CANCER DIAGNOSIS & PROGNOSIS *6*: 236-244 (2026)
doi: 10.21873/cdp.10523

Patient-reported Outcomes of Adverse Events After Perioperative Chemotherapy for Breast Cancer: A Prospective Observational Study

TAKAAKI FUJII[1,2,3], KEI ICHIBA[4], MAYU AOKI[3], KEIKO TANABE[3], MISATO OGINO[3], SAYAKA OBAYASHI[3] and HIROYUKI TAKEI[1]

[1]Department of Breast Surgery and Oncology, Nippon Medical School, Tokyo, Japan;
[2]Department of Breast Surgery and Oncology, Nippon Medical School Chiba Hokusoh Hospital, Chiba, Japan;
[3]Division of Breast and Endocrine Surgery, Department of General Surgical Science, Graduate School of Medicine, Gunma University, Maebashi, Japan;
[4]Nursing, Gunma University Hospital, Maebashi, Japan

Abstract

Background/Aim: Chemotherapy for breast cancer is associated with several adverse events (AEs), many of which are under-reported when assessed solely by physicians. Patient-reported outcomes (PROs) obtained *via* structured questionnaires allow for more accurate assessment of the patients' symptoms. This prospective observational study used a PRO-based questionnaire to assess the long-term course of AEs among patients with breast cancer who underwent perioperative chemotherapy.

Patients and Methods: Patients with operable breast cancer who received perioperative chemotherapy with a docetaxel/cyclophosphamide (TC) or anthracycline- and taxane-based chemotherapy regimen (A+T) were enrolled. A PRO-based questionnaire, prepared for this study and aligned with the Common Terminology Criteria for Adverse Events, was administered at the end of each patient's chemotherapy regimen and 6 months later. The questionnaire covered nausea, vomiting, oral mucositis, constipation, diarrhea, dysgeusia, insomnia, neuropathy, nail loss, and alopecia. The frequency and severity of each AE were compared between regimens, and longitudinal changes were analyzed.

Results: A total of 115 patients (median age 50 years) were evaluated. Nausea, vomiting, mucositis, constipation, dysgeusia, insomnia, peripheral neuropathy, and nail loss were common at the end of the patients' chemotherapy regimens, but 6 months later the frequency of gastrointestinal symptoms had decreased. Several AEs persisted beyond 6 months; notably, neuropathy, dysgeusia, insomnia, and nail loss. Grade 3 symptoms persisted for neuropathy, and nail loss was confirmed to have increased at 6 months. Compared to the TC chemotherapy, peripheral sensory neuropathy persisted longer in the A+T group.

continued

Takaaki Fujii, MD, PhD, FACS, Department of Breast Surgery and Oncology, Nippon Medical School Chiba Hokusoh Hospital, 1715 Kamagari, Inzai, Chiba 270-1694, Japan. Tel: +81 0476991111, Fax: +81 0476991907, e-mail: f-takaaki@nms.ac.jp

Received December 24, 2025 | Revised January 22, 2026 | Accepted February 5, 2026

Conclusion: PROs are thought to capture persistent symptoms that are often underestimated in conventional clinical practice. In the present breast cancer series, PRO-based monitoring revealed regimen-specific AE profiles and the persistence of neuropathy, dysgeusia, and nail changes beyond chemotherapy. These findings highlight the importance of monitoring not only during chemotherapy, but also in the months after the chemotherapy's completion, when patients continue to suffer from persistent symptoms. Incorporating structured PRO-based questionnaires into follow-up care may be crucial for optimizing supportive management.

Keywords: Breast cancer, chemotherapy, adverse event, PRO, perioperative therapy, long-term toxicity.

Introduction

Systemic therapies are necessary for patients with early breast cancer, and adjuvant chemotherapy has been shown to decrease mortality due to breast cancer (1). However, patients with breast cancer who have undergone adjuvant chemotherapy have often suffered from adverse effects (AEs), including nausea, diarrhea, peripheral neuropathy, stomatitis, taste disorder, and insomnia, which significantly impact the patients' quality of life (QOL) and their treatment adherence. Assessments of AEs are conducted using the Common Terminology Criteria for Adverse Events (CTCAE), but these assessments are often based on the clinician's evaluation, leading to a tendency to underestimate subjective symptoms such as nausea, dysgeusia, insomnia, and neuropathy (2-5).

