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WEIGHT LOSS PRIOR TO LUNG TRANSPLANTATION IS ASSOCIATED WITH IMPROVED SURVIVAL

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Abstract

Background—Obesity is associated with increased mortality following lung transplantation and is a relative contraindication to transplant. Whether weight reduction prior to transplantation ameliorates this risk is unknown. Our objective was to determine whether weight loss prior to lung transplantation improves survival.

Methods—This is a two-center, retrospective cohort study of lung transplant recipients between 1/1/2000 and 11/5/2010. Change in weight, demographics, transplant details, lung allocation score, length of intensive care and mechanical ventilator days, and graft and patient survival were abstracted. Wilcoxon signed-rank test and Cox Proportional Hazard model were used for analysis where appropriate.

Results—355 patients (55% male; median age 59 years) satisfied inclusion and exclusion criteria. After adjusting for standard demographic and clinical measures, a one unit reduction in BMI pre-transplant was associated with a reduced risk of death with a hazard ratio 0.89 (95% confidence interval 0.82 to 0.96; $p = 0.004$). This survival benefit persisted in the group with a baseline BMI ≥ 25 kg/m^2 (overweight and obese), hazard ratio 0.85 (95% CI 0.77 to 0.95; $p = 0.003$) but not in those with a BMI ≤ 24.9 kg/m^2. One unit reduction in BMI was also associated with a 6.1% decrease in median mechanical ventilator days ($p = 0.02$) and a trend towards decreased intensive care unit length of stay ($p = 0.06$).

Conclusions—A reduction in the BMI prior to lung transplantation was associated with a reduction in the risk of death and mechanical ventilator days. A greater reduction in BMI was associated with a greater survival benefit.

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Introduction

Median survival following lung transplantation remains suboptimal at approximately 5.5 years (1). Prior studies have demonstrated higher mortality among lung transplantation recipients who are obese (defined as a Body mass index - BMI ≥ 30 kg/m^2) (2). These results have been confirmed in larger trials (3, 4). More recently, obese lung transplant recipients have been found to have a two-fold higher risk for developing primary graft dysfunction (5, 6). Hence, obesity is considered a relative contraindication for lung transplantation (7). Obesity continues to be a major public health problem in the United States with more than 32% of the adult population categorized as obese (8). It is therefore expected that management of the obese candidate will be a common occurrence. It is unclear if weight loss prior to lung transplantation ameliorates the increased risk of mortality. Improving lung transplant outcomes by normalizing modifiable risk factors such as obesity deserves further study. Our objective was to determine if weight loss prior to lung transplant is associated with improved survival. Some of the results have been previously reported in abstract form (9).

Materials and Methods

Patient Selection

We reviewed a retrospective cohort of research consenting patients who underwent single and double lung transplantation at Mayo Clinic, Rochester, MN or Jacksonville, FL, between 1/1/2000 and 11/5/2010. The study was approved by Institutional Review Board of Mayo Clinic (IRB 10-007684).

Inclusion criteria and Exclusion criteria

Patients who were 18 years or older at the time of lung transplantation were included in the study. Retransplantation or multi-organ transplant candidates were not included. Patients with an initial BMI <18.5 kg/m^2 were excluded from survival analysis.

Data Collection

Demographic data, transplant diagnosis and type including secondary pulmonary hypertension, transplant details, BMI at the date of initial evaluation and the date of transplantation, creatinine prior to transplantation, pre-existing diabetes mellitus or prednisone use, lung allocation score (LAS), and need for intensive care unit (ICU) or mechanical ventilation prior to transplant were abstracted. We also abstracted postoperative ICU and mechanical ventilator days, date of last follow up visit or communication, and date and cause of death. For a post-hoc analysis examining post-transplant weight gain we abstracted weights at six and twelve months.

Definitions

We defined normal weight as a BMI between 18.5 and 24.9 kg/m^2. We defined overweight as a BMI between 25 and 29.9 kg/m^2. We defined obese as a BMI ≥ 30 kg/m^2. Diagnostic categories included: COPD, cystic fibrosis, idiopathic pulmonary fibrosis, pulmonary fibrosis (other), lymphangiomyomatosis, pulmonary arterial hypertension (PAH), sarcoidosis, bronchiolitis obliterans, eosinophilic granuloma, bronchiectasis, immotile cilia syndrome, bronchoalveolar cell carcinoma, and silicosis. Diagnoses were further separated into restrictive diseases (idiopathic pulmonary fibrosis, pulmonary fibrosis other, and sarcoidosis with fibrosis). In addition non-PAH patients with a resting pulmonary artery mean pressure on right heart catheterization greater than or equal to 25 mm Hg were defined as having secondary pulmonary hypertension.

