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The impact of pre-transplant mechanical ventilation on short- and long-term survival after lung transplantation

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Abstract

Lung transplantation in mechanically ventilated (MV) patients has been associated with decreased post-transplant survival. Under the Lung Allocation Score (LAS) system, patients at greatest risk of death on the waiting list, particularly those requiring MV, are prioritized for lung allocation. We evaluated whether pre-transplant MV is associated with poorer post-transplant survival in the LAS era. Using a national registry, we analyzed all adults undergoing lung transplantation in the U.S. from 2005-2010. Propensity scoring identified non-ventilated matched referents for 419 subjects requiring MV at the time of transplantation. Survival was evaluated using Kaplan-Meier methods. Risk of death was estimated by hazard ratios employing time-dependent covariates. We found that pre-transplant MV was associated with decreased overall survival after lung transplantation. In the first six-months post-transplant, ventilated subjects had a two-fold higher risk of death compared to non-ventilated subjects. However, after six-months post-transplant, survival did not differ by MV status. We also found that pre-transplant MV was not associated with decreased survival in non-cystic fibrosis obstructive lung diseases. These results suggest that under the LAS, pre-transplant MV is associated with poorer short-term survival post-transplant. Notably, the increased risk of death appears to be strongest the early post-transplant period and limited to certain pre-transplant diagnoses.

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Keywords

lung transplantation; artificial respiration; survival; lung allocation score; propensity score

Introduction

Lung transplantation has the potential to increase survival and improve quality of life for patients suffering from end-stage lung disease.(1) These positive outcomes have driven increased demand for the procedure with the number of transplants performed increasing every year.

Due to the shortage of available donor organs and high mortality on the waiting list, the allocation system for lung transplantation in the United States has undergone considerable evolution over the past decade. Prior to 2005, the allocation system was based upon the amount of time accrued on the waiting list. Under this system, patients with rapidly progressive diseases, such as idiopathic pulmonary fibrosis (IPF) frequently died before receiving a donor organ.(2) (3) To address this disparity, in May of 2005, the Organ Procurement and Transplantation Network (OPTN) implemented an entirely new allocation system based on the Lung Allocation Score (LAS). The LAS uses weighted models based on clinical data to assign each patient a score that incorporates their medical urgency (risk of dying on the waiting list) and their expected outcome (likelihood of surviving one-year after transplant).(2)

Patients whose lung disease has advanced to the point of requiring ongoing support by mechanical ventilation are likely to receive a high LAS. This higher LAS reflects the net weighting of both higher medical urgency and worse expected outcome associated with mechanical ventilation.(2) Studies performed prior to the introduction of the LAS system suggest that mechanical ventilation is a risk factor for death following lung transplantation.(4-8) Thus, mechanical ventilation remains a strong relative contraindication to lung transplantation.(1, 9) Prior analyses, however, have been complicated by small sample size, institutional bias, lack of a comparable referent population, pooling of pediatric and adult data, and, perhaps most saliently, heavy reliance on data that predate implementation of the current LAS system by a decade or more.(4-6, 8, 10-14)

In light of these significant limitations, it remains unclear whether pre-transplant mechanical ventilation is truly a risk factor for reduced post-lung transplant survival in the current LAS era. In this study, we sought to determine whether pre-transplant mechanical ventilation is associated with poorer post-transplant survival. To address this question we used a large national data set, restricted analysis to adults in the LAS era, used a propensity scoring approach to achieve appropriate referent matching, and analyzed patterns for apparent risk both over varying time frames following transplantation and by diagnostic category.

