### Original Article

# Pulmonary rehabilitation improves lung function and exercise tolerance in elderly non-surgical NSCLC patients

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Abstract: Objective: To evaluate the clinical efficacy and safety of pulmonary rehabilitation exercise training in improving lung function, exercise tolerance, cancer-related fatigue, and quality of life in elderly patients with non-surgical non-small cell lung cancer (NSCLC). Methods: A total of 186 elderly NSCLC patients who received non-surgical treatment at The First Affiliated Hospital of Chongqing Medical and Pharmaceutical College from April 2023 to October 2024 were retrospectively enrolled. Among them, 95 received routine treatment (control group), and 91 received pulmonary rehabilitation training in addition to routine treatment (rehabilitation group). The intervention lasted 8 weeks. Evaluation indicators included lung function, exercise tolerance, respiratory function, cancer-related fatigue, quality of life, negative emotions, and sleep quality. Adverse reactions were also recorded. Results: By week 4, the social and emotional function in the EORTC QLQ-C30 showed no significant improvement, but by week 8, the rehabilitation group exhibited significantly better outcomes than the control group. Moreover, the rehabilitation group demonstrated significantly greater improvements in lung function, exercise tolerance, respiratory symptoms, cancer-related fatigue, and psychological status than the control group at week 8 (*P*<0.05). In addition, the incidence of adverse reactions in the rehabilitation group was significantly lower (*P*<0.05). Conclusion: Pulmonary rehabilitation training can effectively improve lung function and exercise capacity in elderly non-surgical NSCLC patients, alleviate fatigue and anxiety, enhance quality of life, and is safe for clinical application.

Keywords: Pulmonary rehabilitation, non-small cell lung cancer, elderly patients, exercise tolerance

#### Introduction

In the context of an aging population, the incidence and mortality of lung cancer among the elderly have risen markedly in recent years [1]. According to surveys, lung cancer has consistently ranked among the leading malignancies in incidence and mortality among elderly populations in China. Especially among those aged ≥65, the average annual incidence exceeds 300 per 100,000, and the mortality rate approaches 240 per 100,000, which is significantly higher than in younger and middle-aged groups [2]. Owing to prevalent comorbidities, diminished lung function, and elevated perioperative risks, many elderly patients are not suitable candidates for curative lung resection. Consequently, treatment often centers on nonsurgical modalities such as chemotherapy and radiotherapy to manage disease progression

[3, 4]. However, although non-surgical treatments can help control tumor growth, they are frequently associated with further decline in pulmonary function, reduced exercise tolerance, and impaired quality of life, seriously compromising patients' independence and survival quality [5, 6]. In addition, studies have shown that pulmonary dysfunction in lung cancer patients is influenced not only by aging and underlying pulmonary diseases but also by the tumor's pathophysiological effects [7]. Direct invasion or compression of the airways, destruction of lung parenchyma, cancer-related inflammation, and cancer cachexia can all lead to restrictive or obstructive ventilatory impairment, resulting in significantly lower forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>4</sub>), and diffusion capacity compared with age-matched healthy individuals [4, 8].

These impairments often worsen during nonsurgical treatments such as chemotherapy and radiotherapy, further compromising quality of life and exercise tolerance [9]. Therefore, enhancing pulmonary function and exercise capacity while mitigating the physical burden of disease remains a critical challenge in the supportive care of elderly patients with lung cancer.

In recent years, pulmonary rehabilitation has become an increasingly well-established intervention for managing chronic respiratory disorders such as chronic obstructive pulmonary disease (COPD) and interstitial lung disease, and its application has gradually extended to patients with lung cancer [10, 11]. Evidence indicates that pulmonary rehabilitation can improve pulmonary ventilation, enhance exercise capacity, relieve fatigue and anxiety, and thus improve overall quality of life through respiratory muscle training, aerobic exercise, and behavioral interventions [12, 13]. For elderly patients ineligible for surgery, pulmonary rehabilitation is not only safe but may also improve treatment tolerance and reduce the risk of adverse events [14]. Importantly, the role of pulmonary rehabilitation differs between lung cancer patients and those with non-cancerous chronic lung diseases. In COPD and interstitial lung disease, pulmonary rehabilitation primarily mitigates chronic airway remodeling, facilitates secretion clearance, and strengthens respiratory muscle endurance, thereby slowing disease progression [15, 16]. In contrast, for lung cancer patients, pulmonary rehabilitation addresses exercise limitation caused by deconditioning and respiratory muscle weakness, enhances tolerance to anticancer treatments, and may indirectly improve therapeutic efficacy by enhancing systemic immune function [17, 18]. Therefore, developing individualized, standardized pulmonary rehabilitation protocols for elderly patients with non-surgical lung cancer holds considerable clinical value.

Based on this background, the present study focused on elderly patients with non-small cell lung cancer (NSCLC) who did not undergo surgery. Using a retrospective design, we investigated whether an 8-week pulmonary rehabilitation program could improve lung function, exercise capacity, fatigue, respiratory symp-

toms, psychological state, and quality of life. A total of 186 patients were included. We compared changes in both physical performance tests and questionnaire scores before and after the 8-week period between the rehabilitation and the control groups. This study aims to provide evidence-based support for the rehabilitation management in elderly non-surgical lung cancer patients, fill gaps in existing research, and offer data and practical guidance for developing standardized pulmonary rehabilitation strategies and elderly-adapted training programs.

#### Materials and methods

Study design

This retrospective study analyzed clinical data from 186 elderly patients with NSCLC who underwent non-surgical treatment at The First Affiliated Hospital of Chongqing Medical and pharmaceutical College between April 2023 and October 2024. Based on treatment type, 95 patients received standard therapy alone (control group), while 91 received pulmonary rehabilitation exercise training in addition to standard therapy (rehabilitation group) (Figure 1). This study was approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical and Pharmaceutical College.