Standard care of overweight and obese patients

All transplant patients meet with a registered dietician and are required to enroll in pulmonary rehabilitation as part of our standard pre-transplant protocol. Overweight and obese patients receive patient education regarding diet and exercise and are encouraged to lose weight prior to lung transplantation.

Data Analysis

A statistical software package (JMP, version 9; SAS 9.2 Institute Inc; Cary, NC; R 2.14) was used for data analysis. Median and Interquartile Range (IQR) for continuous variable and frequency and percentage for categorical variables were used to summarize the data. Wilcoxon Signed Rank was used for weight change comparisons. Time to death or last follow-up was analyzed using Cox Proportional Hazard model and Kaplan-Meier methods. P-values less than 0.05 were considered statistically significant. Linear regression was performed using log transformation models to evaluate ICU days and mechanical ventilator days. Model selection was done using stepwise model selection on clinically important predictors excluding variables that provided no significant improvement in the quality of the model. The Cox Model was adjusted for relevant clinical covariates (age, sex, and race).

Results

Demographics

Patient characteristics are summarized in Table 1. Three hundred and fifty-five patients satisfied the inclusion and exclusion criteria. Of these, 351 patients had data for BMI at the time of transplant evaluation and 341 patients had data for BMI at the time of lung transplant. Final cohort size for weight change analyses were therefore 341 patients. Median age at transplantation was 59 years, interquartile range (IQR) 52 – 65 years. Fifty-five percent were male and 88% were white. Thirty-seven percent (N=130) underwent transplantation for chronic obstructive pulmonary disease and 38% (N=134) underwent transplantation for idiopathic pulmonary fibrosis. Fifty-two percent (N=184) underwent single lung transplantation while the remainder underwent double lung transplantation. Median lung allocation score (LAS) was 39.8 (IQR 34.4 to 54.5). LAS was not available in 101 patients due to the date of transplant.

Pre-transplantation change in BMI

Thirty-eight percent had a BMI in the normal range, while 34% were overweight and 22% were obese at initial evaluation (see Table 2). BMI data was not available in four patients. At transplantation 43% had BMI ≤ 24.9 kg/m^2, 42% were overweight and 9% remained obese. Sixty-four percent had a decrease in BMI before transplantation. Median decrease in

BMI in the entire group was 0.6 kg/m^2 (IQR −0.2 to 2.15). However, in the obese patients the median decrease in BMI was 2.9 kg/m^2 (IQR 1.4 to 4.5), corresponding to weight loss of 8.5 kg (IQR 4.0 to 12.6 Kg). Fifty-six percent (N=41) of obese patients were able to lose weight and achieve a BMI ≤ 29.9 kg/m^2. The median interval between the initial evaluation and lung transplantation was 272 days (IQR 115 to 534 days).

Differences between patients who lost weight and those who did not

We evaluated differences between patients able to achieve weight loss and those that did not (Table 3). Patients did not differ with respect to use of bypass, ischemic time, or single versus bilateral lung transplant. Significant differences were found in patients by diagnosis (including presence of restrictive disease and secondary pulmonary hypertension) and in BMI at evaluation and at transplant.

Change in BMI and Survival

Simple Cox model and time-dependent models of survival were constructed to evaluate the effect of BMI reduction following lung transplantation. Median survival was 5 years representing 157 deaths in 329 patients. Figure 1 demonstrates this survival data categorized by BMI. The simple Cox model shows that after adjusting for demographics (age, sex, and race) and clinical information (initial BMI and days spent on mechanical ventilator) a one unit reduction in pre-transplant BMI was associated with reduced risk of death, shown in Table 4 [Hazard Ratio (HR): 0.89; 95% CI 0.82 - 0.96; p-value = 0.004]. When looking more closely at the reduction in pre-transplant BMI effect on survival, we find weak evidence that the effect varies over time. Variables such as recipient diagnosis (including secondary pulmonary hypertension), pre-operative use of steroids, and ischemic time were not significant predictors of survival and were therefore not included in the model. Although single versus bilateral transplant and use of bypass were important in univariate analysis, they were not important variables in the multivariate model. Interestingly, when we split the analysis for patients with a baseline BMI ≤ 24.9 kg/m^2 and baseline BMI ≥ 25 kg/m^2, weight loss in patients with a baseline BMI ≥ 25 kg/m^2 demonstrated a survival benefit (HR= 0.85; 95% CI 0.77 to 0.95; p = 0.003) whereas weight loss in patients with a baseline BMI ≤ 24.9 kg/m^2 did not (HR= 0.95; 95% CI 0.81 to 1.12; p=0.55) (Table 4). The most common cause of death was respiratory failure regardless of BMI category (Table 5).

