Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1351090
J Health Sci Med. 2023;6(5):1087-1092

Preoperative pulmonary rehabilitation in medical inoperable patients with early stage non-small cell lung cancer and postoperative results

Seray Hazer[1], Seher Satar[2], İpek Candemir[3], Pınar Ergün[4], Leyla Nesrin Üstün Acar[1], Selim Şakir Erkmen Gülhan[1]

[1]Department of Thoracic Surgery, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Turkey
[2]Department of Chest Diseases Pulmonary Rehabilitation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Turkey
[3]Department of Thoracic Surgery, Ankara Etlik City Hospital, Ankara, Turkey
[4]Department of Chest Diseases, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Turkey

Cite this article as: Hazer S, Satar S, Candemir İ, Ergün P, Üstün Acar LN, Gülhan SŞE. Preoperative pulmonary rehabilitation in medical inoperable patients with early stage non-small cell lung cancer and postoperative results. *J Health Sci Med.* 2023;6(5):1087-1092.

Received: 28.08.2023 ◆ **Accepted**: 12.09.2023 ◆ **Published**: 28.09.2023

ABSTRACT

Aims: The impact of postoperative complications after surgery for lung cancer is substantial, with the increasing age of patients and the presence of comorbidities. Impairment in exercise capacity is a potential modifiable risk factor for postoperative complications. This study aimed to assess the contribution of preoperative pulmonary rehabilitation (PR) for increasing operability conditions in non-small cell lung cancer (NSCLC) for patients with limited pulmonary functions and postoperative results.

Methods: The patients with NSCLC who had preoperative pulmonary rehabilitation and underwent surgical resection in our clinics between 2010-2019 were evaluated retrospectively. The patients enrolled in a comprehensive, multidisciplinary, supervised outpatient 10-day duration PR program preoperatively, consisting of bronchial hygiene, breathing control, energy conservation techniques, exercise training (endurance and strength), psychological support, and nutritional support. Exercise capacity and VO2 peak were evaluated by using an incremental shuttle walk test (ISWT).

Results: Eighteen patients who underwent surgery due to NSCLC and had a pre-operative pulmonary rehabilitation program were evaluated. All the cases were male; the mean age was 66.2 (53-77) years. The squamous cell/adenocarcinoma ratio was 2.6 (13:5), and the mean tumor size was 4.6 (8-18) cm. The postoperative hospital stay was 12.7 (4-42) days, and they were followed up for an average of 30.2 (2-83) months.

Conclusion: Complete surgical resection is the most effective curative treatment for lung cancer. However, many patients with lung cancer also have severe COPD, increasing their risk of postoperative complications and their likelihood of being considered "inoperable." Preoperative pulmonary rehabilitation (PR) has been proposed as an intervention for risk modification and to decrease surgical morbidity and mortality. The results of our study also revealed the importance of preoperative pulmonary rehabilitation in centers where lung cancer surgery was performed.

Keywords: Non-small cell lung cancer, surgery, preoperative pulmonary rehabilitation

INTRODUCTION

Complete surgical resection is currently the superior curative treatment for lung cancer. The histopathologic tumor-node-metastasis (TNM) stage is known to be the most significant prognostic factor for surgically treated patients with NSCLC. Nevertheless, patient comorbidities are also important prognostic factors for survival. Age and smoking are strongly associated with comorbidities such as chronic obstructive pulmonary disease (COPD) and cardiovascular disease, which generally coexist with NSCLC. These comorbidities may have independent negative impacts on survival and influence the outcomes of NSCLC treatment, such as surgery or adjuvant therapy. Therefore, several comorbidities may significantly impact the prognosis of high-risk patients with NSCLC than the cancer stage.[1] Even without complications, lung cancer surgery is associated with significant reductions (approximately 10%-18%) in functional capacity (FC). Poor FC strongly predicts postoperative complications, mortality, and long-term survival in lung cancer.[2]

Corresponding Author: Seray Hazer, drserayhazer@gmail.com

Many patients with lung cancer have severe COPD, increasing their risk of postoperative complications and the probability of being considered "medically inoperable."[3] Advanced age, cancer stage, associated diseases and impaired cardiorespiratory fitness (CRF) are predictive factors of major postoperative complications and long-term survival.[4] Cardiopulmonary exercise testing (CPET) describes the accepted standard for evaluating CRF and the response to a rehabilitation program.

