RESEARCH ARTICLE

Reliability and Validity of the EORTC QLQ-CIPN20 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Chemotherapy-Induced Peripheral Neuropathy 20-Item Scale) among Thai Women with Breast Cancer Undergoing Taxane-Based Chemotherapy

Nida Rattanakrong[1,2], Somsri Thipprasopchock[3], Akkradate Siriphorn[1], Sujitra Boonyong[1]*

Abstract

  Objective: The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Chemotherapy-Induced Peripheral Neuropathy 20-item scale (EORTC QLQ-CIPN20) is the common method for determining taxane-induced peripheral neuropathy (TIPN) symptoms. However, there have been no studies on the psychometric properties of the Thai Version of EORTC QLQ-CIPN20. The aim of this study was to evaluate the test–retest reliability, concurrent validity, and contrasting group validity of the Thai Version of EORTC QLQ-CIPN20 among women with breast cancer who received taxane-based chemotherapy. **Methods:** Twenty-eight breast cancer patients and 28 healthy controls participated in the study. Internal consistency, test–retest reliability, and inter-rater reliability were assessed using Cronbach α and the intraclass correlation coefficient (ICC). Concurrent validity was assessed via the Spearman correlation coefficient of the total scale of the EORTC QLQ-CIPN20 and the Total Neuropathy Score clinical version (TNSc), and contrasting group validity was assessed via the Mann-Whitney U test. **Results:** The internal consistency, test–retest reliability, and inter-rater reliability of the Thai Version of EORTC QLQ-CIPN20 was high to excellent (Cronbach α = 0.89, ICC = 0.84–0.95 and 0.78–0.94, respectively). However, the concurrent validity between the Thai Version of EORTC QLQ-CIPN20 and TNSc was not considered statistically significant. Contrasting group validity demonstrated statistically significant differences between breast cancer patients and healthy controls. **Conclusions:** The results support that the Thai Version of EORTC QLQ-CIPN20 is reliable and valid in measuring TIPN symptoms in Thai women with breast cancer. The findings suggest that the Thai Version of EORTC QLQ-CIPN20 may be used to distinguish TIPN symptoms between healthy controls and women with breast cancer undergoing taxane-based chemotherapy.

Keywords: Taxane-induced peripheral neuropathy- breast cancer- EORTC QLQ-CIPN20- reliability- validity

Introduction

   Taxane-based chemotherapy agents are the most commonly used to cure both early-stage and metastatic breast cancers (Bachegowda et al., 2014). Unfortunately, these agents could affect peripheral nerves such as sensory nerves and motor nerves (Barbuti and Chen, 2015). Taxane-induced peripheral neuropathy (TIPN) is the occurrence of signs or symptoms of peripheral nervous problems such as numbness, tingling, pain, and distal muscle weakness (Argyriou et al., 2008). In addition, long-term sensory and motor symptom impairments

can lead to poor posture stability, increased risk of deterioration, and reduced quality of life (Gewandter et al., 2013; Ness et al., 2013; Winters-Stone et al., 2017).

   The European Organization for Study and Treatment of Cancer Quality of Life Questionnaire–Chemotherapy-Induced Peripheral Neuropathy 20-item scale (EORTC QLQ-CIPN20) is a specific tool for determining TIPN symptoms. This patient-reported questionnaire comprises 20 items that can be divided into 3 subscales (sensory, motor, and autonomic subscales). The literature suggests that the EORTC QLQ-CIPN20 has good psychometric properties. This questionnaire was developed by Postma