Materials and Methods

Overview and Study Population

To investigate the effects of pre-transplant mechanical ventilation on post-transplant survival, we performed a case-referent analysis using national data from the Organ Procurement and Transplantation Network (OPTN) registry (Standard Transplant Analysis and Research file #020910-16) supplied by the United Network for Organ Sharing (UNOS). We included all adults (age ≥ 18) who underwent lung or heart-lung transplantation from May 4, 2005 until October 29, 2010. We excluded subjects supported by extracorporeal membrane oxygenation (ECMO) at the time of organ matching. Ventilated subjects were defined as those subjects dependent on invasive mechanical ventilation at the time of organ matching, consistent with OPTN coding definitions. For each ventilated patient, a matched patient not receiving mechanical ventilation was identified using propensity score techniques. Demographic data was extracted for analysis from the Transplant Candidate Form and clinical data from the Transplant Report Form; preference was always given to the data most proximal to the date of organ matching. This study was reviewed by the Committee on Human Research at UC San Francisco and met exempt status (Exempt Project #09035487).

Development of Propensity Score

Pre-transplant candidates supported with mechanical ventilation were likely to differ from all other candidates in many important characteristics that might also affect the likelihood of survival. To address these potentially confounding differences, we used logistic regression to generate a propensity score predicting the likelihood of mechanical ventilation for each recipient prior to lung transplantation.⁽¹⁵⁾ To develop the score, we considered variables in the OPTN registry known to predict mechanical ventilation⁽¹⁶⁾ or known to be associated with post-transplant survival. Allen-Cady backward stepwise regression ($p < 0.2$ threshold) was used to select covariates for inclusion in the propensity score. Variables selected for the final model included: age (in categories), body mass index (BMI), diagnostic category, % predicted forced expiratory volume in 1 second (FEV₁), arterial blood gas partial pressure of carbon dioxide (pCO₂), LAS, and year of transplantation. Age was categorized based on categories used for survival analyses in the annual registry report of the International Society for Heart and Lung Transplantation.⁽¹⁾ Specific listing diagnoses were categorized into the four groups used to determine the LAS (Table 3).⁽²⁾ Based on the propensity score, a nearest-neighbor matching without replacement algorithm identified a non-ventilated match for each ventilated patient.⁽¹⁵⁾ Wilcoxon rank-sum test was used to ensure that the distribution of propensity scores between the ventilated and non-ventilated subjects within each stratum were balanced. By balancing the pre-transplant characteristics of the ventilated and non-ventilated subjects, use of a propensity score reduces confounding by factors associated with both mechanical ventilation and post-transplant survival.^(17, 18) The concordance index (c-index) was used to test the discriminatory power of the propensity score model. Attempts to include center volume and transplant type in the propensity score resulted in failure to meet the balancing hypothesis. Because these variables could not be included in the propensity score, multivariate adjustment accounting for center volume and transplant type were performed in all subsequent models.

Outcome Measure

The primary outcome analyzed was post-transplant survival. Survival was calculated from the date of lung transplantation until the date of the last follow-up recorded in the OPTN registry. The status of subjects is reported at each follow-up interval: registrants are listed as dead, alive, or lost to follow-up. Patient survival time was right-censored if they were alive at the time of their last follow-up visit. Dates of death were corroborated with the Social Security Master Death File (SSMDF). Forty-seven subjects who underwent transplant did not have a date of follow-up or a date of death on the SSMDF. Since the actual survival time of these subjects could not be determined, we conservatively right-censored their survival time at one day post-transplant.

Data Analysis

Variables with 15% missing data in the OPTN database were not included in our analyses. For variables with <15% missing data (serum creatinine, FEV₁, pCO₂, and education), we replaced missing values using 20-fold multiple imputation.⁽¹⁹⁾ Imputation was modeled using variables without missing data (age, sex, category of listing diagnosis, BMI, ethnicity, and smoking history) with the Stata/IC 11.1 multiple imputation package (StataCorp, College Station, TX). The use of multiple imputation minimizes bias that can be introduced when subjects with incomplete data are selectively excluded.⁽²⁰⁾

Survival was graphically assessed using Kaplan-Meier methods. To evaluate the proportionality of hazards, we plotted scaled Schoenfeld residuals with respect to time and assessed log-negative-log plots. We further tested the proportional hazards assumption with the Schoenfeld test. Significant violations of proportionality were detected in the early-post transplant time period. We addressed this in two ways. First, we used non-parametric methods (Wilcoxon-Breslow test) to test equality in overall mortality between ventilated and non-ventilated subjects. Second, we used Cox proportional hazard models employing time-dependent covariates to evaluate mortality differences conditional upon survival at 6 months and 2 years of follow-up; these time points were determined based on visual inspection of plots used to evaluate for violations of proportionality. Non-independence of matched subjects was accounted for in all Cox models by specifying the clustering of paired data formed by each ventilated subject and their unique non-ventilated propensity score-based match.