Inclusion criteria: (1) age ≥65 years; (2) pathologically or cytologically confirmed NSCLC; (3) medically ineligible for surgery due to comorbidities, or refusal of surgical intervention after clinical evaluation; (4) good treatment compliance; (5) adequate cardiopulmonary reserve and musculoskeletal function to participate in rehabilitation exercise, as assessed by a physiotherapist; (6) complete medical record. Exclusion criteria: (1) diagnosis of dementia, severe depression, schizophrenia, or other psychiatric disorders interfering with compliance; (2) history of lobectomy or pneumonectomy; (3) severe cardiovascular or neurological disease; (4) recent acute respiratory infection or unstable pulmonary function; (5) severe visual or hearing impairment that could interfere with participation in exercise training or assessments; (6) concurrent enrollment in any other structured pulmonary or physical rehabilitation intervention.

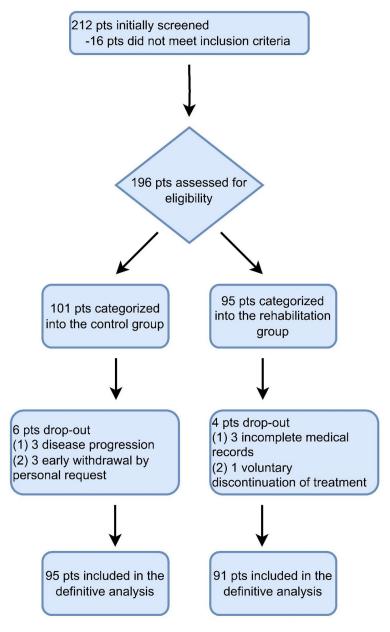


Figure 1. Patient inclusion process.

#### Intervention methods

Patients in the control group received routine exercise rehabilitation. They were educated on lung cancer and its treatment, advised on dietary practices during the treatment period, and instructed to walk for 30 min per session, 5 times a week, for a total duration of 8 weeks.

The rehabilitation group underwent a structured pulmonary rehabilitation program in addition to the aforementioned routine care. The intervention was developed based on the offi-

cial pulmonary rehabilitation guidelines jointly issued by the American Thoracic Society (ATS) and the European Respiratory Society (ERS), with modifications tailored to the physical status of oncology patients [19]. All training activities were demonstrated by qualified professionals, and instructional videos were provided during the first session to ensure accurate mastery of the exercises. The training program included the following components:

#### Comprehensive assessment

Each patient underwent a comprehensive assessment, including nutritional, neurological, circulatory, and respiratory evaluations. Particular attention was given to treatment-related adverse effects and therapeutic efficacy, and individualized rehabilitation plans were formulated accordingly.

## Pulmonary rehabilitation implementation

(1) Breathing exercises: Patients were instructed to sit upright on a chair or bed. Training consisted of nasal inhalation for approximately two seconds to achieve full lung expansion, followed by slow oral exhalation through pursed

lips, mimicking a whistling posture. Each session lasted 10 min and were performed three times daily.

(2) Airway clearance: A "deep breath-breath-hold-forceful cough" technique was introduced to patients to facilitate mucus clearance. Crossing the arms over the chest was encouraged to enhance expiratory force. When necessary, staff assisted with chest percussion or trained patients in using handheld vibrating devices. Sessions lasted 10 to 15 min and were repeated twice daily.

(3) Physical exercise: Upper limb exercises included weighted arm lifts using dumbbells or water bottles, lifting both arms overhead then slowly lowering them. Resistance training involved pulling elastic bands outward with both hands. Each exercise was performed for 20-30 repetitions per set, 2-3 sets per session, twice daily. Lower limb exercises included stair climbing or stationary cycling, 30 min per session, five times per week, adjusted based on patient tolerance.

#### Monitoring and follow-up

To promote adherence, patients were provided with a daily training log, completed by themselves or their caregivers, to record session duration and any symptoms experienced. Rehabilitation staff reviewed these records weekly. In addition, weekly follow-up calls were made to monitor progress, answer questions, and adjust the training regimen as needed. The entire program lasted for 8 weeks.

#### Observation indicators and evaluation criteria

In this study, all patients were systematically evaluated at baseline, as well as at the 4th and 8th weeks after intervention. Evaluations encompassed pulmonary function, exercise tolerance, respiratory function, quality of life, cancer-related fatigue, psychological status, sleep quality, and adverse events.

#### Primary outcomes

Pulmonary function: key respiratory parameters included FEV<sub>1</sub>, FVC, and peak expiratory flow (PEF).

Exercise tolerance: The 6-minute walk test (6MWT) [20] was used to evaluate functional exercise capacity. The test was conducted in a quiet 30 m hallway, with a trained therapist encouraging patients to walk as far as possible within 6 min. A practice trial was performed beforehand. If chest pain, dyspnea, or dizziness occurred, the test was stopped immediately and documented. Additionally, a cardiopulmonary exercise testing system (COSMED, Italy, model K4b2) was used to measure peak oxygen uptake (VO<sub>2</sub>max), maximum workload (MWL), and anaerobic threshold (AT).

Respiratory symptoms: Dyspnea was assessed using the modified Medical Research Council

(mMRC) scale [21], which grades severity from 0 to 4. Higher score indicates more severe symptoms. The St. George's Respiratory Questionnaire (SGRQ) was also administered to assess the impact of respiratory symptoms on quality of life, with higher scores reflecting greater impairment [22]. In addition, all adverse reactions occurred during the intervention period were recorded.

#### Secondary outcomes

Cancer-related fatigue: The Piper Fatigue Scale (PFS) was used to assess multidimensional fatigue, with higher scores indicating greater fatigue severity. This instrument has been validated in oncology populations [23].

Quality of life: The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) was used to evaluate multiple quality-of-life domains, including physical, emotional, cognitive, social, and role functioning. Each domain was scored from 0 to 100, with higher scores indicating better function and overall well-being [24].

Psychological and sleep status: The Hamilton Anxiety Scale (HAMA) and Hamilton Depression Scale (HAMD) were used to assess negative emotional states [25]. The Pittsburgh Sleep Quality Index (PSQI) was employed to evaluate sleep quality [26]. Higher total scores on these scales represent more severe emotional or sleep-related issues.

