

## Relationship between Chemotherapy-induced Peripheral Neuropathy and Quality of Life in Patients with Hematologic Malignancies

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**Purpose:** This study was aimed to identify the incidence and severity of chemotherapy-induced peripheral neuropathy (CIPN) among patients with hematologic malignancies and to examine the relationship between the quality of life (QOL) and CIPN. **Methods:** A total of 66 patients with CIPN-related symptoms participated in this study. Data were collected through self-reported questionnaires consisted of the European Organization for Research and Treatment of Cancer QLQ-C30 version 3.0 and the 16-item QLQ-CIPN20. Data were analyzed with SPSS/WIN20 for descriptive statistics using the Mann-Whitney and Kruskal-Wallis tests, and Spearman's rho. **Results:** The mean lower and upper extremity scale scores were 31.95 and 23.16 respectively for the 16-item QLQ-CIPN20. The mean QLQ-C30 subcategory scores were 46.84 for global health status, 58.72 for functional scales, and 34.85 for symptom scales. The CIPN-related lower extremity scale symptoms correlated negatively with the QOL subscales. There was no correlation between CIPN-related upper extremity symptoms and health-related QOL. **Conclusion:** Patients with hematologic malignancies treated with neurotoxic chemotherapeutic agents had CIPN-related symptoms in the lower extremities mainly, and their QOL functional subscale scores were relatively lower than those of other cancer patients. Interventions need to be developed for patients with hematologic malignancies to alleviate CIPN and enhance their QOL.

**Key Words:** Quality of life, Chemotherapy, Peripheral neuropathies, Hematologic malignancy

### INTRODUCTION

Cancer patients treated with neurotoxic chemotherapeutic agents may develop chemotherapy-induced peripheral neuropathy (CIPN)[1]. Comprised of motor, sensory, and/or autonomic neuron dysfunction and resulting in peripheral neuropathic signs[2], indolent symptoms of CIPN include numbness, loss of postural balance, muscle weakness, tingling, systemic weakness, and concentration disorders. Pain may manifest as burning, myalgia (muscle pain), stabbing, or prickling[3] and is dependent upon the type of chemotherapeutic agent used; cumulative chemotherapy agent dosages; prior

chemotherapy treatments[4] the presence of diabetic mellitus, alcohol abuse, or nutrient deficiencies and patient age[5]. CIPN concomitant with hereditary neuropathy is associated with a higher risk of severe and irreversible CIPN[5].

The prevalence and morbidity rates of CIPN, which have major dose-limiting toxic effects, vary widely with regard to drug type, dose, and the patients' pathological entities[3]. Neurotoxic chemotherapeutic agents, such as vincristine, thalidomide, lenalidomide (a thalidomide analogue), and bortezomib, are components of regimens for hematologic malignancies, including acute lymphocytic leukemia (ALL), non-Hodgkin lymphoma (NHL), and multiple myeloma (MM). Vincristine is used

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to treat ALL and MM, and vincristine-induced peripheral neuropathy morbidity accounts for approximately 70% of all CIPN cases in patients with malignant lymphoma[5]. Thalidomide, lenalidomide, and bortezomib are widely used as primary therapies for MM. The prevalence of thalidomide-induced CIPN is reported to be up to 50%, with the motor dysfunction occurs in 30~40% of cases[6]. When used after exposure to thalidomide, bortezomib, or vincristine, lenalidomide can cause mild to severe CIPN[6]. The incidence rate of bortezomib-induced CIPN in patients with newly diagnosed MM ranged from 11% to 81%[7-9], and rigorous measures are required to control bortezomib-induced CIPN as demonstrated by its severity-dependent dosimetry guidelines [10]. Given the risks involved, it is crucial to assess the relevance of CIPN, identify high-risk factors for CIPN prior to administering known neurotoxic agents, and conduct routine CIPN monitoring and medical interventions to alleviate CIPN symptoms in accordance with therapy plans.

The exacerbation of CIPN symptoms due to a lack of adequate CIPN-related symptom identification and early intervention can lead to dose reductions and therapy postponement or discontinuation, thus affecting therapy outcomes[8] and daily patient activities, such as enjoying pleasant events, pursuing hobbies, and sleeping, which exert negative influences on patient quality of life (QOL) [11-14]. Therefore, intensive studies are currently underway to prevent and alleviate CIPN symptoms[15-19], and attempts are being made to standardize CIPN assessments[20]. Nevertheless, there are a limited number of studies concerning the QOL of cancer patients who experience CIPN-related symptoms[11,20,21], and studies on the CIPN-QOL relationship in patients with hematologic malignancies are rare.

