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Acute Kidney Injury Increases Mortality After Lung Transplantation

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Abstract

Background—Acute kidney injury requiring renal replacement therapy (RRT) is associated with increased mortality after cardiac surgery. Studies examining the impact of RRT after lung transplantation (LTx) are limited. We evaluated risk factors and outcomes associated with RRT after LTx.

Methods—We retrospectively reviewed all LTx recipients in the United Network for Organ Sharing database. Preoperative renal function was stratified by glomerular filtration rate (GFR) as determined by the Modification of Diet in Renal Disease formula (strata: 90, 60 to 90, and <60 mL · min⁻¹ · 1.73m⁻²). Primary outcomes were 30-day, 1-year, and 5-year survival and need for post-LTx RRT. Risk adjusted multivariable Cox proportional hazards regression examined mortality. A multivariable logistic regression model evaluated risk factors for RRT.

Results—From 2001 to 2011, 12,108 patients underwent LTx. After LTx, 655 patients (5.51%) required RRT. Patients requiring post-LTx RRT had decreased survival at 30 days (96.7% versus 76.0%, $p < 0.001$), 1 year (85.5% versus 35.8%, $p < 0.001$), and 5 years (56.4% versus 20.0%, $p < 0.001$). These differences persisted on multivariable analysis at 30 days (hazard ratio [HR] 7.98 [6.16 to 10.33], $p < 0.001$), 1 year (HR 7.93 [6.84 to 9.19], $p < 0.001$), and 5 years (HR 5.39 [4.75 to 6.11], $p < 0.001$). Preoperative kidney function was an important predictor of post-LTx RRT for a GFR of 60 to 90 (odds ratio 1.42 [1.16 to 1.75], $p = 0.001$) and a GFR less than 60 (odds ratio 2.68 [2.07 to 3.46], $p < 0.001$). High center volume was protective.

Conclusions—In the largest study to evaluate acute kidney injury after LTx, the incidence of RRT is 5.51%. The need for post-LTx RRT dramatically increases both short- and long-term mortality. Several variables, including preoperative renal function, are predictors of post-LTx RRT and could be used to identify transplant candidates at risk for acute kidney injury.

Acute kidney injury (AKI) is a common complication after lung transplantation (LTx), occurring in 25% to 62% of LTx recipients [1–5]. In 5% to 16% of patients, AKI is severe enough to require renal replacement therapy (RRT) [2–6]. Both AKI and severe AKI necessitating RRT have been associated with significant morbidity and as much as a fourfold increase in mortality [4–7]. Although a limited number of studies have examined risk factors for AKI and the impact of this complication on LTx outcomes, few studies have focused specifically on RRT. Moreover, existing studies of RRT after LTx are limited to single institutional experiences consisting of relatively small sample sizes [4, 6]. The United

Network for Organ Sharing (UNOS) database of all LTx in the United States offers a unique opportunity to evaluate the incidence, impact, and risk factors for RRT after LTx in a large cohort.

Material and Methods

Data Source

For this study, we utilized the UNOS database from the UNOS registry, an open cohort of all patients undergoing LTx in the United States. The Johns Hopkins Medicine Institutional Review Board approved this study.

Study Design

This study is a retrospective cohort design of all adults (aged 18 years or older) who underwent LTx from 2000 to 2010. Patients undergoing retransplantation, combined heart-lung transplants, multiorgan transplants, patients on preoperative RRT, and patients missing preoperative creatinine were excluded. Primary stratification was according to the perioperative need for post-LTx RRT. Subgroup analysis was performed to compare patients before and after the Lung Allocation Score (LAS) era.

Variables Examined and Outcomes Measured

We examined pertinent covariates in the data set, including recipient demographics and comorbidities, recipient hemodynamics and measures of acuity, donor demographics and comorbidities, and transplant variables.

Recipient preoperative glomerular filtration rate (GFR) was calculated according to the Modified Diet in Renal Disease equation [8] as follows:

$$\text{GFR} = 175 \times (\text{Creatinine}_{\text{serum}})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if black ethnicity})$$

Based on their GFR, recipients were stratified by renal function: stratum 1, GFR $90 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ or more; stratum 2, GFR 60 to $90 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$; and stratum 3, GFR less than $60 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$.

The primary endpoints were 30 day, 1-year, and 5-year mortality. Risk factors for RRT were evaluated.

Statistical Analysis

We compared patient baseline characteristics using the *t* test (continuous parametric variables), the Wilcoxon rank-sum test (continuous nonparametric variables), and the χ^2 or Fisher's exact test (categorical variables) as appropriate. Survival was estimated using the Kaplan-Meier method.

