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LONG TERM SURVIVAL FOLLOWING KIDNEY TRANSPLANTATION IN PREVIOUS LUNG TRANSPLANT RECIPIENTS - AN ANALYSIS OF THE UNOS REGISTRY

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Abstract

BACKGROUND—Kidney transplantation has been advocated as a therapeutic option in lung recipients who develop end-stage renal disease. This analysis outlines patterns of allograft survival following kidney transplantation in previous lung recipients (KAL).

METHODS—Data from the UNOS lung and kidney transplantation registries (1987–2013) were cross-linked to identify lung recipients who were subsequently listed for and/or underwent kidney transplantation. Time-dependent Cox models compared survival in KAL patients vs. those waitlisted for renal transplantation who never received kidneys. Survival analyses compared outcomes between KAL patients and risk-matched recipients of primary, kidney-only transplantation with no history of lung transplantation (KTx).

RESULTS—270 lung recipients subsequently underwent kidney transplantation (KAL). Regression models demonstrated a lower risk of post-listing mortality for KAL patients compared with 346 lung recipients on the kidney waitlist who never received kidneys ($p < 0.05$). Comparisons between matched KAL and KTx patients demonstrated significantly increased risk of death and graft loss ($p < 0.05$), but not death-censored graft loss, for KAL patients ($p = 0.86$).

CONCLUSIONS—KAL patients enjoy a significant survival benefit compared with waitlisted lung recipients who do not receive kidneys. However, KAL patients do poorly compared with KTx

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DISCLOSURES

Authors have complete autonomy for data collection, analysis and interpretation, as well as full rights to approve study publication. Authors have no other relevant financial or industry related disclosure.

patients. Decisions about KAL transplantation must be made on a case-by-case basis considering patient and donor factors.

Keywords

Lung transplantation; Kidney transplantation; Survival; Kidney after lung transplantation

INTRODUCTION

Lung transplantation is controversial in patients with significant dysfunction in another major organ system^{1–3}. Allocating lungs to candidates with advanced renal disease is particularly risky given the known nephrotoxicity of standard immunosuppressant regimens – especially calcineurin inhibition – and the resultant increased likelihood of accelerated renal deterioration post-transplantation^{4–6}. Previous work from our group has advocated for lung transplantation in patients with marginal renal function provided that contingency plans are in place for kidney transplantation should end stage renal disease occur after lung transplantation^{4,7}. This analysis aims to explore the incidence and outcomes of kidney transplantation in previous lung recipients (KAL – Kidney after lung). Authors assess recipient and renal allograft outcomes to determine whether transplantation in this population (KAL) is associated with appropriate longevity when compared with recipients of primary, kidney only transplantation (KTx).

MATERIALS AND METHODS

Institutional Review

The protocol for the retrospective analysis was approved by the Institutional Review Board at Duke University Medical Center, Durham, NC. Individual consent was not required.

Data Source

The United Network for Organ Sharing (UNOS) national database contains data on all transplantation procedures performed in the United States since 1987. For this analysis UNOS files were queried for lung transplantations prospectively recorded between October 1987 and December 2011, and kidney transplantations between October 1987 and December 2013.

Study Design and Patient Selection

All patients undergoing kidney and lung transplantation within the study dates were considered for inclusion in the study. Exclusion criteria included age less than 18 years, non-primary transplantation, simultaneous multi-organ transplantation (including concurrent lung-kidney transplantation) or kidney transplant prior to lung transplantation. Following exclusions, records from the lung and kidney transplantation databases were cross-matched to identify patients with a history of lung transplantation who were subsequently listed for kidney transplantation. The final study cohort was made up of lung recipients who ultimately underwent kidney transplantation (KAL) [Figure 1].

