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Review Article

Effects of Physical Exercise on Chemotherapy-Induced Peripheral Neuropathy: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: The aim of this systematic review and meta-analysis is to systematically collect, evaluate, and critically synthesize research findings on the effects of physical exercise on chemotherapy-induced peripheral neuropathy (CIPN).

Method: The Joanna Briggs Institute (JBI) methodology for systematic reviews was adopted for this study. We searched the Medline®, CINAHL, SportDiscus, and Scopus databases to identify relevant articles published from inception to March 2024. This review was reported in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Results: Twelve studies met the inclusion criteria, totaling 928 participants. Interventions ranged from aerobic and resistance exercises to balance and strength training. A range of physical exercise interventions was explored, including brisk walking, endurance training, weight exercises, and resistance bands, as well as combined programs of aerobics, resistance, and balance training, all tailored to improve symptoms and quality of life in patients with chemotherapy-induced peripheral neuropathy. The meta-analysis focused on five studies that used the FACT/GOG-Ntx scale indicated a standardized mean difference of 0.50 (95% CI: 0.26, 0.74), favoring exercise, reflecting significant improvements in neuropathy symptoms. The heterogeneity among the studies was low ($I^2 = 2\%$), suggesting consistency in the beneficial effects of exercise.

Conclusions: From the results analyzed, the descriptive analysis of the 12 included studies shows promising outcomes not only related to individuals' perceptions of CIPN severity but also in terms of physical functioning, balance, ADL (Activities of Daily Living) performance, pain, and quality of life. The findings support the integration of structured exercise programs into oncological treatment plans.

The increase in cancer incidence continues to be a significant global health issue, affecting an increasing number of individuals each year (Sung et al., 2021). Advances in early detection and treatment have led to improved survival rates, yet the prevalence of cancer-related challenges remains high (Siegel et al., 2022). Chemotherapy, one of the most common and effective treatments for cancer, but it is not immune to its adverse effects (Tanay et al., 2021; Zhang et al., 2023). Among these, chemotherapy-induced peripheral neuropathy (CIPN) stands out as the most common neurological side effect involving cytostatic drugs (*platinium* derivatives, vinca alkaloids, taxanes, proteasome inhibitors and modern antibody-based therapies) and is a debilitating side effect, impacting patients' quality of life (Loprinzi et al., 2020; Majithia et al., 2016; Sommer et al., 2018; Streckmann et al., 2022).

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CIPN is a condition characterized by damage to the peripheral nerves caused by certain chemotherapy drugs. It manifests as sensory, motor, and autonomic symptoms, including numbness, tingling, pain, and weakness, predominantly in the hands and feet (Loprinzi et al., 2020; Majithia et al., 2016; Sommer et al., 2018; Zhang et al., 2021). Bonomo & Cavaletti (2021) summarize the issue of symptoms as a mix of motor, sensory, and autonomic signs, emphasizing that the pain associated with CIPN can be prolonged and intense, making its treatment challenging. This makes the assessment of CIPN fundamental. Evaluation involves various methods, from patient-reported outcomes to clinical examinations (Loprinzi et al., 2020). Effective pharmacological treatments are limited, making CIPN a persistent and challenging condition to manage (Papadopoulou et al., 2023). The symptoms can be dose-limiting, leading to modifications or discontinuation of chemotherapy, complicating the treatment and prognosis for cancer patients (Streckmann et al., 2022).

In the latest update of the recommendations by the American Society of Clinical Oncology (ASCO) regarding the prevention and management of CIPN in adult survivors, it is indicated that there is still no evidence supporting the implementation of strategies (pharmacological or non-pharmacological) for the prevention of CIPN. For treatment, once CIPN is established, the only drug that has demonstrated efficacy (moderate level of evidence) is duloxetine (Loprinzi et al., 2020). This lack of robust evidence from studies supporting prevention or effective interventions to mitigate CIPN, aside from dose reduction, drug delays, or discontinuation of chemotherapy, presents a significant challenge (Brewer et al., 2016; Duregon et al., 2018; Loprinzi et al., 2020).

The discouragement brought about by the lack of therapeutic responses has led to the emergence of studies in areas such as nutritional supplementation, integrative medicine, and exercise programs (Dorsey et al., 2019; Li et al., 2020; Zhang et al., 2023). Recent studies have highlighted the potential benefits of physical exercise as a non-pharmacological intervention to manage CIPN (Crichton et al., 2022; Tanay et al., 2021; Zhang et al., 2021). As cancer incidence rises and more individuals undergo chemotherapy, the need for effective, supportive interventions becomes increasingly critical. Research indicates that exercise can mitigate the adverse effects of chemotherapy by enhancing muscle strength, improving balance, and promoting better physical and mental well-being (Jones et al., 2022; Papadopoulou et al. 2023; Tamburin et al., 2022). These findings suggest that incorporating structured exercise programs into the care plans for cancer patients could offer a valuable approach to managing CIPN, providing both physical and psychological benefits. Physical exercise stands out as a viable option, offering hope for improved outcomes and quality of life for cancer survivors struggling with the debilitating effects of CIPN.

