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Rehabilitative goals for patients undergoing lung retransplantation

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Lung retransplantation (LRT) involves a second or subsequent lung transplant (LT) in a patient whose first transplanted graft has failed. LRT is the only treatment option for irreversible lung allograft failure caused by acute graft failure, chronic lung allograft dysfunction, or postoperative complications of bronchial anastomosis. Prehabilitation (rehabilitation before LT), while patients are on the waiting list, is recognized as an essential component of the therapeutic regimen and should be offered throughout the waiting period from the moment of listing until transplantation. LRT is particularly fraught with challenges, and prehabilitation to reduce frailty is one of the few opportunities to address modifiable risk factors (such as functional and motor impairments) in a patient population in which there is clearly room to improve outcomes. Although rehabilitative outcomes and quality of life in patients receiving or awaiting LT have gained increased interest, there is a paucity of data on rehabilitation in patients undergoing LRT. Frailty is one of the few modifiable risk factors of retransplantation that is potentially preventable. As such, it is imperative that professionals involved in the field of retransplantation conduct research specifically exploring rehabilitative techniques and outcomes of value for patients receiving LRT, because this area remains unexplored.

Keywords: Graft rejection; Lung transplantation; Rehabilitation; Survival; Treatment outcome

Introduction

Lung retransplantation (LRT) involves a second or subsequent lung transplant (LT) in a patient in whom the first transplanted graft has failed [1]. LRT is the only treatment option for irreversible lung allograft failure caused by acute graft failure, chronic lung allograft dysfunction, or postoperative complications associated with bronchial anastomosis [2-7]. Chronic lung allograft dysfunction is characterized by a decline in forced expiratory volume in the first second of ≥ 20% from the reference value, which persists for 3 months [5]. The postoperative onset of allograft dysfunction at 5 years appears to be equivalent in both first-time transplantation and retransplantation [8]. It has been estimated that the median survival after LRT is 2.5 years, and many variables contribute to the decision to pursue retransplantation, such as age, burden of comorbidities, functional performance, and psychosocial factors [9,10]. Several types of LRT procedures have been described, including single and double LRT, and ipsilateral, contralateral, or bilateral approaches [3,6,11]. LRT carries a higher risk than first-time transplantation, especially in patients with poor functional status or

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those requiring mechanical ventilatory support [2,3]. It has been estimated that LRT accounts for 4% to 6% of all LTs [1,4,12] and a longer time between the initial transplant and retransplant is associated with better outcomes [12]. As a bridge to LRT, extracorporeal membrane oxygenation (ECMO) is associated with worse 30-day survival at 67.3%, compared with 91.2% in those not receiving ECMO [13]. At the same time, patients bridged to transplantation with awake ECMO have higher survival rates with awake ECMO than with mechanical ventilation [14].

Prehabilitation while waiting for lung retransplant

Prehabilitation (rehabilitation before LT), while patients are on the waiting list, has been recognized as an essential component of the therapeutic regimen and has been recommended throughout the waiting period from the moment of listing until transplantation [15]. LRT is particularly fraught with challenges, and prehabilitation to reduce frailty is one of the few opportunities to address modifiable risk factors (such as functional and motor impairments) in a patient population where there is clearly room to improve outcomes. In the case of LRT, patients have already experienced and have a general understanding of how to achieve their expected functional goals. When approaching retransplantation, patients often face a clinical deterioration that can be demoralizing. In this regard, it has been found that an 8-week cognitive behavioral stress management and relaxation training intervention is excellent for patients requiring solid organ transplantation [16]. Directing rehabilitative interventions towards goals that focus on maintaining function and avoiding physical deconditioning is of paramount importance in the preoperative period before LRT.

