

The efficacy of pulmonary rehabilitation training program for patients after lung transplantation

Jie Mei^{1#}, Jing Hu^{2#}, Eric M. Krause³, Toyofumi F. Chen-Yoshikawa⁴, Antonio Alvarez⁵, Xiaojun Wang¹

¹Department of Operating Room, Shanghai Pulmonary Hospital, Shanghai, China; ²Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Shanghai, China; ³Division of Thoracic Surgery, University of Maryland, Baltimore, MD, USA; ⁴Department of Thoracic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan; ⁵Department of Thoracic Surgery and Lung Transplantation, University Hospital Reina Sofía, Córdoba, Spain

Contributions: (I) Conception and design: J Mei, J Hu; (II) Administrative support: X Wang; (III) Provision of study materials or patients: J Mei, X Wang; (IV) Collection and assembly of data: J Mei; (V) Data analysis and interpretation: J Mei, J Hu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Xiaojun Wang, BS. Department of Operating Room, Shanghai Pulmonary Hospital, 507 Zhengmin Road, Yangpu District, Shanghai 200000, China. Email: woailuyue0701@126.com.

Background: Pulmonary rehabilitation is recognized widely as one of the most effective measures to promote postoperative recovery of lung transplant recipients (LTRs), and it has positive effects on both short- and long-term quality of life (QoL) and survival outcomes. However, no standardized pulmonary rehabilitation training programs exist specifically for LTRs. The pulmonary rehabilitation programs widely used in clinical practice focus mainly on exercise or respiratory training, to some extent neglecting other therapeutic methods that could promote patient health, such as nutrition support, pain control, spiritual comfort, and so on. This study aimed to develop a postoperative pulmonary rehabilitation training program for LTRs and evaluate its effectiveness.

Methods: Using convenience sampling, all patients who underwent lung transplantation (LTx) at Shanghai Pulmonary Hospital from January 2021 to December 2022 were screened for inclusion and exclusion criteria, and a total of 68 patients were finally included in this study. A non-synchronous quasi-experimental design was used, with patients who underwent LTx in 2021 as the control group and patients who underwent LTx in 2022 as the experimental group. The control group received routine treatment, health education, and rehabilitation guidance when patients determined the date of surgery. In addition to this, the experimental group received pulmonary rehabilitation training. The incidence of postoperative pulmonary complications (pulmonary infections), duration of chest tube drainage, intensive care unit (ICU) length of stay, postoperative pain scores, postoperative QoL, pulmonary function, oxygenation index, and the distance in the 6-minute walking test (6MWD) were compared between the two groups.

Results: The length of ICU stay and duration of chest tube drainage in the experimental group were lower than those in the control group, and the results of oxygenation index, 6MWD, and St. George's Respiratory Questionnaire (reflecting the QoL) were better than those of the control group (P<0.05). There was no significant difference in the pain of the two groups 1 week after surgery and 3 months after surgery, and the pain score of the experimental group was lower than that of the control group at 1 month after surgery (P<0.05). There was no significant difference in the incidence of complications between the two groups (P>0.05).

Conclusions: The postoperative pulmonary rehabilitation training program for LTRs is safe and effective. It can shorten both the duration of chest tube drainage and ICU stay, it can also improve patients' exercise capacity and pulmonary function while also promote safety outcomes of LTRs, and improve QoL scores.

Keywords: Lung transplantation (LTx); pulmonary rehabilitation training; multi-disciplinary approach

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Introduction

Lung transplantation (LTx) is an effective treatment for end-stage lung disease (1). Pulmonary rehabilitation is recognized widely as one of the most effective measures to promote postoperative recovery of lung transplant recipients (LTRs), and it has positive effects on both short- and long-term quality of life (QoL) and survival outcomes (2-4). Studies have shown that early intervention after LTx has more advantages in reducing complications and improving lung function and QoL (5-7). Therefore, pulmonary rehabilitation is a key focus of perioperative management and postoperative follow-up for patients. It is also crucial for prolonging patients' lives and improving their QoL (8,9).

