Study protocol

Title: Comparative Effectiveness of Buerger–Allen Exercises Versus Mechanical Compression Therapy on Lower-Limb Perfusion and Chemotherapy-Induced Peripheral Neuropathy: A Randomized Clinical Trial

NCT Number: Not yet assigned

Protocol Version: 1.1

Date of modification: 20 September 2026

Study Site:

Ayady Almostakbal Cancer Treatment Hospital, Alexandria, Egypt

Introduction

Chemotherapy remains one of the most widely used conventional treatments for various types of cancer and plays a crucial role in treatment and improving patients' outcomes. However, its therapeutic benefits is accompanied by numerous adverse effects that affect both physiological and psychological well-being of patients [(1)]. One of its major complications is myelosuppression, which results in anemia, leukopenia, and thrombocytopenia, leading to increasing susceptibility to fatigue, infection, and bleeding [(2)]. Another major complication associated with chemotherapy is Chemotherapy-Induced Peripheral Neuropathy (CIPN), which is a cluster of symptoms resulting from damage to the peripheral nerves caused by chemotherapeutic agents used in cancer treatment [(3)]**.** Several widely used chemotherapeutic drugs are known to induce endothelial dysfunction, impair vasodilation, and diminish blood flow to distal tissues **[(4, 5)].**

In addition, chemotherapy induced autonomic neuropathy can interfere with normal vasomotor control, causing cold extremities and unstable circulation. Certain chemotherapeutic agents may also increase blood viscosity and promote thrombus formation, resulting in venous stasis or arterial obstruction, which further reduces lower limb perfusion. Clinically, these vascular and neural disturbances may be present as numbness, pallor, delayed capillary refill, edema, or worsening neuropathic symptoms [(5, 6)]**.**

Chemotherapy itself is the primary precipitating factor for CIPN, but the severity and pattern of symptoms can be influenced by treatment related variables, such as the type, dose, and duration of chemotherapy, as well as patient specific risk factors including autoimmune diseases, Raynaud's phenomenon, anemia, and impaired renal function. Platinum-based and taxane-based chemotherapy regimens are particularly associated with CIPN, and treatment characteristics may further modulate symptom severity [(7)]**.** Chemotherapy-Induced Peripheral Neuropathy predominantly affects sensory rather than motor function. Common sensory manifestations include allodynia, cold-induced neuropathy, impaired heat perception, paresthesia, dysesthesia, numbness, tingling, and neuropathic pain [(8)]**.**

Chemotherapy induced peripheral neuropathy significantly diminishes patients' quality of life. In Egypt, its incidence was reported to be approximately 30% to 40% in 2018. Although symptoms may improve over time, only about half of affected individuals experience full recovery [(9)]**.** According to a 2020 report by the Health Promotion Administration, Ministry of Health and Welfare of Taiwan, more than 56% of newly diagnosed cancer patients received chemotherapy in

Taiwan in 2018 [10]. Internationally, CIPN prevalence varies substantially, affecting between 11% and 80% of patients depending on the stage of chemotherapy exposure. Symptoms can emerge shortly after treatment initiation and may persist for several years after therapy completion. Globally, reported CIPN incidence in 2021 ranged from 19% to 85% [11].

Exercise has emerged as a valuable non-pharmacological strategy for managing chemotherapy induced complications, particularly peripheral neuropathy. Early implementation of physical interventions, that promote circulation and support neural recovery is essential to prevent irreversible damage [12]. Among the available rehabilitative techniques, Buerger's Allen Exercises are widely used to enhance peripheral blood flow through systematic limb elevation and dependency. These position-based maneuvers harness gravitational effects to facilitate venous drainage, improve arterial refilling, and increase tissue oxygenation, thereby reducing ischemic pain and discomfort [13, 14]. Conversely, Mechanical Compression Therapy, applied via elastic compression garments or pneumatic compression devices, exerts controlled external pressure to mobilize venous blood, limit edema formation, and enhance microvascular circulation, which can indirectly alleviate neuropathic symptoms [15].

Although both approaches aim to improve perfusion and reduce neuropathic manifestations, they differ in mechanism and level of patient involvement. Buerger's Allen Exercises consist of leg elevation from 45-90 degrees followed by the dependency of the leg and finally resting with the leg in the horizontal position, to induce reactive hyperemia, and returning to a neutral position, which stimulate vasomotor responses, arteriolar dilation, and collateral blood flow. When practiced regularly, these exercises also engage sensory and motor pathways, potentially aiding in the recovery of nerve function [16].