Patient-reported outcomes (PROs), collected through structured questionnaire surveys, have emerged as a complementary tool that captures patients' direct experience of symptoms, thereby providing more accurate and patient-centered toxicity data (2, 3). Discrepancies between physician-reported and patient-reported AE profiles in breast cancer chemotherapy have been identified (2, 3). Large-scale surveys in Japan have also highlighted unmet patient needs regarding AE management and the importance of pretreatment information on the expected course and impact of AEs (3). However, few studies have prospectively monitored the course and persistence of chemotherapy-induced toxicity by using PROs after the end of treatment. Our research group has conducted a prospective observational study on chemotherapy-induced alopecia (which significantly impairs patients' QOL), and we used PROs to evaluate the course of alopecia according to the treatment regimen and patients' age (6-9). In the present study, we evaluated chemotherapy-induced AEs by obtaining PROs via a structured questionnaire, focusing on outcomes after the completion of chemotherapy and 6 months later in order to examine the frequency and progress of the AEs.

Patients and Methods

Patients. This single-center prospective observational study included 115 patients with primary breast cancer who underwent perioperative chemotherapy at Gunma University (Maebashi, Japan) between January 2016 and March 2023, based on the approved study protocol. This study was approved by the ethics committee of Gunma University (approval no. 1405, January 28, 2016). The oncologic management for all of the patients included breast surgery with the appropriate axillary lymph node procedures, including the lymph node sentinel procedure and lymph node dissection, radiotherapy, chemotherapy, hormonal therapy according to the patient's age and the tumor's hormonal status, and a trastuzumab ± pertuzumab regimen for human epidermal growth factor receptor 2 (HER2)-positive breast cancer.

Treatment. The patients received a standard anthracycline- and taxane (A+T)-based chemotherapy regimen, *e.g.*, FEC (5-fluorouracil, epirubicin, and cyclophosphamide) or AC (adriamycin and cyclophosphamide) followed by docetaxel or paclitaxel, or docetaxel plus cyclophosphamide (TC). The HER2-positive patients received additional trastuzumab

± pertuzumab therapy. The chemotherapy protocols were as follows. The FEC regimen was a combination of epirubicin 100 mg/m^2, cyclophosphamide 500 mg/m^2, and 5-fluorouracil 500 mg/m^2 for four cycles every 3 weeks. The AC regimen was a combination of doxorubicin 60 mg/m^2 and cyclophosphamide 600 mg/m^2 every 2-3 weeks for a total of four cycles and docetaxel 75 mg/m^2 every 3 weeks for four cycles or weekly paclitaxel 80 mg/m^2 for 12 cycles. The TC regimen was a combination of docetaxel 75 mg/m^2 and cyclophosphamide 600 mg/m^2 for four cycles every 3 weeks. Only one patient (scheduled for the A+T regimen) could not receive taxane due to AEs, resulting in the administration of AC alone.

Outcomes (patient-reported adverse events). PROs were collected *via* a structured self-administered questionnaire designed specifically for this study. The questionnaire was provided to each patient at the completion of her chemotherapy regimen and then again 6 months later. The end-of-treatment questionnaire assessed the presence of nausea, vomiting, oral mucositis, constipation, diarrhea, dysgeusia, insomnia, neuropathy, and nail loss. PROs were collected via a structured self-administered questionnaire developed for this study. The questionnaire focused on symptomatic AEs that commonly occur during perioperative breast cancer chemotherapy and that can be self-reported (nausea, vomiting, oral mucositis, constipation, diarrhea, dysgeusia, insomnia, peripheral neuropathy, and nail loss). For each AE, response options were written in patient-friendly language and anchored to the descriptive criteria of the Common Terminology Criteria for Adverse Events (CTCAE; version 4.0), such as frequency (*e.g.*, vomiting episodes/day) and functional impact (*e.g.*, interference with oral intake or activities of daily living). Because CTCAE was originally developed for clinician-reported grading, we used a CTCAE-informed grading scheme for patient self-reporting rather than clinician-assigned CTCAE. The questionnaire was reviewed by breast oncologists and oncology nurses for content/face validity and feasibility before study initiation. The questionnaire was administered at completion of the chemotherapy regimen and again 6 months later using the same grading scheme.

Clinical variables. Clinical and pathological data were collected from medical records: the patient's age, tumor TNM stage, estrogen receptor (ER) expression status, progesterone receptor (PgR) expression status, and the HER2 score of the primary tumor. The ER and PgR statuses were assessed by using the Allred score ≥3 points, which indicates ER and PgR positivity (10, 11). HER2 overexpression was determined by an immunohistochemistry (IHC) analysis and a fluorescence in situ hybridization (FISH) analysis with IHC 3+ or IHC 2+/FISH+ scores indicating HER2 positivity (10). Breast cancer subtypes were defined based on the patient's ER, PgR, and HER2 status as luminal-type breast cancer (ER-positive, HER2-negative), luminal-HER2 type (ER-positive and HER2-positive), HER2 type (ER-negative and HER2-negative), and triple-negative (ER-negative and HER2-negative) breast cancer.

