



Preoperative Exercise Reduces Postoperative Pulmonary Complications in Lung Cancer Surgery: A Systematic Review and Meta-Analysis

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Abstract

Background: Preoperative exercise has emerged as a promising approach to reducing the risk of postoperative pulmonary complications (PPCs) in patients undergoing surgery. However, its effectiveness in lung cancer surgery remains a topic of debate, largely due to varying results across studies. This meta-analysis aims to clarify the role of preoperative exercise in preventing PPCs among lung cancer patients.

Methods: We conducted a comprehensive search of randomized controlled trials (RCTs) in databases including PubMed, Medline, Embase, and the Cochrane Central Register of Controlled Trials, covering research published up to November 8, 2023. The primary focus was on the incidence of PPCs, while secondary outcomes included postoperative lung infections, atelectasis, pleural effusion, respiratory failure, and the length of hospital stay. We also performed subgroup analyses based on factors such as age, type of exercise, and the duration of the preoperative exercise program.

Results: A total of eleven studies, involving 949 patients, were included in our analysis. The results showed that preoperative exercise significantly reduced the incidence of PPCs (Relative Risk [RR] = 0.41, 95% Confidence Interval [CI]: 0.32–0.51). It also decreased the rates of postoperative lung infections (RR = 0.76, 95% CI: 0.61–1.00), atelectasis (RR = 0.43, 95% CI: 0.28–0.65), and respiratory failure (RR = 0.31, 95% CI: 0.12–0.80). Additionally, patients who participated in preoperative exercise programs had a shorter hospital stay, with a mean reduction of 2.67 days (95% CI: –3.59 to –1.76). Subgroup analysis showed no significant differences in outcomes based on age or the specific type of exercise.

Conclusions: Our findings suggest that preoperative exercise can effectively reduce PPCs and shorten hospital stays in lung cancer surgery patients. We propose integrating preoperative exercise into enhanced recovery after surgery (ERAS) protocols.

Keywords

Exercise, Preoperative, Lung Cancer, Complications

Abbreviations

MD: Mean Difference; SD: Standard Deviation; COPD: Chronic Obstructive Pulmonary Disease; LC: Lung Cancer; EC: Esophageal Cancer; EXP: Experimental; CON: Control; IMT: Inspiratory Muscle Training; AET: Aerobic Endurance Training

Introduction

Lung cancer is one of the most prevalent and deadly malignancies worldwide, with surgical resection as the cornerstone of curative treatment, particularly in early-stage disease. Despite the potential for favorable outcomes, lung cancer surgeries are often complicated by postoperative pulmonary complications (PPCs), which significantly impede recovery and worsen prognosis. The incidence of PPCs in lung cancer surgeries ranges from 30% to 50%, markedly higher than the 5% to 19% observed in other surgical populations [1]. PPCs, including pneumonia, atelectasis, respiratory failure, and pleural effusion, are influenced by multiple factors, including respiratory muscle weakness, pre-existing lung dysfunction, impaired postoperative sputum clearance, and the effects of intraoperative and postoperative mechanical ventilation [2]. These complications contribute to prolonged hospital stays, increased healthcare costs, and higher postoperative mortality [3].

In this context, preoperative exercise training emerges as a promising intervention to mitigate the risk of PPCs. Preoperative exercise programs typically include respiratory muscle training, abdominal breathing exercises, pursed-lip breathing, and aerobic conditioning such as stair climbing. These exercises aim to enhance respiratory muscle strength and endurance, improve lung function, and optimize overall physical fitness prior to surgery [4]. By improving the patient's pulmonary reserve and physical status, preoperative exercise may potentially reduce the severity of PPCs and improve postoperative outcomes.

Despite mechanistic plausibility, clinical translation remains contentious due to inconsistent evidence. One major barrier to its widespread implementation is the presence of conflicting results in the existing literature. For instance, Benzo et al. reported no significant reduction in PPCs or postoperative hospital stay with preoperative exercise [5], whereas Lai et al. found a significant decrease in hospital stay duration [6].

