Impact of Chemotherapy-induced Peripheral Neuropathy on Quality of Life in Patients with Advanced Lung Cancer Receiving Platinum-based Chemotherapy

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Abstract

Purpose: Chemotherapy-induced peripheral neuropathy (CIPN) is a common adverse event of cancer treatment that may affect quality of life (QoL). The purposes of this study were to: assess the levels of CIPN, depression, general QoL, and CIPN-related QoL; and identify the factors related to CIPN-related QoL and general QoL in patients with advanced lung cancer (LC) receiving platinum-based chemotherapy.

Methods: This cross-sectional study examined patients with advanced LC who received platinum-based chemotherapy from the thoracic oncology inpatient wards of a medical center in northern Taiwan. Structured questionnaires were used to measure patients' CIPN, depression, general QoL, and CIPN-related QoL.

Results: Of the 93 patients with advanced LC studied, 53.8% and 47.3% reported CIPN-sensory impairment and CIPN-motor impairment, respectively. The most common CIPN symptoms were difficulty getting or maintaining an erection and difficulty in climbing stairs or getting up out of a chair. Poor CIPN-related QoL was associated with more CIPN-sensory and more CIPN-motor impairment. Poor general QoL was associated with a higher level of depression, more CIPN-sensory impairment, and a higher cumulative dose of chemotherapy.

Conclusion: More than half of LC patients report impairment related to CIPN. This finding highlights the importance of treating these symptoms which significantly impair QoL. A holistic approach – including patient health education, dietary adjustment, nutritional supplements, aerobic exercise, and balance training – is needed to relieve the distressful peripheral neurological symptoms and emotional distress of CIPN during and after treatment for advanced LC.

Introduction

Lung cancer (LC) is the most common cancer worldwide, with an estimated 2.1 million new cases and approximately 1.76 million deaths expected annually [1]. In Taiwan, some 12,000 new LC cases are reported per year [2]. About 75% of patients are diagnosed at an advanced stage, and chemotherapy is the major treatment modality [3]. Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of several classes of chemotherapy agents, including platinum-based agents, such as cisplatin and carboplatin [4]. Approximately 70–100% of patients treated with platinum-based antineoplastics report CIPN [4], which may develop 1–2 weeks after initiating treatment, persist for several months after completing treatment, and depend on the cumulative dose exposure [5].

CIPN refers to motor, sensory, and autonomic neurons dysfunction, which presents as peripheral neuropathic signs and symptoms, and includes sensory damage. The predominant symptoms of CIPN are paresthesia, numbness and tingling, dulled sensations in the peripheral nerves, burning and shooting pain, or electric shock-like pain [3,6]; motor damage can be manifested as weakness, gait and balance disturbance, and difficulty with fine motor skills [6]. Autonomic damage dysfunction presents as constipation, orthostatic hypotension, and urinary incontinence [7]. The neuropathy symptoms may

cause dose reduction [8], refusal to continue treatment [9], psychological distress [10], neurological impairment [11], and reduced quality of life (QoL) [12,13].

Although previous studies have explored these issues, most research has focused on patients with colorectal cancer [14–16], breast cancer [17], or those in Western countries [18–20]; or on other chemotherapy regimens such as taxane [18,19], paclitaxel [19,20], or carboplatin [19,20]. Clinical observation indicates that LC patients treated with platinum-based regimens report CIPN-related symptoms that affect daily function and QoL, and insufficient attention has been devoted to this important topic. Therefore, the purposes of this study were to (1) examine the levels of CIPN, depression, general QoL, and CIPN-related QoL; and (2) identify the factors associated with CIPN-related QoL and general QoL among advanced LC patients receiving platinum-based chemotherapy.

