Egyptian Journal of Physical Therapy and Rehabilitation (EJPTR)

Faculty of Physical Therapy

e-ISSN: 2974-3605
p-ISSN: 2974-3591

Review Article

Effect of Therapeutic Exercise on Lung Cancer Related Fatigue: A systematic review

Eman Koutb Ali [1, *], **Khadra Mohamed Ali** [1], **Ahmed Mohamed Abd-Elfatah Amer** [2], **Nada Mohamed Yousef** [1]

[1] Department of Physical Therapy for Surgery, Faculty of Physical Therapy, Cairo University, Egypt.
[2] Department of chest Diseases, Faculty of medicine, Kasr El-Ainy, Cairo University, Egypt.

***Correspondence:** Eman Koutb Ali; **Email**: emankoutb8@gmail.com

DOI: https://doi.org/ 10.21608/ejptr.2024.311645.1011

Abstract

Background: The most prevalent and upsetting side effect of lung cancer and its therapy is now known to be fatigue. Cancer treatments, such as radiation, chemotherapy, and radiotherapy, can cause fatigue, which may already be present prior to the start of treatment. A wide range of psychological and physical symptoms are linked to lung cancer and its therapy, and these side effects can last for years after a patient finishes treatment. Fatigue may increase with treatment, so healthcare professionals should emphasize the role of fatigue management to decrease patient stress and improve quality of life, especially during treatment, to encourage patients to continue their treatment. Functional issues such soft tissue tightness, joint stiffness, fatigue, edema or swelling, and muscle weakness can all be improved with exercise treatment while also enhancing HRQoL.

Purpose: To determine the effect of therapeutic exercise on fatigue as primary outcome and secondary outcomes as HRQoL for any lung cancer patient.

Materials and Methods: Randomized controlled trials concerning the effectiveness of exercise training on lung cancer patients Related fatigue were included. Data Sources: We searched in MEDLINE, Embase, Scopus, SPORT Discus, and Web of Science from January 2022to October2023. Data Synthesis: thirteen studies were included. Data were assessed in a random-effects model.

Results: Data Extraction: This Study was extracted using Methodological quality assessment (PEDro Scale, Sackett scale). Risk of bias: was assessed by the Revised Cochrane Risk of Bias Tool for Randomized Trials searching for Recommendations, Assessment, Development and Evaluation**.**

Conclusion: From clinical evidence the therapeutic exercise had positive effect on lung cancer related fatigue and HRQoL**.**

Keywords: Lung Cancer; Cancer-related fatigue; Exercise; HRQL; Meta-analysis ; systemic review; NSCL,SCLC.

Citation: Ali EK, Ali KM, Amer AMA, Yousef NM. Effect of Therapeutic Exercise on Lung Cancer Related Fatigue: A systematic review. Egyptian Journal of Physical Therapy and Rehabilitation. 2025 Feb.;4(1):19-26.

Received: Aug. 2024
Accepted: Aug. 2024
Published: Feb. 2025

Introduction:

With over 1.35 million new cases identified annually, lung cancer is the most common disease diagnosed globally. Uncontrollably growing abnormal lung cells are the first sign of lung cancer. Any part of the respiratory system may be affected by these cells' invasion of adjacent tissues, tumor formation, and other effects. Cancer cells have the ability to metastasize, or spread, to other body areas and lymph nodes **(1).**

Treatment for lung cancer varies according to type in the form of chemotherapy, radiotherapy or combination. Lung cancer has a bad prognosis with many associated side effects. One of the most distressing side effects is fatigue. Fatigue affects quality of life, may increase during treatment, and may lead to treatment discontinuation. A wide range of psychological and physical symptoms are linked to lung cancer and its therapy, and these side effects can last for years after a patient finishes treatment. Exercise may decrease inflammation, improve immunity, decrease patient stress, improve fatigue, and improve quality of life, especially during treatment **(2).**

Breathing exercise can improve the fatigue of lung cancer by changing breathing depth and frequency, as one type of no pharmacological interventions, has demonstrated the benefit of pain relief in various conditions **(3).**

Aerobics exercise has the capacity to improve the fatigue of lung cancer by enhancing the immune response. A regular aerobic exercise regimen of fast walking has been demonstrated in experimental studies to improve certain immune system defenses, such as the T cell (T lymphocyte) response and the antibody response **(4).** The aim of this study is to determine the role of exercise training on fatigue for lung cancer patients.

