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Pulmonary Rehabilitation Exercises Effectively Improve Chronic Cough After Surgery for Non-small Cell Lung Cancer

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Abstract

Introduction: Cough is a major complication after lung cancer surgery, potentially impacting lung function and quality of life. However, effective treatments for managing long-term persistent postoperative cough remain elusive. In this study, we investigated the potential of a pulmonary rehabilitation training program to effectively address this issue.

Methods: Between January 2019 and December 2022, a retrospective review was conducted on patients with non-small cell lung cancer (NSCLC) who underwent lobectomy and lymph node dissection via video-assisted thoracoscopic surgery (VATS) at Daping hospital. Based on their postoperative rehabilitation methods, the patients were categorized into 2 groups: the traditional rehabilitation group and the pulmonary rehabilitation group. All patients underwent assessment using the Leicester cough questionnaire (LCQ) on the third postoperative day. Additionally, at the 6-month follow-up, patients' LCQ scores and lung function were re-evaluated to assess the long-term effects of the pulmonary rehabilitation training programs.

Results: Among the 276 patients meeting the inclusion criteria, 195 (70.7%) were in the traditional rehabilitation group, while 81 (29.3%) participated in the pulmonary rehabilitation group. The pulmonary rehabilitation group showed a significantly lower incidence of cough on the third postoperative day (16.0% vs 29.7%, $P = .018$) and higher LCQ scores in the somatic dimension ($5.09 \pm .81$ vs 4.15 ± 1.22, $P = .007$) as well as in the total score (16.44 ± 2.86 vs 15.11 ± 2.51, $P = .018$, whereas there were no significant differences in psychiatric and sociological dimensions. At the 6-month follow-up, the pulmonary rehabilitation group continued to have a lower cough incidence (3.7% vs 12.8%, $P = .022$) and higher LCQ scores across all dimensions: somatic ($6.19 \pm .11$ vs 5.75 ± 1.20, $P = .035$), mental (6.37 ± 1.19 vs 5.85 ± 1.22, $P = .002$), sociological (6.76 ± 1.22 vs 5.62 ± 1.08, $P < .001$), and total (18.22 ± 2.37 vs 16.21 ± 2.53, $P < .001$). Additionally, lung function parameters including FVC, FVC%, FEV1, FEV1%, MVV, MVV%, DLCO SB, and DLCO% were all significantly higher in the pulmonary rehabilitation group compared to the traditional group.

Conclusion: Pulmonary rehabilitation exercises significantly reduced the incidence of postoperative cough and improved cough-related quality of life in patients undergoing lobectomy, with sustained benefits observed at the 6-month follow-up.

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Additionally, these exercises demonstrated superior lung function outcomes compared to traditional rehabilitation methods.

Plain Language Summary

Pulmonary rehabilitation exercises significantly reduced the incidence of postoperative cough and improved cough-related quality of life in patients undergoing lobectomy, with sustained benefits observed at the 6-month follow-up. Additionally, these exercises demonstrated superior lung function outcomes compared to traditional rehabilitation methods.

Keywords

postoperative cough, pulmonary rehabilitation, video-assisted thoracoscopic surgery, non-small cell lung cancer, pulmonary function

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Introduction

Postoperative cough is one of the most common complications after lung cancer surgery.[1] Approximately 25%-50% of patients presented with short-term postoperative cough.[2,3] Short-term cough after lung cancer surgery was more often associated with surgery and anesthesia, such as injury to the vagus nerve or its branches,[4] lymph node dissection,[5] anesthetic drugs,[6] and tracheal intubation.[7] Unlike short-term postoperative cough, some patients may suffer from a persistent chronic cough that persisted beyond the initial recovery period from surgery.[8] This chronic cough can significantly impact lung function and the overall quality of life for lung cancer patients.[1,9,10] Unfortunately, there is currently no effective treatment for managing this long-term, persistent postoperative cough.

Pulmonary rehabilitation is defined as an "evidence-based, multidisciplinary and comprehensive intervention for patients with chronic respiratory disease who are symptomatic and often have decreased daily life activities".[11] This approach is essential for enhancing pulmonary function and quality of life for patients with chronic pulmonary diseases such as interstitial lung disease,[12,13] chronic obstructive pulmonary disease, and sarcoidosis.[14] The therapeutic concept of pulmonary rehabilitation can also benefit non-small cell lung cancer (NSCLC) patients in postoperative care, potentially reducing persistent cough and improving quality of life.[15] However, the exact efficacy of pulmonary rehabilitation in mitigating postoperative cough in NSCLC patients remains to be elucidated.