Methods

Design and sample selection

A descriptive cross-sectional study was conducted with a convenience sample from the thoracic oncology inpatient wards of a medical center in northern Taiwan. Data were collected from September 2017 through June 2019. The inclusion criteria were: (1) diagnosis of stage III B or IV LC; (2) receiving platinum-based chemotherapy with cisplatin or carboplatin regimens; (3) receiving at least four cycles of chemotherapy; (4) agreement to participate in the study after explanation of its purposes and procedures; and (5) aged 20 years or older. Patients were not eligible if they had a mental disorder, hypothyroidism, alcoholism, vitamin B1 or B12 insufficiency, discontinuation of scheduled treatment more than 2 months since prior treatment cycles, other comorbid conditions potentially causing CIPN (diabetes, thyroid disease, or preexisting neuropathy), or a physical performance less than 60 on the Karnofsky Performance Status Scale (KPS) [21].

The chemotherapy treatment protocol for unresectable advanced LC is a platinum-based regimen of cisplatin or carboplatin given at 75 mg/m² every 3 weeks for 4 to 6 cycles [22].

Ethical considerations

Ethical approval was obtained from the Institutional Review Board of the study institution (Number: 201701101B0). The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants after the study goals and procedures were explained to each in detail.

Data collection

LC patients who met the inclusion criteria were contacted by a research nurse. Participants filled out the structured questionnaires by self-report in the wards; when necessary, the research nurse read each item of the questionnaire, which took around 10–15 minutes.

Measures

European Organization for Research and Treatment of Cancer quality of life questionnaire–chemotherapy–induced peripheral neuropathy 20

CIPN was assessed using the European Organization for Research and Treatment of Cancer quality of life questionnaire-chemotherapy-induced peripheral neuropathy 20 (EORTC QLQ-CIPN20) [23]. The 20-item scale includes three subscales: sensory (9 items), motor (8 items), and autonomic (3 items). Each item is scored from 1 (not at all) to 4 (very much). The summed scores of each subscale and the overall CIPN scale are converted into standardized scores ranging from 0 to 100, with higher scores representing more CIPN-related symptom distress. The scale was translated into Chinese, and previous cancer-related studies reported satisfactory psychometric properties for the EORTC QLQ–CIPN20 [14,17]. The EORTC QLQ–CIPN20 has been demonstrated to be reliable in a cancer-related study [24]. The Cronbach's α for this study was 0.88.

Hospital Anxiety and Depression Scale Depression Subscale

Depression was assessed using the Hospital Anxiety and Depression Scale (HADS) Depression Subscale [25]. Each of the 7 items in the HADS Depression Subscale was scored from 0 (not at all) to 3 (always) and the total score ranges from 0 to 21, with a higher score indicating greater depression. Scores of 0 to 7 indicate the absence of depression, scores of 8 to 10 indicate borderline depression, and scores of 11 to 21 indicate clinical depression [25]. The scale was translated into Chinese, and a previous cancer-related study reported satisfactory psychometric properties for the HADS [26]. Cronbach's alpha for the HADS-Depression Subscale in the present study was 0.88.

Functional Assessment of Cancer Therapy /Gynecologic Oncology Group-Neurotoxicity subscale

The CIPN-related QoL was assessed using the Functional Assessment of Cancer Therapy /Gynecologic Oncology Group-Neurotoxicity subscale (FACT/GOG–Ntx) [29]. The instrument consists of 11 items, with responses scored on a Likert scale from 0 (not at all) to 4 (very much). The summed scores of each item are reverted into standardized scores ranging from 0 to 44, with a higher score indicating a lower level of neurological toxicity and less effect on QoL. Satisfactory psychometric properties were reported in a previous study [29]. Cronbach's alpha for the FACT/GOG–Ntx was 0.90.

Functional Assessment of Cancer Therapy–Lung

The Functional Assessment of Cancer Therapy-Lung (FACT–L) was used to assess general QoL in patients with LC [27]. The 27 item FACT–L contains 5 domains: physical well-being (PWB) (7 items), social/family well-being (SWB) (7 items), emotional well-being (EWB) (6 items), and functional well-being (FWB) (7 items) [27]. Each item is scored on a scale of 0 to 4, with a higher score indicating a better QoL.

The FACT–L has been demonstrated to be reliable in a cancer-related study [28]. In the present study, the Cronbach's α was 0.88.