[1]Human Movement Performance Enhancement Research Unit, Department of Physical Therapy, Faculty of Allied Health Sciences, Chulalongkorn University, Bangkok, Thailand. [2]Department of Rehabilitation Medicine, Physical Therapy Unit, Chulabhorn Hospital, Bangkok, Thailand. [3]The National Cancer Institute of Thailand, Bangkok, Thailand. *For Correspondence: Sujitra.B@Chula.ac.th

et al., (2005) to assess the complication of chemotherapy treatment due to functional impairment. The findings of the preliminary evaluation of the 3 subscales showed strong internal accuracy based on Cronbach α (0.73–0.82). Similarly, Lavoie Smith et al., (2013) observed high internal consistency (0.78–0.88) and suggested that this questionnaire could be used properly to differentiate peripheral neuropathy symptoms between individuals administered neurotoxic agents and individuals who did not undergo chemotherapy. Furthermore, the reduced version—CIPN15—of the EORTC QLQ-CIPN20 has been shown to be reliable (Cronbach α = 0.91) and valid with 5 items of the Total Neuropathy Score clinical version (TNSc) (r = 0.57) and able to differentiate between slight changes in peripheral neuropathy symptoms (Smith et al., 2018). In addition, a previous study assessed the psychometric properties of the Chinese version of EORTC QLQ-CIPN20. The findings revealed that the Chinese version of EORTC QLQ-CIPN20 had reasonable reliability, validity, and responsiveness in the assessment of patients with peripheral neuropathy complications (Barbuti and Chen, 2015). The EORTC QLQ-CIPN20 was already translated into Thai by means of the EORTC quality of life group translation procedure (Prasertsri, 2017). However, the Thai Version of EORTC QLQ-CIPN20 test–retest reliability, concurrent validity, and contrasting group validity was not documented. The objective of this study was to determine the psychometric properties of the Thai Version of EORTC QLQ-CIPN20 including test–retest reliability, concurrent validity, and contrasting group validity among women with breast cancer undergoing taxane-based chemotherapy.

Materials and Methods

Design and setting

This cross-section study was performed to test the psychometric properties of the Thai Version of EORTC QLQ-CIPN20 in women with breast cancer undergoing taxane-based chemotherapy. Patients were recruited from the National Cancer Institute of Thailand and Bhumibol Adulyadej Hospital, Thailand, between October and November 2020.

Participants

Twenty-eight women with breast cancer and 28 healthy women aged between 40 and 70 years participated in the study, which used a convenient sample method. The instructions and informed consent form were provided to all participants prior to their participation in this study. The study protocol was approved by the Ethics Review Committee for Research Involving Human Projects, Chulalongkorn University (under study ID: COA No. 144/2563), National Cancer Institute of Thailand (under study ID: 021_2020T_OUT663), and Bhumibol Adulyadej Hospital (under study ID: IRB No.84/63) before data collection.

The eligibility criteria were (1) aged between 40 and 70 years, (2) undergoing taxane-based chemotherapy equal to or more than 2 cycles, and (3) able to speak and understand the Thai language. Breast cancer patients

were excluded if they (1) had musculoskeletal diseases or neurological conditions with peripheral neuropathic signs such as diabetes and multiple sclerosis, (2) were administered other chemotherapy agents, or (3) were unable to participate through the completion of the study. The eligibility criteria for healthy controls were (1) aged between 40 and 70 years, (2) able to communicate in and understand the Thai language, (3) no history of cancer, and (4) no history of musculoskeletal disorders or neurological diseases with peripheral neuropathy symptoms.

Instruments
Thai version of EORTC QLQ-CIPN20

The Thai version of EORTC QLQ-CIPN20 is a patient-reported questionnaire composed of 20 items, including 3 subscales: sensory, motor, and autonomic scales. Each item is scored on a 4-point Likert scale, which ranges from 1 to 4 (1 = "not at all," 2 = "a little," 3 = "quite a bit," 4 = "very much"). The patients report the score level that represents their symptoms during the past week. The method for the score of the Thai version of EORTC QLQ-CIPN20 was measured and converted into a 0–100 scale using the formula Score = [1 - (RS - 1)/range] × 100, where RS is RawScore, which is the total of all scores for each subscale divided by the number of items answered on each subscale, and the range is the maximum score minus the minimum score for each item (4 – 1 = 3). Higher scores indicate more severe symptoms. Many studies have demonstrated that the scale has good psychometric properties (Postma et al., 2005; Lavoie Smith et al., 2013; Lavoie Smith et al., 2017). The Thai version of EORTC QLQ-CIPN20 was found to have good internal consistency (Cronbach α = 0.79) (Prasertsri, 2017).