We also considered important cofactors that might impact post-transplant survival. Foremost, centers with higher procedural volume were more likely to perform lung transplantation for subjects supported by mechanical ventilation (Table 2). We therefore adjusted all analyses for center volume (categorized as 20, 21-34, and 35 transplants yearly). We also adjusted analyses for transplant type (single-lung vs. bilateral-lung vs. heart lung). A stratified analysis of survival by diagnostic group was also performed. Tests of interaction between diagnostic subgroups were performed.

Additionally, we aimed to identify pre-transplant characteristics predictive of 1-year post-transplant survival. Survival time after transplant was dichotomized at one year. Employing either t-test or Wilcoxon rank sum test statistics, we tested differences in demographic

characteristics, clinical data, transplant type, and center volume in those subjects who survived less than one year to those who survived one year or more. We then performed multiple logistic regression taking into consideration all of these predictors as covariates in a single model.

Further analysis was performed excluding those subjects who underwent heart-lung transplantation in order to assess the impact of this subset on the overall results. For that analysis, we first excluded the 8 subjects who underwent heart-lung transplantation from the dataset. We then regenerated propensity scores predicting mechanical ventilation and identified unique non-ventilated matches as previously described.

Analyses were performed using Stata/IC 11.1 (StataCorp, College Station, TX).

Results

Of the 8,040 subjects who underwent lung transplantation over the five and a half year study period, 424 (5.3%) were receiving mechanical ventilation at the time of transplantation. We successfully identified non-ventilated propensity-scored matches for 99% (419 of 424) of the ventilated subjects (Table 1); propensity scores ranged from 0.011 to 0.749 (the theoretical range of propensity scores is 0 to 1). The median difference in propensity scores between the ventilated and non-ventilated matches was 6×10^{-5} (25th, 75th %: 3.1×10^{-6} , 7×10^{-4}). The propensity score distribution stratified by diagnostic category was not statistically different ($p = 0.18$). The discriminatory power of the propensity score model was good (c-index = 0.802). The surgical characteristics for the ventilated and the non-ventilated groups were balanced for donor age, donor sex, and lung ischemic time, however slightly more subjects in the ventilated group underwent bilateral lung transplantation (Table 2).

In non-parametric testing, pre-transplant mechanical ventilation was associated with decreased overall survival ($p < 0.005$) (Figure 1a). Cumulative survival for ventilated subjects at 6 months, 1 year, 2 years, and 3 years was 76%, 68%, 61%, and 56% compared to 86%, 80%, 71%, and 60% for non-ventilated subjects. In examining specific time periods following lung transplantation, analysis restricted to the first 6 months post-transplant demonstrated that ventilated subjects had a two-fold higher rate of death than non-ventilated subjects (HR 1.92, 95% CI: 1.3 to 2.8; $p < 0.0005$) (Table 4). Cumulative survival was not statistically different between the ventilated and non-ventilated recipients once subjects had survived to 6 months following transplant ($p = 0.55$) (Figure 1b). Cumulative survival for subjects that survived to 6 months for ventilated subjects at 1, 2, and 3 years was 90%, 80%, and 73% compared to 94%, 84%, and 76% for non-ventilated subjects.

