The efficacy of pulmonary rehabilitation exercise training on complications and mortality after lung cancer resection: a systematic review and meta-analysis

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Background: The efficacy of pulmonary rehabilitation exercise training for patients after lung cancer resection has been controversial. We sought to evaluate the efficacy of pulmonary rehabilitation on the incidence of complications and mortality in patients after lung cancer resection.

Methods: Search English databases PubMed, EMBASE, Medline to obtain literature. The literature compared the effect of pulmonary rehabilitation exercise training intervention or not on the efficacy of patients after lung cancer resection, and the outcomes included postoperative complications and mortality. The quality of the included literature was assessed according to the Cochrane risk of bias assessment work. The chi-square test was used to test for heterogeneity. When there is heterogeneity, a random effect model is used; when there is no heterogeneity, a fixed effect model is used.

Results: A total of 9 prospective clinical studies (comprising 1,338 patients) were included in this meta-analysis. Among the patients, there were 571 cases in the rehabilitation group and 767 cases in the control group. The incidence of postoperative complications in the rehabilitation group was lower than that in the control group. The odds ratio (OR) value was 0.66 and 95% confidence interval (CI) was 0.47–0.94 (P=0.02). There was no heterogeneity among studies and no publication bias. The incidence of postoperative pulmonary complications in the rehabilitation group was lower than that in the control group, OR =0.33 (95% CI: 0.22–0.50) (P<0.00001). There was no heterogeneity among studies and no publication bias. There was no significant difference in postoperative mortality between the 2 groups (OR =0.77; 95% CI: 0.26–2.30; P=0.65). There was no heterogeneity among studies and no publication bias.

Discussion: Implementing pulmonary rehabilitation significantly reduced postoperative complications and the risk of pulmonary complications in lung cancer patients, but had no significant effect on mortality. Pulmonary rehabilitation exercise training is recommended for patients undergoing lung cancer resection.

Keywords: Pulmonary rehabilitation; complications; mortality; lung cancer resection.

Introduction

Lung cancer is a common malignant tumour threatening human health, and is also the primary cause of cancer-related death in China and worldwide (1). According to the latest data released by the International Agency for Research on Cancer of the World Health Organization, by 2020, lung cancer will rank 2nd in the global new cancer incidence rate and 1st in the worldwide cancer mortality rate (2). An epidemiological investigation illustrated that the 5-year survival rate of lung cancer was only about 13% (3). Cancer places a heavy disease burden on patients.

Surgery is commonly used in the clinical treatment of lung cancer patients. However, due to the effects of various factors during surgery and the characteristics of patients, the risk of postoperative complications is increased and the postoperative rehabilitation of patients is affected. Under current surgical technology and nursing approaches, about 20–30% of patients experience postoperative pulmonary complications (4), which result in prolonged hospitalization and increased hospitalization expenses and also seriously affects the quality of life of patients after operation.

Pulmonary rehabilitation is a meaningful intervention for treating chronic obstructive pulmonary disease or other chronic respiratory diseases. The American Thoracic Society/European Respiratory Society defines lung rehabilitation as a "comprehensive intervention based on a thorough evaluation of patients, and [a] tailor-made treatment for patients, including but not limited to exercise training, education and behaviour changes, [which is] aimed at improving the physical and psychological status of patients with chronic respiratory diseases and promoting long-term adherence to promote healthy behaviour" (5-7). Among them, exercise training is the core content of pulmonary rehabilitation. Thus, lung rehabilitation programs often include exercise training, drug treatment, smoking cessation, nutritional support, behavioural changes, and health education (6). However, the efficacy of pulmonary rehabilitation exercise training for patients after lung cancer resection has been controversial. A study pointed out that pulmonary rehabilitation can improve the quality of life of patients and reduce the mortality of patients (8). Therefore, we believe that a meta-analysis is necessary. However, some studies suggest that pulmonary rehabilitation exercise training does not affect the survival of patients after lung cancer resection (9). The aim of this study was to further investigate the efficacy of pulmonary rehabilitation exercise training on the incidence of complications and mortality in patients after lung cancer resection through literature search and meta-analysis. We present the following article in accordance with the PRISMA and MOOSE reporting checklists (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-978/rc).

Methods

Article retrieval

The English databases for retrieval are PubMed, EMBASE, Medline. The search method used medical subject words combined with free words. The English search subject words included "lung OR pulmonary" AND "operation OR resection OR surgery" AND "rehabilitation OR exercise".