Materials and Methods:

Protocol and Registration: This systematic review and meta-analysis was conducted with the Preferred Reporting Items for Systematic Review (PRISMA-NMA).

Eligibility criteria: The selection criteria for that review were based on Methodological and clinical factors such as population, intervention, comparison, outcome, study design.

Search strategy: we searched through The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, MEDLINE, EMBASE, CINAHL, PEDRO, LILACS, Google Scholar.

Time of search All the articles were systemically searched from January 2022 to October 2023. Only fully written articles in English were allowed to be submitted. Several websites, the linked article feature in PubMed, Web of Science, and Scopus were also used to look for citations.

Study design Meta-analysis was performed in a systematic manner on thirteen randomised controlled trials (RCT).

Population study participants were any lung cancer patients with SCLC or NSCLC, or lung cancer patients undergoing chemotherapy or radiotherapy, surgery with no Restrictions to age or sex.

Intervention and comparison: All population are divided into two groups': (intervention, control) groups; Then allocated to receive either exercise training or no exercise training as yoga, aerobic exercise, light Resisted breathing exercises, Balance; to enhance fatigue, HRQoL of any lung cancer patients. Included trials tested exercise interventions initiated during active cancer treatment or usual care treatment.

Outcomes: Studies were included if they assessed primary, secondary outcomes and presented data.

When CRF was assessed with More than two articles, represented numerically or graphically.

Selection criteria Included articles assessed any lung cancer patients with full articles in English language according to PICO:

P: any lung cancer patients

I: Therapeutic exercise

C: usual care or non-exercise training

O: primary outcome: enhance fatigue

Secondary outcome: improving HRQOL.
Excluded article:

- Studies assessed the effect of exercise training on normal people.
- Published abstracts with no full text articles available.
- Published studies not in English language.

B-Data extraction: this systematic search will be conducted using (wide electronic database) with no lower date limit but only English language will be used. searches will be performed with a combination of MESH (medical subject's headings) terms and keywords. Studies was searched in a systematic manner on fatigue and HRQOL. The methodological quality of the included studies will be assessed using Physical Therapy Evidence Database (Pedro) scale.

It includes 11 items assessing randomization, blinding and other criteria and categorizes them by score as follows: excellent (9–10), good (6–8), fair (4–5), and poor (<4). The modified Sackett's scale **(5)** will be used to identify the level of evidence. This research was approved by the ethical committee, Cairo University (No:P.T.REC/012/004525).

Risk of bias was assessed by the Revised Cochrane Risk of Bias Tool for Randomized Trials. According to the level of Recommendations, Assessment, Development and Evaluation.

Results:

Sensitivity analysis showed that the effect of therapeutic exercise on fatigue at post-treatment was significant after excluding one trial (Lin et al., 2019) with low heterogeneity and good stability. There was no significant difference in overall effect of fatigue at follow up between intervention group and control group. The effect on quality of life at post-treatment was significant after excluding one trial (Lin et al., 2023) and results for this meta-analysis showed stability. There was significant difference in overall effect of quality of life at follow up between intervention group and control group.

Over All strength of evidence

The quality of life and fatigue of lung cancer patients were the outcome variables used to assess data collected at the end of the intervention period in this meta-analysis. Standardized mean differences (SMDs), which were estimated using the Review Manager program for Windows (RevMan software, version 5) **(6),** were used to produce pooled statistics to enable comparison of data from various scales. To compute SMDs, the means, mean change, and standard deviations (SDs) for the intervention and control groups were analyzed. For every trial that was included in the meta-analysis, the forest plots were calculated using the means, SD, and sample size effect for the control group vs the intervention group. If the action research outcome is a continuous variable and the outcome variable was reported in at least two studies, the estimated effect size was computed. To look at differences, metrics of rehabilitation outcomes with 95% confidence intervals were employed. The I2 statistic and the random effects model were used to examine the study's heterogeneity and variability **(7).** The values listed below were applied: I2=0%–30% indicates no heterogeneity; I2=30%–49% indicates moderate heterogeneity; I2=50%–74% indicates significant heterogeneity; and I2=75%–100% indicates significant heterogeneity.