The Total Neuropathy Score clinical version (TNSc)

The Total Neuropathy Score (TNS) is a valid and accurate tool for assessing peripheral neuropathy symptoms, especially in patients with cancer (Cornblath et al., 1999; Cavaletti et al., 2007; Smith et al., 2018). Among other reduced variants of the TNS, the TNSc is a clinical tool widely used to evaluate peripheral neuropathy in patients undergoing neurotoxic chemotherapy (Cavaletti et al., 2007; Hughes, 2008; Frigeni et al., 2011; Cavaletti et al., 2013). The TNSc is a robust composite tool for assessing TIPN symptoms that combines subjective assessment (sensory, motor, and autonomic symptoms) and objective assessment (such as pin response, pressure sensitivity, manual muscle monitoring, and deep tendon reflex). This tool consists of 7 items (only based on clinical evaluation of signs and symptoms), and each item score ranges from 0 to 4, with the total ranging from 0 to 28. Higher scores indicate severe symptoms. Good reliability (Cronbach α of 0.8) has been shown, as well as good validity compared with the modified Inflammatory Neuropathy Cause and Treatment (INCAT) group sensory sum score (mISS) (r = 0.7). Good test–retest and inter-rater reliability of the TNSc (r = 0.84) was also shown in a previous study (Cavaletti et al., 2013).

Procedures

Prior to participating to the study, all participants were

informed about the objective and testing procedures, and written informed consent was obtained immediately. For the test–retest, the patients completed the Thai version of EORTC QLQ-CIPN20 at 2 different time points, 1 day apart. The Thai version of EORTC QLQ-CIPN20 was tested for inter-rater reliability by two independent researchers. Concurrent validity was tested by calculating the correlation between the total scale of the Thai version of EORTC QLQ-CIPN20 and the total score of TNSc assessed on the same day (Day 1). In addition, the contrasting group validity was assessed by the disparity in the total scale of the Thai version of EORTC QLQ-CIPN20 of women with breast cancer and healthy controls.

Data Analysis

The statistical analysis was performed using SPSS Statistic version 23 for Windows (IBM, Armonk, NY). Descriptive data were examined to describe the participants' characteristics. The Shapiro-Wilk test was used to test the normality of the data. Cronbach α was used to determine the strength of internal consistency values over 0.7 demonstrate strong reliability (Bland and Altman, 1999). The intraclass correlation coefficient (ICC) was used to calculate the test–retest reliability (ICC3,1) and inter-rater reliability (ICC2,1). The ICC values are interpreted as follows: ICC greater than 0.9 implies excellent reliability, 0.76–0.89 indicates strong reliability, 0.51–0.75 indicates modest reliability, and less than 0.5 indicates poor reliability (Koo and Li, 2016). In addition, the normal measurement error (SEM) was calculated using the following equation: SEM = SD × $\sqrt{1 - ICC}$. The formula MDC = 1.96 × SEM × $\sqrt{2}$ was used to determine the minimal detectable change (MDC) at the 95% confidence interval. The Spearman correlation coefficient between the total scale of the EORTC QLQ-CIPN20 and total TNSc score was used to evaluate concurrent validity. The Mann-Whitney U test was used to assess the contrasting group validity by comparing the mean scores of patients with the mean scores of healthy women. The significance level was set at p < 0.05.

Results

Sample demographic characteristics

Fifty-six participants were divided into 2 groups (breast cancer and healthy control). All of those with breast cancer received taxane-based chemotherapy, and the average cumulative dosage was 551.86 mg (192.32) (SD = 192.32). More than half of patients with breast cancer (68%) completed the second cycle, 25% completed the third cycle, and 7% completed the fourth cycle (7.14%) (Table 1).

The prevalence of symptoms for each item is shown in Table 2. Most of the participants reported the degree of symptoms as "not at all." The degree of symptoms of "quite a bit" was reported by breast cancer patients (items 3, 4, 9, 10, 12, 13, 15, and 19). Items 19 and 20 of the questionnaires were conditional, so some participants did not respond to these questions. However, 8 patients with breast cancer and 11 healthy women responded to item 19; no one responded to item 20 because this question inquired about the difficulties of maintaining an erection in males.