The National Cancer Institute Common Terminology Criteria for Adverse Events 4.03v

The US National Cancer Institute Common Terminology Criteria for Adverse Events 4.03v (NCI-CTCAE) is widely used in oncology care as the standard classification and severity grading scale for adverse events in cancer therapy clinical trials and other oncology settings [30]. Severity of peripheral motor neuropathy or peripheral sensory impairment is assessed in 5 grades, ranging from 0 to 5: Grade 1, Asymptomatic, clinical or diagnostic observations only; intervention not indicated/ loss of deep tendon reflexes or paresthesia; Grade 2, Moderate symptoms; limiting instrumental activities of daily living (ADL); Grade 3, Severe symptoms; limiting self-care ADL; assistive device indicated; Grade 4, Life-threatening consequences; urgent intervention indicated; and Grade 5, Death [30]. The inter-rater reliability for this study was 0.99 between the research nurse and the oncologist who provided training to the research nurse.

Karnofsky Performance Status Scale

The KPS scale, used to assess a patient's performance status, ranges from 100% (normal function) to 0% (death) [21]. The KPS has been used in clinical cancer studies to assess cancer patients' level of physical function [31,32]. An inter-observer reliability coefficient of 0.98 was reported in the present study.

Demographic and clinical characteristics form

Demographic data (age, gender, occupation, marital status, education level, and religion) and characteristics of the cancer and treatment (histology type, cancer stage, number of chemotherapy cycles, chemotherapy modalities, total chemotherapy dose, time since diagnosis, and time since the completion of previous chemotherapy) were extracted from the medical record.

Statistical methods

SPSS, version 26.0 for Windows (IBM Corp., Armonk, NY, USA) was used to analyze the data. Descriptive statistics (frequency distribution, percentage, means, standard deviation errors [SE]) were used to analyze the demographic and clinical characteristics; and the levels of CIPN, depression, CIPN-related QoL, and general QoL. Multiple stepwise regression was used to identify factors associated with CIPN-related QoL and general QoL. The independent variables included marital status, number of chemotherapy cycles, cumulative chemotherapy dose, the EORTC QLQ-CIPN20 scores (CIPN-sensory score, CIPN-motor score, CIPN-autonomic score), and depression.

Results

Demographic and clinical characteristics

Of 100 eligible patients approached, 7 declined to participate because they had no time or interest, for a total of 93 patients in the study, 93.0% of all patients approached. Patients' average age was 59.24 ± 1.20 years. The majority were male ($n = 54, 58.1\%$), unemployed ($n = 66, 71.0\%$), married ($n = 65, 69.9\%$), had a junior high school education or less ($n = 48, 51.7\%$), and held Buddhist/Taoist religious beliefs ($n = 62, 66.7\%$). A majority of patients were diagnosed with non-small cell lung cancer ($n = 74, 79.6\%$) and stage IV disease ($n = 76, 81.7\%$). The average number of chemotherapy cycles was 5.53; most patients received four cycles of chemotherapy ($n = 45, 48.4\%$); the most common regimen was cisplatin ($n = 70, 75.3\%$); the mean total platinum dose was 682.94 mg (SE = 49.57, range: 121 to 2756 mg); and all patients had satisfactory KPS scores (60–100). CIPN assessed using the NCI-CTCAE reported that a total of 53.8% ($n = 50$) of the study subjects had CIPN—sensory impairment with toxicity grade I (36.6%, $n = 34$) or grade II (17.2%, $n = 16$), and a total of 47.3% ($n = 44$) had CIPN—motor impairment with toxicity grade I (32.3%, $n = 30$) or grade II (15.0%, $n = 14$). The rest of the patients reported no CIPN—sensory (46.2%, $n = 43$) or CIPN—motor (52.7%, $n = 49$) impairment. The average time since diagnosis was 10.67 months and the average time since the completion of previous chemotherapy was 4.28 weeks (Table 1).