Peak oxygen consumption (peakVo2) deliberates the ability of the pulmonary capacity to deliver oxygen to the working skeletal muscles maximally. Cutoff values for peakVo2 of approximately 16 mL/kg per minute and a 10- to 12-mL/kg per minute anaerobic threshold (AT) have been shown helpful in discriminating between patients at low risk and those at higher risk of major postoperative complications.[5]

In patients with lung cancer, peakVo2 is, on average, 25% to 30% lower than in age- and sex-matched individuals without cancer.[4] No intervention has been proven to reduce the risk of postoperative complications in patients with resectable lung cancer and poor lung function.

Pulmonary rehabilitation (PR) is a procedure to increase exercise capacity in severe COPD. It is recommended as preoperative adjunctive therapy to reduce the risk of postoperative pulmonary complications.[3] To our best knowledge, a limited number of studies reveal the effect of preoperative multidisciplinary comprehensive 10-day duration PR on postoperative results in patients with limited exercise capacity and pulmonary functions.

This study aimed to evaluate the contribution of preoperative pulmonary rehabilitation (PR) to improving operability conditions in non-small cell lung cancer (NSCLC) for patients with limited pulmonary functions and postoperative results.

METHODS

This retrospective study was carried out with the permission of the Ankara Atatürk Sanatorium Training and Research Hospital Ethics Committee (Date: 24.08.2023, Decision No. 2012-KAEK-15/2760). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

The patients with non-small lung cancer who had preoperative pulmonary rehabilitation and underwent surgical resection in our clinics between 1st January 2010- 31st December 2019 were evaluated retrospectively. Inclusion criteria were The patients who completed Pulmonary Rehabilitation, Operable Non-Small Cell Lung Cancer patients, and those who underwent surgery in our Thoracic Surgery Department. Exclusion criteria were: A previously received neoadjuvant/adjuvant treatment, incomplete pulmonary rehabilitation, refused or had an inadequate performance for surgery, and operated on in other clinics after PR were excluded.

Outcome Parameters

The demographic and clinical characteristics included age, sex, smoking status, pulmonary function, echocardiography findings, tumor histology, pathological stage, surgery type, and adjuvant therapy history. The histopathological staging was determined using the eighth edition of the TNM classification.[6] The surgical procedures were classified as sub-lobar, lobectomy, or extended resection. After completing pulmonary rehabilitation, all patients were operated by the same surgery team. All patients were followed up in the intensive care unit for one day after surgery. Postoperative hospital stay, number of 30-day emergency visits and readmissions, complications and survival status data of the patients were recorded from the hospital database.

The demographic and clinical characteristics included age, sex, smoking status, pulmonary function, echocardiography findings, tumor histology, pathological stage, surgery type, and adjuvant therapy history. The histopathological staging was determined using the eighth edition of the TNM classification. The surgical procedures were classified as wedge resection, sub-lobar resection, lobectomy, pneumonectomy or extended resection.

Preoperative Pulmonary Rehabilitation Program

The program was multidisciplinary, comprehensive, and compact (5 consecutive days a week) and lasted two weeks, ten sessions. In patients with transportation problems, the program was undertaken in an inpatient manner. PPR program consisting of (a) educational support, medication advice, bronchial hygiene techniques, breathing control techniques, energy conservation, relaxation, and dietary advice. Two chest physicians, two physical therapists, a dietician, one respiratory nurse, and a psychologist delivered educational sessions. (b) exercise training, (c) a nutritional intervention, and (d) psychological counseling, if needed. The exercise training program was individually tailored to each patient. A physical therapist supervised all exercise training sessions. Exercise included cycle ergometer training (15 min), treadmill training (15 min), upper and lower extremity strength training (5-10 min), breathing therapies (10-20 min), and relaxation therapies (5-10 min) for total 50-70 min/day. Patients underwent both cycle