This study aimed to provide basic data regarding the management of CIPN-related symptoms in patients with hematologic malignancies receiving therapy with neurotoxic agents. Manifested peripheral neuropathy characteristics were itemized by performing a secondary data analysis according to the study by Kim et al.,[22]. Specifically, this study had the following objectives: 1) to determine the degree of relevancy between CIPN-related symptoms and health-related QOL in patients with hematologic malignancies, 2) to determine score differences between the CIPN-related symptoms and health-related QOL of patients with hematologic malignancies according to their general and clinical characteristics, and 3) to determine the relationship between CIPN-related symptoms and health-related QOL of patients with hemato-

logic malignancies.

## METHODS

### 1. Study Design

This study was a descriptive survey study, which aimed to determine the characteristics of CIPN and the degree of QOL experienced by patients with hematologic malignancies treated with neurotoxic chemotherapeutic agents.

### 2. Participants

This study was a secondary data analysis based on the study by Kim et al.,[22]. Kim et al.,[22] verified the reliability and validity of the Korean version of the European Organization for Research and Treatment of Cancer quality of life questionnaire - chemotherapy-induced peripheral neuropathy (EORTC QLQ-CIPN20) on patients with solid tumors (including breast, gastric, and colorectal cancers) and hematological malignancies (malignant lymphoma, MM, and leukemia) after obtaining approval from the Institutional Review Boards (IRB) of the C National University H Hospital, located in J Province (IRB No 2012-148), and the C National University Hospital, located in J Province (IRB No 2012-10-002-001), in South Korea.

Inclusion criteria for this study were an age 18 years, medical records showing treatment with 1 or more neurotoxic chemotherapeutic agents, including vincristine, thalidomide, bortezomib, and lenalidomide, and the experience of peripheral neuropathy. The presence or absence of symptoms was verified in screened patients and, among patients with symptoms, those who understood the purpose of this study and agreed to participation were included. Patients experiencing symptoms before exposure to chemotherapeutic agents were excluded. ALL, NHL, and MM patients who experienced CIPN-related symptoms were the participants of the secondary data analysis. The number of patients with hematologic malignancies in the study by Kim et al., was 71; however, the current study used data from 66 patients after excluding 2 patients with acute myelocytic leukemia (AML) and 3 patients with inexact data.

The number of participants needed was calculated according to Cohen's sampling formula using the sample size calculation program G\*power 3.1.3. Based on the calculation results, with a correlation analysis significance level of .05, a medium effect size (d) of .30, and a

power of .80, the minimum sample size required for this study was 64[23].

### 3. Measurement

#### 1) General and clinical characteristics

The questionnaire form contained 13 questions concerning gender, age, education level, employment status, Eastern Cooperative Oncology Group performance status (ECOG PS), diagnosis, duration of diagnosis, current chemotherapy, duration of CIPN, and exposure to neurotoxic agents.

#### 2) Chemotherapy-induced peripheral neuropathy (CIPN)

CIPN was assessed using the 16-item QLQ-CIPN20, which was validated by Smith et al.,[24]. The original EORTC QLQ-CIPN20, developed by Postma et al.,[2] as a subscale of the European Organization for the Research and Treatment of Cancer quality of life questionnaire core 30 items (EORTC QLQ-30), was comprised of 20 questions (on a 4-point Likert scale) that assessed CIPN, and included 3 subscales to assess motor (8 items), sensory (9 items), and autonomic (3 items) symptoms, as well as function [2]. Three items from the autonomic scale ("Were you dizzy when standing up from a sitting or lying position?", "Did you have blurred vision?", and "Did you have difficulty getting or maintaining an erection?") and 1 item from the sensory scale (Did you have difficulty hearing?) were eliminated from the 20-item original tool because of low inter-item correlations[24]. A factor analysis performed after omitting these 4 yielded 2 factors, the "lower extremity CIPN" and "upper extremity CIPN" subscales. According to the tool's scoring guidelines, the higher the score, the higher the degree of severity of CIPN-related symptoms along a score range of 0-100[25]. Smith et al., determined the Cronbach's  $\alpha$  coefficient of the 16-item QLQ CIPN20 to be .90 (.84 in our study) for the lower extremity subscale and .91 (.70 in our study) for the upper extremity subscale[24].

