

Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-23-1774>

Reviewer A

The manuscript entitled "Evaluation of the construction and application effect of a postoperative pulmonary rehabilitation training program for lung transplant patients" has been reviewed. My recommendations are depicted below:

General:

The MS describes a benefit of pulmonary rehabilitation on the clinical outcomes following single and double lung transplantation.

It is a retrospective study comparing the outcomes in a group of patients who did and did not undergo pulmonary rehabilitation.

For the most part the MS is well written and easy to read.

Comment 1: A major question is, do you routinely collect pain data and SGRQ score in all transplant patients even if not recruited in the study? If that is so, please state as such and include that this data was retrieved by a chart review.

Was this data collected from the electronic medical records or the paper charts?

Reply 1: The ICU nurses would record the pain status of all lung transplant patients on a daily basis, and record the pain score on the electronic nursing record sheet. We collected the pain data by retrieving the electronic nursing record sheet. SGRQ scores were collected regularly by members of the pulmonary rehabilitation team, and only the recruited patients in the study were collected through a questionnaire survey.

Comment 2: The study data in the control group, was this collected prospectively or just retrieved from the chart? Please answer the same question for the study group.

Reply 2: The data of the control group were obtained by retrieving patient history and nursing records, except for the SGRQ score (which was obtained by questionnaire survey of patients by members of the pulmonary rehabilitation team). The study group's data is same.

Comment 3: How long in advance did you plan the study prior to implementing the rehabilitation program?

Reply 3: We planned the study three months in advance. We first developed a pulmonary rehabilitation training plan and revised it through two rounds of expert consultations, which took two months. In addition, we recruited members of the pulmonary rehabilitation team and conducted corresponding training and assessment for all members, which took about 1 month. At the same time as the pulmonary rehabilitation group was established, we began to collect corresponding data for the control group.

Comment 4: In the control group 14 patients underwent LTx for "Acute exacerbation of COPD". This doesn't seem to be correct practice? Please support your practice with substantial evidence.

Reply 4: "Acute exacerbation of COPD" refers to "severe COPD" here, which is a mistake in our expression. We have modified our text (see Page 7, line 318-322).

Changes in the text: 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.

Comment 5: In the "Evaluation indicators" section please provide the frequency of data collection for each of the indicators.

Reply 5: We added the frequency of data collection for each of the indicators (see Page 6, line 269-273).

Comment 6: The title of the MS is too wordy, please revise.

Reply 6: Change to "The efficacy of pulmonary rehabilitation training program for patients after lung transplantation".

Comment 7: Term "Lung Rehabilitation" is misleading, consider using the term "Pulmonary Rehabilitation". Please use this term all throughout the MS. Else describe the difference between "Lung" and "Pulmonary Rehabilitation".

Reply 7: We have modified our text as advised.

Comment 8: Please change the statement "However, he did not compare....." to "However, authors did not compare...." [Line 103]

Reply 8: We have modified our text as advised (see Page 4, line 135-137).

Changes in the text: 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.

Comment 9 : Change the sentence "Patients undergoing lung transplantation at the Shanghai Pulmonary Hospital from January 2021 to December 2022 were recorded." to "..... were included in the study." [Lines 117-118]

Reply 9: We have modified our text as advised (see Page 4, line 151-152).

Changes in the text: Patients undergoing lung transplantation at the Shanghai Pulmonary Hospital from January 2021 to December 2022 were included in the study.

Comment 10: "A total of 68 patients were included in this study, using non-synchronous controlled experimental research methods, including 38 patients who received LTx in 2022 as the experimental group (Figure 1A), and 30 patients who underwent LTx in 2021 as the control group (Figure 1B). The general information of the participants is shown in Table 1." This information belongs to the result section! [Lines 125-129]

Reply 10: We have deleted this part.

Comment 11: Typo: Lines 154-155, "Each" has been used twice.

Reply 11: We have deleted one “each” (see Page 5, line 224).

Comment 12: Typo: Line 157: ,,

Reply 12: We have deleted one “,”.

Comment 13: “Quality Management” and “Intervention for the control group” sections needs to be written in past tense.

Reply 13: We have modified our text as advised (see Page 6, line 245-263).

Comment 14: Baseline information comparison: Silicosis is also an occupational lung disease. Use a term, “Other occupational lung diseases” to describe other entities.

Reply 14: We have modified our text as advised (see Page 7, line 318-321).

Changes in the text: 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.

Comment 15: Please provide definition of the oxygenation index.

Reply 15: We added the definition of the oxygenation index (see Page 8, line 364).

Changes in the text: The oxygenation index is a measure of the efficiency of oxygen exchange by the lungs.

Comment 16: Discussion section: There are two subsets of conclusions! They need to be merged.

Reply 16: We have modified our text as advised.

Comment 17: Omit figure 1

Reply 17: We have omitted figure 1.

Comment 18: Typo: Table 5 [Oxygenation index]

Reply 18: We have modified our text as advised (see Page 22, line 707)

Reviewer B

Thank you for inviting me to review the article titled “Evaluation of the construction and application effect of a postoperative pulmonary rehabilitation training program for lung transplant patients”. I would like to commend the authors of this paper for studying this essential topic and finding measurable outcomes to report. Postoperative pulmonary rehab is one of the necessary tools to allow for better outcomes in the immediate postoperative period which will undoubtedly improve long term lung transplant outcomes.

Dedicated pulmonary rehabilitation is rare in the postoperative lung transplant recipient however the management used in this study has been reported in various studies without defined

measurable outcome. I believe this paper is an essential addition to the literature as it may motivate further research in the area.

I have the following feedback for the authors.

The small sample size presents challenges in comparing the number of variables in the study. Regardless, it appears that pulmonary rehabilitation is safe and effective in reducing ICU length of stay. As a single center study, there will be bias in terms of internal practices. While it would be ideal for this to be extended to a multi center experience, this may have challenges due to practice differences amongst centers.

Comment 1: Please elaborate on specific time frame for inclusion/exclusion criteria.

Reply 1: We added one inclusion criteria as advised (see Page 4, line 156-157).

Changes in the text: (V) Patients undergoing lung transplant surgery between January 2021 and December 2022.

Comment 2: Line 175: Please list ‘other activities’ from control group.

Reply 2: We added the details of the control group in pulmonary rehabilitation training (see Page 6, line 258-263).

Changes in the text: 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*).

Table 3: Pulmonary rehabilitation training for control group.

