



# Weight Change in Underweight or Obese Patients Awaiting Lung Transplantation Does Not Impact Post-Transplant Survival

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## Results

### Abstract

**Background:** Lung transplantation remains the definitive treatment for end-stage COPD, respiratory complications of cystic fibrosis, and interstitial lung diseases. However, long-term survival after lung transplantation remains poor, with an overall 5-year survival rate of 54%. Initial selection of lung transplant candidates includes evaluation of body mass index (BMI), since obesity is a relative contraindication to lung transplantation. However, BMI changes occurring while waiting for transplantation may not reflect initial listing BMI and may be associated with poorer long-term survival.

**Objective:** To determine the effects of pre-transplant BMI change on long-term survival following lung transplantation.

**Methods:** A retrospective chart review of adult lung transplantations performed between January 2004 and May 2016 was conducted. Patient demographics, survival status, and date of death, hours on the mechanical ventilator (MV hours), and ICU length of stay (ICU LOS) were collected. Cases were categorized as underweight (BMI < 20 kg/m<sup>2</sup>) or obese (BMI > 30 kg/m<sup>2</sup>), with change in BMI from time of listing to time of transplantation as subsets. Kaplan-Meier plots were constructed to summarize differences in overall survival between BMI groups. The log rank test was used to assess differences between survival curves. A Z-test using Greenwood's formula was performed to compare post-transplant survival rates at 1, 3, and 5 years. P-values were adjusted using the false discovery rate (FDR).

**Results:** There were 460 cases included in this study. The group sizes were as follows: underweight and lost weight (BMI < 20 kg/m<sup>2</sup> -), 35; underweight and gained weight (BMI < 20 kg/m<sup>2</sup> +), 47; obese and lost weight (BMI > 30 kg/m<sup>2</sup> -), 61; obese and gained weight (BMI > 30 kg/m<sup>2</sup> +), 25. Patients with initial BMI between 20.1 kg/m<sup>2</sup> - 29.9 kg/m<sup>2</sup> were assigned to the control group (n = 292). There were no differences in 1-year, 3-year, or 5-year survival rates (1-year: control 87.6%; BMI < 20 kg/m<sup>2</sup> - , 91.3%; BMI < 20 kg/m<sup>2</sup> + 86.4%; BMI > 30 kg/m<sup>2</sup> - 93.%; BMI > 30 kg/m<sup>2</sup> + 71.2%; all comparisons non-significant [NS]) (3-year: 71.1%; 49.2%; 54.1%; 69.8%; 56.6%, NS) (5-year: 61.1%; 35.1%; 45.9%; 49.1%; 50.9%, NS). Kaplan-Meier plots similarly showed no differences in overall survival (p = 0.203). There were no significant differences among the groups in ICU LOS or MV hours.

**Conclusion:** Weight change in obese or underweight patients prior to lung transplantation does not affect overall survival. Therefore, BMI > 30 kg/m<sup>2</sup> at the time of listing may not be a relative contraindication to lung transplantation.

### Introduction

Lung transplantation is a final treatment option for carefully selected patients suffering from end-stage lung disease. Though the treatment goals are to prolong life and improve quality of life, the long-term survival after lung transplantation remains poor, with an overall 5-year survival rate of 53.6%.<sup>1</sup> To improve outcomes following lung transplantation and more carefully allocate donated lungs, it is necessary to study modifiable risk factors associated with worse survival and increased incidence of postoperative complications.

Though the relationship between body mass index (BMI) at time of transplantation and post-operative survival has been studied, little data is available regarding the effects of BMI changes during the waiting period which can span months.<sup>2</sup> Previous studies have shown a decreased survival among obese (BMI ≥ 30 kg/m<sup>2</sup>) lung transplantation patients,<sup>3-6</sup> making obesity a relative contraindication to lung transplantation.<sup>7</sup> Underweight and malnutrition (BMI < 20 kg/m<sup>2</sup>) are also associated with decreased survival.<sup>4,8,9</sup> The available data analyzes the relationship between BMI status at the time of transplantation and long-term survival, though in practice a patient's BMI is evaluated prior to listing for transplantation. It is unclear whether weight change occurring during the waiting period impacts outcomes. This study aims to investigate the postoperative and long-term survival outcomes of weight change in obese and underweight patients undergoing lung transplantation.

