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Reliability and Validity of the Korean Version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire to Assess Chemotherapy-induced Peripheral Neuropathy

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Purpose: This study was performed to assess the reliability and validity of the Korean version of European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Chemotherapy-induced peripheral neuropathy 20 items (EORTC QLQ-CIPN20) in patients receiving neurotoxic chemotherapy. **Methods:** A convenience sample of 249 Korean cancer patients, previously or currently, being treated with peripheral neurotoxic chemotherapeutic agents were asked to fill in the questionnaire. Collected data were analyzed using SPSS 21.0 and AMOS 21.0. Construct validity, known-group validity, concurrent validity, and internal consistency reliability of the Korean version of the QLQ-CIPN20 were evaluated. **Results:** Factor analysis confirmed 3 dimensions of CIPN: sensory, motor, and autonomic. The factor loadings of the 20 items on the 3 subscales ranged from .38 to .85. The 3 subscale-model was validated by confirmatory factor analysis (GFI = .90, AGFI = .86, RMSR = .05, NFI = .87, and CFI = .94), and concurrent validity was demonstrated with the EORTC QLQ-C30. Furthermore, the QLQ-CIPN20 established known-group validity. The Cronbach's alpha coefficients for internal consistency of the subscales ranged from .73 to .89. **Conclusion:** The Korean version of the EORTC QLQ-CIPN20 showed satisfactory construct, concurrent, and known-group validity, as well as internal reliability.

Key words: Validity, Reliability, Chemotherapy, Peripheral neuropathies

INTRODUCTION

Chemotherapy indiscriminately affects both cancerous and normal cells, leading to systemic complications. Platinum-based chemotherapy agents, taxanes, and vinca alkaloids often damage nerve fibers, leading to chemotherapy-induced peripheral neuropathy (CIPN)[1], a major, distressing side effect of neurotoxic chemotherapy[2]. CIPN, a dysfunction of motor, sensory, and/or autonomic neurons, results in peripheral neuropathic signs and symptoms, such as tingling, numbness, and burning or shooting pain. The incidence of CIPN varies according to the type of chemotherapeutic agent, cumulative dose, patients' comorbidities, and other as-yet-unidentified risk factors[3], and CIPN is estimated

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to occur in 30~70% of patients treated with chemotherapy[4,5].

Most CIPN symptoms dissipate within a few weeks or months after the final chemotherapy administration. For some patients, however, the symptoms take years to fade or may even persist without improvement. These symptoms negatively affect quality of life (QOL) by reducing activities of daily living and exercise[6-8], which may be particularly important during cancer treatment and recovery[3]. Furthermore, the neuropathy may be so severe that it necessitates limiting the administered dose of chemotherapy, thus reducing the potential for curative treatment[3,9]. Therefore, it is important for both clinical oncology research and practice to periodically evaluate CIPN in a valid and reliable manner and effectively manage CIPN symptoms[2].

Several grading scales can be used to assess the severity of CIPN based on physical examinations: the National Cancer Institute's Common Terminology Criteria for Adverse Events version 3.0, the Eastern Cooperative Oncology Group (ECOG) Neuropathy Scale, and the CIPN scale developed by the World Health Organization. Although such grading scales are effective, they are limited because they are uni-dimensional in nature and lack sensitivity and specificity[10-12]. Instruments used to evaluate neuropathic symptoms, such as the Total Neuropathy Scale, the Neuropathy Symptom Profile, and the Neurological Disability Score, do not provide information on severity, distress, timing, or impacts on daily activities[2].

A patient-reported QOL questionnaire assessing CIPN (QLQ-CIPN20) was designed as an outcome instrument to supplement the European Organization for Research and Treatment of Cancer (EORTC) QOL questionnaire[2,13]. The QLQ-CIPN20 contains 3 subscales that evaluate sensory, motor, and autonomic symptoms and functioning[2]. The validity and reliability of this instrument were verified through multisite international study[13], and numerous recent studies have used it to measure CIPN-related symptoms[14-16]. The QLQ-CIPN20 is valuable because it provides subjective, patient-reported information that is not captured by objective physical examinations, nerve conduction studies, or quantitative sensory testing. Furthermore, the QLQ-CIPN20 is particularly important as it provides information that can aid decisions making for determining the need for dosage adjustments prior to each chemotherapy administration[2].