We next performed survival analyses stratified by diagnostic category (Table 3). For diagnostic Group A, a group dominated by COPD (81%), there was no difference in survival between the ventilated and non-ventilated subjects ($p = 0.1$ for all timepoints) (Figure 2a and Table 4). Of note, ventilated subjects demonstrated a non-significant trend towards improved survival in the first 6 post-transplant months (HR 0.5, 95% CI: 0.2 – 1.2; $p = 0.11$). For diagnostic Groups C and D, however, ventilated subjects manifested a 3-5 fold

higher odds of death within the first 6 post-transplant months (Figure 2b and 2c, Table 4). The relative risk of death during the first 6 months post-transplant for Groups C and D were each significantly different from Group A ($p=0.006$ and $p=0.001$ for interaction terms, respectively). The relative risk of death in Group C was not significantly different from Group D (interaction $p=0.43$). After 6 months, the risk of death in ventilated subjects was not different from their non-ventilated matches regardless of diagnostic group. Data for Group B ($n=14$) was too small to draw any meaningful conclusions (data not shown).

Despite an increased risk of mortality within the first 6 post-operative months, the majority of subjects receiving invasive mechanical ventilation at the time of transplant survived at least one year. Factors statistically associated with survival beyond the first year post-transplant were: younger age, better renal function, non-fibrotic lung disease, and bilateral lung transplantation (Table 5). Center volume did not significantly impact survival in either univariate or multivariate analysis ($p>0.05$ for each category in all cases).

We performed a sensitivity analysis excluding subjects who underwent heart-lung transplantation. After excluding eight subjects who underwent heart-lung transplantation and regenerating propensity scores, 411 ventilated subjects and unique non-ventilated matches were analyzed. Cumulative survival estimates, Kaplan Meier curves, and hazard ratio point estimates that excluded the eight subjects who underwent heart-lung transplantation were not substantively different from estimates that included these subjects (data not shown).

Discussion

We found that lung transplantation for adults dependent on mechanical ventilation was associated with poorer overall survival compared to non-ventilated, propensity score-matched referents. In contrast to prior analyses, our findings indicate that the observed decrease in survival appears limited to the first 6-months following lung transplantation. Indeed, among those surviving the early post-transplant period, subjects who received pre-transplant mechanical ventilation no longer manifested an increased in risk of death. Post-transplant survival at 3 years in the ventilated and non-ventilated groups was nearly equivalent.

Although some prior studies implicate pre-transplant mechanical ventilation as a “universal” risk factor for all transplant recipients, our results suggest otherwise. Notably, we found that mechanical ventilation is *not* associated with decreased survival for subjects falling into diagnostic Group A, a group dominated by COPD. Among recipients with conditions in Group C and D, however, mechanical ventilation is a powerful predictor of poor outcomes at 6 months. Group C is overwhelmingly comprised of subjects with cystic fibrosis (96%) and, although Group D is a heterogeneous category, pulmonary fibrosis is the dominant condition within this group (67% in this analysis). This pattern of risk suggests that mechanical ventilation leading up to transplant for cystic fibrosis or underlying fibrotic lung diseases demarcates particularly vulnerable subgroups.

In addition to observing heterogeneity between diagnostic groups, we also observed variation in the risk of death across time. Our observation of a time-limited mortality risk

that appears to attenuate beyond 6 months post-transplant is consistent with the hypothesis that pre-transplant mechanical ventilation is associated with reversible or treatment-responsive conditions or surgically-related factors. These factors could be as straightforward as ventilator-associated and other invasive care-related infections (21-23), but could also be related to acquired peripheral(24) or diaphragmatic(25) muscle weakness, acute renal failure(26), malnourishment(27), or venous thromboembolism(28). Surgically-related factors could include allograft selection as well as technical complications.