### Methods

#### Patient selection

We conducted a retrospective review of patients who underwent single, double, or bilateral lung transplantation at a single institution between January 1, 2004 and May 31, 2016. Pediatric patients (< 18 years old) and one combined heart-lung transplantations were excluded. This study was approved by the institutional review board of the University of Texas Southwestern Medical Center.

#### Data collection

Patient data were prospectively maintained according to the Society of Thoracic Surgeons' Data Collection Forms 2.52, 2.61, 2.73, and 2.81. In this study, we included patient demographic data, diagnosis, date of listing, height and weight at time of listing, height and weight at time of transplantation, and date of transplantation. Missing data were retrospectively obtained from the electronic medical record. BMI was calculated as the weight in kilograms divided by the height in centimeters squared. Collected post-operative data include length of stay following surgery, length of ICU stay, number of mechanical ventilator days, post-operative peak creatinine, incidence of wound infections, incidence of other adverse events, and date of death.

#### Definitions

Underweight was defined as BMI < 20 kg/m<sup>2</sup>, the normal BMI range as BMI 20 kg/m<sup>2</sup> to 29.9 kg/m<sup>2</sup>, and obesity as BMI ≥ 30 kg/m<sup>2</sup>. Because overweight, defined by the World Health Organization as BMI between 25 kg/m<sup>2</sup> and 29.9 kg/m<sup>2</sup>,<sup>10</sup> is not a contraindication to lung transplantation,<sup>7</sup> overweight patients were grouped with normal weight patients for the purpose of selecting lung transplantation candidates. Additionally, diagnoses were categorized into four groups: chronic obstructive pulmonary diseases (COPD), pulmonary vascular diseases, cystic fibrosis, and restrictive diseases.<sup>1</sup>

#### Data Analysis

Characteristics of the sample were summarized using descriptive statistics. Means and standard deviations (or medians and interquartile ranges) were reported for continuous variables; frequencies and percentages were reported for categorical variables. Select risk factors and outcomes were compared between BMI groups using the chi-square test and the Kruskal-Wallis test. Kaplan-Meier plots were created to summarize the differences in overall survival between the BMI groups. The log rank test was performed to detect any difference in overall survival curves. A modification of the z-test using Greenwood's formula for variance was used to compare the survival rates at 1, 3, and 5 years. Since multiple testing increases the Type I error rate, these p-values were adjusted using the false discovery rate (FDR). This adjustment controls the expected number of false significant results. Statistical significance is indicated by p < 0.05.

Table 1: Demographics

Age <sup>1</sup> (y)	59.0 (49.0-65.0)
Sex	
Female	187 (40.2%)
Male	278 (59.8%)
Race	
Black, non-Hispanic	44 (9.7%)
Hispanic	35 (7.7%)
White, non-Hispanic	356 (78.8%)
Other, non-Hispanic	17 (3.8%)
Days on waiting list <sup>1</sup>	78.0 (22.0-231.0)
BMI at listing <sup>2</sup> (kg/m <sup>2</sup> )	25.4 (±4.8)
< 20 kg/m <sup>2</sup> (n)	83 (18.0%)
> 30 kg/m <sup>2</sup> (n)	87 (18.8%)
20kg/m <sup>2</sup> - 30 kg/m <sup>2</sup> (n)	292 (63.2%)
BMI at transplant (kg/m <sup>2</sup> ) <sup>2</sup>	25.1 (±4.5)
BMI < 20 kg/m <sup>2</sup> , - (n)	35 (7.6%)
BMI < 20 kg/m <sup>2</sup> , + (n)	47 (10.2%)
BMI > 30 kg/m <sup>2</sup> , - (n)	61 (13.3%)
BMI > 30 kg/m <sup>2</sup> , + (n)	25 (5.4%)
BMI 20 kg/m <sup>2</sup> – 30 kg/m <sup>2</sup> (n)	292 (63.5%)