Multivariable Cox proportional hazards regression models were constructed to estimate the risk of death with censoring for death and loss to follow-up. A multivariable logistic regression model was constructed to determine risk factors for post-LTx RRT. To construct all multivariable models, independent covariates were first tested in univariate fashion. Variables associated with mortality on exploratory analysis ($p < 0.20$), those with biological plausibility, and those previously reported in the literature to be significant were incorporated in a forward and backward stepwise fashion into the multivariable model. The likelihood ratio test and Akaike's information criterion were utilized in a nested model approach to identify which model had the greatest explanatory power.

For all analyses, p less than 0.05 (2-tailed) was considered statistically significant. Mean values are displayed with their standard deviations and median values are displayed with their interquartile ranges. Hazard ratios (HR) and odds ratios are presented with their 95% confidence intervals (CI). Statistical analysis was performed using STATA 11.2 (StataCorp LP, College Station, TX).

Results

Cohort Statistics

From 2001 to 2010, 13,499 patients receiving a LTx were included in the UNOS database. After excluding pediatric patients ($n = 533$), redo LTx ($n = 497$), multiorgan transplants ($n = 34$), patients requiring preoperative RRT ($n = 9$), and patients missing preoperative creatinine ($n = 318$), the final cohort comprised 12,108 patients.

The mean age of the entire cohort was 52 ± 13 years, and 6,657 (55.0%) were male. By strata, 5,273 recipients (43.6%) had a GFR 90 or more, 5,476 recipients (45.2%) had a GFR of 60 to 90, and 1,359 recipients (11.2%) had a GFR less than $60 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$. The most common indication for LTx was chronic obstructive pulmonary disease (COPD [$n = 4,227$; 34.9%]) followed by idiopathic pulmonary fibrosis (IPF [$n = 3,369$; 27.8%]). In the 6,835 patients transplanted in the post-LAS era, the mean LAS was 43.7 ± 14.7 . Overall, 655 patients (5.51%) required post-LTx RRT.

Baseline Characteristics

An analysis of baseline characteristics stratified by the need for post-LTx RRT revealed several differences (Table 1). Patients requiring post-LTx RRT were more likely to be female, more likely to have diabetes mellitus, had poorer renal function, and were less likely to have COPD but more likely to have primary pulmonary hypertension (PPH). The RRT cohort had higher mean pulmonary artery pressures, were more likely to be hospitalized, to require intensive care unit care, and to require ventilatory or extracorporeal membrane oxygenation (ECMO) support before LTx. These patients were also more likely to undergo a bilateral lung transplantation, had longer ischemic times, a higher LAS, and were more likely to undergo LTx at lower volume centers. Although there were other statistically significant baseline differences, the absolute differences were small and unlikely clinically relevant.

Of patients requiring RRT, patients in the post-LAS era were older (49 ± 13 years versus 52 ± 13 , $p < 0.001$), more likely to have IPF (57 of 269 [21.2%] versus 109 of 386 [28.2%], $p < 0.04$), less likely to have PPH (30 of 269 [11.2%] versus 19 of 386 [4.9%], $p < 0.003$), more likely to require ventilatory support (6 of 269 [2.2%] versus 48 of 386 [12.4%], $p < 0.001$) and ECMO support (1 of 269 [0.4%] versus 20 of 386 [5.2%], $p < 0.001$), and more likely to undergo a bilateral lung transplantation (184 of 269 [68.4%] versus 298 of 386 [77.2%], $p < 0.01$).

Survival

On unadjusted analysis stratified by the need for RRT, the need for post-LTx RRT was associated with significantly decreased survival at 30 days (96.7% [96.3% to 97.0%] versus 76.0% [72.5% to 79.1%], $p < 0.001$), at 1 year (85.5% [84.8% to 86.2%] versus 35.8% [32.0% to 39.6%], $p < 0.001$; Fig 1A), and at 5 years (56.4% [55.2% to 57.5%] versus 20.0% [16.6% to 23.7%], $p < 0.001$; Fig 1B). Of patients who died the first year, the mean age was 53 ± 12 years. Although early mortality appeared to be a significant factor in predicting long-term survival, 5-year survival conditional on surviving to 1 year was still

significantly worse in the RRT cohort (65.9% [64.7% to 67.1%] versus 56.0% [47.8% to 63.4%], $p < 0.01$; Fig 1C).