The QLQ-CIPN20 has been widely translated and used to assess CIPN-related symptoms [13,14,16]. Many oncologists are also interested in CIPN-related symptoms and need a valid and reliable CIPN questionnaire[15,17, 18], The EORTC QLQ-CIPN20 has been translated and back translated into Korean, but the applicability and final version of the EORTC QLQ-CIPN20 needs to be confirmed through cross-cultural validation with Korean cancer patients. Therefore, the purpose of this study was to examine the psychometric properties of the Korean version of the EORTC QLQ-CIPN20 in order to establish its utility in oncology clinical practice and research.

METHODS

1. Study design

This study adopted a methodological research design to test the validity and reliability of the Korean version of the QLQ-CIPN20.

2. Pilot tests

The first interim Korean version of the EORTC QLQ-CIPN20 was produced by EORTC Quality of Life Group using rigorous translation and back translation processes[19]. After obtaining the first interim version from the EORTC Quality of Life Group, the first pilot test was performed from September 3 to 21, 2012, with 18 cancer patients undergoing chemotherapy with regular follow-up care in the outpatient clinic of Chonnam National University Hwasun Hospital in Korea. The pilot test results indicated that all the items except number 9 and 14 were not associated with difficulty in answering, nor were they confusing, difficult to understand, upsetting, or offensive. In addition, no patient indicated that they would ask these questions in a different way. Therefore, "Did you have problems standing or walking because of difficulty feeling the ground under your feet?" in question 9 was revised to "Did you have problems standing or walking because feeling the ground under your feet had decreased?" In addition, "Did you have difficulty walking because your feet dropped downwards?" in question 14 was revised to "Did you have difficulty walking because of dropping symptoms in your feet downwards?" Thus, by modifying questions 9 and 14, we completed the second intermediary version. With the second version, we performed a second pilot test with 10 hematology/oncology cancer patients from September 28 to October 12, 2012. This time none of the items were associated with difficulty for any of the patients. Finally the second version of the QLQ-CIPN20 in Korean was approved by the EORTC Quality of Life Group and ready for psychometric evaluations.

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3. Participants and data collection

Data for psychometric evaluation of the QLQ-CIPN20 in Korean was collected from January to May 2013. The convenience sample was 249 cancer patients previously treated or currently being treated with peripheral neurotoxic chemotherapeutic agents, including paclitaxel, oxaliplatin, vincristine, thalidomide, cisplatin, vinorelbine, and bortezomib, at Chonnam National University Hwasun Hospital and Chonbuk National University Hospital in South Korea. All patients underwent neurological examination by an oncologist to assess the presence of CIPN. Patients in this study were at least 18 years old, able to provide written consent, and able to complete study questionnaires. Those who had shown symptoms before being exposed to chemotherapeutics were excluded from the study.

The required sample size for testing the reliability and validity of a measuring tool is 5 times the number of items, or preferably 10 times the number of items to ensure the reliability of the tests[20]. The sample size in this study was 249 for 20 items. Thus, it satisfied the required sample size.

Ethical approval was obtained in September 2012 from the Institutional Review Boards (IRB) at Chonnam National University Hwasun Hospital (IRB No. 2012-148) and Chonbuk National University Hospital (IRB No. 2012-10-002-001). Participants provided written consent to take part in the survey after being informed about the study such as purpose, procedure, voluntary participation, guaranteed anonymity, and the possibility to leave the study any time. It took participants an average of 15~20 minutes to complete the study questionnaire consisting of items about participants' general and clinical characteristics and two instruments from the EORTC, QLQ-CIPN20 and QLQ-C30.