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	(1) Lung transplantation's expectations; (2) the necessity of the ECMO support therapy and mechanical ventilation; (3) the effectiveness and necessity of pulmonary rehabilitation; (4) respiratory function training method; (5) exercise training methods.		

Mental nursing	Nurses combined with family members of patients provided psychological support for patients.
-----------------------	--

Reviewer C

In this work, Jie Mei, et al report their experience following the implementation of a new rehabilitation program training after lung transplantation in their LTx center in Shanghai. To assess the potential benefits effects of this program, they compared some end-point during peri- and post-LTx between a cohort of LTx recipients with this experimental rehab program and an historical control group.

The advantage of rehabilitation program remains a crucial issue in the field of lung transplantation. The authors should be congratulated for their laborious work to assess the effect of their new rehab program. Nevertheless, important issues are to be considered to assess precisely the additional value of the rehab: in particular, the selection of the historical patients should be precised; additional data concerning characteristics should be provided to better check that the 2 groups are similar; other statistical tests should be performed comparing the 2 groups; modifications of what was really performed as a rehab program in the historic control group and the experimental group should be clearly included in Tables, short-term survival of patients seems also interesting for the readers (see below).

Comment 1: Modifications of the rehabilitation program from the controls group period to the experimental group period.

The authors have planned a pulmonary rehabilitation training plan for the experimental group, which is detailed in Table 3. A large number of ITEMS in this program have been included in this Table 3. It includes, among many other ITEMS (n > 15 ITEMS), nebulizations for airway clearance; for example: gradual reduction of the ECMO flow for ECMO assistance; breathing trainer for respiration training; etc, ... Among the ITEMS of the program, numerous ITEMS are concerning standard of care clinical practice, such as protective ventilation, switch to NIV after extubation, cough training. The authors should separate clearly all ITEMS of the program that were applied in the historic control group, and all those which were exclusively implanted as a new rehab program in the experimental program.

In the application of the rehab program, both period of pre-LTx and post-LTx period are concerned by implementations of new aspect in the rehab program, as compared, if I well understand, with the historic control groups. Again, in the same way, this should also be stated in the methods, separating all aspects of the program which was already performed in the historical controls and those in the pre-LTx exclusively performed in the experimental group. This concern also the paragraph beginning line 168: details of what were really performed as rehab in the control groups.

These suggestions and modifications of what was really performed as a rehab program in the historic control group and the experimental group, respectively, will allow a better comparison of outcome among the 2 groups.

Reply 1: We added the details of the control group in pulmonary rehabilitation training (see Page 6, line 258-263).

Changes in the text: 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*).

Table 3: Pulmonary rehabilitation training for control group.

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	(1) Lung transplantation's expectations; (2) the necessity of the ECMO support therapy and mechanical ventilation; (3) the effectiveness and necessity of pulmonary rehabilitation; (4) respiratory function training method; (5) exercise training methods.		
Mental nursing	Nurses combined with family members of patients provided psychological support for patients.		

Comment 2: Number of patients included in the 2 groups.

the number of patients from the historical group who were excluded for “postoperative conditions that make it difficult to cooperate with pulmonary rehabilitation training”, those with “inability to comprehend or to communicate”, and those with “unwillingness to participate in the study or inability to cooperate with long-term follow-up”, should be mentioned.

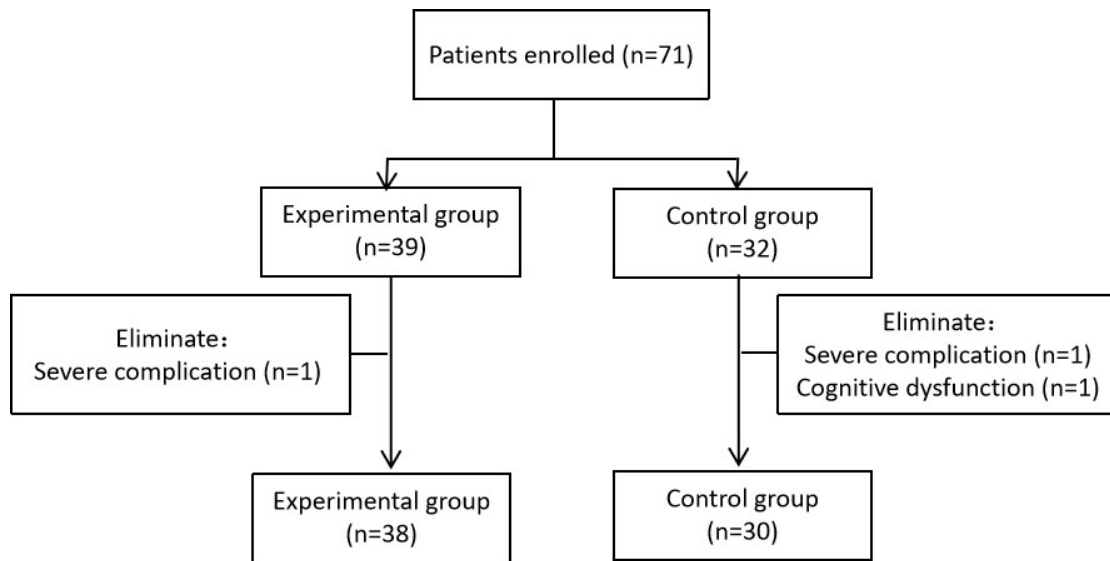
The number of patients excluded in the experimental period, if any, should be mentioned.

A flow-chart of patients could be provided to add for the clarity for the readers.

This is an important aspect, because it will possibly allow to assess a possible bias with the comparison with the historic arm control. In all cases, this probably may introduce a bias when comparing the 2 groups, because such patients with “inability to understand” were not excluded from the control group.

Reply 2: We added the flowchart as you suggested (see Page 16, line 667-668).

Changes in the text:



Comment 3: Short-term survival results: I would suggest to add short-term results of survival of the 2 groups, for example at 9-12 months post-LTX, an end-point available for the 2 groups.
 Reply 3: Due to the time limitation of this study, the data of survival outcomes of patients 9-12 months after lung transplantation have not been collected at present, and we will continue to pay attention to the survival results of patients in the later stage.

Comment 4: Comparison of the 2 groups.

Results of the study show significant difference for early end-point functional results between the 2 groups, such as for 6WT at 3 months, oxygenation at 3 months.