Statistical analysis

1. Fatigue:

At post-treatment: Three studies assessed cancer related fatigue at post-treatment between intervention group and control group in cancer patients. There was considerable heterogeneity in fatigue at post-treatment among three studies (n= 3 studies, n= 416 participants, P<0.00001; I2=99%). There was no significant difference (P= 0.37; P>0.05) in overall effect of fatigue (SMD= -1.39; 95% CI, -4.41 to 1.63) between intervention group and control group (Forest plot 1) **(Figure 1).** The effect on fatigue at post-treatment was significant after excluding one trial **(Lin et al., (8)** with low heterogeneity.

Results for this meta-analysis showed stability (Forest plot 2) **(Figure 2).**

At Follow up: One study assessed cancer related fatigue at follow up between intervention group and control group in cancer patient. There was no significant difference (P= 0.42; P<0.05) in overall effect of fatigue at follow up (SMD= -0.38; 95% CI, -1.29 to 0.53) between intervention group and control group (Forest plot 3) **(Figure 3).**

Quality of life (HRQOL)

At post-treatment: Eleven studies assessed cancer related QoL at post-treatment between intervention and control group in cancer patients. There was considerable heterogeneity among eleven studies (n= 11 studies, n= 629 participants, P<0.00001; I2= 97%). There was no significant difference (P= 0.70; P>0.05) in overall effect of QoL (SMD= -0.25; 95% CI, -1.55 to 1.04) between intervention group and control groups (Forest plot 4) **(Figure 4).** Sensitivity analysis showed that effect on quality of life at post-treatment was significant after excluding one trial **(Lin et al., 2023) (8)** and results for this meta-analysis showed stability (Forest plot 5) **(Figure 5).**

At Follow up

Three studies assessed cancer related quality of life at follow up between intervention group and control group in cancer patients. There was significant difference (P= 0.03; P<0.05) in overall effect of quality of life at follow up (SMD= 1.13; 95% CI, 0.14 to 2.11) between intervention group and control group (Forest plot 6) **(Figure6).**

