 0.51, respectively). A correlation of 0.7 was observed between PNQ sensory scores and the Ntx subscale scores. PNQ sensory scores were significantly correlated with the NCI CTC sensory scores (r = 0.44), but PNQ motor scores were not associated with NCI CTC motor scores (r = 0.16)</td>
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<td>Smith et al., 2010</td>
<td>TNSr, TNSr-SF</td>
<td>Sample included 75 females and 42 males with a mean age of 58.86 (SD = 11.66). Diagnoses included breast (n = 28), lung (n = 27), gastrointestinal (n = 25), head and neck (n = 11), genitourinary (n = 8), gynecologic (n = 13), and other (n = 5) cancers. Patients had received neurotoxic chemotherapy within the past three months.</td>
<td>Cronbach alpha of TNSr was 0.56, resulting in item deletion. Cronbach alpha of NPS-CIN was excellent (0.96).</td>
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CI—confidence interval; CIPN—chemotherapy-induced peripheral neuropathy; CIPNAT—CIPN Assessment Tool; CTC—Common Toxicity Criteria; ECOG—Eastern Cooperative Oncology Group; FACT/GOG-Ntx12—Functional Assessment of Cancer Therapy/Gynecologic Oncology Group—Neurotoxicity 12 subscale; FACT/GOG-Taxane—Functional Assessment of Cancer Therapy/Gynecologic Oncology Group—Taxane subscale; FACT/GOG-Ntx—Functional Assessment of Cancer Therapy/Gynecologic Oncology Group—Neurotoxicity subscale; mTNS—modified Total Neuropathy Score; NCI—National Cancer Institute; NPS—CIN—chemotherapy-induced neuropathy specific pain scale; PNQ—Patient Neurotoxicity Questionnaire; PNS—Peripheral Neuropathy Scale; QLQ-CIPN20—Quality of Life Questionnaire—CIPN20; TNS—Total Neuropathy Score; TNSc—Total Neuropathy Score—clinical; TNSr—Total Neuropathy Score—reduced; TNSr-SF—Total Neuropathy Score—reduced short form; SCIN—Scale for Chemotherapy Induced Long-Term Neuropathy.
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<td>Tofthagen et al., 2011</td>
<td>CIPNAT</td>
<td>Cancer types included breast, lung, colon, and gynecologic malignancies; other solid tumors; and hematologic malignancies. Sample included 167 participants with a mean age of 58 years (SD = 11.91) with breast, lung, colon, or gynecologic malignancies; other solid tumors; and hematologic malignancies. 127 participants were receiving neurotoxic chemotherapy, and 40 participants were in the comparison group. 60% of participants were female, and 40% were male. CIPNAT scores were positively and significantly correlated with the FACT/GOG-Ntx (r = 0.83, p &lt; 0.001). Test-retest scores were found on total CIPNAT (r = 0.93, p &lt; 0.001), symptom experience (r = 0.89, p &lt; 0.001), and interference items (r = 0.93, p &lt; 0.001). Cronbach alphas for the total CIPNAT, symptom experience items, and interference items were 0.95, 0.93, and 0.91, respectively.</td>
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<td>Wampler et al., 2006</td>
<td>TNS, mTNS</td>
<td>Sample included 20 women with breast cancer and 20 healthy controls with a mean age of 50.35 years (SD = 9.34). Women with breast cancer had completed taxane therapy within the past 30 days. TNS and mTNS very strongly correlated (r = 0.99, p &lt; 0.001). mTNS discriminated between treatment and control groups. Only pain did not correlate with mTNS.</td>
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studies, combined with subjective report of sensory, motor, and autonomic items (Cavaletti et al., 2003). The instrument has been tested in a variety of tumor types that were treated with platinum-derived compounds, taxanes, thalidomide, or vinca alkaloids.

The TNS and its other versions were compared to several measures to assess validity, including the National Cancer Institute Common Toxicity Criteria (NCI CTC), Ajani grading scale, Eastern Cooperative Oncology Group (ECOG) grading scale, pin prick, vibration, balance, physical performance, and quality of life (Cavaletti et al., 2003, 2006, 2007). The TNS score highly correlated with NCI CTC, Ajani, and ECOG score (r = 0.654–0.75, 0.676, and 0.666, respectively) and was more sensitive than the NCI CTC in severe cases of CIPN (Cavaletti et al., 2003, 2007). Reduced versions of the TNS were developed because the original instrument was time consuming (about one hour to complete), and oncology practices cannot perform nerve conduction studies.

