



Going the distance: predictors of multi-decade survival following lung transplantation

A. Justin Rucker, Matthew G. Hartwig

Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University Medical Center, Durham, NC, USA

Correspondence to: A. Justin Rucker, MD, MPH. Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University Medical Center, 2301 Erwin Road, Durham, NC 27710, USA. Email: alvin.rucker@duke.edu.

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Lung transplantation (LTx) is the final therapeutic option for select patients with end-stage lung disease. Despite this, long-term outcomes in LTx lag far behind those in other solid organ transplants. Growing experience with LTx over the past several decades has resulted in improvements in surgical technique, perioperative critical care, waitlist allocation, and immunosuppression. While these changes have primarily manifest as improvements in short-term outcomes, increasing numbers of patients are surviving for greater than 20 years post-LTx. As this cohort grows, it is becoming increasingly possible to understand factors that may promote favorable long-term outcomes in these patients. Thus far analyses focusing on 20+ years survivors post-LTx have been limited to small, single institution retrospective analyses (1). Therefore, in an attempt to identify predictive factors of long-term survival amongst LTx recipients from a national cohort, Miggins and colleagues (2) performed a retrospective analysis of the United Network for Organ Sharing (UNOS) database.

The authors identified 6,172 patients that underwent LTx from 1987 to 2002 and survived at least 1-year post-transplant. Of these, 472 (7.6%) LTx recipients survived 20 years or more. In multivariable analysis, protective factors associated with 20+ years survival included younger recipient age (25–45 years old), longer waitlist times (>1 year), and female-to-female donation. In contrast, factors negatively associated with 20+ years survival notably included older patient age (>55 years old), single LTx, recipient glomerular filtration rate

(GFR) <10, and chronic obstructive pulmonary disease (COPD)/emphysema as the indication for transplant. In corroboration with these findings, using a single-institution cohort, Sithampanathan and colleagues similarly found that 20+ years survivors post-LTx were younger on average at the time of transplant (31.8 *vs.* 40.8 years) and more likely to have received bilateral LTx than single LTx (1).

In addition to their multivariable analysis, the authors performed several propensity score matched analyses comparing survival in patients based on receipt of unilateral LTx, cold ischemia time, or donor sex for female recipients. Through these, they found that female-to-female donation remained significantly associated with improved likelihood of 20+ years survival even after accounting for factors such as donor-recipient size matching. Prior data on the importance of donor-recipient sex concordance in lung transplant primarily comes from single institution studies and has been mixed. For example, Demir and colleagues utilized an institutional dataset to examine 461 LTx recipients and found that donor-recipient sex mismatch was associated with worsened 5-year survival (3). However, several other analyses have found that donor-recipient sex mismatch was not associated with significant differences in survival following LTx (4–6). Therefore, further research is needed to clarify the potential role of donor-recipient sex matching in LTx outcomes to inform whether it should be considered as a factor during the allocation of lung allografts.

When the authors broadened their analysis to include all patients that survived at least 10 years post-LTx, risk factors associated with survival largely paralleled those for 20+ years survival except that recipient ages 25–65 were all positively associated with improved survival. Findings from the present study align with those from previous analyses examining factors associated with 10+ years survival post-LTx, indicating that these studies may still provide valuable insight into factors associated with multi-decade survival (7–10). For example, in a retrospective analysis using the UNOS database examining patients that underwent LTx from 1987–1997, Weiss and colleagues found that 10-year survival was more likely in younger patients [18–35] and bilateral LTx recipients (9). Since implementation of the Lung Allocation Score (LAS) in 2005, older recipients are increasingly undergoing LTx (11). Although the cohort used for both the Weiss study as well as the present study by Miggins *et al.* are from the pre-LAS era, studies examining recipients that were transplanted post-LAS have demonstrated similar risk factors for long-term survival (7,8). For instance, our group recently looked at risk factors associated with 10+ years survival for LTx recipients transplanted between 2005–2009 using the UNOS database and similarly found that recipients that were older than 45 years of age and those that received single LTx were less likely to survive beyond 10 years post-LTx. In addition to these factors, we also found that increasing donor age was negatively associated with 10+ years survival post-LTx in multivariable analysis (7).