#### Statistical analysis

All statistical analyses were performed using SPSS version 22.0. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Variables with a normal distribution were expressed as mean ± standard deviation ( $\bar{x}\pm s$ ) and compared using the independent-samples t-test. Non-normally distributed variables were presented as median  $[M(Q_1, Q_3)]$ and analyzed using the Mann-Whitney U test. For repeated measurements across multiple time points, pairwise comparisons were conducted using LSD test or Nemenyi test. Categorical variables were presented as frequency and percentage [n (%)] and analyzed using the  $\chi^2$  test or Fisher's exact test. Graphs and charts were generated with GraphPad Prism

Table 1. Comparison of baseline characteristics between the two groups

	Control group (n=95)			
Sex			0.982	0.322
Male	59 (62.11)	50 (54.95)		
Female	36 (37.89)	41 (45.05)		
Age	70.39±5.92	70.48±5.26	0.114	0.909
Educational level				0.471*
Primary school	40 (42.11)	31 (34.07)		
Secondary school	33 (34.74)	41 (45.05)		
High school	18 (18.95)	17 (18.68)		
Graduation	4 (4.21)	2 (2.20)		
BMI (kg/m <sup>2</sup> )				0.424*
<18.5	17 (17.89)	24 (26.37)		
18.5-23.9	51 (53.68)	39 (42.86)		
24.0-27.9	23 (24.21)	23 (25.27)		
≥28	4 (4.21)	5 (5.49)		
Smoking status			3.473	0.176
Never	5 (5.26)	9 (9.89)		
Current	31 (32.63)	37 (40.66)		
Former	59 (62.11)	45 (49.45)		
Pathological type			0.074	0.786
Adenocarcinoma	52 (54.74)	48 (52.75)		
Squamous carcinoma	43 (45.26)	43 (47.25)		
Stage				0.467*
IIB	2 (2.11)	1 (1.10)		
IIIA	25 (26.32)	32 (35.16)		
IIIB	63 (66.32)	51 (56.04)		
IIIC	5 (5.26)	7 (7.69)		
Treatment			3.366	0.186
Radiotherapy alone	37 (38.95)	32 (35.16)		
Sequential chemoradiotherapy	25 (26.32)	35 (38.46)		
Concurrent chemoradiotherapy	33 (34.74)	24 (26.37)		
ALB (g/L)	35.29 (32.34, 38.73)	35.84 (34.10, 37.91)	0.886	0.376
PAB (mg/L)	146.95 (136.56, 155.24)	142.64 (135.51, 151.16)	1.429	0.153
Hb (g/L)	122.32 (116.80, 132.22)	125.78 (118.24, 131.19)	0.730	0.465

ALB: albumin, PAB: prealbumin, Hb: hemoglobin. \*: Fisher's exact tests.

software. Statistical significance was defined as a two-sided *P*<0.05.

#### Results

Comparison of baseline characteristics between the two groups

There were no significant differences between the control and rehabilitation groups regarding sex, age, educational level, BMI, smoking status, pathological type, clinical stage, treatment regimen, or nutritional status (P>0.05) (**Table 1**).

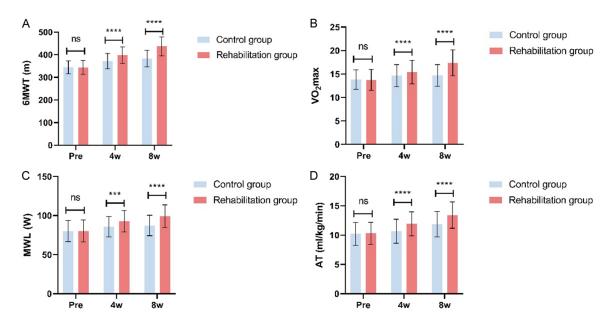
Comparison of pulmonary function outcomes between the two groups

At baseline, pulmonary function measures showed no significant differences between the two groups (P>0.05). However, by weeks 4 and 8 of the intervention, the rehabilitation group demonstrated significantly greater improvements in PEF, FVC, and FEV $_1$  compared to the

**Table 2.** Comparison of pulmonary function between the two groups  $[M(Q_1, Q_2)]$ 

			± 0		
		Control group (n=95)	Rehabilitation group (n=91)	Ζ	Р
PEF (L/min)	Baseline	323.61 (296.87, 355.35)	337.77 (317.31, 355.84)	1.951	0.051
	Week 4	357.29 (312.55, 398.73)*	365.45 (335.31, 425.67)*	2.203	0.028
	Week 8	376.81 (333.43, 418.55)*,#	396.58 (364.52, 438.27)*,#	2.432	0.015
FVC (L)	Baseline	2.64 (2.43, 2.89)	2.69 (2.31, 2.97)	0.360	0.718
	Week 4	2.83 (2.58, 3.08)*	3.05 (2.77, 3.29)*	3.445	<0.001
	Week 8	2.94 (2.42, 3.26)*	3.12 (2.82, 3.65)*,#	3.577	<0.001
FEV <sub>1</sub> (L)	Baseline	2.06 (1.86, 2.32)	2.00 (1.85, 2.29)	0.215	0.829
	Week 4	2.12 (1.96, 2.26)	2.32 (2.17, 2.48)*	5.190	<0.001
	Week 8	2.29 (2.11, 2.47)*,#	2.51 (2.28, 2.67)*,#	4.482	<0.001

PEF: peak expiratory flow, FVC: forced vital capacity, FEV $_1$ : forced expiratory volume in one second, M: Median,  $Q_1$ : 1st Quartile,  $Q_2$ : 3st Quartile. \*: P < 0.05 compared with baseline; #: P < 0.05 compared with week 4.



**Figure 2.** Comparative analysis of exercise tolerance indicators between the control and rehabilitation groups. A. 6MWT; B. VO<sub>2</sub>max; C. MWL; D. AT. 6MWT: 6-minute walk test, VO<sub>2</sub>max: peak oxygen uptake, MWL: maximum workload, AT: anaerobic threshold. ns: not significant; \*\*\*P<0.001; \*\*\*\*P<0.0001.

control group (*P*<0.05). These findings suggest that pulmonary rehabilitation training effectively enhances respiratory function in elderly patients with non-surgical NSCLC (**Table 2**).