In our study, we investigated the effects of pulmonary rehabilitation on postoperative cough and lung function in patients who underwent lobectomy for NSCLC. Our results have the potential to contribute to clinical progress in patient management and care.

Methods

Ethical and Guideline Statements

This study was reviewed and approved by the institutional review board of the Daping Hospital, Army Medical University (No. 2023-217). Written informed consent was obtained from all patients participating in this study. This research has followed the STROBE guideline.[16]

Patients

From January 2019 to December 2022, a total of 394 NSCLC patients who underwent video-assisted thoracoscopic surgery (VATS) lobectomy and systematic lymph node dissection in a single medical group of Daping Hospital were initially reviewed. Of these patients, the following were excluded: (I) age <18 or >70 years; (II) have cough symptoms within 2 weeks before surgery; (III) with neoadjuvant therapy; (IV) intraoperative conversion to thoracotomy due to various reasons; (V) pTNM stage IV; (VI) patients who refused to be followed up (Figure 1).

Data Collection and Definition

Data regarding age, gender, BMI, smoking status, FEV1, FEV1%, tumor location, operation time, blood loss, type of incision, histological type, pTNM stage, post-operative cough, overall complications (including pleural effusion, postoperative air leak over 5 days, pulmonary infection, pulmonary embolism, chylothorax, and arrhythmia), duration of drainage and hospitalization. The histologic classification was determined in accordance with the 2011 guidelines provided by the international association for the study of lung cancer/ American thoracic society, and European respiratory society.[17] The pTNM staging system was assessed based on the eighth edition of the American joint committee on cancer's classification criteria for lung cancer.[18]

Assessment of Cough

All patients were required to complete the Leicester cough questionnaire (LCQ) on the third post-operative day and 6 months later.[19] Although the LCQ is typically utilized for assessing chronic cough, recent studies have demonstrated its

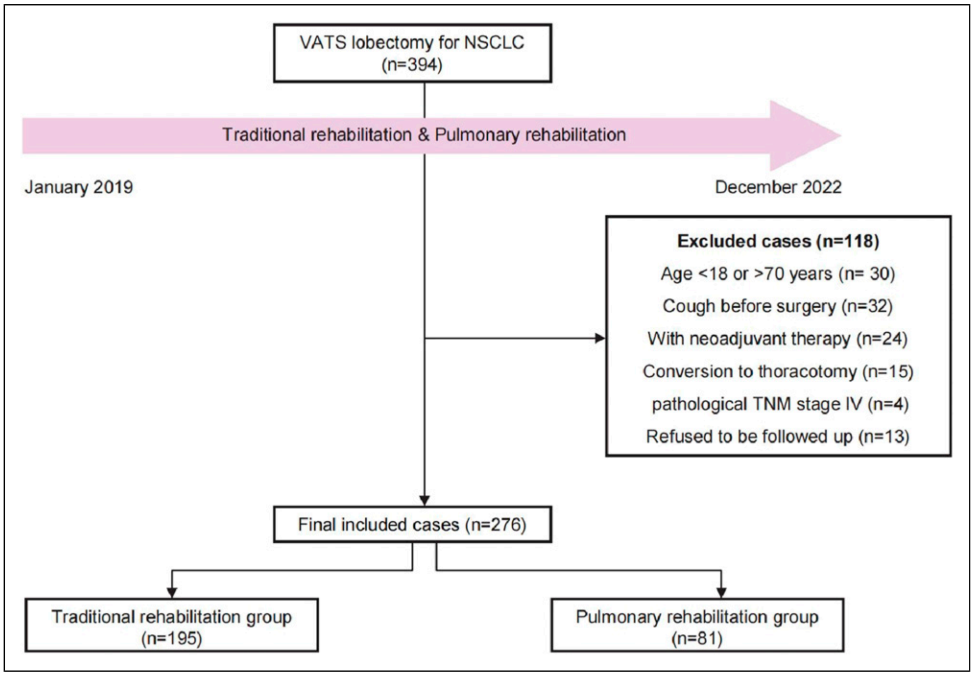

Figure 1. Patient selection process. VATS, video-assisted thoracoscopic surgery. *Abbreviation*: NSCLC, Non-small cell lung cancer.

