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Transplanting Candidates with Stacked Risks Negatively Affects Outcomes

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Abstract

Purpose: Lung transplant (LT) centers are increasingly evaluating patients with multiple risk factors for adverse outcomes. Effects of these stacked risks remains unclear. Our aim was to determine the relationship between number of comorbidities and post-transplant outcomes.

Methods: We performed a retrospective cohort study using the National Inpatient Sample (NIS) and UNOS Starfile (USF). We applied a probabilistic matching algorithm using 7 variables (transplant: month, year and type; recipient: age, sex, race, payer). We matched recipients in the USF to transplant patients in the NIS between 2016 to 2019. The Elixhauser methodology was used to identify comorbidities present on admission. We determined the associations between mortality, LOS, total charges and disposition with comorbidity number using penalized cubic splines, Kaplan-Meier, and linear and logistic regression methods.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

Results: From 28,484,087 NIS admissions, we identified 1,821 LT recipients. Matches were exact in 76.8% of the cohort. While the remaining cohort had a probability match of 0.94. Penalized splines of Elixhauser comorbidity number identified 3 knots defining 3 groups of stacked risk: low (<3), medium (3-6) and high risk (>6). Inpatient mortality increased from low to medium to high risk categories: (1.6%, 3.9% and 7.0%; $p < 0.001$), as did LOS (16, 21, 29 days, $p < 0.001$), total charges (\$553,057, \$666,791, \$821,641.5; $p = 0.004$) and discharge to skilled nursing facility (15%, 20%, 31%; $p < 0.001$).

Conclusion: Stacked risks adversely affect post-LT mortality, LOS, charges and discharge disposition. Further study to understand the details of specific stacked risks is warranted.

Keywords

lung transplant; Candidate Selection; Comorbidities; Outcomes

Guidelines for lung transplant candidate selection were first published as a joint statement between International Society for Heart and Lung Transplantation (ISHLT), American Thoracic Society (ATS), and European Respiratory Society (ERS) in 1998.¹ Though revised in 2006,² 2014,³ and again in 2021,⁴ most of the guidelines outlined in these documents are based on expert opinion rather than randomized clinical trials.⁵ Despite several decades of experience, the evaluation, determination of candidacy, and listing of candidates continue to pose challenges.⁴

There is variability in acceptance of candidate risk between centers but no system, framework or metric to account for combinations of risk factors that are taken into consideration in candidate selection or continued candidacy on the waitlist after initial listing.⁶ Current guidelines stress the importance of the cumulative effect of multiple potential risk factors but highlight the difficulty estimating an individual's post-transplant survival based on published literature.⁴ The LAS was designed to minimize waitlist death while preventing futile transplants.⁷ It was not designed to predict long-term survival or define which candidates are at higher risk for graft failure.⁸ The composite allocation score (CAS) will replace the LAS in early 2023 as part of continuous distribution but is similarly not designed to facilitate center and patient decision making.⁹ Appropriate selection of candidates and decisions for listing at a particular center rely heavily on center experience rather than universal guidelines.¹⁰

Given the subjectivity in candidate decision making, there is significant concern that geographic, racial and socioeconomic disparities present an ongoing challenge to lung transplantation.^{6,11} Additionally, it is becoming increasingly difficult to make decisions for accepting candidates for transplant with multiple relative contraindications, otherwise known as stacked risks. It is likely that anecdotal experiences overshadow objective assessment as the literature does not address stacked risk in potential candidacy.

The objective of our study was to determine the relationship between number of comorbidities and inpatient mortality, length of stay (LOS), total charges, and disposition using a probabilistic matching algorithm linking two administrative databases.

Methods

Study Population

Data were obtained from the United Network for Organ Sharing (UNOS) Standard Transplant Analysis and Research (STAR) File and the Healthcare Cost and Utilization Project National Inpatient Sample (NIS). The cohort was composed of all adult lung transplant candidates listed for lung transplant between January 1st, 2016 to December 21st, 2019. Candidates were excluded if their age at transplant was <18 years of age. Institutional review board approval (Protocol #: 848398), data use agreements (DATA0006379) and Health Resources and Services Administration approvals were obtained. All work presented is in compliance with the ISHLT ethics policies.

Description of Administrative Datasets and Matching algorithm

The NIS is a publically available administrative database developed through Federal-State-Industry partnership and sponsored by the Agency for Healthcare Research and Quality (AHRQ).¹² The NIS database combines data collection efforts from states, hospital associations, private data organizations, and the federal government to create a national encounter-level sample of healthcare data. The NIS is produced and released annually and engineered to be nationally representative of the total discharges from US hospitals.

The STAR files are limited datasets that contain patient-level information about transplant recipients, deceased and living donors, and waiting list candidates. Unique encrypted donor, candidate, hospital, and organ procurement organization identifiers are internally consistent and used to maintain confidentiality.