Statistical analysis. We conducted a univariate statistical analysis using Fisher's exact test or the χ^2-test with Yates' correction. Continuous variables such as age were evaluated for normality using the Shapiro-Wilk test. Since the distribution of age in both groups did not follow a normal distribution, intergroup differences were assessed using the Mann–Whitney *U*-test. A p-value <0.05 was considered significant. Longitudinal changes between the end of the chemotherapy regimen and the 6-month timepoint were evaluated.

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

Results

Patient characteristics. Table I provides the details of the 115 female breast cancer patients who received perioperative chemotherapy during the study period. The median age was 50 years (range=24-76 years), and 48

Table I. *Clinical characteristics of 115 female breast cancer patients who received perioperative chemotherapy.*

	All cases (n=115)
Age [y.o., median (range)]	50 (24-76)
NAC or Adjuvant (n)	
NAC	48 (41.7%)
Adjuvant	67 (58.3%)
Stage (n)	
I	21 (18.3%)
II	56 (48.7%)
III	38 (33.0%)
Subtype (n)	
Luminal	56 (48.7%)
Luminal-HER2	30 (26.2%)
HER2	12 (10.4%)
TN	17 (14.8%)
Regimen (n)	
A	1 (0.9%)
A + T	53 (46.1%)
A + T+antiHER2	39 (33.9%)
TC or T	19 (16.5%)
T+antiHER2	3 (2.6%)

NAC: Neoadjuvant chemotherapy; TN: triple negative; TC: docetaxel/cyclophosphamide; A: anthracycline based chemotherapy; T: taxane based chemotherapy regimen.

Table II. *The incidence of adverse events (AE) in all 115 cases.*

	All cases (n=115)	
Adverse events, (n)	End of CT	After 6 months
Nausea		
Grade 1	35 (30.4%)	14 (12.1%)
Grade 2	44 (38.3%)	6 (5.2%)
Grade 3	0	0
Vomiting		
Grade 1	17 (14.8%)	2 (1.7%)
Grade 2	2 (1.7%)	0
Grade 3	1 (0.9%)	0
Mucositis oral		
Grade 1	43 (37.4%)	17 (14.8%)
Grade 2	3 (2.6%)	4 (3.5%)
Grade 3	15 (13.0%)	1 (0.9%)
Constipation		
Grade 1	37 (32.2%)	23 (20.0%)
Grade 2	43 (37.4%)	22 (19.1%)
Grade 3	4 (3.5%)	2 (1.7%)
Diarrhea		
Grade 1	47 (40.9%)	20 (17.4%)
Grade 2	9 (7.8%)	3 (2.6%)
Grade 3	3 (2.6%)	1 (0.9%)
Dysgeusia		
Grade 1	49 (42.6%)	34 (29.6%)
Grade 2	42 (36.5%)	17 (14.8%)
Grade 3	9 (7.8%)	4 (3.5%)
Insomnia		
Grade 1	36 (31.3%)	36 (31.3%)
Grade 2	53 (46.1%)	16 (13.9%)
Grade 3	0	0
Peripheral sensory neuropathy		
Grade 1	57 (49.6%)	53 (46.1%)
Grade 2	27 (23.5%)	13 (11.3%)
Grade 3	15 (13.0%)	8 (7.0%)
Nail loss		
Grade 1	34 (29.6%)	50 (43.5%)
Grade 2	11 (9.6%)	10 (8.7%)
Grade 3	0	0

CT: Chemotherapy.

patients (41.7%) underwent neoadjuvant chemotherapy (NAC). The breast cancer subtypes were luminal in 56 patients (48.7%), luminal-HER2 in 30 patients (26.2%), pure HER2 in 12 patients (10.4%), and triple-negative in 17 patients (14.8%). The treatment regimens were A+T in 53 patients (46.1%), A+T plus anti-HER2 therapy in 39 patients (33.9%), TC therapy in 19 patients (16.5%), TC therapy plus anti-HER2 therapy in 3 patients (2.6%), and AC therapy alone in a single patient (0.9%).