Taken together these studies suggest that preferentially performing bilateral LTx on younger patients is beneficial for long-term outcomes post-transplant. However, while recipient age clearly impacts long-term survival in these analyses, end-stage lung disease more commonly manifests in the elderly and excluding older patients from LTx because of compromised extended survival is not feasible, nor ethical. This is particularly important as some studies have suggested that extremes of age on either end may be detrimental for survival post-LTx (12). Critical to this discussion, there are limited means to completely account for recipient co-morbidities or indices of frailty in the UNOS database. Consequently, the relationship between patient age and long-term survival seen in this study may reflect confounding from these variables. Therefore, while prioritizing the transplantation of younger, fitter recipients could bolster long-term survival with LTx, it may also severely disadvantage many older patients for which LTx would still offer a substantial benefit. Currently,

there are no clear recommendations for restriction of LTx based on age. However, consensus guidelines from the International Society for Heart and Lung Transplantation caution for careful selection of transplant candidates over age 65 (13). Further research is needed into metrics for the assessment of frailty and other factors that may help to better classify risk for older potential LTx candidates. With these, we may develop patient selection strategies beyond the assessment of numerical age alone which more adequately balance improvement of long-term outcomes while ensuring that appropriately selected older patients still have access to LTx.

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References

1. Sithamparamanathan S, Thirugnanasothy L, Clark S, et al. Observational study of lung transplant recipients surviving 20 years. *Respir Med* 2016;117:103–8.

2. Miggins JJ, Reul RM Jr, Barrett S, et al. Twenty-year survival following lung transplantation. *J Thorac Dis* 2023;15:2997-3012.
3. Demir A, Coosemans W, Decaluwé H, et al. Donor-recipient matching in lung transplantation: which variables are important?†. *Eur J Cardiothorac Surg* 2015;47:974-83.
4. Fessart D, Dromer C, Thumerel M, et al. Influence of gender donor-recipient combinations on survival after human lung transplantation. *Transplant Proc* 2011;43:3899-902.
5. Alvarez A, Moreno P, Illana J, et al. Influence of donor-recipient gender mismatch on graft function and survival following lung transplantation. *Interact Cardiovasc Thorac Surg* 2013;16:426-35.
6. Roberts DH, Wain JC, Chang Y, et al. Donor-recipient gender mismatch in lung transplantation: impact on obliterative bronchiolitis and survival. *J Heart Lung Transplant* 2004;23:1252-9.
7. Jawitz OK, Raman V, Becerra D, et al. Factors associated with short- versus long-term survival after lung transplant. *J Thorac Cardiovasc Surg* 2022;163:853-860.e2.
8. Blitzer D, Copeland H, Roe D, et al. Long term survival after lung transplantation: A single center experience. *J Card Surg* 2020;35:273-8.
9. Weiss ES, Allen JG, Merlo CA, et al. Factors indicative of long-term survival after lung transplantation: a review of 836 10-year survivors. *J Heart Lung Transplant* 2010;29:240-6.
10. de Perrot M, Chaparro C, McRae K, et al. Twenty-year experience of lung transplantation at a single center: Influence of recipient diagnosis on long-term survival. *J Thorac Cardiovasc Surg* 2004;127:1493-501.
11. Chambers DC, Perch M, Zuckermann A, 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.
12. Lehr CJ, Blackstone EH, McCurry KR, et al. Extremes of Age Decrease Survival in Adults After Lung Transplant. *Chest* 2020;157:907-15.
13. Leard LE, Holm AM, Valapour M, et al. Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant* 2021;40:1349-79.

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