Literature screening

To be eligible for inclusion in the meta-analysis studies had to meet the following inclusion criteria: (I) comprise subjects who were lung cancer patients who had undergone lung cancer resection; (II) the study consisted of the rehabilitation and the control groups.; (III) The interventions in the rehabilitation group included pulmonary rehabilitation exercise training; (IV) include at least 1 of the following outcome measures: postoperative complications, postoperative pulmonary complications, and mortality; and (V) be prospective cohort study or randomized controlled trial. Articles were excluded from the meta-analysis if they met any of the following exclusion criteria: (I) some or all patients in the study did not receive surgical treatment; (II) the article was a news report, expert opinion, critical literature, or abstract; (III) the data had been published previously; and/or (IV) the article data was unavailable.

Document data extraction

According to the above inclusion and exclusion criteria, 2 professional researchers independently screened the articles, determined the final included articles, and extracted the data according to a pre-determined data extraction table. If questions or differences in opinion arose in the process of the literature screening and extraction, a 3rd researcher was asked to resolve the issue or the issue was decided via discussion at a meeting if necessary.

Literature quality evaluation

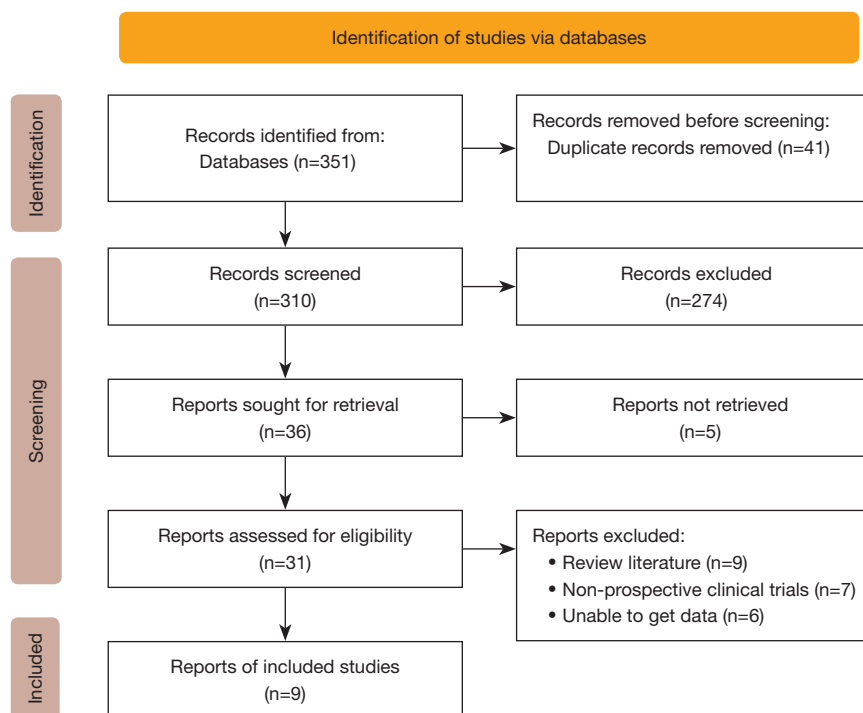The quality of the included articles was evaluated according to the Cochrane risk bias assessment. Prospective cohort

Figure 1 Literature screening process and results.

studies were assessed using the NOS assessment criteria for cohort studies on the Newcastle-Ottawa Scale (NOS). The quality of each included article was assessed independently by the 2 researchers and then cross-checked. If any differences in opinion arose, the 2 researchers discussed the issue until an agreement was reached or a 3rd researcher was consulted.

Statistical method

This study used Cochrane software RevMan5.4 for the statistical analysis of all the data. The efficacy of pulmonary rehabilitation on the postoperative complication and mortality rates were statistically described by calculating the odds ratios (ORs) and 95% confidence intervals (CIs). A P value <0.05 was considered statistically significant in the fixed-effects model or random-effects model. A Chi-square test was used to test the heterogeneity between among studies. When the I^2 results corrected by degrees of freedom was >50%, the results were considered heterogeneous, and a random-effects model was used. When the I^2 results corrected by degrees of freedom was ≤50%, the results were considered non-heterogeneous, and a fixed-effects model was used. The potential publication bias was estimated by

Deeks' funnel plots and Egger test.