In addition to providing a more complete picture of mortality risk associated with pre-transplant mechanical ventilation in the LAS era, our study has other notable strengths. The application of propensity scoring utilized by our study addresses a fundamental methodological limitation since subjects requiring mechanical ventilation are likely to have more severe lung disease and therefore may be less likely to survive after transplant than subjects not requiring mechanical ventilation.(29) Our study also benefits from over 5 years of national lung transplant data since the LAS was implemented in 2005, significantly exceeding what has been reported in any other study on adults to date. The study sample derived from national data allowed us to evaluate the impact of mechanical ventilation on post-transplant survival among different diagnostic categories. In this way, our study builds on the important observations made by Mason et al. by focusing exclusively on those transplanted under the current organ allocation system.(16) By limiting our analysis only to adults transplanted specifically under the current lung allocation system we were also able to avoid any historical biases or trends that may no longer be operative in the present era of lung transplantation. Further, our analysis also takes into account very recent developments in the field of transplantation which suggest that center volume and type of transplant (bilateral vs. single) may be determinants of post-transplant outcomes.(30, 31) We found that center volume did not appreciably impact post-transplant survival among mechanically ventilated patients. This is consistent with the findings that procedural volume explains only a small proportion of center-specific variation in post-transplant survival.(31) By taking a multi-pronged approach of employing propensity score-based matching, focusing exclusively on adults with data from the LAS era, and adjusting for recently identified risk factors for poor outcomes, we were able to unmask important patterns of risk previously obscured by temporal and diagnostic heterogeneity. Consequently, our findings provide information that may assist physicians in weighing risks and benefits among mechanically ventilated patients presently being considered for lung transplantation in the U.S.

Despite these strengths, our analysis also faces certain limitations. First, it is important to note that the OPTN registry does not capture potentially relevant recipient factors such as indication for, or duration of, mechanical ventilation leading up to transplantation, infection, mobility status, deconditioning, or nutritional compromise. The registry also does not provide detailed donor factors including duration of donor intubation, maximum PaO₂, and evidence of infection, edema and pulmonary contusion. These limitations of the registry make identifying causal mechanisms for our findings difficult to account for in our analysis. Ideally, registry data would include comprehensive information on the indications for intubation (e.g., hypoxia vs. hypercarbia), the duration of mechanical ventilation leading up to lung transplant, functional status while ventilated (e.g., ambulatory versus heavily sedated), markers of infection (cultures, antibiotic use, maximal daily temperatures,

leukocytosis), and nutritional status (nitrogen balance, pre-albumin, and c-reactive protein levels). Nevertheless, even if such information were available, controlling for factors that could be considered on the causal pathway often yield results that are even more challenging to interpret. Second, it is possible that data in the OPTN registry (and thus the LAS) may not adequately capture subjects' clinical status at the time of organ matching. This may be particularly true of measurements of lung function. In our experience, patients experiencing clinical worsening (e.g., those at risk of progressing to the point of requiring mechanical ventilation) are more likely to have recently updated clinical data captured by the registry. Therefore, it is probable that the data for mechanically ventilated patients in the registry were more "up to date" relative to matched controls. Our propensity score matching would have therefore identified an inappropriately "healthy" non-ventilated cohort as a comparison group. Such a bias would favor finding a difference between groups. In the case of our analysis, we found no difference in survival between groups after 6-months and for patients with non-CF obstructive lung disease, lending further strength to these findings. Third, limited sample size within certain stratified diagnostic categories (e.g. Group C) may have reduced our ability to detect smaller effect sizes that might have been otherwise statistically significant in larger populations. Nonetheless, the sample sizes within diagnostic categories in our study exceed those of most prior studies. Moreover, for Groups A and D which both included over 200 subjects, the associations we did observe were unlikely to have been due to chance at traditional statistical levels for error. Fourth, limited data on cause of death after transplant restricts our ability to disentangle biological pathways by which mechanical ventilation preceding lung transplant might lead to increased risk of 6-month mortality. Finally, while not explicitly a limitation, our findings should be interpreted as a "best-case" scenario; they reflect actual clinical practice in which the complex decision making involved in offering lung transplantation to mechanically ventilated patients is subsumed within our findings. Transplant physicians surely evaluate many clinical and non-clinical factors not captured by the registry (or reflected in allocation scoring) in deciding to proceed with transplant despite the known negative impact of mechanical ventilation on post-transplant survival. Thus, our results should not be extrapolated to all ventilated patients.