Expected outcomes following lung retransplant

While the 1-year survival after LRT remains inferior (76%) to that after primary LT (84%) [17,18], outcomes have improved over time, although these improvements have been considerably less robust than those seen in other LT indications [19]. Early clinical experiences with LRT dating back to the 1990s indicated 1-year survival rates that were better in patients who were ambulatory and non-ventilated (64% ± 55%) than in those who were non-ambulatory and ventilated (33% ± 4%) [20]. One-year survival improved somewhat in the 2000s in patients requiring LRT because of primary graft dysfunction (34.8% survival) and bronchiolitis obliterans syndrome (72.5% survival) [21]. During the same period, even ventilated patients undergoing LRT saw an increase in 1-year survival to 50% [12,19]. Functional status is an important and modifiable predictor of post-LRT outcomes. Recipients in need of total assistance at the time of retransplantation are much more likely to experience continuing functional limitations after LRT that require the same assistance [22]. Although rehabilitative outcomes and quality of life in patients receiving or awaiting LT have gained increasing interest [23,24], there is a paucity of data regarding rehabilitation in patients undergoing LRT. Indeed, we found no published experience describing the rehabilitation of patients who have undergone LRT, and it seems that this topic is unexplored. This may be because conventional wisdom maintains that rehabilitation in LRT is not different from that in first-time transplantation. Considering the distinct risks and exposure of patients receiving retransplantation, this assumption may not hold true. In the literature, we found only one case report discussing rehabilitation and providing insights into the clinical issues of rehabilitative interest that can arise after LRT, such as post-transplant musculoskeletal syndrome [25]. This condition may adversely affect the patients' flexibility, pain, and strength, although it can be improved using manual and respiratory techniques, such as global postural reduction [25].

Rehabilitative features in lung transplantation

Because of the distinct complexities associated with LRT, rehabilitative interventions should focus on different primary goals depending on preoperative and postoperative needs (Table 1) [25,26].

Currently, there are no specific guidelines for rehabilitating patients undergoing LRT. Therefore, fundamental aspects pertaining to LT candidates and recipients should be used as a guide. We speculate that treatment frequency, intensity (related to patients' clinical status), exercise duration, and expected outcomes likely

Table 1. Rehabilitative outcomes in lung retransplantation

Prehabilitation	Postoperative rehabilitation
Patients should already be accustomed to exercise and aware of expected outcomes since they have already been subjected to rehabilitation at the time of the first transplant. Primary goals focus on preserving residual functional ability and management of worsening dyspnea.	Musculoskeletal issues could be present and can be addressed with manual techniques such as global postural reeducation [25]. Motor reconditioning and respiratory exercises are consistent parts of treatment [26].

vary between first-time LT and LRT candidates and recipients.

While rehabilitation techniques in LRT do not differ substantially from those utilized in patients undergoing first-time LT, the physical condition of patients receiving retransplantation is often impaired by greater medical complexity. While patients are on the waiting list, prehabilitation can be offered under different modalities, including home-based, outpatient, and inpatient programs [27,28]. In a review of rehabilitative interventions in candidates for LT, it was reported that the majority of care was delivered in an outpatient setting, although mixed (outpatient and home-based) and inpatient forms of care were also available [27]. Home-based and inpatient settings are preferred for patients who face barriers to travel, have limited autonomy, or require a high amount of supplemental oxygen during exertion. Telerehabilitation has received increased attention and gained popularity, particularly during the coronavirus disease 2019 pandemic, as a solution to barriers impeding participation in in-person rehabilitative programs [29]. For LT candidates, telerehabilitation programs can substantially increase and facilitate treatment adherence compared to outpatient hospital-based rehabilitation [30]. However, a lack of access to home exercise and monitoring equipment could be potential obstacles to successful home-based exercise programs in LT candidates and recipients [31].

Prehabilitation programs are expected to last from 3 to 12 weeks, with a minimum frequency of at least three sessions per week, ranging from 0.5 to 2 hours per single session. Similarly, postoperative rehabilitation programs typically last 4 to 14 weeks and mainly consist of exercise training. Stretching, resistance exercises, aerobic training, respiratory muscle strength training, and breathing exercises are the most commonly used techniques for rehabilitating LT candidates and recipients [27,32-34]. In addition, it has been found that interval training (consisting of bouts of peak work activity alternating with 30 seconds of rest) is associated with lower dyspnea than continuous training in candidates for LT [35], making such an approach appealing for patients with intense dyspnea.