#### 3) Quality of life (QOL)

To assess health-related QOL, we used the Korean version of the EORTC QLQ-C30 (3.0 version)[26], which was translated from the validity-tested QLQ-C30 (3.0 version) developed by the EORTC. This tool comprised 3 subscales: the global health status, functional, and symptom scales. The global health status scale comprised 2 items (1 health status and 1 QOL item), the functional scale comprised 15 items (5 physical, 2 role, 4 emotional, 2 cognitive, and 2 social items), and the

symptom scale comprised 13 items (3 fatigue, 2 nausea/vomiting, 2 pain, 1 dyspnea, 1 insomnia, 1 appetite loss, 1 constipation, 1 diarrhea, and 1 financial problem item). The 2 global health status-related items were designed for a 7-point answer scale, while all other items were designed for a 4-point scale. Scores were converted to a 100-point scale according to the scoring manual[25], with the QOL increasing in proportion to the global health status and functional scale scores. In contrast, the lower the symptom scales score, the higher the QOL. The Cronbach's  $\alpha$  coefficient in a study by Yun et al.,[26] was .70 or higher, aside from the cognitive functional scale (.60). The Cronbach's  $\alpha$  coefficient values in the study by Kim et al.,[22] were .77, .83, and .78, respectively, for the global health status, functional, and symptom scales, while the coefficient values of the present study were .88, .78, and .75, respectively.

### 4. Data Collection

Data were collected from January to May 2013 and the researcher collected the data by using the questionnaire targeting for the outpatients who visited the Division of Hematology of the C National University H Hospital and the inpatients who are receiving the chemotherapy. All patients underwent neurological examination by an oncologist to assess the presence of CIPN. Those who had shown symptoms before being exposed to chemotherapeutics were excluded from the study. Participants were informed of the purpose and procedure of this study, voluntary participation, guaranteed anonymity, and the choice to abandon the trial, and written consent was obtained. 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. The questionnaire was answered by the patient and only when being asked for help, the researcher read it and helped with their response.

### 5. Data Analysis

The statistical software package SPSS/WIN 20.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. A 5% level of statistical significance was used. The collected data did not display a normal distribution; therefore, nonparametric statistical tests were used. The general and clinical characteristics of the participants are expressed in real numbers and percentages. To express the

participants' degrees of CIPN-related symptoms and health-related QOL, the means and standard deviations were computed. The differences in scores between the CIPN-related symptoms and health-related QOL according to the participants' general and clinical characteristics were analyzed using the Mann-Whitney and Kruskal-Wallis tests. Finally, the relationship between CIPN-related symptoms and the health-related QOL was analyzed using Spearman's rho.

## RESULTS

### 1. General and Clinical Characteristics

The general and clinical characteristics of the partic-

ipants are outlined in Table 1. The percentage of male patients was 65.2% (n=43). The mean age was 57.94 years. In addition, 66.7% (n=44) of patients were unemployed, and 63.7% (n=42) had high school or a higher level of education. Eighty-eight point three percent (n=55) of patients had an ECOG PS score of 0-1. MM, NHL, and ALL diagnoses accounted for 47.0% (n=31), 42.4% (n=28), and 10.6% (n=7) of the cases, respectively. An analysis of the duration of therapy determined that 31.8% (n=21) of patients underwent therapy for >2 years, and 69.7% (n=46) of patients were receiving peripheral neuropathy-associated chemotherapy at the time of the survey. Overall, 39.4% (n=26), 34.8% (n=23), and 25.8% (n=17) of participants experienced CIPN symptoms at durations of 4 months, 5-24 months, and