From the significant difference, they make the hypothesis that such differences between the 2 groups are due to the difference of rehab applied in the 2 groups. In an attempt to increase the evidence of the gain from rehab, I would suggest first to include a greater number of the characteristics of the 2 groups in Table 1, that may influence the early/late functional outcome, such as other characteristics of recipients, donors, surgical procedure, immunological data: 1 Known significant extra-thoracic disease in LTx candidates of the 2 groups: such as coronary disease, (detection (or not) of preformed donor-specific antibody (DSA), initial disease (to be compared in table 1) ,2/ Body mass index (BMI) in preTx and obesity before Tx (>30 BMI), 3/ use of superemergency procedure (or not) if available in the center, 4/use of ECMO in perioperative period, 5/ use of induction therapy (or not), 6/presence of CMV mismatch (D+/R-) and to perform a comparison of each characteristics between the 2 groups. If significant differences are observed, other statistical tests should be performed to exclude potential bias that could explain significant differences in 6WT and O2 at 3 months between the 3 groups.

Reply 4: We added the general data in Table 4 (see Page 21, line 695).

Changes in the text:

Table 4: General data of patient series.

	Experimental group (n=30)	Control group (n=38)	P value
Sex			
Male	34(90)	27 (90)	
Female	4 (10)	3 (10)	

Age (years)	52.37±10.87	52.13±8.06	
BMI	20.539±2.803	20.044±1.961	0.630
SLT	20.329±2.191	20.168±2.00	0.912
DLT	20.773±3.410	19.950±1.988	
ECMO			
With ECMO	19	9	0.083
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			
SLT	20 (52)	13 (43)	
DLT	18 (48)	17 (57)	
Pulmonary complications			
SLT	8 (40)	7 (53)	0.44
DLT	15 (83)	16 (94)	0.32
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

DLT: Double lung transplant; SLT: Single lung transplant. Data are presented as n (%) or mean ± SD. ECMO: extracorporeal membrane oxygenation.

Comment 5: There was no significant difference of pain scores at 1 week and 3 months between the 2 groups. This result appears rather unanticipated if we keep in mind that this modified rehab program applied in the experimental group should rather lead towards lower global pain. This lack of difference for pain among the 2 groups seems also in contradiction with the better SGRQ observed in the experimental group. Could the authors have a comment about the lack of difference in pains reported between the 2 groups?

Reply 5: Because the patient experienced surgical trauma and had more indwelling catheters in the first week after surgery, doctors would pay more attention to the patient's pain, and relatively more sedative and analgesic drugs were used, so the patient's pain was at a high level. With postoperative recovery process, the patients with surgical trauma effect is abate, along with all kinds of support measures to reduce life, lien pipeline decreases, the patient pain gradually ease, the 3 months postoperatively, the patient pain is at a relatively low level. In this study, the mean pain score of the experimental group was lower than that of the control group, and the difference was not statistically significant, which may be related to the relatively small sample size of this study.

Comment 6: In the discussion paragraph (line 267): Could the authors cite some reference, after their introducing sentence saying that “Long term these interventions (rehabilitation programs) also improve survival “, for the survival item?

Reply 6: We added some references and modified this sentence in the text (see Page 14, line 609-621).

References:

1. Florian J, Watte G, Teixeira PJZ, Altmayer S, Schio SM, Sanchez LB, Nascimento DZ, Camargo SM, Perin FA, Camargo JJ, Felicetti JC, Moreira JDS. Pulmonary rehabilitation improves survival in patients with idiopathic pulmonary fibrosis undergoing lung transplantation. *Sci Rep.* 2019 Jun 27;9(1):9347. doi: 10.1038/s41598-019-45828-2. PMID: 31249363; PMCID: PMC6597536.
2. Hume E, Ward L, Wilkinson M, Manifold J, Clark S, Vogiatzis I. Exercise training for lung transplant candidates and recipients: a systematic review. *Eur Respir Rev.* 2020 Oct 28;29(158):200053. doi: 10.1183/16000617.0053-2020. PMID: 33115788; PMCID: PMC9488968.
3. Wu T, Zhou S, Wu B, Chen J, Zhu X, Cai Y. The effect of early tracheal extubation combined with physical training on pulmonary rehabilitation of patients after lung transplantation: a randomized controlled trial. *J Thorac Dis.* 2022 Apr;14(4):1120-1129. doi: 10.21037/jtd-22-119. PMID: 35572910; PMCID: PMC9096297.

Changes in the text: These interventions have long been beneficial to patients and have improved their quality of life.

Reviewer D

This study described respiratory rehabilitation in the perioperative period of lung transplantation (LTx). It has been previously reported that rehabilitation for pre- and post-LTx improves lung function, exercise tolerance, and health-related quality of life, the content of this study was not novel. Although the importance of comprehensive respiratory rehabilitation is noted, it is inadequately evaluated in terms of respiratory subjective symptoms, pulmonary function, physical function, and psychological assessment.

Comment 1: Regarding Evaluation indicators, authors list as an evaluation indicator, postoperative pulmonary infection rate and pre- and post-operative pulmonary function tests as an evaluation item, but we can't find them. Lung function is essential. This is because it concludes that lung function has improved. Without the results of this test, it is impossible to evaluate lung function. Similarly, the incidence and severity of postoperative complications and pre- and postoperative quality of life scores, but we could not find these either. This information is necessary for safety assessments and comparisons between groups.

Reply 1: In the first draft, we actually compared and analyzed the lung function of patients before and after surgery, but considering that there were too many data, it would make the article lengthy, so the analysis of the corresponding data was deleted. According to your suggestion, we realized the importance of lung function data, so we increased the analysis of relative data again (see Page 8 line 369-374 and Table 6).

Comment 2: About the research group, criteria is not clear. In the inclusion criteria, that should be based on specific and objective numbers, not on vague criteria such as stable vital signs after surgery. Exclusion criteria should provide specific and objective criteria for severe postoperative conditions.

Reply 2: We modified our Inclusion and exclusion criteria (see Page 4 line 151-159, Page 5 line 197-200 and Table 5).

Changes in the text: Patients undergoing lung transplantation at the Shanghai Pulmonary Hospital from January 2021 to December 2022 were included in the study. Patients who met all of the following standard were included in the study: (I) aged 18-75 years; (II) successful lung transplantation; (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 long-term follow-up. This study was approved by the Ethics Committee of Shanghai Pulmonary Hospital (No. Q21-347).

Comment 3: Since it is considered an important part of comprehensive respiratory rehabilitation, it should be specifically mentioned in the content of pre-lung transplant health education, pre-rehabilitation training, and adaptive training.