The TNSr excluded the motor symptoms, autonomic symptoms, and vibration sensation sections of the TNS. The TNSr correlated with the TNS (r = 0.98) (Cavaletti et al., 2003). Cavaletti et al. (2006) demonstrated that the TNSr was moderately to strongly correlated with the NCI CTC sensory, ECOG sensory, NCI CTC motor, and ECOG motor scales (r = 0.666, 0.747, 0.491, and 0.492, respectively) (Cavaletti et al., 2006). Differences in TNSr score changes were highly significant, demonstrating that the TNSr is more sensitive in identifying sensory and motor components of CIPN than the NCI CTC (Cavaletti et al., 2007).

Wampler et al. (2006) tested the modified TNS (mTNS) in patients with breast cancer receiving taxane therapy. The mTNS is a modified version of the TNS, excluding the nerve conduction studies. The mTNS and TNS were highly correlated (r = 0.99, p < 0.001). In addition, the mTNS discriminated between the treatment and control groups.

Smith, Cohen, Pett, and Beck (2010) performed additional psychometric testing with the TNSr and a chemotherapy-induced neuropathy–specific pain scale (NPS-CIN). Reliability of the TNSr was poor (Cronbach alpha = 0.56), and the reliability of the NPS-CIN was excellent (Cronbach alpha = 0.96), leading to deletion or modification of several items. The new scale was renamed the TNSr-Short Form (TNSr-SF). Factor analysis demonstrated that the TNSr-SF and NPS-CIN formed two distinct factors, providing evidence of structural validity (Smith et al., 2010).

**Patient Neurotoxicity Questionnaire**

The psychometric properties of the PNQ were reported in two articles. This questionnaire consists of two items that identify the incidence and severity of sensory and motor disturbances, with reference to the neurosensory and neuromotor components of the clinician-based NCI CTC instrument (Shimozuma et al., 2009). The developers of the PNQ spent years interviewing and eliciting information on key symptoms of CIPN (Shimozuma et al., 2009). The sensory PNQ grade was moderately correlated with the sensory NCI CTC grade (r = 0.58, p < 0.05) and the FACT-Taxane (r = 0.51), and the motor
Quality of Life Questionnaire—Chemotherapy-Induced Peripheral Neuropathy 20

The psychometric properties of the QLQ-CIPN20 questionnaire were reported in two articles. This 20-item questionnaire evaluates sensory, motor, and autonomic symptoms and is scored using a four-point Likert-type scale ranging from 1 (not at all) to 4 (very much). Sensory raw scale scores range from 1–36, motor raw scale scores range from 1–32, and autonomic raw scale scores range from 1–12 for men and 1–8 for women. All scale scores are linearly converted to a 0–100 scale, with higher scores indicating more symptoms. The generation of items for the QLQ-CIPN20 scale was described in detail by Postma et al. (2005). Content validation included review by a panel of 15 physicians. Internal consistencies were acceptable to good (Cronbach alpha = 0.82–0.88, 0.73–0.88, and 0.76–0.78 for the sensory, motor, and autonomic scales, respectively) (Lavoie Smith et al., 2013a; Postma et al., 2005). However, low item-item correlations were found between the items on the autonomic scale and hearing loss (r ≤ 0.5) (Lavoie Smith et al., 2013a). Construct validity was measured using confirmatory factor analysis, which revealed a statistically significant chi-square (X² = 2,462.09, p < 0.01), indicating a poor fit. Exploratory factor analysis performed using Bartlett’s test of sphericity indicated that the correlation matrix was favorable (X² = 653.81, p = 0.0001), and the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was adequate at 0.83. Convergent validity was evaluated by comparing the QLQ-CIPN20 with other neuropathy measures; correlations with the Common Terminology Criteria for Adverse Events (CTCAE) sensory grading scale were weak (r = −0.2, 0.2, and 0.03, respectively), and the correlations with Brief Pain Inventory—Short Form (BPI-SF) pain severity questions were weak to moderate. Responsiveness to change over time was evaluated by calculating effect size (Cohen’s d). Based on change in sensory scores, effects were 0.82 and 0.48 for the motor scale.