4. Instruments

1) Quality of life questionnaire - chemotherapy-induced peripheral neuropathy

The QLQ-CIPN20 was designed for use among a wide range of cancer patients of various disease stages who have been treated with potentially neurotoxic chemotherapy, and it comprises 20 items (each using a 4-point Likert scale) assessing peripheral neuropathic side effects of chemotherapy. The QLQ-CIPN20 included 3 subscales assessing sensory (9 items), motor (8 items), and autonomic (3 items) symptoms and functioning[2]. The individual items and multi-item scales were scored such that higher scores represented more symptoms/problems (i.e., higher score = worse). The scores were converted to a 100-point scale according to the scoring manual[21]. The EORTC QLQ-CIPN20 was shown to have internal consistency reliability on the basis of Cronbach's alpha coefficients of .82, .73, and .76 for the sensory, motor, and autonomic scales, respectively[2].

2) Quality of life questionnaire

To evaluate the concurrent validity of the Korean version of the QLQ-CIPN20, we used the Korean version of the QLQ-C30 version 3.0[22], which was translated and validity-tested from the QLQ-C30 (version 3.0) in English and developed by EORTC[23]. This instrument comprised of 3 subscales: global health status (2 items), functional (15 items assessing physical, role, emotional, cognitive, and social aspects), and symptom (13 items assessing fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial problems). The 2 global health status-related items were scored using a 7-point scale, and the functional and symptom items were scored using a 4-point scale. The scores were converted to a 100-point scale according to the scoring manual[21], with QOL increasing in proportion to the global health status and functional scale scores. In contrast, the lower the symptom scale score, the higher the QOL. In a study by Yun et al., the Cronbach's alpha coefficient was .70 or higher in all but the cognitive functional scale (.60)[22]. In the present study, the Cronbach's alpha coefficients were .77, .83, and .78 for the global health status, functional, and symptom scales, respectively.

3) Eastern Cooperative Oncology Group performance status

To verify the known-group validity of the Korean version of the QLQ-CIPN20, we used the Eastern Cooperative Oncology Group performance status (ECOG PS)[24], which classifies physical activity status of cancer patients into scores from zero to five; the score of zero representing fully active, able to carry out all pre-disease tasks without restriction; one representing restricted from physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work and office work; two representing ambulatory, capable of all self-care but unable to carry out any work activities, and up and about more than 50% of waking hours; three representing capable of only limited self-care and confined to bed or chair more than 50% of waking hours; four representing completely disabled, unable to carry out any self-care, and totally confined to bed or chair; and five being dead. The ECOG PS scores, which were assessed by the doctors at the time of administering the QLQ-CIPN20 questionnaire, were collected from the

electronic medical records of the patients.

4) General and clinical characteristics

A total of 10 items were used to assess age, gender, occupation, education level, type of cancer, duration of diagnosis, cancer stage, current chemotherapy, major chemotherapeutic drug regimen, and duration of CIPN.

5. Data analysis

Data were managed and analyzed using SPSS® version 21.0 and AMOS 21.0. A 5% level of statistical significance was used. Descriptive statistics on the general and clinical characteristics of participants, such as percentage, mean, and standard deviation, were calculated. Internal consistency was determined using Cronbach's alpha coefficient.

The construct validity test was confirmed based on the construct reliability of substructures, convergent and discriminant validity between substructures, and a model fit test of the entire structure by item as determined through confirmatory factor analysis (CFA). Concurrent validity was determined by Pearson correlations with the QLQ-C30. To assess the known-group validity of the instrument, the differences in QLQ-CIPN20 scores according to the ECOG PS group classification were analyzed with one-way ANOVA.

RESULTS

1. Participants' characteristics

The general and clinical characteristics of the participants are summarized in Table 1. The mean age was 59.92 years (SD=11.62), and 54.6% (n=136) of participants were women. In addition, 77.1% (n=192) of the participants were unemployed, and 58.7% (n=146) had high school or a higher level of education. Thirty-two point nine percent (n=82) of the participants had breast cancer, and 20.5% (n=51) and 28.5% (n=71) had colorectal cancer and hematological malignancies (a combination of the participants with malignant lymphoma, multiple myeloma, and leukemia), respectively. Forty point one percent (n=100) of patients had a duration of diagnosis of 1 year or less, and 58.4% (n=104) of solid tumor patients had stage 4 disease. Sixty-seven point nine percent (n=169) of participants were receiving chemotherapy at the time of study. With regard to the duration of CIPN, 29.3% (n=73) of patients had experienced CIPN for <5 months, 27.3% (n=68) for 5~12 months, and 24.1% (n=60) for >2 years. Finally, 28.5% (n=71) of patients had an ECOG PS score of 0, 60.6% (n=151) had a score of 1, and 10.9% (n=27) had a score of 2 (Table 1).