At present, a large amount of research-based evidence has proved that pulmonary rehabilitation is beneficial to patients with end-stage lung disease, but in practice it is rarely used. Even in countries with mature pulmonary rehabilitation programs, the utilization rate has not been optimized. For example, less than 1.2% of patients with chronic obstructive pulmonary disease (COPD) in the United States have received pulmonary rehabilitation

Highlight box

Key findings

• The pulmonary rehabilitation program after lung transplantation established in this study can improve patients' exercise ability and lung function, promote early rehabilitation of lung transplant recipients (LTRs), and improve patients' quality of life (QoL).

What is known and what is new?

- Pulmonary rehabilitation is recognized widely as one of the most effective measures to promote postoperative recovery of LTRs. The pulmonary rehabilitation programs widely used in clinical practice focus mainly on exercise or respiratory training.
- This study developed a comprehensive multidisciplinary pulmonary rehabilitation program and compared it with patients receiving a conventional pulmonary rehabilitation program.

What is the implication, and what should change now?

 LTRs should receive multidisciplinary comprehensive pulmonary rehabilitation training after operation to promote the recovery of postoperative pulmonary function. intervention (10). This rate is even lower in China.

In 2013, the American Thoracic Society/European Respiratory Society defined pulmonary rehabilitation as a comprehensive treatment plan based on a thorough patient evaluation, including but not limited to exercise training, education, and behavioral changes; all with the goal of improving the patient's physical and mental conditions while also promoting long-term adherence to healthy behaviors (11). However, the current pulmonary rehabilitation training for LTR mainly focuses on exercise training, and there is no standardized and comprehensive pulmonary rehabilitation training program after LTR. The pulmonary rehabilitation programs widely used in clinical practice focus mainly on exercise or respiratory training (8,12), to some extent neglecting other therapeutic methods that could promote patient health. Furthermore, many patients find these programs burdensome and complicated, resulting in poor patient compliance. There are differences between various versions of pulmonary rehabilitation programs, and the rehabilitation measures are relatively singular, with a lack of characteristic intervention indications and standardized training plans. In addition, the low level of psychological and social attention given to patients makes it difficult to ensure their physical and mental safety (13).

Candemir *et al.* (6) investigated the efficacy of a multidisciplinary and comprehensive pulmonary rehabilitation program in the early pre- and post-operative stages of double LTx (DLT). However, authors did not compare the efficacy of multidisciplinary and comprehensive pulmonary rehabilitation programs to standard of care, so it is unclear if the benefits seen were due to the intervention or the transplant itself.

Based on the American Thoracic Society/European Respiratory Society Pulmonary Rehabilitation Guidelines, we developed a comprehensive and feasible pulmonary rehabilitation training program and applied it to lung transplant patients. We then retrospectively compared those results to patients who had undergone a transplant at our facility the year before implementing our multi-disciplinary and comprehensive rehabilitation program. We present this article in accordance with the TREND reporting checklist (available at https://jtd.amegroups.com/article/

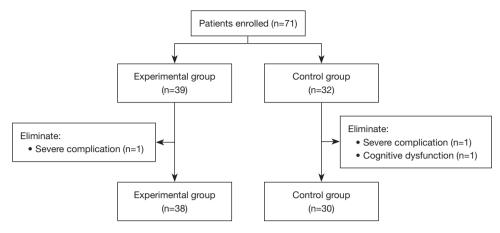


Figure 1 Flowchart of this study.

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Methods

Participants

Patients undergoing LTx at the Shanghai Pulmonary Hospital from January 2021 to December 2022 were included in the study. Patients who met all of the following standards were included in the study: (I) aged 18-75 years; (II) successful LTx; (III) clear mind and able to communicate normally; (IV) voluntarily participate in the study, sign informed consent, and be able to conduct long-term follow-up; (V) patients undergoing lung transplant surgery between January 2021 and December 2022. Patients who met any of the following criteria were excluded: (I) severe postoperative complications; (II) postoperative cognitive dysfunction; (III) short-term death; (IV) are not willing to participate in research or unable to cooperate with longterm follow-up. A total of 68 subjects were included in this study (Figure 1). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Shanghai Pulmonary Hospital (No. Q21-347, HL-C5) and informed consent was taken from all the patients.