**Table 1.** Mean Rank Differences in CIPN and QOL, according to the General and Clinical Characteristics (N=66)

Characteristics	Categories	n (%)	CIPN				QOL					
			Lower extremity scales		Upper extremity scales		Global health status scales		Functional scales		Symptom scales	
			Mean rank	P	Mean rank	P	Mean rank	P	Mean rank	P	Mean rank	P
Gender	Male	43 (65.2)	34.94	.403	34.37	.612	34.53	.544	31.88	.349	34.44	.585
	Female	23 (34.8)	30.80		31.87		31.57		36.52		31.74	
Age (year)	≤ 49	15 (22.7)	19.67	.004	30.07	.759	44.33	.038	47.20	.014	21.87	.060
	50-59	20 (30.3)	35.55		36.78		34.98		31.60		38.60	
	60-69	15 (22.7)	33.03		34.07		28.27		30.10		35.30	
	≥ 70	16 (24.2)	44.34		32.09		26.41		26.22		36.34	
Education	≤ Middle school	24 (36.3)	41.69	.009	30.19	.287	27.71	.060	25.92	.015	38.81	.089
	≥ High school	42 (63.7)	28.82		35.39		36.81		37.83		30.46	
Employment	Yes	22 (33.3)	32.16	.688	31.41	.529	32.07	.664	33.64	.967	30.64	.391
	No	44 (66.7)	34.17		34.55		34.22		33.43		34.93	
ECOG PS	≤ 1	55 (83.3)	31.05	.020	33.05	.665	36.25	.008	35.99	.018	31.92	.134
	≥ 2	11 (16.7)	45.73		35.77		19.73		21.05		41.41	
Diagnosis	ALL	7 (10.6)	24.86	<.001	38.21	.778	25.86	.309	30.50	.097	35.79	.303
	NHL	28 (42.4)	24.21		33.36		37.09		39.41		29.27	
	MM	31 (47.0)	43.84		32.56		31.98		28.84		36.81	
Duration of diagnosis (months)	≤ 4	18 (27.3)	24.36	.025	33.58	.837	29.11	.063	33.86	.027	35.86	.093
	5-12	18 (27.3)	30.33		30.83		43.75		43.53		23.83	
	13-24	9 (13.6)	37.94		32.11		29.06		32.83		37.39	
	≥ 25	21 (31.8)	42.14		36.31		30.38		24.88		38.10	
Current chemotherapy	Yes	46 (69.7)	33.72	.889	34.29	.609	32.71	.606	31.17	.135	37.80	.006
	No	20 (30.3)	33.00		31.68		35.33		38.85		23.60	
Duration of CIPN (month)	≤ 4	26 (39.4)	21.02	<.001	33.87	.833	32.15	.173	36.42	.008	31.83	.071
	5-12	17 (25.8)	36.72		29.25		41.16		41.63		25.34	
	13-24	6 (9.0)	38.00		35.00		32.42		31.17		31.67	
	≥ 25	17 (25.8)	46.06		34.50		26.82		20.29		42.47	
Exposure to neurotoxic agents	Single	45 (68.2)	26.83	<.001	32.83	.678	35.16	.298	37.42	.015	30.02	.031
	Multiple	21 (31.8)	47.79		34.93		29.95		25.10		40.95	

CIPN=chemotherapy-induced peripheral neuropathy; QOL=quality of life; ECOG PS=Eastern Cooperative Oncology Group performance status; ALL=Acute lymphocytic leukemia; NHL=non-Hodgkin lymphoma; MM=multiple myeloma.

25 months, respectively. Finally, 68.2% (n=45) of patients had the number of CIPN-related drugs of single.