high validity and responsiveness in evaluating acute and postoperative cough as well.[20-22] The questionnaire comprised 19 items, each representing an adverse event resulting from coughing. Responses were scored using a 7-point Likert scale. These items were categorized into 3 domains: psychological (e.g., the impact of cough on embarrassment/anxiety), physical (e.g., cough-related chest and stomach pain), and social (e.g., the effect of cough on work, daily activities, and entertainment). Scores were calculated for each domain and totaled, with domain scores ranging from 1 to 7 and the overall score from 3 to 21. Higher scores indicated better health outcomes.[23] This comprehensive approach allowed for a detailed assessment of the impact of cough on patients' overall well-being.

Pulmonary Rehabilitation

In contrast to traditional rehabilitation, pulmonary rehabilitation involved specialized assessments and interventions conducted by a physical therapist. Based on established guidelines and clinical practices, patients in the rehabilitation group underwent a standardized postoperative pulmonary rehabilitation program.[5] This comprehensive program spanned both the hospital stays and the post-discharge period, encompassing various exercises designed to improve respiratory function (Table 1). These pulmonary rehabilitation exercises mainly included the following items: (1). Breathing apparatus: Adopted three-ball breathing apparatus for respiratory function exercise.[24] First, patients get comfortable. Afterwards, patients position the three-ball breathing device in the same plane as their eyes and take slow, controlled breaths while holding the tube in their mouths. The balls will rise in response to the patients' deep inhalations. Then they breathe out.; (2). Pursed lips breathing: Patients inhale through the nose for 2s, followed by holding the breath for 2s, then exhale slowly through pursed lips for 10-20s.; (3). Deep breathing: Deep breathing is similar to pursed lips breathing. Inhaled deeply to maximum, followed by holding the breath for 2s, then exhaled slowly for 10-20s.; (4). Coughing: During hospitalization, the patients are asked to cough actively or with assistance to expel sputum and promote pulmonary expansion. After discharge, patients are required to practice active coughing as they are already competent.; (5). Expelling sputum: Manual back patting, and postural vibratory expectoration to expel sputum.; (6). Stretching exercise: Stretching exercise include head, neck, shoulder, limb, and chest expansion exercises. It could increase the strength of the muscles, including the respiratory muscles.; (7). Aerobic exercise: According to the patient's physical recovery, moderate to high intensity aerobic exercise, such as walking or jogging, should be taken.[25]

Postoperative Management

All patients were sent back to the thoracic surgery unit after surgery. Trained nurses diligently monitored and documented their postoperative vital signs, 24-hour drainage, urine output, fluid intake, and other relevant information. Patients were provided with proper guidance to cough and expectorate efficiently, while also being encouraged to get out of bed and move around as early as possible after their operation. Additionally, on the first day following the operation, patients

Table 1. Items of Pulmonary Rehabilitation Exercise.

Hospitalisation		At Home	
Name of Exercise	Description	Name of Exercise	Description
Breathing apparatus	Adopted three-ball breathing apparatus for respiratory function exercise. 3min * 3/day	Breathing apparatus	Adopted three-ball breathing apparatus for respiratory function exercise. 5min * 3/day
Pursed lips breathing	Inhaled through the nose for 2s, followed by holding the breath for 2s, then exhaled slowly through pursed lips for 10-20s. 5-10min * 3/day.	Pursed lips breathing or deep breathing	Inhaled deeply to maximum, followed by holding the breath for 2s, then exhaled slowly for 10-20s. 10-15min * 3/day.
Coughing	Active or assisted coughing. 2min * 3/day	Coughing	Active coughing. 2min * 3/day
Expelling sputum	Manual back patting, and postural vibratory expectoration. 5min * 3/day	Stretching exercise	Including head, neck, shoulder, limb, and chest expansion exercises. 5-10min * 3/day
Stretching exercise	Including head, neck, shoulder, limb, and chest expansion exercises 3-5min * 3/day	Aerobic exercise	According to the patient's physical recovery, moderate to high intensity aerobic exercise, such as walking or jogging. 10-30min * 3/day

underwent a chest radiograph, as well as blood and electrolyte tests. Those patients who had less than 200 mL of chest drainage over a 24-hour period, revealed no pneumothorax on their chest radiograph, and had no air leakage from their chest tube, were permitted to have their chest tube removed.