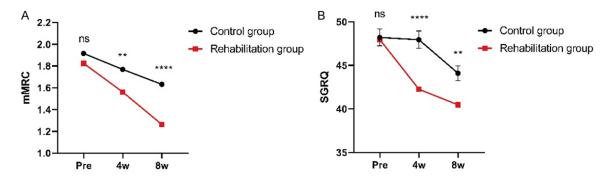
Comparison of exercise tolerance between the two groups

As shown in **Figure 2A**, the rehabilitation group achieved significantly longer walking distances in the 6MWT at both 4 and 8 weeks, indicating marked improvements in functional endurance. As shown in **Figure 2B**, VO<sub>2</sub>max was markedly higher in the rehabilitation group at both time points, indicating enhanced cardio-

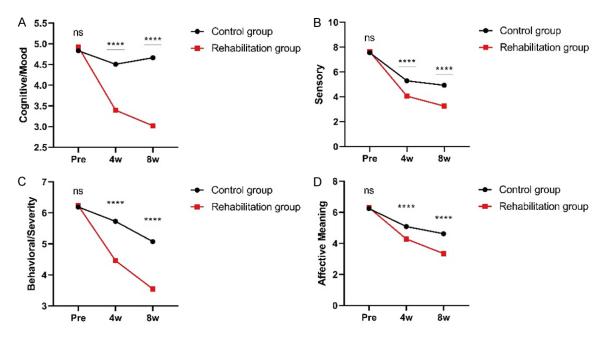
pulmonary fitness. Figure 2C shows a notable increase in MWL in the rehabilitation group, suggesting improved physical performance and exercise tolerance. Figure 2D shows that the rehabilitation training improved aerobic metabolic efficiency and delayed the onset of anaerobic threshold.

Comparison of respiratory function between the two groups

At baseline, there were no significant differences in respiratory function scores between the two groups. Following the intervention, patients in the rehabilitation group demonstrated significant differences in the rehabilitation group demonstrated significant differences.



**Figure 3.** Comparison of respiratory function between the two groups. A. mMRC; B. SGRQ. mMRC: modified Medical Research Council, SGRQ: St. George's Respiratory Questionnaire. ns: not significant; \*\*\*P<0.01; \*\*\*\*P<0.0001.



**Figure 4.** Comparison of cancer-related fatigue scores between the control and rehabilitation groups. A. Cognitive/mood; B. Sensory; C. Behavioral/severity; D. Affective meaning. ns: not significant; \*\*\*\*P<0.0001.

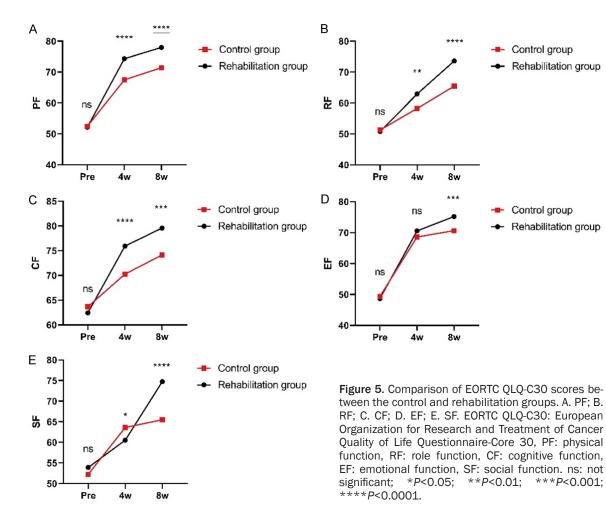
nificantly lower scores on both the mMRC dyspnea scale and the SGRQ, compared to the control group. These findings suggest that pulmonary rehabilitation effectively alleviated dyspnea and improved overall respiratory function (Figure 3).

Comparison of cancer-related fatigue scores between the two groups

As shown in **Figure 4**, scores across all four dimensions of cancer-related fatigue were significantly reduced in the rehabilitation group at both weeks 4 and 8, and were obviously better than the control group.

Comparison of EORTC QLQ-C30 scores between the two groups

After intervention, the rehabilitation group showed significant improvement across all functional domains of the EORTC QLQ-C30 compared with the control group. Physical, role, cognitive, emotional functions improved more quickly and more significantly in the rehabilitation group at both weeks 4 and 8, whereas improvements in the control group were limited. In the domain of social functioning, the rehabilitation group scored slightly lower than the control group at week 4 but surpassed it by week 8 (Figure 5).



Comparison of psychological status and sleep quality between the two groups

At baseline, no significant differences were observed between the two groups in terms of psychological well-being and sleep quality. However, following the intervention, the rehabilitation group demonstrated markedly greater reduction in anxiety and depression scores, along with improved sleep quality, compared with the control group (Figure 6).

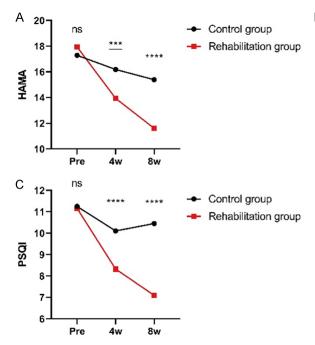
Comparison of incidence of adverse events between the two groups

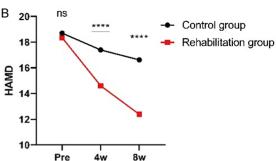
The total incidence of adverse events in the rehabilitation group was 18.68% (17/91), which was significantly lower than that in the control group (38.95%, 37/95) ( $\chi^2$ =9.265, P=0.002) (**Table 3**).

Multivariate logistic regression analysis of pulmonary rehabilitation as an independent predictor of pulmonary function

Pulmonary function was defined as the primary outcome. Based on standard clinical thresholds, good pulmonary function was classified as  $\text{FEV}_1 \geq 1.5 \text{ L}$ ,  $\text{FVC} \geq 2.5 \text{ L}$ , and  $\text{PEF} \geq 300 \text{ L/min}$  (coded as 0), whereas poor pulmonary function was defined as any value below these thresholds (coded as 1). The intervention variable was whether pulmonary rehabilitation was performed. To control for potential confounders, age, sex, and BMI were included as covariates in the logistic regression analysis.