Research methods

Development of pulmonary rehabilitation training program for LTRs

Using both Chinese and international sources, we reviewed clinical practice guidelines, expert consensus, original research, and other related materials on pulmonary rehabilitation programs. From this research, an initial training plan for pulmonary rehabilitation for LTRs was created. Next, we selected an expert discussion group consisting of senior leaders in pulmonary nursing, nursing management, and anesthesia. The detailed responsibilities of team members are shown in *Table 1*. Based on the experts' opinions, the pulmonary rehabilitation training plan was modified and finalized, and the final plan for pulmonary rehabilitation training for LTRs is detailed in *Table 2*.

Application of lung transplant rehabilitation program

In the intensive care unit (ICU), each recipient in the experimental group was assigned a pulmonary rehabilitation team consisting of one respiratory therapist, one lung transplant specialist, one rehabilitation therapist, and two critical care nurses. The pulmonary rehabilitation team conducts a comprehensive assessment of the patient before surgery, provides health education manuals, training videos, and on-site demonstrations through multiple modes of health education, and implements pre-rehabilitation training and adaptive training. After surgery, personalized and full-course pulmonary rehabilitation training plans are developed according to the patient's different stages and are adjusted in real-time based on the patient's specific recovery situation. Each recipient also received standard of care in regards to fluid management, integrated basic rehabilitation care measures, immunosuppression, antiinfective prophylaxis, nutritional support, psychological support, sleep management, and pain treatment.

Quality management

In this study, the pulmonary rehabilitation program was

Table 1 Ieam members responsibilities				
Members	Responsibilities			
Respiratory therapist	Supervise and manage the entire pulmonary rehabilitation work to ensure the effective implementation of the plan			
Lung transplant specialist physician	Dynamically assess the compatibility of the pulmonary rehabilitation plan and patient condition, and comprehensively evaluate the patient's respiratory, circulatory, nervous, and coagulation indicators before each pulmonary rehabilitation training session to determine whether the training plan can be implemented			
Rehabilitation therapist	Assist patients in implementing various training plans during the training process (such as guiding patients in early activity, respiratory muscle training, and exercise on the bed)			
Critical care specialist nurse	Responsible for closely monitoring the patient's vital signs throughout the process, especially when implementing non-invasive ventilation, being vigilant about aspiration, avoiding mask leakage, and ensuring the effectiveness of non-invasive ventilation			
	In case of any abnormal situation, the responsible nurse should immediately report to the respiratory therapy specialist nurse and the lung transplant specialist physician			

Table 1 Team members responsibilities

initiated within 24 hours after surgery and continued until the patients were discharged from the hospital. The patients were followed up at 1 and 3 months after surgery. For the experimental group, the pulmonary rehabilitation therapist was responsible for recording daily rehabilitation logs. The critical care specialist nurse was responsible for recording vital signs, patient complaints and complications. The respiratory therapist was responsible for implementing the daily goals and adjusting them as clinically indicated. The entire team met at regular intervals to evaluate the patient's progress and to make indicated changes to the care plan.

Intervention for the control group

After LTx surgery, the critical care specialist nurse implemented routine nursing interventions for the patient, including basic care, skin care, nebulization therapy, turning and percussion, oscillation sputum suction, and so on. Patients in the control group received rehabilitation training led by primary nurses. Primary nurses assumed the responsibility of pulmonary rehabilitation guidance on the basis of providing overall quality nursing for patients. Primary nurses cooperated with doctors to provide patients with appropriate treatment and rehabilitation guidance, and carried out health education and psychological nursing for patients in the whole process (*Table 3*).

Evaluation indicators

- (I) Postoperative pulmonary infection rate;
- (II) Postoperative chest tube duration;
- (III) ICU hospitalization time;

- (IV) 6-minute walking test (6MWT) (3 months after LTx) (2);
- (V) Pulmonary function: oxygenation index (3 months after LTx and 6 months after LTx);
- (VI) QoL: St. George's Respiratory Questionnaire (SGRQ) (6 months after LTx) (14);
- (VII) Pain: Numeric Rating Scale (NRS) (1 week, 1 month and 3 months after LTx) (15).