Results

Literature search results

A total of 351 relevant articles were retrieved following the database search. After retrieving and collecting the articles, EndNote X9 management software was used to remove duplicate articles. The pre-determined inclusion and exclusion criteria were applied in a preliminarily screening in which the titles and abstracts of the articles were read, and the remaining articles then underwent a re-screening in which the full texts of the articles were read. Ultimately, 9 articles (7-15) (comprising 1,338 patients) met the criteria and were included in the meta-analysis, The specific screening process and results are shown in *Figure 1*.

Basic characteristics and quality evaluation of articles

The 9 included studies were all English-language articles, and comprised 5 randomized controlled studies and 4 prospective cohort studies. The basic information of the included articles are set out in *Table 1*. In 6 studies,

Table 1 Basic characteristics of the included articles

Author	Type of study	Preoperative/ postoperative pulmonary rehabilitation	Sample size		Complications		Pulmonary complications		Mortality		NOS	Cochrane
			Pulmonary rehabilitation group	Control group	Pulmonary rehabilitation group	Control group	Pulmonary rehabilitation group	Control group	Pulmonary rehabilitation group	Control group		
Benzo 2011 (7)	Randomized controlled trial	Preoperative	9	8			3	5			–	Low risk of bias
Pehlivan 2011 (15)	Randomized controlled trial	Preoperative	30	30	1	5					–	Low risk of bias
Bradley 2013 (8)	Prospective cohort study	Preoperative + Postoperative	58	305			5	49	2	6	7	–
Arbane 2014 (9)	Randomized controlled trial	Postoperative	67	68	20	22	10	16			–	Low risk of bias
Gao 2015 (10)	Prospective cohort study	Preoperative	71	71	12	59	5	25			6	–
Glogowska 2017 (12)	Prospective cohort study	Preoperative + Postoperative	215	187	32	37					7	–
Chesterfield-Thomas 2016 (11)	Prospective cohort study	Preoperative	33	9					0	1	7	–
Licker 2017 (13)	Randomized controlled trial	Preoperative	74	77	27	39	17	33	2	2	–	Low risk of bias
Laurent 2020 (14)	Randomized controlled trial	Preoperative	14	12			2	10	0	1	–	Low risk of bias

| | Rehabilitation | | Control | | | Odds Ratio | Odds Ratio |
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Arbane 2014	20	67	22	68	21.9%	0.89 [0.43, 1.85]	
Gao 2015	12	71	59	71	20.9%	0.04 [0.02, 0.10]	
Glogowska 2017	32	215	37	187	23.0%	0.71 [0.42, 1.19]	
Licker 2017	27	74	39	77	22.3%	0.56 [0.29, 1.07]	
Pehlivan 2011	1	30	5	30	11.9%	0.17 [0.02, 1.58]	
Total (95% CI)		457		433	100.0%	0.33 [0.11, 0.96]	
Total events	92		162				

Heterogeneity: Tau² = 1.22; Chi² = 36.05, df = 4 (P < 0.00001); I² = 89%
Test for overall effect: Z = 2.04 (P = 0.04)

0.01   0.1   1   10   100
Favours [experimental]   Favours [control]

Figure 2 Forest chart of the postoperative complication rates between the rehabilitation group and control group.

| | Rehabilitation | | Control | | | Odds Ratio | Odds Ratio |
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Arbane 2014	20	67	22	68	19.6%	0.89 [0.43, 1.85]	
Gao 2015	12	71	59	71	0.0%	0.04 [0.02, 0.10]	
Glogowska 2017	32	215	37	187	43.1%	0.71 [0.42, 1.19]	
Licker 2017	27	74	39	77	31.1%	0.56 [0.29, 1.07]	
Pehlivan 2011	1	30	5	30	6.2%	0.17 [0.02, 1.58]	
Total (95% CI)		386		362	100.0%	0.66 [0.47, 0.94]	
Total events	80		103				

Heterogeneity: Chi² = 2.37, df = 3 (P = 0.50); I² = 0%
Test for overall effect: Z = 2.30 (P = 0.02)