In contrast, Mechanical Compression Therapy operates passively, using rhythmic pressure gradients to displace pooled venous blood and augment arterial inflow without requiring physical effort, making it particularly suitable for weak or fatigued chemotherapy patients [17]. However, while compression therapy is superior in managing edema and accelerating venous return, it lacks the neuromuscular stimulation provided by Buerger's Allen Exercises. Therefore, Buerger's Allen Exercises may be more advantageous for neurovascular rehabilitation, whereas compression therapy may be preferable for hemodynamic stabilization. A combined approach, incorporating both active positioning and passive compression, may offer the most comprehensive therapeutic

benefit for chemotherapy patients experiencing both circulatory insufficiency and neuropathic complications [18].

Nurses play a pivotal role in mitigating chemotherapy induced complications through early assessment, targeted intervention, and continuous support. Their responsibilities extend beyond basic care to encompass proactive screening for symptoms of peripheral neuropathy and lower limb vascular insufficiency, enabling timely management. A key component of their role lies in patient education, where they teach and reinforce lifestyle modifications, positioning techniques, and therapeutic exercise routines tailored to individual capabilities [19].

Also, Nurses play a vital role in teaching and supervising the proper performance of Buerger's Allen Exercises and guiding patients in the correct application of mechanical compression devices to optimize blood circulation. Through consistent monitoring, they promote adherence to therapy and assess the effectiveness of these interventions, making necessary adjustments when needed. By integrating structured circulatory exercises and compression therapies into routine oncology care, nurses significantly enhance functional outcomes, symptom control, and overall quality of life for patients undergoing chemotherapy [20].

Significance of the study:

Chemotherapy-induced peripheral neuropathy (CIPN) and impaired lower-limb circulation are common adverse effects that can compromise patients' mobility, comfort, balance, functional independence, and quality of life and may increase the risk of falls. Although Buerger–Allen exercises and mechanical compression therapy are non-pharmacological approaches that may improve peripheral circulation and alleviate neuropathic symptoms, evidence directly comparing these interventions among patients receiving chemotherapy remains limited, particularly in Egypt. This study will address this gap and may inform feasible, nurse-led strategies for supportive oncology care.

Aim of the study:

This study will aim to compare the effects of Buerger–Allen exercises and mechanical compression therapy on lower-limb perfusion and peripheral neuropathy among patients undergoing chemotherapy.

Hypothesis:

H0: There will be no statistically significant differences between the Buerger–Allen exercise group and the mechanical compression therapy group in lower-limb perfusion or peripheral neuropathy outcomes across the study assessment points.

H1: Patients receiving Buerger–Allen exercises will demonstrate significantly greater improvement in lower-limb perfusion than patients receiving mechanical compression therapy.

H2: Patients receiving mechanical compression therapy will demonstrate a significant reduction in peripheral neuropathy symptoms following the intervention.

H3: Changes in lower-limb perfusion and peripheral neuropathy outcomes will differ significantly between the Buerger–Allen exercise group and the mechanical compression therapy group over time.

Materials and Methods

Materials

Research design:

Randomized control trail research design will be used.

Setting

The study will be conducted in the inpatient chemotherapy department at Ayady Almostakbal Cancer Treatment Hospital, Alexandria Governorate, Egypt. The hospital is a specialized, non-governmental, charitable medical center that provides cancer treatment services to residents of Alexandria Governorate and surrounding areas.

Subjects:

A purposive sample of 100 eligible patients will be recruited and allocated equally to two intervention groups: the Buerger–Allen exercise group (n = 50) and the mechanical compression therapy group (n = 50).

Inclusion criteria:

- Adult male and female patients aged 20–60 years who have been receiving chemotherapy for at least six months and who are willing to participate will be eligible for inclusion.

Exclusion criteria:

- Patients with uncontrolled diabetes mellitus or other medical conditions that may affect lower-limb perfusion or peripheral nerve function will be excluded.
- Patients with burns or extensive wounds of the lower limbs will be excluded.
- Patients with a lower-limb amputation will be excluded.
- Patients receiving another physical, pharmacological, or mechanical treatment regimen directed at the lower limbs will be excluded.

Sample size calculation

The required sample size will be estimated using Epi Info version 7 based on an accessible population of approximately 120 patients over three months, an expected frequency of 50%, a 5% margin of error, and a 95% confidence level. The calculated minimum sample will be 91 patients. To compensate for possible attrition and incomplete data, 100 patients will be recruited and allocated equally to the two intervention groups (n = 50 per group).

Tools for data collection:

- Two principal assessment tools will be used for data collection in addition to the Patient Demographic Profile and clinical data including age, gender, educational level, marital status, and occupation the patient's past and current health history.