Change in BMI and immediate post-operative outcomes

Weight loss pre-transplant was associated with improvement in perioperative morbidity. Median number of intensive care unit days and mechanical ventilator days post-transplant were 4 (IQR 3 to 8) and 2 days (IQR 1 to 3) respectively. After adjusting for age, a one-unit reduction in BMI was associated with a 4.4% decrease in the median number of days spent in the ICU (p= 0.06). In addition after adjusting for age and race, a one-unit reduction in BMI was associated with a 6.1% decrease in the median number of days spent on a mechanical ventilator (p= 0.02).

Post-transplant weight gain

At six months post-transplant patients did not gain weight with a mean difference of loss of −0.1 kg ($p=0.84$). Patients did gain weight at 12 months post-transplant with a mean increase of 3.3 kg ($p<0.001$). When analyzed by BMI weight gain was significantly different depending on BMI at transplant ($p<0.001$). Patients who were underweight at transplant (BMI <18.5 kg/m^2) gained a mean of 8.1 kg, while those with a BMI between 18.5 and 24.9 kg/m^2 gained a mean of 5.2 kg at 12 months post transplant. Overweight patients (BMI 25-29.9 kg/m^2) gained a mean of 1.6 kg while obese patients (BMI of 30 kg/m^2 or more at transplant) gained only a mean of 0.26 kg at 12 months following transplant. Interestingly patients who were obese or overweight at the time of evaluation (the same group that lost a median of 8.5 kg pre-transplant) gained only a median of 1.9 kg at 12 months.

Discussion

Our study demonstrated that weight loss prior to lung transplantation was associated with improved survival and decreased perioperative morbidity when adjusted for gender and age. Specifically, we found that a one-unit reduction in BMI pre-transplantation was associated with a reduced risk of death and decreased number of mechanical ventilator days. There was a trend towards decrease length of ICU stay. When evaluated further this mortality benefit was demonstrated in the patients with a baseline BMI ≥25 kg/m^2 (the patients who were obese or overweight at baseline). Interestingly this benefit appeared to persist over time with HR after four years demonstrating persistent significance.

In addition, our study addresses the feasibility of weight loss pre-transplant. In our cohort, sixty-four percent were able to achieve some weight loss with a median decrease in BMI of 2.9 kg/m^2 in obese patients. In fact, fifty-six percent of initially obese patients were able to lose weight to achieve a BMI < 29.9 kg/m^2. This suggests that not only is weight loss associated with benefits for survival and morbidity, but it is a reasonable expectation for the majority of pre-transplant obese patients. Our median time between initial evaluation and transplant was 272 days suggesting that patients had a median of nine months to lose excess weight. Patients with a life expectancy of shorter duration may not be able to achieve equivalent weight loss.

Finally our study briefly looks at post-transplant weight gain. Our overweight and obese patients lost a median of 8.5 kg pre-transplant. At twelve months following these patients gained a median of 1.9 kg suggesting that most of the pre-transplant weight loss was sustained.

It has been reported previously that obese recipients have poor post-transplant survival (2-4). In addition, pre-transplant obesity is a risk factor for reduced physical quality of life after lung transplantation and for primary graft dysfunction.(6, 10). Our study is the first to demonstrate evidence that pre-transplant obesity is a modifiable risk factor with respect to mortality. It is uncertain if weight loss pre-transplant improves post-transplant quality of life.