ergometer and treadmill training. Both workloads for cycling and walking speed for the treadmill ergometer were calculated from incremental shuttle walking test (ISWT) results using formulations. St. George's Respiratory Questionnaire (SGRQ) is a questionnaire that evaluates the quality of life in patients with chronic obstructive pulmonary disease (COPD) and includes three parts (symptoms, activity, and impacts) divided into 76 items. The questionnaire is self-administered but may be read to illiterate persons. BORG dyspnea scores 4-6 were also used for prescribing exercise. Patients were trained at 50% of peak workload and 50-80% of peak VO2. Quadriceps resistance training was applied using free weights for five consecutive days a week according to a 1-repetition maximum starting at 50% for three sets and ten repetitions per set in the ten sessions. Upper extremity training consisted of one set, ten repetitions per set for ten sessions. Loads were recorded as kilograms.[7]

Postoperative hospital stay, number of 30-day emergency visits and readmissions, complications and survival status data of the patients were recorded from the hospital database.

Statistical Analysis

All data obtained during the study and recorded in the study form were analyzed using the IBM SPSS 20.0 (Chicago, IL, USA) statistical program. After evaluating whether the data were normally distributed, the Shapiro-Wilk test, histogram, and Q-Q plot were used to express the mean±standard deviation (SD) for normally distributed data. The median quartiles were used for non-normally distributed or ordinal data. The categorical variables were presented as the number of cases and the percentage. A paired test t-test compared two dependent groups regarding customarily distributed continuous variables. The 95% confidence intervals (95% CIs) were also calculated when appropriate, and a p-value less than 0.05 was considered statistically significant.

RESULTS

Eighty-three patients diagnosed with lung cancer who were admitted to a multidisciplinary pulmonary rehabilitation program were analyzed retrospectively. Forty-three patients completed the preoperative pulmonary rehabilitation program, and 18 of them who underwent surgery due to Non-Small Lung Cancer were evaluated. Demographics of the patients are shown in Table 1. All the cases were male; the mean age was 66.2 (53-77) years. All patients had a smoking history; their average consumption was 58.55 packs/year (19-110), and 27.7% were active smokers preoperatively.

When measurements and gains were evaluated before and after pulmonary rehabilitation, FEV1 increased from 54.06±12.9 to 57.89±11.19 (p: 0.23), FVC increased from 65.72±16.907 to 68.28±16.03 (p: 0.46), ISWT increased from 328.89±119.79 to 392.78±123.61 (p: 0.001) and SGRQ score increased from 54.2±17.7 to 29.05±8.7 (p<0.01), (Table 2).

Table 1. Demographics of the patients

Patient no	Age	Surgery	Histopathology	Stage	Complication	Hospital stay	Mortality	Mortality reason	Follow-up
1	67	LLL	A	IIIA	-	9	-	-	83
2	77	R BiL Inf	SCC	IIB	-	18	-	-	18
3	77	RUL	SCC	IIB	-	16	-	-	13
4	53	LSLL	SCC	IIIA	-	9	22nd month	Esophageal Fistula	22
5	69	LP	SCC	IA	-	7	-	-	64
6	55	RUL	SCC	IIB	Atelectasis	18	-	-	75
7	74	RLL	SCC	IIIA	VRE Pneumonia, PTE	42	42nd day	Sepsis	1
8	63	LP	SCC	IIB	-	8	-	-	11
9	59	LUL	A	IB	-	7	-	-	24
10	67	R BiL Inf	SCC	IIIA	Atelectasis, PAL	15	-	-	25
11	57	LSLL	SCC	IIA	-	8	-	-	43
12	72	RLL	SCC	IVA	-	8	5th month	Pneumonia	5
13	72	LV-UW	SCC	IA	-	4	-	-	6
14	65	LLL	SCC	IIIA	-	19	-	-	31
15	59	RUL	A	IB	Atelectasis, PAL	15	-	-	32
16	73	RV-LL	A	IA	Subcutaneous Emphysema	7	-	-	39
17	63	RUL	A	IB	-	10	-	-	24
18	69	RUW	SCC	IIB	-	9	-	-	8