There is no individual linking variable to combine the NIS to the UNOS Starfile (USF); therefore, we applied a probabilistic matching algorithm using 7 variables (transplant: month, year and type; recipient: age, sex, race, payer) to match deidentified patients without a linking key. Given the size and the computational requirements for use of the full datasets, a multi-step strategy was employed. The first step retained only index lung transplant admissions identified by 28 ICD-10-CM/PCS codes (see supplement) between 2016 to 2019 in the NIS. The second step, harmonized the 7 matching variable labels. Next, we utilized “relink2” implemented in Stata which is used for merging two datasets with no linking key.¹³ After merging the datasets, clerical review of all multiple matches was performed and adjudication was based on length of stay reported in both datasets (only identical or closest match was retained). Sensitivity analyses were performed using deletion of all replicates and retention of all replicates with >90% probability matches.

Primary and secondary endpoints

The primary endpoint was inpatient mortality. Secondary endpoints included hospital length of stay (LOS), total charges for index admission, need for mechanical ventilation and ECMO at 72 hours, and discharge disposition.

Statistical Analysis

We performed all data management and analysis using Stata v14.2 (Stata Corp, College Station, Tx). Summaries of clinical factors are reported with means and standard deviations or medians and interquartile ranges for continuous measures, and percentages for binary measures. All reported P values are 2-sided.

We determined candidate comorbidities using the Elixhauser comorbidity index implemented in Stata (“elixhauser”) which generates 31 categorized comorbidities based on ICD-10-CM codes present on admission and not related to the primary diagnosis of lung transplantation. The Elixhauser methodology was chosen because it outperforms other ICD coding and medication based indices that exclude acute conditions that could be complications of care.¹⁴⁻¹⁶ We used penalized splines (“pspline” implemented in STATA 14.2 which fits a penalized spline regression and plots the function to identify knots with equally spaced quantiles) to determine an estimation of the dose response function to the exposure of comorbidity number on inpatient mortality.^{17,18} We focused on inpatient mortality as the outcome variable because it is extreme and uncommon, thereby reducing the potential for type I error. We used logistic regression to develop a model to predict inpatient mortality to assess the simultaneous effect of multiple variables on the stacked risk classifier following lung transplant. For time to event analysis, we used Kaplan-Meier analysis with logrank test and restricted mean survival time (RMST). Hospital length of stay and inpatient mortality were stratified by transplant type (single, bilateral) for comparison.

Results

During the study period, there were 28,484,087 hospital admissions captured in the NIS and 9,853 transplants recorded in the USF. From these cohorts, 2,877 lung transplant recipients were matched and 145 (4.8%) were unable to be matched secondary to missing values required for matching. Probabilistic matching identified 76.8% perfect matches, 19.6% with a probability match of 0.97 and 3.5% with a probability match of 0.94. 1,140 (39.6%) patients had only a single match while the remainder (60.4%) had multiple matches with identical probabilities scores which required further clerical review. After adjudication, 1,821 lung transplant recipients were identified representing 18.5% of all lung transplants performed over the study period (CONSORT diagram in Figure 1). Cohort demographics are summarized in Table 1.

We used the Elixhauser methodology to define comorbid conditions as the score provides the capability to adjust for disease burden in patients. The number of conditions was normally distributed and ranged between 0-12 with the mean being 4.64 ± 1.9 SD (Figure 2). The frequency of each diagnosis is summarized in Table 2. The top five most common comorbid conditions excluding Chronic Lung Disease were Fluid and Electrolyte Disorders (68.1%), Cardiac Arrhythmias (49.6%), Coagulopathy (40.3%), Pulmonary Circulation Disorders (39.5%), and Uncomplicated Hypertension (34.9%).

We utilized penalized splines to define inflection points for dose response effects on inpatient mortality. Risk increased with increasing comorbidities ($p=0.012$). Three knots were identified at 3, 6 and 9 comorbid conditions which were used to define low (0-3),

medium (4-6) and high (>6) risk categories. Demographics of these risk groups are summarized in Table 3. Between risk categories, there were significant differences in age, race, diagnosis group, lung allocation score, elective admission status, body mass index of the recipient and no significant differences in donor characteristics.

The risk of inpatient mortality increased with the number of comorbidities in a dose dependent fashion (Figure 3, Table 4). By risk categories, inpatient mortality significantly increased from low to high risk ($1.6\% \pm 12.5$ SD, $4.1\% \pm 19.7$ SD, $6.9\% \pm 25.4$ SD; $p=0.001$). This risk persisted and was consistent at 90-days, 1-year, 3-years and 5-years ($p=0.0007$, Figure 4). Compared to low risk, there was significant decrease in restricted mean survival time (measure of average survival from time 0 to a specified time point) at 3 years demonstrated with medium risk (-44.4 [95% CI: $-13.9, -74.9$] days, $p=0.004$) and high risk (-89.6 [95% CI: $-42.7, -136.5$] days, $p<0.0001$) categories. Given the significant differences in recipient characteristics identified, multivariate analysis of inpatient mortality by Elixhauser defined risk categories remained a consistent independent predictor of inpatient mortality (odds ratio of 1.9 [95% CI: 1.3; 2.8]; $p=0.001$). Candidate age (OR 1.01 [95% CI: 0.99; 1.04]; $p=0.37$), race (OR 1.05 [95% CI: 0.83; 1.32]; $p=0.70$), diagnostic group (OR 0.92 [95% CI: 0.76; 1.12]; $p=0.40$), initial LAS (OR 1.00 [95% CI: 0.98; 1.02]; $p=0.9$), elective admission (OR 0.51 [95% CI: 0.20; 1.29]; $p=0.16$), transplant type (OR 1.23 [95% CI: 0.65; 2.32]; $p=0.52$) and BMI (OR 1.03 [95% CI: 0.97; 1.09]; $p=0.30$) did not predict inpatient mortality. Within this model using the low risk group as a reference, medium risk (OR 2.33 [95% CI: 1.08; 5.05]; $p=0.03$) and high risk (OR 3.8 [95% CI: 1.63; 8.93]; $p=0.002$) increased in dose dependent fashion.