Univariate logistic regression revealed a significant association between pulmonary rehabilitation and pulmonary function outcomes. Patients who received pulmonary rehabilitation





**Figure 6.** Comparison of psychological status and sleep quality outcomes between the two groups. A. HAMA; B. HAMD; C. PSQI. HAMA: Hamilton Anxiety Rating Scale, HAMD: Hamilton Depression Rating Scale, PSQI: Pittsburgh Sleep Quality Index. ns: not significant; \*\*\*P<0.001; \*\*\*\*P<0.0001.

**Table 3.** Comparison of incidence of adverse events between the two groups

	Control group (n=95)	Rehabilitation group (n=91)	$\chi^2$	Р
Total adverse events	37 (38.95)	17 (18.68)	9.265	0.002
Nausea/Vomiting	21 (22.11)	11 (12.09)		
Pneumonia	8 (8.42)	4 (4.40)		
Atelectasis	5 (5.26)	2 (2.20)		
Pneumothorax	3 (3.16)	0		

had a markedly lower risk of poor pulmonary function than those who did not (P<0.001). After adjusting for age, sex, and BMI, multivariate logistic regression confirmed pulmonary rehabilitation as an independent protective factor for pulmonary function (P<0.001) (**Table 4**).

#### Discussion

Lung cancer is frequently accompanied by dyspnea, weight loss, cough, pain, fatigue, and sleep disturbances, and most patients are elderly with comorbidities such as COPD or cardiovascular disease, complicating treatment decisions [27, 28]. Current therapeutic approaches include radiotherapy, chemotherapy, targeted therapy, and immunotherapy [29]. However, conventional options such as radiotherapy and platinum-based chemotherapy often lead to radiation pneumonitis, pulmonary

fibrosis, and drug-related declines in lung function, thereby exacerbating respiratory burden, impairing physical performance, and diminishing quality of life [30]. Systemic toxicity is another concern, as these regimens can cause both acute and long-term adverse effects across multiple organ systems [31]. In this context, supportive care plays a crucial

role in maintaining patient well-being and treatment tolerance.

A recent consensus from the European Society for Radiotherapy and Oncology (ESTRO) and the European Society for Medical Oncology (ESMO) emphasized several supportive strategies, including smoking cessation, nutritional support, exercise during treatment, and management of key symptoms such as esophagitis, cough, dyspnea, and nausea. The statement also highlighted the importance of protecting cardiovascular health, optimizing radiotherapy, and tailoring chemotherapy to reduce toxicity [32]. Notably, the consensus underlined that aerobic and resistance training can help restore functional status and recommended incorporating structured exercise interventions before and during chemoradiotherapy. Yet, despite strong supporting evidence, these recom-

Table 4. Univariate and multivariate logistic regression analyses of pulmonary function outcomes

	Univariate analysis				Multivariate analysis					
	β	S.E	Z	Р	OR (95% CI)	β	S.E	Z	Р	OR (95% CI)
Pulmonary rehabilitation training										
NO					1.00 (Reference)					1.00 (Reference)
Yes	-1.49	0.38	-3.87	<0.001	0.23 (0.11-0.48)	-1.46	0.39	-3.76	<0.001*	0.23 (0.11-0.50)

<sup>\*:</sup> adjusted for age, sex, and BMI.

mendations remain underutilized in routine clinical practice.

Preoperative rehabilitation has been shown to offer substantial benefits for patients with early-stage NSCLC, as supported by several clinical studies [33, 34]. A 2020 review reported that individuals with NSCLC who engaged in physical training prior to lung surgery were 67% less likely to experience postoperative pulmonary complications. Additionally, they also had chest drains removed about three days earlier, hospital stays shortened by four days, 6-minute walking distances improved by 18 meters, and slightly better preoperative lung function [35] but is associated with a risk of postoperative pulmonary complications (i.e. pneumonia (new infiltrate coupled with either fever (>38°C))). In post-surgical setting, the effects of exercise training on exercise capacity and adverse events are also well documented. In a 2019 review by Cavalheri et al., which included eight randomized controlled trials with a total of 450 participants, structured exercise interventions after surgery led to significant improvements in both exercise tolerance and walking distance [36]. In contrast, studies investigating the impact of pulmonary rehabilitation in elderly non-surgical lung cancer patients are rare, and the available evidence remains limited.

In clinical practice, our team observed that elderly NSCLC patients unfit for surgery often experienced not only cancer-related symptoms but also progressive fatigue and breathlessness. This led us to explore whether structured breathing and movement exercises might offer meaningful improvements. The results showed that after 4 and 8 weeks of intervention, the rehabilitation group outperformed the control group on multiple key indicators. These results suggest that pulmonary rehabilitation training is feasible, safe, and clinically valuable this vulnerable patient population.

Previous studies have indicated that pulmonary rehabilitation can enhance lung compliance and respiratory muscle efficiency through breathing exercises and aerobic training, thereby improving ventilation-perfusion disorders and enhancing lung function and exercise capacity [37, 38]. According to the ATS guidelines released by Rochester et al., patients with chronic respiratory diseases who undergo pulmonary rehabilitation experience notable improvements in 6MWD and FEV, along with reduced hospitalization days and symptom burden [11]. Although these guidelines primarily target diseases like COPD, the underlying intervention principles and rehabilitation model align closely with those applied in this study. A systematic review by He et al. also indicated that, in patients with severe or very severe COPD, pulmonary rehabilitation improved the 6MWD by an average of 30-70 m and significantly enhanced aerobic endurance and quality-of-life indicators [10]. In line with these findings, participants in the rehabilitation group in our study demonstrated significant improvements in 6MWD, VO<sub>2</sub>max, AT, and MWL by week 8, indicating that such interventions are equally beneficial for elderly patients with non-surgical lung cancer.