A research nurse collected data on length of time a chest tube was in place, ICU length of stay, incidences and severity of post-operative complications, pre- and post-operative lung function and oxygenation levels, pre- and post-operative QoL scores, pain scores, 6-minute walk test distance (6MWD) at 3 months post-transplant.

Statistical methods

EpiData software (EpiData, Buenos Aires, Caba, Argentina) was used for double data entry, and after validation, the data were imported into SPSS 26.0 (IBM Corp., Armonk, NY, USA) for data analysis.

For quantitative data, the normality is tested by graphical method. And the normally distributed metric data were expressed as mean \pm standard deviation, and an independent sample *t*-test was used for inter-group comparison. Non-normally distributed metric data were expressed as median (25–75% quartile), and non-parametric tests were performed. Count data were expressed as composition ratio or rate, and the chi-square test was used. Logistic regression analysis was used for multivariate analysis of related factors,

ECMO + ventilator assistance	Ventilator assistance	Active rehabilitation training
Gradually reduce the ECMO flow rate to 2.5–3.0 L/min; the blood oxygen saturation is maintained above 95%	Early removal of tracheal intubation; spontaneous breathing trial for 30–120 min	Breathing function training combining deep breathing, abdominal breathing, and pursed-lip breathing
		Breathing trainer: 10–15 min of inhalation training; exhalation training, gradually increase the training frequency and duration
Protective lung ventilation strategy: maintain positive end-expiratory pressure ventilation at 5–10 cmH ₂ O; oxygen concentration should be as low as possible (\leq 40%), maintaining peripheral arterial oxygen pressure at 70–80 mmHg, oxygen saturation >95%	Remove mechanical ventilation early: spontaneous breathing trial, 30–120 min; the oxygenation index >200 mmHg, remove the tracheal tube	Switching to non-invasive continuous positive airway pressure ventilation and high-flow nasal cannula oxygen therapy, achieve conventional oxygen therapy finally
Nebulization inhalation; suction as needed; percussion; postural drainage; flexible bronchoscopy as needed; do not recommend using oscillatory sputum excretion device	Nebulized inhalation; suction as needed, percussion; postural drainage; perform fiberoptic bronchoscopy as needed; oscillatory sputum clearance device as needed, avoiding the surgical incision area	The following measures should be added: (I) effective cough training; (II) vibration positive pressure respiratory treatment system: twice a day, 5 sets per session
Joint movement of the limbs: twice a day, 10 min once	Limb strength training: (I) upper limb training: arm lifting exercises using grip trainers and resistance against gravity; (II) lower limb training: straight leg raises, bridge exercises, and bed cycling	Independent walking: more than 20 min, without assistance, 2–3 times per day
Bed sitting training: 20 min, twice a day	Bedside sitting training: 2–3 times a day, 20 min each time	
Upper limb exercise: Passive movement 2–3 times a day, 20 min each time	Standing training: 2–3 times a day, 20 min each time	
Lower limb exercise: 2–3 times a day, 20 min each time	Walking training: 2–3 times per day	
target feeding volume within 24-48 hours	, , , , , , , , , , , , , , , , , , , ,	No swallowing dysfunction: start oral feeding as early as possible
of initiation of feeding		Swallowing dysfunction: enteral nutrition, with a target feeding volume of 105–126 kJ/kg/day and a target protein requirement of 1.2–2.0 g/kg/day
	Gradually reduce the ECMO flow rate to 2.5–3.0 L/min; the blood oxygen saturation is maintained above 95% Protective lung ventilation strategy: maintain positive end-expiratory pressure ventilation at 5–10 cmH ₂ O; oxygen concentration should be as low as possible (≤40%), maintaining peripheral arterial oxygen pressure at 70–80 mmHg, oxygen saturation >95% Nebulization inhalation; suction as needed; percussion; postural drainage; flexible bronchoscopy as needed; do not recommend using oscillatory sputum excretion device Joint movement of the limbs: twice a day, 10 min once Bed sitting training: 20 min, twice a day Upper limb exercise: Passive movement 2–3 times a day, 20 min each time Lower limb exercise: 2–3 times a day, 20 min each time Enteral nutrition: aim to reach 50% of the target feeding volume within 24–48 hours	Gradually reduce the ECMO flow rate to 2.5–3.0 L/min; the blood oxygen saturation is maintained above 95%Early removal of tracheal intubation; spontaneous breathing trial for 30–120 minProtective lung ventilation strategy: maintain positive end-expiratory pressure ventilation at 5–10 cmH2O; oxygen concentration should be as low as possible (≤40%), maintaining peripheral arterial oxygen pressure at 70–80 mmHg, oxygen saturation >95%Remove mechanical ventilation early: spontaneous breathing trial, 30–120 min; the oxygenation index >200 mmHg, remove the tracheal tubeNebulization inhalation; suction as needed; percussion; postural drainage; flexible bronchoscopy as needed; do not recommend using oscillatory sputum excretion deviceNebulized inhalation; suction as needed, percussion; postural drainage; perform fiberoptic bronchoscopy as needed; oscillatory sputum clearance device as needed, avoiding the surgical incision areaJoint movement of the limbs: twice a day, 10 min onceLimb strength training: (1) upper limb training: arm lifting exercises, using gravity; (1) lower limb training: straight leg raises, bridge exercises, and bed cyclingBed sitting training: 20 min, twice a day, 20 min each timeBedside sitting training: 2–3 times a day, 20 min each timeUpper limb exercise: Passive movement 2–3 times a day, 20 min each timeStanding training: 2–3 times a day, 20 min each timeLower limb exercise: 2–3 times a day, 20 min each timeWalking training: 2–3 times per dayUpper limb exercise: 2–3 times a day, 20 min each timeGradually increase the feeding volume of enteral nutrition