Reply 3: We added the details of the control group in pulmonary rehabilitation training (see Page 6, line 258-263 and Table 3).

Changes in the text: 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*).

Table 3: Pulmonary rehabilitation training for control group.

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	(1) Lung transplantation's expectations; (2) the necessity of the ECMO support therapy and mechanical ventilation; (3) the effectiveness and necessity of pulmonary rehabilitation; (4) respiratory function training method; (5) exercise training methods.		

Mental nursing	Nurses combined with family members of patients provided psychological support for patients.
-----------------------	--

Minor comments

Comment 4: Statistical methods not used in this analysis should not be described.

Reply 4: We deleted one paragraph in the text (see Page 7).

Comment 5: Basic patient data such as height and weight are necessary to understand the analysis population.

Reply 5: We added some basic patient data in the text (including BMI, duration of surgery, etc.) (see Page 7 line 321-322 and Table 4).

Comment 6: About the discussion, no data on upper or lower extremity muscle strength, respiratory muscles, or mental health can be discussed in this study.

Reply 6: We do have these issues, and we've removed the stuff related to muscle strength, respiratory muscle strength and mental health (see Page 9).

Comment 7: It should be added to the study limitations that this study was conducted on recipients whose postoperative status was stable.

Reply 7: We added this limitation in the text (see Page 11, line 480-482).

Changes in the text: Fourth, our study was conducted among recipients who were stable after surgery and thus cannot be representative of all LTR patients.

Comment 8: As the authors pointed out, a multidisciplinary and comprehensive respiratory rehabilitation is very important for lung transplant patients. We look forward to future research.

Reply 8: Further studies will be conducted as soon as possible. Thank you.

Reviewer E

The potential novelty and contribution of this paper was its promise to describe the process the authors used to develop a lung transplant specific pulmonary rehabilitation protocol, the inclusion of a replicable pulmonary rehab protocol, and rigorous evaluation of its efficacy. Yet the authors did not meet these expectations. The process for developing the intervention is anecdotal and not scientific. There is no conceptual model provided to justify the selection of elements of the rehab program (physical, mental and behavioral) or how it may overcome the barriers that LTRs face participating in conventional PR programs, or the role that LTRs play in learning self-management, behavior change techniques to sustain the effects. A description of the published evidence to justify the inclusion of elements in the experimental intervention versus standard care is lacking. If Table 3 is intended to reflect the actual protocol for the experimental condition, it lacks adequate detail regarding steps, indications for readiness, individual customization, initiation, or timing of delivery to guide any attempt by others to replicate the intervention. Table 3 does not address the mental health aspects or behavior change

techniques for the successful rehab program the authors claim to have developed. Rationale for the selection of outcome variables that are sensitive to the intervention, the specific measures, and the timing of early and longer-term assessment intervals are lacking. In general, there is no evidence that the experimental condition is unique to LTRs or different from usual post-operative clinical management of LTRs.

Below are a few specific comments; this is not an exhaustive list of issues which were too many to mention.

Comment 1: Line 36: authors should consistently use the conventional term: “pulmonary” rehab throughout the paper and delete “lung” rehab

Reply 1: We modified our text as advised.

Comment 2: Line 42: provide examples of some other therapeutic methods that are neglected

Reply 2: We have modified our text as advised (see Page 2, line 44-45).

Comment 3: Line 45: Convenience sampling without discussion of recruitment rates or how representative the final sample of LTRs was of the program or LTRs in general.

Reply 3: We have modified our text as advised (see Page 2, line 48-51).

Changes in the text: 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.

Comment 4: Methods: the description of the study design is unclear. Line 47 the use of term “controlled experimental design” does not seem appropriate, perhaps “quasi” experimental design?

Reply 4: We have modified our text as advised (see Page 2, line 51).

Comment 5: Line 109 mentions a retrospective assessment of outcomes comparing results pre and post implementation of the rehab intervention. Line 126 mentions using non-synchronous controlled experimental research methods

Reply 5: We modified our text (see Page 4, line 140-143).

Changes in the text: We then compared the result of the implementation of multi-disciplinary comprehensive rehabilitation program with the result of receiving the routine rehabilitation program at our hospital one year before.

Comment 6: Line 49-50: Describe specifics of control group intervention and experimental intervention conditions.

Reply 6: We added the details of the control group in pulmonary rehabilitation training (see Page 6, line 258-263).

Changes in the text: 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*).

Table 3: Pulmonary rehabilitation training for control group.

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	(1) Lung transplantation's expectations; (2) the necessity of the ECMO support therapy and mechanical ventilation; (3) the effectiveness and necessity of pulmonary rehabilitation; (4) respiratory function training method; (5) exercise training methods.		
Mental nursing	Nurses combined with family members of patients provided psychological support for patients.		

Comment 7: Line 51: it is unclear when in the peri-operative period the experimental rehab intervention starts. Line 149 mentions that in the ICU the experimental group is assigned a PR team, yet the team conducts an assessment of the patient before surgery and initiates education and training pre-op. Is the pre-op assessment and training part of standard care or only the experimental condition? When exactly is the pre-transplant assessment performed (at the time of listing or once a donor is identified and transplant is scheduled)? The timing is critical since times on the transplant wait list vary so the duration of training will vary between LTRs. Some of the experimental rehab intervention was delivered (while LTRs were still hospitalized)? And when the outcome variables to evaluate the “effect” of the intervention were measured.

Reply 7: We have added a specific period when the experimental rehab intervention starts (see Page 2, line 53-55). The pre-op assessment and training is only the experimental condition. The pre-transplant assessment is performed at the time that the transplantation is scheduled, which partially reduced the bias of the experimental results due to differences in the duration of rehabilitation training. Some patients were waiting in the hospital for lung transplantation, while others were waiting at home. When lung transplantation is scheduled, the patient who is waiting at home is urgently admitted to the hospital and has some appropriate preoperative workup, at which time the pulmonary rehabilitation team will deliver the patient the experimental rehab intervention. Therefore, we only taught the patients some specific practices of pulmonary rehabilitation training before surgery to ensure that the patients could cooperate

with the training after surgery, rather than conducting pulmonary rehabilitation training for the patients who were already in the hospital for a period of time.

Comment 8: Line 57: Use the term “Results or Findings” of oxygenation index, 6MWD, and St. George’s Respiratory Questionnaire were better, instead of the “number of”

Reply 8: We have modified our text as advised (see Page 2, line 62).