0.01   0.1   1   10   100
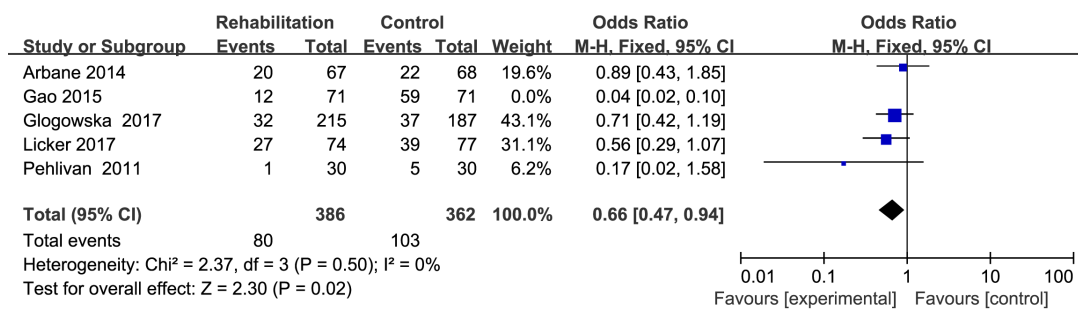Favours [experimental]   Favours [control]

Figure 3 Comparison of postoperative complication rates between the rehabilitation group and the control group after sensitivity analysis.

the rehabilitation exercise training plan was implemented before surgery. In 1 study, the rehabilitation exercise training plan was implemented after surgery. In 2 studies, the rehabilitation exercise training plan was implemented both before and after surgery. Of the 9 studies, 5 examined complication outcome indicators, 6 examined pulmonary complication outcome indicators, and 4 examined mortality indicators.

The Cochrane risk bias assessment tool was used to evaluate the 5 randomized controlled studies, and the 4 prospective cohort studies were evaluated using the evaluation criteria of the NOS. The scores were shown in *Table 1*.

Meta-analysis results

Postoperative complications

The outcome indicators of the postoperative complications were examined in 5 studies (9,10,12,13,15), comprising 890 patients. The results of the heterogeneity test for these 5 studies were as follows: χ^2=36.05, P<0.00001, I²=89%. Thus, the results indicated that there was heterogeneity among the 5 included studies, and a random-effects model was used

to combine the outcome indicators for the postoperative complications. The meta-analysis results showed that the OR value for postoperative complications between the rehabilitation group and the control group was 0.33 (95% CI: 0.11–0.96), and the difference between the 2 groups was statistically significant (z=2.04; P=0.04). The results are shown in *Figure 2*. There was obvious heterogeneity among the 5 literatures, and we used sensitivity analysis to find the source of heterogeneity. The heterogeneity mainly comes from the study of Gao *et al.* (10). There is no heterogeneity among the documents after removal. The OR value of postoperative complications between the rehabilitation group and the control group was 0.66 (95% CI: 0.47–0.94), and there was a statistical difference between the two groups, Z=2.30 (P=0.02). The sensitivity analysis results were consistent with the previous results, and the results were stable, as shown in *Figure 3*. Additionally, as the funnel chart shows, most of the points fell within the confidence interval, and the funnel type was inverted (see *Figure 4*). Egger's test P>0.05, there is no publication bias.

Postoperative pulmonary complications

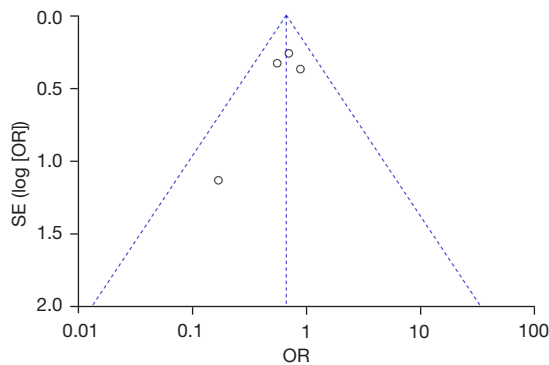The outcome indicators of postoperative pulmonary

Figure 4 Funnel chart of the postoperative complication rates between the rehabilitation group and control group.
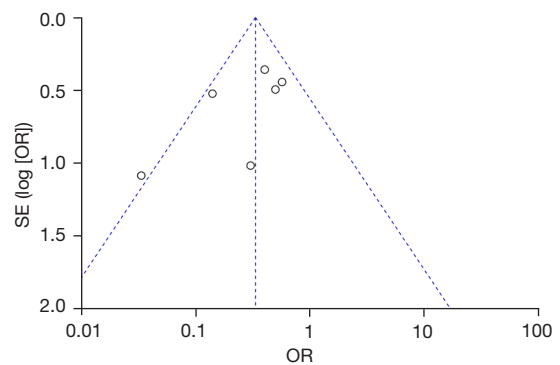

