Falls and Functional Impairments in Breast Cancer Patients with Chemotherapy-Induced Peripheral Neuropathy

Hiroko Komatsu¹, Kaori Yagasaki¹, Yasuhiro Komatsu², Hideko Yamauchi³, Teruo Yamauchi⁴, Toshio Shimokawa⁵, Ardith Z. Doorenbos⁶,⁷

¹Faculty of Nursing and Medical Care, Keio University, Tokyo, ²Department of Healthcare Quality and Safety, Gunma University Graduate School of Medicine, Gunma, ³Department of Breast Surgical Oncology, St. Luke’s International Hospital, Tokyo, ⁴Division of Medical Oncology, St. Luke’s International Hospital, Tokyo, ⁵Department of Medical Data Science, Graduate School of Medicine, Wakayama Medical University, Wakayama, Japan, ⁶Department of Biobehavioral Health Science, College of Nursing, University of Illinois at Chicago, Chicago, IL, ⁷Department of Biobehavioral Health Science, College of Nursing, University of Illinois at Chicago and Department of Biobehavioral Nursing and Health Informatics, School of Nursing, University of Washington, WA, USA

Corresponding author: Hiroko Komatsu, PhD, RN
Faculty of Nursing and Medical Care, Keio University, Tokyo, Japan
Tel: +81-3-5363-3733; Fax: +81-3-5363-2039
E-mail: komah@sfc.keio.ac.jp
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ABSTRACT

Objective: We investigated the incidence of falls and functional impairments in breast cancer patients with chemotherapy-induced peripheral neuropathy (CIPN). Additionally, we examined whether taxane-induced peripheral neuropathy was associated with the patients’ falls and functional impairments. Methods: We conducted a cross-sectional study including 88 patients with breast cancer who received taxane-based chemotherapy and were recognized as having peripheral neuropathy symptoms (Common Terminology Criteria for Adverse Events Grade ≥1). Patients completed the Functional Assessment of Cancer Therapy-Gynecologic Oncology Group-Neurotoxicity questionnaire for neuropathy and described falls from the onset of the taxane-based chemotherapy to the time of the survey. Functional impairments were defined using the Activities of Daily Living subsection of the Vulnerable Elder’s Scale. Data were analyzed using descriptive statistics and logistic regression. Results: Of the participants, 40.9% experienced falls and 38.4% reported functional impairments. Most falls occurred on flat ground. Bone fracture due to falls was observed in 11.4% of the participants. Logistic regression revealed that CIPN was not significantly associated with the reported incidence of falls. However, it was significantly associated with functional impairments (odds ratio, 6.415; 95% confidence interval: 1.271–32.379; \( P = 0.024 \)). Conclusions: CIPN was associated with functional impairments, but not with the onset of the taxane-based chemotherapy to the time of the survey. Functional impairments were defined using the Activities of Daily Living subsection of the Vulnerable Elder’s Scale. Data were analyzed using descriptive statistics and logistic regression. Results: Of the participants, 40.9% experienced falls and 38.4% reported functional impairments. Most falls occurred on flat ground. Bone fracture due to falls was observed in 11.4% of the participants. 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incidence of falls. Patients should be informed prior to the onset of anticancer therapy that CIPN is a risk factor for functional impairments.

Key words: Breast cancer, chemotherapy, chemotherapy-induced peripheral neuropathy, falls, functional impairments, peripheral neuropathy

Introduction

Taxane-based chemotherapy (e.g., paclitaxel or docetaxel) is used in the management of early-stage and metastatic breast cancer,[1] the most common cancer in women. Taxane-induced peripheral nerve damage can lead to motor and sensory symptoms such as bilateral paresthesia manifested as numbness, tingling, and burning pain.[2] A systematic review on chemotherapy-induced peripheral neuropathy (CIPN) showed that the prevalence of CIPN among patients with all cancer types was 68.1% (95% confidence interval [CI]: 57.7–78.4) in the 1st month after chemotherapy, 60.0% (95% CI: 36.4–81.6) after three months, and 30.0% (95% CI: 6.4–53.5) after six months or more.[3] The overall incidence of peripheral neuropathy among all patients with cancer varies for the different taxanes, with reported rates of 57%–83% for patients treated with paclitaxel and 11%–64% for patients treated with docetaxel.[4] It has also been shown that the prevalence of taxane-induced peripheral neuropathy among patients with breast cancer was 70.8% (95% CI: 43.5–98.1).[3]