Comment 9: Lines 63-65: safety outcomes? Check spelling and punctuation

Reply 9: We have modified our text as advised (see Page 2, line 82).

Changes in the text: 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.

Comment 10: Line 67: Why nursing care? This is supposedly a multi-disciplinary approach

Reply 10: We have modified our text as advised (see Page 2, line 84-85).

Comment 11: Line 75: The references cited refer to impact of pre-operative interventions for lung cancer, be more specific about this claim as the evidence for LTRs and post-operative management

Reply 11: We have modified our references 5-7 and our text (see Page 2, line 93-94).

Changes in the text: Studies have shown that early intervention after lung transplantation has more advantages in reducing complications and improving lung function and QoL (5-7).

Comment 12: Line 90-91: The claim that no PR training programs specifically for LTRs overlooks the work described in several publications about lung transplant specific exercise protocols

For example:

- Langer D, Burtin C, Schepers L, Ivanova A, Verleden G, Decramer M, Troosters T, Gosselink R. Exercise training after lung transplantation improves participation in daily activity: a randomized controlled trial. *Am J Transplant*. 2012 Jun;12(6):1584-92. doi: 10.1111/j.1600-6143.2012.04000.x. Epub 2012 Mar 5. PMID: 22390625 Q1 . Additional Supporting Information about the exercise protocol may be found in the on-line version of this article
- Wickerson L, Rozenberg D, Janaudis-Ferreira T, Deliva R, Lo V, Beauchamp G, Helm D, Gottesman C, Mendes P, Vieira L, Herridge M, Singer LG, Mathur S. Physical rehabilitation for lung transplant candidates and recipients: An evidence-informed clinical approach. *World J Transplant*. 2016 Sep 24;6(3):517-31. doi: 10.5500/wjt.v6.i3.517 . PMID: 27683630; PMCID: PMC5036121.
- Hergenroeder AL, Willey B, Vendetti M, Dabbs AD. Exercise Progression Protocol for Lung Transplant GO: A Multicomponent Telerehab Exercise Intervention for Patients After Lung Transplantation. *Cardiopulm Phys Ther J*. 2023 Jan;34(1):2-12. doi: 10.1097/CPT.000000000000203 . Epub 2022 Mar 23. PMID: 36644217; PMCID: PMC9838685.

Reply 12: Most of the published articles on pulmonary rehabilitation training for LTR are single exercise training, while the pulmonary rehabilitation training we mentioned is a comprehensive training, including exercise training, respiratory training, pain management, etc. We made a mistake in our presentation, which has now been corrected (see Page 3, line 108-111).

Changes in the text: 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.

Comment 13: Line 98: The authors provide no citations to support the claim: In addition, the low level of psychological and social attention given to patients makes it difficult to ensure their physical and mental safety.

Reply 13: We added one citation to support the claim (Smith, PJ, Snyder, LD, Palmer, SM, et al. Depression, social support, and clinical outcomes following lung transplantation: a single-center cohort study. *Transplant International*. 2018;31: 495-502.).

Comment 14: Line 117: eligibility criteria such as “stable vital signs after surgery” make it difficult to determine the generalizability of the program to all LTRs

Reply 14: We modified our Inclusion and exclusion criteria (see Page 4-5, line 152-197).

Changes in the text: Patients undergoing lung transplantation at the Shanghai Pulmonary Hospital from January 2021 to December 2022 were included in the study. Patients who met all of the following standard were included in the study: (I) aged 18-75 years; (II) successful lung transplantation; (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 long-term follow-up. This study was approved by the Ethics Committee of Shanghai Pulmonary Hospital (No. Q21-347).

Comment 15: Line 118: clarify what is meant by “were recorded”

Reply 15: We made a mistake in our presentation, which has now been corrected (see Page 4, line 151-152).

Changes in the text: Patients undergoing lung transplantation at the Shanghai Pulmonary Hospital from January 2021 to December 2022 were included in the study.

Comment 16: All tables should report the “n” in all title or relevant column headers. Table 1 and 4 could be combined to compare between group differences in sample characteristics and outcomes. Hospital length of stay? Discharge destination between groups?

Reply 16: According to your suggestion, we have added "n" to all the tables, and we have merged part of the contents in Table 5 into Table 4 (see Page 21-22, line 695-700).

Changes in the text:

Table 4: General data of patient series.

	Experimental group (n=30)	Control group (n=38)	P value
Sex			
Male	34(90)	27 (90)	
Female	4 (10)	3 (10)	

Age (years)	52.37±10.87	52.13±8.06	
BMI	20.539±2.803	20.044±1.961	0.630
SLT	20.329±2.191	20.168±2.00	0.912
DLT	20.773±3.410	19.950±1.988	
ECMO			
With ECMO	19	9	0.083
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			
SLT	20 (52)	13 (43)	
DLT	18 (48)	17 (57)	
Pulmonary complications			
SLT	8 (40)	7 (53)	0.44
DLT	15 (83)	16 (94)	0.32
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

DLT: Double lung transplant; SLT: Single lung transplant. Data are presented as n (%) or mean ± SD. ECMO: extracorporeal membrane oxygenation.

Table 5 Comparison of perioperative results

	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	0.69
	1 month	1.75±0.72	2.46±0.52	<0.01
	3 months	0.45±0.51	0.46±0.52	0.95
	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

DLT, double lung transplantation; ICU: intensive care unit; SGRQ: St. George's Respiratory Questionnaire; SLT: single lung transplantation. Data are presented as n (%) or mean ± SD.

Comment 17: Many of the terms are not appropriate to their meaning in English (e.g., “rational” oxygen therapy, “evacuate” mechanical ventilation early).

Reply 17: We modified “rational” to “appropriate”, “evacuate” to “remove” (see Page 17-20, line 687-690, Table 2).

Reviewer F

Thank you for the opportunity to review this article. Constructive feedback has been diligently provided to enhance this valuable work, and more importantly to increase the benefit to the reader.

Overall, this paper is well-constructed, contributing to the current literature in terms scope of topic and aligning with existing findings. While it has some weaknesses, they do not interfere with the validity of the results.

The aim of this study is clearly presented as it assesses the outcomes of a postoperative pulmonary rehabilitation training program for 68 lung transplant patients.