Another noteworthy finding of this study is that, after the intervention, the rehabilitation group outperformed the control group across all four dimensions of the Piper Fatigue Scale (PFS). This result can be explained from both physiological and psychological perspectives. Physiologically, moderate and regular exercise training enhances peripheral muscle oxygenation and metabolic efficiency, thereby alleviating the physical manifestations of cancer-related fatigue [39]. Psychologically, the sense of accomplishment and autonomous participation in the training process may foster positive emotions and mitigate emotional exhaustion [40, 41]. Additionally, the rehabilitation group achieved better scores than the control group in HAMA, HAMD, and PSQI measures, suggesting that pulmonary rehabilitation not only enhanced exercise capacity but also supported mental well-being and sleep quality. Recent studies have shown that exercise training can effectively alleviate fatigue, anxiety and sleep disorders in cancer patients during treatment [42]. This mechanism may be partly attributed to exercise-induced enhancement of BDNF expression and regulation of 5-HT metabolic pathways in the brain, thereby improving the functional state of the central nervous system [43].

It is noteworthy that, at week 4 of the intervention, the rehabilitation group showed slightly lower scores in social functioning compared to the control group. We speculate that, during the early stage of rehabilitation training, patients were still adapting to the training, with limited improvement in physical strength, and might have reduced social interaction due to fatigue and anxiety. However, as emotional stability and self-confidence improved, patients became more inclined to participate in social interactions, thus improving social functioning [44]. A similar delayed improvement was noted in emotional functioning, underscoring the necessity for sustained and long-term pulmonary rehabilitation to achieve optimal benefits. Accordingly, the EORTC QLQ-C30 may be particularly suitable for tracking the medium- and long-term impacts of rehabilitation training.

Regarding adverse reactions, the incidence of adverse reactions in the rehabilitation group was significantly lower than that in the control group. This may be attributed to the multifaceted benefits of pulmonary rehabilitation, including improved ventilation, enhanced sputum clearance, and increased muscular strength and endurance [45]. In particular, atelectasis and pneumonia occurred less frequently among patients in the rehabilitation group, suggesting that breathing exercises and airway clearance techniques may offer additional protection against treatment-related complications. In addition, rehabilitation training may improve drug tolerance, thereby reducing the likelihood of chemotherapy-related discomfort such as nausea and vomiting [20, 46, 47].

Naturally, this study has several limitations. First, as a single-center retrospective study, it is subject to potential selection bias in patient

inclusion. Second, discrepancies may exist between the recorded and actual implementation of interventions and compliance monitoring, leading to potential information asymmetry. In the future, multi-center, prospective cohort studies can be used to improve sample representativeness. Another limitation lies in the wide variability among elderly patients. Due to wide variations in baseline physical conditions, comorbidities, and willingness to participate in rehabilitation, it is still difficult to achieve complete consistency in training frequency and implementation quality, even under uniform rehabilitation guidelines, which may have a certain impact on the effectiveness of the intervention. Future research should consider stratified study designs that adjust training intensity based on patients' physical capabilities and document actual participation levels to more accurately assess outcomes.

#### Conclusion

Pulmonary rehabilitation exercise training can significantly improve lung function, enhance exercise endurance, reduce fatigue, and improve quality of life in elderly patients with nonsurgical lung cancer. It also demonstrates a favorable safety profile, supporting its feasibility and potential for broader clinical application.

#### Disclosure of conflict of interest

None.

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#### References

- [1] Baladi A, Tafenzi HA, Zouiten O, Afani L, Essaadi I, El Fadli M and Belbaraka R. Immunotherapy for elderly patients with advanced non-small cell lung cancer: challenges and perspectives. Int J Mol Sci 2025; 26: 2120.
- [2] Liu YY, Li DJ, Wu SS, Zhang S, Fu YF and He YT. Cancer incidence, mortality and trends among elderly in Hebei province, 2011-2020. Zhonghua Zhong Liu Za Zhi 2025; 47: 228-236.

- [3] Wang H, Yao Z, Kang K, Zhou L, Xiu W, Sun J, Xie C, Yu M, Li Y, Zhang Y, Zheng Y, Lin G, Pan X, Wu Y, Luo R, Wang L, Tang M, Liao S, Zhu J, Zhou X, Zhang X, Xu Y, Liu Y, Peng F, Wang J, Xiang L, Yin L, Deng L, Huang M, Gong Y, Zou B, Wang H, Wu L, Yuan Z, Bi N, Fan M, Xu Y, Tong R, Yi L, Gan L, Xue J, Mo X, Chen C, Na F and Lu Y. Preclinical study and phase II trial of adapting low-dose radiotherapy to immunotherapy in small cell lung cancer. Med 2024; 5: 1237-1254, e9.
- [4] Zhang R, Jiang X, Liu W, Zhang N and Shang J. Effect of graded exercise rehabilitation based on pulmonary function classification on dyspnea, pulmonary function, and exercise capacity in elderly lung cancer patients. Am J Transl Res 2024; 16: 6552-6563.
- [5] Nikitas J, Yanagawa J, Sacks S, Hui EK, Lee A, Deng J, Abtin F, Suh R, Lee JM, Toste P, Burt BM, Revels SL, Cameron RB and Moghanaki D. Pathophysiology and management of chest wall pain after surgical and non-surgical local therapies for lung cancer. JTO Clin Res Rep 2024; 5: 100690.
- [6] Tsang MW, Kam MK, Leung SF and Chan ATC. Non-surgical treatment of lung cancer: personalised stereotactic ablative radiotherapy. Hong Kong Med J 2014; 20: 529-536.
- [7] Edbrooke L, Granger CL, Francis JJ, John T, Kaadan N, Halloran E, Connolly B and Denehy L. Rehabilitation outcomes for people with lung cancer (UNITE): protocol for the development of a core outcome set. BMJ Open Respir Res 2023; 10: e001571.
- [8] Takemura N, Cheung DST, Fong DYT, Hui D, Lee AWM, Lam TC, Ho JC, Kam TY, Chik JYK and Lin CC. Tai Chi and Aerobic exercise on cancer-related dyspnea in advanced lung cancer patients: a randomized clinical trial. J Pain Symptom Manage 2024; 68: 171-179.
- [9] Murison KR, Warkentin MT, Khodayari Moez E, Brhane Y, Liu G and Hung RJ. Respiratory function as a prognostic factor for lung cancer in screening and general populations. Ann Am Thorac Soc 2025; 22: 591-597.
- [10] He W, Wang J, Feng Z, Li J and Xie Y. Effects of exercise-based pulmonary rehabilitation on severe/very severe COPD: a systematic review and meta-analysis. Ther Adv Respir Dis 2023; 17: 17534666231162250.
- [11] Rochester CL, Alison JA, Carlin B, Jenkins AR, Cox NS, Bauldoff G, Bhatt SP, Bourbeau J, Burtin C, Camp PG, Cascino TM, Dorney Koppel GA, Garvey C, Goldstein R, Harris D, Houchen-Wolloff L, Limberg T, Lindenauer PK, Moy ML, Ryerson CJ, Singh SJ, Steiner M, Tappan RS, Yohannes AM and Holland AE. Pulmonary rehabilitation for adults with chronic respiratory disease: an official American thoracic society