2. Reliability

The Cronbach's alpha coefficient for internal consistency was .88 for the QLQ-CIPN20. The Cronbach's alpha coefficients for the sensory, motor, and autonomic subscales in the QLQ-CIPN20 were .89, .88, and .73, respectively (Table 2).

Table 1. General and Clinical Characteristics (*N*=249)

Characteristics	Categories	n (%)	M ± SD
Age (year)	<49	50 (20.1)	59.92 ± 11.62
	50-59	84 (33.7)	
	60-69	61 (24.5)	
	≥70	54 (21.7)	
Gender	Female	136 (54.6)	
	Male	113 (45.4)	
Occupation	Employed	57 (22.9)	
	Unemployed	192 (77.1)	
Education	Under or equal to elementary school graduate	62 (24.9)	
	Middle school graduate	41 (16.4)	
	High school graduate	101 (40.6)	
	Over or equal to college graduate	45 (18.1)	
Type of cancer	Breast cancer	82 (32.9)	
	Colon & rectal cancer	51 (20.5)	
	Gastric cancer	24 (9.6)	
	Esophageal cancer	4 (1.6)	
	Bile duct cancer	5 (2.8)	
	Ovarian cancer	4 (1.6)	
	Lung cancer	3 (1.2)	
	Malignant lymphoma	31 (12.4)	
	Multiple myeloma	32 (12.9)	
	Leukemia	8 (3.2)	
	Others	5 (1.3)	
Time since diagnosis (month)	<5	35 (14.0)	
	5-12	65 (26.1)	
	13-24	48 (19.3)	
	25-36	37 (14.9)	
	37-48	18 (7.2)	
	≥49	46 (18.5)	
Stage (n=178)	Stage 2	22 (12.4)	
	Stage 3	52 (29.2)	
	Stage 4	104 (58.4)	
Current chemotherapy	Yes	169 (67.9)	
	No	80 (32.1)	
Duration of CIPN (month)	<5	73 (29.3)	
	5-12	68 (27.3)	
	13-24	48 (19.3)	
	≥25	60 (24.1)	
ECOG PS	0	71 (28.5)	
	1	151 (60.6)	
	2	27 (10.9)	

CIPN=Chemotherapy-induced peripheral neuropathy; ECOG PS=Eastern Cooperative Oncology Group performance status.

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3. Validity

The construct validity test was confirmed based on the construct reliability of substructures, convergent validity and discriminant validity between substructures[25], and a model fit test of the entire structure in item as determined through CFA.

The items within the QLQ-CIPN20 showed a correlation that varies between .42 and .54 (Table 2). The substructures of the QLQ-CIPN20 (sensory, motor, and autonomic subscales) showed that the composite reliability (CR) for all 3 substructures had a standard value of =.70[25]. The CR for the sensory subscale was the highest (.90), and the CR for the autonomic subscale was the lowest (.74). The average variance extracted (AVE) for each of the substructures was .50, .52, and .60 for the sensory, motor, and autonomic subscales, respectively. Thus, all satisfied the AVE standard value of =.50[25]. In addition, the AVE was larger than the squared value of the inter-subscale correlations (Table 2), confirming convergent and discriminant validity between the substructures[25].

The model fit of the QLQ-CIPN20 was analyzed using CFA. The results showed that χ^2 =231.89 (df=147), which was significant. The CFA results showed goodness of fit (GFI), adjusted goodness of fit index (AGFI), root mean square residual (RMSR), normal fit index (NFI), and comparative fit index (CFI) values of .90, .86, .05, .87, and .94, respectively (Table 3).