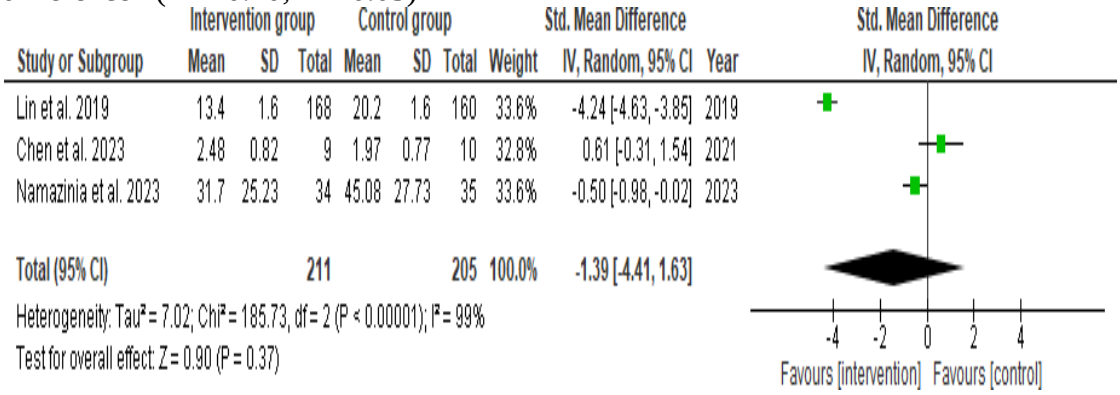

Figure 1. Forest plot (1): SMD (95% CI) of fatigue at post-treatment

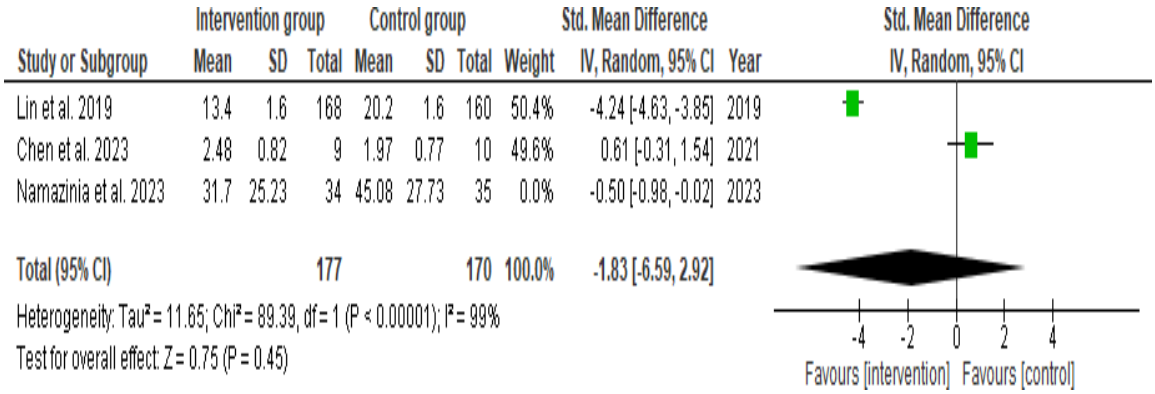

Figure 2. Forest plot (2): SMD (95% CI) of fatigue at post-treatment

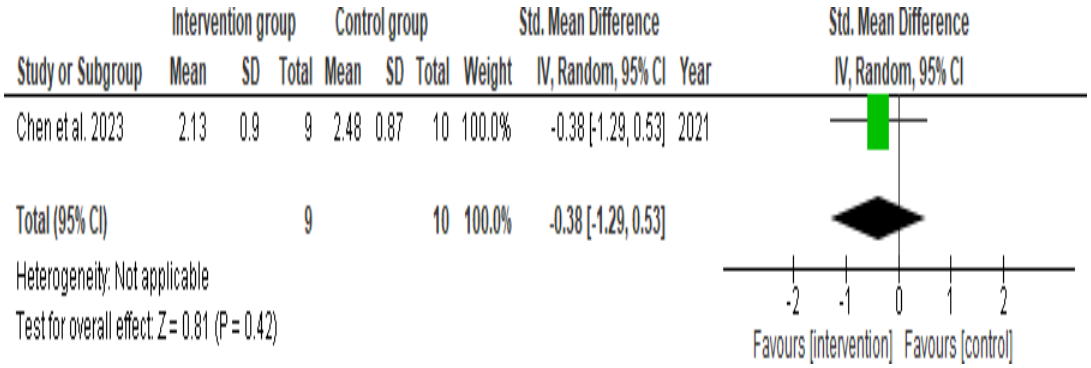

Figure 3. Forest plot (3): SMD (95% CI) of fatigue at follow up.