Another important aspect of the duration of exercise programs is their length; it has been found that a shorter duration is not necessarily associated with lower-quality outcomes. Instead, shorter programs allow patients to obtain benefits comparable to longer programs (7 weeks vs. 14 weeks) in terms of exercise capacity, muscle strength, and quality of life in recipients of LT [36]. Exercise is a cornerstone of rehabilitation in these patients and determines an increase in physical functioning and quality of life postoperatively [15,37,38]. Cognitive-behavioral interventions and nutritional management also boost patient satisfaction and happiness and prevent body mass index deterioration and malnutrition, thereby optimizing the preoperative timeframe [39-41].

Conclusion

LRT can be a life-saving procedure for patients who develop postoperative complications that are not amenable to medical therapy after initial transplantation. The limited availability of organs for transplantation can create ethical issues regarding offering a second or third transplant to individuals who have already received an organ, while first-time LT candidates wait for surgery. At the same time, it should not be forgotten that research in the field of artificial lungs is ongoing, and in the foreseeable future, it may be possible to construct new lungs with progenitor cell cellularization [42,43]. Such advances would dramatically change the capacity of LRT to meet its full potential, offering a broader patient base opportunities to overcome chronic lung allograft dysfunction.

Postural issues and coordination are other potential aspects worthy of further consideration, as it has been found that approximately one-third of recipients receiving LT experience residual postural impairments postoperatively [44].

Frailty is one of the few potentially preventable or modifiable risk factors of retransplantation. As such, it is imperative that professionals involved in the field of retransplantation conduct research specifically directed at exploring rehabilitative techniques and outcomes of value for patients receiving LRT, because this area remains unexplored.

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References

1. Magee JC, Barr ML, Basadonna GP, Johnson MR, Mahadevan S, McBride MA, et al. Repeat organ transplantation in the Unit-