CIPN is not life threatening. However, it restricts daily activities[5] and thereby impairs the physical and role functioning[6] and quality of life[6,7] of patients. Diminished sensation and loss of neuromuscular control in the lower extremities may escalate to eventually interfere with balance and gait.[8]

In a study using secondary data analysis to investigate serious health outcomes in 512 female patients with cancer in the US, CIPN was found to have an impact on both physical function impairment and falls.[9] Falls are the second leading cause of accidental or unintentional injury deaths and are a growing public health problem worldwide.[10] Falls are a serious health concern and are a leading cause of injury and death in humans, especially among the elderly in the US.[11] Gewandter et al.[12] reported that CIPN, primarily motor neuropathy, was associated with falls and functional impairments in patients with cancer. Their data suggest that patients with cancer who received taxane were more likely to experience a fall or have a functional impairment. Bao et al.[13] demonstrated that there was a significant relationship between the severity of CIPN and the high fall rate in patients with breast cancer who received taxane-based chemotherapy in the US. However, there have been no reports on the prevalence of falls in breast cancer patients with CIPN caused by taxane-based chemotherapy (e.g., paclitaxel or docetaxel) or on the relationship between CIPN and falls or functional impairments in Asian populations. We conducted this study to determine the prevalence of falls and their association with functional impairments in breast cancer patients diagnosed with CIPN after receiving taxane-based chemotherapy.

Methods

Participants and study design

We used a cross-sectional study design. The setting was a general hospital in Tokyo with approximately 500 beds. The attending physician, who was also a member of the research team, identified potential participants from their medical records based on the inclusion and exclusion criteria. Once potential participants were identified, the attending physician approached the patients at their scheduled visit, and if they showed interest, they were introduced to a researcher who explained the research overview and methods using a written document and obtained the participant’s consent.

The inclusion criteria were: (1) age 20–79 years; (2) ability to provide written informed consent; (3) patients with breast cancer who received taxane anticancer agents between January 1, 2013 and August 31, 2015, and presented peripheral neuropathy symptoms (Common Terminology Criteria for Adverse Events [CTCAE] Grade 1 or above); and (4) fluency in spoken and written Japanese. The exclusion criteria were: (1) unsuitability for participation due to cognitive or mental disorder present at the time of recruitment as judged by an attending physician; (2) presence of brain metastasis; (3) physician’s prognosis of <6 months; and (4) registration in another clinical trial.

After consent was obtained, the participants were invited to complete the survey during their visit to the clinic. The survey took approximately 20 min to complete. The majority of the participants completed the survey at the time of their visit to the clinic and returned it directly to the researcher. Some participants completed the survey at home and returned it by mail.
**Instruments for measurement**

**Severity of chemotherapy-induced peripheral neuropathy**  
The severity of CIPN due to chemotherapy or targeted therapy was determined according to the clinical grade, based on the National Cancer Institute-CTCAE version 4.0 (Japan Clinical Oncology Group). The CTCAE grade was determined by reviewing the medical records, and the highest grade observed during the treatment period, from the onset of chemotherapy till the time of the study, was used for the study.

**Symptoms of chemotherapy-induced peripheral neuropathy**  
A subjective evaluation of each participant’s CIPN was performed using the Functional Assessment of Cancer Therapy-General (FACT-G) scale and the Gynecologic Oncology Group-Neurotoxicity (GOG-Ntx) subscale, which measures neural toxicity. The basic scale FACT-G, developed by Cella et al., is a 27-item self-completed questionnaire which consists of four subscales addressing physical (7 items), social/family (7 items), emotional (6 items), and functional well-being (7 items). The reliability and validity of the Japanese version of the FACT-G has been established.