## 2. CIPN-related Symptoms and Health-related QOL Scores

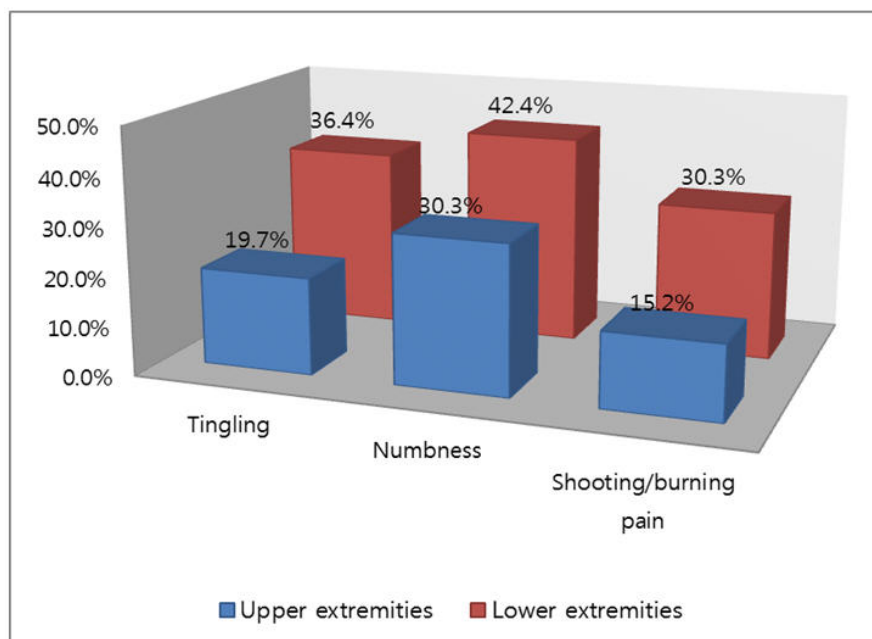
The manifestation rates for tingling, numbness, and shooting/burning pain were 19.7%, 30.3%, and 15.2%, respectively, in the upper extremities and 36.4%, 42.4%, and 30.3%, respectively, in the lower extremities when respondents' answers regarding CIPN-related symptoms were "quite a bit" or "very much". Symptoms were more intense in the lower extremities than the upper extremities (Figure 1). The average CIPN lower and upper extremity scale scores were 31.95 and 23.16 points, respectively (Table 2).

The average global health status, functional, and symptoms scale scores of the health-related QOL were 46.84, 58.72, and 34.85 points, respectively. Of the functional scale subscales, the emotional scales were the highest (71.46 points) and the social scales were the lowest (41.16 points). Of the symptom scales, fatigue and financial problems had relatively high scores (55.22 and 52.53 points, respectively), and nausea/vomiting and diarrhea had low scores (11.11 and 12.12 points, respectively) (Table 2).

**Table 2.** Scores from the 16-item QLQ-CIPN20 Subscales and EORTC QLQ-C30 Subscales (N=66)

Variables		M±SD
16-item QLQ-CIPN20	Lower extremity scales	31.95±23.30
	Upper extremity scales	23.16±19.01
EORTC QLQ-C30	Global health status scales	46.84±21.62
	Functional scales	58.72±20.61
	Physical scales	56.24±21.71
	Role scales	51.01±36.97
	Emotional scales	71.46±25.61
	Cognitive scales	62.12±28.58
	Social scales	41.16±36.19
	Symptom scales	34.85±16.79
	Fatigue	55.22±27.90
	Nausea & vomiting	11.11±16.10
	Pain	30.56±30.74
	Dyspnea	41.41±35.60
	Insomnia	37.88±38.73
Appetite loss	37.88±36.46	
Constipation	22.22±36.20	
Diarrhea	12.12±21.59	
Financial problem	52.53±40.95	

16-item QLQ-CIPN20=16-item quality of life questionnaire-chemotherapy-induced peripheral neuropathy; EORTC QLQ-C30=European Organization for the Research and Treatment of Cancer quality of life questionnaire core 30 items.



**Figure 1.** Percentage of patients who reported "quite a bit" or "very much" tingling, numbness, and/or shooting/burning pain on the 16-item QLQ-CIPN20 sensory scales.

### 3. Mean Rank Differences in CIPN and QOL according to the General and Clinical Characteristics

Among the CIPN-related lower extremity scores according to the general and clinical characteristics, significant mean rank differences existed with respect to age ( $p=.004$ ), education ( $p=.009$ ), ECOG PS ( $p=.020$ ), diagnosis ( $p<.001$ ), duration of diagnosis ( $p=.025$ ), duration of CIPN ( $p<.001$ ), and exposure to neurotoxic agents ( $p<.001$ ). There were no differences in CIPN-related upper extremity symptom scores (Table 1).

For health-related QOL, analyzing the global health status scale scores according to general and clinical characteristics determined significant mean rank differences for age ( $p=.038$ ) and ECOG PS ( $p=.008$ ). For the functional scale scores according to general and clinical characteristics, significant mean rank differences existed for age ( $p=.014$ ), education ( $p=.015$ ), ECOG PS ( $p=.018$ ), duration of diagnosis ( $p=.027$ ), duration of CIPN ( $p=.008$ ), and exposure to neurotoxic agents ( $p=.015$ ). In addition, for the symptom scale scores according to general and clinical characteristics, significant mean rank differences existed for current chemotherapy ( $p=.006$ ) and exposure to neurotoxic agents ( $p=.031$ ) (Table 1).