Incidence and severity of adverse events. Table II shows the incidence of AEs in all 115 cases. The frequency of AEs at the end of the chemotherapy regimens, across all grades, was as follows: nausea 68.7%, vomiting 17.4%, oral mucositis 53.0%, constipation 73.0%, diarrhea 51.3%, dysgeusia 87.0%, insomnia 77.4%, peripheral neuropathy 86.1%, and nail loss 39.1%. The AEs with particularly high frequencies were dysgeusia, peripheral neuropathy, insomnia, and constipation. At 6 months post-chemotherapy, the incidence rates for all grades were: nausea 17.4%, vomiting 1.7%, oral mucositis 19.1%, constipation 40.9%, diarrhea 20.9%, dysgeusia 47.8%, insomnia 45.2%, peripheral neuropathy 64.3%, and nail loss 52.2%. Although gastrointestinal symptoms such as nausea and oral mucositis had decreased, constipation remained relatively common. Neuropathy, dysgeusia, insomnia, and nail loss were still frequently observed at the 6-month timepoint. Grade 3 symptoms persisted for

neuropathy, and nail loss was confirmed to have increased at 6 months, emphasizing the importance of long-term PRO monitoring.

Comparison between regimens (TC vs. A+T). Table III summarizes the background characteristics of the TC group and the A+T group. TC chemotherapy is administered as postoperative adjuvant therapy, and no cases of NAC were observed in this patient series. The A+T group included more cases with higher stages and a higher proportion of HER2-positive and TN cases. In the comparison of the groups' AEs (Table IV), peripheral sensory neuropathy also occurred more frequently and persisted longer in the A+T group (71.0% *vs.* 36.4% at 6 months). The incidence of nail loss in the A+T group was relatively higher at 6 months than at the end of chemotherapy (55.9% *vs.* 34.4%). The incidence of AEs by grade is detailed in Table V. Most of the symptoms were Grade 1-2, but persistent Grade 3 neuropathy and dysgeusia were observed in some patients who had received A+T therapy.

Table III. *The background characteristics of the TC group and the A+T group.*

	TC (n=22)	A + T (n=93)	*p*-Value
Age [≥50 y.o., n (%)]	9 (40.9%)	51 (54.8%)	0.343
NAC or Adjuvant (n)			<0.001
NAC	0	48 (51.6%)	
Adjuvant	22 (100%)	45 (48.4%)	
Stage (n)			0.001
I	6 (27.3%)	15 (16.1%)	
II	16 (72.7%)	40 (43.0%)	
III	0	38 (40.7%)	
Subtype (n)			<0.001
Luminal	19 (86.4%)	37 (39.8%)	
Luminal-HER2	3 (13.6%)	27 (29.0%)	
HER2	0	12 (12.9%)	
TN	0	17 (18.3%)	
Regimen (n)			0.014
anti-HER2	3 (13.6%)	39 (41.9%)	

NAC: Neoadjuvant chemotherapy; TN: triple negative; TC: docetaxel/cyclophosphamide; A: anthracycline based chemotherapy; T: taxane based chemotherapy regimen.

Discussion

The results of our analyses of 115 patients demonstrated that PRO-based monitoring, specifically through a structured patient questionnaire aligned with the CTCAE, provides important insights into chemotherapy-induced symptoms after perioperative treatment for breast cancer. The design of the questionnaire allowed for systematic collection of patient-reported symptom severity and recovery timing across multiple AEs, including nausea, vomiting, oral mucositis, constipation, diarrhea, dysgeusia, insomnia, neuropathy, and nail loss. The persistence of AEs beyond 6 months underscores the necessity of continuing toxicity monitoring beyond the treatment period. This study revealed that patients continue to suffer long-term symptoms such as peripheral neuropathy, nail loss, dysgeusia and insomnia even after their chemotherapy ends, which can significantly impair patients' QOL and daily functioning (12-15).

Persistent chemotherapy-induced peripheral neuropathy (CIPN) is a significant problem for patients. CIPN has been shown to significantly affect patients' QOL (12, 13). Rivera *et al.* emphasized the impact of CIPN on treatment discontinuation (16), and other researchers reported that CIPN is associated with psychological distress and falls (17). Our group recently demonstrated the potential efficacy of mirogabalin in managing taxane-related CIPN during perioperative breast cancer chemotherapy (18). These findings confirm that effective interventions are both necessary and feasible through symptom monitoring.

In addition to neuropathy, our findings revealed the long-term persistence of nail disorders among the patients. Nail changes induced by taxane-based agents are highly prevalent, occurring in up to 89% of patients, with functional impairment reported in approx. 32% (14). It has been reported that nearly half of paclitaxel-treated patients developed Grade 2 nail toxicity, including painful hemorrhagic onycholysis, which significantly impacted the patients' daily lives (19). Our findings corroborate these observations, underscoring the importance of (*i*) providing accurate information to patients regarding nail toxicity and (*ii*) systematic PRO-based assessment.