Physical exercise is increasingly recognized as an essential component of nursing care, particularly in the field of oncology (Fernandes et al., 2018; Paul, 2017). It is essential that nurses include physical activity guidelines when providing holistic and person-centered care (Hirschey et al. 2021; Paul, 2017). By integrating structured exercise programs, nurses can directly contribute to the management and relief of symptoms associated with CIPN, improving the well-being and functional capacity of patients.

Despite numerous studies on exercise and CIPN, there is still a lack of synthesized evidence on the efficacy, adherence, and outcomes of interventions, and the type of exercise, particularly concerning their effects and their application. This review is essential as it reflects the most recent and comprehensive research on the impact of physical exercise on patients with chemotherapy-induced peripheral neuropathy, aiming to fill the gap not only by summarizing the effects of exercise on CIPN but also by examining the quality of existing research to guide future studies and clinical applications more effectively. Thus, this review aims to find evidence from clinical trials on the effects of physical exercise on chemotherapy-induced peripheral neuropathy.

Methods

Study Design

This systematic review was conducted using the framework proposed by the Joanna Briggs Institute (JBI) manual and our methods and results are presented in accordance with the guidelines and checklist of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for 2020 (Aromataris et al., 2024; Page et al., 2021). The research protocol was registered on the Open Science Framework platform DOI: 10.17605/OSF.IO/WY2MS.

Search Strategy

Following these guidelines, we formulated our research question and then searched for and identified relevant studies in this area. We selected studies based on our inclusion and exclusion criteria, extracted the data, and collated, summarized, and reported the results. In our research strategy, we sought to broaden the scope of the results by not imposing publication date restrictions. The bibliographic search was performed in May 2024 and was structured based on the PICO strategy (which stands for Population, Intervention, Comparator, Outcome) (Aromataris et al., 2024). The population of interest comprised individuals experiencing chemotherapy-induced neurotoxicity. The intervention under investigation was physical exercise or exercise programs, with usual care serving as the comparator. We focused on outcomes related to have an impact on CIPN. We specifically sought randomized controlled trials, as the types of studies to include.

Our search encompassed a variety of databases, including Medline®, CINAHL®, Sports Discuss® and Scopus®. To determine the keywords and terms for our investigation, we relied on descriptors indexed in each database (Example such as MeSH and CINAHL Headings) as well as descriptors associated with the study area (natural language and adapted for the other databases). To meet our research objectives, we formulated search equations that combined the descriptors using Boolean operators AND and OR, following the structure provided in the Supplementary table. Additionally, we conducted a backward citation search by examining the reference lists of all publications included in the review to identify any additional relevant studies (“Backward citation search”) (Appendix 1).

Eligibility Criteria

For this systematic review, the studies considered in the analysis must satisfy the following inclusion criteria: (a) randomized controlled trials (RCTs), (b) involving adult cancer patients (aged ≥18 years) who were receiving neurotoxic chemotherapy, (c) including a pre-post comparison of exercise interventions with the training program beginning during chemotherapy, and (d) a control group receiving usual care or health education without performing physical therapy. Additionally, the studies (e) must be published in English, French, Spanish, or Portuguese, (f) demonstrated methodological quality, and (g) measure outcomes relate to CIPN.

Studies were excluded if they: (a) tested passive exercise interventions, such as whole-body vibration, passive range of mo-

Table 1
JBI Critical Appraisal Tool for Randomized Controlled Trials.

ID	Criteria													Total
	C1	*C2*	*C3*	*C4*	*C5*	*C6*	*C7*	*C8*	*C9*	*C10*	*C11*	*C12*	*C13*	
E1	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	10/13
E2	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	10/13
E3	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	11/13
E4	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	11/13
E5	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	10/13
E6	Y	U	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	9/13
E7	Y	U	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	10/13
E8	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	10/13
E9	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	10/13
E10	N	N	Y	N	N	Y	Y	Y	NA	Y	Y	Y	N	7/12
E11	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	11/13
E12	N	U	Y	U	U	U	Y	Y	NA	Y	Y	Y	N	7/13

Y = yes; N = no; U = unclear; NA = not applicable

tion, and splinting; (b) involving concurrent non-exercise physiological interventions, such as drugs, supplements, and transcutaneous electrical nerve stimulation; (c) investigated other neurological conditions or involved patients who were not currently undergoing chemotherapy with neurotoxic potential, or (d) were noneligible publication types such as abstracts, protocols, review articles, editorials, comments, guidelines, and case reports.

Study Selection

All articles were retrieved and imported to Rayyan QCRI® web application (Rayyan QCRI; https://rayyan.qcri.org/, Qatar) to streamline the review process, since a single reviewer remove duplicates. Following the removal of all duplicate articles, two reviewers initiate the screening of studies relied on title and abstract information alone, conducted to identify studies for comprehensive text evaluation. Subsequently, two reviewers independently assessed the studies, and any discrepancies were resolved through consensus with a third reviewer to confirm the eligibility of the publications.