Table 1
Demographic and clinical characteristics of patients (N= 93)

Variable	Number (%)	Mean (SE)	Range
Age (years)		59.24(1.20)	27–89
Sex			
Male	54(58.1)		
Female	39(41.9)		
Occupation			
Unemployed	66(71.0)		
Employed	27(29.0)		
Marital status			
Unmarried	28(30.1)		
Married	65(69.9)		
Education level			
None	4(4.3)		
Elementary	18(19.4)		
Junior high	26(28.0)		
Senior high	28(30.1)		
College and above	17(18.2)		
Religion			
None	27(29.0)		
Buddhism/ Taoism	62(66.7)		
Christianity/ Catholicism	4(4.3)		
Histology type			
NSCLC	74(79.6)		
SCLC	19(20.4)		
<i>SD</i> , standard deviation; <i>RT</i> , radiotherapy; <i>CT</i> , chemotherapy; <i>CCRT</i> , combined chemotherapy and radiotherapy; <i>KPS</i> , Karnofsky performance score			
CIPN, Chemotherapy–Induced Peripheral Neuropathy			
NCI-CTCAE– The Common Terminology Criteria for Adverse Events (CTCAE) 4.03v.			

Variable	Number (%)	Mean (SE)	Range
Cancer stage			
IB	17(18.3)		
IV	76(81.7)		
Number of chemotherapy cycle	5.53(2.75)		4–22
4	45(48.4)		
5	24(25.8)		
≥ 6	24(25.8)		
Chemotherapy modalities			
Cisplatin	70(75.3)		
Carboplatin	5(5.4)		
Cisplatin + docetaxel	15(16.1)		
Carboplatin + docetaxel	3(3.2)		
Chemotherapy, total dose, mg		682.94(49.57)	121–2756
Severity of CIPN–sensory impairment			
No CIPN impairment	43(46.2)		
NCI-CTCAE grade ^a			
I	34(36.6)		
II	16(17.2)		
III	0(0)		
Severity of CIPN–motor impairment			
No CIPN impairment	49(52.7)		
NCI-CTCAE grade ^a			
I	30(32.3)		

SD, standard deviation; *RT*, radiotherapy; *CT*, chemotherapy; *CCRT*, combined chemotherapy and radiotherapy; *KPS*, Karnofsky performance score

CIPN, Chemotherapy–Induced Peripheral Neuropathy

NCI-CTCAE– The Common Terminology Criteria for Adverse Events (CTCAE) 4.03v.

Variable	Number (%)	Mean (SE)	Range
II	14(15.0)		
III	0(0)		
KPS score (level)		85.74(0.45)	70–90
90 to 100	10(10.8)		
80 to 90	61(65.6)		
70 to 80	16(17.2)		
60 to 70	6(6.5)		
Time since diagnosis (months)		10.67(1.46)	2–84
Time since the completion of previous chemotherapy (weeks)		4.28(0.21)	1–11
<i>SD</i> , standard deviation; <i>RT</i> , radiotherapy; <i>CT</i> , chemotherapy; <i>CCRT</i> , combined chemotherapy and radiotherapy; <i>KPS</i> , Karnofsky performance score			
CIPN, Chemotherapy–Induced Peripheral Neuropathy			
NCI-CTCAE– The Common Terminology Criteria for Adverse Events (CTCAE) 4.03v.			

Top chemotherapy-induced peripheral neuropathy (CIPN) symptoms

The highest-scoring CIPN symptoms in descending ranking were: “did you have difficulty getting or maintaining an erection?” (mean = 56.02, SE = 4.33); “did you have difficulty climbing stairs or getting up out of a chair because of weakness in your legs?” (mean = 40.59, SE = 2.02); and “did you have blurred vision?” (mean = 37.63, SE = 1.56) (Table 2).