Figure 6 Funnel chart of the postoperative pulmonary complications in the rehabilitation group and control group.
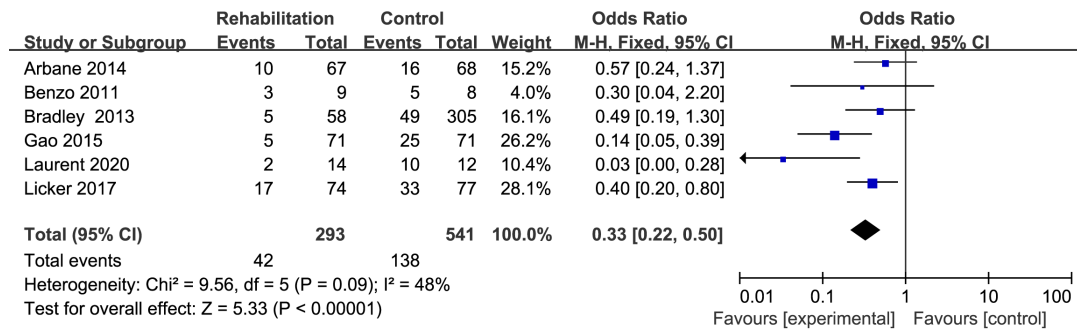

Figure 5 Forest chart of the postoperative pulmonary complications in the rehabilitation group and control group.

complications were examined in 6 studies (7-10,13,14), comprising 834 patients. The results of the heterogeneity test were as follows: χ^2=9.56, P=0.09, I^2=48%. Thus, the results indicated that there was heterogeneity among the 6 included studies, and the fixed-effects model was adopted, and the data were combined. The meta-analysis results indicated that the OR value of postoperative pulmonary complications between the lung rehabilitation and control groups was 0.33 (95% CI: 0.22–0.50), and the difference between the 2 groups was statistically significant (z=5.33; P<0.00001). Thus, the implementation of lung rehabilitation programs appeared to significantly reduce the incidence of postoperative pulmonary complications in lung cancer patients. The results are set out in *Figure 5*. Additionally, as the funnel chart shows, most of the points fell within the confidence interval, and the funnel type was inverted (see *Figure 6*). Egger's test P>0.05, there is no publication bias.

Postoperative mortality

The outcome indicators of postoperative mortality were

examined in 4 studies (8,11,13,14), comprising 582 patients. The results of the heterogeneity test were as follows: χ^2=3.24, P=0.36, I^2=8%. Thus, there appeared to be no heterogeneity among the 4 included studies, and the fixed-effects model was adopted, and the data were combined. The meta-analysis results illustrated that the OR value of postoperative pulmonary complications between the lung rehabilitation and control groups was 0.77 (95% CI: 0.26–2.30), and there was no significant difference between the 2 groups (Z=0.46, P=0.65). Thus, compared to the control group, implementing a rehabilitation program for lung cancer patients who underwent resections did not change the postoperative mortality. The results are set out in *Figure 7*. Additionally, as the funnel chart shows, most of the points fell within the confidence interval, and the funnel type was inverted (see *Figure 8*). Egger's test P>0.05, there is no publication bias.

Discussion

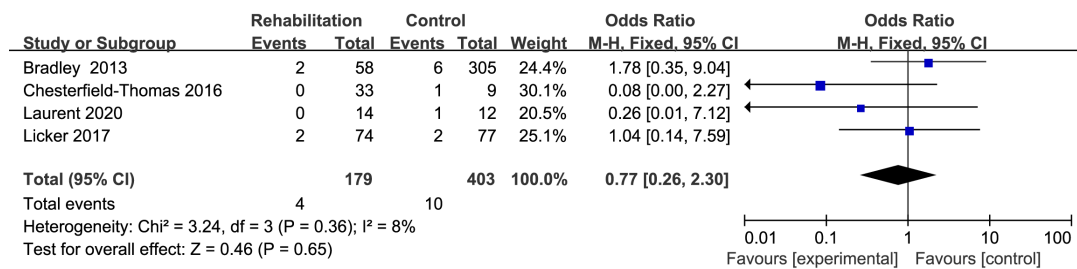Lung cancer is the leading cause of cancer-related death