ECMO salvage at 72-hours post-transplant consistently increased from 2.8% for low risk to 4.4% for medium risk to 11.2% for high risk groups ($p<0.001$). This corresponded to need for mechanical ventilation which also exhibited the same relationship (21.7%; 27.5%; 37.6%; $p<0.001$).

Hospital length of stay also demonstrated a significant dose response in accordance with comorbid risk (Table 4). Overall length of stay increased from 16 [IQR: 11; 27.5] to 21 [IQR: 14; 37] to 29 [IQR: 18; 50] days among the low medium and high risk groups, respectively ($p<0.0001$). This was consistent in both single (12.5 [IQR: 10; 20], 15 [IQR: 11; 25]; 25 [IQR: 14; 41]) and bilateral lung transplants (17 [IQR: 12; 30], 23 [IQR: 15; 40], 29 [IQR: 18; 53]).

Consistent with increasing length of stay, total hospital charges for the index admission demonstrated a similar relationship ($p=0.0037$). Median cost overall between risk groups increased from \$549,593 [IQR: 397,047; 911,928] for low risk to \$665,666 [IQR: 463,642; 1,161,165] for medium risk to \$816,576 [IQR: 553,376; 1,261,809] in the high risk category. This trend remained regardless of transplant type (Single: \$504,809 [IQR: 356,636; 906,914.5]; \$502,071 [IQR: 378,923; 960,064]; \$735,919 [IQR: 526,755; 1,463,928]; Bilateral: \$566,470 [IQR: 414,477; 941,223]; \$707,612 [IQR: 502,246.5; 1,251,858]; \$830,990 [IQR: 574,395; 1,232,098]).

To gain an understanding of resource utilization, discharge disposition was evaluated Table 4. Among the low, medium and high risk groups there was a decrease in discharge to home (47.6%, 39.1% and 31.7%, $p < 0.001$). Conversely, discharge to skilled nursing facility or intermediate care facility increased with increasing risk from 14.8% to 20.4% and 31.0% ($p < 0.001$), respectively. Discharges to short term hospitals was rarely used and only for low and medium risk groups (1.4%; 1.1%; $p < 0.001$, respectively).

Sensitivity analyses were performed to determine if alternate strategies for cohort identification and curation affected results. We contrasted a strategy of keeping all matches when more than one match was possible due to ties in probability score and a strategy of deleting all but the first best match to our presented curation adjudication method based on length of stay matching. Alternative strategies both demonstrated identical cut points for risk categorization and similar adverse effects (data in supplement).

Discussion

Increasing number of recipient comorbidities (stacked risks) increases risk of mortality, need for prolonged mechanical ventilation, ECMO salvage and costs after lung transplantation. Stacked risks further significantly limit discharge disposition to home at the expense of increased placement in skilled nursing facilities, suggesting suboptimal functional short-term outcomes.

Transplant center evaluation of candidates with stacked risks is well recognized but understudied because of the limitations posed on available administrative datasets. This study demonstrated linkage of the USF and the NIS is possible in lung transplant patients despite lack of identifiers.¹⁹ Moreover, the ability to link real-world comorbidities to the USF has important and significant applications which can address variability in acceptance of candidate risk between centers.²⁰ The potential to develop a metric to account for stacked risks could improve candidate selection, waitlist and post-transplant survival modeling, and regulatory oversight, particularly if automated methods are employed using ICD-10 coding structures which are uniformly defined. This work is a first step for developing such a metric and more work needs to be done refining and optimizing stacked risk definitions and determining which comorbid conditions are driving the associations identified.

It makes intuitive sense that the absolute number of comorbid conditions increases mortality at any time point and this study confirms that assumption. Surprisingly, the number of diagnoses that contribute to the risk categories were not those routinely considered potential risk factors (e.g. hypertension, diabetes, obesity, weight loss, fluid and electrolyte disorders, anemia, depression, hypothyroidism, cardiac arrhythmias) which, based on our analysis, if present in the same candidate would define a high risk candidate. It is unlikely a transplant center would consider a potential candidate with any combination of the 7 to 9 risk factors listed above as high risk; therefore, a better understanding of associated individual Elixhauser comorbidities and patterns of comorbidities is needed. While the NIS is roughly representative of 20% of annual US inpatient admissions and therefore about 20% of annual lung transplants, the Medicare dataset includes roughly 40% of all lung transplants. Future

work will seek to use both the NIS and Medicare data to capture roughly 50% of all annual US transplants.