Furthermore, studies by Morano et al. and Bradley et al. have produced mixed results, with some showing improvements in specific pulmonary outcomes and others indicating no substantial benefits [7,8]. These inconsistencies may be attributed to variations in exercise protocols, patient populations, study designs, and outcome measures. As a result of these conflicting findings, clinicians are left without clear guidance on the efficacy of preoperative exercise, leading to its underutilization in clinical practice. The ambiguity in the literature underscores the necessity for a comprehensive and systematic evaluation of the available evidence.

This systematic review and meta-analysis aim to critically assess the impact of preoperative exercise on the incidence of PPCs and postoperative outcomes in lung cancer surgery patients. By synthesizing data from recent randomized controlled trials (RCTs), this study seeks to provide robust evidence to inform clinical practice and enhance perioperative care strategies for lung cancer patients.

Methods

Protocol Registration:

The protocol for this meta-analysis was registered in the PROSPERO database (<https://www.crd.york.ac.uk/PROSPERO>; registration number: CRD42023459104).

Search Strategy:

We followed the recommended process described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [9]. We searched for articles on published clinical trial studies in English from inception to November 8, 2023, in PubMed, Medline, Embase, and the Cochrane Central Register of Controlled Trials. Informal searches were performed on OpenGrey, National Technical Information Service, and Bielefeld Academic Search Engine. Additionally, articles that met the criteria were hand-searched from references. The search terms used

Table-1: Search Strategy

Criteria	Keywords
Patient (P)	(respiratory tract OR respiratory system OR respiratory OR pulmonary OR lung OR bronchia* OR bronchus) AND (cancer OR neoplasm OR carcinoma OR tumo*r)
Intervention (I)	Preoperative AND (physical exercise OR exercise OR physical activity OR exercise training OR aerobic exercise OR acute exercise OR isometric exercise)
Comparison (C)	Control group
Outcome (O)	postoperative pulmonary complication* OR postoperative complication* OR post*operative pulmonary complication* OR post*operative complication* OR respiratory infection* OR respiratory failure OR pleural effusion OR atelectas*s OR pneumothorax OR bronchospasm OR respiratory complication* OR respiratory tract infection* OR respiratory system infection* OR respiratory insufficiency OR pneumonia OR pulmonary atelectas*s OR pulmonary infection OR lung collapse

medical subject headings (MeSH) and terms relevant to postoperative respiratory complications based on the European Perioperative Clinical Outcome (EPCO) definitions [10], with Boolean operators "AND" and "OR" as shown in **Table-1**.

Eligibility Criteria:

Inclusion Criteria: (1) The study subjects were lung cancer patients, who aged 18 or over; (2) The intervention was preoperative exercise; (3) Non-cardiac surgery was eventually performed; (4) The type of study was a randomized controlled trial (RCT); (5) The outcome measures included postoperative complications.

Exclusion Criteria: (1) The full text could not be obtained; (2) The outcome measures were not available; (3) The literature was duplicated; (4) Outcome included exercise-induced asthma.

Literature Processing:

All retrieved documents were imported into EndNote software for management. Duplicate documents were first removed. Preliminary screening was conducted by reading the titles and abstracts of the articles to exclude irrelevant literature, followed by a careful reading of the full text to determine whether to include it. Two authors independently processed documents and extracted data. Any disagreement was resolved by discussion until consensus was reached or by consulting a third author.

Risk of Bias Assessment:

Following the Cochrane Manual of Evaluation criteria [Higgins JP, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0. The Cochrane Collaboration, 2011], we evaluated each study in the following seven aspects: (1) Selection bias when

generating random sequences; (2) Selection bias when allocation concealment was performed; (3) Performance bias when blinding investigators and participants; (4) Measurement bias in outcome evaluation; (5) Attrition bias for outcome data completeness; (6) Reporting bias for selective reporting; (7) Other biases from other sources. Each aspect was evaluated as "low", "unclear", and "high".