Impact/Novelty

Several studies in the current literature support the positive outcomes of pulmonary rehabilitation after lung transplantation (Langer, Burtin et al. 2012, Song, Park et al. 2018, Andrianopoulos, Gloeckl et al. 2019, Candemir, Ergun et al. 2019, Hume, Ward et al. 2020, Kerti, Bohacs et al. 2021). Most notable is a recent study by (Kerti, Bohacs et al. 2021) which included 14 patients, however had no control group, and another study by (Langer, Burtin et al. 2012) which included 34 lung transplant patients, however dated. The study under review adds to the current literature by having a larger sample size than previous studies (therefore having more power) and including a control group. Moreover, this study does not only incorporate exercise training into its program but also includes training modules for ECMO and ventilation assistance in its rehabilitation program. This is the major aspect that sets it apart from previous studies.

A systematic review by (Gutierrez-Arias, Martinez-Zapata et al. 2021) claims that the evidence supporting the practice of exercise training in a lung transplant population is unclear, which calls for the demand of more evidence on this topic, which this study provides.

This study also has outcomes not previously analyzed, such as incidence of complications, ICU stay time, duration of chest tube drainage, pain scores, and oxygen index. However, an important indicator, FEV1, even though mentioned in evaluation indicators, was not included in the results section.

Strengths

The intervention procedures have been detailed in depth, and when combined with training modules (Table 3) allows easy reproducibility of this study.

There was appropriate use of statistical tests (Unpaired t-test for comparing two quantitative variables, and chi-square test for comparing categorical variables).

There was appropriate use of p values <0.05 for significance. Standard deviation and p values were provided for all outcome analysis.

Limitations section transparently describes how sample size and lack of long-term follow-up limited the study's power. It also mentions how the analysis did not consider other medical factors that could have influenced the transplant outcomes, although specific examples of such factors were not provided.

Tables and figures are clear making it easy for the reader to interpret the results.

Comment 1: The abstract is concise and reflects the most important findings except for the pain score outcomes which should be included in the results paragraph.

Reply 1: The description of the results in the abstract section is indeed missing and has been supplemented at present. We have added content in the abstract section (see Page 2, line 64-67).

Changes in the text: We have added content in the abstract section. "There was no significant difference in the pain of the two groups one week after surgery and three months after surgery, and the pain score of the experimental group was lower than that of the control group at one month after surgery ($p < 0.05$)."

Comment 2: Line 60, "adverse events" should be reworded to "complications" to reflect the same wording found in the paper's main results section maintaining consistency of phrasing.

Reply: We modified our text as you mentioned (see Page 6, line 250; Page 2, line 68).

Comment 3: Line 165, mentioning the follow-up's interval and total duration is important as evidence of consistency of protocol among all patients included. It also allows this study to be more accurately compared with other studies.

Reply 3: This study starts pulmonary rehabilitation program in 24 hours after surgery, the scheme to patients discharged from the hospital, a month after surgery and postoperative follow up three months for the patient (see Page 6, line 245-247).

Changes in the text: In this study, the pulmonary rehabilitation program was initiated within 24 hours after surgery and continued until the patients were discharged from the hospital. The patients were followed up at 1 month and 3 months after surgery.

Comment 4: Patient compliance/adherence should be addressed and whether non-compliant patients have been excluded or included in the analysis. Including non-compliant or lost-to-follow-up patients would classify this study as an intention-to-treat analysis, thereby enhancing its strength.

Reply 4: The inclusion and exclusion criteria for patients in this study were respecified, and patients who were unwilling to adhere to the pulmonary rehabilitation protocol or who had poor adherence were excluded (see Page 4-5, line 151-200).

Changes in the text: Patients who met all of the following standard were included in the study: (I) aged 18-75 years; (II) successful lung transplantation; (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 long-term follow-up.

Comment 5: This is also especially important as this study was conducted during the COVID-19 pandemic. It should be addressed how the isolation precautions and the quarantine affected the compliance and the application of the rehabilitation program.

Reply 5: In this study, all lung transplant patients were housed in a single room, in a separate

laminar flow unit during intensive care and in a single room during the ward, and all disinfection was performed according to uniform hospital regulations. During the ICU, the family members were not contacted. During the ward, the family members were fixed to accompany them. The ward was equipped with hand sanitizer, masks, isolation gowns, gloves and other materials with corresponding protection levels. The patients with abnormal nucleic acid refused to enter the ward. If the patient's nucleic acid was abnormal, the emergency treatment plan for COVID-19 confirmed patients was started to improve the level of protection.

Comment 6: Line 182, pulmonary function outcome mentioned in the evaluation indicators list is not mentioned in the results section.

Reply 6: We have supplemented the lung-function results (see Page 22-23, line 707-725).

Changes in the text:

Table 6: Changes in oxygenation index before and after lung transplantation.

Oxygenation index (mmHg)	Group	Stage		
		Pre-transplant	3 months post-transplant	6 months post-transplant
	EG	162.76±26.67	328.96±26.39* [#]	385.89±17.13 [#]
	CG	158.42±28.43	306.75±32.21 [#]	393.10±39.33 [#]
	DLT			
	EG	157.62±27.24	314.35±21.04* [#]	373.92±25.26 [#]
	CG	156.11±26.51	300.76±17.89 [#]	360.20±21.76 [#]
VC(L)	SLT			
	EG	1.99±0.21	2.47±0.15* [#]	3.02±0.14 [#]
	CG	1.96±0.16	2.28±0.28 [#]	2.93±0.26 [#]
	DLT			
	EG	1.81±0.24	2.29±0.09* [#]	2.85±0.21 [#]
	CG	1.77±0.23	2.03±0.48 [#]	2.81±0.23 [#]
FEV ₁ (L)	SLT			
	EG	1.51±0.22	2.58±0.22* [#]	2.95±0.29* [#]
	CG	1.49±0.18	2.34±0.27 [#]	2.71±0.26 [#]
	DLT			
	EG	1.42±0.21	2.39±0.16* [#]	2.67±0.15* [#]
	CG	1.46±0.28	2.05±0.29 [#]	2.55±0.16 [#]
MVV(L)	SLT			
	EG	54.06±5.86	75.86±4.60* [#]	86.22±5.93 [#]
	CG	54.78±4.19	69.52±4.48 [#]	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±4.54 [#]	63.91±3.91 [#]

* Comparison with the control group significant (p<0.05). [#] Comparison with pre-transplant is also significant (p<0.05). CG: control group; DLT: double lung transplantation; EG: experimental group; SLT: single lung transplantation.