Propensity Matching

To analyze outcomes in the KAL cohort, KAL patients were matched 1:2 with recipients of primary, kidney only transplantation (KTx) based on the propensity score method as outlined by Rosenbaum and Rubin, D'Agostino and Rubin, and Austin⁸⁻¹¹. Using a logistic regression model with covariate selection based on backward elimination, we calculated a propensity score for each patient, which represents the “risk” of being a KAL recipient. Our model controlled for differences in age, race, gender, body mass index (BMI), etiology of renal disease, functional status and type of kidney donor (living vs. deceased) between KAL and KTx cohorts. Each KAL recipient was subsequently matched with two KTx patients to create the 1:2 matched cohort for analysis of outcomes.

Per convention for managing missing data in propensity score analysis, a value of 0 was imputed in empty fields for continuous variables with creation of a new, binary variable indicating those records that have missing entries. For categorical variables, an additional level was created for missing data^{10,12,13}. Comparisons between cohorts were made using standardized differences with values less than 0.2 indicating negligible differences in a given patient characteristic^{14,15}.

Primary Analysis

Primary outcomes include allograft and patient survival following kidney transplantation. For comparisons in matched KAL vs. KTx populations, Kaplan-Meier and Cox-regression analyses use the date of kidney transplantation as the start time. Additional analyses explored death-censored graft survival to better isolate comparisons of renal allograft longevity between KAL and KTx cohorts.

To further outline the benefits of kidney transplantation in lung recipients with ESRD, comparisons were made between KAL patients and lung recipients who were waitlisted but did not end up undergoing kidney transplantation. These comparisons were performed using multivariable, time dependent Cox-regression models that appropriately assigned time on the waitlist for KAL patients to the waitlist arm of the analysis. Starting time for these analyses was date of listing for kidney transplantation or date of transplantation for recipient of living donor kidneys who were never waitlisted.

Secondary Analysis

Secondary analyses used multivariable cox-regression models to explore predictors of improved outcomes in KAL cohorts. Additionally, we compared outcomes in primary, lung only recipients (LTx) to an aggregated cohort of KAL recipients and lung recipients who were listed for kidneys but did not receive them. Analyses were performed using time-dependent Cox-regression models that explored implications of going on dialysis and of undergoing kidney transplantation on outcomes in patients with a history of lung transplantation.

Statistical Analysis

Statistical analyses were performed using SAS v9.3 (SAS Institute Inc., Cary, NC). Variables in propensity matched analysis were compared with standardized differences as

previously described. For non-matched comparisons continuous variables were compared using the student's T-test while categorical variables were compared using the Chi-Square statistic. Survival analyses were performed using Kaplan-Meier and Cox Regression analyses as described. Variables were included in multivariable models if they had p value < 0.2 on univariate or bivariate analysis. Final multivariable models were determined using a backward selection algorithm.

Per convention, the threshold for statistical significance of analyses was set at < 0.05 . Variables were included in analyses if they were at least 80% populated, with most having complete data for more than 95% of patients included in the study.

RESULTS

Patient Characteristics

Of 20,572 lung recipients who met study criteria, 616 (2.9 %) were subsequently listed for kidney transplantation. 270 of these patients (1.3%) ultimately underwent kidney transplantation [Figure 1]. In the overall cohort of lung recipients, only 65 patients (0.23%) were on dialysis at the time of lung transplantation. Notably, 18 recipients of simultaneous lung-kidney transplantation were excluded from this analysis based on criteria describe in the methods. Compared with lung recipients who were not listed for renal transplantation, patients who were listed for and/or underwent kidney transplantation were younger at the time of lung transplantation (49 years vs. 57 years, $p < 0.0001$), more often female (54.9% vs. 44.1%, $p < 0.0001$), more likely to have undergone bilateral lung transplantation (66.1% vs. 57.4%, $p < 0.0001$), more likely to have undergone lung transplantation for cystic fibrosis/bronchiectasis (31.2% vs. 14.3%) and more likely at the time of lung transplantation to be independent in performing activities of daily living (Based on a rating of 7 or higher on the Karnofsky scale, 33.8% of those listed for renal transplant vs 27.6% for those who were not). [Table 1]. Few patients were on hemodialysis at the time of lung transplantation (0.59% in the group of patients who were listed for and/or received kidney transplantation vs. 0.24% in the group who were not, $p = 0.1365$).