The factor loading analysis of each item resulted in values =.5 in all items except for 2 (range=.54-.85, Table 2). In this study, the items having low factor loading were "Did you have cramps in your hands?" (.38) and "If you are a man, did you have difficulty getting or maintaining an erection?" (.39). To examine whether the suitability of the overall model increases when these 2 less-explanatory items are excluded, a comparative analysis was performed between the suitability of Model 1 (with the 2 items) and Model 2 (without the 2 items). When analyzing the validity of the QLQ-CIPN20 with latent variables of all 20 items (Model 1) against that of the model with 18 items (Model 2), the GFI, AGFI, RMSR,

Table 2. Construct Validity and Reliability

Constructs	Items	Factor loading	Error estimate	CR	AVE	Inter-subscale correlation	Cronbach's alpha
Sensory	Did you have tingling fingers or hands?	.62	.46	.90	.50	.42~.53*	.89
	Did you have tingling toes or feet?	.70	.43				
	Did you have numbness in your fingers or hands?	.68	.44				
	Did you have numbness in your toes or feet?	.72	.38				
	Did you have shooting or burning pain in your fingers or hands?	.66	.44				
	Did you have shooting or burning pain in your toes or feet?	.67	.45				
	Did you have problems standing or walking because of difficulty feeling the ground under your feet?	.85	.29				
	Did you have difficulty distinguishing between hot and cold water?	.54	.55				
	Did you have difficulty hearing?	.54	.55				
Motor	Did you have cramps in your hands?	.38	.78	.89	.52	.53~.54*	.88
	Did you have cramps in your feet?	.70	.50				
	Did you have a problem holding a pen, which made writing difficult?	.80	.38				
	Did you have difficulty manipulating small objects with your fingers (for example, fastening small buttons)?	.71	.40				
	Did you have difficulty opening a jar or bottle because of weakness in your hands?	.83	.30				
	Did you have difficulty walking because your feet dropped downwards?	.67	.47				
	Did you have difficulty climbing stairs or getting up out of a chair because of weakness in your legs?	.68	.49				
	If you drive a car, did you have difficulty using the pedals?	.66	.44				
Autonomic	Were you dizzy when standing up from a sitting or lying position?	.83	.30	.74	.60	.42~.54*	.73
	Did you have blurred vision?	.78	.39				
	If you are a man, did you have difficulty getting or maintaining an erection?	.39	.75				

*p<.001; CR=Composite reliability; AVE=Average variance extracted.

Table 3. Model Fit Test

Model	Items	Absolute fit index					Incremental fit index	
		χ^2 (p)	χ^2/df	GFI	AGFI	RMSR	NFI	CFI
Model 1	20	231.89 (<.001)	1.58	.90	.86	.05	.87	.94
Model 2	18	209.66 (<.001)	1.58	.91	.87	.05	.87	.95

GFI=Goodness of fit index; AGFI=Adjusted goodness of fit index; RMSR=Root mean square residual; NFI=Normal fit index; CFI=Comparative fit index.

NFI, and CFI values were .90, .86, .05, .87, and .94 and .91, .87, .05, .87, and .95, respectively. Thus, when the suitability index of Model 2 was compared to Model 1, the value improvement was very slight. Therefore, the 2 items with low factor loading were not excluded, and the QLQ-CIPN20 with all 20 items was chosen as the final model (Table 3).

When testing correlations between the substructures of the Korean version of the QLQ-CIPN20 and QLQ-C30, all had p values of .001 or less (Table 4).

Known-group validity estimates how well the QLQ-CIPN20 discriminates between groups. To test known-group validity, the QLQ-CIPN20 subscale scores between groups classified by the ECOG PS were compared with ANOVA. The results showed statistically significant differences between ECOG PS groups in all sensory, motor, and autonomic subscales ($F=13.28$, $p<.001$; $F=12.62$, $p<.001$; $F=10.34$, $p<.001$). In other words, groups with poor physical activity status had higher CIPN scores (Table 5).