  Tool 1: Lower-Limb Perfusion Assessment. This part will be adapted from Abouelala et al. (2022) (21) and will assess lower-limb skin color and temperature, distal circulation, capillary refill, active and passive range of motion, edema, preferred sleeping or sitting position, limb circumference, and skin condition.

  Tool 2: Peripheral Neuropathy Assessment. This tool will be adapted from Abouelala et al. (2022) (21) and will be used to assess lower-limb sensation and pain.

Proposed Study Procedures

- Official permission to conduct the study will be obtained from the authorized administration of Ayady Almostakbal Cancer Treatment Hospital before recruitment begins.
- The study tools will be prepared or adapted by the researchers after reviewing the relevant literature.

- The tools will be evaluated for content validity and relevance by a panel of five experts in medical-surgical nursing and oncology. Their recommendations will be considered when preparing the final versions.
- A pilot study will be conducted with 10% of the calculated sample to assess the clarity, feasibility, and applicability of the study tools and procedures and to identify potential barriers to data collection. Necessary modifications will be made accordingly. Participants included in the pilot study will be excluded from the main study sample and analyses.
- The internal consistency of the study tools will be evaluated using Cronbach's alpha. Reliability coefficients will be calculated using pilot-study data before the tools are applied in the main study.

- Patients who meet the eligibility criteria will be allocated equally to the Buerger–Allen exercise group (n = 50) and the mechanical compression therapy group (n = 50).
- Written informed consent will be obtained from each participant after the study purpose, intervention procedures, potential risks, and expected benefits have been explained.
- Participants in Group 1 will receive Buerger–Allen exercises. The researchers will explain and demonstrate the exercise and will ask each participant to return-demonstrate the following three steps:
    - Step 1—Elevation: The participant's lower extremities will be elevated to approximately 45° and supported in this position until blanching occurs, for approximately three minutes.
    - Step 2—Dependency: The participant's feet and legs will then be lowered below the level of the body until redness appears, for approximately 10 minutes.
    - Step 3—Horizontal rest: The participant's legs will be placed flat on the bed for 10 minutes.
- The three-step Buerger–Allen exercise cycle will be repeated three times per session. Participants will be instructed to complete three sessions per day for five consecutive days, with performance monitored and reinforced by the researchers.

- Participants in Group 2 will receive mechanical compression therapy once during each chemotherapy session for one month, for a total of three sessions, with each session lasting 20 minutes.
- In both groups, the assigned intervention will be delivered during administration of the prescribed chemotherapy.
- Intervention sessions will be conducted individually in a quiet, private environment, with a caregiver present when appropriate. Lower-limb perfusion and peripheral neuropathy outcomes will be assessed at baseline, immediately after the intervention, and at two- and four-week follow-ups using the same standardized tools.

Proposed Statistical Analysis

Data will be coded, entered, cleaned, and analyzed using an appropriate statistical software package. Descriptive statistics will summarize demographic and clinical characteristics and study outcomes. Baseline comparability between groups will be examined using independent-samples tests appropriate to the level and distribution of the data. Changes in lower-limb perfusion and peripheral neuropathy across baseline, immediate post-intervention, two-week, and four-week assessments will be evaluated using repeated-measures or generalized models appropriate to each outcome. Effect estimates, 95% confidence intervals, and exact p values will be reported, with statistical significance set at $p < .05$.

Ethical Considerations

- Ethical approval will be obtained from the Research Ethics Committee of the Faculty of Nursing, Damanhour University, Egypt, before study implementation. The approval date and research code will be documented in the final study report.
- The purpose and procedures of the study will be explained to all eligible patients, and written informed consent will be obtained before enrollment in either intervention group.
- Participants will be assured that their anonymity, privacy, voluntary participation, and confidentiality will be protected throughout the study.
- Participants will have the right to withdraw from the study at any time without penalty or any effect on their treatment or care.
- The mechanical compression device will be inspected and approved for safe use by oncology and vascular specialists before the intervention begins.