There is increasing interest in defining outcomes by more than just mortality.²¹ Alive at one year but institutionalized or unable to function independently is arguably not a positive outcome. Determining the risk of candidates who present for transplant evaluation is complex, subjective and variable.^{6,11} As a first step in creating an objective candidate assessment metric, we evaluated the disposition of lung transplant recipients based on their stacked risk assessment. We identified an inverse relationship in discharge to home with respect to stacked risks. Consequently, the number of patients requiring discharge to a skilled nursing facility (SNF) doubled from low to high risk. When arbitrarily defining poor outcome as inpatient death or discharge to SNF, about ~40% of the high risk group have a poor outcome compared to ~16% for the low risk group. Better understanding of risk and poor outcomes are needed to facilitate frank discussions with candidates.

There are limitations to this study. The Elixhauser comorbidity methodology is crude and identified patients with diagnoses not normally seen in lung transplant. We acknowledge only 31 comorbidities can be identified using the Elixhauser methods. This method of identifying comorbidities is standardized and commonly used for adjustment for hospital quality comparisons.²² Nonetheless, our future work will utilize the Clinical Classifications Software Refined (CCSR) which is one in a family of databases and software tools developed as part of the Healthcare Cost and Utilization Project. The CCSR may be superior to the Elixhauser methodology because it aggregates ICD-10 codes into 530 clinical categories across 22 body systems giving finer granularity. With respect to candidates identified with diagnoses that would not be transplant candidates (e.g. metastatic cancer, lymphoma or solid tumors), we have assumed that those patients were treated in the past and had met the cancer free survival requirements defined by guidelines.⁴ Categorical designations of low, medium and high risk based on Elixhauser diagnosis numbers limits granularity in terms of risk prediction. Our decision to use a categorical rather than continuous measure was made to ensure that this relatively small dataset could be used for analysis. Our intention is to refine and optimize this classifier to improve granularity and facilitate discussion in the clinic between providers and patients and at the listing conferences between providers utilizing a larger dataset combining HCUP, Medicare and UNOS administrative data. NIS data prior to 2016 were not included. In late 2015 ICD-10 was implemented in the US making data pre-2016 complicated due to mixed coding structures. We decided to omit all data years prior to 2016 in order to ensure consistent comorbidity identification. Center was not used as a linking variable because the NIS no longer provides State and hospital identifiers in order to protect patient confidentiality. Additionally, there is a correlation of comorbidity number and age ($\rho = 0.125$, $p < 0.001$). While this is expected to some degree, we have refrained from suggesting cutoffs or implying certain patient populations not be transplanted because more work will need to be done to further validate and generalize our observations. Lastly, our current metric does not discriminate the level of risk among individually defined diagnoses meaning pulmonary hypertension and uncomplicated diabetes are considered to have similar risk. Future work with an expanded cohort will focus on associated risks of specific diagnoses to better characterize each associated risk and potential interactions.

In summary, stacked risks defined by number of Elixhauser comorbidities are associated with increased mortality, need for prolonged mechanical ventilation, salvage ECMO, hospital length of stay, cost and discharge to a skilled nursing facility. In addition, we successfully demonstrated it is feasible to link the NIS with the USF using probabilistic matching which provides a powerful investigative toolset. Further study of stacked risks is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

AHRQ	Agency for Healthcare Research and Quality
ATS	American Thoracic Society
CCSR	Clinical Classifications Software Refined
CAS	Composite Allocation Score
ECMO	Extracorporeal Membrane Oxygenation
ERS	European Respiratory Society
ICD	International Classification of Diseases
ISHLT	International Society for Heart and Lung Transplantation
LAS	Lung Allocation Score
LT	Lung Transplant
LOS	Length of Stay
NIS	National Inpatient Sample
USF	UNOS Starfile
RMST	Restricted Mean Survival Time
SNF	Skilled Nursing Facility
STAR	Standard Transplant Analysis and Research