LLL: Left Lower Lobectomy, R Bil Inf: Right bi-lobectomy Inferior, RUL: Right Upper Lobectomy, LSLL: Left Sleeve Lower Lobectomy, LP: Left Pneumonectomy, RLL: Right Lower Lobectomy, LUL: Left Upper Lobectomy, LV-UW: Left VATS Upper Wedge, RV-LL: Right VATS Lower Lobectomy, RUW: Right Upper Wedge Resection, A: Adenocarcinoma, SCC: Squamous Cell Carcinoma, PAL: Prolonged Air Leakage

Table 2. Outcome measures before and after the PR program

Parameters	Before PR	After PR	Mean differences with 95%CI	P value
FVC	65.72±16.907	68.28±16.03	-2.55 (-9.7 to 4.6)	0.46
FEV_1	54.06±12.9	57.89±11.19	-3.8 (-10.4 to 2.7)	0.23
ISWT	328.89±119.79	392.78±123.61	-63.8 (-95.9 to -31.7)	0.001
SGRQ	54.2±17.7	29.05±8.7	25.1 (18.05 to 32.2)	<0.001

Complications and death were determined as a composite outcome (5 patients had a composite outcome.) The amount of change in patients with and without a composite result was compared in terms of relevant data. There was no significant relation between FEV1 (p:0.737), FVC (p:0.358), ISWT (p:0.534) and Saint George's Respiratory Questionnaire (SGRQ) (p:0.220) with composite outcomes.

Surgical approaches were lobectomy for 50% (n: 9), wedge resection for 16.7% (n:3), pneumonectomy for 11.1% (n:2), Sleeve lobectomy for 11.1% (n:2), and bi-lobectomy inferior for 11.1% (n:2) of patients. The postoperative hospital stay was 12.7 (4-42) days.

The squamous cell/adenocarcinoma ratio was 2.6 (13:5), and the mean tumor size was 4.6 (8-18) cm. The participants were followed up for an average of 28.5 (1-83) months, and mortality occurred in three patients (16.66%) on the 42nd day, 5th month and 22nd month of follow-up. No mortality occurred in the first 30 days postoperatively. However, one patient died on the 42nd day due to Vancomycin-resistant Enterococci pneumonia and pulmonary thromboembolism. One patient who underwent cranial metastasectomy (Stage IV-A) was deceased due to pneumonia after chemotherapy in 5th month of the surgery. The other patient who underwent sleeve left lower lobectomy with Squamous Cell Ca (Stage III-A) died of esophageal fistula in the 22nd month.

Complications developed in 5 patients (27.77%). Atelectasis occurred in three cases (16.66%), prolonged air leakage occurred in two cases (11.11%), subcutaneous emphysema occurred in 1 (5.55%), pneumonia occurred in one (5.55%), pulmonary thromboembolism occurred in one patient (5.55%). A 55-year-old male who underwent a right upper lobectomy had atelectasis and was treated with repeating bronchoscopies. A 67-year-old male who underwent bi-lobectomy inferior and a 59-year-old male who underwent right upper lobectomy had prolonged air leakage and atelectasis. Bronchoscopy was performed for both patients. Pleurodesis was used for one of the patients, and the other underwent secondary chest tube insertion for prolonged air leakage. Subcutaneous emphysema occurred, and a fasciotomy was needed in a 73-year-old patient who underwent a right lower lobectomy with VATS.

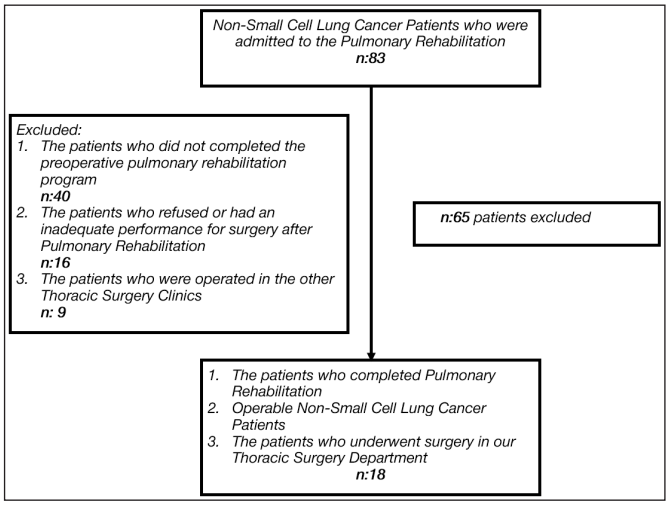

Figure 1.