Within the group of patients who were listed for and/or underwent kidney transplantation, there were some differences in populations that ultimately received kidneys (KAL) compared to those on the wait list who did not undergo renal transplantation. KAL patients were on average younger (Median age 53 vs. 58 years at the time of listing [or at kidney transplantation for recipients of living donor transplantation who were never listed], $p < 0.0001$), less likely to already be on dialysis (41.4% vs. 56.1%, $p = 0.0009$), more likely to be Caucasian (94.8% vs. 87.3%, $p = 0.0015$) and more likely to have undergone lung transplantation for a diagnosis of cystic fibrosis/bronchiectasis (38.5% vs. 25.4%, $p = 0.0004$) [Table 2]. Median time between lung transplantation and listing for kidneys was similar in the two groups (82 vs. 76 months, $p = 0.3191$), as was median time between lung transplantation and initiation of HD (83 vs. 68 months, $p = 0.1109$).

Primary Analysis

Univariate time dependent cox-regression models comparing KAL patients to lung recipients listed for kidney transplantation who never received kidneys, demonstrated a lower risk of post-listing mortality for KAL patients (HR 0.38, 95% CI 0.29 – 0.50, $p < 0.001$). Bivariate time dependent models identified recipient age, gender, etiology of renal pathology, type of lung transplantation (single vs. double) and etiology of initial pulmonary pathology as potential modifiers of this relationship (All with $p < 0.05$). Time-dependent multivariate modelling incorporating all these factors demonstrated a persistent mortality benefit for KAL patients compared to lung recipients listed for kidney transplantation who never received kidneys (HR 0.40, 95% CI 0.2 – 0.56, $p < 0.001$) [Table 3]. This multivariable model selected for relevant predictors using a backward selection algorithm, ultimately identifying age, gender, type of lung transplantation and etiology of renal pathology as significant predictors of mortality in our cohort of 616 lung recipients who were subsequently listed for kidney transplantation, whether or not they received kidneys (All $p < 0.05$) [Table 3].

The 270 KAL patients were matched 1:2 with 540 recipients of primary, kidney only transplantation (KTx) based on the propensity score method described earlier. After matching, KAL and matched KTx cohort were similar in age, race, gender, etiology of renal disease, ADL independence, BMI, proportion of deceased donor transplantation and overall donor characteristics (All with Standardized Difference < 0.2) [Table 4]. Fewer patients in the KAL group were on dialysis at the time of transplantation (61.4% vs. 74.1%, Standardized Difference = 0.2803). 33.3% of KAL patient underwent deceased donor kidney transplantation vs. 36.9% of kidney only recipients (Standardize Difference = 0.0754).

Cox regression analysis comparing patient survival in KAL vs. risk matched KTx cohorts demonstrated a significantly increase mortality risk for KAL patients (HR 2.14, 95% CI 1.72 – 2.65, $p < 0.0001$) [Figure 2]. Similarly, the risk of graft loss was higher for KAL patients (HR 1.96, 95% CI 1.57 – 2.46, $p = 0.0317$) [Figure 3A]. Additional cox-regression models exploring comparative death-censored graft survival demonstrated no significant differences between the two groups (HR 1.05, 95% CI 0.63 – 1.75, $p = 0.8586$) [Figure 3B].

Secondary Analysis

Cox-regression models were created to identify factors associated with improved survival following kidney transplantation in patients with a prior history of lung transplantation (I.e. KAL patients). Univariate models identified increasing age, diagnosis of obstructive lung disease, receipt of single lung transplantation (vs. bilateral) and receipt of deceased donor kidney transplantation (vs. living donor) as being associated with increased mortality post kidney transplantation (All $p < 0.05$). When combined in a multivariable model (including BMI which had univariate $p = 0.1396$), only age and receipt of deceased donor kidney transplantation maintained their associations with increased mortality (Both $p < 0.05$) [Table 5].