For publication bias assessment on the primary outcome, we used Egger's test in R language (version 4.0.3). We set $\alpha = 0.05$, and there was no significant evidence for publication bias if $p \geq 0.05$. If publication bias existed, we would trim and fill the data to assess it. To ensure the quality of evidence for each study, we used GRADEpro (version 3.6) according to the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group system [11]. Each study was evaluated as "very low", "low", "moderate", or "high" from different aspects, including risk of bias, inconsistency, indirectness, imprecision of effect estimates, and publication bias.

Data Extraction

The following data were extracted: title, author, year of publication, area, sample size, mean age, control group treatment, experimental group intervention, frequency, duration, PPCs, and postoperative hospital stay, and shown in one table. If the necessary data were not available, we contacted the author. Postoperative hospital stay was shown as mean and standard deviation, and a formula was used to translate if data were shown as quartiles [12–15].

The main outcome indicator was the incidence of PPCs. According to EPCO [15] definitions, PPCs include respiratory infection, respiratory failure, pleural

effusion, atelectasis, pneumothorax, and bronchospasm. The effect measure was risk ratio.

The secondary outcome was the length of postoperative hospital stay, which means the period between surgery and discharge. The effect measure was mean difference (days).

Statistical Analysis

Meta-analysis was performed using R language (version 4.0.3). Mean difference (MD) was used as the statistical variable for continuous measures, and relative risk (RR) was used for categorical measures, with 95% confidence intervals (CI) indicating the effect size. Heterogeneity between studies was evaluated using the I^2 test, with $\alpha = 0.1$. If $p \geq 0.1$ and $I^2 < 40\%$, heterogeneity between studies was considered small, and a fixed-effect model was used for pooled analysis. If $p < 0.1$ and $I^2 \geq 40\%$, heterogeneity between studies was considered substantial, and a random-effects model was used. Sensitivity analysis was performed by removing one study at a time and recalculating the combined estimate for the remaining studies. If I^2 was reduced by at least 10%, the excluded study was considered to affect the stability of the results, indicating that the difference between the excluded study and the remaining studies caused the heterogeneity. Subgroup analysis was also conducted by the age of patients. If all patients were elderly (age over 65), they were divided into one group, and the rest into another group.

Results

Literature Search and Final Inclusion Results:

A comprehensive computer search identified 37 articles in PubMed, 55 in Medline, 138 in Embase, and 91 in the Cochrane Central Register of Controlled Trials, totaling 321 articles. No relevant searches were found on Opengrey, National Technical Information Service, and Bielefeld Academic Search Engine. Initially, 119 duplicate articles were removed, leaving 202 papers for preliminary screening. During this screening, 109 non-randomized controlled clinical studies were excluded, along with 77 irrelevant studies. The remaining 16 articles underwent secondary screening; 3 full texts could not be obtained, 1 was poorly randomized, and 1 was unrelated, resulting in 11 articles being included.

The specific selection process is shown in **Fig-1**. The basic information of the included articles is presented in **Table-2**.

Table-2.

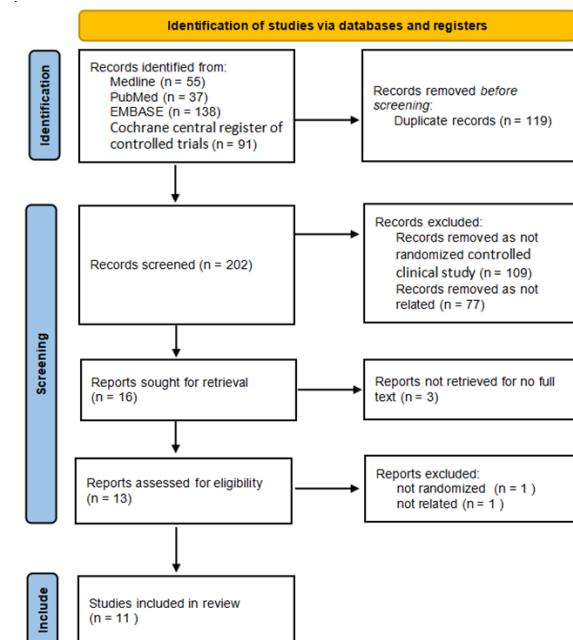


Fig-1:

Flow diagram of the screening process of the initial literature search

IMT: Inspiratory Muscle Training - includes respirator training, abdominal breathing training, lip breathing, blowing up balloons training, chest expansion training and spirometer training

AET: Aerobic Endurance Training - includes Nustep instrument, stair climbing training, fast walking, running, biking and high-intensity interval training

Quality and Risk of Bias of Studies:

The primary high-risk bias identified was attrition bias, related to patient withdrawal due to the inability to complete the training plan. These studies exhibited bias due to loss to follow-up because of exercise difficulties. Selection bias was noted in the study by Pehlivan, E. et al., where patients were randomly selected according to hospital record numbers. Regarding publication bias, due to the relatively small number of included studies, the Egger test was employed to analyze potential bias in the combined effect of each index. The results indicated no publication bias in the incidence of PPCs ($t = -0.67$, $P = 0.52$) and the length of postoperative hospital stay ($t = -1.39$, $P =$

0.20). According to the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group system, the quality of evidence was considered high for PPCs and moderate for the length of postoperative hospital stay.

Effect of Preoperative Exercise on the Incidence of PPCs in Surgery for Lung Cancer Patients:

Eleven studies reported on the effect of preoperative exercise on the incidence of PPCs in lung cancer surgery patients. The included studies demonstrated good homogeneity ($P = 0.69$, $I^2 = 0\%$), allowing the use of a

fixed-effect model for pooled analysis. The results showed that preoperative respiratory exercise significantly reduced the incidence of PPCs in lung cancer surgery patients ($RR = 0.41$, 95% CI: 0.32–0.51, $Z = -7.53$, $P < 0.01$). Forest plots for primary outcomes are presented in **Fig-2**. Patients were divided into three subgroups by age (over 65 or not), mode of exercise (IMT + AET vs. IMT). The results indicated that preoperative exercise was effective for all subgroups, but there was no significant difference in the incidence of PPCs between the age subgroup ($P = 0.34$), mode of exercise subgroup ($P = 0.75$).

Table-2: The Basic Information of the Included Articles

Aurthor	Year	Area	Disease	Number		Age (MD±SD)		Intervention		Outcomes*
				EXP	CON	EXP	CON	Mode and Frequency	Duration	
Gao, K. et al	2015	Sichuan, China	LC	71	71	66.3±10.17	59.57±13.0	IMT 20min/2-4 set/day	3-7 days	①②③⑤
Pehlivan, E. et al	2011	Istanbul, Turkey	LC	30	30	54.1±8.53	54.76±8.45	IMT 2 set/day	1 week	①②④
Lai, Y. et al	2019	Sichuan, China	LC	34	34	64.2±6.8	63.4±8.2	IMT 3 set/day	1 week	①②③④⑤
Kökeç, H. et al	2023	Antalya, Turkey	LC	30	30	54.8±11.18	54.8±8.72	IMT 3 set/day	1 week	①②③④
Sebio, R. et al	2017	A Coruña, Spain	LC	10	12	70.9±6.1	69.4±9.4	IMT 2 set/day	every week	①
Benzo, R. et al	2011	Minnesota, USA	LC	9	8	70.2±8.61	72.0±6.69	IMT 15-20min/day	1 week	①②③④⑤
Laurent et al	2020	Clermont-	LC	14	12	64±7	62±9	IMT 30 min/day	3 weeks	①②⑥
Lai, Y. Huang, J	2017	Sichuan, China	LC	30	30	72.5±3.4	71.6±1.9	IMT 20min/2 set/day	1 week	①②③④⑤⑥
Licker, M. et al	2017	Geneva, Switzerland	LC	74	77	64±13	64±10	AET 2-3 set/day	3-4 weeks	①②③④
Lai, Y. Su, J. et al	2017	Sichuan, China	LC	51	50	63.8±8.2	64.6±6.6	IMT 15min/3 set/day	1 week	①②③④⑥