Table 2
Top ten CIPN measurement by EORTC QLQ–CIPN 20 (N= 93)

Variable	Domain	Mean (SE)
20. Did you have difficulty getting or maintaining an erection?	Autonomic	56.02(4.33)
15. Did you have difficulty climbing stairs or getting up out of a chair because of weakness in your legs?	Motor	40.59(2.02)
17. Did you have blurred vision?	Autonomic	37.63(1.56)
16. Were you dizzy when standing up from a sitting or lying position?	Autonomic	36.56(1.60)
4. Did you have numbness in your toes or feet?	Sensory	34.95(1.84)
3. Did you have numbness in your fingers or hands?	Sensory	34.14(1.66)
11. Did you have a problem holding a pen, which made writing difficult?	Motor	30.65(1.22)
9. Did you have problems standing or walking because of difficulty feeling the ground under your feet?	Sensory	30.11(1.24)
18. Did you have difficulty hearing?	Sensory	30.11(1.30)
12. Did you have difficulty manipulating small objects with your fingers (for example, fastening small buttons)?	Motor	29.30(1.30)
<i>EORTC QLQ-CIPN 20</i> , European Organization for Research and Treatment of Cancer quality of life questionnaire–chemotherapy-induced peripheral neuropathy 20, each item rated on a scale of 0–4 (not at all = 1, a little = 2, quite a bit = 3, and very much = 4), theoretical scoring range 0-100.		

Levels of CIPN, depression, CIPN–related quality of life (QoL), and general QoL

The overall mean CIPN score was 31.56 (SE = 0.84). Mean scores for the subscales were: sensory, 29.15 (SE = 0.57); motor, 31.83 (SE = 0.93); and autonomic, 33.81 (SE = 1.45). The mean score for depression was 6.67 (SE = 0.49). According to the HADS classification, 23.7% (n = 22) and 17.2% (n = 16) of patients were classified as having clinical depression and borderline depression, respectively. The mean score for CIPN–related QoL was 40.44 (SE = 0.57). The mean score for overall general QoL was 78.08 (SE = 1.68). Mean scores for the subscales were: PWB, 20.79 (SE = 0.59); SFWB, 20.31 (SE = 0.43); EWB, 19.01 (SD = 0.50); and FWB, 17.97 (SE = 0.68) (Table 3).

Table 3
Scores for CIPN, depression, CIPN–related QoL, and general QoL (N= 93)

Variable	Mean/N	SE/%	Range	Theoretical scoring range
CIPN (EORTC QLQ–CIPN 20)	31.56	0.84	0–38.89	0–100
- Sensory	29.15	0.57	0–38.89	0–100
- Motor	31.83	0.93	0–32.14	0–100
- Autonomic	33.81	1.45	0–62.50	0–100
Depression (HADS–depression subscale)	6.67	0.49	0–17	0–21
- Noncases	55	59.10		
- Borderline Cases	16	17.20		
- Clinical Cases	22	23.70		
CIPN–related QoL (Ntx subscale)	40.44	0.57	11–44	0–44
- I have trouble feeling the shape of small objects when they are in my hand	3.88	0.46	1–4	0–4
- I have trouble hearing	3.81	0.56	1–4	0–4
- I have trouble buttoning buttons	3.80	0.58	1–4	0–4
- I have joint pain or muscle cramps	3.76	0.76	0–4	0–4
- I have trouble walking	3.75	0.72	0–4	0–4
General QoL (FACT–G)	78.08	1.68	26–102	0–108
- Physical well-being (PWB)	20.79	0.59	5–28	0–28
- Social/family well-being (SFWB)	20.31	0.43	0–24	0–28
- Emotional well-being (EWB)	19.01	0.50	1–24	0–24
- Functional well-being (FWB)	17.97	0.68	3–28	0–28
EORTC QLQ–CIPN 20, European Organization for Research and Treatment of Cancer quality of life questionnaire–chemotherapy–induced peripheral neuropathy 20, theoretical scoring range 0–100; HADS–depression subscale, Hospital Anxiety and Depression Scale–depression subscale, theoretical scoring range: 0–21; Ntx subscale, The Functional Assessment of Cancer Therapy–Neurotoxicity subscale, theoretical scoring range: 0–44; FACT–G, The Functional Assessment of Cancer Therapy–General, theoretical scoring range: 0–108.				