There was no difference in the incidence of RRT before and after the implementation of the LAS (269 of 5,111 [5.3%] versus 386 of 6,767 [5.7%], $p < 0.30$). Although patients requiring RRT had similar 30-day survival before and after the LAS era (76.4% [70.8% to 81.1%] versus 75.7% [71.1% to 79.7%], $p < 0.73$), there was a trend toward decreased 1-year survival (40.9% [34.9% to 46.7%] versus 31.6% [26.6% to 36.6%], $p < 0.07$) and 2-year survival (35.1% [29.4% to 40.9%] versus 26.3% [21.4% to 31.4%], $p = 0.057$; Fig 2) among LTx patients requiring RRT in the post-LAS era.

On adjusted analysis, the need for post-LTx RRT was associated with worse 30-day mortality (HR 7.87 [6.07 to 10.20], $p < 0.001$; Table 2), 1-year mortality (HR 7.89 [6.80 to 9.15], $p < 0.001$; Table 3), and 5-year mortality (HR 5.35 [4.72 to 6.07], $p < 0.001$). At all three time points, age greater than 55 years and the need for intensive care unit or ECMO support pre-LTx were associated with an increased hazard of mortality. Increasing center volume was protective of mortality. Centers that performed 18 or fewer LTx each year tended to have lower 1-year survival ($p < 0.001$) and 5-year survival ($p < 0.001$; Fig 3).

Risk of Renal Replacement Therapy

To evaluate risk factors for developing AKI requiring RRT after LTx, a multivariable logistic regression model was constructed. On adjusted analysis, increasing age, ethnicity other than white, decreasing renal function, increasing body mass index, a diagnosis of IPF or PPH, need for intensive care unit support, need for ECMO support, bilateral lung transplantation, and increasing ischemic time were all predictive of the need for post-LTx RRT (Table 4). Both a diagnosis of COPD and increasing center volume were protective. Further investigation of the impact of center volume on the need for RRT found that for each additional LTx performed annually, there was a corresponding decrease in the risk of RRT by 1% (odds ratio 0.99 [0.989 to 0.996], $p < 0.001$).

Comment

This analysis represents the largest study to date to examine the incidence, impact, and risk factors for requiring RRT in the perioperative period after LTx. In our study of 12,108 LTx, we found a 5.51% incidence of RRT. The need for RRT after LTx was associated with decreased survival at 30 days, 1 year, and 5 years on both univariate and multivariable analysis. Although much of the difference in mortality occurs early, the need for RRT is still associated with increased 5-year mortality among patients who survive to 1 year. Additionally, implementation of the LAS has not changed the incidence of RRT, although there is a trend toward a higher associated mortality in the post-LAS era. Finally, a detailed analysis of risk factors for RRT demonstrated that, among other risk factors, poor preoperative renal function, a diagnosis of IPF or PPH, the need for ventilatory or ECMO support preoperatively, and bilateral lung transplantation were strongly predictive of RRT. Increasing center volume and a diagnosis of COPD were protective of the need for RRT.

Acute kidney injury has been previously associated with poor outcomes in critically ill patients [9], patients undergoing cardiac surgery [7, 10–12], and solid organ transplant recipients [13]. All patients with AKI, and particularly those requiring RRT, are at increased risk of mortality [7, 9–11]. Previous studies suggest that patients undergoing LTx are at particularly high risk of renal dysfunction, with AKI developing in 25% to 62% of recipients [1–5] and 5% to 16% requiring RRT [2–6]. Chronic renal failure in this population is also problematic as more than 90% of LTx recipients will have renal dysfunction, and an increasing number of patients will require RRT as time passes [6, 14].

Numerous explanations have been offered to explain why LTx recipients are at high risk of renal dysfunction. First, several authors have suggested that lung injury damages the kidneys through “lung biotrauma.” In this paradigm, lung injury results in the release of inflammatory mediators that mediate renal epithelial apoptosis, resulting in AKI [5, 15, 16]. Second, lung injury and the resulting fluid retention and hypoxemia may be associated with renal hypoperfusion [17]. Such injury may be exacerbated by perioperative hemodynamic instability [18]. Third, the postoperative administration of nephrotoxic agents including calcineurin inhibitors and nephrotoxic antibiotics [1, 19]. Finally, in an effort to protect the allograft and avoid primary graft dysfunction, LTx recipients undergo aggressive diuresis in an effort to maintain a negative fluid balance [5, 20, 21]. Although this practice can improve graft function, it may result in iatrogenic AKI.

The incidence of AKI after LTx reported in the literature varies widely and is dependent on the definition utilized. Therefore, we examined the need for RRT because it is a concrete marker of severe AKI. In our study, we found an overall incidence of RRT of 5.51%. As in other studies, the need for RRT was independently associated with dramatically decreased survival at 30 days, 1 year, and 5 years [4–6]. The exact reason for this increased mortality is unclear. The need for RRT is likely a surrogate for critical illness [7]. Additionally, AKI places patients at risk of chronic renal failure, which may increase their long-term mortality [6].