ed States, 1996-2005. Am J Transplant 2007;7(5 Pt 2):1424–33.
2. Keshavjee S. Retransplantation of the lung comes of age. J Thorac Cardiovasc Surg 2006;132:226–8.
3. Kawut SM. Lung retransplantation. Clin Chest Med 2011;32:367–77.
4. Aigner C. Retransplantation. Curr Opin Organ Transplant 2015;20:521–6.
5. Bedair B, Hachem RR. Management of chronic rejection after lung transplantation. J Thorac Dis 2021;13:6645–53.
6. Rucker AJ, Nellis JR, Klapper JA, Hartwig MG. Lung retransplantation in the modern era. J Thorac Dis 2021;13:6587–93.
7. Michel E, Galen Hartwig M, Sommer W. Lung retransplantation. Thorac Surg Clin 2022;32:259–68.
8. Yusen RD, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Goldfarb SB, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-second Official Adult Lung and Heart-Lung Transplantation Report--2015; Focus Theme: Early Graft Failure. J Heart Lung Transplant 2015;34:1264–77.
9. Schaheen L, D'Cunha J. Re-do lung transplantation: keys to success. J Thorac Dis 2019;11:5691–3.
10. Wallinder A, Danielsson C, Magnusson J, Riise GC, Dellgren G. Outcomes and long-term survival after pulmonary retransplantation: a single-center experience. Ann Thorac Surg 2019;108:1037–44.
11. Kon ZN, Bittle GJ, Pasrija C, Sanchez PG, Griffith BP, Pierson RN 3rd. The optimal procedure for retransplantation after single lung transplantation. Ann Thorac Surg 2017;104:170–5.
12. Harhay MO, Cherikh WS, Toll AE, Christie JD, Stehlik J, Chambers D, et al. Epidemiology, risk factors, and outcomes of lung retransplantation: an analysis of the International Society for Heart and Lung Transplantation Thoracic Transplant Registry. J Heart Lung Transplant 2022;41:1478–86.
13. Hayanga JW, Aboagye JK, Hayanga HK, Luketich JD, D'Cunha J. Extracorporeal membrane oxygenation as a bridge to lung re-transplantation: is there a role? J Heart Lung Transplant 2016;35:901–5.
14. Warnecke G, Haverich A. Lung re-transplantation: review. Curr Opin Organ Transplant 2012;17:485–9.
15. Annema C, De Smet S, Castle EM, Overloop Y, Klaase JM, Janaudis-Ferreira T, et al. European Society of Organ Transplantation (ESOT) consensus statement on prehabilitation for solid organ transplantation candidates. Transpl Int 2023;36:11564.
16. Jutagir DR, Saracino RM, Cunningham A, Foran-Tuller KA, Driscoll MA, Sledge WH, et al. The feasibility of a group stress management Liver SMART intervention for patients with end-stage liver disease: a pilot study. Palliat Support Care 2019;17:35–41.
17. Pereira RO, Rodrigues ES, Martin AK, Narula T, Ball CT, Alvarez F, et al. Outcomes after lung retransplantation: a single-center retrospective cohort study. J Cardiothorac Vasc Anesth 2022;36:1366–72.
18. Randhawa SK, Yang Z, Morkan DB, Yan Y, Chang SH, Hachem RR, et al. One-year survival worse for lung retransplants relative to primary lung transplants. Ann Thorac Surg 2022;113:1265–73.
19. Chambers DC, Perch M, Zuckermann A, Cherikh WS, Harhay MO, Hayes D Jr, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-eighth adult lung transplantation report - 2021; Focus on recipient characteristics. J Heart Lung Transplant 2021;40:1060–72.
20. Novick RJ, Stitt LW, Al-Kattan K, Klepetko W, Schäfers HJ, Duchatelle JP, et al. Pulmonary retransplantation: predictors of graft function and survival in 230 patients. Pulmonary Retransplant Registry. Ann Thorac Surg 1998;65:227–34.
21. Aigner C, Jaksch P, Taghavi S, Lang G, Reza-Hoda MA, Wisser W, et al. Pulmonary retransplantation: is it worth the effort?: a long-term analysis of 46 cases. J Heart Lung Transplant 2008;27:60–5.
22. Kilic A, Beaty CA, Merlo CA, Conte JV, Shah AS. Functional status is highly predictive of outcomes after redo lung transplantation: an analysis of 390 cases in the modern era. Ann Thorac Surg 2013;96:1804–11.
23. Polastri M, Dell'Amore A, Eden A, Pehlivan E. Does preoperative rehabilitation influence the quality of life in patients who are candidates for lung transplant? Exp Clin Transplant 2022;20:543–8.
24. Polastri M, Dell'Amore A, Reed RM, Pehlivan E. Handgrip strength in lung transplant candidates and recipients. Exp Clin Transplant 2023;21:547–55.
25. Polastri M, Paganelli GM, Dolci G, Di Ciaccio E, Prediletto I. Musculoskeletal syndrome treated with global postural re-education in double-redo lung transplantation: a case report with an 8-month follow-up. Reumatismo 2022;74:29–35.
26. Wickerson L, Rozenberg D, Janaudis-Ferreira T, Deliva R, Lo V, Beauchamp G, et al. Physical rehabilitation for lung transplant candidates and recipients: an evidence-informed clinical approach. World J Transplant 2016;6:517–31.
27. Quint EE, Ferreira M, van Munster BC, Nieuwenhuijs-Moeke G, Te Velde-Keyzer C, Bakker SJ, et al. Prehabilitation in adult solid organ transplant candidates. Curr Transplant Rep 2023;10:70–82.