Synthesis of Results

We summarize our data synthesis featuring the following: (a) general study details, (b) type of study, objective, participants characteristics including number, diagnosis and type of chemotherapy, (c) detailed descriptions of the exercise intervention, encompassing information regarding their type, intensity, frequency, and duration, adherence rates and compliance, (d) the outcomes along with a general overview of their findings. A summary of the results obtained in these studies, all presented in Table 1.

Quality Assessment

The methodological quality of the included randomized controlled trials was assessed using the JBI Critical Appraisal Checklist for RCT (Barker et al., 2023). For this systematic review, we established a criterion that reviews scoring above moderate quality, as per the 13-point assessment defined in the JBI manual in the Critical Appraisal Instrument for RCT, would be considered acceptable (Barker et al., 2023). Before proceeding the assessment, we determined that studies meeting at least 7 of the validated criteria would be eligible for inclusion in this review, as outlined in Table 2. This table presents a summary of the results obtained in assessing the quality of the studies included in this systematic review. All studies were included in the review, as they score more than half of the observed criteria.

Data Analysis

The Revman 5.4 software was used to analyze the mean scores and standard deviations from the included studies, presenting the results as pooled means, effect sizes, and 95% confidence intervals. Heterogeneity among studies was assessed using Cochran's Q test and the I^2 index, with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively, according to Higgins et al. (2003). Due to variability in the interventions of the studies, a random-effects model was adopted for a more generalized interpretation of the results. Low heterogeneity was observed among the studies ($p < .00001$, $I^2 = 2\%$). Therefore, it was decided to retain all the articles initially included, and the results confirmed the statistical significance of the primary findings.

Results

Figure 1 displays the PRISMA flowchart depicting the progression of our literature search and selection procedure. In total, we identified and thoroughly assessed 12 RCT (Bahar-Ozdemir eta al., 2020; Bao et al., 2020; Cao et al., 2023; Dhawan et al., 2020; Gui et al., 2021; Ikio et al., 2022; Kanzawa-Lee et al., 2022; Kleckner et al., 2018; Saraboon & Siriphorn, 2021; Visovsky et al., 2014; Vollmers et al., 2018; Zimmer et al., 2018), that satisfied the inclusion criteria, and these reviews underwent comprehensive data extraction and statistical evaluation.

Studies Characteristics

The studies included in this analysis encompass a diverse range of physical exercise interventions aimed at alleviating CIPN symptoms in cancer patients. These studies span various countries, including Canada, the USA, India, Japan, Germany, Turkey, Thailand and China and were conducted between 2014 and 2023. With a total of 928 participants, the most common cancer type in the included studies was breast cancer, with treatments involving neurotoxic chemotherapy agents like taxane and platinium derivates. Table 2 presents a summary that provides an overview of the participants (number, gender and age), types of cancer and chemotherapy, and the variety of exercise interventions employed.

Participants Characteristics

The participant demographics varied across studies. Sample sizes ranged from 19 participants (E9) to 355 participants (E5).

Table 2
Presentation of Studies Characteristics (ID, Author, Participants, Type of Cancer and Chemotherapy, Exercise Program, Outcomes Measures, Adverse events and Compliance).