Internal consistency, test–retest reliability, and inter-rater reliability

The internal consistency of the total scale of the Thai version of EORTC QLQ-CIPN20 indicated good reliability, as shown by the Cronbach α of 0.89. Of the 3 subscales, both sensory and motor scales had a reasonable Cronbach α of 0.76, whereas the autonomic scale had a Cronbach α below the acceptable level (Table 3).

The Thai version of EORTC QLQ-CIPN20 test–retest reliability (ICC), SEM, and MDC are presented in Table 4. Both the total and the subscale showed high to excellent reliability (ICC3,1 = 0.84–0.95). The total scale ICC was 0.95 (SEM = 1.69; MDC = 4.68), the sensory scale ICC was 0.88 (SEM = 2.98; MDC = 8.30), the motor scale ICC was 0.90 (SEM = 3.16; MDC = 8.75), and the autonomic scale ICC was 0.84 (SEM = 11.09; MDC = 12.27).

In the same way, the inter-rater reliabilities of the total Thai version of EORTC QLQ-CIPN20 and its subscales were high to excellent (ICC2,1 = 0.78–0.94). The total scale and motor scale ICC showed excellent reliability (0.94 and 0.92), whereas the sensory scale ICC and motor scale ICC were high (0.87 and 0.78) (Table 4).

Concurrent Validity and Contrasting Groups Validity

Concurrent validity between the Thai version of EORTC QLQ-CIPN20 and TNSc was found not to be statistically significant (p > 0.05). The contrasting groups validity of the Thai version of EORTC QLQ-CIPN20

Table 1. Demographic Characteristics of the Participants (N = 56)

Characteristics	Breast cancer (n=28)	Healthy (n=28)
Age (years) [mean (SD)]	55.25 (9.98)	57.61 (8.61)
Weight (kg) [mean (SD)]	62.87 (12.02)	64.88 (10.45)
Height (m) [mean (SD)]	1.56 (0.06)	1.59 (0.56)
BMI (kg/m²) [mean (SD)]	25.60 (4.76)	25.61 (4.53)
Cumulative dose (mg) [mean (SD)]	551.86 (192.32)	-
Cycle number [N (%)]		
2 cycles	19 (67.85)	-
3 cycles	7 (25.00)	-
4 cycles	2 (7.14)	-

Table 2. Taxane-Induced Peripheral Neuropathy (TIPN) Symptoms Prevalence in Women with Breast Cancer and Healthy Control