Table IV. *Comparison of adverse events (all grades) between TC and A+T groups.*

Adverse events, (n)	TC (End of CT)	A+T (End of CT)	*p*-Value (End of CT)	TC (After 6 months)	A+T (After 6 months)	*p*-Value (6 months)
Nausea	13 (59.1%)	66 (71.0%)	0.312	6 (27.3%)	14 (15.1%)	0.211
Vomiting	3 (13.6%)	17 (18.3%)	0.761	1 (4.5%)	1 (1.1%)	0.347
Mucositis oral	8 (36.4%)	53 (57.0%)	0.186	5 (22.7%)	17 (18.3%)	0.763
Constipation	16 (72.7%)	68 (73.1%)	1.000	11 (50.0%)	36 (38.7%)	0.333
Diarrhea	10 (45.5%)	49 (52.7%)	0.542	4 (18.2%)	20 (21.5%)	1.000
Dysgeusia	20 (90.9%)	80 (86.0%)	1.000	11 (50.0%)	44 (47.3%)	0.820
Insomnia	17 (77.3%)	82 (88.2%)	0.186	9 (40.9%)	43 (46.2%)	0.812
Peripheral sensory neuropathy	19 (86.4%)	80 (86.0%)	1.000	8 (36.4%)	66 (71.0%)	0.005
Nail loss	11 (50.0%)	34 (36.6%)	0.245	8 (36.4%)	52 (55.9%)	0.153

CT: Chemotherapy; TC: docetaxel/cyclophosphamide; A: anthracycline based chemotherapy; T: taxane.

Insomnia emerged as another important symptom persisting 6 months post-treatment in our patient population. Ancoli-Israel *et al.* reported that 30%-75% of cancer patients experience sleep disturbances and that chemotherapy frequently exacerbates insomnia (20). A resent prospective study of breast cancer patients undergoing chemotherapy confirmed that the severity of insomnia is strongly associated with impaired QOL (15). Our findings align with these reports, highlighting the importance of monitoring sleep disturbances as part of supportive care strategies.

We also observed that gastrointestinal (GI) symptoms such as nausea, diarrhea, and constipation, though prevalent during active chemotherapy, generally resolved within months after the chemotherapy's completion. The Chemo-Gut Study conducted by Deleemans *et al.* demonstrated that while some survivors report persistent GI complaints, the majority experience a resolution of acute GI symptoms over time (21). Similarly, gastrointestinal symptoms were reported to be only rarely persistent in long-term breast cancer survivors (22). These findings are consistent with our present results, suggesting that although the management of patients' GI symptoms is crucial during active therapy, long-term follow-ups should prioritize persistent symptoms such as neuropathy, nail disorders, and insomnia. In this study, among gastrointestinal symptoms, dysgeusia was found to be relatively common and potentially persistent. Evaluating dysgeusia may be important for nutritional management in early-stage breast cancer patients undergoing chemotherapy (23, 24).

Our study is among the few prospective investigations using PROs to capture chemotherapy symptoms longitudinally. The utility of PRO-CTCAE to characterize long-term AEs in breast cancer survivors has been described (25), supporting the validity of our methodology. By explicitly using a questionnaire as a PRO tool, our study ensured that the patients' voices were central in the evaluation of treatment-related AEs. Electronic PRO (ePRO) systems represent the next step in AE monitoring. They allow real-time symptom reporting, integration into clinical workflows, and automated alerts for clinicians. A recent systematic review confirmed the value of ePRO systems in cancer care, describing improved monitoring capabilities and patient engagement (26). In addition, digital follow-up methods may be cost-effective alternatives to traditional surveillance for breast cancer (27), enhancing both efficiency and patient-centered care.