Id	Author/ Year	Participants	Cancer and Chemo Type	Supervision	Type	Intensity	Frequency	Duration	Outcomes measures	Adverse Events	Compliance
E1	Cao et al., 2023	134 IG, n = 69 CG, n = 65 All Women Age Mean (SD) 57.5 (8.3)	Ovarian cancer Carboplatin and paclitaxel (82%) *(34 participants missing data about chemotherapy)*	Home-based	Aerobic exercise, mainly brisk walking,	Moderate	Aiming for 150 min per week.	6 months	FACT/GOG-Ntx	No AE	83.8% of participants in the exercise intervention group met 80% of the exercise goal
E2	Dhawan et al., 2020	45 IG n = 22 (male=4) CG = 23 (male = 3) Age Mean (SD) IG = 50.5 (7.9) CG = 52.5 (6.6)	Ovarian, cervix, lung and head and neck cancer Carboplatin and paclitaxel	Home-based	Muscle strengthening and balancing exercises.	Moderate	30 min daily	10 weeks	Leeds Assessment of Neuropathic Symptoms and Signs pain scale. European Organisation for Research and Treatment of Cancer QOL Chemotherapy-Induced Peripheral Neuropathy Assessment Tool Nerve Conduction Velocity (NCV) Test	No AE	68% of patients adhered to the exercise program
E3	Ikio et al., 2022	39 IG: n = 19 (male=11) CG: n = 20 (male=11) Age Mean (SD) IG = 69 (7.25) CG = 64 (7.5)	Hematological malignancies and gastrointestinal cancer Vinca alkaloids, taxanes, platinum agents, and proteasome inhibitors	Home-based	Combined hand exercise intervention, including muscle strength exercises, manual dexterity training, and sensory function training	Moderate intensity (40-60% of maximum muscle strength for muscle strength exercises)	30 min a day for 3 or more days per week	Over two chemother-apy cycles	Upper-extremity function - Michigan Hand Outcomes Questionnaire (MHQ) Functional assessment, QoL FACT/GOG - Ntx	No AE	IG, the average exercise adherence was 73.3%.
E4	Kanzawa-Lee et al., 2022	57 IG n = 29 (male=23) CG *n* = 28 (male=13) Age Mean (SD) 57.88 (10.68)	Gastrointestinal cancer Oxaliplatin as part of FOLFOX or FOLFIRINOX regimens.	Home-based	Brisk walking with motivational Interviewing support	Moderate to vigorous	Progressive dosages of 10 to 60 min 3 to 5 days per week	8 weeks	Oxaliplatin-Induced Peripheral Neuropathy (OIPN): CIPN20 sensory subscale. Quality of Life (QOL) Physical Function: self-reported Emotional Function: self-reported Physical Activity: Monitored with Fitbit	No AE	Good compliance with walking program.
E5	Kleckner et al., 2018	355 participants IG n = 170 (male=15) CG n = 185 (male= 11) Age Mean (SD) 55.8 (10.8)	Breast cancer (79%), Lymphoma, Colon, Lung and other. Taxane-, platinum-, or vinca alkaloid-based chemotherapy.	Home-based	Walking and resistance exercise program. Control: Standard care for chemotherapy without additional exercise intervention.	Low to moderate	Daily for walking and resistance band exercises 3.5 d per week on average.	6 weeks	CIPN symptoms assessed via patient-reported numbness, tingling, hot/coldness in hands/feet.	All adverse events were unrelated to the exercise intervention	77% of exercise participants reported performing at least some resistance exercise during the study. Control Group 7% reported any resistance exercise.
E6	Vollmers et al., 2018	36 Women IG, n = 17 CG, n = 19 Age range 20.08 – 68.67	Breast cancer Paclitaxel	Supervised	Sensorimotor exercises, general strength training (upper and lower extremities), exercises focused on balance training	13-15 on the Borg Scale (moderate)	Twice a week, 30 min	During the Paclitaxel treatment and for six weeks after chemother-apy	Postural stability - Fullerton Advanced Balance Scale scores. Strength and Quality of life	Not mentioned	Not provided

(*continued on next page*)

Table 2 (*continued*)

Id	Author/ Year	Participants	Cancer and Chemo Type	Supervision	Type	Intensity	Frequency	Duration	Outcomes measures	Adverse Events	Compliance
E7	Zimmer et al., 2018	30 IG: n = 17 (male n = 5) CG: n = 13 (male n = 4) Age range 50-81	Colorectal cancer FOLFIRI, FOLFOX, 5-fluorouracil, capecitabine	Supervised	Multimodal exercise: endurance, resistance and balance training		Each session lasted 60 min. 2x/week	8 weeks	FACT/GOG-Ntx Balance assessed using the GGT-Reha	No AE	The mean training frequency was reported as 88.3%. Overall adherence 80%.
E8	Bao et al., 2020	41 IG: n = 21 CG: n = 20	Breast, Uterine and Ovarian cancer. Carboplatin, Docetaxel and Carboplatin	Combine (in person classes 2x week and at home 5x week)	Yoga (mind-body exercises)	Light to moderate	Daily	Each session lasted 60 min, 8 weeks	FACT/GOG-Ntx Pain assessment NRS (numerical rating scale)	3 incidents of myalgia and 1 leg cramp	IG: 76.2% completing the outcome assessments at week 8
E9	Visovsky et al., 2014	19 women Demographics: Age range 24-65 years;	Breast cancer Paclitaxel	Home-based	Aerobic and strength training exercise	Light to moderate	30 min per session Aerobic exercises 5-7 days per week Strength training: 3x per week	12 weeks	FACT/GOG-TAXANE Timed Up and Go Test (TUG) for gait and balance	No AE	Not detailed
E10	Bahar-Ozdemir et al., 2020	60 IG, n = 24 (10 males) CG, N = 36 (19 males) Age Mean (SD) IG = 52 (9.99) CG = 53.58 (11.92)	Colorectal, Gastric, Lung, Ovarian, Breast, Endometrial, Pancreas and Head and Neck Cancer. Paclitaxel, Carboplatin, Oxaliplatin, Cisplatin, Docetaxel	Home-based	Lower limb strengthening and balance exercises	Progressive resistance and balance exercises. 20 min (10 min of strengthening and 10 min of balance exercises)	5 days a week	10 weeks	Balance: Berg Balance Scale (BBS) and Neurocom Balance Master. Neuropathic pain: PainDETECT questionnaire (PD-Q). Quality of life: EORTC-QLQ-C30	No serious AE	Not reported
E11	Saraboon & Siriphorn, 2021	30 Female Age (years) 45.53 ± 4.64 (CG) 45.07 ± 3.88 (IG)	Gynecologic cancer Taxane-based chemotherapy	Supervised	The IG performed foam pad balance exercises	Exercises included variations with eyes open and closed, and different postural challenges	60 min per day, twice a week	6 weeks	FACT/GOG-Taxane Fullerton Advanced Balance (FAB) Scale Short Physical Performance Battery (SPPB) Michigan Diabetic Neuropathy Score (MDNS)	No AE	Not detailed
E12	Gui et al., 2021	79 IG, n = 51 (34 male) CG, n = 28 (18 male) Mean age ±SD IG 50±8 CG 52±7	Colorectal, Gastric, Pancreatic and liver cancer Folfox, Xelox, Folfirinox and EOX	Home-based	Comprehensive gymnastics (raising arms, stretching and drawing) and quick walking training	Moderate	3 times every morning and evening (each session: 30 min)	2 weeks	FACT/GOG-Ntx Functional tests Brief Pain Inventory (BPI)	No AE	52.9% of patients in the IG previously exercised regularly and continued with the prescribed exercise rehabilitation program