Comparative time dependent cox-regression models with start point at the time of lung transplantation compared recipients of primary, lung only transplantation who never got

listed for kidneys (LTx) to those lung recipients who made it onto the waitlist for kidneys and/or subsequently underwent kidney transplantation. Models exploring the effect of hemodialysis demonstrated increased mortality risk for lung recipients who require renal replacement therapy, compared with those who don't (HR 1.29, 95% CI 1.09 – 1.53, $p = 0.0030$). Conversely, there was a clear decrease in mortality risk for those who ultimately underwent transplantation (KAL) compared with the rest of the lung transplantation cohort, whether or not these patients were ever listed for kidney transplantation or required dialysis (HR 0.73, 95% CI 0.62 – 0.86, $p = 0.0002$). Notably, both of the models described in this paragraph were set up such that survival time prior to dialysis or kidney transplantation was appropriately attributed to the LTx group. In other words, survival of KAL patients prior to kidney transplantation was classified as LTx survival to try to mitigate the effects of lead time bias.

COMMENT

Renal insufficiency is not uncommon after lung transplantation, likely related to the widespread use of nephrotoxic calcineurin inhibition regimes post-transplantation^{5,7}. The current study represents the first dedicated analysis of the national experience with kidney transplantation in lung recipients (KAL). Our analysis suggests that renal transplantation in patients with a history of prior lung transplantation confers significant survival benefit when compared with waitlisting for ESRD without subsequent receipt of a kidney allograft. However, renal transplantation in patients with a prior history of lung transplantation is associated with a significantly higher risk of graft loss when compared with recipients of first time, kidney only transplantation. Analyses of death-censored graft survival suggest that much of this increased risk of graft loss is driven by patient mortality, hinting at a potential opportunity for customizing the allocation of kidneys to patients in this unique subset of kidney candidates. Study findings lend support to efforts to optimize allocation of kidney allografts by matching expected donor allograft longevity with overall expected patient survival in certain unique groups.

The median time between lung transplantation and listing for kidneys was 82 months, suggesting that practitioners believe that late kidney transplantation is a better option in this population. One might speculate that this allows lung recipients to declare their resilience and thus support their candidacy for a second organ transplant. That said, it remains unclear what the ideal time for kidney transplantation is following lung transplantation. Kidney transplantation too late after lung transplantation may be associated with increased likelihood of bronchiolitis obliterans syndrome (BOS) which would confer unacceptably high rates of early mortality following renal transplantation. This issue is particularly pungent when considering patients for potential living donor transplantation given the disproportionate comparative longevity for kidneys donated from living donors vs. long term recipients of lung transplantation. Ideally kidney transplantation should not be considered an option in the setting of known declining lung function, unless options for lung re-transplantation are also being explored. Although excluded from our analysis, there were 18 simultaneous lung-kidney transplants performed within the study dates and this remains an options for patients. However, the relatively infrequency of this occurrence is likely related to traditional descriptions of ESRD – which would represent “significant dysfunction in

another organ system” – as a contra-indication to lung transplantation. Further supporting this hypothesis is the fact that only 0.23% of patients were on dialysis at the time of lung transplantation.

Our results comparing KAL patients to those who underwent primary, lung only transplantation provide further evidence of the survival benefit of kidney transplantation in this population as KAL patients enjoy improved longevity compared to lung only recipients. Findings are robust even in models that account for the inherent longevity bias enjoyed by lung recipients who live long enough to make it to listing for a kidney. This further highlights the need to continue to consider lung recipients who develop ESRD for kidney transplantation even in the face of significantly increased mortality compared with primary kidney only transplantation.

Models in KAL cohorts identified younger age and receipt of living donor kidney transplantation (vs. deceased donor transplantation) as factors associated with improved survival in this population. While KAL living donor recipients are still at increased risk for death related graft loss, prioritizing living donor transplantation in this group would improve overall longevity and might contribute to alleviating concerns about competition for deceased donor organs with kidney only candidates who will on average derive longer term benefit from kidney transplantation. In this setting, it will be important for living donors to be alerted to the likely shorter lifespan of their organ compared to the potential lifespan if given to a patient who did not have a history of lung transplantation. Notwithstanding, high rates of death censored graft loss suggest that KAL recipients of living donation will likely enjoy benefit from donated organs for the duration of their lives, a fact that will likely temper the news of decreased organ longevity for the potential living kidney donor.