This study had several limitations. The number of cases was relatively small (n=115); however, the data were based on self-reported questionnaires, and while sampling bias may have occurred, there was no researcher bias at the time of sampling. Moreover, the study results were derived from patients' subjective outcome reports, not from objective findings by researchers. It should be noted that CTCAE was designed as a clinician-reported

Table V. *The incidence of adverse events of TC and A+T groups by grade.*

	TC (n=22)		A + T (n=93)	
Adverse events, (n)	End of CT	After 6 months	End of CT	After 6 months
Nausea				
Grade 1	5 (22.7%)	4 (18.2%)	30 (32.3%)	10 (10.8%)
Grade 2	8 (36.4%)	2 (9.1%)	36 (38.7%)	4 (4.3%)
Grade 3	0	0	0	0
Vomiting				
Grade 1	3 (13.6%)	1 (4.5%)	14 (15.1%)	1 (1.1%)
Grade 2	0	0	2 (2.2%)	0
Grade 3	0	0	1 (1.1%)	0
Mucositis oral				
Grade 1	7 (31.8%)	5 (22.7%)	36 (38.7%)	12 (12.9%)
Grade 2	0	0	3 (3.2%)	4 (4.3%)
Grade 3	1 (4.5%)	0	14 (15.1%)	1 (1.1%)
Constipation				
Grade 1	7 (31.8%)	5 (22.7%)	30 (32.3%)	18 (19.4%)
Grade 2	9 (40.9%)	6 (27.3%)	34 (36.6%)	16 (17.2%)
Grade 3	0	0	4 (4.3%)	2 (2.2%)
Diarrhea				
Grade 1	7 (31.8%)	4 (18.2%)	40 (43.0%)	16 (17.2%)
Grade 2	2 (9.1%)	0	7 (7.5%)	3 (3.2%)
Grade 3	1 (4.5%)	0	2 (2.2%)	1 (1.1%)
Dysgeusia				
Grade 1	11 (50.0%)	7 (31.8%)	38 (40.9%)	27 (29.0%)
Grade 2	7 (31.8%)	4 (18.2%)	35 (37.6%)	13 (14.0%)
Grade 3	2 (9.1%)	0	7 (7.5%)	4 (4.3%)
Insomnia				
Grade 1	7 (31.8%)	7 (31.8%)	39 (41.9%)	29 (31.2%)
Grade 2	10 (45.5%)	2 (9.1%)	43 (46.2%)	14 (15.1%)
Grade 3	0	0	0	0
Peripheral sensory neuropathy				
Grade 1	15 (68.2%)	7 (31.8%)	42 (45.2%)	46 (49.5%)
Grade 2	3 (13.6%)	1 (4.5%)	24 (25.8%)	12 (12.9%)
Grade 3	1 (4.5%)	0	14 (15.1%)	8 (8.6%)
Nail loss				
Grade 1	9 (40.9%)	6 (27.3%)	25 (26.9%)	44 (47.3%)
Grade 2	2 (9.1%)	2 (9.1%)	9 (9.7%)	8 (8.6%)
Grade 3	0	0	0	0

CT: Chemotherapy; TC: docetaxel/cyclophosphamide; A: anthracycline based chemotherapy.

grading framework. For patient self-reporting, the National Cancer Institute developed and validated the Patient-Reported Outcomes version of the CTCAE (PRO-CTCAE) (28), which captures symptomatic toxicities using patient-reported frequency, severity, and interference items. In addition, the questionnaire was developed for this study and used a CTCAE-informed grading scheme for patient self-reporting; it was not psychometrically validated against PRO-CTCAE or clinician-assigned CTCAE, which may have introduced measurement error. Future studies involving a larger number of cases and using an ePRO system are necessary.

In conclusion, the PRO-based monitoring of patients treated with perioperative chemotherapy revealed persistent symptoms, especially neuropathy, nail changes, and insomnia, while gastrointestinal symptoms generally resolved after treatment. Importantly, adverse events persisted even at 6 months after the completion

of the patients' chemotherapy regimens, indicating that monitoring should continue beyond the completion of treatment. Integrating PROs, or potentially ePRO systems, into clinical practice could enhance patient-centered care and improve supportive care in breast cancer chemotherapy.

Conflicts of Interest

The Authors have no conflicts of interest to declare.

Authors' Contributions

TF analyzed data and wrote the initial draft of the manuscript. KI, MA, KT, MO and SO collected data and were involved in the initial study conception and design. TF, KI, MA, KT, MO and HT were involved in drafting and revising the manuscript. All Authors have read and approved the final manuscript.

Acknowledgements

We thank the Gunma University School of Nursing for their cooperation.

Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (DeepL) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual data were generated or modified using generative AI or machine learning–based image enhancement tools.