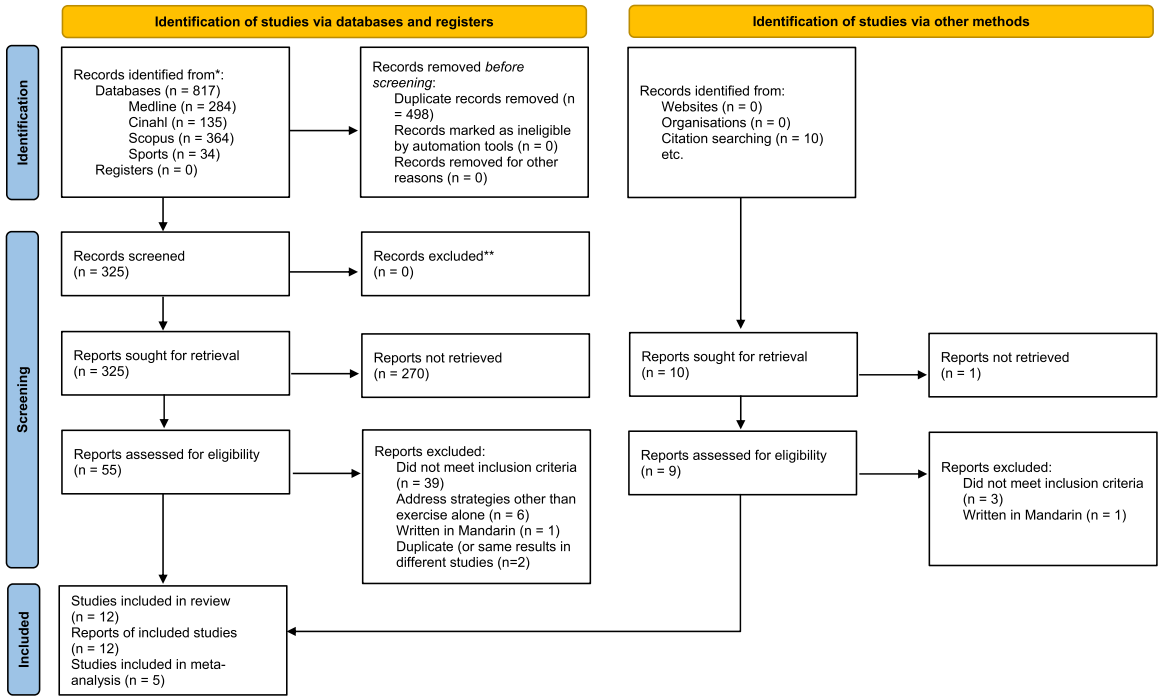

Figure 1. PRISMA flow diagram

Most studies focused on female participants, particularly those with breast or ovarian cancer (E1, E6, E8, E9, E11), although the other studies included mixed-gender cohorts (E2, E3, E7, E10, E12). Participant ages also varied, with some studies including younger adults (E6, E9), while others included older adults (E3, E7). The mean ages ranged from early 20s to late 60s, providing a broad representation of adult cancer patients represented in the research.

Intervention Characteristics

Based on the analysis of the included studies, the summary of exercise interventions for CIPN is presented in Table 2, revealing several patterns and observations emerge. Interventions varied in type, intensity, frequency, and duration, reflecting the diversity in exercise regimens applied to counter CIPN symptoms.

Professional supervision during the intervention is variable through the studies: interventions ranged from home-based exercises (more common) (E1, E2, E3, E4, E5, E9, E10) to regularly supervised (E6, E7, E11), with one study incorporating a combination of supervised and home-based components (E8). This is suggesting that flexibility in intervention delivery can accommodate patient preferences and logistical constraints.