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physical therapy ECMO, extracorporeal membrane oxygenation.

Training modules	ECMO + ventilator assistance	Ventilator assistance	Active rehabilitation training	
Respiratory function training	Lung-protective ventilation strategy; airway management; atomization treatment; suction secretions as required	Early extubation; diaphragmatic protective ventilation strategy; airway management; atomization treatment; suction secretions as required	Respiratory function training (abdominal contraction lip breathing and effective cough, etc.)	
Exercise training	Passive movement of extremities (muscle massage, flexion, extension, adduction, abduction)	Active phased physical exercise; assisted ambulation	Upper and lower limb weight training; autonomous walking training; stair climbing training	
Health education	 (I) Lung transplantation's expectations; (II) the necessity of the ECMO support therapy and mechanical ventilation; (III) the effectiveness and necessity of pulmonary rehabilitation; (IV) respiratory function training method; (V) exercise training methods 			
Mental nursing	Nurses combined with family member	rs of patients provided psychological support	for patients	

Table 3 Pulmonary rehabilitation training for control group

ECMO, extracorporeal membrane oxygenation.

with $P \leq 0.05$ indicating statistical significance.

Results

Baseline information comparison

A total of 68 patients were enrolled in the study, 38 in the experimental group and 30 in the control group. The experimental group's underlying diagnoses were COPD in 19 cases, interstitial lung disease in 12 cases, idiopathic pulmonary fibrosis in 4 cases, pulmonary arterial hypertension in 1 case, and acute respiratory distress syndrome complicated with severe pneumonia in 2 cases. The control group's underlying diagnoses were similar with severe COPD in 14 cases, interstitial lung disease in 9 cases, idiopathic pulmonary fibrosis in 3 cases, bronchiectasis in 2 cases, occupational lung disease in 1 case, and other occupational lung diseases in 1 case. There was no significant difference in gender, age, and main diagnosis between the two groups (*Table 4*).

Comparison of perioperative results

As shown in *Table 4*, there was no significant difference in the incidence of complications after single LTx (SLT) or DLT between the experimental group and the control group (χ_1^2 =0.609, P₁=0.435; χ_2^2 =1.005, P₂=0.316).

ICU stay time in the experimental group (SLT: 14.05±3.14 days; DLT: 24.61±4.83 days) was significantly shorter than in the control group (SLT: 17.77±3.24 days; DLT: 28.24±4.63 days) (SLT: t_1 =3.284, P₁<0.01; DLT: t_2 =2.26, P₂=0.03) (*Table 4*).