Scale for Chemotherapy-Induced Long-Term Neuropathy

Oldenburg, Fossa, and Dahl (2006) reported the psychometric properties of the SCIN, which has three subscales: neuropathy (two items), Raynaud’s phenomenon (two items), and ototoxicity (two items). The SCIN questionnaire was initially developed based on interviews with testicular cancer survivors (TCSs) and a review of the literature on long-term morbidity in TCSs. The SCIN was tested with 206 TCSs, but limited psychometric evaluation was performed (Oldenburg et al., 2006). Internal consistency was reported at greater than 0.7. Oldenburg et al. (2006) used the known group’s technique to measure construct validity. A significant difference was found in scores between the chemotherapy alone group and the radiation or surgery alone group (p < 0.001), indicating that the questionnaire accurately discriminates between these groups. Criterion validity was measured by comparing the scale scores with subjective measures of CIPN, such as clinician-based toxicity criteria and other self-report neuropathy scales.

Chemotherapy-Induced Peripheral Neuropathy Assessment Tool

The psychometric properties of the CIPNAT questionnaire were described in one article. The CIPNAT was developed based on the Theory of Unpleasant Symptoms (Lenz, Pugh, Milligan, Gift, & Suppe, 1997), with information obtained from 14 people with CIPN, and was validated by five experts who recommended minor revisions (Toft Hansen, McMillan, & Kip, 2011). The questionnaire contains 36 items that evaluate the occurrence, severity, distress, and frequency of nine neuropathy symptoms and 14 items that evaluate neuropathic interference with activities. Mean scores on the CIPNAT of patients expected to have symptoms of neurotoxicity and scores of a comparison group differed significantly (t = 7.66, p < 0.01), and scores on the CIPNAT and the FACT/GOG-Ntx were highly correlated (r = 0.83, p < 0.001, n = 167). Test-retest reliability was excellent for the total CIPNAT, symptom experience, and interference items (r = 0.93, 0.89, 0.93, respectively; p < 0.001). Cronbach alphas were excellent for the total CIPNAT, the symptom experience items, and the interference items (Cronbach alpha = 0.95, 0.93, and 0.91, respectively).

Discussion

No clear consensus exists on what is the most appropriate patient self-report instrument for assessing CIPN. The FACT/GOG-Ntx and TNS (and its other versions) have been extensively studied. The FACT/GOG-Ntx has acceptable reliability and validity and is recommended for use in patients with gynecologic malignancies. However, additional studies should be conducted with other tumor types to determine if this scale is valid and reliable in these populations. The original TNS is not feasible for use in routine practice because it includes nerve conduction studies. The simplified versions of the TNS scale, including the TNSc, Tnsr, TNSr-SF, and mTNS, appear to be valid; however, data on the reliability of the mTNS and TNSr-SF are lacking, and continued psychometric testing is recommended.

The PNS, FACT-Taxane, PNQ, QIQ-CIPN20, and CIPNAT have been studied in limited ways. The FACT-Taxane and PNQ appear to be valid questionnaires to measure sensory symptoms associated with CIPN, but reliability data are lacking. Additional psychometric testing is recommended before routine use of these tools can be recommended. The PNS, QIQ-CIPN20, and CIPNAT all appear to be valid and reliable, but, because a limited number of studies have evaluated these tools, routine use is not recommended at this time.

The SCIN has been validated in patients who had previously received chemotherapy, but it is unclear whether the SCIN is appropriate for use in patients actively receiving chemotherapy. Therefore, data to recommend the use of the SCIN are lacking.

One issue with psychometric testing of CIPN instruments is that it is not entirely clear what is the most appropriate method.
Implications for Practice

- Assess for chemotherapy-induced peripheral neuropathy (CIPN) using a combination of subjective and objective measures.
- Use the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group—Neurotoxicity to assess CIPN in patients with gynecologic malignancies undergoing chemotherapy.
- Consider the Total Neuropathy Score—clinical for use in a broader oncology population because this scale has been tested on more than one tumor type.

CIPN in patients with gynecologic malignancies undergoing chemotherapy. The TNSc could be considered for use with a broader oncology population because this scale has been tested on more than one tumor type.

References


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