The GOG-NTX, a scale by which patients subjectively evaluate their sensory disturbance caused by CIPN, is composed of 11 items related to neuropathy, including sensory neuron disorders, motor neuron disorders, acoustic nerve disorders, and functional impairment. The GOG-NTX score ranges between 0 and 44, with lower scores indicating more severe neuropathy. The 11-item GOG-Ntx subscale correlated moderately and significantly with several objective measures of neuropathy, and unlike its more standard counterparts, it distinguished patients with known neurotoxicity from chemotherapy-naive patients. The reliability and validity of the Japanese version of the FACT-G has been confirmed.

**Incidence of falls**  
We defined a fall as described by Tinetti and Speechley, that is, “unintentionally coming to rest on the ground or at some other lower level, not as a result of a major intrinsic event (e.g., a stroke or syncope) or overwhelming hazard.” Using a self-administered questionnaire, the participants were asked whether they had experienced any falls from the onset of the taxane-based chemotherapy to the time of the survey; if that was the case, they were asked to describe the reasons for each fall, location of the fall, the presence or absence of injury, and the nature of the injury.

**Functional impairments**  
Functional impairments were measured using the Vulnerable Elders Survey (VES) developed by Saliba et al.

The VES-13 is a validated survey used to identify patients at risk of functional decline. It is comprised of 13 items that assess age, self-rated health, and difficulty performing six physical activities and five functional activities of daily living (ADLs), resulting in a score from 0 to 10. We selected the VES because it has also been used to identify cancer patients with disability who are at a risk of adverse outcomes.

Functional impairment was determined based on the method of Gewandter et al., who examined the relationship between functional impairment in cancer survivors and peripheral neuropathy using the VES. A subsection of the VES assesses functional impairment using a series of “yes or no” questions to inquire whether the respondent is unable to perform or needs help with daily living activities (e.g., shopping for personal items, managing money, walking across the room, doing light housework, and bathing) due to his/her health problems. Any participant who reported an inability to perform the activity or needed assistance with any of the listed activities was considered to have a functional impairment.

**Data analysis**  
Descriptive statistics were used to analyze the participants’ history of falls, demographics, cancer stage and cancer treatment, severity of the peripheral neuropathy (as assessed by the [NCI]-CTCAE version 4.0), subjective evaluation of the peripheral neuropathy (as assessed by the FACT/GOG-NTX), and functional impairments (as assessed by the subscale of VES). To compare the demographics, breast cancer stage and its treatment history, and variables related to CIPN between fallers and nonfallers and between those with and without any functional impairments, we used the Mann–Whitney U-test and Fisher’s exact test for continuous and categorical data, respectively. We performed logistic regression to identify factors associated with falls and the presence of any functional impairments. Simultaneous variable selection was used in the logistic regression. Statistical tests were two tailed, and the significance level was set at \( P < 0.05 \). Statistical analyses were performed using Statistical Package for the Social Sciences software version 22.0 (IBM Corp., Armonk, NY, USA).

**Ethical approval**  
This study was approved by the Institutional Review Board of the Faculty of Nursing and Medical Care, Keio University (Approval No. 243), and the Internal Review Board of St. Luke’s International Hospital (15-R026). All participants provided written informed consent.
Results

Characteristics of participants

A total of 98 participants were identified from the medical records to be eligible for the study. Of these, ten participants did not complete the survey. We were unable to contact three potential participants, two withdrew from chemotherapy, and five participants had brain metastasis. Thus, a total of 88 participants successfully completed and returned the survey (response rate: 89.8%).

The participants’ demographic and clinical characteristics at the time of the survey are summarized in Table 1. Their mean age was 54.1 (standard deviation [SD] = 10.0) years. Of the 88 participants, 71 (80.7%) had college level or higher education, and approximately 50% were employed. Only two participants (2.3%) had a history of diabetes. Fifty (56.8%) participants had Stage I/II cancer at the time of the diagnosis, and eight participants (9.1%) reported recurrence or metastasis at the time of the survey. Fifty-nine participants (67.0%) used a paclitaxel-based regimen, 27 participants (30.7%) used a docetaxel-based regimen, and two participants (2.3%) used both types of regimen.