Exercise types or modalities included different approaches. Aerobic exercise (like brisk walking, aerobic or endurance training) was used frequently, emphasizing its cardiovascular benefits (E1, E4, E5, E9, E12). Resistance training includes muscle strengthening and was performed with another modality, such as aerobic (E5, E9, E12), with balance training (E2, E10) or with balance and sensorimotor exercises (E6). Another combined approach that has been described in E3 and E7, incorporate aerobic, resistance and balance training, indicating a recognition of the need for comprehensive fitness to address multiple dimensions of CIPN. The balance training was performed in five studies (E2, E6, E7, E10, E11). Yoga was specifically highlighted in one study for its mind-body benefits (E8). The studies that performed one component of exercise alone are E1, E4, E8 and E11 (Table 2).

Exercise programs varied in intensity, ranging from light to moderate to vigorous, often tailored to the phase of chemotherapy or specific patient capabilities. Moderate intensity was the standard in many studies (E1, E2, E3, E4, E5, E7, E10 and E12), ensuring that exercises were sufficiently challenging yet manageable for patients experiencing chemotherapy side effects. Some studies included light-to-moderate (E8 and E9) or moderate-to-vigorous intensity levels (E4). However, the level of intensity was not reported in three studies (E6, E7, and E11).

About the frequency, the interventions ranged from daily sessions (E2, E3, E8, E9) to 3 to 5 days per week (E4, E5, E8, E12), to two times per week (E6, E7, E11) with session durations ranging from 20 to 60 minutes. Notice that exercise programs like muscle strengthening and balance, yoga and combined hand exercise (E2, E8, E3), were conduct daily. Exercises like walking were performed three to five times per week (E4, E5, E9) and in E1, the frequency is not mentioned, only the aim per week – 150 minutes. The duration of interventions varied, from as 2 weeks (E12) to 6 weeks (E5, E6 and E11) to as long as 6 months (E1). Notably, intervention periods often coincided with chemotherapy cycles or extended slightly beyond them to capture post-treatment effects (E2, E3, E6 and E7).

Adherence to exercise protocols was generally high, with several studies reporting compliance rates exceeding 70% (E1, E3, E5, E7, E8). In general, it is important to note the adherence and safety related to the intervention: High adherence rates across all studies indicate that the exercise interventions were well accepted and feasible for participants (E1, E3, E5, E7 and E8). Adverse events were rare and, when reported, were mostly minor and not related to the exercise interventions (E5, E8).

Outcomes

The primary outcomes measured across the studies were varied, focusing on different aspects of CIPN and related parameters. These outcomes were assessed using a range of scales and instruments to capture the effects of exercise interventions on CIPN symptoms, functionality and quality of life.

Neuropathic symptoms were the most common outcome assessed across the reviewed studies (E1, E2, E3, E4, E5, E6, E7, E8, E9, E11, E12), and used various measurement tools: FACT/GOG-Ntx, Chemotherapy-Induced Peripheral Neuropathy Assessment Tool, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (QLQ)–CIPN20 sensory subscale, Patient-reported 0-10 scale (Numbness/ Tingling and Hot/cold sensitivity), FACT-Taxane, Michigan Diabetic Neuropathy Score (MDNS). The more frequent utilized was the FACT/GOG-Ntx, employed in five studies (E1, E3, E7, E8, E12) and FACT-TAXANE (E9, E11).

Other frequently used outcome measures included pain assessment scales – Leeds Assessment of Neuropathic Symptoms (E2), PainDETECT Questionnaire (E10) and NRS (Numerical Rating Scale) used in study E8 to assess pain intensity. These pain measures were critical in determining the effectiveness of exercise in managing CIPN-related discomfort. Studies often assessed physical function through various means. There were instruments to evaluate the physical functionality (E3, E8, E10, E11, E12), such as Michigan Hand Outcomes Questionnaire (MHQ), Short Physical Performance Battery (SPPB), Chair to Stand Test, 6-Hole Shirt Time, Walking 50 Steps, Coin Test. The balance of participants was measured in eight studies (E2, E3, E6, E7, E8, E10, E11, E12). The measurement tools were Fullerton Advanced Balance Scale (FAB), GGT-Reha, Functional Reach Test, NeuroCom Balance Master and Berg Balance Scale (BBS).

Two studies assessed strength of participants using Digital Hand Dynamometer, hypothetic One-Repetition Maximum (h1RM) for bench press, leg press, lat pulldown (E3, E7).

Quality of life was also an outcome that many studies search (E2, E6, E7, E8, E9, E10, E11) by applying self-reported instruments like European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30, BR23, CIPN20), Functional Assessment of Cancer Therapy-Taxane (FACT-Taxane).

The FACT/GOG-Ntx was an instrument prominently used to evaluate neuropathy symptoms severity. The consistent application of this measure across multiple studies (E1, E3, E7, E8 and E12) allows for comparative analysis of the intervention effects.