DISCUSSION

This study showed a significant improvement in the incremental shuttle walk test (ISWT) and SGRQ with preoperative pulmonary rehabilitation in patients with Lung Cancer with COPD coexistence. Patients were safely taken to surgical treatment after pulmonary rehabilitation.

Lung cancer is the leading cause of cancer death worldwide, and the most effective treatment in the early stages of NSCLC remains complete surgical resection.[8,9] Elder age, cancer stage, co-morbidities, and impaired cardiorespiratory fitness (CRF) are predictive factors of major postoperative complications and long-term survival.[10] Even without complications, lung cancer surgery is associated with significant reductions (approximately 10%-18%) in functional capacity (FC). Poor FC strongly predicts postoperative complications, mortality, and long-term survival in lung cancer.[2] Enhancing FC by the exercise of the individual to enable them to withstand an incoming stressor such as surgery has been termed prehabilitation. Preoperative exercise training has significantly improved physical function before thoracic surgery approaches, with fewer pulmonary complications, shorter hospital stays, and better quality of life. Additionally, patients with lung cancer are at nutritional risk due to reduced food intake and underlying metabolic derangements leading to delayed recovery and mortality. Furthermore, these patients often experience psychological stress, such as anxiety and depression, after the diagnosis.[2,11]

Varela et al.[12] used a cross-sectional configuration with historical controls to consider the cost-effectiveness of chest physiotherapy following lobectomy. One hundred nineteen subjects undergoing lobectomy, more commonly by video-assisted thoracoscopic surgery (VATS) than by thoracotomy, received intensive chest physiotherapy one day before surgery and continued until hospital discharge. They were compared with a historical control group of 520 patients who had a lobectomy, more commonly by muscle-sparing thoracotomy than VATS at the same hospital. Nosocomial pneumonia and atelectasis rates were higher in the control group. However, only atelectasis rates demonstrated a significant difference (2% vs. 7.7%, odds ratio 0.20; 95% CI 0.05-0.86). The median length of stay was 5.7 days (range 3-22 days) in the physiotherapy group and 8.3 days (range 3-40 days) in the control group (p<0.0001). Cost analysis indicated a reduction in overall cost for hospital treatment in the physiotherapy group, but this did not include out-of-hospital charges caused by complications. The authors, therefore, refute that the difference between the groups could be accounted for by the more extensive use of the VATS approach in the physiotherapy group.[12,13] In our study, atelectasis occurred in three cases (16.66%), and the median length of stay was 12.7 (4-42) days. VATS lobectomy was performed in two patients (11.11%).

Li et al.[14] 2019 executed a meta-analysis of 404 patients from 7 randomized controlled trials (RCTs) on the effect of preoperative exercise therapy on surgical outcomes in lung cancer patients, with or without COPD. In 5 studies that reported postoperative pneumonia, there was no decrease in postoperative pneumonia frequency in those receiving preoperative exercise before lung cancer surgery. The length of stay in patients who underwent preoperative exercise training was shorter, with a standardized mean difference of minus 4.23 days (p=0.02).[15] Additional subgroup analysis of patients with COPD and lung cancer simultaneously found no advantage of preoperative exercise intervention in the incidence of PPC but a similar reduction in length of stay. Patients who received preoperative exercise before surgery reported an improved exercise capacity with an increase in 6-minute walking distance (6MWM) and a higher VO2 peak; however, no significant difference in pulmonary function was observed.