- clinical practice guideline. Am J Respir Crit Care Med 2023; 208: e7-e26.
- [12] Xiong T, Bai X, Wei X, Wang L, Li F, Shi H and Shi Y. Exercise rehabilitation and chronic respiratory diseases: effects, mechanisms, and therapeutic benefits. Int J Chron Obstruct Pulmon Dis 2023; 18: 1251-1266.
- [13] Ma Q, Lu M, Yang Q, Gong F, Zhou L and Xu D. Effects of aerobic exercise-based pulmonary rehabilitation on quality of life in pediatric asthma: a systematic review and meta-analysis. Heart Lung 2025; 69: 11-30.
- [14] Kocamaz D, Dinler E, Yamak D, Hatimoğulları K, Bayramlar K and Yıldırım M. The effect of pulmonary rehabilitation on quality of life and functional capacity after chemotherapy in patients with small cell lung cancer. Support Care Cancer 2024; 32: 678.
- [15] Cheng SWM, McKeough ZJ, McNamara RJ and Alison JA. Pulmonary rehabilitation using minimal equipment for people with chronic obstructive pulmonary disease: a systematic review and meta-analysis. Phys Ther 2023; 103: pzad013.
- [16] Lindell KO. Nonpharmacological therapies for interstitial lung disease. Curr Pulmonol Rep 2018; 7: 126-132.
- [17] Mikkelsen MK, Lund CM, Vinther A, Tolver A, Johansen JS, Chen I, Ragle AM, Zerahn B, Engell-Noerregaard L, Larsen FO, Theile S, Nielsen DL and Jarden M. Effects of a 12-week multimodal exercise intervention among older patients with advanced cancer: results from a randomized controlled trial. Oncologist 2022; 27: 67-78.
- [18] Avancini A, Sartori G, Gkountakos A, Casali M, Trestini I, Tregnago D, Bria E, Jones LW, Milella M, Lanza M and Pilotto S. Physical activity and exercise in lung cancer care: will promises be fulfilled? Oncologist 2020; 25: e555-e569.
- [19] Rochester CL, Vogiatzis I, Holland AE, Lareau SC, Marciniuk DD, Puhan MA, Spruit MA, Masefield S, Casaburi R, Clini EM, Crouch R, Garcia-Aymerich J, Garvey C, Goldstein RS, Hill K, Morgan M, Nici L, Pitta F, Ries AL, Singh SJ, Troosters T, Wijkstra PJ, Yawn BP and ZuWallack RL; ATS/ERS Task Force on Policy in Pulmonary Rehabilitation. An official american thoracic society/european respiratory society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. Am J Respir Crit Care Med 2015; 192: 1373-1386.
- [20] Ferté JB, Boyer FC, Taiar R, Pineau C, Barbe C and Rapin A. Impact of resistance training on the 6-minute walk test in individuals with chronic obstructive pulmonary disease: a systematic review and meta-analysis. Ann Phys Rehabil Med 2022; 65: 101582.

- [21] Sunjaya A, Poulos L, Reddel H and Jenkins C. Qualitative validation of the modified Medical Research Council (mMRC) dyspnoea scale as a patient-reported measure of breathlessness severity. Respir Med 2022; 203: 106984.
- [22] Swigris JJ, Esser D, Conoscenti CS and Brown KK. The psychometric properties of the St George's Respiratory Questionnaire (SGRQ) in patients with idiopathic pulmonary fibrosis: a literature review. Health Qual Life Outcomes 2014; 12: 124.
- [23] Berardi A, Graziosi G, Ferrazzano G, Casagrande Conti L, Grasso MG, Tramontano M, Conte A and Galeoto G. Evaluation of the psychometric properties of the revised piper fatigue scale in patients with multiple sclerosis. Healthcare (Basel) 2022; 10: 985.
- [24] Nolte S, Liegl G, Petersen MA, Aaronson NK, Costantini A, Fayers PM, Groenvold M, Holzner B, Johnson CD, Kemmler G, Tomaszewski KA, Waldmann A, Young TE and Rose M; EORTC Quality of Life Group. General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the Unites States. Eur J Cancer 2019; 107: 153-163.
- [25] Shahrokhi M, Ghaeli P, Arya P, Shakiba A, Noormandi A, Soleimani M and Esfandbod M. Comparing the effects of melatonin and zolpidem on sleep quality, depression, and anxiety in patientswithcolorectalcancerundergoingchemotherapy. Basic Clin Neurosci 2021; 12: 105-114.
- [26] Xie Y, Liu S, Chen XJ, Yu HH, Yang Y and Wang W. Effects of exercise on sleep quality and insomnia in adults: a systematic review and meta-analysis of randomized controlled trials. Front Psychiatry 2021; 12: 664499.
- [27] Berg CD, Schiller JH, Boffetta P, Cai J, Connolly C, Kerpel-Fronius A, Kitts AB, Lam DCL, Mohan A, Myers R, Suri T, Tammemagi MC, Yang D and Lam S; International Association for the Study of Lung Cancer (IASLC) Early Detection and Screening Committee. Air pollution and lung cancer: a review by international association for the study of lung cancer early detection and screening committee. J Thorac Oncol 2023; 18: 1277-1289.
- [28] Song C and Yao L. The experience of social alienation in elderly lung cancer patients: a qualitative study. Asian Nurs Res (Korean Soc Nurs Sci) 2024; 18: 281-287.
- [29] Antonio M, Saldaña J, Linares J, Ruffinelli JC, Palmero R, Navarro A, Arnaiz MD, Brao I, Aso S, Padrones S, Navarro V, González-Barboteo J, Borràs JM, Cardenal F and Nadal E. Geriatric assessment may help decision-making in elderly patients with inoperable, locally ad-