Meta-Analysis Results

Given the variability of instruments used, it was only possible to meta-analyze the data using the FACT/GOG-Ntx scale (Cheng et al., 2020). This scale measures neuropathic symptoms, where a lower FACT-GOG/Ntx score indicates greater severity of CIPN (Huang et al., 2007; McCrary et al., 2019). Specifically, the analysis included five studies that utilized the FACT/GOG-Ntx measurement tools. The overall effect size of 0.50 indicates a moderate positive effect of exercise interventions in reducing CIPN symptoms, favoring the exercise group. This result is statistically significant, as shown by the 95% confidence interval (0.26; 0.74). The I^2 value of 2% suggests very low heterogeneity among the included studies, indicating that the results are consistent across different studies. The Tau^2 value of 0.00 and the non-significant Chi^2 test ($p = .39$) further corroborate the low variability among the studies. Cao et al., 2023 contributed the most to the overall weight (46.3%), followed by Gui et al., 2021 (24.6%) (Figure 2). The forest plot below illustrates the standardized mean differences and confidence intervals for the included studies.

The forest plot suggests that exercise interventions have a moderate beneficial effect on reducing CIPN symptoms in cancer patients undergoing chemotherapy. The low heterogeneity indicates that the findings are consistent across the included studies, making the results robust and reliable. This supports the integration of exercise programs into clinical practice for managing CIPN.

Discussion

This systematic review and meta-analysis sought to critically synthesize the effects of physical exercise on chemotherapy-induced peripheral neuropathy (CIPN), using recent evidence from randomized clinical trials (RCTs). At this point, we analyzed the relationship between exercise programs and the positive outcomes found in participants. Despite the variability of the instruments used to determine outcomes across the different studies included, we generally obtained data on neuropathic symptoms (Cao et al., 2023; Gui et al., 2021; Saraboon & Siriphorn, 2021; Visovsky et al., 2014), neuropathic pain (Bahar-Ozdemir et al., 2020; Bao et al., 2020; Cao et al., 2023; Ikio et al., 2022), and measures of physical function related to balance and gait (Saraboon & Siriphorn, 2021; Vollmers et al., 2018), strength (Ikio et al., 2022; Zimmer et al., 2018), and quality of life (Cao et al., 2023; Dhawan et al., 2020; Vollmers et al., 2018). Statistically significant differences were observed between the intervention group and the control group regarding neuropathic symptoms in nearly all studies, except in one (Kanzawa-Lee et al., 2022). The results are consistent with previous research (Courneya et al., 2013; Guo et al., 2023; Kneis et al., 2019; Mijwel et al., 2018) and recent reviews on non-pharmacological approaches (Li et al., 2020; Tamburin et al., 2022). These findings align with other studies on the effects of exercise on peripheral neuropathy, including diabetic neuropathy (Streckmann et al., 2022).

The analysis indicates that exercise interventions, particularly those involving aerobic, strength, and balance exercises, had an impact on neuropathic symptoms, pain, balance, physical function, and quality of life in cancer patients undergoing chemotherapy. Studies such as those by Cao et al. (2023); Kanzawa-Lee et al. (2022); Kleckner et al. (2018), and Gui et al. (2021) highlighted the use of aerobic exercises, mainly brisk walking. These programs ranged from home-based walks with specific weekly goals (Cao et al., 2023) to supervised walks with motivational support (Gui et al., 2021; Kanzawa-Lee et al., 2022; Kleckner et al., 2018).

Studies by Dhawan et al. (2020); Vollmers et al. (2018); Zimmer et al. (2018), and Bahar-Ozdemir et al. (2020) combined strength and balance exercises. Strength exercises can be complemented with activities that aim to improve balance and coordination, which are crucial for fall prevention and enhancing the functional capacity of patients, particularly cancer patients (Lu & Zheng, 2024).

Some studies, such as those by Bao et al. (2020); Zimmer et al. (2018), and Saraboon & Siriphorn (2021), explored the efficacy of more holistic exercise regimens combining multiple modalities, including yoga. Bao et al. (2020) focused on yoga as an intervention encompassing both physical and mental benefits, executed through a combination of in-person sessions and home practices. Conversely, Zimmer et al. (2018) applied a multimodal training regimen that included resistance, endurance, and balance training, showing a comprehensive approach to addressing multiple aspects of neuropathy. These multiple modalities underscore the importance of integrative approaches that not only

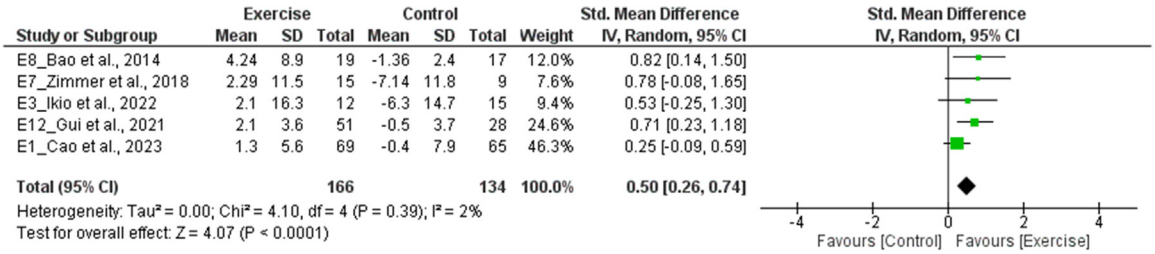

Figure 2. Forest plot of the included studies.

strengthen the body but also support patients' emotional and mental well-being (Gentile et al., 2024).