Pulmonary Function Tests

Pulmonary function tests were performed at the 6-month postoperative follow-up. Indicators of lung function are collected including forced vital capacity (FVC), FVC%, forced expiratory volume in one second (FEV1), FEV1%, maximum ventilatory volume (MVV), MVV%, the single breath diffusing capacity of the lung for CO (DLCO SB), and DLCO%.

Surgical Techniques

The patient was placed in the healthy lateral position and underwent double-lumen intubation and the healthy side one-lung ventilation under general anesthesia during surgery. The surgery was performed by single or two-port thoracoscopic approach. All patients underwent a 3- to 5-centimeter aperture at the fourth or fifth intercostal space in the anterior axillary line. The observation hole is located in the mid-axillary line at the seventh intercostal space. Lobectomy and lymph node dissection were performed. Lymph nodes were grouped according to the eighth edition lung cancer stage classification.[26]

Statistical Analysis

Data were analyzed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < .05$ for all tests. Categorical variables were presented as frequencies and percentages (%), and comparisons between the 2 treatment groups were made using either the standard chi-square test or fisher's exact test. For continuous variables, those following a normal distribution were summarized as mean ± standard deviation and compared between groups using the independent samples t-test or corrected t-test. On the other hand, continuous variables that did not adhere to a normal distribution were described using the median, 25th percentile (Q1), and 75th percentile (Q3). Comparisons for these non-normally distributed variables were conducted using the Wilcoxon rank-sum test.

Results

Baseline Characteristics

A total of 276 patients were enrolled in this study, 195 (about 71%) were assigned to the traditional rehabilitation group and 81 (about 29%) to the pulmonary rehabilitation group. Patient baseline characteristics are presented in Table 2. The 2 groups were well equivalent for age, gender, BMI, smoking status, FEV1, FEV1 rate, tumor location, type of incision, histological type and pTNM stage.

Perioperative Outcomes

Perioperative outcomes for both the traditional rehabilitation group and the pulmonary rehabilitation group were summarized in Table 3. R0 resection was successfully achieved in all cases, with no postoperative deaths reported within 30 days. When comparing the 2 groups, no significant differences were observed in operative time, blood loss, duration of thoracic drainage, incidence of overall postoperative complications (in pulmonary rehabilitation group, there were 3 cases of pleural

Table 2. Baseline Characteristics of Patients.

Characteristics	Pulmonary Rehabilitation (n = 81)	Traditional Group (n = 195)	Statistical Value	*P*-Value
Age(years)	57.48 ± 8.33	59.31 ± 9.49	t = 1.326	.186
Gender (n [%])				
Male	63 (77.8%)	132 (67.7%)	χ^2 = 2.807	.094
Female	18 (22.2%)	63 (32.3%)		
BMI (kg/m^2)	23.06 ± 2.85	22.52 ± 2.94	t = 1.393	.165
Smoking status				
Absent	32 (39.5%)	87 (44.6%)	χ^2 = .609	.435
Present	49 (60.5%)	108 (55.4%)		
FEV1 (L)	2.05 ± .44	2.03 ± .35	t = .245	.807
FEV1 %	86.36 ± 14.92	85.90 ± 16.16	t = .222	.824
Tumor location				
Right upper lobe	25 (30.9%)	65 (33.3%)	χ^2 = 1.297	.862
Right middle lobe	2 (2.5%)	9 (4.6%)		
Right lower lobe	20 (24.7%)	41 (21.0%)		
Left upper lobe	19 (23.5%)	48 (24.6%)		
Left lower lobe	15 (18.5%)	32 (16.4%)		
Type of incision				
Single-port VATS	66 (81.5%)	139 (71.3%)	χ^2 = 3.116	.078
Two-port VATS	15 (18.5%)	56 (28.7%)		
Histological type				
Adenocarcinoma	69 (85.2%)	163 (83.6%)	χ^2 = .109	.742
squamous carcinoma	12 (14.8%)	32 (16.4%)		
pTNM stage				
I	48 (59.3%)	129 (66.1%)	χ^2 = 3.471	.176
II	17 (21.0%)	44 (22.6%)		
III	16 (19.8%)	22 (11.3%)		

Table 3. Perioperative Outcomes.