Figure 7 Forest chart of postoperative mortality in the rehabilitation group and control group.
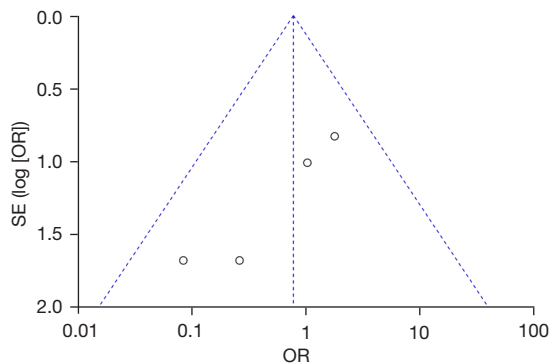

Figure 8 Funnel chart of postoperative mortality in the rehabilitation group and control group.

worldwide, is the 2nd most common cancer among men and women, and accounts for about 15% of all new cancer cases (16). Approximately 80% of all lung cancer cases are non-small cell lung cancer (17). Surgical resection is the first choice for patients with stage I–IIIa lung cancer. Lung cancer resection provides the highest survival potential for patients. However, patients often experience postoperative complications, pulmonary complications, cancer recurrence, and severe and even life-threatening risks. A previous study shown that the incidence of postoperative complications among lung cancer patients is about 38–58%, of which 15–25% are directly related to respiratory health, such as pulmonary infection and pneumonia, which lead to prolonged hospitalization, impaired functional performance, reductions in patients' quality of life, and increased cancer recurrence, readmission, and mortality rates (18).

As a therapeutic intervention, pulmonary rehabilitation exercise training is usually used in chronic obstructive pulmonary disease and is also recommended for other chronic lung diseases, interstitial lung diseases, cystic fibrosis, and lung cancer. Pulmonary rehabilitation measures include exercise training, drug treatment, smoking cessation, nutritional support, behaviour change, and health education. Research has shown that (7) rehabilitation exercise training positively affects muscle strength, exercise endurance, wellbeing, and health status. Various surgical specialties, including cardiothoracic surgery, have also advocated for the use of lung rehabilitation exercise training in recent years. Several studies have reported on the clinical value of lung rehabilitation exercise training in lung cancer resection (10,13,14). For patients who must undergo lung surgery, a lung rehabilitation exercise training plan can be implemented before and/or after surgery.

Many systematic reviews and meta-analyses have been conducted to examine the effects of lung rehabilitation exercise training on postoperative lung cancer patients, including its effects on hospital stay, functional status, health-related quality of life, postoperative complications, and mortality. Notably, Gravier *et al.* (19) reviewed the effects of pre-pneumonectomy exercise training on patients with non-small cell lung cancer, and found that exercise training improved patients' exercise ability, lung function, quality of life, and depression levels. Mao *et al.* (1) reviewed prospective and retrospective studies on the effects of lung rehabilitation exercise training on complications and mortality after lung cancer resection before 2020. Additionally, Pu *et al.* (18) reviewed the effects of preoperative respiratory movement on the postoperative outcomes of lung cancer patients undergoing radical pneumonectomy. Xu *et al.* (20) examined the effects of preoperative and postoperative rehabilitation exercise training programs on postoperative pulmonary complications and hospital stay among lung cancer patients. The present study sought to update these findings using the data of the latest prospective studies to analyze the efficacy of lung rehabilitation exercise training programs on the postoperative complication and mortality rates of lung cancer patients.

A total of 1,338 patients were included in 9 prospective studies, of which 254/890 patients reported postoperative complications. A total of 180/834 patients reported postoperative pulmonary complications, and 14/582 patients reported mortality. The results demonstrated that implementing pulmonary rehabilitation exercise training programs reduced the risk of postoperative complications and pulmonary complications by 67%. However, in terms of mortality, there was no significant difference between the pulmonary rehabilitation group and the control group.

This study had some limitations. The efficacy of pulmonary rehabilitation exercise training on patients after the operation was multifaceted; for example, it affected the length of hospitalization, and patients' functional status and health-related quality of life. This study only sought to analyze the incidence of complications, but other aspects also deserve attention. Future research should seek to analyze other key postoperative factors based on more clinical trial data.

In sum, the implementation of pulmonary rehabilitation exercise training was found to significantly reduce the incidence of postoperative complications and pulmonary complications in lung cancer patients. However, it had no significant effect on mortality. Our findings suggest that surgical experts should formulate preoperative or postoperative pulmonary rehabilitation exercise training plans for patients according to their actual situations to improve their postoperative clinical efficacy.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the PRISMA and MOOSE reporting checklists. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-978/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-978/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved.

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