### 4. Correlation between the CIPN-related Symptoms and Health-related QOL

The CIPN-related lower extremity symptoms of patients with hematologic malignancies correlated negatively with the global health status ( $\rho=-.243$ ,  $p=.050$ ) and functional scales ( $\rho=-.469$ ,  $p=.002$ ) and correlated positively with the symptom scale ( $\rho=.463$ ,  $p=.002$ ). There was no correlation between CIPN-related upper extremity symptoms and health-related QOL (Table 3).

**Table 3.** Correlation between Health-related QOL and Peripheral Neuropathy Status (N=66)

Subscales in EORTC QLQ-C30	Subscales in 16-item QLQ-CIPN	
	Lower extremity rho ( $p$ )	Upper extremity rho ( $p$ )
Global health status	-.243 (.050)	-.075 (.550)
Functional	-.469 (.002)	-.236 (.057)
Symptom	.463 (.002)	.126 (.314)

QOL=quality of life; 16-item; QLQ-CIPN20=16-item quality of life questionnaire-chemotherapy-induced peripheral neuropathy; EORTC QLQ-C30=European Organization for the Research and Treatment of Cancer quality of life questionnaire core 30 items.

## DISCUSSION

According to long term surviving and remission extension due to effective cancer therapy, side effects of the therapy and health-related quality of life appear as important outcome variables. Up to the present time it is true that effective intervention methods for CIPN have been insufficient[2]. Based on the results of this study, we aim to provide the basic materials of intervention development for alleviation of CIPN and QOL improvement.

First, this study evaluated only 16 of the 20 original items of the EORTC QLQ-CIPN20 tool[24] as four items were deleted during the validity test. To justify the elimination of these 4 items as non-CIPN-related problems, Smith et al[24], argued that dizziness, blurred vision, and erectile dysfunction could manifest as a result of non-CIPN-related drugs or comorbid diseases, and hearing loss was likely to occur in patients treated with chemotherapeutics associated with ototoxicity, such as cisplatin, which was not typically administered. This study included patients with hematologic malignancies and a high possibility of comorbid anemia, a high proportion of elderly patients (47% $\geq$ 65 years of age), and patients unexposed to chemotherapeutics associated with ototoxicity. Therefore, the 16-item QLQ-CIPN20 was selected as a tool with which to assess CIPN.

CIPN is a troublesome symptom for cancer patients exposed to neurotoxic chemotherapeutic agents, with tingling and numbness being the most frequently reported symptoms[5]. Consistent with the studies by Kim et al[21], and Wolf et al[27], this study determined the most common CIPN-related symptom among participants to be numbness, followed by tingling and shooting/burning pain. And, the mean CIPN scores for the lower and upper extremity scales as in this study were 31.95 and 23.16 points, respectively, demonstrating more severe CIPN-related symptoms in the lower extremities. These results are similar to those of previous studies[1, 27], which CIPN-related symptoms were more frequent and intense in the lower extremities than in the upper extremities. Patients experiencing peripheral neuropathy from the administration of neurotoxic chemotherapeutic agents with severe symptoms in the lower extremity are at high risk of falling, calling for safe, prudent nursing care. Furthermore, in patients with hematologic malignancies who have been administered neurotoxic chemotherapeutic agents, CIPN assessment must accompany a comparison of the lower and upper extremity symptoms[21]. Moreover in this study, the lower extremity scale scores were significantly different with re-

gard to age, education, ECOG PS, diagnosis, duration of diagnosis, duration of CIPN, and exposure to neurotoxic agents. The results of this study have supported the previous studies[11,21,28] that reported that CIPN level is related to age, ECOG PS, duration of diagnosis, duration of CIPN, and exposure to neurotoxic chemotherapeutic agents. Therefore, the variables that led to differential scores in the lower-extremity peripheral neuropathy section should be incorporated into the education and counseling materials for patients with hematologic malignancies who have been administered neuro-toxic chemotherapeutic agents.