While our analysis provides a useful framework in which to assess the risks of mechanical ventilation, the decision to perform lung transplantation in any given patient ultimately remains individual, clinical, and ethically complex. Indeed, the decision of whether to offer a ventilated patient lung transplantation presents a dilemma in which the survival benefit to an individual patient may deviate from the collective benefit of maximizing the survival time derived from each donor organ. On the other hand, it is important to bear in mind that the LAS scoring algorithm appropriately recognizes that mechanically ventilated patients listed for lung transplantation have a short-term mortality that likely approaches 100% without transplant. To help address these issues, future studies should focus on identifying other factors not captured in the OPTN registry responsible for the observed early increase in short-term mortality for patients dependent on mechanical ventilation at the time of lung transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of non-standardized abbreviations

IPF	Idiopathic pulmonary fibrosis
OPTN	Organ Procurement and Transplantation Network
LAS	Lung Allocation Score
FEV₁	% predicted forced expiratory volume in 1 second
pCO₂	arterial blood gas partial pressure of carbon dioxide
SSMDF	Social Security Master Death File
ECMO	extracorporeal membrane oxygenation
UNOS	United Network for Organ Sharing

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Figure 1.

Figure 2.

Table 1

Baseline Characteristics after matching

Characteristic	Mechanical ventilation support	No mechanical ventilation support
Data presented as n (%), mean $\pm$ SD, or median (25%, 75%)		
N	419	419
Age Category		
18-49	164 (39.1)	152 (36.2)
50-60	114 (27.2)	129 (30.8)
60-65	81 (19.3)	89 (21.2)
>65	60 (14.3)	49 (11.7)
Sex (female)	175 (41.8)	189 (45.1)
Indication for Transplant by Diagnostic Category*		
Group A	100 (23.9)	123 (29.4)
Group B	14 (3.3)	6 (1.4)
Group C	72 (17.2)	61 (14.6)
Group D	233 (55.6)	229 (54.7)
Ethnicity		
White, non- Hispanic	359 (85.9)	327 (78.0)
Black	30 (7.2)	49 (11.7)
Hispanic	22 (5.3)	31 (7.4)
Asian	8 (1.9)	12 (2.9)
Prior cigarette use	224 (54.9)	241 (59.1)
Body Mass Index	25.3 $\pm$ 5.5	25.1 $\pm$ 5.1
Creatinine (mg/dl)	0.80 (0.6, 1.0)	0.80 (0.6, 1.0)
pCO ₂ (mm Hg)	53.7 $\pm$ 18.4	52.7 $\pm$ 16.8
FEV ₁ (% of predicted)	32 (20, 50)	37 (21, 51)
FVC (% of predicted)	43 (33, 55)	43 (33, 56)
Lung Allocation Score	65.9 (40.5, 88.3)	66.3 (41.2, 88.4)
Wait-time while listed (days)	27 (8, 111)	48 (13, 159)

pCO₂ = arterial partial pressure of carbon dioxide; FEV₁ = Forced expiratory volume in 1 second; FVC = Forced vital capacity

* Diagnostic categories used for calculation of the Lung Allocation Score

Table 2

Surgical Characteristics

Data presented as n (%) or mean $\pm$ SD			
Characteristic		Mechanical ventilation support	No mechanical ventilation support
N		419	419
Donor age (years)		34.6 $\pm$ 14.3	35.1 $\pm$ 14.0
Donor sex (female)		187 (45%)	197 (47%)
Transplant Type			
	Bilateral lung	329 (78.5)	311 (74.2)
	Single lung	82 (19.6)	104 (24.8)
	Heart-Lung	8 (1.9)	4 (1)
Ischemic Time (hours)		5.5 $\pm$ 1.6	5.4 $\pm$ 1.8
Center Volume *			
	1-20	73 (17.4)	104 (24.8)
	21-34	80 (19.1)	77 (18.4)
	35	266 (63.5)	238 (56.8)

* Center volume = number of transplants performed yearly

Table 3

Diagnostic categories and component diagnoses used in calculating the Lung Allocation Score. Adapted from Egen, et al.(2)

Group A	Group B	Group C	Group D
Bronchiectasis COPD	Eisenmenger's syndrome	Cystic Fibrosis Immune Deficiency	Bronchoalveolar carcinoma (BAC)
Emphysema (including A1ATD) LAM	Primary PAH Pulmonary vascular disease		Eosinophilic granuloma Hemosiderosis IPF
Sarcoidosis (without PAH)			Restrictive lung disease
			Sarcoidosis with PAH Scleroderma/CREST Following lung transplant: Bronchiolitis obliterans Primary graft failure