* Outcomes : ① the incidence of postoperative pulmonary complications ② length of postoperative hospital stay ③ the incidence of postoperative lung infections ④ the incidence of postoperative atelectasis ⑤ the incidence of postoperative pleural effusion ⑥ the incidence of postoperative respiratory failure

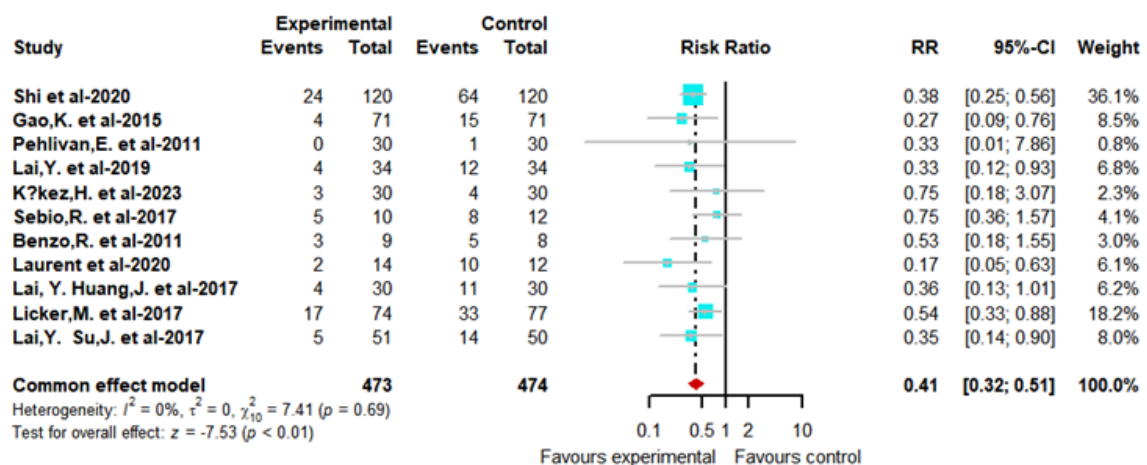


Fig-2:

Summary effect size of incidence of PPCs in thoracic cancer patients. RR, risk ratio; CI, confidence interval.

Original Article

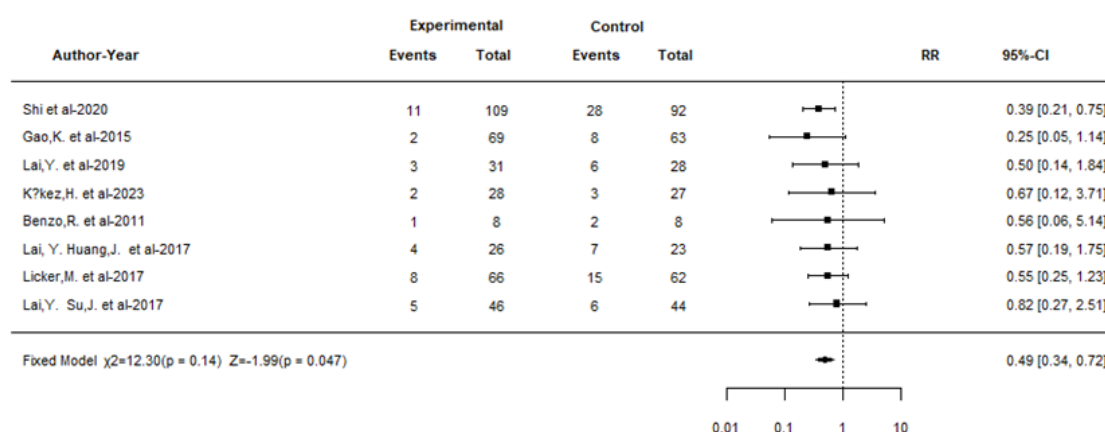


Fig-3:

Summary effect size of preoperative exercise on postoperative lung infections in lung cancer patients. RR, risk ratio; CI, confidence interval.