Patients who needed RRT in the post-LAS period tended to have worse survival than patients in the pre-LAS era. While several explanations are possible, a comparison of their baseline characteristics suggests that patients in the post-LAS era tend to be older, have more comorbidities, and are of higher acuity at the time of transplant.

In analyzing predictors of RRT, worse preoperative renal function is associated with an increased incidence of post-LTx RRT. Although seemingly intuitive, the literature is divided on this question. Most previous studies have found GFR not to be associated with AKI but predictive of chronic renal dysfunction [1, 2, 4–6, 22]. This highlights the power of the UNOS database. Poor renal function is a relative contraindication to LTx. Therefore, most centers transplant only a small number of patients with poor baseline renal function. However, in the national experience as a whole, many patients with poor renal function have undergone LTx, which provides the statistical power to detect the impact of this risk factor.

As in previous studies, a diagnosis of COPD was protective whereas a diagnosis either IPF or PPH was predictive of RRT [4, 14]. In contrast to previous reports, these findings were independent both of the type of transplant performed and the age of the recipient. Previous reports have also suggested that cystic fibrosis is predictive of AKI [23]. Further analysis is necessary to understand the reasons for the differential risk of RRT.

The need for both ventilatory and ECMO support were highly predictive of post-LTx RRT. In both cases, these variables are markers of high recipient acuity. These patients often have or will have infections and multiorgan dysfunction, causing or predisposing them to kidney injury. They are thus less likely to tolerate perioperative hemodynamic instability, nephrotoxic medications, or aggressive diuresis without having AKI requiring RRT.

Finally, increasing annual center volume was protective of RRT when considered both as a continuous variable and when stratified by quartiles. This finding is consistent with previous reports that increasing annual center volume is associated with increased survival after LTx [24]. Concerns about allograft function lead to aggressive efforts to maintain a negative fluid balance but may exacerbate kidney injury. It is likely that with their accumulated experience, high volume centers are better able to maintain the delicate balance between healthy lungs and prerenal azotemia.

Although some data suggest that mild AKI is not associated with higher mortality in LTx, the need for post-LTx RRT is unequivocally associated with worse outcomes [4, 5]. Although several risk factors such as low preoperative GFR and ECMO support are strongly predictive of post-LTx AKI, and thereby increased mortality, we are not suggesting any of these factors should be viewed as absolute contraindications to LTx. Rather, potential LTx recipients should be evaluated for their overall risk of mortality. Their risk of post-LTx RRT is one important component of this evaluation. For high-risk patients, referral to high volume centers should be considered. For recent LTx recipients who are high risk, after optimizing hemodynamics and carefully avoiding nephrotoxic drugs, particular attention should be paid to their fluid status. Although preservation of the allograft is of penultimate concern, it must be carefully weighed against the dramatically increased mortality associated with the need for RRT. Finally, given the mortality associated with AKI requiring RRT after LTx, strategies including combined lung-kidney transplants or early renal transplantation after LTx merit additional consideration.

Study Limitations

Although we have chosen RRT as a concrete marker of severe AKI, this outcome lacks the sensitivity to encompass the broader range of renal dysfunction as defined by recent consensus criteria such as RIFLE (an acronym for risk, injury, failure, loss, end stage) [25, 26]. Therefore, our findings of the incidence, impact, and risk factors for severe AKI should be seen as focused on AKI requiring RRT.

One reason for avoiding RIFLE and other definitions for renal dysfunction in this study is the absence of longitudinal renal function measurements in the UNOS database. Given the uncertain impact of less severe AKI on survival, future inclusion of these data in the database should be considered.

Additionally, the data concerning RRT in the UNOS database are limited. We do not know whether peritoneal, intermittent, or continuous RRT were utilized. Moreover, although previous studies suggest that recovery of renal function may not completely mitigate the impact on mortality, duration of RRT is also not available.

Finally, our study is a retrospective cohort study, and thus it is not possible to control for all confounders. Other important variables, including the dosing of nephrotoxic medications and perioperative hypotension, are not included. In particular, there are no data on the need for cardiopulmonary bypass during implantation. Cardiopulmonary bypass may be associated with AKI, and previous work suggests that the use of cardiopulmonary bypass may protect against rejection. Furthermore, the database does not include the dates of various postoperative complications; therefore, it is impossible to determine whether implementation of RRT is temporally related to a particular complication. For example, although drug-treated rejection was associated with the need for RRT on univariate analysis (odds ratio 1.82 [0.996 to 3.33], $p = 0.052$), we do not know if rejection occurred before AKI. Therefore, we have excluded these covariates, although they may be risk factors for RRT.