Results	Pulmonary Rehabilitation (n = 81)	Traditional Group (n = 195)	Statistical Value	*P*-Value
Operative duration (min)	140 (85, 165)	125 (80, 155)	Z = 1.666	.096
Blood loss (mL)	120 (70, 200)	110 (60, 150)	Z = 1.546	.122
Post-operative cough	13 (16.0%)	58 (29.7%)	Z = 5.617	.018
Overall complications	8 (9.9%)	24 (12.3%)	χ^2 = .330	.566
Drainage (days)	3 (2, 5)	3 (2, 6)	Z = .285	.776
Hospital stays (days)	7 (5, 9)	7 (4, 10)	Z = .139	.889

effusion, 3 cases of air leak, 1 case of arrhythmia, and 1 case of pulmonary embolism in the traditional rehabilitation group, there were 6 cases of pleural effusion, 9 cases of air leak, 5 cases of lung infection, 3 cases of pulmonary embolism, and 1 case of chylothorax), or length of hospital stay. However, the pulmonary rehabilitation group exhibited a significantly lower incidence of postoperative cough. This observation underscored the potential benefits of pulmonary rehabilitation in mitigating postoperative cough and enhancing patient recovery.

Postoperative Lung Function and Cough Analysis

In comparison between the pulmonary rehabilitation group and the conventional group, we observed a significantly lower incidence of cough at 3 days postoperatively in the pulmonary rehabilitation group (16.0% vs 29.7%, $P = .018$). Pulmonary rehabilitation group also exhibited higher LCQ scores, particularly in the physical dimension (5.09 ± .81 vs 4.15 ± 1.22, $P = .007$) and the total score (16.44 ± 2.86 vs 15.11 ± 2.51, $P = .018$). No significant differences were noted in the psychiatric and sociological dimensions (Figure 2). At the 6-month postoperative follow-up, the pulmonary rehabilitation group continued to show a lower incidence of cough (3.7% vs 12.8%, $P = .022$) and significantly higher LCQ scores across all dimensions, including the physical (6.19 ± .11 vs 5.75 ± 1.20, $P = .035$), mental (6.37 ± 1.19 vs 5.85 ± 1.22, $P = .002$), and social (6.76 ± 1.22 vs 5.62 ± 1.08, $P < .001$), resulting in a higher total score (18.22 ± 2.37 vs 16.21 ± 2.53, $P < .001$)

(Figure 3). Furthermore, pulmonary function tests at the 6-month follow-up revealed significant improvements in the pulmonary rehabilitation group compared to the conventional group. Specifically, FVC (2.63 ± .71 vs 2.17 ± .64, $P = .003$), FVC% (80.32 ± 17.51 vs 72.39 ± 11.32, $P = .008$), FEV1 (1.87 ± .61 vs 1.54 ± .39, $P = .009$), FEV1% (76.63 ± 15.30 vs 71.89 ± 13.30, $P = .024$), MVV (72.16 ± 15.59 vs 67.19 ± 13.56, $P = .024$), MVV% (78.59 ± 19.51 vs 72.50 ± 20.12, $P = .028$), DLCO SB (6.87 ± 2.12 vs 5.73 ± 1.41, $P = .037$), and DLCO% (85.31 ± 21.41 vs 71.24 ± 14.97, $P = .027$) were all significantly higher in the pulmonary rehabilitation group (Figure 4). These findings suggested that pulmonary rehabilitation effectively reduced postoperative cough and enhanced pulmonary function following lobectomy, highlighting its potential benefits in improving patient outcomes.

Discussion

Our study found that pulmonary rehabilitation exercises were effective in reducing cough incidence after surgery for NSCLC patients, both in the short-term and long-term postoperatively. Furthermore, the pulmonary rehabilitation exercises did not lead to an increase in postoperative complications, drainage time, or length of hospital stay. Additionally, pulmonary rehabilitation training can improve the lung function of patients.