The mechanism by which obesity affects survival in lung transplantation recipients is not clear. The increased mortality risk appears to effect mortality in the early post-transplant period (11). There is a general sense that the procedure is more protracted. Longer ischemic and cardiopulmonary bypass times would increase risk of primary graft dysfunction (PGD) and possibly effect mortality (3, 5, 12, 13). Our study did not support this theory. There was no difference in patients with weight loss versus those without weight loss in terms of cardiopulmonary bypass use or ischemic time suggesting this was not the reason for the improved Hazard Ratio. Furthermore, ischemic time and use of cardiopulmonary bypass were not important predictors in the Cox Model.

Another theory to explain the increased mortality associated with obesity is that obese patients have increased risks of complications and respiratory failure perioperatively (14). A decrease in ventilator days and trend towards decreased ICU length of stay in our study suggest that improvement in perioperative morbidity may be one mechanism of pre-transplant weight loss benefit. Respiratory failure was the most common cause of death but this was true regardless of BMI.

Another theory of obesity's effect on survival is that obese patients may suffer from a pro-inflammatory state. It is known that obesity leads to increased production and release of proinflammatory mediators including leptin, resistin, vistafatin, interleukin 6 (IL-6), and Tumor necrosis factor-α (TNF-α) (15, 16). In addition, fatty acids are increased contributing to Toll-like receptor activated systemic inflammation (16, 17). In animal models leptin has been shown to produce acute lung injury and fibroproliferative changes leading to lung fibrosis (18, 19). In obese recipients higher leptin levels are associated with development of PGD (6). In fact, obese lung transplant recipients have a two-fold higher risk for developing PGD (5, 6). PGD is associated with an increased risk of bronchiolitis obliterans syndrome (BOS), and the severity of PGD correlates with decreased survival (20, 21). Acute lung injury sustained during PGD might predispose patients to BOS later and thus lead to worsened survival (20). Due to the retrospective nature of our study we do not have leptin or adiponectin levels from our cohort to support or refute this hypothesis.

Obese patients may also suffer worsened survival due to a detriment in respiratory mechanics. Obesity decreases the total lung capacity, functional residual capacity and vital capacity, restricting lung volumes and leading to a decrease in respiratory system compliance with a tendency for atelectasis and worsening gas exchange (14). The accumulation of visceral adiposity in patients with obesity increases the gastric pressure, decreases the tone of the lower esophageal sphincter, and increases the risk for aspiration, a known risk factor for BOS (22-25). We did find a difference in those with restrictive physiology versus those without when comparing patients who lost weight versus those who did not pre-transplant. Diagnosis, including restriction, was not ultimately important in the Cox Model.

Finally obesity may simply be associated with increased risk of co-morbidities. Compared with normal weight recipients, obese recipients are more likely to die from infection, cardiac disease, cancer and respiratory failure (3). The presence of a longer-term mortality benefit in our study raises the question of whether this effect is due to changes in co-morbidities.

Weight loss prior to transplantation could reverse several of these risk factors and improve survival. Although we do include a cause of death break down by BMI further study is needed to explore this hypothesis.

Limitations

Our study is a retrospective cohort study and therefore we cannot control for all known or unknown confounding factors. For example, due to the retrospective nature we could not reliably adjust for transfusion rates in this study. It is possible that ability to achieve weight loss reflected a subset of patients that were in general more compliant with medical recommendations. Patients with increased medical compliance would potentially have other behaviors that could enhance outcomes. In addition it is possible that some of the patients suffered unintentional rather than volitional weight loss. Caution is warranted in such patients. Further study is needed to differentiate whether unintentional weight loss provides the same benefit to patients. Our routine practice is that obese and overweight patients meet with a registered dietician to receive standard education regarding weight loss. It is possible that patients who achieved weight loss were more physically active than those who did not achieve weight loss leading to a benefit from increased physical activity. At our transplant centers, however, all pre-transplant patients are encouraged to exercise and pulmonary rehabilitation enrollment is standard practice. Due to current selection criteria guidelines few patients in this study were morbidly obese (BMI ≥ 35 kg/m^2) and therefore further study is needed for that group of patients. Finally, the number of cystic fibrosis patients in our cohort was small (N=21) with only one obese cystic fibrosis patients at evaluation and therefore it is unknown whether our results are applicable to the cystic fibrosis population.