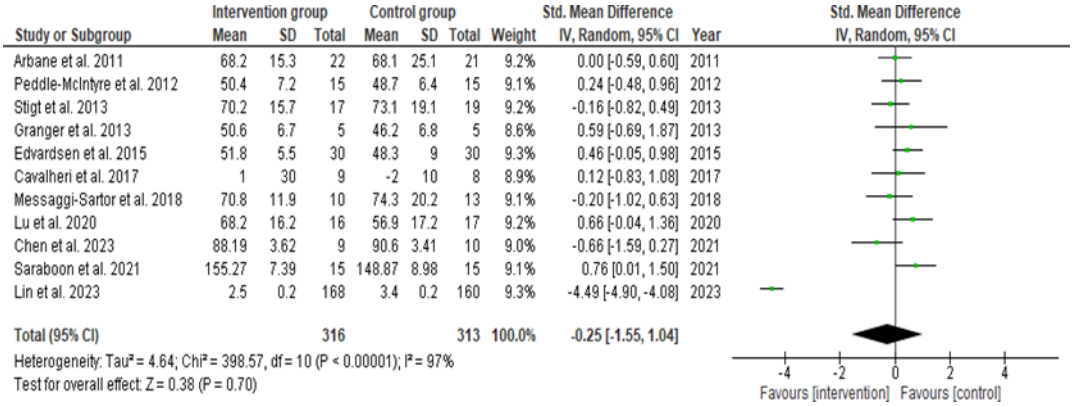

Figure 4. Forest plot (4): SMD of QOL at post-treatment as compared with a control from 11 studies.

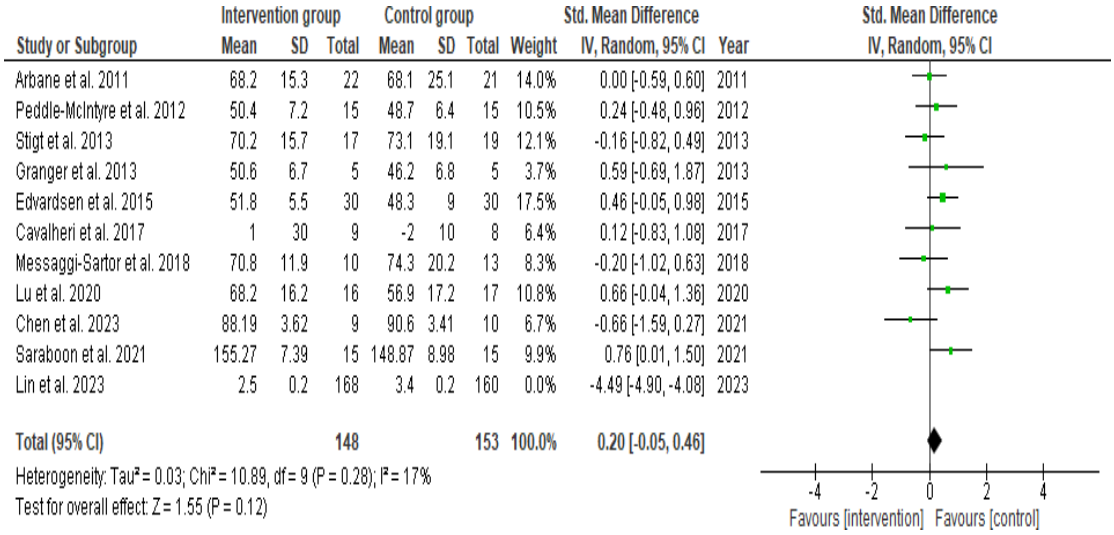

Figure 5. Forest plot (5): SMD of QOL at post-treatment

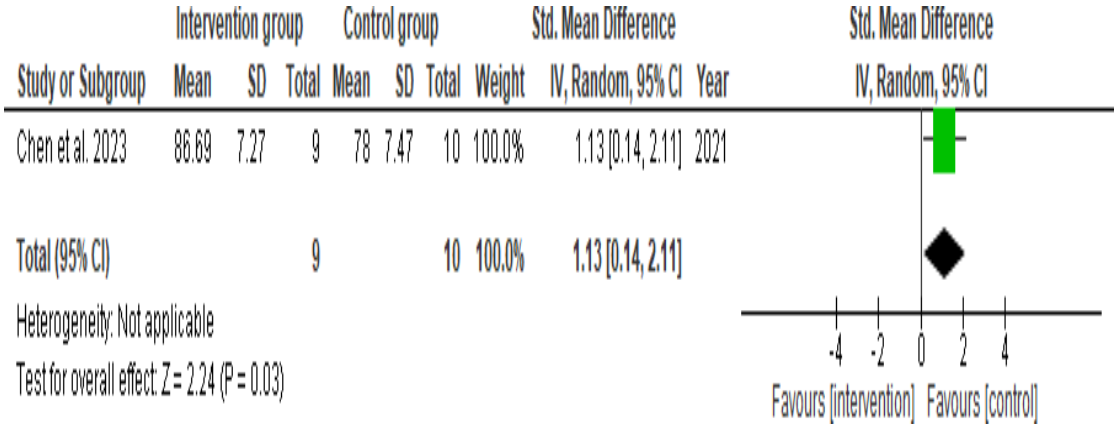

Figure 6. Forest plot (6): Standardized mean differences (95% CI) of quality of life at follow up.