References

1 Early Breast Cancer Trialists' Collaborative Group (EBCTCG): Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. Lancet 379(9814): 432-444, 2012. DOI: 10.1016/S0140-6736(11)61625-5

2 Arahori H, Kondo K, Imai Y, Bando T, Inoue H, Sasa S, Takizawa H: Symptomatic adverse events of chemotherapy in breast cancer patients: Using CTCAE, PRO-CTCAE, and EORTC QLQ-C30. J Med Invest 71(1.2): 82-91, 2024. DOI: 10.2152/jmi.71.82

3 Hara F, Nagasaki R, Minami R, Izutani T, Yoshida T, Arai A, Nihei A, Sakurai N, Ohno S: Survey on adverse events associated with drug therapy for breast cancer patients. BMC Womens Health 24(1): 545, 2024. DOI: 10.1186/s12905-024-03355-x

4 Ardavanis-Loukeris G, Kokkali S, Perdikari K, Karatrasoglou E, Talagani S, Tzovaras A, Ardavanis A: A real-world study of everolimus plus aromatase inhibitor in hormone receptor-positive, HER2-negative advanced breast cancer. Anticancer Res 44(4): 1559-1565, 2024. DOI: 10.21873/anticanres.16953

5 Aoyama T, Hashimoto I, Maezawa Y, Esashi R, Yamamoto S, Shimada K, Kazama K, Numata K, Uchiyama M, Tamagawa A, Saito A, Yukawa N: Perioperative anemia is an independent prognostic factor for gastric cancer patients who receive curative treatment. Anticancer Res 44(12): 5551-5557, 2024. DOI: 10.21873/anticanres.17381

6 Fujii T, Ichiba K, Honda C, Tokuda S, Nakazawa Y, Ogino M, Kurozumi S, Obayashi S, Yajima R, Shirabe K: Prospective observational study of chemotherapy-induced alopecia after sequential FEC+taxane and the effects of age in breast cancer patients. Breast Cancer 28(2): 329-334, 2021. DOI: 10.1007/s12282-020-01161-5

7 Fujii T, Ichiba K, Aoki M, Tanabe K, Ogino M, Obayashi S, Takei H: Effectiveness of scalp-cooling therapy for preventing chemotherapy-induced alopecia in patients with breast cancer: a prospective observational study focusing on scalp, eyebrow, and eyelash hair loss. In Vivo 39(6): 3596-3601, 2025. DOI: 10.21873/invivo.14158

8 Ono M, Nagasaki R, Nakamura M, Hamaguchi K, Yokoi M, Matsuura N, Utsugi K, Kataoka A, Takano T, Watanabe M: Appearance-related needs and challenges among cancer patients undergoing systemic therapy: a comprehensive survey study. Int J Clin Oncol 30(3): 469-479, 2025. DOI: 10.1007/s10147-025-02705-5

9 Lemieux J, Maunsell E, Provencher L: Chemotherapy-induced alopecia and effects on quality of life among women with breast cancer: a literature review. Psychooncology 17(4): 317-328, 2008. DOI: 10.1002/pon.1245

10 Nakazawa Y, Nakazawa S, Kurozumi S, Ogino M, Koibuchi Y, Odawara H, Oyama T, Horiguchi J, Fujii T, Shirabe K: The pathological complete response and secreted protein acidic and rich in cysteine expression in patients with breast cancer receiving neoadjuvant nab-paclitaxel chemotherapy. Oncol Lett 19(4): 2705-2712, 2020. DOI: 10.3892/ol.2020.11354