After lobectomy and lymph node dissection surgery for NSCLC patients, the incidence of cough in the early postoperative period was 29.7% and 16.0% in the traditional and pulmonary rehabilitation groups, respectively. Furthermore, after 6 months of recovery, the cough symptoms with incidence rates of 12.8% in traditional group and 3.7% in

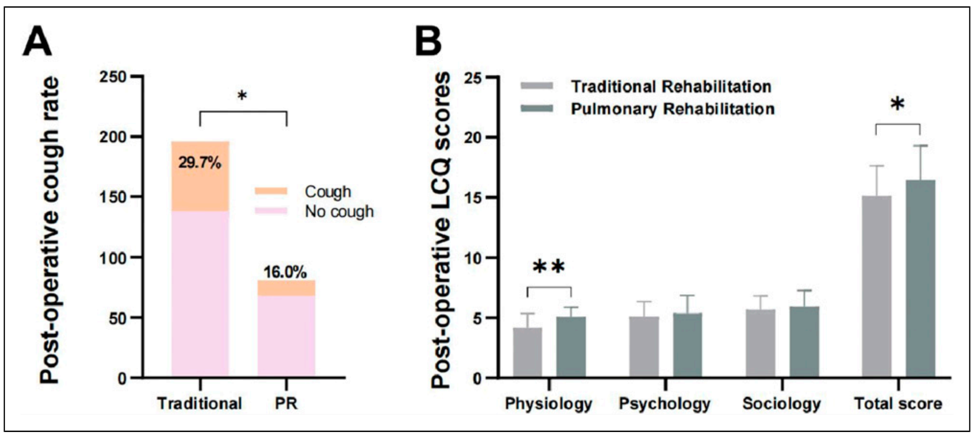

Figure 2. Short-term comparison of patients on postoperative cough and postoperative LCQ scores. (A) postoperative cough rate between traditional rehabilitation group and pulmonary rehabilitation group. (B) postoperative LCQ scores between traditional rehabilitation group and pulmonary rehabilitation group. *Abbreviation*: LCQ, Leicester Cough Questionnaire.

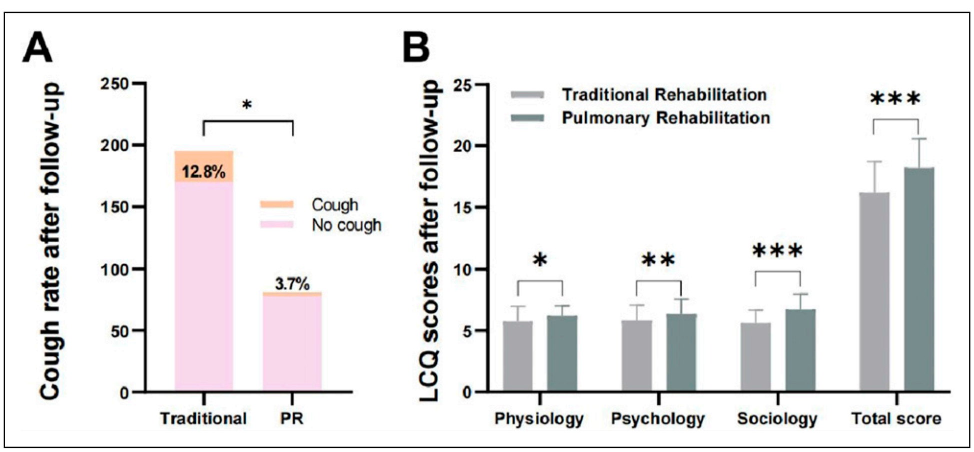

Figure 3. Comparison of postoperative cough and LCQ scores in patients at 6-month follow-up. (A) postoperative cough rate between traditional rehabilitation group and pulmonary rehabilitation group. (B) postoperative LCQ scores between traditional rehabilitation group and pulmonary rehabilitation group. *Abbreviation*: LCQ, Leicester Cough Questionnaire.