In conclusion, in the largest study to evaluate AKI requiring RRT after LTx, the incidence of RRT is 5.51%. The need for post-LTx RRT is independently associated with both short-term and long-term mortality. Several variables, including preoperative renal function, are predictors of post-LTx RRT and could be used to identify transplant candidates at risk for RRT.

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Abbreviations and Acronyms

AKI	acute kidney injury
CI	confidence interval
CMV	cytomegalovirus
COPD	chronic obstructive pulmonary disease
ECMO	extracorporeal membrane oxygenation
GFR	glomerular filtration rate
HR	hazard ratio
IPF	idiopathic pulmonary fibrosis
LAS	lung allocation score
LTx	lung transplantation
PPH	primary pulmonary hypertension
RIFLE	risk, injury, failure, loss, end stage
RRT	renal replacement therapy
UNOS	United Network for Organ Sharing

References

1. Al-Naamani N, Maarouf OH, Wilt JS, et al. The modification of diet in renal disease (MDRD) and the prediction of kidney outcomes after lung transplantation. *J Heart Lung Transplant*. 2008; 27:1191–1197. [PubMed: 18971090]
2. Barraclough K, Menahem SA, Bailey M, Thomson NM. Predictors of decline in renal function after lung transplantation. *J Heart Lung Transplant*. 2006; 25:1431–1435. [PubMed: 17178337]
3. Jacques F, El-Hamamsy I, Fortier A, et al. Acute renal failure following lung transplantation: risk factors, mortality, and long-term consequences. *Eur J Cardiothorac Surg*. 2011 Jun 10. [E-pub ahead of print].
4. Rocha PN, Rocha AT, Palmer SM, Davis RD, Smith SR. Acute renal failure after lung transplantation: incidence, predictors and impact on perioperative morbidity and mortality. *Am J Transplant*. 2005; 5:1469–1476. [PubMed: 15888056]
5. Arnaoutakis GJ, George TJ, Robinson CW, et al. Severe acute kidney injury according to the RIFLE (risk, injury, failure, loss, end stage) criteria affects mortality in lung transplantation. *J Heart Lung Transplant*. 2011; 30:1161–1168. [PubMed: 21620737]
6. Mason DP, Solovera-Rozas M, Feng J, et al. Dialysis after lung transplantation: prevalence, risk factors and outcome. *J Heart Lung Transplant*. 2007; 26:1155–1162. [PubMed: 18022082]
7. Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. *Am J Med*. 1998; 104:343–348. [PubMed: 9576407]
8. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function—measured and estimated glomerular filtration rate. *N Engl J Med*. 2006; 354:2473–2483. [PubMed: 16760447]
9. Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA*. 2005; 294:813–818. [PubMed: 16106006]

10. Kuitunen A, Vento A, Suojäranta-Ylinen R, Pettilä V. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. *Ann Thorac Surg.* 2006; 81:542–546. [PubMed: 16427848]
11. Cooper WA, O'Brien SM, Thourani VH, et al. Impact of renal dysfunction on outcomes of coronary artery bypass surgery: results from The Society of Thoracic Surgeons National Adult Cardiac Database. *Circulation.* 2006; 113:1063–1070. [PubMed: 16490821]
12. Arnaoutakis GJ, Bihorac A, Martin TD, et al. RIFLE criteria for acute kidney injury in aortic arch surgery. *J Thorac Cardiovasc Surg.* 2007; 134:1554–1561. [PubMed: 18023682]
13. Ojo AO, Held PJ, Port FK, et al. Chronic renal failure after transplantation of a nonrenal organ. *N Engl J Med.* 2003; 349:931–940. [PubMed: 12954741]
14. Esposito C, De Mauri A, Vitulo P, et al. Risk factors for chronic renal dysfunction in lung transplant recipients. *Transplantation.* 2007; 84:1701–1703. [PubMed: 18165784]
15. Imai Y, Parodo J, Kajikawa O, et al. Injurious mechanical ventilation and end-organ epithelial cell apoptosis and organ dysfunction in an experimental model of acute respiratory distress syndrome. *JAMA.* 2003; 289:2104–2112. [PubMed: 12709468]
16. Gurkan OU, O'Donnell C, Brower R, Ruckdeschel E, Becker PM. Differential effects of mechanical ventilatory strategy on lung injury and systemic organ inflammation in mice. *Am J Physiol Lung Cell Mol Physiol.* 2003; 285:L710–L718. [PubMed: 12754185]
17. Kilburn KH, Dowell AR. Renal function in respiratory failure. Effects of hypoxia, hyperoxia, and hypercapnia. *Arch Intern Med.* 1971; 127:754–762. [PubMed: 5555500]
18. Navis G, Broekroelofs J, Mannes GP, et al. Renal hemodynamics after lung transplantation. A prospective study. *Transplantation.* 1996; 61:1600–1605. [PubMed: 8669104]
19. Bloom RD, Reese PP. Chronic kidney disease after nonrenal solid-organ transplantation. *J Am Soc Nephrol.* 2007; 18:3031–3041. [PubMed: 18039925]
20. Christie JD, Kotloff RM, Pochettino A, et al. Clinical risk factors for primary graft failure following lung transplantation. *Chest.* 2003; 124:1232–1241. [PubMed: 14555551]
21. Currey J, Pilcher DV, Davies A, et al. Implementation of a management guideline aimed at minimizing the severity of primary graft dysfunction after lung transplant. *J Thorac Cardiovasc Surg.* 2010; 139:154–161. [PubMed: 19909995]
22. Cardinal H, Poirier C, Fugère JA, Ferraro P, Girardin C. The evolution of kidney function after lung transplantation: a retrospective cohort study. *Transplant Proc.* 2009; 41:3342–3344. [PubMed: 19857746]
23. Broekroelofs J, Navis G, Stegeman C, et al. Long-term renal outcome after lung transplantation is predicted by the 1-month postoperative renal function loss. *Transplantation.* 2000; 69:1624–1628. [PubMed: 10836372]
24. Weiss ES, Allen JG, Meguid RA, et al. The impact of center volume on survival in lung transplantation: an analysis of more than 10,000 cases. *Ann Thorac Surg.* 2009; 88:1062–1070. [PubMed: 19766782]
25. Bellomo R, Kellum J, Ronco C. Acute renal failure: time for consensus. *Intensive Care Med.* 2001; 27:1685–1688. [PubMed: 11810109]
26. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) group. *Crit Care.* 2004; 8:R204–R212. [PubMed: 15312219]