Comment 7: Since the rate of complications between the intervention and the control group are similar, possible explanations for that should be addressed in the discussions section.

Reply 7: The similar complication rates are explained in the Discussion section (see Page 10, line 452-459).

Changes in the text: 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, infection is the most common cause of death after lung transplantation. In this study, the incidence of infection in the experimental group was lower than that in the control group in both single and bilateral lung transplantation patients, but the difference was not statistically significant, which may be related to the sample size of this study.

Reference: Perch M, Hayes D Jr, Cherikh WS, Zuckermann A, Harhay MO, Hsich E, Potena L, Sadavarte A, Lindblad K, Singh TP, Stehlik J; International Society for Heart and Lung Transplantation. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-ninth adult lung transplantation report-2022; focus on lung transplant recipients with chronic obstructive pulmonary disease. *J Heart Lung Transplant*. 2022 Oct;41(10):1335-1347. doi: 10.1016/j.healun.2022.08.007. Epub 2022 Aug 20. PMID: 36050206; PMCID: PMC10257980.

Comment 8: Line 267 and 337, the author should provide some reasoning behind the conclusion that these interventions would improve survival and quality of life. This is particularly important given that the study reported no difference in rate of complications or pain scores.

Reply 8: We added some references and modified this sentence in the text (see Page 9, line 393-394).

References:

1. Florian J, Watte G, Teixeira PJZ, Altmayer S, Schio SM, Sanchez LB, Nascimento DZ, Camargo SM, Perin FA, Camargo JJ, Felicetti JC, Moreira JDS. Pulmonary rehabilitation improves survival in patients with idiopathic pulmonary fibrosis undergoing lung transplantation. *Sci Rep*. 2019 Jun 27;9(1):9347. doi: 10.1038/s41598-019-45828-2. PMID: 31249363; PMCID: PMC6597536.

2. Hume E, Ward L, Wilkinson M, Manifold J, Clark S, Vogiatzis I. Exercise training for lung transplant candidates and recipients: a systematic review. *Eur Respir Rev*. 2020 Oct 28;29(158):200053. doi: 10.1183/16000617.0053-2020. PMID: 33115788; PMCID: PMC9488968.

3. Wu T, Zhou S, Wu B, Chen J, Zhu X, Cai Y. The effect of early tracheal extubation combined with physical training on pulmonary rehabilitation of patients after lung transplantation: a randomized controlled trial. *J Thorac Dis*. 2022 Apr;14(4):1120-1129. doi: 10.21037/jtd-22-119. PMID: 35572910; PMCID: PMC9096297.

Changes in the text: These interventions have long been beneficial to patients and have improved their quality of life.

Comment 9: Line 319, the assertion that the rehabilitation program is safe requires reporting whether any complications related to rehabilitation procedures have occurred.

Reply 9: No complications related to the rehabilitation procedure occurred during the study.

Comment 10: Line 71, use of the better reference is advised as the cited paper does not study lung transplantation as a treatment for end-stage lung disease, rather it only mentions it in its introduction.

Reply 10: We changed reference 1.

1.Meyer KC. Recent advances in lung transplantation. *F1000Res*. 2018 Oct 23;7:F1000 Faculty Rev-1684. doi: 10.12688/f1000research.15393.1. PMID: 30416706; PMCID: PMC6206601.

Comment 11: Line 75, these references do not mention the effectiveness of lung rehabilitation.

Reply 11: We changed reference 2-4.

2.Kerti M, Bohacs A, Madurka I, Kovats Z, Gieszer B, Elek J, Renyi-Vamos F, Varga JT. The effectiveness of pulmonary rehabilitation in connection with lung transplantation in Hungary. *Ann Palliat Med*. 2021 Apr;10(4):3906-3915. doi: 10.21037/apm-20-1783. Epub 2021 Mar 9. PMID: 33691452.

3.Hume E, Ward L, Wilkinson M, Manifold J, Clark S, Vogiatzis I. Exercise training for lung transplant candidates and recipients: a systematic review. *Eur Respir Rev*. 2020 Oct 28;29(158):200053. doi: 10.1183/16000617.0053-2020. PMID: 33115788; PMCID: PMC9488968.

4.Florian J, Watte G, Teixeira PJZ, Altmayer S, Schio SM, Sanchez LB, Nascimento DZ, Camargo SM, Perin FA, Camargo JJ, Felicetti JC, Moreira JDS. Pulmonary rehabilitation improves survival in patients with idiopathic pulmonary fibrosis undergoing lung transplantation. *Sci Rep*. 2019 Jun 27;9(1):9347. doi: 10.1038/s41598-019-45828-2. PMID: 31249363; PMCID: PMC6597536.

Comment 12: Line 76, these references assess rehabilitation in lung resection in lung cancer patients and not lung transplant patients, which is not closely related to this study's focus on lung transplant patients.

Reply 12: We changed reference 5-7.

5.Andrianopoulos V, Gloeckl R, Boensch M, Hoster K, Schneeberger T, Jarosch I, Koczulla RA, Kenn K. Improvements in functional and cognitive status following short-term pulmonary rehabilitation in COPD lung transplant recipients: a pilot study. *ERJ Open Res*. 2019 Sep 16;5(3):00060-2019. doi: 10.1183/23120541.00060-2019. PMID: 31544112; PMCID: PMC6745414.

6.Candemir I, Ergun P, Kaymaz D, Demir N, Taşdemir F, Sengul F, Egesel N, Yekeler E. The Efficacy of Outpatient Pulmonary Rehabilitation After Bilateral Lung Transplantation. *J Cardiopulm Rehabil Prev*. 2019 Jul;39(4):E7-E12. doi: 10.1097/HCR.0000000000000391. PMID: 31241521.

7.Song JH, Park JE, Lee SC, Kim S, Lee DH, Kim EK, Kim SY, Shin JC, Lee JG, Paik HC, Park MS. Feasibility of Immediate in-Intensive Care Unit Pulmonary Rehabilitation after Lung Transplantation: A Single Center Experience. *Acute Crit Care*. 2018 Aug;33(3):146-153. doi: 10.4266/acc.2018.00129. Epub 2018 Aug 31. PMID: 31723878; PMCID: PMC6786695.

Comment 13: Line 79, again, these references assess rehabilitation in COPD patients and not

lung transplant patients.

Reply 13: We changed reference 8-9.