Items	EORTC QLQ-CIPN20	Breast cancer [N (%)]				Healthy [N (%)]			
		Not at all	A little	Quite a bit	Very much	Not at all	A little	Quite a bit	Very much
1	Tingling fingers or hands	24 (85.7)	4 (14.3)	0 (0.0)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
2	Tingling toes or feet	24 (85.7)	4 (14.3)	0 (0.0)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
3	Numbness in your fingers or hands	9 (32.1)	12 (42.9)	7 (25.0)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
4	Numbness in your toes or feet	8 (28.6)	14 (50.0)	6 (21.4)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
5	Shooting or burning pain in your fingers or hands	27 (96.4)	1 (3.6)	0 (0.0)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
6	Shooting or burning pain in your toes or feet	24 (85.7)	4 (14.3)	0 (0.0)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
7	Cramps in your hands	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)	21 (75.0)	7 (25.0)	0 (0.0)	0 (0.0)
8	Cramps in your feet	26 (92.9)	2 (7.1)	0 (0.0)	0 (0.0)	15 (53.6)	13 (46.4)	0 (0.0)	0 (0.0)
9	Problems standing of walking because of difficulty feeling the ground under your feet	15 (53.6)	11 (39.3)	1 (3.6)	1 (3.6)	27 (96.4)	1 (3.6)	0 (0.0)	0 (0.0)
10	Difficulty distinguishing between hot and cold water	24 (85.7)	3 (10.7)	1 (3.6)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
11	A problem holding a pen, which made writing difficult	18 (64.3)	10 (35.7)	0 (0.0)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
12	Difficulty manipulating small objects with your fingers	16 (57.1)	9 (32.1)	3 (10.7)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
13	Difficulty opening a jar or bottle because of weakness in your hands	17 (60.7)	7 (25.0)	4 (14.3)	0 (0.0)	26 (92.9)	2 (7.1)	0 (0.0)	0 (0.0)
14	Difficulty walking because your feet dropped downwards	26 (92.9)	2 (7.1)	0 (0.0)	0 (0.0)	28 (100)	0 (0.0)	0 (0.0)	0 (0.0)
15	Difficulty climbing stairs or getting up out of a chair because of weakness in your legs	12 (42.9)	13 (46.4)	3 (10.7)	0 (0.0)	25 (89.3)	3 (10.7)	0 (0.0)	0 (0.0)
16	Dizzy when standing up from a sitting or lying position	18 (64.3)	10 (35.7)	0 (0.0)	0 (0.0)	17 (60.7)	11 (39.3)	0 (0.0)	0 (0.0)
17	Blurred vision	23 (82.1)	5 (17.9)	0 (0.0)	0 (0.0)	25 (89.3)	3 (10.7)	0 (0.0)	0 (0.0)
18	Difficulty hearing	26 (92.9)	2 (7.1)	0 (0.0)	0 (0.0)	27 (96.4)	1 (3.6)	0 (0.0)	0 (0.0)
19	Difficulty using pedals (conditional)	3 (37.5)	5 (62.5)	0 (0.0)	0 (0.0)	11 (100)	0 (0.0)	0 (0.0)	0 (0.0)
20	Difficulty maintaining erection (conditional)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Abbreviation: EORTC QLQ-CIPN20, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Chemotherapy-Induced Peripheral Neuropathy 20-Item Scale (Thai Version)

between women with breast cancer and healthy controls showed statistically significant differences in total scale ($p < 0.001$), sensory scale ($p < 0.001$), and motor scale ($p < 0.002$) but not autonomic scale (Table 5).

Table 3. Internal Consistency Reliability of the Thai Version of EORTC QLQ-CIPN20 in Women with Breast Cancer

EORTC QLQ-CIPN20	Cronbach's α
Total scale	0.89
Subscale	
Sensory scale	0.76
Motor scale	0.76
Autonomic scale	0.18

Abbreviation: EORTC QLQ-CIPN20, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Chemotherapy-Induced Peripheral Neuropathy 20-Item Scale (Thai Version).

Discussion

This study examined the reliability and validity of the Thai version of EORTC QLQ-CIPN20 in patients with breast cancer who received taxane-based chemotherapy. The findings of the study indicated that the total scale of the Thai version of EORTC QLQ-CIPN20 and 2 subscales (sensory and motor scales) had high to excellent reliability (internal consistency, test–retest reliability, and inter-rater reliability). However, the internal consistency of the autonomic scale did not reach the acceptable level (Cronbach α less than 0.7). Concurrent validity between the Thai version of EORTC QLQ-CIPN20 and TNSc was not found to be statistically significant. Although there was a statistically significant difference in the total scale, sensory scale, and motor scale between breast cancer patients and healthy women, the autonomic scale was not found to be statistically significant.

Table 4. Test-Retest Reliability of the Thai Version of EORTC QLQ-CIPN20 in Women with Breast Cancer

EORTC QLQ-CIPN20	Scale score (Mean±SD)		ICC (95% CI)	SEM	MDC
	Time 1	Time 2			
Total scale	11.01±7.69	10.39±7.44	0.95 (0.90-0.97)	1.69	4.68
Subscale					
Sensory scale	11.64±9.05	11.77±8.49	0.88 (0.75-0.94)	2.98	8.3
Motor scale	10.82±10.17	9.50±9.85	0.90 (0.50-0.95)	3.16	8.75
Autonomic scale	8.93±10.62	7.74±11.55	0.84 (0.68-0.92)	11.09	12.27

Abbreviation: 95% CI, confidence intervals; EORTC QLQ-CIPN20, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Chemotherapy-Induced Peripheral Neuropathy 20-Item Scale (Thai Version); ICC, intraclass correlation coefficient; MDC, minimal detectable change; SEM, standard error of measurement.