Lai et al.[16] presented a randomized trial of 68 patients with NSCLC undergoing VATs lobectomy to examine the impact of preoperative physical training. In those who underwent physical training preoperatively, the study found that preoperative physical training can improve cardiopulmonary tolerance, reduce PPCs and shorten in-hospital LOS. In Laurent et al.'s[17] study, 26 patients eligible for NSCLC resection were evaluated for the impact of preoperative respiratory muscle endurance training. Those in the intervention group (n=14) were found to have improved exercise capacity with increased minute ventilation [+15(±)16 vs. −2(±)17, p=0.004] and increased endurance time [+299(±)199 vs. −5 (±)371, p=0.001]. Those in the respiratory muscle endurance training group had fewer PPCs (2 vs. 10, p=0.037). However, there was no difference in LOS between groups.

Lee et al.[1] evaluated 471 patients with NSCLC who underwent surgery, and they were classified into high-risk (HR) (n=77) and standard-risk (SR) (n=394) groups according to the American College of Surgeons Oncology Group criteria (Z4099 trial).[18] In Lee et al.'s[1] study, the patients in the HR group experienced more postoperative complications (p≤0.001), hospital stays were significantly longer in the HR group than in the SR group and mortality was seen more often without disease recurrence. Pneumonia was the most frequent complication in HR patients, and its incidence was significantly higher than in SR patients. However, HR patients without postoperative complications had a survival rate similar to that of SR patients. In the present study, complications occurred in 5 patients (27.77%). The complications were atelectasis, prolonged air leakage, subcutaneous emphysema, pneumonia, and pulmonary thromboembolism. Early mortality occurred in a patient on the 42nd day due to pneumonia and pulmonary thromboembolism.

Pouwels et al.'s[19] systematic reviews (11 studies; 916 participants) investigated the effect of preoperative exercise therapy on patients undergoing lung surgery. Meta-analysis was not possible due to study heterogeneity. However, the review showed that a preoperative moderate to intense exercise program improved aerobic capacity, physical fitness, and quality of life, with a possibility that it might reduce postoperative complications and length of hospital stay. Preoperative physical therapy for cardiac surgery patients was evaluated in Hulzebos et al.'s[20] meta-analyses. Preoperative physical therapy that includes mixed interventions such as aerobic exercises, breathing exercises, and inspiratory muscle training compared with no treatment or sham therapy reduced postoperative atelectasis after elective cardiac surgery in four trials and pneumonia in five trials, but not the necessity for mechanical ventilation extended than 48 hours or mortality. The postoperative hospital stay was significantly faster for those in the physical therapy groups. A meta-analysis of 65 randomized controlled trials concluded that pulmonary rehabilitation was more effective than standard community-based care for functional exercise capacity.[21] The six-minute walk distance was greater following pulmonary rehabilitation than with community care. It transcended the clinical significance threshold (mean

difference 43.93 meters, 95% CI 32.64 to 55.21). Maximal exercise testing in participants assigned to pulmonary rehabilitation compared with usual care revealed increased maximal workload. Our study evaluated measurements and improvements before and after pulmonary rehabilitation. FEV1 increased from 54.06±12.9 to 57.89±11.19 (p: 0.23), FVC increased from 65.72±16.907 to 68.28±16.03 (p: 0.46), ISWT 328.89±119.79 from 392.78±123.61 (p: 0.001) and SGRQ score increased from 54.2±17.7 to 29.05±8.7 (p<0.01).