8.Langer D, Burtin C, Schepers L, Ivanova A, Verleden G, Decramer M, Troosters T, Gosselink R. Exercise training after lung transplantation improves participation in daily activity: a randomized controlled trial. *Am J Transplant*. 2012 Jun;12(6):1584-92. doi: 10.1111/j.1600-6143.2012.04000.x. Epub 2012 Mar 5. PMID: 22390625.

9.Shiner CT, Woodbridge G, Skalicky DA, Faux SG. Multidisciplinary Inpatient Rehabilitation Following Heart and/or Lung Transplantation-Examining Cohort Characteristics and Clinical Outcomes. *PM R*. 2019 Aug;11(8):849-857. doi: 10.1002/pmrj.12057. Epub 2019 Mar 14. PMID: 30609218

Comment 14: Line 85, “This rate is even lower for LTRs”. A reference is needed here to support this statement.

Reply 14: We have misexpressed this sentence. We want to express that the implementation rate of pulmonary rehabilitation is lower under the medical conditions in China (see Page 3, line 103).

Changes in the text: This rate is even lower in China.

Comment 15: Line 91, while the author claims otherwise, standardized lung rehabilitation training programs do exist specifically for lung transplant recipients (Schuurmans, Benden et al. 2013).

Reply 15: The pulmonary rehabilitation program we refer to in this article is a nurse-led multidisciplinary pulmonary rehabilitation program. However, most published pulmonary rehabilitation has been led by surgeons (see Page 3, line 108-111).

Changes in the text: 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.

Comment 16: Line 108, in the introduction, the authors mention that their program “has demonstrated good clinical results”. If this phrase refers to a prior publication from the authors’ group, please add citation. If this phrase refers to the findings of the current study, then anticipating findings in the introduction would not be appropriate. If it only reflects the authors’ personal clinical or preliminary experience, mentioning how the author came to that determination, and whether it is subjective in nature, would clarify the phrase’s meaning.

Reply 16: We modified our text (see Page 4, line 138-140).

Changes in the text: 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.

Comment 17: Line 171, “the critical care specialist nurse implements routine nursing interventions for the patient, including basic care, skin care, nebulization therapy and so on”. The expression “and so on” would not be appropriate as not all readers are familiar with routine care. It also assumes that routine care is universally similar. Listing the rest of routine interventions done in the control group would help in contrasting them with the interventions

made in the intervention arm.

Reply 17: We added specific measures for the control intervention (see Page 6, line 256-263). Changes in the text: 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*).

Table 3: Pulmonary rehabilitation training for control group.

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	(1) Lung transplantation's expectations; (2) the necessity of the ECMO support therapy and mechanical ventilation; (3) the effectiveness and necessity of pulmonary rehabilitation; (4) respiratory function training method; (5) exercise training methods.		
Mental nursing	Nurses combined with family members of patients provided psychological support for patients.		

Comment 18: Line 196 and line 203, line 198 and line 207, there is some repetition of the methods used. The independent (unpaired) t test and the chi square test is mentioned twice. Lines 203 and 207 alone are enough for conveying the methods used, while also avoiding redundancy.

Reply 18: We have deleted the repeated content (see Page 7, line 299-302).

Comment 19: Line 203, “normal distribution was checked”. Specifying exactly how it was checked would improve the validity of that claim.

Reply 19: The normality of quantitative data (each recipient in the experimental group) was tested by the graphical method (see Page 7, line 299-302).

Changes in the text: For quantitative data, the normality is tested by graphical method.

Comment 20: Line 215, “total of 68 patients (out of 71)”, It is unclear as to how the number 71 was formed.

Reply 20: A patient screening flowchart was generated and inclusion and exclusion criteria were updated (see Page 16, line 667-668).

Changes in the text:

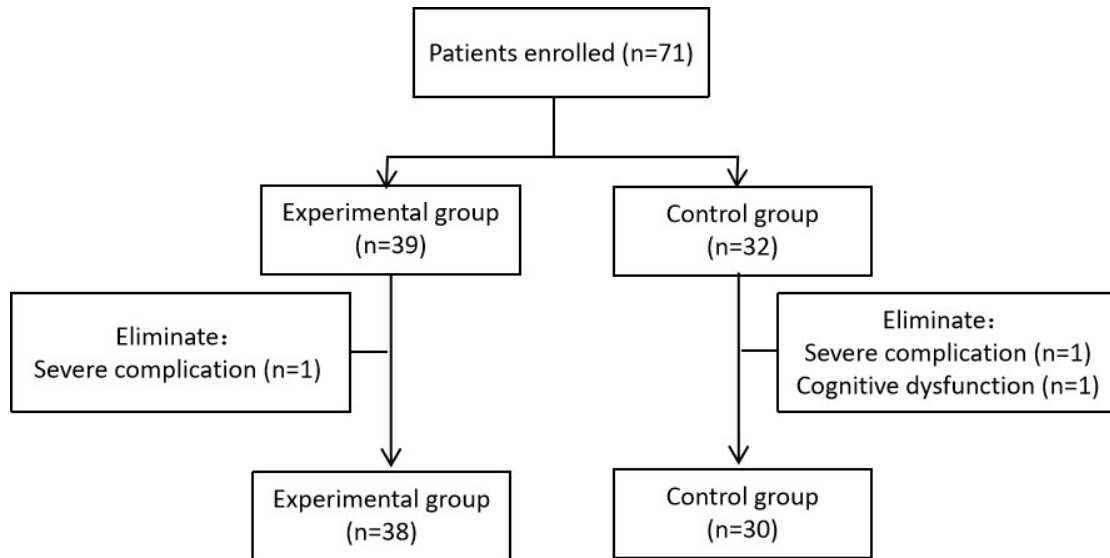


Figure 1: Flowchart of this study.

Comment 21: Line 329, providing specific examples of other medical factors that could have had an influence on the transplant outcomes would increase the transparency of the limitations section.

Reply 21: Example: such as cold ischemia time, immune rejection, etc.

Comment 22: Units of measurement is not mentioned in some parts of the paper. For example: line 231, days for ICU stay time. Line 234, days for the duration of the chest tube drainage Line 293, meters for 6MWD. Table 1, “%” sign for the number in brackets.

Reply 22: We added the units of measurement in the text (see Page 7-8, line 330-353).

Comment 23:

Line 65, “promote” instead of “promot”

Line 461, “oxygenation” instead of “loxygenation”

Line 155, “Each each recipient also”. Word duplication.

Reply 23: We have modified these words in the text (see Page 3, line 82; Page 22, line 707; Page 5, line 224).