Fig. 1. Kaplan-Meier estimates of (A) 1-year survival and (B) and 5-year survival stratified by the need for post-lung transplantation renal replacement therapy (RRT). (C) Five-year survival conditional on 1-year survival stratified by the need for post-lung transplantation renal replacement therapy. The p value is based on the log rank test. (Solid lines = no RRT; dashed lines = RRT.)

Fig. 2. Kaplan-Meier estimates of 2-year survival of patients requiring post-lung transplantation renal replacement therapy stratified by implementation of the lung allocation score (LAS). The p value is based on the log rank test. (Solid line = pre-LAS; dashed line = post-LAS.)

Number at risk

≤ 18 LTx/year	3083	2483	2317	2155	2012
19-31 LTx/year	3178	2818	2653	2458	2304
32-48 LTx/year	2831	2506	2332	2175	2012
≥ 49 LTx/year	2930	2680	2480	2233	2079

A

Number at risk

≤ 18 LTx/year	3083	1983	1528	1162	852	624
19-31 LTx/year	3178	2267	1708	1340	1039	760
32-48 LTx/year	2831	1970	1496	1166	857	625
≥ 49 LTx/year	2930	2047	1430	968	621	356

B

Fig. 3. Kaplan-Meier estimates of (A) 1-year survival and (B) and 5-year survival in all lung transplantation (LTx) recipients stratified by annual center volume: black lines = 18 or fewer LTx annually; red lines = 19 to 31; blue lines = 32 to 48; green lines = 49 or more. The p value is based on the log rank test.

Table 1

Baseline Characteristics Stratified by Need for Postoperative Renal Replacement Therapy (Post-LTx RRT)