Table 5. Inter-Rater Reliability of the Thai Version of EORTC QLQ-CIPN20 in Women with Breast Cancer

EORTC QLQ-CIPN20	Scale score (Mean±SD)		ICC (95% CI)
	Rater 1	Rater 2	
Total scale	11.01±7.69	10.26±7.13	0.94 (0.88-0.97)
Subscale			
Sensory scale	11.64±9.06	11.37±8.66	0.87 (0.73-0.93)
Motor scale	10.82±10.17	9.33±9.22	0.92 (0.83-0.96)
Autonomic scale	8.93±10.62	8.33±10.63	0.78 (0.57-0.89)

Abbreviation: 95% CI, confidence intervals; EORTC QLQ-CIPN20, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Chemotherapy-Induced Peripheral Neuropathy 20-Item Scale (Thai Version); ICC, intraclass correlation coefficient.

The current research was the first to test the reliability and validity of the Thai version of EORTC QLQ-CIPN20 in women with breast cancer relative to healthy controls. The internal consistency of the total scale of the Thai version of EORTC QLQ-CIPN20 was as reliable as in previous studies using the EORTC QLQ-CIPN20 (Cronbach α of 0.79–0.91) (Postma et al., 2005; Smith et al., 2018). Acceptable levels were reached for the sensory and motor scales, but not for the autonomic scale. These findings are not unexpected because the signs of TIPN are a mixed sensorimotor neuropathy. Generally, the early symptoms of TIPN cause sensory dysfunction and may impair motor functions as well. Autonomous symptoms of this type are uncommon and rare (Argyriou et al., 2008; Velasco and Bruna, 2015).

The test–retest reliability of both the total scale and subscales of the Thai version of EORTC QLQ-CIPN20 was high to excellent. These results are in agreement with those of Smith (2018) who evaluated the test–retest reliability of a reduced version-CIPN15-of the EORTC QLQ-CIPN20 in 121 patients with cancer who received neurotoxic

Table 6. Contrasting Groups Validity in Women with Breast Cancer and Healthy Control

EORTC QLQ-CIPN20	Breast cancer	Healthy	P
Total scale	11.01±7.69	2.67±2.38	< 0.001 [a]
Subscale			
Sensory scale	11.63±9.05	0.26±1.40	< 0.001 [a]
Motor scale	10.82±10.17	4.12±4.50	< 0.002 [a]
Autonomic scale	8.93±10.62	8.33±10.63	0.84

Abbreviation: EORTC QLQ-CIPN20, The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Chemotherapy-Induced Peripheral Neuropathy 20-Item Scale (Thai Version). [a], significant difference between patients with breast cancer and healthy women

agents. Participants completed the questionnaire twice (1–2 hours apart). The results showed excellent test–retest reliability based on the Pearson correlation (r = 0.86; CI, 0.80–0.90) (Smith et al., 2018).

However, most of the participants in our study reported their degree of symptoms as "not at all" and "a little," and a couple of the participants indicated "a little bit," whereas only one of the women with breast cancer indicated "very much." Approximately 68% of women with breast cancer reported a total Thai version of EORTC QLQ-CIPN20 score lower than 15%. These results suggest that the Thai version of EORTC QLQ-CIPN20 has a significant floor effect. Similarly, Cheng (2019) measured the EORTC QLQ-CIPN20 floor and ceiling effects. The findings revealed significant floor effects, as about 28%–47% of respondents reached the lowest EORTC QLQCIPN20 score (Cheng and Molassiotis, 2019). One possible explanation for these findings is that most women with breast cancer had only completed the second cycle of chemotherapy, and only a few patients had completed the fourth cycle. The literature suggests that most patients with cancer who undergo taxane-based chemotherapy have TIPN effects in Cycle 3 (Hilkens et al., 1997). Unsurprisingly, most participants reported a low severity of TIPN symptoms. The findings suggest that the EORTC QLQCIPN2020 scores should be interpreted carefully. The SEM and MDC of the total scale of the Thai version of EORTC QLQ-CIPN20 appear to be small in this study (SEM = 1.69; MDC = 4.68). However, the SEM and MDC of the subscales, especially of the autonomous scale, were quite high (SEM = 2.98, 3.16, 11.09; MDC = 8.30, 8.75, 12.27, respectively).