- vanced non-small-cell lung cancer. Br J Cancer 2018; 118: 639-647.
- [30] Evin C, Razakamanantsoa L, Gardavaud F, Papillon L, Boulaala H, Ferrer L, Gallinato O, Colin T, Moussa SB, Harfouch Y, Foulquier JN, Guillerm S, Bibault JE, Huguet F, Wagner M and Rivin del Campo E. Clinical, dosimetric and radiomic features predictive of lung toxicity after (chemo)radiotherapy. Clin Lung Cancer 2025; 26: 93-103, e1.
- [31] Luo Y, Zhang L, Mao D, Yang Z, Zhu B, Miao J and Zhang L. Symptom clusters and impact on quality of life in lung cancer patients undergoing chemotherapy. Qual Life Res 2024; 33: 3363-3375.
- [32] De Ruysscher D, Faivre-Finn C, Nackaerts K, Jordan K, Arends J, Douillard JY, Ricardi U and Peters S. Recommendation for supportive care in patients receiving concurrent chemotherapy and radiotherapy for lung cancer. Ann Oncol 2020; 31: 41-49.
- [33] Voorn MJJ, Bastiaansen EMW, Schröder CD, van Kampen-van den Boogaart VEM, Bootsma GP, Bongers BC and Janssen-Heijnen MLG. A qualitative stakeholder analysis of beliefs, facilitators, and barriers for a feasible prehabilitation program before lung cancer surgery. J Cancer Res Clin Oncol 2023; 149: 15713-15726.
- [34] Moyen A, Fleurent-Grégoire C, Gillis C, Zaks R, Carli F, Scheede-Bergdahl C, Spicer J, Cools-Lartigue J, Najmeh S, Morais JA, Mazurak V and Chevalier S. Novel multimodal intervention for surgical prehabilitation on functional recovery and muscle characteristics in patients with non-small cell lung cancer: study protocol for a randomised controlled trial (MMP-LUNG). BMJ Open Respir Res 2025; 12: e002884.
- [35] Cavalheri V and Granger C. Preoperative exercise training for patients with non-small cell lung cancer. Cochrane Database Syst Rev 2017; 6: CD012020.
- [36] Cavalheri V, Burtin C, Formico VR, Nonoyama ML, Jenkins S, Spruit MA and Hill K. Exercise training undertaken by people within 12 months of lung resection for non-small cell lung cancer. Cochrane Database Syst Rev 2019; 6: CD009955.
- [37] Borghetti P, Branz J, Volpi G, Pancera S, Buraschi R, Bianchi LNC, Bonù ML, Greco D, Facheris G, Tomasi C, Pini L, Bezzi M, Grisanti S, Gallazzi MS, Borghesi A and Buglione di Monale e Bastia M; ASST Spedali Civili of Brescia Lung Unit. Home-based pulmonary rehabilitation in patients undergoing (chemo)radiation therapy for unresectable lung cancer: a prospective explorative study. Radiol Med 2022; 127: 1322-1332.

- [38] Hockele LF, Sachet Affonso JV, Rossi D and Eibel B. Pulmonary and functional rehabilitation improves functional capacity, pulmonary function and respiratory muscle strength in post COVID-19 patients: pilot clinical trial. Int J Environ Res Public Health 2022; 19: 14899.
- [39] Xin X, Huang L, Pan Q, Zhang J and Hu W. The effect of self-designed metabolic equivalent exercises on cancer-related fatigue in patients with gastric cancer: a randomized controlled trial. Cancer Med 2024; 13: e7085.
- [40] Malveiro C, Correia IR, Cargaleiro C, Magalhães JP, de Matos LV, Hilário S, Sardinha LB and Cardoso MJ. Effects of exercise training on cancer patients undergoing neoadjuvant treatment: a systematic review. J Sci Med Sport 2023; 26: 586-592.
- [41] Herranz-Gómez A, Cuenca-Martínez F, Suso-Martí L, Varangot-Reille C, Prades-Monfort M, Calatayud J and Casaña J. Effectiveness of therapeutic exercise models on cancer-related fatigue in patients with cancer undergoing chemotherapy: a systematic review and network meta-analysis. Arch Phys Med Rehabil 2023; 104: 1331-1342.
- [42] Lu L, Chen X, Lu P, Wu J, Chen Y, Ren T, Li Y and Zhong X. Analysis of the effect of exercise combined with diet intervention on postoperative quality of life of breast cancer patients. Comput Math Methods Med 2022; 2022: 4072832.

- [43] Loureiro J, Costa-Pereira JT, Pozza DH and Tavares I. The power of movement: how exercise influences chemotherapy-induced peripheral neuropathy. Biomedicines 2025; 13: 1103.
- [44] Farver-Vestergaard I, Volpato E, Hansen H and Steed L. Editorial: psychosocial issues and interventions in pulmonary rehabilitation. Front Rehabil Sci 2025; 6: 1562337.
- [45] Okrzymowska P, Kurzaj M, Seidel W and Rożek-Piechura K. Eight weeks of inspiratory muscle training improves pulmonary function in disabled swimmers-a randomized trial. Int J Environ Res Public Health 2019; 16: 1747.
- [46] Rehman M, Ahmad U, Waseem M, Ali B and Tariq MI. Effects of exercise training in patients with lung cancer during chemotherapy treatment. Malays J Med Sci 2023; 30: 141-152.
- [47] Luo N, Dai F, Wang X, Hu B, Zhang L and Zhao K. Pulmonary rehabilitation exercises effectively improve chronic cough after surgery for non-small cell lung cancer. Cancer Control 2024; 31: 10732748241255824.