<sup>1</sup> Median and interquartile range are reported

<sup>2</sup> Median and standard deviation are reported

Table 2: Pre-transplantation weight change by BMI group

BMI < 20 kg/m <sup>2</sup> , -	-0.65 (-0.98 – -0.30) kg/m <sup>2</sup>
BMI < 20 kg/m <sup>2</sup> , +	1.05 (0.37 – 2.33) kg/m <sup>2</sup>
BMI > 30 kg/m <sup>2</sup> , -	-1.54 (-2.88 – -0.66) kg/m <sup>2</sup>
BMI > 30 kg/m <sup>2</sup> , +	0.33 (0.21 – 1.20) kg/m <sup>2</sup>
BMI 20 kg/m <sup>2</sup> – 30 kg/m <sup>2</sup>	-0.21 (-0.97 – 0.34) kg/m <sup>2</sup>

Median and interquartile range are reported

Table 3: Summary of pre-operative diagnoses

Cystic fibrosis and immunodeficiency	59 (12.7%)
COPD	123 (26.5%)
Restrictive	232 (49.9%)
Pulmonary vascular disease	19 (4.1%)
Other	32 (6.9%)

Table 4: Summary of post-operative course

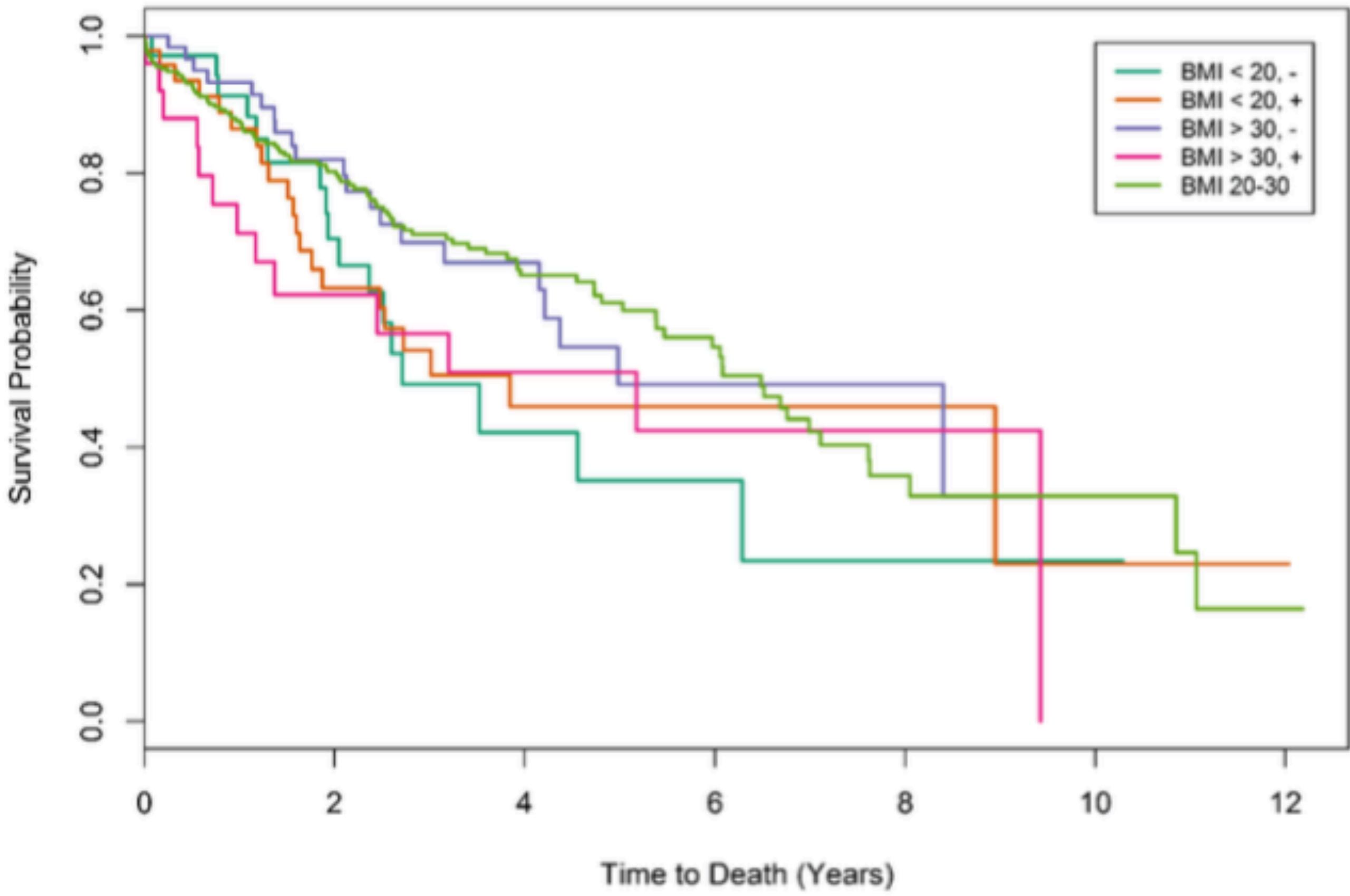
Length of stay (days) <sup>1</sup>	14 (11.0 – 21.0)
Initial ICU hours <sup>1</sup>	137.1 (88.8 – 240.7)
Major complication	
Reoperation	128 (27.5%)
Cardiac arrest	16 (3.4%)
Renal failure requiring dialysis	20 (4.3%)
Stroke	16 (3.4%)
Multi-system organ failure	12 (2.6%)