Similarly, the duration of the chest tube drainage was significantly longer in the control group (SLT: 16.23 ± 3.63 days; DLT: 26.59 ± 3.30 days) than in the experimental group (SLT: 13.80 ± 2.78 days; DLT: 23.50 ± 3.63 days), both for recipients of SLT and for recipients of DLT (SLT: $t_1=2.17$, P₁=0.04; DLT: $t_2=2.63$, P₂=0.01) (*Table 4*).

The difference of SGRQ scores at 6 months after transplantation were shorter by statistical significance in the experimental group (SLT: 38.75±8.26; DLT: 49.28±7.30) compared to the control group (SLT: 50.69±8.61; DLT: 57.47±5.85) (SLT: t_1 =3.993, P₁<0.01; DLT: t_2 =3.650, P₂<0.01).

There was no significant difference in pain scores between the experimental group and the control group at either 1 week (SLT: t_1 =0.390, P_1=0.699; DLT: t_2 =0.975, P_2=0.337) or 3 months post-operation (t_1 =0.063, P_1=0.950; t_2 =0.422, P_2=0.676) (*Figure 2, Table 5*).

Comparison of oxygenation index, vital capacity (VC), forced expiratory volume in one second (FEV_1) and maximum ventilatory volume (MVV) before and after LTx

The oxygenation index is a measure of the efficiency of oxygen exchange by the lungs. The oxygenation indexes at 3 months after unilateral LTx and bilateral LTx in the experimental group (SLT: 328.96 ± 26.39 ; DLT: 314.35 ± 21.04) were significantly different from those in the control group (SLT: 306.75 ± 32.21 ; DLT: 300.76 ± 17.89) (P<0.05). As expected, the oxygenation index of the experimental group and the control group at 3 and 6 months after surgery improved when compared with

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Variables	Experimental group (n=38)	Control group (n=30)	P value
Sex			>0.99
Male	34 [89]	27 [90]	
Female	4 [11]	3 [10]	
Age (years)	52.37±10.87	52.13±8.06	0.653
BMI (kg/m²)	20.539±2.803	20.044±1.961	0.414
SLT	20.329±2.191	20.168±2.00	0.832
DLT	20.773±3.410	19.950±1.988	0.387
ECMO			0.096
With ECMO	19	9	
Without ECMO	19	21	
Duration of surgery (minutes)			
SLT	339.55±72.89	349.92±61.64	0.675
DLT	560.17±114.48	539.76±121.93	0.613
Type of transplant			0.446
SLT	20 [53]	13 [43]	
DLT	18 [47]	17 [57]	
Pulmonary complications			
SLT	8 [21.05]	7 [23.33]	0.435
DLT	15 [39.47]	16 [56.33]	0.316
ICU stay (days)			
SLT	14.05±3.14	17.77±3.24	<0.01
DLT	24.61±4.83	28.24±4.63	0.03
Chest tube (days)			
SLT	13.80±2.78	16.23±3.63	0.04
DLT	23.50±3.63	26.59±3.30	0.01

Table 4 General data of patient series

Data are presented as n [%] or mean ± standard deviation. BMI, body mass index; DLT, double lung transplant; SLT, single lung transplant; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

those before surgery (*Table 6*). The VC, FEV₁ and MVV at 3 months after unilateral LTx and bilateral LTx in the experimental group were significantly different from those in the control group (P<0.05). The VC, FEV₁ and MVV of the experimental group and the control group at 3 and 6 months after surgery were statistically significant compared with those before surgery (P<0.05) (*Table 6*).

Comparison of 6MWD 3 months after LTx

The 6MWD in the experimental group with SLT was

394.15±41.06 meters at 3 months after surgery, whereas the 6MWD in the control group with SLT was $357.85\pm$ 35.57 meters at the same time point (*t*=2.6113, P=0.01). Likewise, the 6MWD for DLT in the experimental group with DLT was 331.50 ± 48.84 meters, whereas it was 296.94±38.58 meters for the control group at 3 months after surgery (*t*=2.3804, P=0.02).