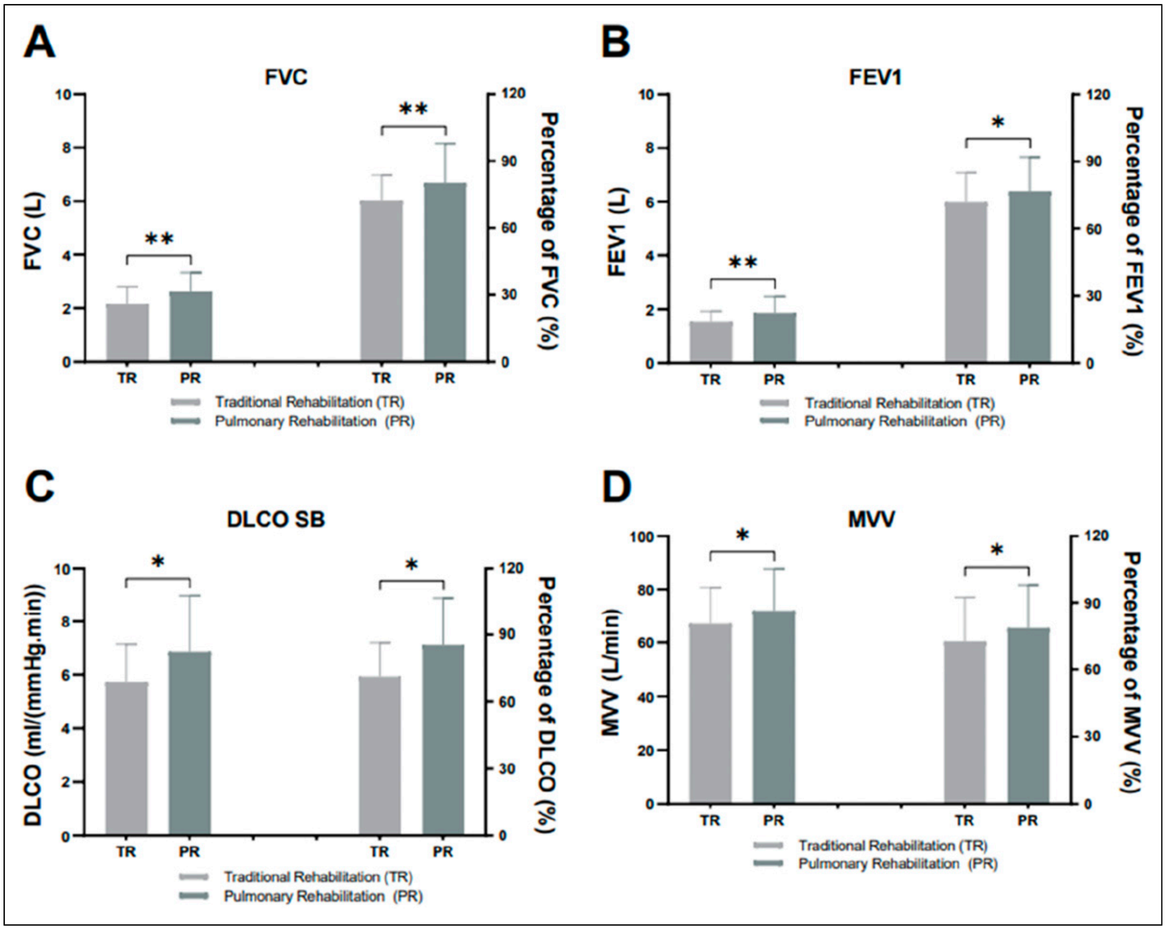

Figure 4. Comparison of postoperative pulmonary function in patients with traditional rehabilitation group and pulmonary rehabilitation group. (A) Comparison of FVC and FVC% of projected value. (B) Comparison of FEV1 and FEV1%. (C) Comparison of DLCO SB and DLCO %. (D) Comparison of MVV and MVV%. FVC, forced vital capacity. FEV1, forced expiratory volume in the first second. DLCO SB, the single breath diffusing capacity of the lungs for carbon monoxide. *Abbreviation*: MVV, maximal voluntary ventilation. TR, traditional rehabilitation. PR, pulmonary rehabilitation.

pulmonary rehabilitation group. This result was not entirely consistent with some other studies. The early study of Sawabata and colleagues[27] showed that the incidence of cough within 1 year after pulmonary surgery was 50%, and there were 18% of patients with postoperative cough lasting more than 1 year. The probable reason for this is that the study was conducted almost 20 years ago, during which time the type of disease and surgical techniques have changed to a great extent.[28] Previously, it was dominated by more invasive open-chest surgery, which included pyothorax, lung destruction, thoracic adhesions, locally advanced lung cancer, large tumor diameters, and so on. All of these may lead to a greater probability of postoperative cough.[29] Meanwhile, thoracic surgery was becoming less traumatic for the patient and less likely to trigger an inflammatory response in the postoperative period.