<sup>1</sup> Median and interquartile range are reported

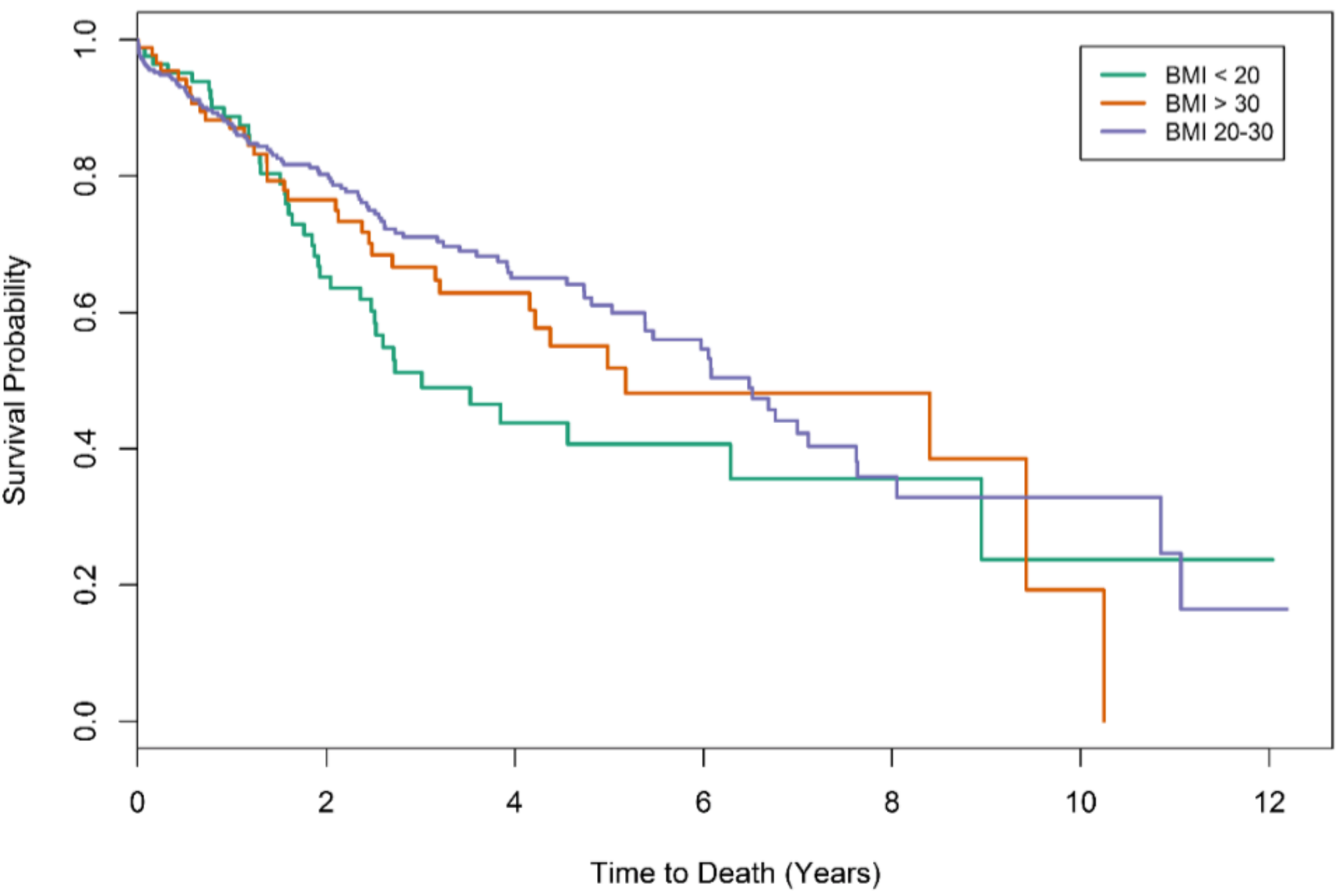
Table 5: Comparison of risk factors and outcomes between BMI groups.