DISCUSSION

The EORTC recently developed the QLQ-CIPN20 instrument, including 3 subscales assessing sensory (9 items), motor (8 items), and autonomic (3 items) symptoms, to measure CIPN as a subcategory of QOL. Because peripheral neuropathy mostly involves subjectively experienced symptoms, understanding patients' subjective symptoms is considered as important as objective evaluation[2]. The purpose of this study was to assess the reliability and validity of the Korean translation of the QLQ-CIPN20, an internationally developed, patient-reported questionnaire. The results provide support for the validity and reliability of this version in measuring CIPN-related symptoms in Korean population.

First, through two rounds of pilot tests, the present study partially revised questions 9 and 14 in the interim Korean version of the QLQ-CIPN20 that underwent rigorous translation and back translation processes by the EORTC Quality of Life Group. Then, a psychometric evaluation was performed upon approval of the revised items from the EORTC Quality of Life Group.

In this study, the Cronbach's alpha coefficient was .88 for the overall instrument and ranged from .73 to .89 for each substructure. Thus, the reliability of the measured variable satisfied the standard of =.70[26]. These results are similar to those of Postma et al.[2] who reported Cronbach's alpha coefficients between .73 and .82 for cancer patients who were previously or currently being treated with peripheral neurotoxic chemotherapeutic agents. Relatively high coefficients were shown, ensuring instrument reliability.

In this study construct validity, concurrent validity, and known-group validity were used as methods of testing validity. To test construct validity, χ^2 statistics, GFI, AGFI, RMSR, NFI, and CFI were calculated through CFA. The χ^2 statistic assesses whether the actual data corresponds to the model in CFA. However, when the sample size increases, it generally becomes significant. Thus, in this research many other suitability indicators were examined in addition to χ^2. The RMSR should be less than .05, and GFI, AGFI, NFI, and CFI should be .70 at a minimum; the suitability of the model is good when it is .90 or more[25]. The AGFI and NFI for all 20 items were at least .70, and the GFI and CFI values were especially high ($\geq .90$). The AGFI and NFI were .86 and .87, respectively, falling marginally short of the gold standard while all the other suitability indicators met the gold standard. Construct validity was deemed as established based on the validity test in a previous study that reported similar results to that of our goodness of fit test through CFA[27]. Validity testing was also attempted in this research by comparing the suitability of the model 1 including all 20 items with a model 2 excluding two items having

Table 4. Correlations between the QLQ-C30 and QLQ-CIPN20 for Concurrent Validity

QLQ-C30	QLQ-CIPN20		
	Sensory	Motor	Autonomic
	r (*p*)	r (*p*)	r (*p*)
Global health status	-.32 (<.001)	-.28 (<.001)	-.30 (<.001)
Functional	-.51 (<.001)	-.58 (<.001)	-.60 (<.001)
Symptom	.49 (<.001)	.51 (<.001)	.57 (<.001)

QLQ-C30=Cancer Core Quality of Life Questionnaire 30 items; QLQ-CIPN20=Quality of life questionnaire chemotherapy-induced peripheral neuropathy 20 items.

Table 5. Known-group Validity Tests

ECOG PS	QLQ-CIPN20					
	Sensory		Motor		Autonomic	
	M ± SD	F (*p*)	M ± SD	F (*p*)	M ± SD	F (*p*)
0	15.39 ± 16.12	13.28 (<.001)	14.92 ± 16.51	12.62 (<.001)	30.97 ± 19.51	10.34 (<.001)
1	28.73 ± 19.57		26.72 ± 19.48		37.18 ± 20.35	
2	39.23 ± 19.85		37.45 ± 17.37		55.00 ± 22.78	

ECOG PS=Eastern Cooperative Oncology Group performance status; QLQ-CIPN20=Quality of life questionnaire chemotherapy-induced peripheral neuropathy 20 items.

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slightly low factor loading values. The results did not reveal much difference between the suitability indexes of the two models, and the original instrument was therefore selected. This is advantageous, as the degree of CIPN-related symptoms among Korean cancer patients can be compared with research from other countries. In addition, the model 2 without the two items can be reevaluated in future research.