References:

1. Rao RD, Michalak JC. Chemotherapy-related toxicity in oncology practice. J Oncol Pract. 2018;14(2):89-96.
2. National Cancer Institute. Chemotherapy and you: support for people with cancer [Internet]. Bethesda (MD): National Institutes of Health; 2021 [cited 2026 Jun 18]. Available at: https://www.cancer.gov/
3. Rahman N, Sukumar J, Maryam B. Chronic chemotherapy-induced peripheral neuropathy: living with neuropathy during and after cancer treatments. Ann Palliat Med. 2025;14(2).
4. Kruger-Genge A, Blocki A, Franke RP, Jung F. Vascular endothelial cell biology. Int J Mol Sci. 2019;20:4411. ***doi: 10.3390/ijms20184411***
5. Starobova H, Vetter I. Pathophysiology of chemotherapy-induced peripheral neuropathy. Front Mol Neurosci. 2017;10:174.
6. Iorga RA, Bratu OG, Marcu RD, Constantin T, Mischianu DLD, Socea B, et al. Thromboembolism in cancer patients treated with chemotherapy—still a clinical concern. Cancers. 2019;18(6):5026-5032. ***doi: 10.3892/etm.2019.8019.***
7. Bandos H, Melnikow J, Rivera DR, Swain SM, Sturtz K, Fehrenbacher L, et al. Long-term peripheral neuropathy in breast cancer patients treated with adjuvant chemotherapy: NRG Oncology/NSABP B-30. J Natl Cancer Inst. 2018;110(2):djx162.
8. Zajączkowska R, Kocot-Kępska M, Leppert W, Wrzosek A, Mika J, Wordliczek J. Mechanisms of chemotherapy-induced peripheral neuropathy. Int J Mol Sci. 2019;20(6):1451. doi:10.3390/ijms20061451.
9. Gaballah A, Shafik A, Elhusseiny K, Ashraf M. Chemotherapy-induced peripheral neuropathy in Egyptian patients: single institution retrospective analysis. Asian Pac J Cancer Prev. 2018;19(8):2223-2227. ***doi: 10.22034/APJCP.2018.19.8.2223.***
10. Health Promotion Administration, Ministry of Health and Welfare. Cancer Registry Annual Report 2020 [Internet]. 2020 [cited 2026 Jun 18]. Available at: https://www.hpa.gov.tw/Pages/Detail.aspx?nodeid=269&pid=13498
11. Sarezky J, Sachs G, Elinzano H, Stavros K. Cancer and peripheral nerve disease. Clin Geriatr Med. 2021;37(2):289-300.

12. Sidhu D, Wilkie JC, Buchan J, Toohey K. Optimising exercise for managing chemotherapy-induced peripheral neuropathy in people diagnosed with cancer. Cancers. 2025;17(15):2533. doi:10.3390/cancers17152533.
13. Hassan Z, Bader El Din S, El Rasek A. Impact of Buerger Allen exercise on improving selected clinical features of peripheral vascular disease among diabetic patients. J Nurs Health Sci. 2020;9(2):4-13.
14. Saleh MA, Ahmed SS, Bakr ZH. Effect of Buerger Allen exercise on lower limb perfusion and peripheral neuropathy among patients with peripheral vascular diseases. Egypt J Health Care. 2024;15(1):1248-1261. ***DOI:10.21608/ejhc.2024.344814***
15. Kaur G, Khandelwal N, Rani B. Trends in pneumatic compression devices and their impact on patient outcomes: a review. Int J Community Med Public Health. 2024;11(2):1016-1021. ***DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20240299***
16. Mollaelahi F, Shahali S. The effect of modified Buerger-Allen exercises on lower extremities edema in late pregnancy: randomized clinical trial. J Obstet Gynaecol India. 2023;73(6):488-495. ***doi: 10.1007/s13224-023-01850-z***
17. Huang Y, Tan T, Liu L, Yan Z, Deng Y, Li G, et al. Exercise for reducing chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis of randomized controlled trials. Front Neurol. 2024;14:1252259. ***doi: 10.3389/fneur.2023.1252259.***
18. Xiaoqian Y, Jiwei H, Lizhi Z, Baojia G, Luyan G, Huiqian X, et al. A randomized controlled trial: effects of compression therapy combined with exercise on chemotherapy-induced peripheral neuropathy in patients with breast cancer. Cancer Treat Res Commun. 2024;42:100871.
19. Okumu RA, Omondi EA, Mageto I, Fitch MI, Oweya E. Evaluating the effectiveness of an educational program on chemotherapy-induced peripheral neuropathy in enhancing competence among nurses in cancer care. Can Oncol Nurs J. 2025;35(4):533-553. ***doi: 10.5737/23688076354533.***
20. Behairy AS, Masry SE. Impact of educational nursing intervention on compression therapy adherence and recurrence of venous leg ulcers: a quasi-experimental study. Ocul Oncol Pathol. 2022;8(2):120-132.
21. Abouelala F, Khalil N, Bahy A, Habiba A. Effect of gradual sitting position on recovery and satisfaction of patients post trans-femoral cardiac catheterization. Egypt J Health