Discussion

It is established that pulmonary rehabilitation programs

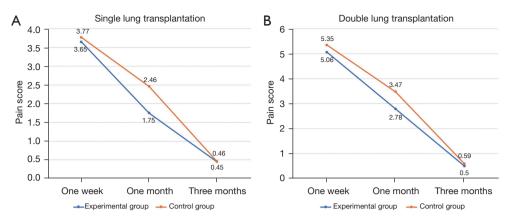


Figure 2 Pain scores. (A) Pain scores of experimental and control groups in single lung transplant recipients. (B) Pain scores of experimental and control groups in double lung transplant recipients.

Item	Type of transplant	Experimental group (n=38)	Control group (n=30)	P value
SGRQ	Pre-operation			
	SLT	49.65±8.98	53.15±9.21	0.675
	DLT	61.00±4.21	62.00±4.27	0.613
	Post-operation			
	SLT	38.75±8.26	50.69±8.61	<0.01
	DLT	49.28±7.30	57.47±5.85	<0.01
Pain score	SLT			
	1 week	3.65±0.93	3.77±0.73	0.699
	1 month	1.75±0.72	2.46±0.52	<0.01
	3 months	0.45±0.51	0.46±0.52	0.950
	DLT			
	1 week	5.06±0.87	5.35±0.93	0.337
	1 month	2.78±0.73	3.47±0.87	0.016
	3 months	0.50±0.62	0.59±0.62	0.676

Table 5 Comparison of perioperative results

Data are presented as mean ± standard deviation. DLT, double lung transplantation; SGRQ, St. George's Respiratory Questionnaire; SLT, single lung transplantation.

are safe and effective post LTx. Pulmonary rehabilitation is a key component of perioperative management of lung transplant patients (16-18). These interventions have long been beneficial to patients and have improved their QoL (3,4,19). In this study, the pulmonary rehabilitation program was initiated within 24 hours of surgery after the appropriate evaluations. The respiratory therapist was responsible for the coordination of care. An individualized, early, loadbearing respiratory training program was developed by the principle of gradual progression, transitioning from passive to active movement. Our results show that our program had statistically significant improvements in lung function, functional exercise capacity, and QoL.

Pulmonary rehabilitation effectively improves pulmonary function by increasing the strength and endurance of respiratory muscles, relieving respiratory muscle damage

literer	Oreure	Stage		
Item	Group	Pre-transplant	3 months post-transplant	6 months post-transplant
Oxygenation index (mmHg)	SLT			
	EG	162.76±26.67	328.96±26.39* [†]	$385.89 \pm 17.13^{\dagger}$
	CG	158.42±28.43	$306.75 \pm 32.21^{\dagger}$	$393.10\pm39.33^{\dagger}$
	DLT			
	EG	157.62±27.24	314.35±21.04* [†]	373.92±25.26 [†]
	CG	156.11±26.51	$300.76 \pm 17.89^{\dagger}$	$360.20\pm21.76^{\dagger}$
VC (L)	SLT			
	EG	1.99±0.21	2.47±0.15* [†]	$3.02\pm0.14^{\dagger}$
	CG	1.96±0.16	$2.28 \pm 0.28^{\dagger}$	$2.93\pm0.26^{\dagger}$
	DLT			
	EG	1.81±0.24	2.29±0.09* [†]	$2.85\pm0.21^{\dagger}$
	CG	1.77±0.23	$2.03\pm0.48^{\dagger}$	$2.81\pm0.23^{\dagger}$
FEV ₁ (L)	SLT			
	EG	1.51±0.22	2.58±0.22* [†]	2.95±0.29* [†]
	CG	1.49±0.18	$2.34{\pm}0.27^{\dagger}$	$2.71\pm0.26^{\dagger}$
	DLT			
	EG	1.42±0.21	2.39±0.16* [†]	2.67±0.15* [†]
	CG	1.46±0.28	$2.05 \pm 0.29^{+}$	$2.55\pm0.16^{\dagger}$
MVV (L)	SLT			
	EG	54.06±5.86	75.86±4.60* [†]	86.22±5.93 [†]
	CG	54.78±4.19	$69.52 \pm 4.48^{\dagger}$	81.96±7.12 [†]
	DLT			
	EG	48.84±4.49	61.28±7.09* [†]	68.72±5.28* [†]
	CG	48.10±6.90	$54.96 \pm 4.54^{\dagger}$	$63.91 \pm 3.91^{\dagger}$