Conclusions

In summary, potential lung transplantation recipients who are obese and overweight should be encouraged to lose weight prior to lung transplantation. A reduction in the BMI prior to lung transplantation is associated with a reduction in the risk of death. Patients who are able to achieve a reduction in BMI have improved long-term survival. Weight reduction also demonstrates an improvement in post-transplant mechanical ventilator days and a trend towards reduced ICU stay. Future studies should focus on the cause of improved survival. Study of the impact of weight loss pre-transplant on inflammatory markers, primary graft dysfunction and subsequent development of BOS would be particularly beneficial. Furthermore studies evaluating for cause-specific mortality may further elucidate the impact of weight loss on obesity-related comorbidities. Finally, further study on the impact of weight loss pre-transplant on the post-transplant quality of life is also needed.

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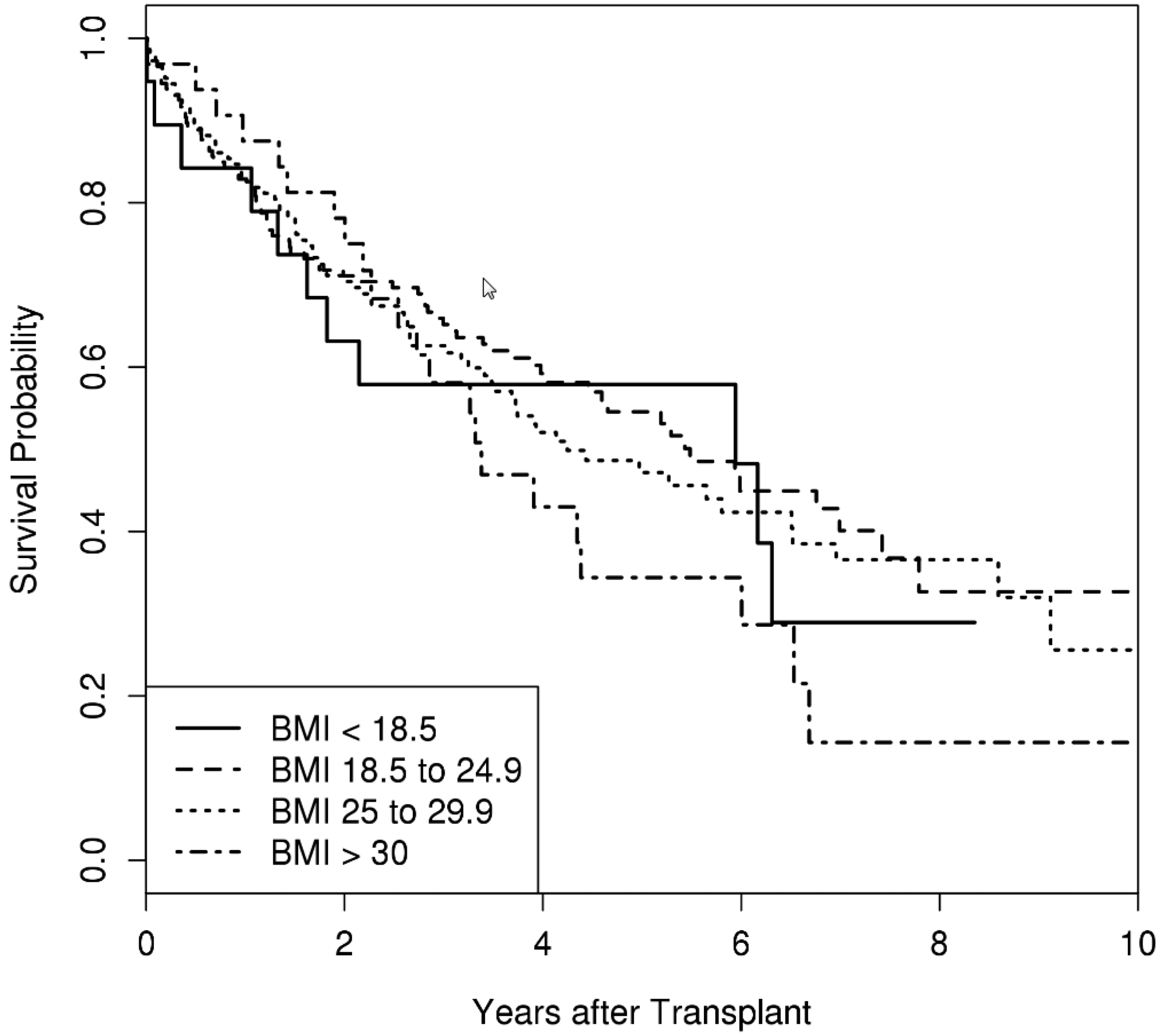

Figure 1.