In order to verify the concurrent validity, the QLQ-C30 questionnaire was utilized in this study to assess the "cancer-related quality of life" variables, which have been suggested by previous studies to be intimately associated with CIPN-related symptoms of cancer patients [6-8,15,17,18]. The QLQ-C30 evaluates attributes that are similar to those evaluated by the QLQ-CIPN20, as it measures cancer treatment-related functional and symptomatic quality of life, whereas the QLQ-CIPN20 measures the degree of CIPN-related symptoms and loss of functions. Thus, our work suggests that the QLQ-C30 is an adequate tool to verify the concurrent validity of the QLQ-CIPN20 because the degree of CIPN-related symptoms experienced by patients can affect their perceptions of cancer-related quality of life. In this study, significant correlations were found between the subscales of the QLQ-CIPN20 and QLQ-C30. However, the range of correlation coefficients for the global health status subscale of the QLQ-C30 and for the subscales of the QLQ-CIPN20 were -.28 to -.30, and thus did not fall within the recommended range for correlation coefficients (r=.40 to r=.80) for establishing concurrent validity[28]. Such a low correlation is presumed to be because the global health status subscale consists of two items that represent the overall health condition, whereas the functional and symptom subscales of the QLQ-C30 measure the degree of symptoms and loss of functions that arise as a result of cancer treatment. Future research should be conducted to evaluate the concurrent validity by testing of the relation of the EORTC QLQ-CIPN20 with directly comparable objective and subjective CIPN instruments.

Finally, this study was the first in which the known-group validity of the QLQ-CIPN20 instrument was assessed. Recently, verification of known-group validity (also known as clinical validity) was performed by some nursing researchers in Korea[29,30]. In particular, health-related QOL scales reflect the impact of the health status by yielding scores that differ between groups in hypothesized ways in a previous study[29]. According to previous studies, the physical activity status of cancer patients is closely linked to CIPN-related symptoms. That is, the lower the patient's physical activity status, the more CIPN-related symptoms the patient reports[15,17,18]. Hence, a significant difference in the CIPN scores of the groups with different physical activity statuses would indicate the known-group validity of the QLQ-CIPN20. Analysis of the differences in CIPN mean scores for each group according to the ECOG PS classification was carried out in this research. As groups with poor physical activity status showed a higher degree of CIPN-related symptoms, the known-group validity of the QLQ-CIPN20 instrument was considered to be established.

In sum, in this study verification of the reliability and validity of the Korean version of the EORTC QLQ-CIPN20, which was composed identically to the original instrument, without excluding any items was accomplished. In addition, as the reliability and validity between each substructure were verified, the degree of CIPN symptoms can be understood in greater depth if the score for each subcategory is examined (sensory, motor, and autonomic). Patients can also identify areas with high and low scores, thus helping to manage symptom areas showing relatively higher scores. However, the limitation of this research is there was no test for responsiveness, which assesses the change in degree of patient-reported CIPN symptoms over time. Therefore, there is a need to test responsiveness through a future longitudinal study. Additionally, the concurrent validity with other subjective and objective CIPN measures was not evaluated in this study. Concurrent validity should be evaluated in future research via testing of the EORTC QLQ-CIPN20's relation with directly comparable other objective and subjective CIPN instruments. In addition, future research should be conducted to evaluate the 2 items that had relatively low factor loading.

CONCLUSION

In conclusion, the final Korean version of the EORTC QLQ-CIPN20 showed adequate reliability and validity among Korean cancer patients experiencing CIPN. As no items had to be excluded from the analysis results to enhance reliability and validity, the original 20 items were retained. The final Korean version of the QLQ-CIPN20 is appropriate for assessing CIPN-related symptoms and their impact on patients' daily lives. Thus, this version will be a useful instrument in clinical trials investigating peripheral neurotoxic chemotherapy and/or potential neuroprotective agents in Korean oncology patient populations. Further research is warranted to investigate responsiveness to changes over time for the QLQ-CIPN20.

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