Study results are consistent with existing literature exploring kidney transplantation in recipients with a history of thoracic organ transplantation^{16–18}. A recent single center analysis by Otani et al. looked at 8 kidney after thoracic organ (lung or heart- lung) transplantation patients with median time of 127 months between thoracic and kidney transplantation. Study findings highlight higher median survival following living donor compared with deceased donor kidney transplantation¹⁷. A 2010 study by Cassuto et al focused on KAL patients who received deceased donor kidney transplantation demonstrating a graft loss HR of 1.61 (95% CI 1.09 – 2.38) for KAL compared with recipients of primary, kidney only transplantation with no history of primary lung or other organ transplantation¹⁸. Authors highlighted that at five years post kidney transplantation, 80% of graft loss in the KAL cohort was secondary to death with a functioning kidney, numbers that correlate with findings in our study.

Similarly, a 2009 study by Lonze et al. analyzed outcomes in 210 KAL patients with median time between lung and kidney transplantation of 90.2 months and average 5 year survival of 62.6%¹⁶. As in our study, death censored graft survival for KAL patients was quite high at 87.6% and comparable to results in matched cohorts of kidney only recipients (91.8%). Authors highlight the fact that survival in KAL patients is determined by progression of lung disease, not by renal pathology. Despite findings of lower survival compared to primary kidney recipients, Lonze et al. advocate for continued consideration of lung recipients for

kidney transplantation, making insightful comparisons to other high risk populations (e.g. elderly candidates for primary kidney transplantation) who continue to receive kidney despite high rates of death related graft loss.¹⁶

Taken together, results in the existing literature and in this present study highlight a few things: 1) Increased graft loss in KAL patients compared with kidney only recipients with no history of lung transplanation is mediated by death related graft loss. In other words, KAL patients are likely to receive kidney allografts that are “too robust” for their particular expected longevity. Factoring in the estimated life expectancy of a given lung recipient will allow for use of extended criteria organs in this population to minimize the controversy associated with maintained kidney allograft function at the time of death. It will be important however to carefully balance risks so that kidney graft loss does not then become the cause of mortality in KAL patients. This is not too unlike current efforts to provide ideal organs for high risk primary kidney only recipients, particularly those with advanced age; 2) Benefits of living vs. deceased donor kidney transplantation for KAL patients are seen in improved graft survival, but also in the logistics of organ allocation as there is somewhat less direct competition with the overall kidney candidate pool since living donors are very often related to recipients. In this setting, the key will be to educate donors about the intricacies of living donation to a KAL patient as previously outlined; and 3) Worse outcomes for lung recipients on the waitlist for kidneys highlight the detrimental effect of ESRD to lung allografts and hint at the benefit of early discussion about options for renal replacement when end stage renal disease is imminent. This will allow recipients and practitioners to evaluate options early and receive kidneys early on in the progression of their disease.

Our study is limited by its retrospective design, which exposes it to the shortcomings associated with non-prospective, non-randomized analyses. Notably, results could be a reflection of confounding based on variables that have not been controlled for, which should be acknowledged when interpreting our findings. Additionally, we recognize that analyses using large data repositories like the UNOS database are fraught with uncertainties related to the completeness and accuracy of available data. For this analysis, all included variables were robustly populated, mitigating this limitation to some degree. A final limitation is found in our consideration of the interplay between renal dysfunction and waitlist outcomes. A considerable proportion of KAL patients underwent living donor renal transplantation and thus were never put on the kidney waitlist. This imposes some limitation in our understanding of time to and circumstances surrounding development of severe kidney disease following lung transplantation.