Although several studies have measured the reliability of the EORTC QLQ-CIPN20, no studies have tested its

inter-rater reliability. The inter-rater reliability of the Thai version of EORTC QLQ-CIPN20 in the current study was high to excellent (ICC2,1 = 0.78–0.94) for both the total and subscales. These findings indicate that the Thai version of EORTC QLQ-CIPN20 should be absolutely reliable and has a minor measurement error for evaluating TIPN symptoms in patients with breast cancer receiving taxane-based chemotherapy. These findings indicate that the Thai version of EORTC QLQ-CIPN20 is not only appropriate for tracking TIPN symptoms in patients with breast cancer who are undergoing taxane-based chemotherapy but is also feasible for use by multiple assessors.

The concurrent validity between the Thai version of EORTC QLQ-CIPN20 and TNSc was found not to be statistically significant. Although the Thai version of EORTC QLQ-CIPN20 and TNSc are both used to test TIPN symptoms, they do so in different ways. The EORTC QLQ-CIPN20 assesses for the degree and level of TIPN symptoms linked to functional impairment, such as "Problems standing or walking because of difficulty feeling the ground under your feet," "A problem holding a pen, which made writing difficult," and "Difficulty climbing stairs or getting up out of a chair because of weakness in your legs." The TNSc, on the other hand, tests TIPN signs related to neurophysiological testing, such as pin sensitivity, vibration sensitivity, strength, and deep tendon reflex. Whereas the EORTC QLQ-CIPN20 assesses the perception of pain, the TNSc does not determine the level of pain.

The contrasting groups validity in this study indicated statistically significant differences in total scale, sensory scale, and motor scale when comparing breast cancer patients' scores and healthy women's scores. These results are similar to those of Smith (2018) who reported statistically significant differences in the total scale of the reduced version—CIPN15—of the EORTC QLQ-CIPN20 when comparing scores of patients with cancer to a healthy control group (Smith et al., 2018). On the other hand, the autonomic scale was not statistically significant when comparing breast cancer patients' scores and healthy women's scores. The autonomic scale included "Dizzy when standing up from a sitting or lying position" (item 16), "Blurred vision" (item 17), and "Difficulty maintaining erection" (item 20); however, the current study only used items 16 and 17. When standing up from a seated or lying position, the dizziness was linked to the orthostatic symptoms. This symptom has not only been observed in patients with TIPN but has also been seen in other patients, such as patients with heart disorders, Parkinson's disease, and diabetes mellitus (Jones et al., 2015). Similarly, blurred vision might have developed in a different condition without signs of TIPN, such as eye disorders. This result shows that the Thai version of EORTC QLQ-CIPN20 total scale, sensory scale, and motor scale could distinguish between patients with or without TIPN symptoms, but the autonomic scale could not be used properly to define TIPN symptoms.

A few limitations must be considered. This research only measured the reliability and validity of the scale for women with breast cancer who received taxane-based chemotherapy and were diagnosed with homogeneous cancer, most of whom had completed a second cycle of chemotherapy treatment. Further research should be conducted with other cancer diagnoses or in various chemotherapy cycles.

In conclusion, the findings showed that the Thai version of EORTC QLQ-CIPN20 is reliable and valid for the assessment of TIPN symptoms in patients with breast cancer receiving taxanic chemotherapy. In addition, this patient-report questionnaire may be used to distinguish and track TIPN symptoms between people with cancer and healthy people.

Author Contribution Statement

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Nida Rattanakrong. The first draft of the manuscript was written by Nida Rattanakrong and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Acknowledgments

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. The study protocols were approved by the Ethics Review Committee for Research Involving Human Projects, Chulalongkorn University (COA No. 144/2563), National Cancer Institute of Thailand (under study ID: 021_2020T_OUT663), and Bhumibol Adulyadej Hospital (under study ID: IRB No.84/63) before data collection.