Kaplan-Meier curve demonstrating survival separated by Body Mass Index (BMI) in kg/m^2. Underweight is BMI <18.5 kg/m^2, normal weight is a BMI 18.5 kg/m^2 - 24.9 kg/m^2, overweight is BMI 25-29.9 kg/m^2, obese is BMI >30 kg/m^2.

Table 1

Baseline demographics are shown for various categories as indicated.

	N (%) unless noted
Total number of patients	355
Caucasian	310 (88.1)
Male	196 (55.1)
Age at transplantation	*59 years, IQR 52 to 65
Diagnosis	
Chronic Obstructive Pulmonary Disease	130 (36.5)
Idiopathic Pulmonary Fibrosis	134 (37.6)
Bronchiectasis (includes Cystic Fibrosis)	32 (9)
Pulmonary fibrosis other	41 (11.5)
Other	19 (5)
Lung allocation scorec∞	*39.8, IQR 34.4 to 54.5
Single lung transplantation	184 (51.7)
Intensive Care Unit pre-transplant	38 (10.7)
Use of prednisone at transplant, %	37.5%
Median dose (in mg) of those on prednisone at transplant (IQR)	10 mg (10-20)
Mechanical ventilator pre-transplant	23 (6.5)

N = number.

∞LAS not available in 101 patients.

*Values presented are median. IQR = interquartile range; BMI = body mass index; Kg = kilogram; ICU = Intensive Care Unit

Table 2

Summary table of body mass index (BMI) data at the initial lung transplant evaluation (column 2), time of lung transplantation (column 3), and the measured change between the two dates (column 4).

	Initial evaluation	At lung transplantation	Change
BMI (kg/m^2)	N (%)	N (%)	
<18.5	23 (6.6)	19 (5.6)	−0.9%
18.5 to 24.9	134 (38.2)	146 (42.8)	+4.1%
25 to 29.9	118 (33.6)	144 (42.2)	+8.6%
≥30	76 (21.7)	32 (9.4)	−11.6%
BMI (kg/m^2)	*25.7, IQR 21.8 to 29.5	*25.2, IQR 21.4 to 27.7	*−0.6
Weight (kg)	*75, IQR 61 to 87.7	*71.1, IQR 61.5 to 84.5	*3.9

N=number; kg=kilogram

*median; IQR= interquartile range. Four patients were missing BMI data at evaluation. Fourteen patients were missing BMI data at transplantation.

Table 3

Comparison of percent of patients with listed characteristics (column 1) divided into those who did not lose weight (column 2) and those who did (column 3). P-values are given in the last column with $p<0.05$ indicating statistical significance.

Characteristic	No weight loss (% unless noted)	Weight loss (% unless noted)	p-value
Secondary Pulmonary Hypertension	48	62.9	0.012
Restrictive diagnosis	35.8	52.5	0.004
COPD	39.6	30.6	0.10
Single lung	49.5	52.9	0.56
Use of bypass	19.2	27.1	0.12
Ischemic time in minutes, median	225*	227*	0.72
Corticosteroid use pre-transplant, median dose in mg	37.5	37.4	0.99

COPD=chronic obstructive pulmonary disease

*median

Table 4

Table shows univariate analysis hazard ratio and corresponding p-values (column 2 and 3) and multivariate analysis hazard ratio and corresponding p-values (column 4 and 5) for listed patient characteristics (column 1). Analyses are further divided demonstrating all patients (top rows), BMI ≤ 24.9 kg/m , and patients with BMI ≥25 kg/m2. Univariate analysis was also performed using diagnosis (idiopathic pulmonary fibrosis versus other), secondary pulmonary hypertension, pre-operative steroid use, and total ischemic time, but none of these variables were significantly associated with survival.