CONCLUSION

Lung recipients who subsequently undergo kidney transplantation enjoy a significant survival benefit when compared with lung recipients who are waitlisted but do not end up receiving kidneys. However, outcomes following kidney after lung transplantation are significantly worse compared with those following primary, kidney only transplantation in patients without a history of lung transplantation, likely mediated by high rates of death related graft loss. Notwithstanding, kidney transplantation should remain a consideration for lung recipients who develop end stage renal disease, particularly when patients demonstrate

robust function of existing lung allografts. Strategies to mitigate controversy of transplantation in this population include focusing on early transplantation, kidney transplantation from living donors, and potentially on extended criteria donation to match expected survival in this patient population.

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Figure 1.
Study Population

Figure 2.
Kaplan-Meier Curves comparing Patient Survival in Kidney after Lung Recipients vs. Risk-Matched patients undergoing primary, Kidney only Transplantation with no prior history of Lung Transplantation

Figure 3.
Kaplan-Meier Curves comparing A) Graft Survival and B) Death Censored Graft Survival in Kidney after Lung Recipients vs. Risk Matched patients undergoing primary, Kidney only Transplantation with no prior history of Lung Transplantation

Table 1

Comparative Characteristics at the time of Lung Transplantation for Lung Recipients who were subsequently listed for and/or underwent Kidney Transplantation vs. Lung recipients who were never considered for kidney transplantation

Variable*	Lung Recipients never listed for kidney transplantation (n = 27,518)	Lung Recipients listed for and/or undergoing kidney transplantation (n = 616)	P Value**	Number Missing
Age (Years)	57 (47 – 63)	49 (35 – 56)	<0.0001	0
Female	12144 (44.1)	338 (54.9)	<0.0001	0
White Race	23593 (85.7)	559 (90.8)	0.0004	0
Independent of ADLs	6777 (27.6)	156 (33.8)	0.0031	3079
BMI (Kg/m ²)	24.78 (20.96 – 28.36)	22.27 (19.11 – 26.12)	<0.0001	228
Etiology (LTx)			<0.0001	0
Obstructive	10373 (37.7)	256 (41.6)		
Restrictive	10557 (38.4)	110 (17.9)		
Cystic Fibrosis	3936 (14.3)	192 (31.2)		
PPH	1226 (4.5)	23 (3.7)		
Other	1426 (5.2)	35 (5.7)		
HD at LTX	62 (0.24)	3 (0.59)	0.1365	2191
Double LTx	15800 (57.4)	407 (66.1)	<0.0001	0
LTx Donor age (Years)	30 (21 – 45)	27 (19 – 40)	<0.0001	0
LTx Donor Female	10641 (38.7)	247 (40.1)	0.4717	0
1 Year Survival after LTx	20284 (80.4)	615 (99.8)	<0.0001	2293
5 Year Survival after LTx	8075 (57.2)	540 (89.3)	<0.0001	7209

* Median (SD) for continuous variables, N (%) for categorical variables

** Student's T-test for continuous variables; X² for categorical variables

LTx – Lung Transplantation; ADLs – Activities of Daily Living; HD – Dialysis; BMI – Body Mass Index; PPH – Primary Pulmonary Hypertension

Table 2

Characteristics of Lung Recipients who underwent Kidney Transplantation compared to those listed for Kidney Transplantation who did not ultimately receive organs