Data availability

The datasets analyzed in this study are not publicly available. Please contact the corresponding author regarding any reasonable requests for the data.

Conflict of interest

The authors declare no conflict of interest.

References

Argyriou AA, Iconomou G, Kalofonos HP (2008). Bortezomib-induced peripheral neuropathy in multiple myeloma: a comprehensive review of the literature. *Blood*, **112**, 1593-9.

Bachegowda LS, Makower DF, Sparano JA (2014). Taxanes: impact on breast cancer therapy. *Anticancer Drugs*, **25**, 512-21.

Barbuti AM, Chen ZS (2015). Paclitaxel Through the Ages of Anticancer Therapy: Exploring Its Role in Chemoresistance and Radiation Therapy. *Cancers (Basel)*, **7**, 2360-71.

Bland JM, Altman DG (1999). Measuring agreement in method comparison studies. *Stat Methods Med Res*, **8**, 135-60.

Cheng HL, Molassiotis A (2019). Longitudinal validation and comparison of the Chinese version of the European Organization for Research and Treatment of Cancer Quality

of Life-Chemotherapy-Induced Peripheral Neuropathy Questionnaire (EORTC QLQ-CIPN20) and the Functional Assessment of Cancer-Gynecologic Oncology Group-Neurotoxicity subscale (FACT/GOG-Ntx). *Asia Pac J Clin Oncol*, **15**, 56-62.

Gewandter JS, Fan L, Magnuson A, et al (2013). Falls and functional impairments in cancer survivors with chemotherapy-induced peripheral neuropathy (CIPN): a University of Rochester CCOP study. *Support Care Cancer*, **21**, 2059-66.

Hilkens PH, Verweij J, Vecht CJ, et al (1997). Clinical characteristics of severe peripheral neuropathy induced by docetaxel (Taxotere). *Ann Oncol*, **8**, 187-90.

Jones PK, Shaw BH, Raj SR (2015). Orthostatic hypotension: managing a difficult problem. *Expert Rev Cardiovasc Ther*, **13**, 1263-76.

Koo TK, Li MY (2016). A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med*, **15**, 155-63.

Lavoie Smith EM, Barton DL, Qin R, et al (2013). Assessing patient-reported peripheral neuropathy: the reliability and validity of the European Organization for Research and Treatment of Cancer QLQ-CIPN20 Questionnaire. *Qual Life Res*, **22**, 2787-99.

Ness KK, Jones KE, Smith WA, et al (2013). Chemotherapy-related neuropathic symptoms and functional impairment in adult survivors of extracranial solid tumors of childhood: results from the St. Jude Lifetime Cohort Study. *Arch Phys Med Rehabil*, **94**, 1451-7.

Postma TJ, Aaronson NK, Heimans JJ, et al (2005). The development of an EORTC quality of life questionnaire to assess chemotherapy-induced peripheral neuropathy: the QLQ-CIPN20. *Eur J Cancer*, **41**, 1135-9.

Prasertsri N, Kaewmani C, Khantichit P, et al(2017). Chemotherapy-Induced Peripheral Neuropathy (CIPN): A Cross-Sectional Study in Cancer Patients. *J Nurs Health Res*, **3**, 52-62.

Smith EML, Knoerl R, Yang JJ, et al (2018). In Search of a Gold Standard Patient-Reported Outcome Measure for Use in Chemotherapy- Induced Peripheral Neuropathy Clinical Trials. *Cancer Control*, **25**, 1073274818756608.

Velasco R, Bruna J (2015). Taxane-Induced Peripheral Neurotoxicity. *Toxics*, **3**, 152-69.

Winters-Stone KM, Horak F, Jacobs PG, et al (2017). Falls, Functioning, and Disability Among Women With Persistent Symptoms of Chemotherapy-Induced Peripheral Neuropathy. *J Clin Oncol*, **35**, 2604-12.