Treatments traditionally used for chronic coughs caused by respiratory diseases can also be beneficial for post-VATS coughs. These included physiotherapy and speech and language therapy.[30] A study by Miyamoto and colleagues found that C-fiber activation contributes to persistent coughing after lobectomy.[31] Oral suplatast tosilate, corticosteroids, and β-agonists can alleviate this type of cough, which may not respond to opioid cough suppressants like codeine.[32] Furthermore, applying betamethasone gel to the tracheal tube can reduce local inflammation due to intubation.[33] In our study, the mainstay of treatment was somatic exercise and cough management education. We utilized breathing techniques, including pursed lips breathing, deep breathing, coughing, and sputum expulsion, along with stretching and aerobic exercises. Pulmonary rehabilitation exercises significantly improved patients' postoperative cough status, aligning with previous research.[34] However, our approach differed in several ways. Unlike previous studies that relied on long-term cough medications like pregabalin and codeine, we emphasized somatic and psychological exercises. Additionally, we incorporated lung function exercises to enhance lung function after lobectomy, which was crucial for improving the long-term quality of life for patients.[35] Overall, our treatment plan effectively improved postoperative cough status and reduced complications. The emphasis on somatic exercises and cough management education proved beneficial for patient outcomes.

Pulmonary rehabilitation exercises offered multifaceted benefits for improving cough symptoms and lung function. Firstly, this comprehensive program educated patients and their families through medical professionals, allaying fears about lung cancer and minor post-operative issues like coughing. This education fostered confidence in the recovery process. Secondly, techniques like deep breathing, pursed-lip breathing, and active coughing exercises can reduce airway sensitivity. Thirdly, somatic exercises aided in post-operative drainage and encouraged the expansion of the remaining lung tissue, thereby increasing effective ventilation volume. Lastly, these exercises enhanced the strength and endurance of respiratory muscle groups. Our study underscored the superiority of pulmonary rehabilitation as a long-term strategy for managing post-operative cough symptoms. Therefore, we strongly advised patients to persist with pulmonary rehabilitation exercises over an extended period for optimal results.

There were certain limitations in our study. Firstly, the inclusion of patients during the COVID-19 epidemic period introduced a potential confounding factor. Specifically, the assessment of postoperative cough may have been complicated by the presence of neo-coronary pneumonia, which could have biased the results. Secondly, while pulmonary rehabilitation was an important aspect of cough management, our exclusive focused on this approach may have been too narrow. Ideally, the management of cough should be individualized and multifaceted, taking into account various patient factors and potential therapeutic strategies. By recognizing these limitations, future studies can aim to address them through more comprehensive designs and analysis.

Conclusion

Pulmonary rehabilitation exercises can significantly decrease the incidence and severity of postoperative cough, both in the short-term and long-term, in NSCLC patients with lobectomy. Furthermore, pulmonary rehabilitation can also significantly enhance postoperative lung function, leading to potential improvements in the quality of life for those patients.

Abbreviations and Acronyms:

NSCLC	Non-small cell lung cancer
VATS	Video-assisted thoracoscopic surgery
LCQ	Leicester cough questionnaire
BMI	Body mass index
FEV1	Forced expiratory volume in one second
pTNM	Pathological TNM
FVC	Forced vital capacity
MVV	Maximum ventilatory volume
DLCO SB	The single breath diffusing capacity of the lung for CO

Author Contributions

Conceptualization, N.L., F.D., L.Z. and K.Z.; Methodology, N.L. and F.D.; Software, N.L. and F.D.; Validation, N.L. and F.D.; Formal Analysis, X.W. and B.H.; Investigation, X.W. and B.H.; Resources, F.D. and X.W.; Data Curation, X.W. and B.H.; Writing – Original Draft Preparation, N.L. and F.D.; Writing – Review & Editing, N.L., L.Z. and K.Z.; Supervision, L.Z. and K.Z.; Funding Acquisition, K.Z and B.H.

Declaration of Conflicting Interests

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Ethical Statement

This study was reviewed and approved by the Institutional Review Board of the Daping Hospital, Army Medical University (No. 2023-217). Written informed consent was obtained from all patients at initial treatment.

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