Factors associated with CIPN–related QoL and general QoL

Multiple regression analysis identified the factors that were significantly and independently associated with CIPN-related QoL and general QoL. Patients who had greater CIPN-sensory scores ($\beta = -0.658$) and CIPN-motor scores ($\beta = -0.215$) were more likely to have worse CIPN-related QoL. These two factors explained 64.5% of the total variance in CIPN-related QoL. Patients who had a higher level of depression ($\beta = -2.768$), who had higher CIPN-sensory scores ($\beta = -0.602$), and who received a greater cumulative dose of chemotherapy ($\beta = 0.006$) were more likely to have worse general QoL. These three factors explained 57.6% of the total variance in general QoL (Table 4).

Table 4
Factors significantly associated with CIPN-related QoL and general QoL based on multiple regression analysis ($N = 93$)

Domains of QoL	Predictive variable	Adjusted R^2	Beta	F	p	95% CI	
						Lower	Upper
CIPN-related QoL (Ntx subscale)	CIPN-sensory	0.645	-0.658	84.754	0.001	-0.798	45.086
	CIPN-motor		-0.215		0.001	-0.329	-0.517
	Constant		44.193		0.001	43.301	-0.101
General QoL (FACT-G)	Depression	0.576	-2.768	42.707	0.001	-3.315	-2.221
	CIPN-sensory		-0.602		0.014	-1.077	-0.127
	Cumulative dose of chemotherapy therapy		0.006		0.039	0.001	0.011
	Constant		136.084		0.001	130.289	141.880
<i>FACT/GOG-Ntx</i> , The Functional Assessment of Cancer Therapy-Neurotoxicity subscale							
<i>FACT-G</i> , The Functional Assessment of Cancer Therapy-General							
Input independent variable: covariates included marital status (not married vs. married), number of chemotherapy cycles (continuous score), cumulative dose of chemotherapy therapy (continuous score), CIPN-sensory (continuous score), CIPN-motor (continuous score), CIPN- autonomic (continuous score), and depression (continuous score).							

Discussion

In this study, among patients with advanced LC who received platinum-based regimens, the prevalence of grade 0, I, II, and III CIPN-sensory adverse events were 46.2% ($n = 43$), 36.6% ($n = 34$), 17.2% ($n = 16$), and 0% ($n = 0$), respectively, and the prevalence of grade 0, I, II, and III CIPN-motor adverse events were 52.7% ($n = 49$), 32.3% ($n = 30$), 15.0% ($n = 14$), and 0% ($n = 0$), respectively. Kautio et al. [33] found that, in patients who received vinca alkaloid, taxane, or platina derivative regimens, 0%, 21%, 42%, and 37% of

patients reported a prevalence of grade 0, I, II, and III sensory CIPN adverse events, respectively, and 52%, 31%, 16%, and 1% of patients reported the prevalence of grade 0, I, II, and III motor CIPN adverse events, respectively. The reduced level of neuropathy may result from the fact that patients in Kautio et al. [33] had received 1–3 cycles of treatment, while our subjects had received at least 4 cycles of chemotherapy; indeed, more than half (51.6%) had received 5 or more cycles of treatment, and were still continuing treatment. CIPN symptoms were present within a few days after starting therapy and lasted for several months after beginning treatment. Healthcare providers should seek to detect CIPN early and continue assessment of CIPN as patients continue their chemotherapy.

Our results showed that the average CIPN-related QoL score of patients with advanced LC was 40.44 (SE = 0.57). The level of CIPN-related QoL among subjects in this study was lower than that reported in another recent study [34]. This difference may be due to the different cycles of chemotherapy during which patients were assessed. Patients in our study received an average of 5.53 cycles of chemotherapy and had not yet completed all cycles of chemotherapy, while patients in the study of Ajewole et al. [34] were enrolled within 2 weeks of the first chemotherapy of cycle 1 and followed for 12 weeks after enrollment. These findings may reflect that the impact of CIPN on QoL increases over time. CIPN in advanced LC patients treated with platinum-based chemotherapy may impact their ability to perform self-care, independently complete ADLs, and return to work, as well as their level of physical activity. Healthcare providers should be aware of patients' reports of outcomes related to CIPN and provide care for their needs.