Table 1: Cancer patients with chemotherapy-induced peripheral neuropathy (n=88): Demographics and the associations of demographic and cancer-related factors with falls and functional impairments

| Variable                                      | Total, n (%) | Any falls, n (%) | No fall, n (%) | P       | Any functional impairment, n (%) | No functional impairments, n (%) | P       |
|-----------------------------------------------|--------------|------------------|----------------|---------|----------------------------------|---------------------------------|---------|
| Age, years                                    |              |                  |                |         |                                  |                                  |         |
| <65                                           | 68 (77.3)    | 26 (74.3)        | 42 (82.4)      | 0.424   | 16 (57.1)                       | 51 (87.9)                       | 0.002   |
| ≥65                                           | 19 (21.6)    | 9 (25.7)         | 9 (17.7)       |         | 12 (42.9)                       | 7 (12.1)                        |         |
| Unknown                                       | 1 (1.1)      |                  |                |         |                                  |                                  |         |
| Educational level                             |              |                  |                |         |                                  |                                  |         |
| High school or less                           | 17 (19.3)    | 10 (27.8)        | 7 (13.7)       | 0.169   | 10 (34.5)                       | 7 (12.1)                        | 0.021   |
| College or above                              | 71 (80.7)    | 26 (72.2)        | 44 (86.3)      |         | 19 (63.5)                       | 51 (87.9)                       |         |
| Employment                                    |              |                  |                |         |                                  |                                  |         |
| Employed                                      | 45 (51.1)    | 18 (50.0)        | 26 (52.0)      | >0.999  | 9 (31.0)                        | 35 (61.4)                       | 0.012   |
| Nonemployed                                    | 42 (47.7)    | 18 (50.0)        | 24 (48.0)      |         | 20 (69.0)                       | 22 (38.6)                       |         |
| Unknown                                       | 1 (1.1)      |                  |                |         |                                  |                                  |         |
| Cancer stage                                  |              |                  |                |         |                                  |                                  |         |
| I/II                                          | 50 (56.8)    | 18 (52.9)        | 32 (68.1)      | 0.247   | 11 (39.3)                       | 38 (71.7)                       | 0.008   |
| III/IV                                        | 32 (36.4)    | 16 (47.1)        | 15 (31.9)      |         | 17 (60.7)                       | 15 (28.3)                       |         |
| Unknown                                       | 6 (6.8)      |                  |                |         |                                  |                                  |         |
| Recurrence/metastasis                         |              |                  |                |         |                                  |                                  |         |
| Yes                                           | 8 (9.1)      | 1 (2.8)          | 7 (13.7)       | 0.133   | 4 (13.8)                        | 4 (6.9)                         | 0.432   |
| No                                            | 80 (90.9)    | 35 (97.2)        | 44 (86.3)      |         | 25 (86.2)                       | 54 (93.1)                       |         |
| Radiation                                      |              |                  |                |         |                                  |                                  |         |
| Yes                                           | 54 (61.4)    | 23 (63.9)        | 30 (60.0)      | 0.823   | 14 (48.3)                       | 39 (68.4)                       | 0.100   |
| No                                            | 33 (37.5)    | 13 (36.1)        | 20 (40.0)      |         | 15 (51.7)                       | 18 (31.6)                       |         |
| Duration of chemotherapy administration (months), mean±SD | 6.6±10.2 | 4.9±6.1          | 7.0±11.2       | 0.297   | 8.7±16.1                        | 5.6±5.4                         | 0.176   |
| Total dose of taxane anticancer agents, mean±SD | 1446.3±1558.8 | 1074.4±512.2 | 1649.1±1927.9 | 0.085  | 1802.7±2442.1 | 1265.4±825.1 | 0.133   |
| Regimen                                       |              |                  |                |         |                                  |                                  |         |
| Docetaxel based                               | 27 (30.7)    | 13 (36.1)        | 14 (27.5)      | 0.290   | 10 (34.5)                       | 17 (29.3)                       | 0.667   |
| Paclitaxel based                              | 59 (67.0)    | 22 (61.1)        | 37 (72.6)      |         | 18 (62.1)                       | 40 (69.0)                       |         |
| Both DOC + PAC                                | 2 (2.3)      | 1 (2.8)          | 0 (0.0)        |         | 1 (3.5)                         | 1 (1.7)                         |         |
| NCI-CTCAE version 4.0 CIPN grade              |              |                  |                |         |                                  |                                  |         |
| 1                                             | 71 (80.7)    | 26 (72.2)        | 45 (88.2)      | 0.090   | 17 (58.6)                       | 53 (91.4)                       | 0.001   |
| ≥2                                            | 17 (19.3)    | 10 (27.8)        | 6 (11.8)       |         | 12 (41.4)                       | 5 (8.6)                         |         |
| Total scores of FACT/GOG-NTX, mean±SD         | 31.4±9.0     | 28.6±8.6         | 33.5±8.7       | 0.011   | 24.8±8.3                        | 34.7±7.5                        | <0.001  |
| Level of any functional impairment            |              |                  |                |         |                                  |                                  |         |
| Yes (>1)                                      | 29 (33.0)    | 16 (45.7)        | 12 (23.5)      | 0.037   |                                  |                                  |         |
| No                                            | 58 (66.9)    | 19 (54.3)        | 39 (76.5)      |         |                                  |                                  |         |

