

# Weight loss prior to lung transplantation is associated with improved survival



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## KEYWORDS:

weight loss;  
lung transplantation;  
survival;  
obesity;  
patient selection

**BACKGROUND:** Obesity is associated with increased mortality after lung transplantation and is a relative contraindication to transplant. It is unknown whether weight reduction prior to transplantation ameliorates this risk. Our objective was to determine whether weight loss prior to lung transplantation improves survival.

**METHODS:** Our investigation was a two-center, retrospective cohort study of lung transplant recipients between January 1, 2000 and November 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's signed-rank test and the Cox proportional hazard model were used for analysis where appropriate.

**RESULTS:** Three hundred fifty-five patients (55% male, median age 59 years) satisfied inclusion and exclusion criteria. After adjusting for standard demographic and clinical measures, a 1-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 baseline BMI  $\geq 25$  kg/m<sup>2</sup> (overweight and obese) and hazard ratio 0.85 (95% CI 0.77 to 0.95;  $p = 0.003$ ), but not in those with a BMI  $\leq 24.9$  kg/m<sup>2</sup>. The 1-unit reduction in BMI was also associated with a 6.1% decrease in median mechanical ventilator days ( $p = 0.02$ ) and a trend toward decreased intensive care unit length of stay ( $p = 0.06$ ).

**CONCLUSIONS:** A reduction in 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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Median survival after lung transplantation remains sub-optimal at approximately 5.5 years.<sup>1</sup> Studies have demonstrated higher mortality among lung transplant recipients who are obese (defined as a body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>).<sup>2</sup> These results have been confirmed in larger

trials.<sup>3,4</sup> More recently, obese lung transplant recipients have been found to have a 2-fold higher risk for developing primary graft dysfunction.<sup>5,6</sup> Hence, obesity is considered a relative contraindication for lung transplantation.<sup>7</sup> Obesity continues to be a major public health problem in the USA, with >32% of the adult population categorized as obese.<sup>8</sup> It is therefore expected that management of the obese candidate will be a common occurrence. It is unclear whether weight loss prior to lung transplantation ameliorates the increased risk of mortality. Improving lung transplant

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outcomes by normalizing modifiable risk factors such as obesity deserves further study. Our objective was to determine whether weight loss prior to lung transplant is associated with improved survival. Some of these results have been reported previously in abstract form.<sup>9</sup>

## Methods

### Patient selection

We reviewed a retrospective cohort of research consenting patients who underwent single- and double-lung transplantation at the Mayo Clinic, Rochester, Minnesota, or Jacksonville, Florida, between January 1, 2000 and November 5, 2010. The study was approved by the institutional review board of the Mayo Clinic (IRB 10-007684).

### Inclusion criteria and exclusion criteria

Patients  $\geq 18$  years of age 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<sup>2</sup> were excluded from the survival analysis.

### Data collection

We abstracted demographic data, transplant diagnosis and transplant type, including secondary pulmonary hypertension, as well as 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. We also abstracted post-operative 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 6 and 12 months.

### Definitions

We defined normal weight as a BMI between 18.5 and 24.9 kg/m<sup>2</sup>. We defined overweight as a BMI between 25 and 29.9 kg/m<sup>2</sup>. We defined obese as a BMI  $\geq 30$  kg/m<sup>2</sup>. Diagnostic categories included: chronic obstructive pulmonary disease (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  $\geq 25$  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

Statistical software (JMP version 9, SAS 9.2; SAS Institute, Inc., Cary, NC) was used for data analysis. Median and interquartile range (IQR) for continuous variables and frequency and percentage for categorical variables were used to summarize the data. Wilcoxon's signed rank was used for weight change comparisons. Time to death or last follow-up was analyzed using the Cox proportional hazard model and Kaplan-Meier methods.  $p < 0.05$  was 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, gender and race).

## Results

### Demographics

Patients' characteristics are summarized in Table 1. Three hundred 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 had data for BMI at the time of lung transplantation. Final cohort size for weight change analyses therefore consisted of 341 patients. Median age at transplant was 59 years and IQR 52 to 65 years. Fifty-five percent were male and 88% were white. Thirty-seven percent ( $N = 130$ ) underwent transplantation

**Table 1** Demographics

	<i>N</i> (%) unless noted
Total number of patients	355
Caucasian	310 (88.1)
Male	196 (55.1)
Age at transplantation	59 <sup>a</sup> years, IQR 52–65
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 score <sup>b</sup>	39.8 <sup>a</sup> , IQR 34.4–54.5
Single lung transplantation	184 (51.7)
ICU pre-transplant	38 (10.7)
Use of prednisone at transplant	37.5%
Median dose (mg) of those on prednisone at transplant (IQR)	10 mg (10–20)
Mechanical ventilator pre-transplant	23 (6.5)

BMI, body mass index; ICU, intensive care unit; IQR, interquartile range; *N*, number.

<sup>a</sup>Values presented are median.

<sup>b</sup>LAS not available in 101 patients.

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