28. Polastri M. Physiotherapy for lung transplant candidates and recipients: time frame from pre-operative to long-term care. Int J Ther Rehabil 2019;26:1–6.
29. Vendetti ML, Esther Moon SJ, Imes CC, Hergenroeder A, Sciurba F, Lendermon E, et al. Design of Lung Transplant Go (LTGO): a randomized controlled trial evaluating the efficacy of a telerehabilitation behavioral exercise intervention to improve physical activity, physical function, and blood pressure control after lung transplantation. Contemp Clin Trials Commun 2023;33:101097.
30. Layton AM, Irwin AM, Mihalik EC, Fleisch E, Keating CL, DiMango EA, et al. Telerehabilitation using fitness application in patients with severe cystic fibrosis awaiting lung transplant: a pilot study. Int J Telemed Appl 2021;2021:6641853.
31. Wickerson L, Helm D, Gottesman C, Rozenberg D, Singer LG, Keshavjee S, et al. Telerehabilitation for lung transplant candidates and recipients during the COVID-19 pandemic: program evaluation. JMIR Mhealth Uhealth 2021;9:e28708.
32. Pehlivan E, Mutluay F, Balcı A, Kılıç L. The effects of inspiratory muscle training on exercise capacity, dyspnea and respiratory functions in lung transplantation candidates: a randomized controlled trial. Clin Rehabil 2018;32:1328–39.
33. Li M, Mathur S, Chowdhury NA, Helm D, Singer LG. Pulmonary rehabilitation in lung transplant candidates. J Heart Lung Transplant 2013;32:626–32.
34. Hume E, Ward L, Wilkinson M, Manifield J, Clark S, Vogiatzis I. Exercise training for lung transplant candidates and recipients: a systematic review. Eur Respir Rev 2020;29:200053.
35. Gloeckl R, Halle M, Kenn K. Interval versus continuous training in lung transplant candidates: a randomized trial. J Heart Lung Transplant 2012;31:934–41.
36. Fuller LM, Button B, Tarrant B, Steward R, Bennett L, Snell G, et al. Longer versus shorter duration of supervised rehabilitation after lung transplantation: a randomized trial. Arch Phys Med Rehabil 2017;98:220–6.
37. Langer D, Burtin C, Schepers L, Ivanova A, Verleden G, Decramer M, et al. Exercise training after lung transplantation improves participation in daily activity: a randomized controlled trial. Am J Transplant 2012;12:1584–92.
38. Ihle F, Neurohr C, Huppmann P, Zimmermann G, Leuchte H, Baumgartner R, et al. Effect of inpatient rehabilitation on quality of life and exercise capacity in long-term lung transplant survivors: a prospective, randomized study. J Heart Lung Transplant 2011;30:912–9.
39. Rodrigue JR, Baz MA, Widows MR, Ehlers SL. A randomized evaluation of quality-of-life therapy with patients awaiting lung transplantation. Am J Transplant 2005;5:2425–32.
40. Weber Gulling M, Schaefer M, Bishop-Simo L, Keller BC. Optimizing nutrition assessment to create better outcomes in lung transplant recipients: a review of current practices. Nutrients 2019;11:2884.
41. Staufer K, Halilbasic E, Hillebrand P, Harm S, Schwarz S, Jaksch P, et al. Impact of nutritional status on pulmonary function after lung transplantation for cystic fibrosis. United European Gastroenterol J 2018;6:1049–55.
42. Nonaka PN, Uriarte JJ, Campillo N, Oliveira VR, Navajas D, Farré R. Lung bioengineering: physical stimuli and stem/progenitor cell biology interplay towards biofabricating a functional organ. Respir Res 2016;17:161.
43. Uriarte JJ, Uhl FE, Rolandsson Enes SE, Pouliot RA, Weiss DJ. Lung bioengineering: advances and challenges in lung decellularization and recellularization. Curr Opin Organ Transplant 2018;23:673–8.
44. Ebenbichler G, Doblhammer S, Pachner M, Habenicht R, Kienbacher T, Mair P, et al. Impairments in postural control and retest reliability of dynamic posturographic measures after lung transplantation. Am J Phys Med Rehabil 2019;98:353–9.