	BMI < 20 kg/m <sup>2</sup> , -	BMI < 20 kg/m <sup>2</sup> , +	BMI > 30 kg/m <sup>2</sup> , -	BMI > 30 kg/m <sup>2</sup> , +	BMI 20 kg/m <sup>2</sup> - 30 kg/m <sup>2</sup>	P-value
Age	35 (26.0 – 58.5)	38 (26.0 – 57.5)	62 (58.0 – 66.0)	61 (54.0 – 65.0)	60 (53.0 – 66.0)	< 0.0001
Sex						0.024
Female	18 (51.4%)	28 (59.6%)	20 (32.8%)	10 (40.0%)	110 (37.7%)	
Male	17 (48.6%)	19 (40.4%)	41 (67.2%)	15 (60.0%)	182 (62.3%)	
Days on wait list	69.0 (21.5 – 247.0)	125 (29.0 – 250.5)	53 (21.0 – 122.0)	71.0 (31.0 – 290.0)	79.0 (20.0 – 231.0)	0.25
Length of stay (d)	14.0 (11.0 – 24.5)	15.0 (11.0 - 22.0)	14.0 (11.0 – 20.0)	14.0 (10.0 – 20.0)	14.0 (11.0 – 22.0)	0.94
Initial ICU hours	133.6 (89.0 – 180.4)	110.5 (82.9 - 234.1)	142.2 (97.9 – 280.1)	140.8 (92.0 – 301.6)	138.6 (88.0 – 241.2)	0.83
Initial ventilation hours	43.9 (29.7 – 78.2)	42.0 (24.0 – 93.3)	62.5 (40.7 – 111.3)	68.1 (42.1 – 105.4)	57.9 (34.0 – 121.6)	0.54

The Kruskal-Wallis test and chi-square test were used to make comparisons of non-normally distributed continuous variables and categorical variables, respectively.



**Figure 1:** Kaplan-Meier plot comparing survival curves for the following groups: initial BMI < 20 kg/m<sup>2</sup> and lost weight (BMI < 20, -); BMI < 20 kg/m<sup>2</sup> and gained weight (BMI < 20, +); BMI > 30 kg/m<sup>2</sup> and lost weight (BMI > 30, -); BMI > 30 kg/m<sup>2</sup> and gained weight (BMI > 30, +); and control (BMI 20-30 kg/m<sup>2</sup>). Survival was statistically similar between each group (p = 0.203).



**Figure 2:** Kaplan-Meier plot comparing survival curves comparing BMI at transplantation, regardless of recent weight change. Obese patients (BMI ≥30 kg/m<sup>2</sup>) trended toward decreased survival, though that relationship did not reach statistical significance (p = 0.121).

### Conclusions

- 1) There was a measurable weight change in each subgroup.
- 2) Weight change was not associated with altered survival
- 3) Requiring patients to obtain more optimal weight while on waitlist may not improve their survival
- 4) Short-term alterations to nutritional status do not counteract the chronic effects of malnutrition or obesity on long-term outcomes following lung transplantation.
- 5) This study validates current lung transplantation selection recommendations because obese patients are expected to have similar outcomes regardless of weight gain or loss during the waiting period.
- 6) Limitations:
  - a. Small subgroup sizes limit the statistical power of the study
  - b. Height and weight were obtained from the EMR and not prospectively measured for the purposes of this study
  - c. We were unable to standardize the time of height and weight measurement relative to the time of listing.
    - i. Height and weight measurements were typically taken within days of listing.

### References

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