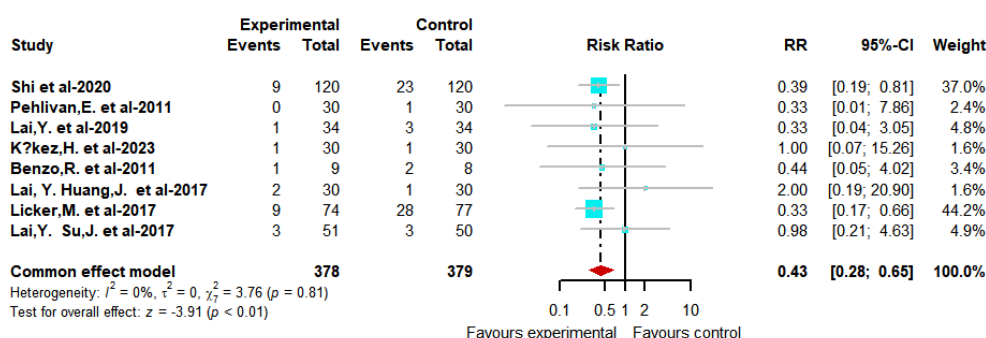


Fig-4:

Summary effect size of preoperative exercise on postoperative atelectasis in lung cancer patients. RR, risk ratio; CI, confidence interval.

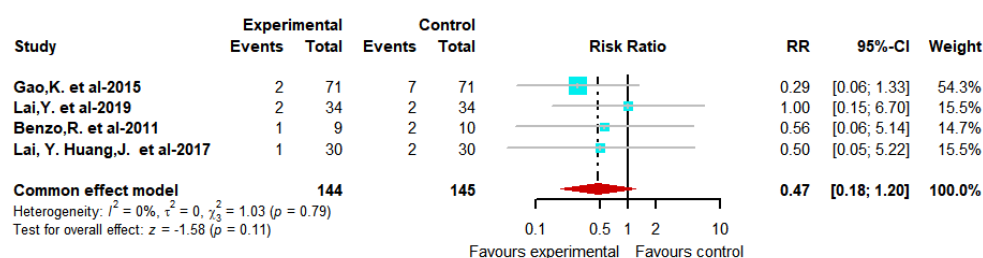


Fig-5:

Summary effect size of preoperative exercise on postoperative pleural effusion in lung cancer patients. RR, risk ratio; CI, confidence interval.

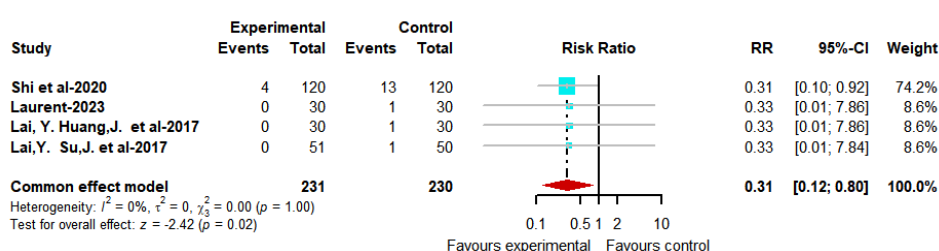


Fig-6:

Summary effect size of preoperative exercise on postoperative respiratory failure in lung cancer patients. RR, risk ratio; CI, confidence interval.