UNOS United Network for Organ Sharing

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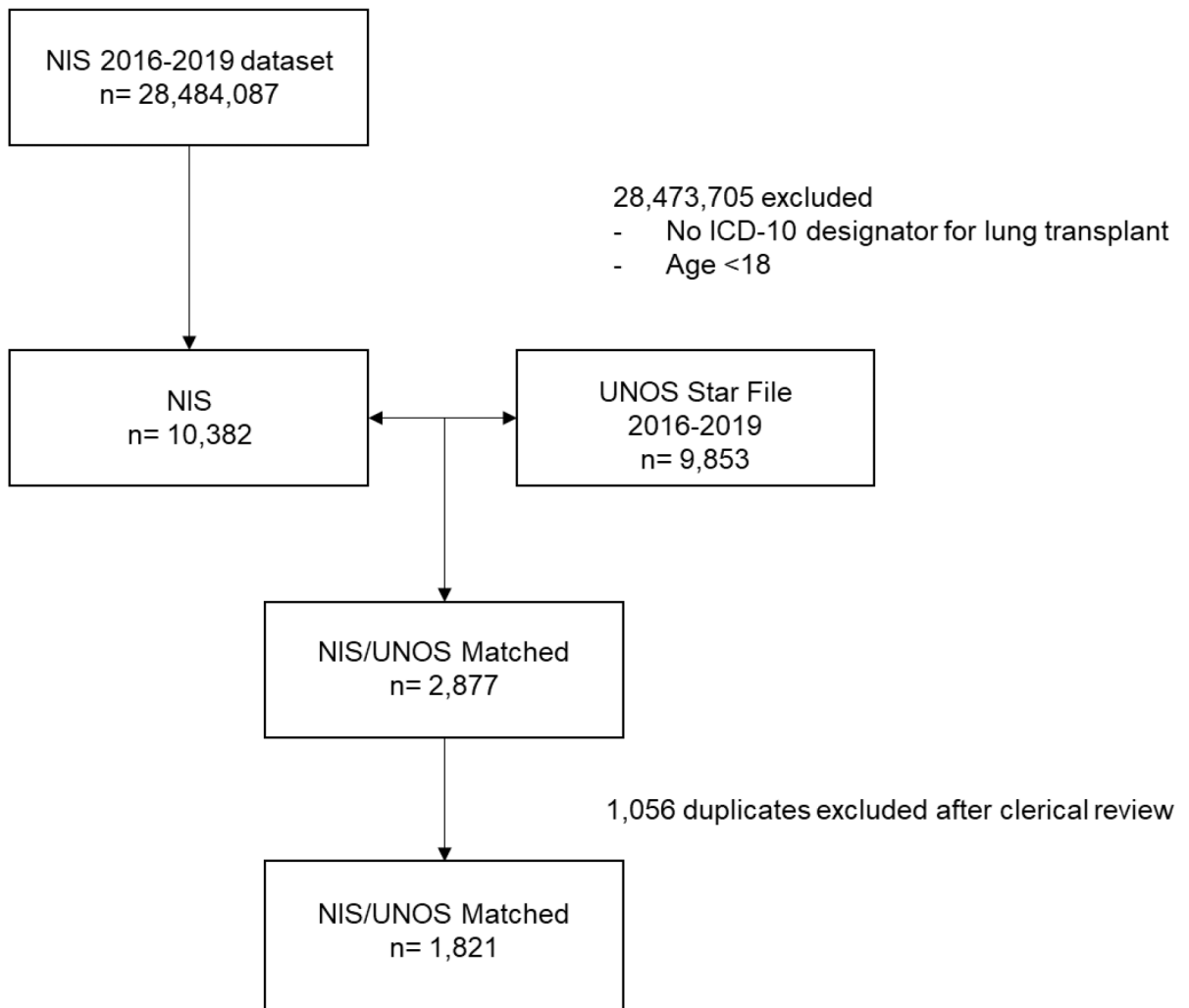