The most highly rated CIPN items for patients in the present study were: difficulty getting/maintaining an erection, difficulty climbing stairs/rising from a chair, blurred vision, dizziness when standing up from a sitting/lying position, and numbness in the toes/feet. These findings agree with those of previous studies of cancer patients treated with CIPN-related regimens, which indicated that tingling or numbness in the fingers/hands, toes/feet were most the common CIPN-related symptoms, and may limit ADLs and diminish QoL [35,36]. In the present study, difficulty getting / maintaining an erection was the most common problem. Male patients may be embarrassed to discuss their perceptions and feelings about sexual dysfunction. Healthcare providers should therefore actively evaluate each patient's concerns about changes in sexual function and encourage male patients in particular to express their feelings.

Results of the present study indicated that patients who had a higher level of depression and who had more severe CIPN-sensory scores were more likely to have worse overall QoL. These results are consistent with those of previous studies [37], which reported that CIPN [36] and depression [37] lead to restrictions in ADLs [37] and decreases in mobility and independency [38] in cancer patients treated with platinum-based antineoplastic agents. Healthcare professionals should evaluate neurological function and provide information on nutritional supplements, aerobic exercise, and balance training that may stimulate peripheral neurological function and enhance daily function, to help patients cope with the adverse effects of chemotherapy.

Limitations

This study had several limitations. First, the present study examined patients with advanced LC who received at least 4 chemotherapy cycles, and although such problems may develop as early as 1–2 weeks after initiating treatment, CIPN following chemotherapy cycles is part of a dynamic process that changes over time. Longitudinal studies are needed, with long-term follow up of patients from the time they undergo treatment through the post-treatment period. Second, we did not consider the effect of nutritional supplements (glutathione, glutamine, vitamin E, or B complex) or dietary supplements (vitamins, minerals, proteins, or amino acids) as factors in CIPN, although such factors may affect outcomes. Thus, future studies should extend their analysis to include the use of nutritional supplements. Finally, patients' initial (pre-treatment) peripheral neurological function and lifestyle, variables not studied here, may have affected the evaluation of CIPN. Further studies are needed to determine the correlation between initial peripheral neurological function, lifestyle, and CIPN.

Conclusions

We found that 53.8% and 47.3% of advanced LC patients receiving platinum-based chemotherapy reported CIPN–sensory impairment and CIPN–motor impairment, respectively. Patients who had a higher level of depression, greater CIPN–sensory impairment, and those receiving a higher cumulative dose of chemotherapy were more likely to have a worse overall general QoL. Patients who had greater CIPN–sensory and CIPN–motor impairment were more likely to have worse CIPN–related QoL. CIPN–sensory impairment was the most important factor associated with overall general QoL and CIPN–related QoL.

Clinical implications

The results of this study provide a reference for clinical assessment of CIPN and the factors associated with CIPN–related QoL and general QoL in patients with advanced LC receiving platinum-based chemotherapy. Based on the results of the current study, these patients need a holistic approach to help them maximize their QoL, including health education, dietary guidance, nutritional supplements, aerobic exercise, and balance training.

Declarations

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Conflicts of interest

The authors declare that they have no conflict of interest.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the University of Wisconsin Health Sciences IRB (Number: 201701101B0) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent to participate and consent for publication

Informed consent was obtained from all individual participants included in the study.

Availability of data and material

The data that support the findings of this study are available from the corresponding author. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of Chang Gung Memorial Hospital Research Program, Chang Gung University of Science and Technology, and Ministry of Science and Technology (MOST) in Taiwan.

Authors' contribution

Conceptualization, H.-W.H. and S.-C.C.; methodology, S.-C.C.; software, H.-W.H.; validation, H.-W.H., C.-Y.L., H.-F.C., and S.-C.C.; formal analysis, H.-W.H. and S.-C.C.; investigation, H.-W.H., C.-Y.L., and S.-C.C.; resources, S.-C.C.; data curation, C.-Y.L.; writing—original draft preparation, C.-Y.L. and S.-C.C.; writing—review and editing; visualization, H.-W.H., C.-Y.L., H.-F.C., and S.-C.C.; supervision, S.-C.C.; project administration, H.-W.H. and S.-C.C. All authors have read and agreed to the published version of the manuscript.

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