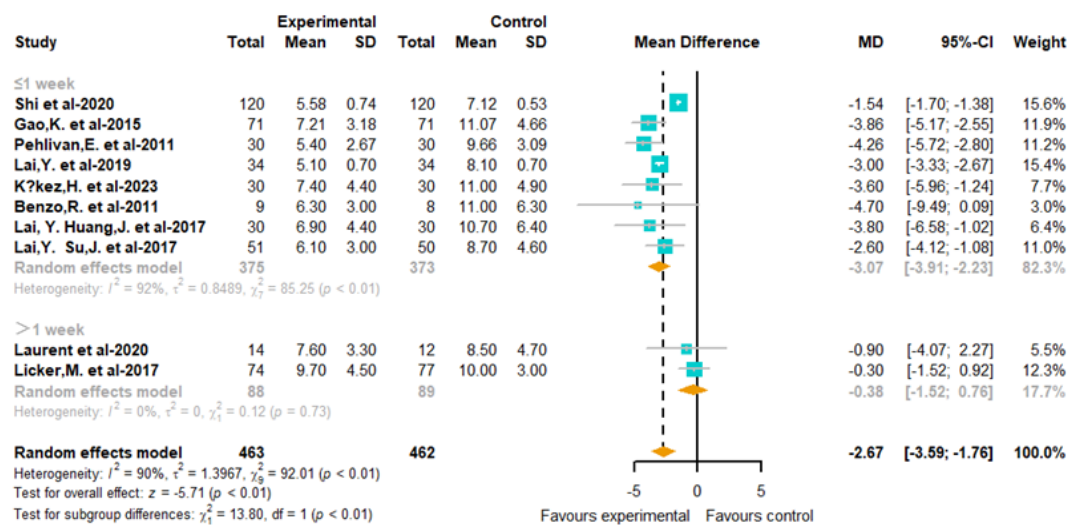


Fig-7:

Summary effect size of preoperative exercise on length of postoperative hospital stay in lung cancer patients. MD, mean difference; SD, standard deviation; CI, confidence interval.

Effect of Preoperative Exercise on the Incidence of Postoperative Lung Infections in Surgery for Lung Cancer Patients:

Eight studies reported the effect of preoperative exercise on the incidence of postoperative lung infections in lung cancer surgery patients, with good homogeneity ($P = 0.94$, $I^2 = 0\%$). The results indicated that preoperative respiratory exercise could reduce the incidence of postoperative lung infections ($RR = 0.49$, 95% CI: 0.34-0.72, $Z = -1.99$, $P = 0.047$). Details are shown in Fig-3.

Effect of Preoperative Exercise on the Incidence of Postoperative Atelectasis in Surgery for Lung Cancer Patients:

Eight studies reported the effect of preoperative exercise on the incidence of postoperative atelectasis in lung cancer surgery patients, demonstrating good homogeneity ($P = 0.81$, $I^2 = 0\%$). The results showed that preoperative respiratory exercise could reduce the incidence of postoperative atelectasis ($RR = 0.43$, 95% CI: 0.28-0.65, $Z = -3.91$, $P < 0.01$). Details are shown in Fig-4.

Effect of Preoperative Exercise on the Incidence of Postoperative Pleural Effusion in Surgery for Lung Cancer Patients:

Four studies reported the effect of preoperative exercise on the incidence of postoperative pleural

effusion in lung cancer surgery patients, with good homogeneity ($P = 0.79$, $I^2 = 0\%$). The results showed no significant evidence that preoperative respiratory exercise could reduce the incidence of postoperative pleural effusion ($RR = 0.47$, 95% CI: 0.18-1.20, $Z = -1.58$, $P = 0.11$). Details are shown in Fig-5.

Effect of Preoperative Exercise on the Incidence of Postoperative Respiratory Failure in Surgery for Lung Cancer Patients:

Eight studies reported the effect of preoperative exercise on the incidence of postoperative respiratory failure in lung cancer surgery patients, with good homogeneity ($P = 1$, $I^2 = 0\%$). The results showed that preoperative respiratory exercise could reduce the incidence of postoperative respiratory failure ($RR = 0.31$, 95% CI: 0.12-0.80, $Z = -2.42$, $P = 0.02$). Details are shown in Fig-6.

Effect of Preoperative Exercise on Length of Postoperative Hospital Stay in Surgery for Lung Cancer Patients:

Ten studies reported the effect of preoperative exercise on the length of postoperative hospital stay in lung cancer surgery patients. The included studies showed poor homogeneity ($P < 0.01$, $I^2 = 90\%$), necessitating pooled analyses using a random-effects model. The results demonstrated that preoperative respiratory exercise significantly reduced the length of

postoperative hospital stay in lung cancer surgery patients (MD=-2.67, 95% CI: -3.59 to -1.76, Z=-5.71, $P<0.01$).