Figure 1.
CONSORT diagram

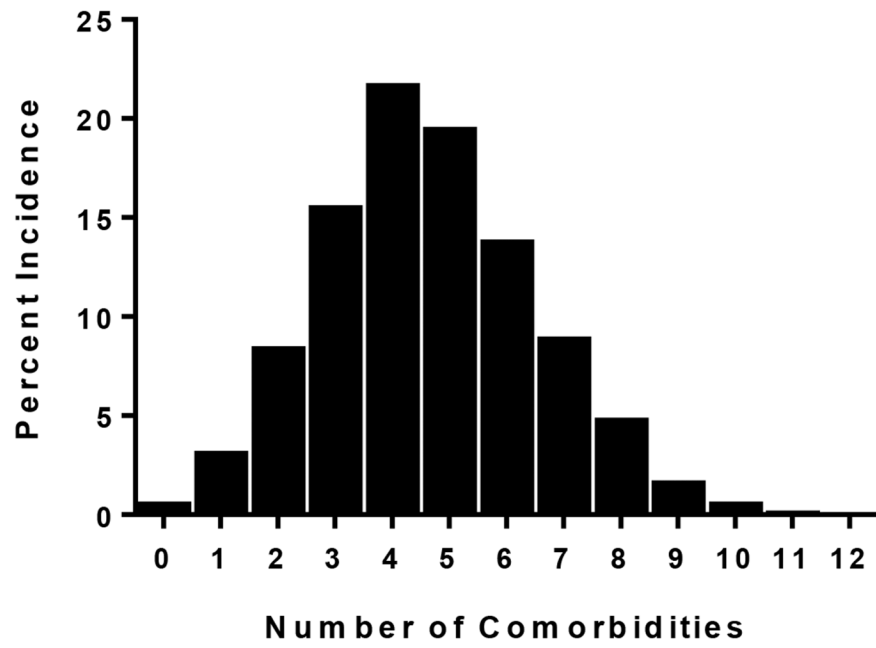


Figure 2.
Distribution of comorbidity number

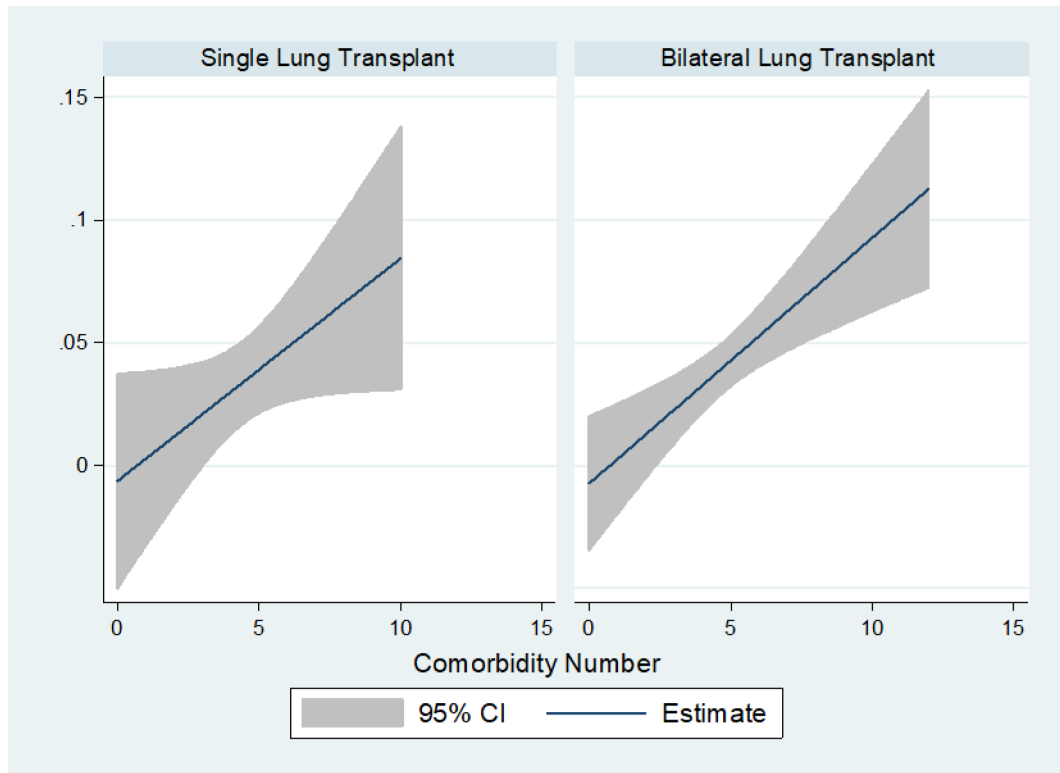


Figure 3. Inpatient mortality risk by number of comorbidities stratified by transplant type

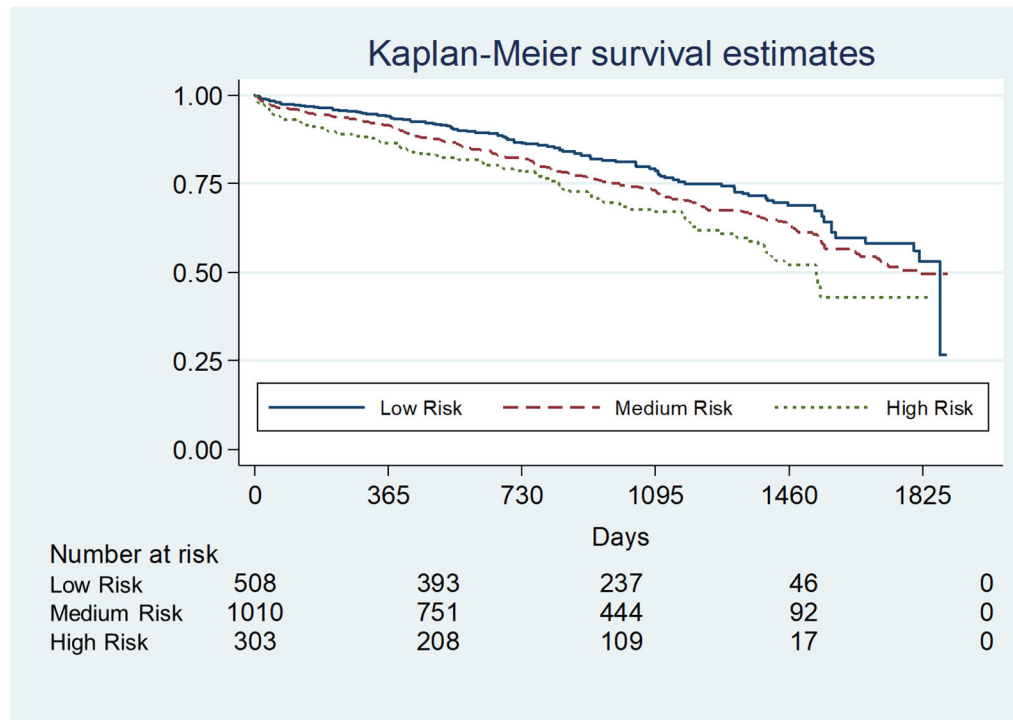


Figure 4.
Post-Transplant Survival

Table 1.