Variable	No Post-LTx RRT (n = 11,223)	Post-LTx RRT (n = 655)	p Value
Recipient demographics and comorbidities			
Age, years	52.5 ± 12.7	51.1 ± 12.9	<0.01
Male (%)	9,728/11,221 (86.7)	503/655 (76.8)	<0.01
White ethnicity (%)	9,728/11,221 (86.7)	503/655 (76.8)	<0.01
Black ethnicity (%)	862/11,221 (7.7)	85/655 (13.0)	<0.01
Hispanic ethnicity (%)	477/11,221 (4.3)	42/655 (6.4)	<0.01
Other ethnicity (%)	154/11,221 (1.4)	25/655 (3.8)	<0.01
Diabetes mellitus (%)	1,498/11,126 (13.5)	117/651 (18.0)	<0.01
Hypertension (%)	1,395/7,377 (18.9)	90/434 (20.7)	0.35
GFR, mL · min ⁻¹ · 1.73m ⁻²	93.8 ± 40.0	88.4 ± 58.9	<0.01
GFR 90, mL·min ⁻¹ ·1.73m ⁻² (%)	4,962/11,223 (44.2)	236/655 (36.0)	<0.01
GFR 60–90, mL· min ⁻¹ · 1.73m ⁻² (%)	5,087/11,223 (45.3)	286/655 (43.7)	0.41
GFR <60, mL · min ⁻¹ · 1.73m ⁻² (%)	1,174/11,223 (10.5)	133/655 (20.3)	<0.01
Total bilirubin, mg/dL	0.5 (0.3–0.7)	0.5 (0.3–0.9)	<0.01
Body mass index, kg/m ²	24.7 ± 7.5	25.1 ± 4.9	0.20
CMV positive (%)	6,077/10,287 (59.1)	379/621 (61.0)	0.34
IPF (%)	3,135/11,223 (27.9)	166/655 (25.3)	0.15
COPD (%)	3,976/11,223 (35.4)	155/655 (23.7)	<0.01
Cystic fibrosis (%)	1,520/11,223 (13.5)	96/655 (14.7)	0.42
PPH (%)	240/11,223 (2.1)	49/655 (7.5)	<0.01
Other diagnosis (%)	2,592/11,223 (23.1)	238/655 (36.3)	<0.01
Recipient hemodynamics, pulmonary function, and need for support			
Cardiac output, L/min	5.3 ± 1.4	5.2 ± 1.7	0.29
Mean PA pressure, mm Hg	26.9 ± 10.6	31.6 ± 14.0	<0.01
FEV ₁ , L	36.0 ± 20.9	38.3 ± 20.9	0.01
FVC, L	49.7 ± 17.6	49.3 ± 18.1	0.59
Hospitalized (%)	1,178/11,223 (10.5)	152/655 (23.2)	<0.01
Intensive care unit (%)	516/11,223 (4.6)	92/655 (14.1)	<0.01
Ventilatory support (%)	378/11,223 (3.4)	54/655 (8.2)	<0.01
ECMO support (%)	44/11,223 (0.4)	21/655 (3.2)	<0.01
Donor and transplant variables			
Age, years	33.1 ± 14.1	33.8 ± 14.5	0.28
Male (%)	6,751/11,223 (60.2)	383/655 (58.5)	0.39
Bilateral LTx (%)	6,394/11,223 (57.0)	482/655 (73.6)	<0.01
Ischemic time, hours	4.9 ± 1.7	5.3 ± 1.9	<0.01
Waitlist time, days	150 (42–466)	159.5 (37–439)	0.93
LAS	43.3 ± 14.4	49.6 ± 18.6	<0.01

Variable	No Post-LTx RRT (n = 11,223)	Post-LTx RRT (n = 655)	p Value
CMV positive (%)	6,737/11,134 (60.5)	404/645 (62.6)	0.28
Sex matching (%)	7,722/11,223 (68.8)	455/655 (69.5)	0.72
HLA mismatch (%)	5,321/9,316 (57.1)	324/548 (59.1)	0.36
Annual center volume (%)			
18 LTx	2,870/11,223 (25.57)	223/655 (34.05)	<0.01
19–31 LTx	2,951/11,223 (26.29)	151/655 (23.05)	0.06
32–48 LTx	2,634/11,223 (23.47)	143/655 (21.83)	0.34
49 LTx	2,768/11,223 (24.66)	138/655 (21.07)	0.04

CMV = cytomegalovirus; COPD = chronic obstructive pulmonary disease; ECMO = extracorporeal membrane oxygenation; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; GFR = glomerular filtration rate; HLA = human leukocyte antigen; IPF = idiopathic pulmonary fibrosis; LAS = lung allocation score; LTx = lung transplantation; PA = pulmonary artery; PPH = primary pulmonary hypertension.

Table 2**Cox Proportional Hazards Model of 30-Day Mortality**

Variable	Multivariable HR (95% CI)	p Value
Renal replacement therapy	7.87 (6.07–10.20)	<0.001
Recipient demographics and comorbidities		
Age 55 years	1.37 (1.04–1.81)	0.02
GFR 90	1 (Reference)	
GFR 60–90	1.03 (0.80–1.33)	0.83
GFR <60	1.22 (0.86–1.72)	0.27
Body mass index 30	1.25 (0.94–1.67)	0.13
IPF	1.03 (0.75–1.41)	0.84
COPD	0.88 (0.63–1.23)	0.46
Cystic fibrosis	0.80 (0.49–1.33)	0.39
PPH	1.32 (0.72–2.43)	0.37
Recipient hemodynamics, pulmonary function, and need for support		
Mean PA pressure, per mm Hg	1.01 (0.99–1.02)	0.11
Intensive care unit status	2.70 (1.94–3.77)	<0.001
ECMO support	3.00 (1.70–5.32)	<0.001
Donor and transplant variables		
Age, per year	0.99 (0.98–1.01)	0.08
Bilateral LTx	0.79 (0.59–1.04)	0.09
Ischemic time, per hour	1.08 (1.01–1.16)	0.04
Annual center volume		
18 LTx	1 (Reference)	
19–31 LTx	0.96 (0.70–1.30)	0.77
32–48 LTx	1.02 (0.75–1.40)	0.88
49 LTx	0.65 (0.46–0.91)	0.01