11 Allred DC, Harvey JM, Berardo M, Clark GM: Prognostic and predictive factors in breast cancer by immunohistochemical analysis. Mod Pathol 11(2): 155-168, 1998.
12 Beijers AJ, Mols F, Dercksen W, Driessen C, Vreugdenhil G: Chemotherapy-induced peripheral neuropathy and impact on quality of life 6 months after treatment with chemotherapy. J Community Support Oncol 12(11): 401-406, 2014. DOI: 10.12788/jcso.0086
13 Mols F, Beijers T, Vreugdenhil G, van de Poll-Franse L: Chemotherapy-induced peripheral neuropathy and its association with quality of life: a systematic review. Support Care Cancer 22(8): 2261-2269, 2014. DOI: 10.1007/s00520-014-2255-7
14 Mittal S, Khunger N, Kataria SP: Nail changes with chemotherapeutic agents and targeted therapies. Indian Dermatol Online J 13(1): 13-22, 2022. DOI: 10.4103/idoj.IDOJ_801_20
15 Eslamijouybari M, Patidar V, Kumar Mudgal S, Gaur R, Hosseini Marznaki Z, Fournier A, Hossein Hakimi M, Khosravi S: Quality of life, insomnia, attitudes and beliefs in women undergoing chemotherapy for breast cancer: a cross-sectional study in Amol city Northern Iran. BMC Womens Health 25(1): 303, 2025. DOI: 10.1186/s12905-025-03853-6
16 Rivera DR, Ganz PA, Weyrich MS, Bandos H, Melnikow J: Chemotherapy-associated peripheral neuropathy in patients with early-stage breast cancer: a systematic review. J Natl Cancer Inst 110(2): djx140, 2018. DOI: 10.1093/jnci/djx140
17 Bao T, Basal C, Seluzicki C, Li SQ, Seidman AD, Mao JJ: Long-term chemotherapy-induced peripheral neuropathy among breast cancer survivors: prevalence, risk factors, and fall risk. Breast Cancer Res Treat 159(2): 327-333, 2016. DOI: 10.1007/s10549-016-3939-0
18 Fujii T, Honda C, Tanabe K, Ogino M, Obayashi S, Shirabe K: Efficacy of mirogabalin for taxane-associated chemotherapy-induced peripheral neuropathy in perioperative chemotherapy for early breast cancer. In Vivo 38(4): 1935-1938, 2024. DOI: 10.21873/invivo.13649
19 Alessandrini A, Starace M, Cerè G, Brandi N, Piraccini BM: Management and outcome of taxane-induced nail side effects: experience of 79 patients from a single centre. Skin Appendage Disord 5(5): 276-282, 2019. DOI: 10.1159/000497824
20 Ancoli-Israel S, Liu L, Rissling M, Natarajan L, Neikrug AB, Palmer BW, Mills PJ, Parker BA, Sadler GR, Maglione J: Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: a 1-year longitudinal study. Support Care Cancer 22(9): 2535-2545, 2014. DOI: 10.1007/s00520-014-2204-5
21 Deleemans JM, Toivonen K, Reimer RA, Carlson LE: The chemo-gut study: a cross-sectional survey exploring physical, mental, and gastrointestinal health outcomes in cancer survivors. Glob Adv Health Med 11: 2164957X221145940, 2022. DOI: 10.1177/2164957X221145940
22 Obispo B, Bailleux C, Cantos B, Zamora P, Jhawar SR, Varghese J, Cabal-Hierro L, Luz P, Berrocal-Almanza L, Xu X: Long-term adverse events following early breast cancer treatment with a focus on the BRCA-mutated population. Cancers (Basel) 17(15): 2506, 2025. DOI: 10.3390/cancers17152506
23 Pedersini R, Zamparini M, Bosio S, di Mauro P, Turla A, Monteverdi S, Zanini A, Amoroso V, Vassalli L, Cosentini D, Grisanti S, Simoncini EL, Berruti A: Taste alterations during neo/adjuvant chemotherapy and subsequent follow-up in breast cancer patients: a prospective single-center clinical study. Support Care Cancer 30(8): 6955-6961, 2022. DOI: 10.1007/s00520-022-07091-6
24 Kinjo T, Kanda K, Fujimoto K: Effects of a self-monitoring intervention in breast cancer patients suffering from taste alterations induced by chemotherapy: A randomized, parallel-group controlled trial. Eur J Oncol Nurs 52: 101956, 2021. DOI: 10.1016/j.ejon.2021.101956
25 Adesoye T, Liao KP, Peterson S, Li L, Zorzi D, Holmes HM, Chavez-MacGregor M, Giordano SH: Patient-reported outcomes in older breast cancer survivors with and without prior chemotherapy treatment. Cancer Med 12(17): 17740-17752, 2023. DOI: 10.1002/cam4.6394
26 Salmani H, Nasiri S, Alemrajabi M, Ahmadi M: Electronic patient-reported outcome systems and capabilities in cancer care: a systematic review. Front Digit Health 7: 1560533, 2025. DOI: 10.3389/fdgth.2025.1560533
27 Peltola M, Blomqvist C, Färkkilä N, Poikonen-Saksela P, Mattson J: Comparing the costs of surveillance of early-stage breast cancer by digital or traditional follow-up methods: randomized crossover study. JMIR Cancer 11: e58113, 2025. DOI: 10.2196/58113
28 Dueck AC, Mendoza TR, Mitchell SA, Reeve BB, Castro KM, Rogak LJ, Atkinson TM, Bennett AV, Denicoff AM, O'Mara AM, Li Y, Clauser SB, Bryant DM, Bearden JD 3rd, Gillis TA, Harness JK, Siegel RD, Paul DB, Cleeland CS, Schrag D, Sloan JA, Abernethy AP, Bruner DW, Minasian LM, Basch E, National Cancer Institute PRO-CTCAE Study Group: Validity and reliability of the US National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). JAMA Oncol 1(8): 1051-1059, 2015. DOI: 10.1001/jamaoncol.2015.2639