Matched Cohort Demographics

Factor	Overall
N	1821
Recipient	
Age, median (IQR)	62.0 (54.0, 67.0)
Female	708 (38.9%)
Race	
White	1367 (75.1%)
Black	180 (9.9%)
Hispanic	141 (7.7%)
Asian or Pacific Islander	29 (1.6%)
Native American	8 (0.4%)
Other	43 (2.4%)
Missing	53 (2.9%)
Diagnosis Grouping	
Obstructive	483 (26.5%)
Pulmonary Vascular	86 (4.7%)
Infective	139 (7.6%)
Restrictive	1113 (61.1%)
LAS, median (IQR)	40.6 (35.2, 51.7)
Elective admission	239 (13.1%)
Transplant type	
Single	444 (24.4%)
Bilateral	1377 (75.6%)
BMI, median (IQR)	26.3 (22.5, 29.3)
Donor	
Donor Age, median (IQR)	33.0 (23.0, 46.0)
Donor Ethnicity	
White	1154 (63.4%)
Black	317 (17.4%)
Hispanic	271 (14.9%)
Asian	57 (3.1%)
American Indian/Alaska Native	7 (0.4%)
Native Hawaiian/Pacific Islander	4 (0.2%)
Multiracial	11 (0.6%)
Cigarette Use	
No	1657 (91.0%)
Unknown	31 (1.7%)
Yes	133 (7.3%)
Cause of Death	
Anoxia	592 (32.5%)

Factor	Overall
Cerebrovascular	490 (26.9%)
Head Trauma	697 (38.3%)
CNS Tumor	6 (0.3%)
Other	36 (2.0%)
BMI, median (IQR)	25.6 (22.6, 29.5)
PO2, median (IQR)	415.0 (308.1, 483.0)

Statistical comparisons are between risk categories overall. Pearson's chi-squared was used for categorical variables and Kruskal-Wallis for continuous factors. Abbreviations: IQR, interquartile range; LAS, Lung Allocation Score; CNS, Central Nervous System; BMI, Body Mass Index; PO2, partial pressure arterial oxygen.

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Table 2.

Frequency of Elixhauser Defined Comorbidities

Diagnosis	Frequency (%)
Fluid and Electrolyte Disorders	68.11
Cardiac Arrhythmias	49.58
Coagulopathy	40.29
Pulmonary Circulation Disorders	39.45
Hypertension, Uncomplicated	34.89
Weight Loss	34.89
Depression	17.97
Diabetes, Complicated	15.08
Congestive Heart Failure	14.13
Hypothyroidism	11.96
Hypertension, Complicated	11.91
Other Neurologic Disorders	10.18
Obesity	9.07
Renal Failure	8.96
Rheumatoid Arthritis/Collagen Vascular Disease	8.9
Liver Disease	7.07
Valvular Disease	5.68
Diabetes, Uncomplicated	5.23
Peripheral Vascular Disorders	4.84
Deficiency Anemia	4.23
Drug Abuse	1.61
Solid Tumor without Metastasis	1.45
Blood Loss Anemia	1.22
Paralysis	1.11
Alcohol Abuse	1
Peptic Ulcer Disease excluding Bleeding	0.78
Psychoses	0.45
Lymphoma	0.22
Metastatic Cancer	0.17
AIDS/HIV	0.06

Table 3.

Demographics of Elixhauser Defined Risk Category

Factor	Low Risk	Medium Risk	High Risk	p-value
N	508	1010	303	
Recipient				
Age, median (IQR)	60.0 (50.0, 66.0)	62.0 (55.0, 67.0)	62.0 (57.0, 67.0)	<0.001
Female	180 (35.4%)	407 (40.3%)	121 (39.9%)	0.17
Race				0.019
White	398 (78.3%)	759 (75.1%)	210 (69.3%)	
Black	31 (6.1%)	106 (10.5%)	43 (14.2%)	
Hispanic	42 (8.3%)	74 (7.3%)	25 (8.3%)	
Asian or Pacific Islander	5 (1.0%)	16 (1.6%)	8 (2.6%)	
Native American	4 (0.8%)	3 (0.3%)	1 (0.3%)	
Other	12 (2.4%)	23 (2.3%)	8 (2.6%)	
Missing	16 (3.1%)	29 (2.9%)	8 (2.6%)	
Diagnosis Grouping				<0.001
Obstructive	113 (22.2%)	286 (28.3%)	84 (27.7%)	
Pulmonary Vascular	19 (3.7%)	46 (4.6%)	21 (6.9%)	
Infective	65 (12.8%)	65 (6.4%)	9 (3.0%)	
Restrictive	311 (61.2%)	613 (60.7%)	189 (62.4%)	
LAS, median (IQR)	39.8 (35.0, 49.0)	40.6 (35.0, 51.9)	42.0 (36.9, 53.3)	0.029
Elective admission	73 (14.4%)	114 (11.3%)	52 (17.2%)	0.019
Transplant type				0.055
Single	140 (27.6%)	243 (24.1%)	61 (20.1%)	
Bilateral	368 (72.4%)	767 (75.9%)	242 (79.9%)	
BMI, median (IQR)	25.8 (22.3, 28.9)	26.3 (22.5, 29.3)	26.9 (23.2, 29.7)	0.008
Donor				
Age, median (IQR)	33.0 (23.0, 46.0)	33.0 (23.0, 46.0)	33.0 (24.0, 46.0)	0.98
Ethnicity				0.64
White	318 (62.6%)	636 (63.0%)	200 (66.0%)	
Black	91 (17.9%)	177 (17.5%)	49 (16.2%)	
Hispanic	85 (16.7%)	147 (14.6%)	39 (12.9%)	
Asian	9 (1.8%)	37 (3.7%)	11 (3.6%)	
American Indian/Alaska Native	2 (0.4%)	5 (0.5%)	0	
Native Hawaiian/Pacific Islander	1 (0.2%)	2 (0.2%)	1 (0.3%)	
Multiracial	2 (0.4%)	6 (0.6%)	3 (1.0%)	
Cigarette Use				0.57
No	461 (90.7%)	926 (91.7%)	270 (89.1%)	
Unknown	9 (1.8%)	14 (1.4%)	8 (2.6%)	
Yes	38 (7.5%)	70 (6.9%)	25 (8.3%)	
Cause of Death				0.38
Anoxia	165 (32.5%)	327 (32.4%)	100 (33.0%)	