The mean QOL scores of our study participants were 46.84 points for the global health status scales, 58.72 points for the functional scales, and 34.85 points for the symptom scales. According to a study on the QOL of oxaliplatin-treated colorectal patients conducted by Kim et al.,[11], the average scores for the global health status, functional, and symptom scales were 59.41, 73.29, and 26.72 points, respectively. According to a report by Kim et al.,[21] on the QOL of patients diagnosed with Paclitaxel-treated breast cancer, the average scores for the global health status, functional, and symptom scales were 46.14, 62.43, and 31.29 points, respectively. So, it appeared that the hematological cancer patients who are the participant of the study have somewhat low QOL in general health status, functional, and symptom status compared to those with the colon cancer[11] and breast cancer[21] who received neurotoxic chemotherapeutic agents. This implies that efforts to prevent the deterioration of the QOL of patients with hematologic malignancies who are exposed to neurotoxic chemotherapeutic agents should be augmented by conducting systematic examinations of their CIPN-related conditions from the outset of chemotherapy. Moreover, the global health status scales showed statistically significant differences depending on age and ECOG-PS; the functional scales differed significantly according to age, education level, ECOG-PS, duration of diagnosis, duration of CIPN, and neurotoxic agent exposure; and the symptom scales differed significantly according to current chemotherapy and neurotoxic agent exposure. Kim et al.,[11] is the only study which identified the difference in QOL score according to the general and clinical characteristics of cancer patients who are experiencing the CIPN and as the clinical characteristics used in the study of Kim et al.,[11] is different from the clinical characteristics used in this study, it's a current situation that it's difficult to compare each other. Therefore, in the future, the study checking the QOL of hematological cancer patients who are expe-

riencing the CIPN and identifying variables associated with QOL is recommended to be implemented.

It is known that there is a significant correlation between CIPN and QOL[11-14]. In this study, as CIPN symptoms in the lower extremities become more severe, global health status and functional performance are lower and overall symptoms are severe. But, CIPN symptoms in the upper extremities showed no correlation with quality of life. It is considered that these results are shown because CIPN symptoms appear more often, sooner and more severely in lower extremities compared than upper extremities[1,27]. Also, as the degradation in the sensory and motor functions of lower extremities induced difficulties in driving, walking, exercising, or engaging in any activity that requires mobility or balance[3], it is considered that such dysfunction has affected quality of life. This result suggests that CIPN symptoms affect QOL, and, to better understand the CIPN-QOL relationship, it is necessary to acknowledge patients' CIPN-related complaints. However, the prevailing attitude of health care workers toward peripheral neuropathy symptom control is perceived by 60% of patients as passive or disinterested[29], which indirectly indicates a lack of CIPN-related interest in health care professionals and countermeasures, resulting in patient suffering[21]. Therefore, there is a need to improve the QOL of cancer patients who are exposed to neurotoxic chemotherapeutic agents through the initiatives of the supervising medical professionals to acquire basic knowledge about CIPN, conduct continuous inspections and monitoring for the early detection of CIPN-related symptoms, and provide adequate interventions to prevent symptom exacerbation, thus improving therapeutic outcomes[21].

Limitations of this study include the fact that its sample size of 66 participants was not large enough for a secondary data analysis, and its nonparametric analytical tests raise an interpretational issue with regard to the study results. Additionally, a replication study is necessary to focus on the high-risk factors and comorbid diseases as influential factors for CIPN (e.g., diabetes, a cumulative dose of neuro-toxic chemotherapeutic agents, etc.), which could not be addressed in this study. Thus, a replication study is necessary to focus on high-risk factors and comorbid diseases as influential factors for CIPN.

## CONCLUSION

In summary, the present study revealed that CIPN-re-

lated symptoms, especially numbness and tingling, in patients with hematologic malignancies who are treated with neurotoxic chemotherapeutic agents manifest more frequently in the lower extremities than the upper extremities, and these patients scored lower on the QOL function subscale when compared to patients with other cancers. To improve the conditions of these patients, oncologists should educate patients who are exposed to neurotoxic chemotherapeutic agents regarding CIPN-related symptoms before treatment and should show interest in and provide remedies for CIPN symptoms reported by their patients. Furthermore, it is necessary to develop effective pharmacological and non-pharmacological interventions to prevent and alleviate CIPN-related symptoms. Finally, this study was not able to consider all of the variables that may affect CIPN. Future studies should include co-morbid diseases and high risk factors in order to identify the effect factors of CIPN in patients with hematologic malignancies.

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