COPD = Chronic obstructive pulmonary disease; A1ATD= Alpha 1 antitrypsin deficiency ; LAM = Lymphangioleiomyomatosis; PAH= Pulmonary arterial hypertension; IPF= Idiopathic pulmonary fibrosis; CREST = Calcinosis, Raynauds, esophageal dysmotility, scleroderma, telangectasias

Table 4

Relative risk of death (hazard ratio) based on survival at follow up*

		Overall cohort	Group A	Group C	Group D
Time since transplant					
	0-6 months	1.9 (1.3 to 2.7) p < 0.0005	0.5 (0.2 to 1.2) p = 0.11	5.1 (1.1 to 23.1) p = 0.03	2.7 (1.7 to 4.4) p < 0.0005
	6 months- 2 years	1.3 (0.9 to 2.0) p = 0.22	1.8 (0.7 to 4.2) p = 0.21	1.3 (0.5 to 3.3) p = 0.65	1.1 (0.6 to 1.9) p = 0.86
	2 years	0.9 (0.5 to 1.9) p = 0.86	1.6 (0.5 to 4.7) p = 0.42	0.8 (0.2 to 3.9) p = 0.77	0.9 (0.3 to 2.3) p = 0.78

* Hazard ratio (95% Confidence Interval) adjusted for center volume and transplant type. A hazard ratio of >1.0 represents greater risk for death for patients requiring pre-transplant mechanical ventilation compared to those not requiring mechanical ventilation.

Table 5

Characteristics of Subjects Surviving Greater than 1 year after transplant

Characteristic		Survived less than 1 year after transplant	Survived 1 year after transplant	p-value
Data presented as n (%) or mean ± SD				
N		115	208	
Age Category				
	18-49	41 (35.7)	92 (44.2)	0.01
	50-60	32 (27.8)	51 (24.5)	
	60-65	32 (27.8)	32 (15.4)	
	>65	10 (8.7)	33 (15.9)	
Sex (female)		143 (40)	150 (42)	0.47
Indication for Transplant by Diagnostic Category *				
	Group A	16 (13.9)	59 (28.4)	0.01
	Group B	5 (4.4)	5 (2.4)	
	Group C	18 (15.7)	42 (20.2)	
	Group D	76 (66.1)	102 (49.0)	
Ethnicity				
	White, non- Hispanic	98 (85.2)	182 (87.5)	0.65
	Black	9 (7.8)	10 (4.8)	
	Hispanic	5 (4.3)	12 (5.7)	
	Asian	3 (2.6)	4 (1.9)	
Prior cigarette use		58 (52.2)	111 (55.0)	0.67
Body Mass Index		24.1 ± 5.2	26.1 (5.6)	0.36
Creatinine (mg/dl)		1.2 ± 0.8	0.9 ± 0.5	< 0.001
pCO2 (mm Hg)		54.4 ± 21.0	52.8 ± 17.0	0.46
FEV ₁ (% of predicted)		38.6 ± 21.0	36.3 ± 20.4	0.33
FVC (% of predicted)		44.5 ± 17.2	45.6 ± 17.9	0.61
Lung Allocation Score		64.8 ± 23.0	63.1 ± 22.6	0.53
Transplant Type				
	Single lung	39 (33.9)	29 (13.9)	0.003
	Bilateral lung	74 (64.4)	174 (83.7)	
	Heart-lung	2 (1.7)	5 (2.4)	
Center volume (transplants performed per year)				
	20	23 (20.0)	36 (17.3)	0.18
	21-34	30 (26.1)	35 (16.8)	
	35	62 (53.9)	137 (65.9)	

pCO₂ = arterial partial pressure of carbon dioxide; FEV₁ = Forced expiratory volume in 1 second; FVC = Forced vital capacity

* Diagnostic categories used for calculation of the Lung Allocation Score