Variable *	Lung recipients who underwent kidney transplantation (n = 270)	Lung recipients who were listed but did <u>NOT</u> undergo kidney transplantation (n = 346)	P Value **	Missing
Age at listing (Years)	53.0 (40.0 – 60.0)	58.0 (47.0 – 64.0)	<0.0001	0
Female	151 (55.9)	187 (54.1)	0.6418	0
White Race	256 (94.8)	302 (87.3)	0.0015	0
Etiology of Kidney Disease (Tubulointerstitial)	133 (63.6)	207 (60.2)	0.4173	63
Independent of ADLs	234 (92.5)	273 (88.4)	0.1003	54
BMI (Kg/m ²)	23.0 (19.9 – 25.9)	23.0 (20.1 – 25.9)	0.4331	80
HD at Listing	84 (41.4)	192 (56.1)	0.0009	71
Time to HD (Months)	83.8 (58.7 – 118.8)	67.9 (42.4 – 99.6)	0.1109	358
Time to listing for kidney (Months)	82.0 (52.1 – 115.0)	76.3 (49.5 – 107.0)	0.3191	60
Time to Transplant (Months)	88.4 (62.6 – 122.9)	NA	NA	0
Etiology (LTx)			0.0004	0
Obstructive	106 (39.2)	150 (43.4)		
Restrictive	32 (11.9)	78 (22.5)		
CF	104 (38.5)	88 (25.4)		
PPH	9 (3.3)	14 (4.1)		
Other	19 (7.0)	16 (4.6)		
HD at LTx	2 (0.97)	1 (0.33)	0.5688	105
Bilateral LTx	180 (66.7)	227 (65.6)	0.7828	0
LTx Donor age (Years)	27.0 (18.0 – 39.0)	27.0 (19.0 – 41.0)	0.2631	0
LTx Donor Female	121 (44.8)	126 (36.4)	0.0348	0
LTX Donor White Race	209 (77.4)	258 (74.6)	0.4139	0

* Median (SD) for continuous variables, N (%) for categorical variables

** Student's T-test for continuous variables; X² for categorical variables

LTx – Lung Transplantation; ADLs – Activities of Daily Living; HD – Dialysis; BMI – Body Mass Index; PPH – Primary Pulmonary Hypertension

Table 3

Results of Time-Dependent Cox Regression Models exploring Mortality in Lung Recipients who underwent Kidney Transplantation compared to those Listed for Kidney Transplantation who did not ultimately receive organs

BIVARIATE*		MULTIVARIATE***	
Variable	HR (95% CI)	Variable	HR (95% CI)
KAL ONLY	KAL – 0.379 (0.287 – 0.501) **		
KAL + Age	KAL – 0.420 (0.317 – 0.556) Age – 1.022 (1.012 – 1.033) **		
KAL + Female Gender	KAL – 0.376 (0.284 – 0.497) Fem – 0.794 (0.637 – 0.990) **		
KAL + Race (White)	KAL – 0.372 (0.281 – 0.493) Whi – 1.245 (0.818 – 1.895)	KAL	KAL – 0.402 (0.285 – 0.566)
KAL + Etiology of kidney disease (Tubulointerstitial)	KAL – 0.358 (0.260 – 0.494) Tub – 0.705 (0.556 – 0.894) **	+ Age	Age – 1.013 (1.001 – 1.026)
KAL + Body Mass Index (BMI)	KAL – 0.359 (0.259 – 0.497) BMI – 0.997 (0.970 – 1.025)	+ Female Gender	Fem – 0.718 (0.558 – 0.924)
KAL + Bilateral Lung Transplantation	KAL – 0.377 (0.285 – 0.498) Bil – 0.600 (0.479 – 0.750) **	+ Etiology of Kidney Disease (Tubulointerstitial)	Tub – 0.763 (0.558 – 0.924)
KAL + ADL Independence	KAL – 0.393 (0.293 – 0.527) ADL – 0.675 (0.457 – 0.995) **	+ Bilateral Lung Transplant	Bil – 0.671 (0.509 – 0.884)
KAL + Etiology of lung disease	KAL – 0.405 (0.305 – 0.536) Obs – 1.449 (1.130 – 1.359) ** Res – 1.201 (0.856 – 1.687)		
KAL + Time to HD	KAL – 0.293 (0.173 – 0.498) HD – 1.000 (1.000 – 1.000)		

* Each time dependent model included an indicator variable for receipt of kidney transplantation vs. remaining on the waitlist (KAL). Bivariate models tested the interaction of KAL with each of the stated variables

** Statistically significant at the 0.05 level

*** All variables from bivariate analysis with significant effect at 0.20 level (Left) were included in the final model. HR from the multivariate model are shown only for variables included in the final model, selected based on backward selection algorithm