CONCLUSION

Preoperative pulmonary rehabilitation improves exercise capacity in patients undergoing surgical resection to manage lung cancer. Many studies support that preoperative exercise significantly reduces postoperative pulmonary complications and hospital length of stay. Referrals to exercise programs should be considered in patients awaiting lung resection, especially those patients considered borderline for suitability for surgical resection. Further studies are needed to investigate the effect of preoperative exercise on mortality and the cost/benefit of this intervention.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Ankara Atatürk Sanatorium Training and Research Hospital Ethics Committee (Date: 24.08.2023, Decision No. 2012-KAEK-15/2760).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Lee S, Roknuggaman M, Son JA, et al. Prognostic impact of postoperative complications in high-risk operable non-small cell lung cancer. *J Chest Surg.* 2022;55(1):20-29.
2. Ferreira V, Minnella EM, Awasthi R, et al. Multimodal prehabilitation for lung cancer surgery: a randomized controlled trial. *Ann Thorac Surg.* 2021;112(5):1600-1608.
3. Benzo R, Wigle D, Novotny P, et al. Preoperative pulmonary rehabilitation before lung cancer resection: results from two randomized studies. *Lung Cancer.* 2011;74(3):441-445.
4. Licker M, Karenovics W, Diaper J. Short-term preoperative high-intensity interval training in patients awaiting lung cancer surgery: a randomized controlled trial. *J Thorac Oncol.* 2017;12(2):323-333.
5. Licker M, Schnyder JM, Frey JG, et al. Impact of aerobic exercise capacity and procedure-related factors in lung cancer surgery. *Eur Respir J.* 2011;37(5):1189-1198.
6. Lababede O, Meziane MA. The eighth edition of TNM staging of lung cancer: reference chart and diagrams. *Oncologist.* 2018;23(7):844-848.
7. Kaymaz D, Ergün P, Candemir I, Gülhan SE, Fındık G, Demir N. Efficacy of preoperative comprehensive pulmonary rehabilitation in patients with lung cancer. *Phys Med Rehabil Int.* 2016;3(6):1103-1115.
8. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin.* 2018;68:7-30.
9. Sherwood JT, Brock MV. Lung cancer: new surgical approaches. *Respirology.* 2007;12:326-332.
10. Licker M, Karenovics W, Diaper J. Short-term preoperative high-intensity interval training in patients awaiting lung cancer surgery: a randomized controlled trial. *J Thorac Oncol.* 2017;12(2):323-333.
11. Cavalheri V.Granger C. Preoperative exercise training for patients with non-small cell lung cancer. *Cochrane Database Syst Rev. Coc.* 2017;6(6):CD012020.
12. Nagarajan K, Bennett A, Agostini P, Naidu B. Is preoperative physiotherapy/pulmonary rehabilitation beneficial in lung resection patients? *Interact Cardiovasc Thorac Surg.* 2011;13(3):300-302.
13. Varela G, Ballesteros E, Jiménez MF, Novoa N, Aranda JL. Cost-effectiveness analysis of prophylactic respiratory physiotherapy in pulmonary lobectomy. *Eur J Cardio-thorac Surg.* 2006; 29(2):216-220.
14. Li X, Li S, Yan, S. Impact of preoperative exercise therapy on surgical outcomes in lung cancer patients with or without COPD: a systematic review and meta-analysis. *Cancer Manag Res.* 2019;11:1765-1777.
15. Bibo L, Goldblatt J, Merry C. Does preoperative pulmonary rehabilitation/physiotherapy improve patient outcomes following lung resection? *Interact Cardiovasc Thorac Surg.* 2021;32(6):933-937.
16. Lai Y, Wang X, Zhou K, Su J, Che G. Impact of one-week preoperative physical training on clinical outcomes of surgical lung cancer patients with limited lung function: a randomized trial. *Ann Transl Med.* 2019;7(20):544-544.
17. Laurent H, Aubreton S, Galvaing G, et al. Preoperative respiratory muscle endurance training improves ventilatory capacity and prevents pulmonary postoperative complications after lung surgery. *Eur J Phys Rehabil Med.* 2020;56(1):73-81.
18. Fernando HC, Timmerman R. American College of Surgeons Oncology Group Z4099/Radiation Therapy Oncology Group 1021: a randomized study of sublobar resection compared with stereotactic body radiotherapy for high-risk stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg.* 2012;144(3):S35-S38.
19. Pouwels S, Fiddelaers J, Teijink JA, Woorst JF, Siebenga J, Smeenk FW. Preoperative exercise therapy in lung surgery patients: A systematic review. *Respir Med.* 2015;109(12):1495-1504.
20. Hulzebos EH, Smit Y, Helders PP, Meeteren NL. Preoperative physical therapy for elective cardiac surgery patients. *Cochrane Database Syst Rev.* 2012;11(11):CD010118.
21. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2015;23;2015(2):CD003793.