CIPN: Chemotherapy-induced peripheral neuropathy, DOC: Docetaxel, PAC: Paclitaxel, NCI-CTCAE: National Cancer Institute Common Terminology Criteria for Adverse Events, SD: Standard deviation, FACT/GOG-NTX: Functional Assessment of Cancer Therapy-Gynecologic Oncology Group-Neurotoxicity. One participant did not answer to the question related to "fall", and the other one participant did not answer to the question related to "functional impairment"
Chemotherapy-induced peripheral neuropathy severity and chemotherapy-induced peripheral neuropathy symptom

In total, 71 (80.7%) and 17 (19.3%) participants were diagnosed with Grade 1 and Grade 2 or above CIPN, respectively [Table 1]. The participants’ mean (SD) total scores for FACT-G and FACT/GOG-Ntx were 74.9 (18.5) and 31.4 (9.0), respectively.

Incidence of falls and any functional impairments

Of the 88 participants, 36 (40.9%) had experienced falls during the period from the onset of taxane-based chemotherapy to the time of the survey. With regard to the frequency of falls in these 36 fallers, 19 reported falling only once, and the other 17 reported falling twice or more.

In the 36 fallers, falls occurred both inside (21 participants) and outside the home (23 participants), at a similar rate. Flat places were the location of falls for 26 participants, with eight participants reporting falls in a hallway, five in a living room, five in a bedroom, five on a sidewalk, and three in an open space. Surprisingly, only 14 participants reported falling in nonflat places, such as the stairs (11 participants) or the bathroom (3 participants), and this number was smaller than that for flat places. The stated reasons for falls included “because my feet were numb, it was hard to walk,” “I could not hold a handrail (at home),” “I could not lift my feet up,” and “I lost my balance.”

As for injuries caused by the falls, 15 participants were injured, 18 participants were not injured, and three participants had no response. The types of injury were bone fracture (10 participants), sprain (5 participants), and not specified (1 participant). Several participants who had bone fractures reported, “When I am about to fall, I cannot support myself because of the numbness not only in my legs but also in my hands.” Among the ten participants who had bone fracture, four were on hormonal therapy. Tamoxifen was prescribed to the two participants on hormonal therapy, whereas the name of the prescribed drug was unknown to the remaining two participants.

Of the 88 participants, 29 (33.0%) reported some functional impairment. Twenty-one (23.9%) participants reported difficulty when shopping, and 17 (19.3%) reported difficulty when performing daily living tasks independently. Difficulties in performing these two tasks were the most prevalent impairments reported.

Factors affecting falls and functional impairments

Table 1 summarizes the associations of demographic and cancer-related factors with falls and functional impairments in our breast cancer patients with CIPN. Among 36 fallers, 26 (72.2%) were associated with CIPN Grade 1 and 10 (27.8%) were associated with CIPN Grade 2 or higher. The fall rate was 26/71 (36.6%) among 71 participants with CIPN Grade 1, whereas it was 10/17 (58.7%) among 17 participants with CIPN Grade 2 or higher. Thus, the fall rate was higher among those with CIPN Grade 2 or higher compared to those with CIPN Grade 1. However, the difference was not statistically significant.