KAL – Kidney after Lung; ADL – Activities of Daily Living; HD – Dialysis; Obs – Obstructive Lung Disease; Res – Restrictive Lung Disease

Table 4

Characteristics of Kidney after Lung Recipients compared with Risk Matched Patients undergoing primary, Kidney only Transplantation with no prior history of Lung Transplantation

Variable *	Recipients of Kidney after Lung Transplantation (KAL) (n = 270)	Recipients of Primary, Kidney only Transplantation with no LTx. History (n = 540)	Std. Diff. **	Missing
Age (Years)	53.5 (41.0 – 61.0)	57.0 (43.5 – 64.5)	0.1468	0
Female	151 (55.9)	325 (60.2)	0.0872	0
White Race	256 (94.8)	508 (94.1)	0.0305	0
Etiology of Kidney Disease (Tubulointerstitial)	216 (80.0)	431 (79.8)	0.0049	0
Independent of ADLs	211 (86.5)	432 (88.2)	0.0482	76
BMI (Kg/m ²)	23.0 (19.9 – 25.9)	22.7 (20.2 – 25.8)	0.0046	202
Hospitalized at transplant	8 (2.96)	14 (2.59)	0.0225	0
Deceased Donor (Vs. Living)	90 (33.3)	199 (36.9)	0.0754	0
HD at Kidney Transplant	164 (61.4)	392 (74.1)	0.2803	14
Donor Age (Years)	42.0 (33.0 – 52.0)	40.0 (30.0 – 51.0)	0.0987	0
Donor Gender (Female)	151 (55.9)	289 (53.5)	0.0482	0
Donor Race (White)	256 (94.8)	479 (88.7)	0.1800	0
Waitlist Time (Months)	7.8 (3.5 – 19.1)	9.1 (3.6 – 23.3)	0.1751	190
1 Year Survival	240 (89.2)	511 (95.5)	0.2387	6
5 Year Survival	128 (60.1)	333 (78.2)	0.3968	171

* Median (SD) for continuous variables, N (%) for categorical variables

** Standardized Difference – This is estimated as the difference in the mean between the two groups being compared, divided by the square root of the pooled variance, with modification to reflect proportions for categorical variables. Values < 0.2 indicate negligible differences between the two groups.

LTx – Lung Transplantation; ADLs – Activities of Daily Living; HD – Dialysis; BMI – Body Mass Index; Std. Diff – Standardized Difference

Table 5

Results of Cox Regression models exploring predictors of Mortality in Lung Recipients who underwent kidney transplantation (KAL)

UNIVARIATE		MULTIVARIATE	
Variable	HR (95% CI)	Variable	HR (95% CI)
Age	1.045 (1.029 – 1.061) **	Age Deceased Kidney Donor (Vs. Living)	1.040 (1.021 – 1.058) 1.547 (1.055 – 2.268)
Female Gender	0.860 (0.621 – 1.190)		
Race (White)	1.794 (0.663 – 4.851)		
Etiology of Kidney Disease (Tubulointerstitial)	0.857 (0.576 – 1.275)		
Body Mass Index	1.032 (0.990 – 1.075)		
Deceased Kidney Donor (Vs. Living)	1.482 (1.062 – 2.070) **		
On dialysis at time of kidney transplant	1.132 (0.800 – 1.600)		
Etiology of lung disease			
Restrictive	1.366 (0.842 – 2.218)		
Obstructive	2.101 (1.517 – 2.910) **		
CF/Bronchiectasis	0.402 (0.227 – 0.583) **		
Bilateral Lung Transplant	0.506 (0.364 – 0.702) **		

* Each univariate model explores the effect of a unit increase in the given continuous variable (or existence in the given state for categorical variable) on mortality in KAL patients

** Statistically significant at the 0.05 level

*** All variables from univariate analysis with significant effect at 0.20 level (Left) were included in the final model. HR from the multivariate model are shown only for variables included in the final model, selected based on backward selection algorithm

KAL – Kidney after Lung; HD – Dialysis