The diversity and complexity of these exercise interventions tested in clinical settings point to the need for more personalized programs that consider the individual characteristics and needs of oncology patients.

Another finding from our review is that adherence to exercise programs was significantly high in the analyzed studies, reflecting not only the feasibility of the interventions but also patient acceptance. This adherence is crucial, as exercise programs with high adherence tend to be more effective in cancer patients (Ximei et al., 2024). For example, Cao et al. (2023) reported that 83.8% of participants achieved 80% of the proposed exercise goal, suggesting that aerobic exercises, such as brisk walking, are well accepted and easily integrated into patients' daily routines.

Additionally, it is important to note that the exercise programs were generally safe, with minimal reports of adverse events, and these were considered mild and not directly related to the exercises. This finding is vital, as it highlights that, in addition to being effective, physical exercise is a safe treatment option, offering symptomatic relief without the risks associated with more invasive or pharmacological interventions. This safety and efficacy emphasize the importance of routinely integrating exercise prescriptions into oncological treatment plans, providing significant physical and psychological benefits for patients during a challenging period of their lives (Gentile et al., 2024; Tamburin et al., 2022).

Nurses in clinical settings can utilize the findings of this study to support the integration of exercise as part of the care plan for patients with CIPN. Nurses play a critical role in assessing pain (Jiahui et al., 2023) and other neuropathic symptoms (Galligan, 2023) and can implement or recommend exercise programs that help improve patients' quality of life (Hirschey et al., 2021; Paul, 2017).

These interventions can be feasibly integrated into routine cancer care, providing a non-pharmacological option for alleviating CIPN symptoms. Exercise prescription recommendations should be issued based on the safety of exercise and its efficacy in improving physical fitness, restoring physical functioning, improving quality of life, and mitigating cancer-related fatigue (Campbell et al., 2019; Patel et al., 2019). Strategies must be developed to integrate exercise programs into routine clinical practice, including creating guidelines for nurses, which will help ensure that these interventions are implemented effectively.

Implications for Practice and Research

The findings of this study have clinical, educational, and research implications that are crucial for managing chemotherapy-induced peripheral neuropathy (CIPN). Clinically, nurses can use these results to support the integration of exercise into care plans, recommending or implementing personalized exercise programs that are safe and effective. In research, there is a wide scope to explore how different intensities and types of exercise specifically affect CIPN across various cancer types and chemotherapy regimens, while developing evidence-based clinical guidelines for nursing practice.

Limitations

We recognize several limitations that require discussion. The included studies varied in sample size and quality, which may affect the reliability of the results. Due to differences in outcome measures utilized in the several studies, we used the FACT/GOG-Ntx to enhance comparability of results. This limits our meta-analysis on one consistent outcome measure present in 5 of the 12 studies reviewed. This focus allowed us to observe low heterogeneity in the statistical analysis; however, we also acknowledge that there is significant variability in the interventions, other outcomes measures and populations/ types of chemotherapy studied overall.

Publication bias is a potential concern, although the funnel plots suggested minimal bias. Lastly, the generalizability of the findings is limited, as most studies concentrated on other outcome measures. Future research should aim to include diverse cancer populations and investigate the long-term effects of exercise on CIPN.

Conclusion

Based on the findings and limitations identified in this systematic review and meta-analysis, several future research directions are proposed to further investigate the impact of exercise interventions on CIPN and to enhance their understanding and implementation in nursing practice. Further research is needed to standardize exercise protocols, determining the optimal type, intensity, frequency, duration, and volume of exercise interventions for maximum benefit. This is crucial for reducing heterogeneity and improving comparability across studies. Exploring the potential for exercise to prevent the onset or progression of CIPN when initiated early during chemotherapy is another important research direction.

Expanding research to include a broader range of cancer types and chemotherapy regimens is necessary to assess the generalizability of exercise interventions. Most current studies focus on breast cancer, so including other cancer types will provide a more comprehensive understanding. It is also important developing strategies for integrating exercise programs into routine clinical practice, including creating guidelines for nurses, will help ensure these interventions are effectively implemented.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Anabela Amarelo: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Marta Campos Ferreira: Writing – review & editing, Supervision, Methodology, Formal analysis. **Carla Sílvia Fernandes:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization.

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