The results also showed that preoperative exercise was effective for both age and training mode subgroups without significant differences. Details are shown in **Fig-7**. Considering the high heterogeneity, sensitivity analysis was conducted. After removing the studies by Shi et al. and Lai, Y. et al., the I^2 of the remaining studies decreased by 21.8% and 14.6%, respectively, without changing the results. Upon reviewing these two studies, it was found that the standard deviation was distinctly smaller (about 0.7) compared to other studies (average about 3.4). This suggested that the patients' conditions were more similar within these two studies but differed from other studies, resulting in closer but different hospital stay durations.

Discussion

The findings of this study demonstrate that preoperative exercise can significantly reduce the incidence of PPCs, including postoperative lung infections, atelectasis, and respiratory failure. Additionally, it shortens the length of postoperative hospital stay in patients undergoing lung cancer surgery. Subgroup analysis indicated that neither age nor mode of exercise significantly influenced the effects of preoperative exercise on the incidence of PPCs and the duration of hospital stay.

Our results are consistent with previous research, which has shown that preoperative exercise can reduce postoperative atelectasis, pneumonia, and hospital stay duration in adults undergoing cardiac and major abdominal surgery [16]. The study by Ting Zhou et al. also found that preoperative exercise improved lung function and shortened hospital stays in lung cancer surgery [17]. These findings reinforce the benefits of preoperative exercise in reducing PPCs and hospital stay duration. We further analyzed specific complications associated with PPCs and found that preoperative exercise effectively reduced the incidence of postoperative lung infections, atelectasis, and respiratory failure. This suggests that preoperative exercise enhances respiratory muscle endurance, facilitating timely sputum discharge post-surgery

[18,19]. Consequently, this reduces the risk of lung infections and ensures proper lung ventilation, decreasing the likelihood of atelectasis and respiratory failure.

However, our study did not find a significant impact of preoperative exercise on the incidence of postoperative pleural effusion. This finding aligns with the study by P.H. Nielsen et al., who suggested that postoperative pleural effusion might be related to postoperative sodium and water retention, exacerbated by age-related relative cardiac decompensation [20]. Factors such as lung cancer, anesthesia, sedative drugs, and surgical trauma increase inflammatory factors, impacting pleural permeability and leading to pleural effusion. Preoperative exercise does not mitigate these elevated inflammatory factors, hence its limited protective effect on pleural effusion. The small sample size in our study further limits the reliability of this conclusion, indicating the need for more high-quality studies.

We also explored the role of preoperative exercise in elderly patients, considering the clinical challenges posed by an aging population. Although our results showed a reduction in the incidence and length of hospital stay for postoperative PPCs in both elderly and non-elderly patients, there was no statistical difference between the groups. This may be due to the small number of elderly patients in our study, affecting the statistical significance. Additionally, we compared respiratory muscle training alone with combined aerobic endurance training and found no difference in improving postoperative PPCs and hospital stay duration. This suggests that in clinical practice, respiratory muscle training alone can enhance operability and patient compliance.

Our study has several limitations. Firstly, half of the included studies were evaluated as having a high risk of bias, which may influence the final analysis. Secondly, the analysis of the length of postoperative hospital stay showed high heterogeneity, reducing the credibility of the evidence. Thirdly, the small sample size in subgroup analyses limits the reliability of the findings. More studies, including those involving esophageal cancer, are needed to better represent thoracic tumor conditions.

Conclusions

In summary, preoperative exercise can reduce the incidence of PPCs, postoperative lung infections, atelectasis, and respiratory failure, and shorten the length of postoperative hospital stay in lung cancer surgery patients. However, due to the limited number of available studies and potential bias in some included randomized controlled trials, these conclusions should be interpreted with caution. Further large-scale, high-quality analyses are needed, particularly those focusing on elderly patients, to provide more robust evidence and inform clinical practice.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

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