Care. 2022;13(1):1421-1438. available at: https://ejhc.journals.ekb.eg/article_227153.html

22. Park H, Park S. Effects of Buerger-Allen exercises on lower extremity circulation and peripheral neuropathy: a randomized controlled trial. J Clin Nurs. 2019;28(9-10):1803-1812.
23. Loprinzi CL, Lacchetti C, Bleeker J, Cavaletti G, Chauhan C, Hertz L, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: ASCO guideline update. J Clin Oncol. 2020;38(28):3325-3348. doi:10.1200/JCO.20.01399.
24. Staff NP, Grisold A, Grisold W, Windebank AJ. Chemotherapy-induced peripheral neuropathy: a current review. Ann Neurol. 2017;81(6):772-781. doi:10.1002/ana.24951.
25. Kaur J, Kaur S, Bhardwaj N. Effectiveness of Buerger Allen exercises on lower extremity perfusion among patients with diabetes mellitus. Int J Nurs Educ. 2019;11(3):45-50.
26. Sharma R, Kaur M. Effectiveness of nursing interventions on improving circulation among patients with peripheral vascular disease. Nurs Midwifery Res J. 2020;16(2):87-94.
27. Dörenkamp S, de Vries M, Hoogeveen A, Noordzij P, van den Houten M, Teijink J, et al. Patient characteristics and comorbidities influence walking distances in symptomatic peripheral arterial disease: a large one-year physiotherapy cohort study. PLoS One. 2016;11(1):e0146821. doi:10.1371/journal.pone.0146821.
28. Sahu P, Das K, Behera S. A study to assess the effectiveness of Buerger Allen exercises on lower extremity perfusion. Indian J Public Health Res Dev. 2020;11(5):234-239.
29. Radhakrishnan S, D'Souza S, Kumar A. Effectiveness of Buerger Allen exercises on improving peripheral circulation among patients with vascular disorders. Clin Epidemiol Glob Health. 2021;10:100685. doi:10.1016/j.cegh.2020.100685.
30. Partsch H. Compression therapy: clinical and experimental evidence. Ann Vasc Dis. 2017;10(4):260-268. doi:10.3400/avd.ra.17-00052.
31. Mosti G, Partsch H, Mortimer P. Compression therapy in venous and lymphatic disease: clinical and experimental evidence. Ann Vasc Dis. 2018;11(3):272-279. doi:10.3400/avd.ra.18-00057.

32. Khan F, Amatya B, Galea M. Rehabilitation interventions in patients with peripheral vascular disease: a systematic review. Arch Phys Med Rehabil. 2020;101(3):556-571. doi:10.1016/j.apmr.2019.10.189.
33. O'Sullivan B, Schmitz J, Fulk G. Physical rehabilitation. 7th ed. Philadelphia: F.A. Davis Company; 2019.
34. Chang D, Yeh Y, Chen S. Effects of exercise interventions on edema and limb function in patients with vascular disorders: a systematic review. Int J Environ Res Public Health. 2021;18(9):4562. doi:10.3390/ijerph18094562.
35. El-Deen A, Mohamed E, Ali A. Impact of Buerger Allen exercises on lower limb circulation and edema among patients with peripheral arterial disease. Egypt J Health Care. 2020;11(3):1120-1132.
36. Gray M, Black M, Baharestani M, Bliss DZ, Colwell C, Goldberg M, et al. Moisture-associated skin damage: overview and pathophysiology. J Wound Ostomy Continence Nurs. 2019;46(2):153-161. doi:10.1097/WON.0000000000000517.
37. Westphal T, Konschake W, Haase H, Vollmer M, Jünger M, Riebe H. Medical compression stockings on the skin moisture in patients with chronic venous disease. Vasa. 2019;48(6):502-508. doi:10.1024/0301-1526/a000812.
38. Smith EML, Pang H, Cirrincione C, Fleishman S, Paskett ED, Ahles T, et al. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced peripheral neuropathy. JAMA. 2013;309(13):1359-1367. doi:10.1001/jama.2013.2813.
39. Hershman DL, Lacchetti C, Dworkin RH, Lavoie Smith EM, Bleeker J, Cavaletti G, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014;32(18):1941-1967. doi:10.1200/JCO.2013.54.0914.
40. Kleckner IR, Dunne RF, Asare M, Cole C, Fleming F, Fung C, et al. Exercise for chemotherapy-induced peripheral neuropathy: a neurophysiological perspective. Support Care Cancer. 2018;26(4):1019-1028. doi:10.1007/s00520-017-4013-0.