Discussion:

Lung cancer has a bad prognosis with many associated side effects. One of the most distressing side effects is fatigue. Fatigue affects lifestyle and quality of life with many psychological problems. Fatigue may increase with treatment, so healthcare professionals should emphasize the role of fatigue management to decrease patient stress and improve quality of life, especially during treatment, to encourage patients to continue their treatment. The role of rehabilitation becomes more important nowadays in treating chest diseases, improving quality of life, improving prognosis, and decreasing mortality.

This systematic review and meta-analysis pooled fatigue and HRQoL data to determine the effect of therapeutic exercise administered to any lung cancer patients compared with usual care or non-exercise training. There was significant effect on fatigue and HRQoL between the intervention and control groups for lung cancer patients. Improvement of HRQoL was determined by aerobic exercise (walking distance) and light resisted breathing exercises.

Fatigue was measured by aerobic exercise (yoga therapy). All the studies measured fatigue assessed aerobic exercise and yoga therapy (Relaxation technique) with different Results through the three RCT studies at post treatment as in studies of **Lin et al ,2019 (8), Chen et al. 2023 (9), Namazine et al. 2023 (10)** and one RCT study measured fatigue at follow up treatment as in the study of **Chen et al. 2023 (9).** All the studies measured fatigue divided all patients into two groups, one intervention group, Received Aerobic exercise or yoga therapy, the other group received usual care with no exercise training, also with good result for all lung cancer patients pre and post operation. Achieving good result at post treatment with 2 weeks and repeated measurement within one month at follow up as in the study of **Chen et al. 2023 (9).**

HRQoL was measured through eleven RCT studies assessed aerobic exercise and light resisted breathing exercises, balance training at post treatment for lung cancer patients divided the patients into two groups , Intervention group assessed walking, aerobic exercise as in studies of **Peddle-McIntyre et al. 2012 (11), Arbane et al. 2011 (12), Cavalheri et al. 2017 (13),** and Balance training as in the study of S**araboon et al. 2021 (14)** and light resisted breathing exercises as in the studies of **Stight et al. 2013 (15), Edvardsen et al. 2015 (16), Messaggi-Sartor et al. 2018 (17), Granger et al. 2013 (18).** The other group received the usual care with no exercise training. HRQoL was measured two weeks post treatment or operation after that measurement within one month at follow up. Only three studies of them measured HRQoL at follow up as in the study of **Chen et al. 2023 (9)** which is a combined study between fatigue and HRQoL and achieved a significant evidence in improving general health and quality of life for all lung cancer patients.

Conclusion: from clinical evidence the therapeutic exercise had positive effect on lung cancer related fatigue and HRQoL.

Funding: Nil.
Data Availability Statement: Not applicable

Acknowledgments: Everyone who took part in this trial is much appreciated and thanked by the authors.