Table 6 Changes in oxygenation index before and after lung transplantation

Data are presented as mean \pm standard deviation. *, significant compared with the control group (P<0.05); [†], significant compared with pre-transplant (P<0.05). CG, control group; EG, experimental group; SLT, single lung transplantation; DLT, double lung transplantation; VC, vital capacity; FEV₁, forced expiratory volume in one second; MVV, maximum ventilatory volume.

and fatigue. Wickerson (20) found that the maximum and functional exercise capacity, skeletal muscle strength, and health-related QoL metrics are improved at 1 month post-transplantation with sustained benefit for at least 6 months. As expected, the oxygenation indexes in both the control and the experimental group were significantly improved compared to preoperative values at 3 and 6 months after LTx. Interestingly, the oxygenation index in the experimental group at 3 months after surgery was significantly better than that in the control group. However, by 6 months the parameters in the experimental group were higher than those in the control group, but with no statistical significance. The results of this study are consistent with previous research, demonstrating that the pulmonary rehabilitation programs, like the one proposed in this study can promote early pulmonary function recovery in patients.

As demonstrated by Langer *et al.* (8,21), the implementation of a pulmonary rehabilitation program for recipients has been shown to effectively improve exercise

capacity, and QoL. Similarly, our program showed a significant improvement in the 6MWD after 3 months compared to the control group for both SLT and DLT recipients (SLT: 394.15 vs. 357.85 meters; DLT: 331.50 vs. 296.94 meters). These results suggest that the pulmonary rehabilitation program can promote early improvement in functional exercise capacity for LTRs.

Langer *et al.* (8) investigated the effects of 3 months of exercise training in LTx patients immediately after surgery and compared it with a control group that received no intervention. The results showed that LTx patients who underwent exercise training immediately after surgery significantly improved their QoL during training, consistent with our results.

Hutchins *et al.* (22) found that 49% of LTRs had pain in different areas. In their study, the prevalence of the syndrome itself (thoracotomy scar pain) after thoracotomy was 33%. This is consistent with the prevalence of chronic pain after thoracotomy for other indications. This explains to a certain extent why short-term pain after LTx in LTRs had no significant relationship with whether pulmonary rehabilitation training was performed.

Limbos (23) showed that LTx patients have poorer QoL than normal individuals. This may be partially explained by increased depression and anxiety as reported by Vermeulen (24). To combat this, we provided health education to patients in one-on-one sessions and in group therapy. We found that QoL improved significantly to be within the normal score range. Therefore, we recommend that mental health disorders should be screened for and treated as part of any pulmonary rehabilitation program post LTx.

The lung is in constant communication with the external environment for a long time. The external microorganisms, the microorganisms of the donor lung itself, and the use of immunosuppressants increase the risk of lung infection. According to the 2022 report of the International Society for Heart and Lung Transplantation (25), infection is the most common cause of death after LTx. In this study, the incidence of infection in the experimental group was lower than that in the control group in both single and bilateral LTx patients, but the difference was not statistically significant, which may be related to the sample size of this study.

Limitations

This study has several limitations. First, the sample size of

LTRs was small and the results reported herein may not be generalizable to other transplant populations. Second, this study lacked long-term follow-up of participants, making it impossible to obtain long-term survival rates and QoL for the cases. Third, the analysis did not take into account other medical factors that could have had an influence in the transplant outcomes, and therefore, some degree of bias must be taken into account. Fourth, our study was conducted among recipients who were stable after surgery and thus cannot be representative of all LTR patients.

Conclusions

The pulmonary rehabilitation program for patients after LTx established in this study is safe and feasible in clinical practice, which might have a role in shortening of ICU and hospital stay, improve patients' exercise ability and lung function, and improve patients' QoL.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Shanghai Pulmonary Hospital (No. Q21-347) and informed consent was taken from all the patients.

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