The total FACT/GOG-NTX score was significantly associated with both falls and functional impairments: mean score for falls = 28.6 versus no falls = 33.5, P < 0.011 and mean score for any functional impairment = 24.8 versus no functional impairment = 34.7, P < 0.001. The CTCAE grade of CIPN was not associated with falls, but it was significantly associated with functional impairment, as follows: Grade 2, falls 27.8% versus no falls 11.8%, P < 0.090; any functional impairment 41.4% versus no functional impairment 8.6%, P < 0.001.

We used logistic regression to evaluate the association between peripheral neuropathy with the two outcomes (falls and any functional impairments) [Tables 2 and 3]. Peripheral neuropathy, as indicated by the CTCAE grade for CIPN, or total score of FACT/GOG-NTX, was not significantly associated with the reported incidence of falls. In contrast, these indicators of peripheral neuropathy were significantly associated with functional impairments, as follows: Grade 2, odds ratio (OR):
6.415, 95% CI: 1.271–32.379, \( P = 0.024 \); total score of FACT/GOG-NTX, OR: 0.874, 95% CI: 0.808–0.946, \( P = 0.001 \) [Table 3].

**Discussion**

In the present cross-sectional study, 40.9% of the breast cancer patients with CIPN symptoms experienced falls. A study by Bao et al.,[13] reported that, among postmenopausal women with a history of Stage I–III breast cancer who received taxane-based chemotherapy, 31.9% and 41.5% of the mild CIPN and moderate-to-severe CIPN groups, respectively, experienced at least one fall after the end of chemotherapy. Our findings, as well as those of Bao et al.,[13] focus on falls as an important area for research and nursing care among those who receive taxane-based chemotherapy.

Regarding the locations of falls, our analyses revealed no differences in the prevalence of falls which occurred indoors and those that occurred outdoors, whereas the number of falls in nonflat places, such as the stairs, was smaller than that for flat places. This result is similar to that reported by Kolb et al.[21] for falls among cancer patients with CIPN due to a taxane- or platinum-based chemotherapeutic agent. Kolb et al.[21] reported that the vast majority of falls occurred indoors in a flat well-lit area, not in the bathroom or on the stairs, and that fall risk mitigation strategies must also recognize that most falls may not occur in these areas of the home. Fall prevention counseling has focused on areas of high risk, such as the bathroom, stairs, and poorly lit areas,[22] but fall prevention strategies clearly need to include the dissemination of awareness that falls can occur indoors in flat and well-lit areas as well.

In our participants with breast cancer, more than 40% of the falls resulted in injury, two-thirds of which were bone fractures. Several participants with a bone fracture stated that they were unable to support themselves due to the numbness in their hands and legs when they were about to fall, thus highlighting the characteristics of falls caused by a peripheral nerve disorder due to a taxane anticancer agent. Paclitaxel induces a bilateral, distal, symmetrical axonal neuropathy that is predominantly characterized by sensory symptoms such as numbness, tingling, and burning pain in a stocking-and-glove distribution; docetaxel induces similar but usually milder symptoms.[2] Therefore, the difficulty in using their hands before a fall hinders them from rebalancing. The falls induced by such episodes can result in one or more bone fractures. The fractures caused by such falls often require emergency treatment and long-term rehabilitation, imposing a high economic burden on both the individual and the society. The risk of bone fracture is associated with endocrine therapy in patients with breast cancer, with a significantly higher fracture risk among women treated with aromatase inhibitors, especially during the treatment period.[23,24] In our study, four participants were on endocrine therapy; however, we could not deduce any association among fracture, osteoporosis, and the use of aromatase inhibitors owing to the lack of information regarding the name of the drug and the small number of participants undergoing endocrine therapy. Future studies on CIPN in patients with breast cancer are needed to elucidate the association between aromatase inhibitors and osteoporosis.

In the present study, we examined whether CIPN is independently associated with falls and/or functional impairments. Our findings demonstrated that peripheral neuropathy symptoms were associated with functional impairments. However, there was no significant relationship between CIPN (total CIPN-Ntx score or CTCAE grade for CIPN) and falls. The lack of association between CIPN and falls may be attributable to the small number of patients with Grade 2 or higher CIPN.