Characteristic	**Univariate Cox model**		**Multivariable Cox Model**	
All Patients	**HR (CI)**	**p-value**	**HR (CI)**	**p-value**
Age	1.014 (0.998,1.030)	0.096	1.012 (0.995,1.030)	0.156
Male	0.92 (0.68,1.25)	0.605	1.05 (0.75,1.46)	0.775
Mech. Vent Days	1.03 (1.02,1.04)	<0.001 *	1.025 (1.014,1.036)	<0.001 *
Race (Ref White)		0.074		0.022 *
Black	0.69 (0.37,1.27)	--	0.59 (0.31,1.11)	
Other	0.27 (0.07,1.09)	--	0.28 (0.07,1.13)	
BMI Baseline	1.01 (0.98,1.04)	0.6	1.052 (1.005,1.101)	0.03 *
BMI reduce	0.950 (0.90,1.01)	0.097	0.89 (0.82,0.96)	0.004 *
Single vs. Bilateral	0.731 (0.54,0.997)	0.047 *	--	--
Bypass	1.13 (0.80,1.60)	0.479	--	--

Initial BMI ≤24.9	**HR (CI)**	**p-value**	**HR (CI)**	**p-value**
Age	1.01 (0.99,1.04)	0.263	1.01 (0.99,1.04)	0.319
Male	1.12 (0.70,1.79)	0.642	1.31 (0.78,2.18)	0.301
Mech. Vent Days	1.03 (1.02, 1.04)	<0.001	1.03 (1.01,1.04)	0.004
Race (Ref White)		0.367		0.299
Black	0.66 (0.24,1.81)	--	0.64 (0.23,1.79)	--
Other	0.32 (0.04,2.33)	--	0.33 (0.04,2.48)	--
BMI Baseline	1.128 (0.99,1.29)	0.076	1.10 (0.96,1.28)	0.179
BMI reduce	0.97 (0.85,1.11)	0.641	0.95 (0.81,1.12)	0.551
Single vs. Bilateral	0.71 (0.44,1.15)	0.16	--	--
Bypass	2.02 (1.15,3.57)	0.013 *	--	--

Initial BMI ≥ 25	**HR (CI)**	**p-value**	**HR (CI)**	**p-value**
Age	1.02 (0.99,1.04)	0.167	1.01 (0.99,1.04)	0.252
Male	0.77 (0.50,1.18)	0.234	0.87 (0.54,1.40)	0.570
Mech. Vent Days	1.02 (1.00,1.04)	0.043 *	1.02 (1.00,1.04)	0.069
Race (Ref White)	--	0.169	--	0.057
Black	0.68 (0.31,1.46)	--	0.59 (0.26,1.36)	--
Other	0.22 (0.03,1.61)	--	0.20 (0.03,1.45)	--

Initial BMI ≥ 25	HR (CI)	p-value	HR (CI)	p-value
BMI Baseline	1.01 (0.96,1.07)	0.605	1.11 (1.02,1.21)	0.014*
BMI reduce	0.93 (0.86,1.00)	0.063	0.85 (0.77,0.95)	0.003*
Single vs. Bilateral	0.75 (0.50,1.13)	0.163	--	--
Bypass	0.87 (0.56,1.36)	0.546	--	--

(BMI= Body mass index; HR=Hazard ratio; CI= Confidence Interval; Mech. Vent days= number of days on mechanical ventilator; BMI baseline=BMI at transplant evaluation; BMI reduce=patients who lost weight at transplant; single versus bilateral=whether patients received a single or double lung transplant; bypass= use of cardiopulmonary bypass for transplant surgery)

*p<0.05 is considered significant.

Table 5

Table demonstrates the cause of death by category (column 1). Columns 2-4 demonstrate number (N) and percentages of all those in each BMI category at transplant (underweight, normal/overweight, and obese).

	Underweight (BMI <18.5 kg/m^2)	**Normal or overweight (BMI 18.5-29.9 kg/m^2)**	**Obese (BMI ≥30 kg/m^2)**
Category	**N (% of column)**	**N (% of column)**	**N (% of column)**
Respiratory failure/Graft failure/Rejection	9 (39.1)	46 (18.11)	13(17.6)
Sepsis/Infection/Pneumonia	3 (13.0)	24 (9.5)	4 (5.4)
Malignancy/PTLD	1 (4.4)	15 (5.91)	9 (12.2)
Neurological	2 (8.7)	4 (1.6)	2 (2.7)
Hematological	0	4 (1.6)	5 (6.8)
Cardiovascular	0	3 (1.18)	1 (14)
Liver failure	0	2(.8)	1(1.4)
Renal failure	0	1(4)	1(1.4)
Unknown	2 (8.7)	30 (11.81)	6 (8.1)
Alive	6 (26.1)	125 (49.2)	32 (43.2)

BMI= Body Mass Index. N=number.