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ECMO = extracorporeal membrane oxygenation; GFR = glomerular filtration rate; HR = hazard ratio; IPF = idiopathic pulmonary fibrosis; LTx = lung transplantation; PA = pulmonary artery; PPH = primary pulmonary hypertension.

Table 3**Cox Proportional Hazards Model of 1-Year Mortality**

Variable	Multivariable HR (95% CI)	p Value
Renal replacement therapy	7.89 (6.80–9.15)	<0.001
Recipient demographics and comorbidities		
Age 55 years	1.52 (1.31–1.75)	<0.001
GFR 90	1 (Reference)	
GFR 60–90	1.02 (0.90–1.17)	0.71
GFR <60	1.24 (1.03–1.49)	0.02
Recipient body mass index 30	0.97 (0.82–1.14)	0.69
IPF	1.04 (0.88–1.23)	0.63
COPD	0.80 (0.67–0.95)	0.01
Cystic fibrosis	0.90 (0.70–1.15)	0.41
PPH	0.94 (0.64–1.37)	0.74
Recipient hemodynamics, pulmonary function, and need for support		
Mean PA pressure, per mm Hg	1.00 (0.99–1.01)	0.44
Intensive care unit status	2.26 (1.86–2.73)	<0.001
ECMO support	2.72 (1.76–4.21)	<0.001
Donor and transplant variables		
Age, per year	1.00 (0.99–1.01)	0.09
Bilateral LTx	0.84 (0.73–0.97)	0.02
Ischemic time, per hour	1.03 (0.99–1.07)	0.14
Annual center volume		
18 LTx	1 (Reference)	
19–31 LTx	0.86 (0.74–1.01)	0.06
32–48 LTx	0.75 (0.63–0.88)	0.001
49 LTx	0.66 (0.56–0.78)	<0.001

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ECMO = extracorporeal membrane oxygenation; GFR = glomerular filtration rate; HR = hazard ratio; IPF = idiopathic pulmonary fibrosis; LTx = lung transplantation; PA = pulmonary artery; PPH = primary pulmonary hypertension.

Table 4

Multivariable Logistic Regression Model of Predictors of the Need for Renal Replacement Therapy (RRT) After Lung Transplantation (LTx)

Variable	Multivariable OR (95% CI)	p Value
Recipient demographics and comorbidities		
Age, per year	1.01 (1.001–1.021)	0.03
Male	1.19 (0.99–1.43)	0.06
White ethnicity	1 (Reference)	
Black ethnicity	1.74 (1.31–2.31)	<0.001
Hispanic ethnicity	1.72 (1.20–2.47)	0.003
Other ethnicity	2.81 (1.72–4.59)	<0.001
GFR ≥90	1 (Reference)	
GFR 60–90	1.42 (1.16–1.74)	0.001
GFR <60	2.67 (2.07–3.46)	<0.001
Total bilirubin, per mg/dL	1.07 (1.03–1.11)	<0.001
IPF	1.07 (1.03–1.11)	<0.001
COPD	0.65 (0.50–0.85)	0.002
Cystic fibrosis	1.04 (0.73–1.49)	0.83
PPH	2.19 (1.47–3.27)	<0.001
All pulmonary fibrosis	0.97 (0.61–1.54)	0.91
Recipient hemodynamics, pulmonary function, and need for support		
Intensive care unit	1.61 (1.10–2.37)	0.01
ECMO support	4.06 (2.24–7.37)	<0.001
Donor and transplant variables		
Bilateral LTx	1.56 (1.24–1.96)	<0.001
Ischemic time, per hour	1.09 (1.03–1.16)	0.002
Annual center volume		
18 LTx/year	1 (Reference)	
19–31 LTx/year	0.62 (0.49–0.79)	<0.001
32–48 LTx/year	0.69 (0.54–0.88)	0.002
49 LTx/year	0.56 (0.43–0.71)	<0.001

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ECMO = extracorporeal membrane oxygenation; GFR = glomerular filtration rate; IPF = idiopathic pulmonary fibrosis; LTx = lung transplantation; OR = odds ratio; PPH = primary pulmonary hypertension.