CIPN (total CIPN-Ntx score or CTCAE grade for CIPN) was significantly associated with functional impairments. The participants in this study comprised only patients with breast cancer who received taxane anticancer agents. Taxanes cause sensory and motor neuropathy symptoms, most commonly muscle weakness.[25] Therefore, difficulties performing daily living activities may be induced by various dysfunctions caused by taxane, including sensory and motor neuropathy symptoms and muscle weakness. On the other hand, no significant relationship was observed between the dosage of taxanes and functional impairment in our data. This may be partly due to the wide variation in individual dosage, leading to a SD of 1558.8, while the mean was 1446.3. Future studies using a prospective study design should collect taxane dosage information and investigate the relationships between regimens and falls or functional impairments in patients with breast cancer.

**Table 3: Multivariate associations of neuropathy and demographic and cancer-related factors with any functional impairment in cancer patients with chemotherapy-induced peripheral neuropathy**

| Predictor                                      | Estimated adjusted OR | OR  | 95% CI | \( P \) |
|------------------------------------------------|-----------------------|-----|--------|---------|
| Age: ≥65 vs. <65 years*                        | 1.108 0.248 4.948 0.893 |     |        |         |
| Educational level: ≤ high school vs. ≥ college | 0.213 0.053 0.858 0.030 | 0.466 0.133 1.639 0.234 |     |        |
| Employment: Unemployed vs. employed            | 0.319 0.198 0.574 0.440 | 1.000 1.000 1.001 0.211 |     |        |
| Metastasis: Yes vs. no                         | 6.415 1.271 32.379 0.024 |     |        |         |
| Total dose of taxane anticancer agents         | 0.874 0.808 0.946 0.001 |     |        |         |
| NCI-CTCAE version 4.0 grade: ≥2 vs. 1          | 0.248 1.000 1.000 1.001 | 1.639 0.133 1.639 0.234 |     |        |

\(*<65\text{ years}=0, \text{ <65 years}=1.\;\text{NCI-CTCAE: National Cancer Institute Common Terminology Criteria for Adverse Events, FACT/GOG-NTX: Functional Assessment of Cancer Therapy-Gynecologic Oncology Group-Neurotoxicity, OR: Odds ratio, CI: Confidence interval}\)
**Limitations**

Due to limitations in the cross-sectional design of this study, we could not establish causality in the relationship between falls and functional impairments in patients with CIPN. Only a one-time evaluation has the potential for recall bias, and future prospective studies need to collect data at multiple time points for evaluation.

There might also have been a recall bias as the fall history was collected based on the self-reports of patients. In addition, we did not collect information on whether the patients were experiencing menopause. Future studies are needed to explore menopause as a potential risk factor for CIPN or incidences of fall. Moreover, the generalizability of the results is limited because the participants were patients with cancer at a single hospital in Japan. Future studies must investigate the causes of falls using a prospective study design including various cancer types and therapy regimens.

**Implications for future research and practice**

Education on fall prevention should incorporate current research findings, such as our finding that falls occur even on flat surfaces and that patients have difficulty in preventing falls when they have a peripheral nerve disorder in the limbs. The effect of an interactive motor adaptation balance training program based on wearable sensors for improving balance has been examined in the elderly with peripheral nerve disorders caused by anticancer agents. Further examinations of walking balance that focus not only on lower-extremity balance, but also on the movement of the upper extremities would be informative. Our analyses suggest that difficulties in the performance of daily living activities are due to dysfunctions caused by taxane-related sensory and motor neuropathy symptoms and muscle weakness. Training on ways of safely and effectively performing daily living activities should be emphasized as self-care strategies for individuals with peripheral nerve disorder.

**Conclusion**

Our study showed that falls and functional impairments occurred in 40.9% and 38.4% of patients, respectively, of taxane-treated breast cancer patients with a peripheral nerve disorder rated >1 using the CTCAE. The presence of peripheral neuropathy symptoms was associated with functional impairments, but not with falls. Prior to the onset of their anticancer therapy, patients should be informed that CIPN is a risk factor for functional impairments, and education on how to cope with these functional impairments needs to be provided.

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**Conflicts of interest**

There are no conflicts of interest.

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