Factor	Low Risk	Medium Risk	High Risk	p-value
Cerebrovascular	137 (27.0%)	273 (27.0%)	80 (26.4%)	
Head Trauma	200 (39.4%)	385 (38.1%)	112 (37.0%)	
CNS Tumor	0	3 (0.3%)	3 (1.0%)	
Other	6 (1.2%)	22 (2.2%)	8 (2.6%)	
BMI, median (IQR)	25.5 (22.7, 29.7)	25.6 (22.6, 29.4)	25.8 (22.7, 29.8)	0.98
PO2, median (IQR)	422.0 (325.0, 487.0)	410.0 (291.0, 477.0)	429.0 (296.0, 493.0)	0.053

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Table 4.

Outcome measure by risk category

Factor	Overall	Low Risk	Medium Risk	High Risk	p-value
N	1821	508	1010	303	
Survival					<0.001
30-day	0.98	0.99	0.98	0.97	
90-day	0.96	0.97	0.96	0.93	
1-year	0.91	0.94	0.91	0.86	
3-year	0.74	0.79	0.73	0.67	
Mechanical Ventilation at 72 Hours					<0.001
No	1315 (72.2%)	396 (78.0%)	730 (72.3%)	189 (62.4%)	
Unknown	4 (0.2%)	2 (0.4%)	2 (0.2%)	0	
Yes	502 (27.6%)	110 (21.7%)	278 (27.5%)	114 (37.6%)	
ECMO at 72 Hours					<0.001
No	1724 (94.7%)	492 (96.9%)	963 (95.4%)	269 (88.8%)	
Unknown	4 (0.2%)	1 (0.2%)	3 (0.3%)	0	
Yes	92 (5.1%)	14 (2.8%)	44 (4.4%)	34 (11.2%)	
Missing	1 (0.1%)	1 (0.2%)	0	0	
iNO at 72 Hours					0.417
No	1662 (91.3%)	471 (92.7%)	919 (91.0%)	272 (89.8%)	
Unknown	11 (0.06%)	3 (0.6%)	5 (0.5%)	3 (1.0%)	
Yes	147 (8.1%)	33 (6.5%)	86 (8.5%)	28 (9.2%)	
Missing	1 (0.05%)	1 (0.2%)	0	0	
Length of Stay					<0.001
Overall	20 [13; 37]	16 [11; 27.5]	21 [14; 37]	29 [18; 50]	
Single	15 [11; 27]	12.5 [10; 20]	15 [11; 25]	25 [14; 41]	
Bilateral	22 [15; 40]	17 [12; 30]	23 [15; 40]	29 [18; 53]	
Disposition					<0.001
Home	735 (40.4%)	242 (47.6%)	397 (39.3%)	96 (31.7%)	
Short Term Hospital	18 (1.0%)	7 (1.4%)	11 (1.1%)	0	
Skilled Nursing Facility	375 (20.6%)	75 (14.8%)	206 (20.4%)	94 (31.0%)	
Home Health Care	623 (34.2%)	176 (34.7%)	355 (35.2%)	92 (30.4%)	
Died	70 (3.8%)	8 (1.6%)	41 (4.1%)	21 (6.9%)	
Total Charges					<0.001
Overall	\$653,024 [454,335; 1,125,028]	\$549,593 [397,047; 911,928]	\$665,666 [463,642; 1,161,165]	\$816,576 [553,376; 1,261,809]	
Single	\$542,419 [386,252; 971,431]	\$504,809 [356,636; 906,914.5]	\$502,071 [378,923; 960,064]	\$735,919 [526,755; 1,463,928]	
Bilateral	\$685,880 [483,949; 1,162,435]	\$566,470 [414,477; 941,223]	\$707,612 [502,246.5; 1,251,858]	\$830,990 [574,395; 1,232,098]	