Conflicts of Interest: There are no conflicts of interest

References

1. **Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D.** Global cancer statistics. CA Cancer J Clin. 2011 Mar-Apr;61(2):69-90.
2. **Noonan KL, Ho C, Laskin J, Murray N.** The Influence of the Evolution of First-Line Chemotherapy on Steadily Improving Survival in Advanced Non-Small-Cell Lung Cancer Clinical Trials. J Thorac Oncol. 2015 Nov;10(11):1523-31.
3. **Elmetwaly RM & El Sayed RA.** Chest Tube Removal: Efficacy of Cold Application and Breathing Exercise on Pain and Anxiety Level. Evidence-Based Nursing Research 2020, 2(4), 12**.**
4. **Pedersen B.K., Saltin B.** Exercise as medicine-evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scand. J. Med. Sci. Sports.* 2015; 25:1–72.
5. **Sacket, D.L., Richardson, W.L., Rosenberg, W., Straus, E.S., Haynes, R.B., Livingstone, C.** Evidence-Based medicine. How to practice and Teach EBM. 2nd Ed 2000. Churchill Livingstone: New York.
6. **Manchikanti:** Evidence-Based Medicines Systematic Reviews, And Guidelines in Interventional Pain Management, Part I: Introduction and General Considerations Pain Physician 2008; 11:161-186.
7. **Higgins JPT, Green S (editors).** *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011.
8. **Lin PJ, Kleckner IR, Loh KP, Inglis JE, Peppone LJ, Janelsins MC, et al.** Influence of Yoga on Cancer-Related Fatigue and on Mediational Relationships Between Changes in Sleep and Cancer-Related Fatigue: A Nationwide, Multicenter Randomized Controlled Trial of Yoga in Cancer Survivors. Integr Cancer Ther. 2019.
9. **Chen X, Li J, Chen C, Zhang Y, Zhang S, Zhang Y, Zhou L, Hu X.** Effects of exercise interventions on cancer-related fatigue and quality of life among cancer patients: a meta-analysis. BMC Nurs. 2023 Jun 13;22(1):200.
10. **Namazinia M, Mazlum SR, Mohajer S, Lopez V.** Effects of laughter yoga on health-related quality of life in cancer patients undergoing chemotherapy: a randomized clinical trial. BMC Complement Med Ther. 2023 Jun 12;23(1):19.
11. **Peddle-McIntyre CJ, Bell G, Fenton D, McCargar L, Courneya KS.** Feasibility and preliminary efficacy of progressive resistance exercise training in lung cancer survivors. Lung Cancer. 2012 Jan;75(1):126-32.
12. **Arbane G, Tropman D, Jackson D, Garrod R.** Evaluation of an early exercise intervention after thoracotomy for non-small cell lung cancer (NSCLC), effects on quality of life, muscle strength and exercise tolerance: randomised controlled trial. Lung Cancer. 2011 Feb;71(2):229-34.
13. **Cavalheri V, Jenkins S, Cecins N, Gain K, Phillips MJ, Sanders LH, Hill K.** Exercise training for people following curative intent treatment for non-small cell lung cancer: a randomized controlled trial. Braz J Phys Ther. 2017 Jan-Feb;21(1):58-68.
14. **Saraboon C, Siriphorn A.** Effects of foam pad balance exercises on cancer patients undergoing chemotherapy: A randomized

control trial. J Bodyw Mov Ther. 2021 Oct; 28:164-171.

15. **Stigt JA, Uil SM, van Riesen SJ, Simons FJ, Denekamp M, Shahin GM, Groen HJ.** A randomized controlled trial of postthoracotomy pulmonary rehabilitation in patients with resectable lung cancer. J Thorac Oncol. 2013 Feb;8(2):214-21.
16. **Edvardsen E, Skjønsberg OH, Holme I, Nordsletten L, Borchsenius F, Anderssen SA.** High-intensity training following lung cancer surgery: a randomised controlled trial. Thorax. 2015 Mar;70(3):244-50.
17. **Messaggi-Sartor M, Marco E, Martínez-Téllez E, Rodriguez-Fuster A, Palomares C, Chiarella S, Muniesa JM, Orozco-Levi M, Barreiro E, Güell MR.** Combined aerobic exercise and high-intensity respiratory muscle training in patients surgically treated for non-small cell lung cancer: a pilot randomized clinical trial. Eur J Phys Rehabil Med. 2019 Feb;55(1):113-122.
18. **Granger CL, McDonald CF, Berney S, Chao C, Denehy L.** Exercise intervention to improve exercise capacity and health related quality of life for patients with Non-small cell lung cancer: a systematic review. Lung Cancer 2011; 72(2): 139-153.